SPATIAL AND ATTENTIONAL FUNCTIONS OF THE MIDBRAIN VISUAL SYSTEM

by

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Abstract

The superior colliculus of the midbrain has been implicated in spatial and attentional behaviours, in particular the redirecting of attention to novel peripheral stimuli. Paradoxically, while certain aspects of sensory and motor organisation within the structure are common to all species studied, others (eg. single unit characteristics) show wide inter-species variation. Models of intracollicular processing and possible functional subdivisions were discussed.

The hippocampal formation and dorsomedial frontal cortex in the rat have also been reported as having spatial and attentional functions. Thus in the present studies, rats with both types of lesion were compared with colliculars on a variety of behavioural measures. Those with bilateral collicular lesions were grossly inattentive towards novel stimuli in a number of situations, regardless of lesion size. Elevation of open field activity occurred in animals with large lesions extensively damaging deeper collicular laminae. Unilateral lesions of colliculus or frontal cortex produced ipsiversive turning when leaving a goaldoor, and contralateral stimulus neglect, though gross locomotion was at worst temporarily affected. Rats with bilateral frontal lesions were normally attentive and tended to exhibit elevated "attentional" behaviour in an open field arena. Hippocampals showed intermittent distractability in a runway and, unlike other groups (but like visual decorticates), exhibited a severe radial maze deficit. Hippocampal "hyperactivity" in an open field was found to result primarily from decreased habituation across test sessions.

It was concluded that hippocampal, dorsomedial frontal cortical, collicular and posterior cortical lesions are dissociable in terms of their behavioural consequences; also that the most likely function of the superior colliculus is the detection of novelty and shifting of attention, though the details of such a function are likely to vary with task, species, amplitude of orientation response, and the location, meaningfulness and other parameters of the stimulus concerned.

Summary

A considerable body of evidence was reviewed which implicates the superior colliculus of the midbrain in spatial and attentional behaviours. However, the parameters of spatial and attentional deficits following collicular lesions have not been identified and it is unlikely that the colliculus performs a "unitary" function. Paradoxically, while certain aspects of sensory and motor organisation within the structure show remarkable cross-species consistency (from amphibian to primate), others (eg. single unit characteristics) are extremely, and unsystematically, variable. Models of intracollicular processing were discussed and it was concluded that while the primary function of the colliculus appears to be the redirecting of attention to novel peripheral stimuli, anatomical, electrophysiological and behavioural evidence points to a division between superficial (primarily visual) and deeper (multimodal, motor) laminae; however, the latter may be necessary for the total coordination of orienting behaviour. It was suggested that the colliculus may be autonomous in organising attentional shifts based on the physical parameters of a (novel) stimulus, but may be especially dependent upon "enhancing", or facilitatory input from extracollicular structures for the shifting of attention to stimuli which are significant by virtue of their meaning, context, species-specific significance or interest to the individual. The latter system is likely to be experience-dependent, and may be provided by the late-developing retino-cortico-tectal (Y-fibre) pathway, and tectal afferents from many brain areas.

A brief anatomical study revealed that descending projections from the rat colliculus to the brainstem reticular formation are similar to those in other species of mammals studied.

The hippocampal formation and the frontal cortical "eye fields" (so called in the monkey; assumed to be represented by dorsomedial frontal cortex in the rat) have also been implicated in spatial and attentional behaviours, and have anatomical connections and electrophysiological features in common with the superior colliculus.

In a series of experiments, groups of rats were given chronic deep, or superficial lesions of the superior colliculus, lesions of medial frontal cortex or the hippocampus and compared on a variety of behavioural measures. Rats with deep, but not superficial, bilateral collicular lesions were hyperactive in an open field and fell into holes drilled in the apparatus floor without initiating investigation of them. Degree of postoperative hyperactivity correlated significantly with the degree of damage inflicted upon deep collicular laminal tissue, but attention was uniformly affected in colliculars regardless of lesion size and depth.

Unilateral superior collicular and medial frontal cortical lesions produced neglect of unexpected visual "distractor" stimuli occurring in visual space contralateral to the lesion, and a tendency to turn towards the lesion side when leaving a goaldoor from which food had been obtained, though (except in the case of very deep-lesioned colliculars) gross locomotion remained surprisingly unaffected. Rats with bilateral superior collicular, and medial frontal cortical lesions were clearly distinguishable; the former showed decreased attentiveness in an open field arena, bilateral visual neglect, increased latency to notice a novel object in a familiar arena and ran straighter than controls in a runway (even when required to turn through 180° in order to localise a target goaldoor). The frontally-lesioned rats, in contrast,showed more "attentional" behaviour than controls in an open field arena, showed normal attention towards novel "distractors", normal latencies in detecting a novel object, had runpaths similar to those of controls when traversing a runway, and tended to make many repetitive goaldoor presses when tested for postoperative retention of runway performance.

Bilaterally hippocampally-lesioned rats were "hyperactive" in the open field but only to the extent that they failed to show intersession habituation. In contrast, deep-lesioned colliculars were grossly hyperactive throughout testing. Hippocampals were intermittently distractable in a runway, showing little response to initial stimulus presentations but some longer latencies at a time when controls had habituated. They showed normal investigation of holes drilled in the apparatus floor.

When tested on the radial maze, rats with large lesions of either hippocampus or posterior (visual) neocortex were impaired though not those with lesions of colliculus or frontal cortex. It was argued that visual cues are important for accurate radial maze performance, and that posterior cortical and hippocampal lesions may affect different aspects of performance. The importance of monitoring individual subjects' response styles was emphasised.

Following training to criterion on a visual (horizontal-vertical stripe) pattern discrimination, rats with collicular lesions were less disrupted than other groups by the temporary relocation of discriminanda in peripheral areas of visual space, and probably attended to peripheral stimuli less.

The results suggest that the superior colliculus mediates shifts of attention towards currently unattended and potentially relevant stimuli; as such it may be regarded as a "unitary" structure. However, on theoretical grounds, it is likely that the form of intracollicular processing, dependence upon extraretinal signals, output commands, amplitude of eye/head/trunk movements will vary depending upon species, stimulus parameters, context, meaningfulness and eccentricity.

From the present and previous studies, some degree of complementary functioning (and in some instances, opposition) is envisaged between the colliculus and cortical eye field; the former appears to be involved in shifting attention to stimuli present in the visual field, the latter to spatial positions determined by an internal schema. The hippocampus and colliculus are likely to be related in the process of sampling and acquiring information, though visuospatial information used in spatial encoding appears to derive from cortex.

ABBREVIATIONS[1]

cgm	medial geniculate nucleus
cn	cochlear nucleus
cp	cerebral peduncle
cst	cerebrospinal tract
dlm	decussation of the medial lemniscus
dpcs	decussation of the superior cerebellar peduncle (decussation of the brachium conjunctivum)
FEF	frontal eye-field (arcuate sulcus)
flm	medial longitudinal fasciculus
fr	fascicularis retroflexus
gnf	genu of n. facialis (Vll)
HPC	hippocampal formation
IC	inferior colliculus
ipn	interpeduncular nucleus
MFC	medial frontal cortex
ngc	nucleus reticularis gigantocellularis
nll	nucleus of the lateral lemniscus
nmd	dorsomedial thalamic nucleus
npc	nucleus reticularis parvocellularis
nrm	nucleus raphe magnus
nro	nucleus raphe obscurus
nrt	nucleus reticularis tegmenti pontis
nlll	oculomotor nucleus
nlV	abducens nucleus
p	pons
pbg	parabigeminal nucleus
pcm	medial cerebellar peduncle (brachium pontis)
PMRF	pontomedullary reticular formation
pvg	periventricular grey substance
rpo	nucleus reticularis pontis oralis
rpc	nucleus reticularis pontis caudalis
scn	superior central nucleus (pontine raphe)
SC	superior colliculus
	LAMINAE:
sz	stratum zonale
sgs	stratum griseum superficiale
so	stratum opticum
sgi	stratum griseum intermediale
sai	stratum album intermediale
sgp	stratum griseum profundum
sap	stratum album profundum
sn	substantia nigra
trs	solitary tract
trsnt	spinal tract of n. trigemini (nV)
tpt	tectopontine tract
vlll	third ventricle
vlV	fourth ventricle

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[1] Except on anatomical diagrams, structures will be introduced with both full name and abbreviation and the abbreviation used thereafter.

For brevity, groups of collicular-lesioned rats, medial frontal cortically-lesioned rats and hippocampally-lesioned rats will sometimes be referred to as SCs, MFCs and HPCs respectively.

CHAPTER 1

THE MORPHOLOGY AND CONNECTIONS OF THE SUPERIOR COLLICULUS

1.1 Morphology

The superior colliculi of the midbrain in mammals consist of paired hillocks of laminar tissue made up of alternating layers of myelinated fibres and neuropil. These laminae are arranged in concentric arcs around the dorsal border of periventricular grey which surrounds the third ventricle and extend between the pretectal and posterior thalamic (pulvinar) nuclei anteriorly and inferior colliculus posteriorly.

Substantial changes have occurred within the colliculus in phylogeny both in terms of extrinsic connections and intrinsic organisation. Thus the colliculus (tectum) of amphibians contains some fifteen laminae which receive limited afferent connections from pallial regions, with dendritic processes that extend across a number of laminae whereas in mammals the colliculus contains only seven major laminae that receive extensive input from cortex (and proportionally fewer directly from the retina), its cellular processes usually extending into adjacent laminae only (Ingle and Sprague, 1975). Lamination in the mammalian colliculus has been extensively studied and two types of classification have been devised. One is based on the appearance in Nissl-stained sections of alternating layers of cells and myelinated fibres

(Winkler and Potter, 1914; Kanaseki and Sprague, 1974). The other is based on the appearance of cells in Golgi-stained sections giving rise to a "zonal" classification according to cell size, shape and orientation of dendrites (Ramon y Cajal, 1954; Langer and Lund, 1974; Tokunaga and Otani, 1976).

A major structural division in both classifications is between superficial and deep laminae. The former comprise layers dorsal to and including the point of entry of retino- and cortico-tectal fibres; strata zonale, griseum superficiale and medullare superficiale (or opticum) of Winkler and Potter (1914), strata I, II and III of Kanaseki and Sprague (1974), and the zones of horizontal cells, vertical cells and optic fibres of Langer and Lund (1974) are virtually synonymous. The deeper laminae comprise strata griseum intermediale, album intermediale, griseum profundum, album profundum and griseum periventriculaire according to Winkler and Potter (1914), strata IV to VIII according to Kanaseki and Sprague (1974), and Langer and Lund's (1974) zone of ganglion cells (Table 1.1). Karten (1975) has suggested, on the basis of retinofugal termination, that the superficial laminae alone represent the true mammalian homologue of the (supraventricular) optic tectum of amphibia and reptilia, although Huber and Crosby (1943) noted that during mammalian embryological development, a seemingly "reptilian" stage is reached when optic fibres form the dorsal surface of the colliculus (overlying laminae which later become "deep" collicular laminae) prior to the further migration of cells outwards to form the superficial laminae. The latter development does not occur in lower animals, and may do so in mammals in response to the neurobiotactic functioning of cortico-tectal afferents in mammals (Huber and Crosby, 1943).

Nonetheless, within the mammalian order, the colliculus, unlike the pretectum, shows strong interspecies anatomical comparability (Kanaseki and Sprague, 1974). The following represents a summary of (i) the laminar organisation and morphology of the main cell types in the cat (Kanaseki and Sprague, 1974) and rat (Langer and Lund, 1974; Tokunaga and Otani, 1976) superior colliculus (SC) , (ii) a summary of the principle afferent and efferent connections of the mammalian SC, and (iii) a summary of speculations which have been made concerning the intrinsic mode(s) of functioning of the mammalian SC on the basis of anatomical findings.

The primary laminal notation adopted will be that of Langer and Lund (1974), for the purpose of describing cell types, though comparisons will be made throughout to the classification of Kanaseki and Sprague (1974). The latter classification will inevitably dominate

Table 1.1 CLASSIFICATIONS OF COLLICULAR LAMINAE

Kanaseki & Sprague (1974) (cat)	Tartuferi (1885) (man)	Winkler & Potter (1914) (cat)	Berman (1958) (cat)	Ramon Y Cajal (1954) (various)	Langer & Lund (1974) (rat)	Tokunaga & Otani (1976) (rat)
I_1	STRATO FIBRILLE PERIFERICHE	STRATUM ZONALE (zonal layer)		ZONE MARGINALE OU DES CELLES HORIZONTALES	ZONE OF HORIZONTAL CELLS	1st LAYER (SUPERFICIAL)
I_2						
II_1	STRATO CAPPA CINEREA	STRATUM GRISEUM SUPERFICIALE (superficial grey layer)	SUPERFICIAL CELL LAYER	ZONE DES CELLES FUSIFORMES VERTICALES		
II_2					ZONE OF VERTICAL CELLS	
II_3						
III_1	STRATO BIANCO CINEREO SUPERFICIALE	STRATUM MEDULLARE SUPERFICIALE (stratum ** opticum or optic fibre layer)	INTERMEDIATE CELL LAYER	ZONE DES FIBRES OPTIQUES OU FIBRES ANTEROPOST--ERIEUSES	ZONE OF OPTIC FIBRES	
III_2						
IV		STRATUM GRISEUM INTERMEDIALE (intermediate grey layer)			GANGLION CELL ZONE	2nd LAYER (INTERMEDIATE)
V		STRATUM ALBUM INTERMEDIALE (intermediate white layer)	DEEP CELL LAYER	ZONE GANGLIONAIRE OU DES FIBRES TRANSVERSALES		3rd LAYER (DEEP)
VI		STRATUM GRISEUM PROFUNDUM (deep grey layer)				
VII		STRATUM ALBUM PROFUNDUM (deep white layer)				
VIII		STRATUM GRISEUM PERI--VENTRICULAIRE * (central grey layer		ZONE DE LA SUBSTANCE GRISE CENTRALE		

NOTES
1. 3 sublayers of stratum zonale have been described in rabbit and goat by Kato (1941) and for rodents, ungulates, carnivores and primates by Yoshida (1957).
2. Kato (1941: goat) and Yoshida (1957) described 3 layers in lamina III.
3. Kato (1941) described 2 sublaminae of IV in goat. Yoshida (1957) distinguished 3 sublaminae of IV for rodents and ungulates but only 2 in carnivores and primates.

*4. Stratum griseum and stratum fibrosum periventriculaire (Huber and Crosby, 1943).

**5. 'Stratum opticum' is the name most frequently adopted for lamina III. Originates with Marburg (1904).

section (ii) as most authors have related afferent and efferent connections to laminae identified from Nissl-stained sections. Unless specifically referenced otherwise, details of morphology in section (i) are taken from Langer and Lund (1974) and Tokunaga and Otani (1976): these reports will be referenced separately at points where they fail to agree or where neuronal classifications conflict.

1.1.1 The zone of horizontal cells

This encompasses both stratum zonale and the upper regions of stratum griseum superficiale (layers I and II of Kanaseki and Sprague, 1974), these being the major terminal laminae for cortical and retinal afferents (Sprague 1975). It is characterised by the presence of small sized cells (approximately 10μ diameter), lying within 250μ (Langer and Lund, 1974) or 260-270μ (Tokunaga and Otani, 1976) of the collicular surface and with long dendritic fields. These extend over distances of 1000μ or more, running parallel to the surface and extending up to 200μ deep. The dendritic processes do not ramify greatly, there being usually 2 primary dendrites branching after 10-50μ into much longer "higher order" dendrites often running obliquely dorsalward or ventralward. Reflexive dendrites are occasionally seen, thus making horizontal cells unique within the SC cell populations. The axon may be formed from a primary or higher order dendrite and branches within the horizontal cell zone. Langer and Lund (1974) infer that the position of the soma is not crucial to the functioning of horizontal cells since these are scattered at various depths within the horizontal cell zone, and variably in relation to the position of processes. Smaller triangular or round shaped cells (5-8μ diameter, the smallest cells in the colliculus), are also found in the most superficial region of the horizontal cell zone (corresponding to the upper half of lamina I, of Kanaseki and Sprague, 1974). These cells, termed "marginal" cells by Ramon y Cajal (1954) are situated among fine myelinated (0.5-5μ diameter) antero-posterior coursing fibres, while in sublayer I_{11} they tend to be ovoid or round, interspersed with many glia. Like all other cells in the SC, except horizontal cells, they come in two varieties which differ in spine density (Langer and Lund, 1974). They project one to five, but usually two, dendrites from the deeper regions of the cell body surface; these branch to form a dense arbor of dendritic processes extending up to 75μ lateral to the cell body and up to 150μ below it, thus remaining within the zone of horizontal cells. A third type of cell in this zone is the piriform cell; alternative names or descriptions of it are type I ganglion cell (Langer and Lund, 1974), the "short ovoidal tufted cell of the zone of horizontal cells" (Ramon y Cajal, 1954), the type II cylindrical neuron (Tokunaga and Otani, 1976). It is found in a highly restricted region along the deep margin of the zone of horizontal cells and therefore lies in the mid- to upper-regions of stratum griseum superficiale. Piriform cells have ovoid or cup-shaped bodies of 10-15μ diameter, and give rise to 2 to 5 dendrites from their superficial surface. These typically climb vertically or obliquely through the horizontal cell processes, branching and terminating in a complex network 150-350μ wide, close to the surface of the SC. Dendrites of piriform cells are almost never seen to pass below the level of the cell body though their axons typically run downward through the zone of vertical cells.

1.1.2 The zone of vertical cells

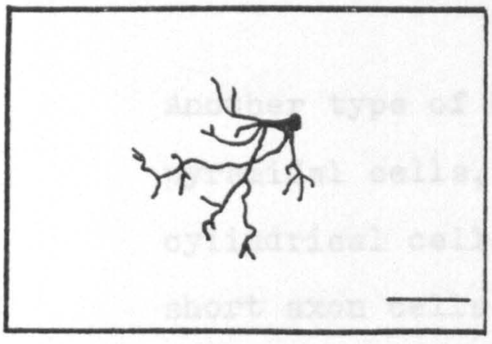
This corresponds to the deeper regions of stratum griseum superficiale (II_{111}) of Kanaseki and Sprague (1974) and contains vertical fusiform cells and pyramidal cells (together termed narrowfield vertical cells by Langer and Lund, 1974), widefield vertical cells and stellate cells. Vertical fusiform cells have soma 10-20μ in diameter and cylindrical, vertically-orientated dendritic fields. Vertical fusiform cells more deeply located, tend to have larger cell bodies (20μ) and send axons into deeper collicular laminae (below stratum opticum). Most vertical cells are bipolar or even multipolar, with two ascending dendritic trunks and two descending dendritic trunks which give rise to separate deep and superficial dendritic fields. The axons of vertical cells commonly arise from one of the lower order dendrites and run deep towards the ganglion cell zone.

Figure 1.1

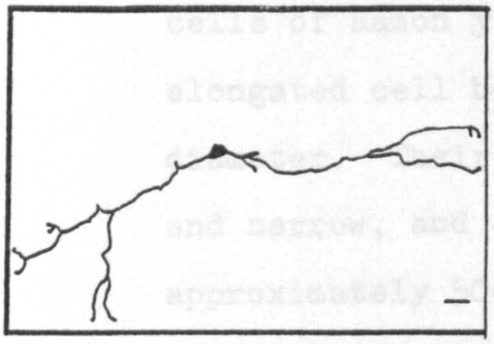
EXAMPLES OF PRINCIPLE CELL TYPES IN THE SC

Redrawn from Langer and Lund (1974).
Names in brackets are taken from Tokunaga and Otani (1976)

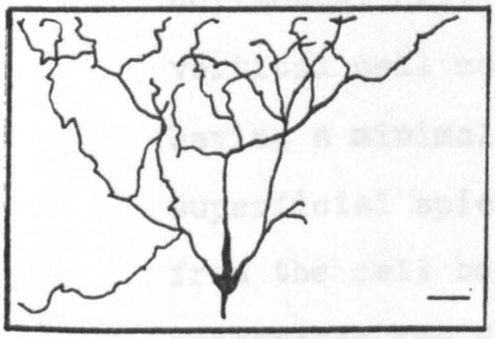
(Calibration bars: 25μ)



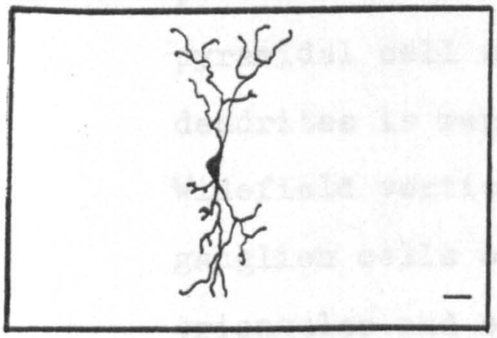
Marginal cell



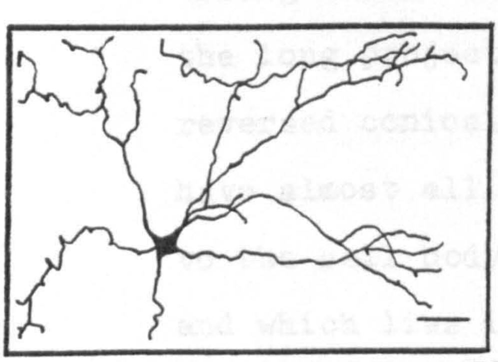
Horizontal cell



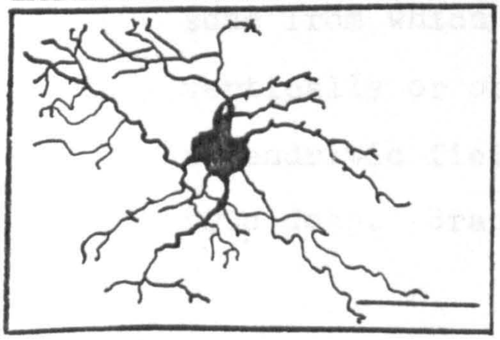
Spiny Piriform cell
or Type I Ganglion cell
(cylindrical neurons with dorsally oriented dendrites)



Narrow Field Vertical cell
(Small Field Cylindrical cell)



Widefield Vertical cell
(Widefield Multipolar cell)



Stellate cell
(Narrowfield Multipolar cell)

Another type of cell found in this zone are the pyramidal cells, alternatively type I and II cylindrical cells (Tokunaga and Otani, 1976), the short axon cells of Valverde (1973), large fusiform cells of Ramon y Cajal, (1954) which have vertically elongated cell bodies of about 15µ transverse diameter. Their dendritic fields, which are long and narrow, and cylindrical in shape, extend approximately 500µ from the upper margin of the horizontal cell zone to the lower margin of the vertical cell zone. They are usually multipolar, having a minimal deep field, withone or two thick superficial apical dendrites. The axon originates from the cell body or a lower order dendrite and penetrates the deep laminae. A second variety of pyramidal cell with dorso-ventrally orientated dendrites is reported by Tokunaga and Otani (1976). Widefield vertical cells, alternatively type II ganglion cells of Langer and Lund (1974), the triangular and ovoidal cells of Ramon y Cajal (1954), the long projecting neurons of Valverde (1973) and reversed conical cells of Tokunaga and Otani (1976) have almost all their dendritic field superficial to the cell body which is about 15-25µ in diameter and which lies in the deep region of the vertical cell zone from which it may send 3-7 primary dendrites vertically or obliquely towards the surface to form a dendritic field in excess of 400µ diameter and 500µ deep. Branching axons from these cells may project either into more superficial or deeper regions. A further type of cell has also been reported, termed type III ganglion cells by Langer and Lund (1974) which correspond with the triangular or stellate cells of Ramon y Cajal (1954) and the widefield multipolar neurons of Tokunaga and Otani (1976). These have a large cell body (20-25μ diameter, often located within stratum opticum) with a patchy and sparse dendritic field but which is quite extensive (often spanning over 1000μ). The cells have 3-6 primary dendrites, some extending below the cell body and an axon which has several collaterals. These invariably run into deep collicular laminae. Also there are stellate cells of various sizes (narrowfield multipolar cells of Tokunaga and Otani , 1976) that possess symmetrical radiating dendritic fields, and which are frequently multipolar and have a variable axon length. They possess a round or eliptical cell body ($15\mu^+$ diameter) and are found in most regions and laminae of the colliculus. They form the bulk of the cell population of laminae below stratum opticum.

1.1.3 The zone of optic fibres

This zone corresponds to stratum opticum (Marburg, 1904), stratum medullare superficiale (Winkler and Potter, 1914) or lamina III of Kanaseki and Sprague (1974), and is the lamina into which afferents from a number of sources enter the SC, and through which many efferents leave. It is therefore composed mainly of fibres, though it also contains scattered small- and medium-sized cells, notably wide-field vertical cells, stellate cells and a population of cells with horizontally-orientated dendritic fields similar to those in the zone of horizontal cells. These are generally found in an intermediate position in the lamina between separate dorsally and ventrally placed layers of fibres which may be regarded as separate laminae according to Kanaseki and Sprague (1974). Of these fibre sublayers, the most dorsal is likely to contain the bulk of retinotectal afferents while more ventral fibres are more likely to originate in the cortex (Singleton and Peele, 1965; but see Kawamura, Sprague and Niimi, 1974).

1.1.4 The zone of ganglion cells

This region encompasses all the intermediate and deep laminae of Winkler and Potter (1914) and laminae IV and V - VIII of Kanaseki and Sprague (1974). It consists mainly of stellate (Langer and Lund, 1974), or multipolar (Tokunaga and Otani, 1976), and vertical (Tokunaga and Otani, 1976) neurons. The multipolar neurons may be medium sized field neurons (20µ diameter cell body) or wide field neurons (30-40µ diameter cell body) whose processes extend across 400µ in places.

Lamina IV

Not all students of the colliculus have placed lamina IV (stratum griseum intermediale) with deeper laminae; Ramon y Cajal (1954) and Berman (1958) grouped it with stratum opticum, while Tokunaga and

and Otani (1976) have isolated it as a major lamina intermediate between superficial and deep zones. (Lund (1966) noted that in the rat, the boundary between stratum opticum and stratum griseum intermedium is poorly defined.) It comprises a well-developed cell layer (the thickest of all collicular laminae) and anteriorly it is continuous with the posterior pretectal nucleus. It is composed of densely arranged small- to medium-sized cells (20µ diameter), but, unlike deeper laminae, it has a unique population of multipolar, large diameter ($40\mu^{+}$) stellate cells located particuarly in lateral regions. Axons of the latter cells (which may form the tectospinal tract/ predorsal bundle according to Tokunaga and Otani, 1976) arise from the soma or from a thick dendritic trunk close to the cell body, and descend into the fibre bundle of stratum album profundum. Other axons from some medium-sized multipolar neurons project dorsally towards the optic layer though it is not known where they distribute (Tokunaga and Otani, 1976). Deep vertical cells are similar to those in more superficial laminae; they have one or two dendrites projecting from the ends of the spindle-like cell body, and their axons intermingle with fibres of stratum album profundum some climbing vertically towards the optic layer. These stellate and vertical cells are found throughout the deeper layers. In addition, a few horizontal cells are observed in deeper laminae; though similar to those in the horizontal cell zone, they possess less extensive dendrites.

Lamina V

This lamina (alternatively known as stratum album intermediate or stratum lemnisci) is predominantly a fibre layer. It is found between layers IV and VI in central and lateral regions of colliculus, but does not extend to the medial collicular border. It contains small- to medium-sized cells, fusiform or triangular in shape, apparently arranged parallel to the incoming spinotectal tract fibres which enter the colliculus at this point. Many fibres in this stratum traverse the SC and enter the posterior thalamus and pretectum anteriorly (Kanaseki and Sprague, 1974).

Lamina VI

Stratum griseum profundum is a well-developed cell layer like lamina but is is less densely packed with cells (types being similar to lamina IV) and contains a number of myelinated fibres of the tectal and posterior commisures. It fades imperceptibly into the nuclei of the posterior commisure anteriorly (Kanaseki and Sprague, 1974).

Lamina VII

Stratum album profundum is a thin fibre layer located between layer VI and the central grey, containing multi-polar (stellate) cells whose dendrites project from the ventral part of the cell body to invade lamina VIII, and tectofugal fibres originating in lamina IV and VI.

Lamina VIII

Though not always included in collicular laminal classifications, the most dorsolateral region of periventricular grey is intimately connected with deep collicular laminae and has been included as the most ventral collicular lamina by Ramon y Cajal (1954) ("zone de la substance grise central"), Kanaseki and Sprague (1974) ("periventricular grey, pars lateralis") and Huber and Crosby (1943) ("stratum griseum et stratum fibrosum periventriculaire"). Medium sized field neurons are shown in this region by Tokunaga and Otani (1976, Figures I and II), some projecting vertically into more superficial regions of the colliculus.

Discussion

While the numerous morphological studies of the SC are in general agreement, some specific contradictory findings have emerged, perhaps reflecting species differences in organisation. For example, Valverde (1973) claimed to have found horizontal cells solely in stratum zonale in his experiments with mice, and these with dendrites aligned wholly in the frontal plane. However Langer and Lund (1974) argue that the "short axon cells" reported by Valverde may represent foreshortened segments of horizontal cells orientated through the plane of section. Both these authors and Tokunaga and Otani (1976) have reported that horizontal cells in the rat occur in dorsal regions of stratum griseum superficiale in addition to stratum zonale, though the suggestion by Langer and Lund (1974) that horizontal cell dendrites are aligned along horizontal and vertical field axes is disputed by Tokunaga and Otani (1976) who failed to observe such orientation preference.

Sterling (1971), in a study of the SC in rhesus monkeys, and Viktorov (1966), in a second study involving comparisons among a range of species did not describe marginal cells. Langer and Lund (1974) attribute this to the possible effect of precipitation in histological treatments, selectively masking the most superficially located cells which in this case are the marginal cells. Furthermore, Sterling (1971) failed to observe horizontal cells, which is especially surprising in view of the presence, in all other species studied so far, of superficial cells with horizontally-orientated dendrites. However, Langer and Lund (1974) report horizontal cells in the rhesus monkey colliculus, though in one respect there may exist a genuine species difference between rat and monkey in that the very long dendritic fields of rat horizontal cells (often extending over 1000µ) have not been seen in the monkey.

Only Yoshida (1957) has reported gross laminal differences between rodents and primates; lamina IV may have 3 distinguishable sublaminae in rodents and ungulates but only 2 in primates and carnivores.

Other reported species differences relate to variations in laminal thicknesses, correlating with the extent to which the visual modality is used in particular species. For example, laminae III and V are particularly thin in bat and shrew (Huber and Crosby, 1943). Since both are notably "non-visual" species, this presumably reflects a reduction in the afferent and efferent pathways in these animals. Of further interest in this respect would be the morphology of the mole SC: the absence of retinal input to the SC (Lund and Lund, 1965) would be predicted to result in a reduction in thickness of the superficial laminae, though in addition the loss or atrophy of particular cell types might represent those in visual mammals particularly involved in the processing of retinal input.

1.2 Connection of the SC

1.2.1 Afferents

There are two main sources of visual input to the SC, the contralateral retina and ipsilateral visual cortex. Retino-tectal fibres from the optic tract pass over the dorsal border of the medial geniculate nucleus and close to, or through, regions of the lateral geniculate nucleus, entering the SC mainly via the lateral collicular brachium (supplying the caudolateral SC) and a few via the medial collicular brachium (supplying the antero-medial SC) (Székely, 1973). They terminate in superficial laminae, specifically in upper regions of stratum griseum superficiale (II_1) and stratum zonale (I) in the cat (Kawamura et al, 1974), maintaining a precise retinotopic organisation and mainly terminating in the caudal ¾ of the SC (Lund, 1972). Lund (1966) reported degeneration throughout sgs following unilateral enucleation in rat, though the deeper degeneration may represent en passant synapses between retinal afferents and deeper cells; Lund (1972) and Langer and Lund (1974) describe the majority of boutons termineaux as being located within 100μ of the SC surface.

While input from the ipsilateral retina is extensive in the cat (see Chapter 2), it is greatly reduced in animals with more lateralised eyes, corresponding to the overall reduction in ipsilateral projections. In the rat, Lund (1966) and Hayhow, Sefton and Webb (1962) observed significant ipsilateral retinotectal projections (estimated at 5-10% of the total) in hooded, but not albino, rats, from tracings of degeneration following unilateral enucleation, though it should be noted that Siminoff, Schwassmann and Kruger (1966) failed to record electro-physiological responses in the hooded rat SC upon stimulation of the ipsilateral eye. Where ipsilateral projections are observed, these generally terminate in rostral SC; for example in the rat they are limited to the anterior third of stratum opticum (Hayhow et al., 1962).

Whether input to the SC is independent of that to the lateral geniculate nucleus is unclear; some authors have suggested that retinocollicular fibres may be small diameter collaterals of geniculostriate fibres (Altman, 1962c; Bishop, Clare and Landau, 1969; Sefton, 1968; see Marrocco and Li, 1977). However Michael (1967) has shown electrophysiologically that in the squirrel monkey, separate populations of retinal ganglion cells project to visual cortex and SC (see Chapter 2), and Schneider (1968) has demonstrated that cortical and SC projections from the retina are separable by their differential rates of maturation. It is likely that some retinocollicular fibres are collaterals of geniculate fibres while others are direct and independent of the lgn (see Sprague, Berlucchi and Rizzolatti, 1973), though the proportion may conceivably vary with species.

Afferent input from the visual cortex to SC has been investigated in a variety of species (for the rat, see Nauta and Bucher, 1954; Lund, 1966), since its earliest demonstration by von Monakow (1889) in cat. While, clearly, input from pallial regions is limited by the extent of their development in lower species, for example in amphibians (Huber and Crosby, 1933), the situation within the mammalian order shows remarkable interspecies consistency. Altman (1962c) reported that following removal of striate cortex (lateral and postlateral gyri) in the cat, numerous degenerating fibres were seen to leave the cortex via the internal capsule and enter the SC (exclusively ipsilaterally) via the lateral collicular brachium, and a few via the medial brachium. Most fibres were seen to traverse the SC in so, turning dorsally to terminate in sgs, though at a deeper level than retinal afferents; such was also reported for the rat by Lund (1966). Magalhaes-Castro et al (1975) showed the cells of origin of cortico-collicular fibres from area 17 to be pyramidal cells in layer V in the cat.

The most extensive tracing of fibre routes from cortex (striate and extra striate) to colliculus was carried out by Crosby and Henderson (1948). They claimed to have identified (in macacca mulatta) at least 7 separate fibre bundles, including an external cortico-tectal tract (from visual association cortex, areas 20, 21) having three separate terminal zones within SC, and an internal tract (occipital and preoccipital divisions), projecting to separate rostro-caudal SC zones. Though their results have been questioned, in that they report cortico-tectal fibres entering the SC via laminae below so (see Lund, 1966), it is clear that the cortico-tectal tract cannot be considered an indivisible unit. Lund (1966) who observed degeneration resulting from area 17 lesions in rats, found that fibres leave the cortex via the internal capsule, to enter the lateral cerebral peduncle, but leave it where it crosses the optic tract to enter the SC via (i) the collicular brachium or (ii) via the lgn and pretectum. Lesions placed in cortex medial to the occipital region result in localised degeneration in rostral stratum album intermediale (see Lund (1966) for an historical review of corticotectal pathways in the rat). In the cat there appear to be two separate corticotectal tracts (Sprague, 1975, Figures 19, 20), one originating in striate cortex and the other in peristriate regions. Many fibres from the latter region appear to enter SC in the medial brachium. Recent work by Updyke (1977) in the cat has demonstrated efferents from striate cortex to SC which terminate in deep sz, sparsely in upper sgs (II_1) and profusely in mid sgs (II_2), except in rostral SC where terminals in upper sgs (II_1) are more numerous. A further group of fibres enter the SC in stratum opticum and spread diffusely into deeper laminae though their precise terminal zone is unknown (Altman, 1962c; S Kawamura et al, 1974; Sprague, 1975).

Topographic visual cortical input from secondary visual areas in the cat terminates in SC laminal zones below those receiving input from primary visual cortex; temporal cortex efferents to SC terminate in lower sgs, from parietal cortex in sai (Sprague, 1975), and from dorsolateral frontal cortex (in the monkey) in laminae below so (Kuypers and Lawrence, 1967). Cerebellar and spinal afferents traverse the SC in lamina V and terminate in lamina VI in the cat (Kanaseki and Sprague, 1974). Astruc (1971) has demonstrated projections in the monkey from area 8 (the rostral bank of arcuate sulcus, or "Frontal Eye Field") to intermediate and deep colliculus, and projections from the (supposedly homologous - see Leonard, 1969, 1972) dorsomedial frontal region in the rat have been reported to terminate in similar regions (Leonard, 1969). Degeneration limited to laminae IV and V in the rat results from lesions in cortex anterior to the striate area (Lund, 1966), elsewhere termed "parietal" cortex (Lund, 1966; Boyd and Thomas, 1976).

Anatomical studies employing standard degeneration techniques have been unsuccessful in demonstrating degeneration in rostral SC following enucleation in monkeys (Wilson and Toyne, 1970), leading to the conclusion that no direct input to SC originates from the foveal retina (corresponding to the central 5% of visual space) and that it must therefore be relayed via visual cortex (see Marrocco and Li (1977) for discussion). However Schiller <u>et al</u> (1974) have demonstrated that in the absence of visual cortex (VI), electrophysiological responses in rostral SC could still be recorded upon stimulation of the fovea. Hubel, Le Vay and Wiesel (1975) have provided autoradiographic evidence for a direct projection. Marrocco and Li (1977) argue that the nature of foveal input may render it particularly difficult to detect. It must be concluded, nonetheless, that direct foveal input from the retina to SC is sparse by comparison to foveal projections to visual cortex, and less significant than input from more peripheral regions of space to which the majority of colliculus is devoted, particularly in the afoveal rat. The 'magnification' of central visual space in the rat is not obvious (if not altogether absent) compared with the cat (compare Forrester and Lal (1962) and Siminoff et al (1975) for the rat with Sprague et al (1975) for the cat). However, the region of retina densest in ganglion cells invariably projects to the rostral pole of the SC, even though in the rat the area of retina concerned is temporally located (Forrester and Lal, 1962) (see Chapter 2).

In addition to the above, there is also substantial input to SC in the cat from the fastigial nucleus (lobule VII) of the cerebellum (Angaut, 1969), acoustic input from the inferior colliculus (Powell and Hatton, 1969) auditory cortices (Garey, Jones and Powell, 1968), input from the reticular formation and central grey (Hamilton, 1973) and extensive input has been identified from extraocular and neck muscles (Abrahams and Rose, 1975a) and fore- and hind-limb muscles (Abrahams and Rose, 1975b).

Subcortical input from the pulvinar nucleus to so and sgs was described by Altman (1960) in the cat, and a recent study of subcortical projections to SC using HRP labelling (Grofova, Ottersen and Rinvik, 1978) has revealed inputs from the parabigeminal nucleus, the midbrain reticular formation, the substantia nigra (pars reticularis), the nucleus of the posterior commisure, pretectum, zona incerta and ventral lgn. The demonstration of input from pretectum is especially interesting in view of the controversy regarding the existence of such a pathway (Goldberg and Robinson, 1979) prior to the development of axonal transport methods in experimental anatomy. No projection from hippocampus to the SC has been reported.

Thus in summary, the superficial laminae receive afferents primarily from visual structures, in particular the ipsilateral visual cortex and contralateral retina in a precise point-to-point topography, different afferent pathways distributing across separate regions of colliculus; in particular striate cortex input is especially dense in rostral colliculus while retinal and nonstriate cortical input predominates caudally. Input from secondary visual sources, notably the ventral lgn, reticular formation and cerebellum, terminates in deep SC where all modalities except gustation and olfaction are represented. The topography of deep projections is much less precise than to superficial laminae although there is a rough topographic correspondence between deep and superficial spatial representations. The range of depth of terminals for each afferent pathway is generally limited to a particular lamina (or adjacent laminae) and it would appear that each afferent source has a particular, characteristic terminal depth profile (though overlapping with terminal depth fields of adjacent inputs). The above organisation would seem to apply to the rat though precise homology between specific afferent pathways is difficult to establish.

1.2.2 Efferents

Efferent pathways from the SC are also divisible into subgroups differing in terms of laminal and/or rostrocaudal regional origins. Using Nauta staining, Altman and Carpenter (1961) reported that following large unilateral lesions in the SC of the cat, anterior projections could be traced to the ipsilateral posterior thalamus (pulvinar complex), the nucleus of the optic tract, pretectum and pars ventralis and dorsalis of the lateral geniculate nucleus. Kawamura (1974) has shown that medial SC projects to rostral and medial regions of the posterior pretectal nucleus, the nucleus of the optic tract and dorsal half of the pulvinar, while the lateral SC projects to the suboptic and posterior pretectal nucleus, nucleus of the optic tract and ventral pulvinar; also that retinotopography exists within these projections. In the tree shrew, the anterior projections to pretectum and pulvinar were shown to arise exclusively from superficial SC laminae (Harting, Hall, Diamond and Martin, 1973), and more recent precise tracing using retrograde axonal transport of horseradish peroxidase (HRP) has further demonstrated that projections to the pulvinar have their cells of origin in lower sgs while projections originating in upper sgs travel to the ventral lgn (Raczkowski and Diamond, 1978). Interestingly, the granular precipitate resulting from the exogenous uptake of HRP is sufficiently dense in many cases to allow the identification of cell type and size. Raczkowski and Diamond (1978) have shown that wide field vertical cells (using Langer and Lund's (1974) terminology) are the most likely cells of origin of the pulvinar projection while lgn_V projections are likely to arise from narrow field vertical cells.

Projections from the deeper SC laminae (below stratum opticum) in cat form at least five major tracts. Altman and Carpenter (1961) found fibres traceable to (i) deep laminae of the contralateral SC, a few degenerating in the contralateral dorsal tegmentum, (ii) profuse degeneration in the ipsilateral tegmentum, (iii) a tectopontine tract coursing laterally round the margin of the inferior colliculus to terminate in the dorsolateral pons, (iv) the predorsal bundle consisting of fibres which cross the midline beneath periventricular grey coursing between nIII and red nucleus in the caudal mesencephalon as the dorsal tegmental decussation many of which terminate in the brainstem reticular formation, others (v) continuing caudally without synapsing in the reticular formation and passing caudally from the medulla as the tecto-spinal tract. These latter fibres are seen to travel in the ventral funiculus and terminate in upper cervical regions of the spinal cord.

The above findings have been refined and extended for a number of species. Edwards (1978) has shown in the cat that intertectal fibres are not homogeneously distributed across the rostrocaudal extent of the SC but selectively connect corresponding points in rostral colliculus, apparently originating in strata grisea intermediale and profundum. He has further demonstrated that in this region of SC the head and face of the animal are somatotopically represented, and speculates that the intertectal pathway may be involved in visual tracking or convergence movements of the eyes. From rostral SC Edwards and Henkel (1978) have traced descending projections beneath periventricular grey which sweep dorsally and medially on the contralateral side to terminate in the region of periventricular grey overlying nIII (oculomotor nucleus). Evidence of connections between nIII and overlying grey matter has also been provided anatomically (Edwards and Henkel, 1978; Ramon y Cajal, 1954), and thus direct tecto-oculomotor contacts are possible (Edwards and Henkel, 1978). The low stimulus thresholds necessary to produce eye movements and activate motoneurons in deep laminae in cat and monkey (Anderson, Yoshida and Wilson, 1971; Robinson, 1972; Schiller and Stryker, 1972) suggest strong and direct driving of oculomotor neurons by the SC (Sprague, 1975). This presumed pathway, by which the SC may exert influence on vertical eye movements with which nIII is especially associated (see Edwards and Henkel, 1978) is especially interesting in view of the controversy regarding the existence of direct anatomic connections between the SC and the oculomotor (extraocular muscle) nuclei.In accordance with the traditional view of the SC as an oculomotor reflex centre, it was anticipated that such direct connections should exist, and indeed early anatomists claimed to have identified them (e.g. Held, 1890). Others, using more modern techniques, specifically denied their existence, though indirect connections via the interstitial nuclei were reported (Altman and Carpenter, 1961; Sprague, 1975; see Edwards and Henkel (1978) for discussion).

Projections to the brainstem have been investigated in the cat by Kawamura, Brodal and Hoddevik (1974) using both Nauta and Fink-Heimer silver degeneration techniques. [1] The ipsilateral tegmental projection is largely restricted to the dorsal one third of the mesencephalic reticular formation and the exclusively contralateral predorsal bundle terminates within two separate reticular foci, one at pontine level in the large- and giant-celled RF, in a terminal zone corresponding to the posterior portion of nucleus reticularis pontis oralis (rpo) and rostral nucleus reticularis pontis caudalis (rpc), while a second focus exists in the more caudally

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[1] The Fink-Heimer technique indicates fields of termination of pathways by selectively staining boutons terminaux.

situated nucleus reticularis gigantocellularis of the medulla. The latter region is virtually coextensive with the region termed the "paramedian reticular formation" [1] (Graybiel, 1977), an area traditionally associated with horizontal eye movements in view of its demonstrable connections with the abducens nerve (nIV) (Sparks and Travis, 1971; Grantyn and Grantyn, 1976). Thus the medullary projection represents a second route by which the SC might exert influence over the oculomotor system. Edwards and Henkel (1978) claim that large cells in sgi of the caudal ¾ of the SC are the cells of origin of connections to the parabducens region. Indeed, electrical thresholds for eliciting intracellular potentials in the abducens nerve decrease on moving from rostral to caudal SC. Small cells (<20μ) in sgi and sgp of rostral SC were reported by Edwards and Henkel (1978) to be the cells of origin of the projection to the oculomotor region (Bucher and Bürgi (1950) also reported small cells to project to the intestitial nucleus of Cajal). However, Kawamura and Hashikawa (1978) found labelled neurons distributed throughout the entire rostrocaudal extent of SC following gigantocellular

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[1] This is not the same as the paramedian reticular nuclei, a more caudal band of cells close to the midline (Sidman, Angevine and Pierce, 1971).

injections of HRP. Unfortunately there is no comparable data for the rat. Species variations in such pathways might be expected; for example these pathways might be less well developed in an animal such as the rat which uses few eye movements, and does not exhibit "convergence" to near objects. The two existing studies in the rat (Tasiro, 1939; Papez and Freeman, 1930) used the Marchi technique and cannot be reliably compared with the above studies in the cat. However, Figure 1.8(taken from Tasiro, 1939) does suggest that in the rat the descending projections are similar to those previously described (see Section 1.2.4).

Weber, Martin, Behan, Huerta and Harting (1978) have suggested that a subtle species difference may exist regarding the population of collicular cells projecting to the spinal cord. In opossum and tree shrew only large ($>40\mu$ diameter) cell bodies are labelled following injections of HRP into the cervical spinal cord while cells of a range of diameters are labelled following similar injections in the cat. Similarly Kawamura and Hashikawa (1978) reported cells of a range of diameters to be labelled following injections of HRP into the brainstem RF in cats. They argue that tectoreticular neurons originate in the rostral $\frac{1}{3}$ of the SC and spinal projections from the caudal $\frac{2}{3}$, a suggestion strongly supported by the recent report of Henkel, Edwards and Kersey (1979). Eighty per cent of tectopontine projecting neurons were of small diameter (10-25µ) while larger multipolar neurons appeared to form the origin of tectoreticular fibres (10-15% 40µ, 20-30% 25-40µ). Raczkowski and Diamond (1978) reported labelling in laminae V to VII following HRP injections into the predorsal bundle at their point of decussation in the caudal mesencephalon. However, in view of the fact that predorsal bundle fibres include tectospinal fibres (Kawamura et al, 1974), labelling following such injections would be predicted to occur in both intermediate (IV) and deep laminae, and thus Raczkowski and Diamond's (1978) results create an anomaly.

Though most studies of collicular efferents are in general agreement, Graham (1977) reported few or no descending projections from lamina IV, though subsequent retrograde transport studies have demonstrated substantial projections from lamina IV to pontomedullary RF in the cat (Edwards and Henkel, 1978; Kawamura and Hashikawa, 1978) and to the spinal cord in cat, opossum and tree shrew (Weber et al, 1979). Thus Graham's result must be considered to have arisen from the vagaries of tracing techniques.

Using an autoradiographic tracing technique in monkeys, Harting (1977) has reported a similar organisation of SC efferents to that in the cat. However, surprisingly little labelling was noted in the medullary reticular formation although the caudal one third of the medial accessory olivary complex was labelled. Harting (1977) also found the parabigeminal nucleus (pbg) (ventrolateral to the inferior colliculus) to receive input from the SC via the most lateral efferent pathway, the tectopontine tract. This might be inferred to represent an isolated species idiosyncrasy (see for example Goldberg and Robinson, 1979), although in fact Harting has elsewhere (Harting et al, 1973) reported that in the tree shrew the pbg nucleus receives tectal efferents. On the other hand while the pbg nucleus was labelled following autoradiographic injections in the SC and pretectum in another study using cats (Graybiel, 1977), injections localised within SC alone failed to result in labelling of this nucleus, though labelling was identified nearby (Graybiel, 1977, Figure 16B, p.72, upper illustration). The pbg might represent a unique structure, possibly receiving afferents from deep SC (Harting 1977; Benevento and Fallon, 1977; Graham, 1977) while projecting to superficial SC (Grofova et al, 1978); see Langer, Sherk and Graybiel (1977).

In the tree shrew, Harting et al (1973) showed the superficial laminae to project to pulvinar, pretectum and dorsal and ventral lgn, while Hashikawa and Kawamura (1977) have demonstrated a modest contribution to the tectopontine tract from small cells in medial SC. Thus not all projections from superficial laminae are rostrally directed. Similarly, not all projections from deep SC are caudally directed; Harting et al (1973) reported projections from deep SC in the tree shrew to the intralaminar thalamic nuclei, subthalamus and the posterior nuclear group of Rose and Woolsey, caudal projections being observed to terminate in the inferior colliculus, pbg nucleus, nucleus reticularis tegmenti pontis, the inferior olive, brainstem reticular formation and facial nucleus. In macacca mulatta, Harting (1977) reported deep lesions to result in additional degeneration in nucleus cuneiformis and the substantia nigra. Benevento and Fallon (1975), also working with monkeys, reported additional projections from superficial SC to the magnocellular portion of the dorsomedial thalamic nucleus (nMD), the lateral posterior nucleus and some intralaminar nuclei, while additional projections from deep SC were recorded to central grey, suprageniculate nucleus and zona incerta, remaining intralaminar nuclei accessory optic tract and the magnocellular portion of the medial geniculate nucleus.

Thus in summary, the SC has a large number of efferent pathways, many of them topographically organised.

While in the cat (Meikle and Sprague, 1964) and in the rat (Krieg, 1947) the pretectum is said to have a direct cortical projection, such has never been observed for the SC, though Sprague et al (1973) note that the SC has a widespread cortical projection lying outside the lgn projection via thalamic relays. Ascending projections are predominantly from superficial laminae and travel mainly to visual structures, for example the pulvinar, via which the SC projects to peristriate cortex. The latter system perhaps represents a "second visual system" (Diamond and Hall, 1969; Harting, Hall and Diamond, 1972). Other collicular-pulvinar-cortical projections terminate in the frontal eye field (Bos and Benevento, 1975; Trojanowski and Jacobson, 1975). An homologous pathway to MFC is not identifyable in the rat, though the pulvinar pathway is represented by the projection from SC to peristriate cortex via thalamic nucleus thalami posterior pars lateralis.

Deep laminae project mainly caudally to the ipsilateral pons and midbrain reticular formation, contralateral pontomedullary reticular formation and spinal cord, while also sending fibres to the contralateral SC, nonspecific thalamic nuclei and other (non primary) visual structures. Some efferent pathways appear to have specific laminal, or restricted rostrocaudal, zones of origin and perhaps originate from specific cell populations.

1.2.3 Intrinsic functional organisation: anatomical considerations

Retinotectal afferents traverse the SC in stratum opticum and almost all run vertically, making en passant synapses through the zone of vertical cells, and terminate in the first 100μ beneath the SC surface. Langer and Lund (1974) have suggested that horizontal cells are the recipients of these incoming afferents (in addition to intrinsic projections). These horizontal cells, which are a feature of all mammalian colliculi, are probably the presynaptic elements in the dendro-dendritic synapses reported in superficial SC laminae (Sterling, 1972). Their dendritic spines have been shown to contain large, flattened vesicles (associated with inhibitory processes; see Sterling, 1972), and to be presynaptic to dendrites or postsynaptic to a variety of terminals including optic terminals (Langer and Lund, 1974). Tokunaga and Otani (1976) calculate that eight retinotectal axons could synapse on one dendrite of a horizontal cell. The extensive dendritic fields of these neurons (in excess of 1000μ in some cases in the rat) suggest that they may mediate processes across a wide area of visual field. However action potentials do not appear to be generated by horizontal cells; their electrophysiology is unknown. The majority of cells from which recordings have been made in superficial SC laminae are likely to be narrowfield and widefield vertical cells (Langer and Lund, 1974). These have dendritic processes extending over 60μ - 350μ. Application of the magnification factor calculated by Siminoff _et al_ (1966), namely that 35μ on the collicular surface corresponds to 1% of visual angle, indicates that the receptive fields of these cells would be expected to be between 2° and 10°. This corresponds to the 2° - 15° reported by Humphrey (1968) for cells in superficial SC of the rat. By the same token horizontal cells would be predicted to have receptive fields of over 30°. Thus the presence of unrecorded horizontal cells may explain why inhibitory influences on the discharge of cells in superficial laminae may be exerted by stimuli presented well outside the cell's receptive field (Rizzolatti, Camarda, Grupp and Pisa, 1975).

Of further interest, assuming Langer and Lund's (1974) model to be correct, evoked potentials recorded from cells in superficial laminae have already crossed at least 2 synapses involving horizontal cells prior to being recorded at the microelectrode. However, Tokunaga and Otani (1976) assume that retinotectal afferents may terminate upon a variety of other cell types in addition to horizontal cells (e.g. piriform cells [1]) though <u>corticotectal</u> fibres are presumed to

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[1] Sprague (1975) proposes that retinotectal fibres terminate on the "bushy dendrites of small cells described by Ramon y Cajal (1911)", probably referring to piriform cells. It should be noted that Lund (1966) reports degeneration throughout sgs in the rat following unilateral enucleation, thus notably in regions below the horizontal cell zone, though the greatest density is found within the horizontal cell zone.

terminate on cells other than horizontals. This implies that at least some retinal input undergoes initial processing at horizontal cell level prior to its influencing corticotectal inputs while corticotectal input is more directly relayed to deeper laminae. However it must be admitted that corticotectal afferents are not easily identified (Langer and Lund, 1974) and thus a better understanding of interactions in superficial laminae awaits further anatomic evidence.

A possible functional role for horizontal cells is suggested by Langer and Lund (1974) in relation to lateral inhibition mechanisms allowing the development of directional selectivity. However, these authors acknowledge that the inter-species variability in directional selectivity as ascertained by single unit recordings in SC, together with relative inter-species invariance of SC cell types may indicate that direct parallels between morphology and electrophysiological responses are premature. In addition, since directional selectivity has been shown to depend upon the integrity of visual cortex in many instances (see Chapter 2) and retinal cells which project to SC have directionally selective properties (Y-cells; Hoffman, 1972) it is probable that directional selectivity is imposed upon retinotectal information at a prior (retinal) level. But this is not to say that lateral inhibition does not occur within the colliculus.

Transfer of information from superficial to deeper laminae is likely to take place via axo- and dendrodendritic contacts between horizontal and vertical cells (Langer and Lund, 1974) with axons of the latter passing mainly into stratum opticum, some passing deeper. Thus two basic modes of intracollicular function are likely: firstly an extensive horizontal interaction at superficial level, and a vertical downward flow from superficial to deeper laminae, the latter maintaining topography throughout its descent (see Sprague, Rosenquist and Palmer; cited Sprague, 1975). In deeper laminae, however, receptive field sizes increase; neurons in the so and sgs of the rat which have been identified electrophysiologically as having large, irregular, patchy visual fields (Humphrey, 1968) are thought by Langer and Lund (1974) to correspond to their type III ganglion cells, and likewise by Tokunaga and Otani (1976) to correspond to their equivalent cell, the widefield multipolar neurons which have irregularly shaped, patchy dendritic fields covering wide horizontal areas. Tokunaga and Otani (1976) favour the idea that narrow field cells in superficial SC are 'nested' with the receptive fields of these deeper neurons, and also that descending information finally reaches, and is integrated by, the large multi-polar neurons in deeper laminae from which efferent pathways emerge. One consequence of such a "descending flow" model is that extrastriate input, organised as successive bands or layers (through which the descending activity must pass) is strategically placed to influence or modulate descending impulses. Langer and Lund (1974) argued similarly that the function of visual cortical input may be to modulate collicular cell responses rather than to 'generate' their response characteristics (see Chapter 3). Rostrally-directed projections from SC arise from superficial laminae - probably from reversed conical (Tokunaga and Otani, 1976) Type II ganglion (Langer and Lund, 1974) cells and widefield multipolar (Tokunaga and Otani, 1976) Type III ganglion (Langer and Lund, 1974) cells. Indeed axons of such cells have been observed to pass into lamina IV which is continuous with the pretectal nuclei anteriorly (Kanaseki and Sprague, 1974). The contention that some deep cells with dorsally running axons may be the source of anterior projections (Tokunaga and Otani, 1976) is disconfirmed by Weber et al (1979) who found labelled cell bodies solely within superficial laminae (specifically wide and narrowfield vertical neurons) following HRP injections into lgn_V and pulvinar in the tree shrew.

Alternatives to the "vertical flow" or "classical" (Mohler and Wurtz, 1976) model of intrinsic collicular organisation have been proposed. Casagrande et al (1972) and Harting et al (1973) have suggested that such a major division exists between superficial and deep regions of the colliculus that they may best be considered separate units with independent afferent and efferent connections; indeed it is possible that each lamina has a large degree of independence in view of the demonstrated laminal specificities of efferent pathways (Weber et al, 1979; Raczkowski and Diamond, 1978; Henkel et al, 1979). Sprague has expressed a similar though more conservative view:

> "We can draw a major functional generalisation, namely that, based on the spatial organisation of receptor surfaces, these (I - VIII) laminas have a certain independence of one another. Stated in another way, the constituent neurons of each lamina can be independently modulated by different afferent sources." (Sprague, 1975, p. 204).

The behavioural evidence for such a division of function will be examined in a later section (Chapter 3). Such an organisation represents an abrupt discontinuity between amphibians and mammals; most authors have generally concluded that while the emphasis has shifted from retinal input to cortical input during phylogeny, that the function of the SC remains similar (albeit under control by different extrinsic influences), and thus a "descending flow" model tacitly assumed for lower animals is presumably expected to apply to mammals (see, e.g. Crosby and Henderson, 1948)

Anatomical evidence for the involvement of the SC in eye movement control is strong; Edwards (1978) has provided evidence of indirect connections to oculomotor nuclei. However in view of the interspecies variation in the extent to which eye movements are used, it might be expected that efferent pathways from

SC would exhibit interspecies variability. This possibility is examined in the experiment in Section 1.2.4. However the extent to which the SC is "responsible" for eye movement generation (via sensorimotor translation of signals from superficial to deep laminae) is a source of controversy. Mohler and Wurtz (1976) who argued against the "descending flow" model of SC function proposed that afferent information from the retina in superficial SC 'converges' in intermediate laminae with ascending information from deeper laminae, resulting in the potential "enhancement" of superficial activity according to the significance or novelty of the sensory stimulus, thus facilitating eye movements to the region of visual space in which the stimulus is located. However, anatomical studies to date have failed to investigate possible modes of organisation among deep neurons and in the absence of such information no comment can be made regarding this theory from an anatomical standpoint.

It has been informally proposed that the superficial and intermediate laminae should be considered 'true' colliculus and that deeper laminae should be considered part of the reticular formation. However since activity in deep neurons is (albeit loosely) topographically related to that in superficial neurons, the structure does appear to operate as a functional unit in many respects. The seemingly nonspecific responses of deeper neurons to the 'presence or absence' of stimuli rather than their precise location (Humphrey, 1968) is likely to be functionally related to the more precise processing of stimulus position and detail in more superficial laminae (Foreman et al, 1978; Mohler and Wurtz, 1976). At a time when the 'diffuse mass' of the reticular formation is being progressively more subdivided into functional units (Brodal, 1969) it would seem a retrograde step to attempt to include the dorsal midbrain simply because neurons show arousal-related multisensory responses.

In conclusion it is evident that potential exists for a widespread division of function between regions of termination of afferent, and regions of departure of efferent projections, laminal independence, horizontal and vertical interactions and collicular cell populations. A strict "unitary function" hypothesis is likely to be an inadequate model of collicular involvement in behaviour; indeed the SC may "function" differently according to the class (i.e. position, modality, novelty, complexity) of stimulus considered.

1.2.4 Preliminary investigation of tecto-reticular projections in the rat: A combined Fink-Heimer, Horseradish Peroxidase study

1.2.4.1 Introduction

Efferent projections from the SC have been the subject of a number of recent studies in opossum (Weber et al, 1979), cat (Altman and Carpenter, 1961; Kawamura et al, 1974; Graham, 1977; Graybiel, 1977; Kawamura and Hashikawa, 1978; Weber et al, 1979), tree shrew (Harting et al, 1973; Raczkowski et al, 1976; Weber et al, 1979), bushbaby (Raczkowski and Diamond, 1978) and monkey (Harting, 1977). In addition to anterograde degeneration or autoradiographic results, a number of studies have used retrograde axonal transport to identify the precise soma of origin of specific pathways (for example, Kawamura and Hashikawa, 1978; Raczkowski and Diamond, 1978). Most have agreed that anatomically, as electrophysiologically (see above review and Chapter 2), the SC is divisible into two separate zones. Cells in the superficial zone (strata zonale, griseum superficiale and opticum) project mainly rostrally to the posterior thalamus, pretectum and lateral geniculate nucleus ipsilaterally. From the deep zone (comprising all intermediate and deep laminae and pars lateralis of stratum griseum periventriculaire), projections terminate mainly in the intralaminar thalamic nuclei, the mesencephalic reticular formation and dorsolateral pontine nuclei ipsilaterally and in the contralateral SC, pontomedullary reticular formation and cervical spinal cord.

Behavioural studies have provided additional evidence for such a division; for example while lesions predominantly involving superficial laminae in the tree shrew produce pattern discrimination impairments, deeper lesions result in visual tracking deficits and a profound inattentiveness (Casagrande _et al_, 1972). In the rat, superficially placed lesions produce attentional deficits, while deeper lesions give rise to additional hyperactivity (Foreman _et al_, 1978), this perhaps resulting from a disruption of collicular influence upon the reticular formation (Isaac, 1971; Foreman _et al_, 1978). However, despite the frequent use of rats as subjects in studies of collicular morphology (Langer and Lund, 1974; Tokunaga and Otani, 1976) and the behavioural consequences of SC lesions (see Chapter 3), no recent experimental anatomical studies have been devoted to the efferent connections of the rat SC, the only available studies being those of Tasiro(1939) and Papez and Freeman (1930) both employing the Marchi technique.
The aim of the present experiment was to observe the pattern of terminal degeneration in the reticular formation following deep SC lesions in the rat using the Fink-Heimer silver impregnation method, and to attempt to identify the soma of origin of tectoreticular projections using retrograde axonal transport of horseradish peroxidase (HRP).

1.2.4.2 Subjects

Ten male hooded rats of the Lister strain (Olac Ltd) were employed in the degeneration study, and 3 albino Wistar rats (supplied by the University of Bergen, Norway) were employed, all weighing approximately 370 gm at surgery.

1.2.4.3 Surgery and Procedure

The 10 hooded rats received unilateral lesions of SC. Surgery was performed under clean aseptic conditions. Animals were weighed and anaesthetised using Equithesin (Sagatal: May and Baker Ltd), at a dose of 60 mg barbiturate/Kg body weight. The head was shaved, and the rat placed in a Kopf stereotaxic apparatus with the upper incisor bar 5.00 mm above the level of the interaural line. Following a medial incision, the skin was retracted bilaterally and the periosteum retracted as far as the temporal muscles. At an appropriate location on the cranium, a hole was drilled using a hand-held dental burr (to avoid heat generation). The underlying dura was lifted and carefully sectioned using the tip of a hypodermic syringe needle. A radiofrequency electrode diameter 0.5 mm connected to a standard radiofrequency lesionmaker (Radionics, RFG-4) was lowered into the SC to a position 5.0 mm posterior to the bregmoidal suture + or - 1.3 mm lateral to the midline and 3.2 mm below the surface of the brain. A grounded electrode was attached to a haemostat in contact with the cut skin. The temperature of the electrode tip was raised to 52.5°C, maintained for 60 secs. One minute after termination of the lesion current the electrode was carefully withdrawn. The wound was sutured and animals were allowed to recover in a warmed cage with free access to food and water.

After 24hr (n = 3), 48hr (n = 3), 72hr (n = 3) or 96hr (n = 1) postoperatively, the animals were killed with an overdose of barbiturate and intracardially perfused with 50 ml saline followed by 100 ml buffered 10% formal saline. Brains were removed and soaked in 20% sucrose solution.

Sections were taken at 20µ - 30µ throughout the mid- and hind-brain on a standard cryostat and mounted on glycerine-coated slides. Half of the brains were cut in coronal and half in horizontal section. Most of the sections were stained according to the Fink-Heimer silver impregnation technique (Fink and Heimer, 1967; Hjorth-Simonson, 1974). Details of solutions and procedure are given in Appendix 1.

The reticular formation was inspected under high-power microscopy for evidence of degeneration. This consists of small, darkly staining dust-like particles which represent degenerated boutons, and broken, irregular and often swollen strands of debris in the case of degenerated fibres (Fink and Heimer, 1967). In order to map the distribution of degeneration selected sections were stained with cresyl violet and compared with parallel, silver-impregnated sections. Neural structures were identified from atlases of the brainstem constructed by Valverde (1962), Petrovicky (1963) and Sidman et al (1962). Degeneration observed microscopically was plotted on tracings of selected sections magnified using a standard Kodak photographic enlarger. In all figures boutons terminaux and passing fibres are shown as dots and wavy lines respectively, densities representing relative intensities of degeneration.

In a second experiment microinjections of horseradish peroxidase (HRP) were made into the brainstem of 3 albino rats, directed at nucleus reticularis gigantocellularis (ngc). The rat was prepared and placed in the stereotaxic headholder as before but with the surface of the skull in the horizontal plane. Using coordinates for ngc devised by Lynch and Crain (1972), a small-diameter drawn glass micropipette was placed 2.00 mm posterior to the lambdoidal suture, +,or -,0.90 mm lateral to the midline and 8.00 mm below the surface of the brain.

A 30% solution of HRP (type VI Sigma) in distilled water was manually injected over a period of 10 minutes. Total volume injected was approximately 30 - 40 nml. Following completion of the injection the pipette was left in place for 5 minutes and then carefully withdrawn. Following a 24 hr recovery period the animals were sacrificed with a lethal dose of Equithesin and intracardially perfused with a 1% glutoraldehyde solution (Kim and Strick, 1976). The tissue was fixed for 24 hr at 4°C, also in a 1% glutoraldehyde solution. Sections were taken at either 20µ or 30µ on a standard cryostat mounted on clean slides and incubated with a 0.05% solution of D.A.B. in Tris buffer for 30 minutes, followed by reaction with a 0.01% solution of H_2O_2 (see Appendix II). The sections were examined under high power and dark-field microscopy for evidence of labelling consisting of a dark

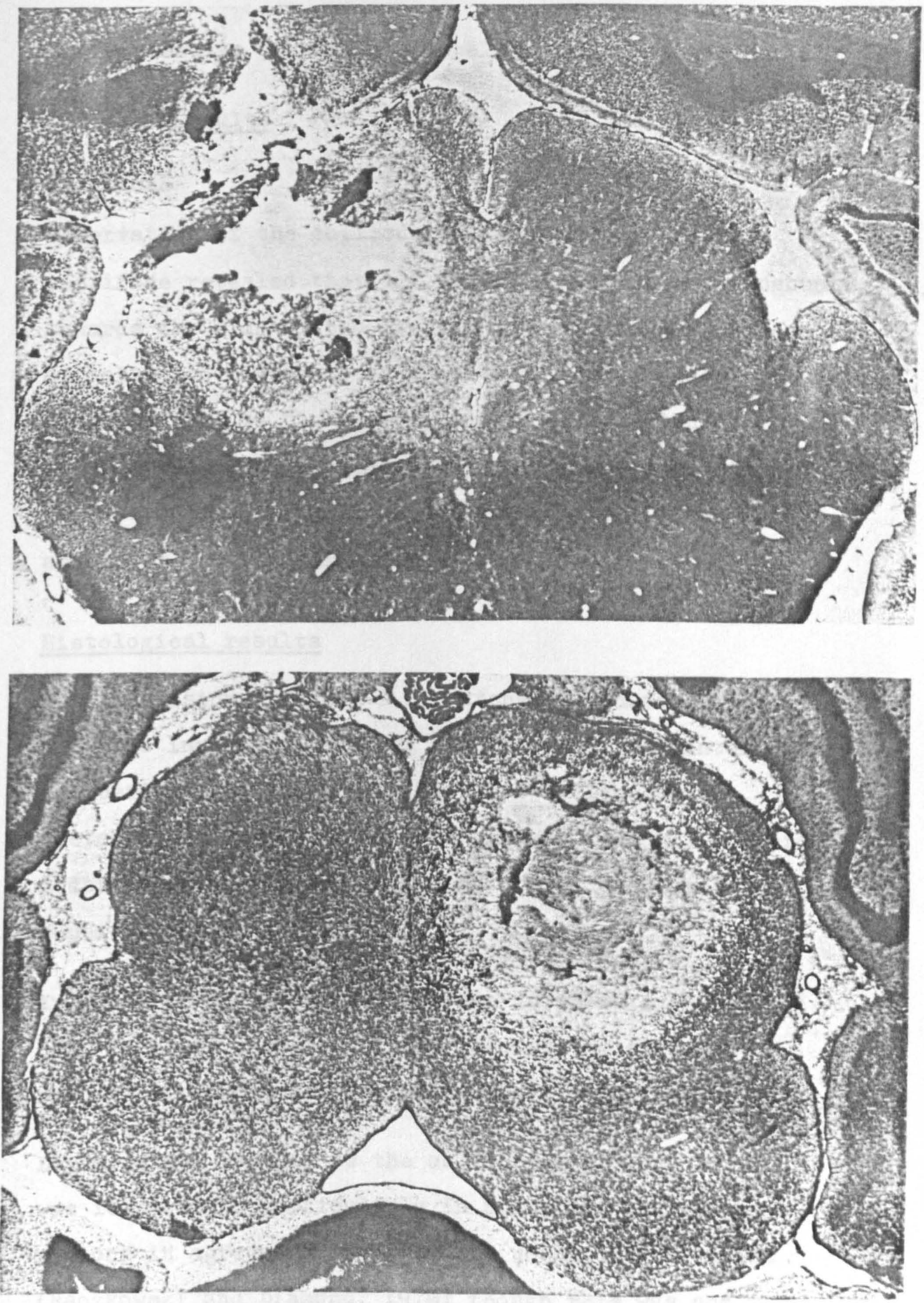


Figure 1.2.
Lesions in rats 3L (above) and 9R, cut in coronal and horizontal planes respectively.

brown granular precipitate localised within the soma.

1.2.4.4 Results

Behaviour

Observation of the collicular-lesioned rats prior to sacrifice revealed that all tended to circle spontaneously towards the side of the lesion. They were clearly less attentive to movements of objects in visual space contralateral to the lesion, and to stimulation of the contralateral vibrissae than to ipsilateral stimulation, in agreement with previous reports (Kirvel, Greenfield and Meyer, 1974; Collin, 1977).

Histological results

Typical lesions (Figure 1.2) extensively damaged the SC but also invaded underlying mesencephalic tegmentum and periventricular grey. Inferior colliculus or pretectum were invaded in some animals, and all sustained moderate damage to subiculum and cortex overlying the superior colliculus.

Evidence of degeneration was seen in animals sacrificed only 24 hours postoperatively, though the clearest results were obtained following 48-72 hours' survival.

Degeneration rostral to the colliculus (Figure 1.4B) was identified, particularly in posterior thalamic regions in agreement with studies using other species (Raczkowski and Diamond, 1978) though this was not pursued in detail. Dense degeneration was predictably seen throughout all remaining ipsilateral collicular

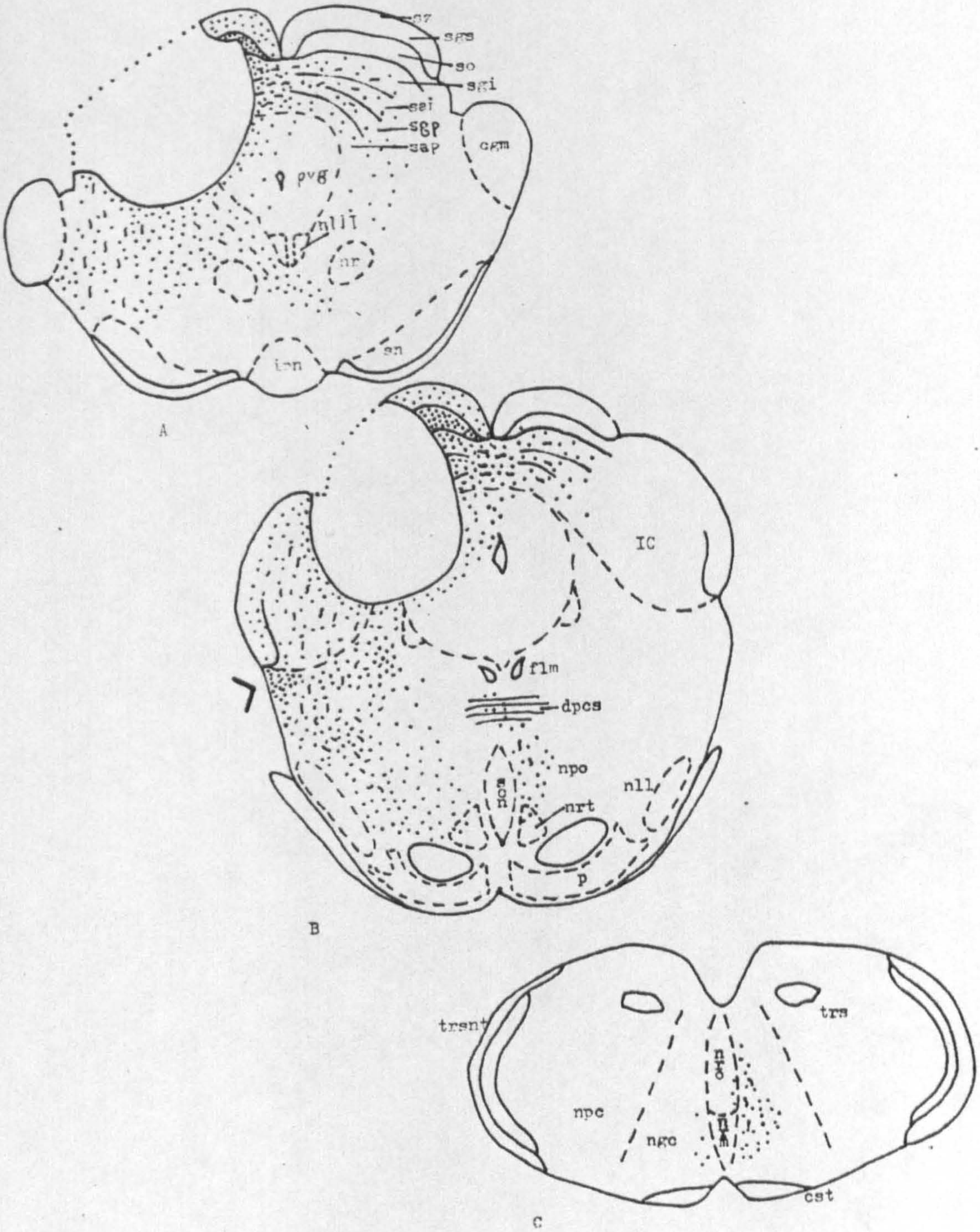


Figure 1.3.
Coronal sections at mesencephalic (A), pontine (B) and medullary (C) levels in rat 3L showing left SC lesion and resulting degenerating fibres (wavy lines) and boutons terminaux (dots). Arrow indicates dense pocket of terminals in the region of the parabigeminal nucleus.

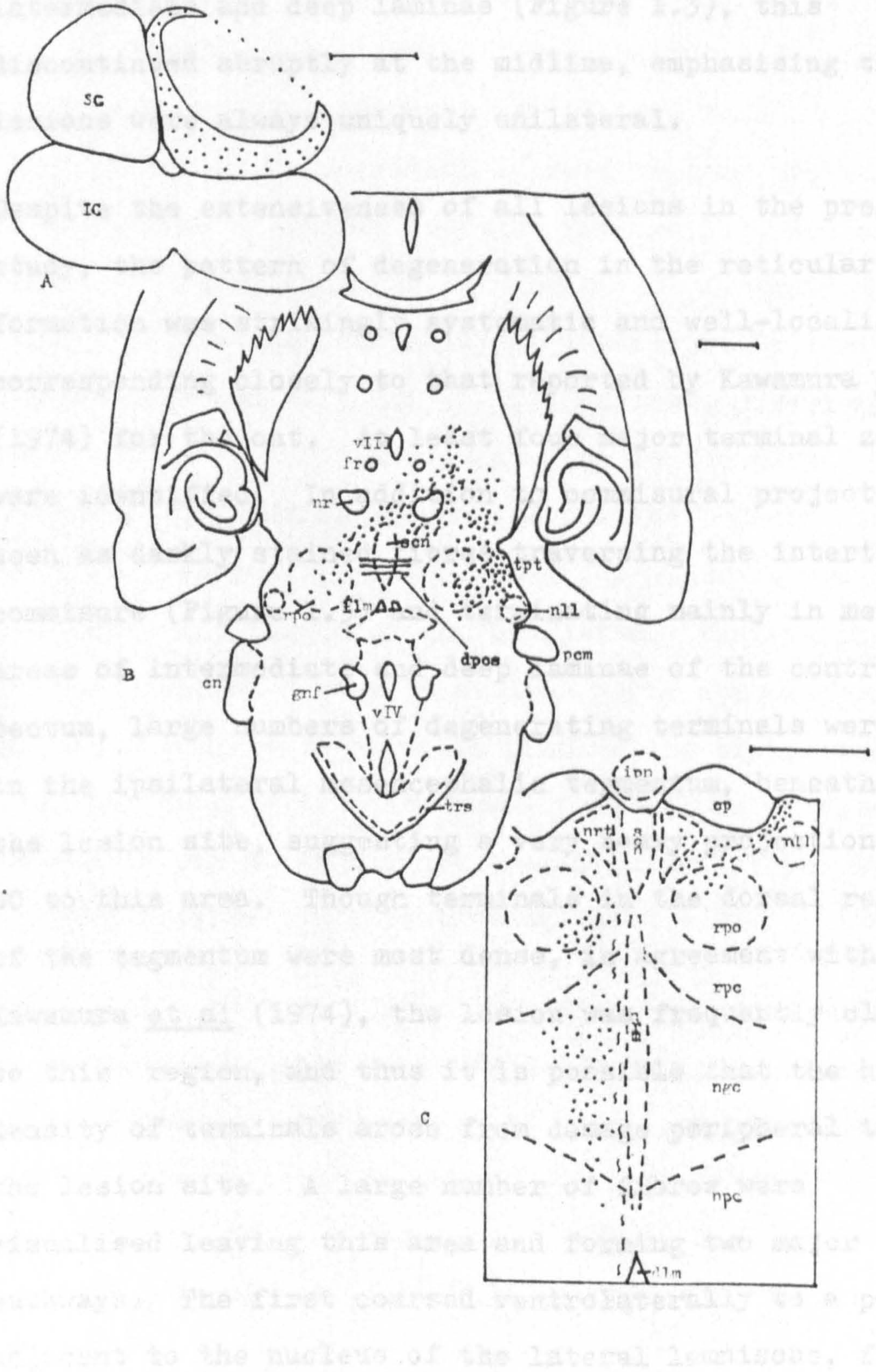


Figure 1.4.
Horizontal sections at the level of the superior colliculus (A), decussation of the superior cerebellar peduncle (B) and interpeduncular nucleus (C) for animal 9R (lesion of R SC). Degeneration as on previous figure. Calibration bars: 1 mm.

tissue due to degenerated intracollicular pathways though except for commissural projections terminating in intermediate and deep laminae (Figure 1.3), this discontinued abruptly at the midline, emphasising that lesions were always uniquely unilateral.

Despite the extensiveness of all lesions in the present study, the pattern of degeneration in the reticular formation was strikingly systematic and well-localised, corresponding closely to that reported by Kawamura et al (1974) for the cat. At least four major terminal zones were identified. In addition to commisural projections seen as darkly stained fibres traversing the intertectal commisure (Figure 1.3) and terminating mainly in medial areas of intermediate and deep laminae of the contralateral tectum, large numbers of degenerating terminals were seen in the ipsilateral mesencephalic tegmentum, beneath the lesion site, suggesting a very heavy projection from SC to this area. Though terminals in the dorsal region of the tegmentum were most dense, in agreement with Kawamura et al (1974), the lesion was frequently close to this region, and thus it is possible that the high density of terminals arose from damage peripheral to the lesion site. A large number of fibres were visualised leaving this area and forming two major pathways. The first coursed ventrolaterally to a position adjacent to the nucleus of the lateral lemniscus, from which it spread out medially to terminate in dorsal pontine nuclei, nucleus reticularis tegmenti pontis and among the more rostral areas of nucleus reticularis pontis oralis (Figures 1.3 and 1.4). Unfortunately the small parabigeminal nucleus, which has been said to receive projections from SC in other species (Harting, 1977; Benevento and Fallon, 1977; Graham, 1977) was not clearly identified. However it is clear that a particularly dense pocket of degeneration appears beneath the inferior colliculus in a lateral position (Figure 1.3) and may represent a projection to this nucleus. A second major pathway passed ventromedially at mesencephalic level, coursing between nIII and the red nucleus, crossing the midline beneath periventricular grey in the dorsal tegmental decussation (predorsal bundle). These fibres could be followed, almost exclusively contralaterally, throughout the length of the brainstem. They follow the most lateral border of nucleus raphé magnus from posterior pontine level, some passing out of the medulla caudally, judging from the small collections of clearly-stained fibres at this level (see Figures 1.3 and 1.4), probably representing the tectospinal tract.

Within the caudal reticular formation, two particular areas contained dense terminal degeneration. These were both coterminous with regions of large and giant-neurons corresponding roughly to nuclei reticularis pontis oralis and medullary nucleus reticularis gigantocellularis (Figures 1.3 and 1.4). Pockets of degenerated boutons were often seen close to the perikarya and proximal dendrites of large and giant neurons as shown (arrowed) in Figure 1.7, in agreement with the results of Kawaumura _et al_ (1974; Figure 1d). Between these two main areas of termination was a fibrous zone containing few large cells and conspicuously few degenerated boutons, though fibres of passage were still present at this level. Throughout the length of the medulla these fibres are found in a medial position, weaving between transverse fibres and the lateral branches of the raphé system.

On the side ipsilateral to the lesion, some degeneration was observed in nucleus pontis oralis, though this terminated abruptly at pontine level as shown in Figure 1.5B. However, a small scatter of degeneration was observed at medullary level in the most ventromedial part of nucleus reticularis gigantocellularis. This was seen in coronal section (Figure 1.3) though such ventral levels of the medulla were not easily investigated on horizontally-cut sections.

As in the cat (Altman and Carpenter, 1961; Kawamura et al, 1974) no terminals were seen in the red nucleus or oculomotor complex (nIII), though fibres pass densely round the borders of each (Figure 1.3A).

Injections of HRP were found to be reasonably well-localised in ngc, extending across the medial two-thirds of the brainstem. Injections appeared to be restricted to one side of the midline. Under light microscopy, labelled cells in the SC contained a reddy brown granular precipitate. This was most clearly seen (as small, reflecting particles) under darkfield microscopy. However, as in previous studies (Weber et al, 1979), few cells were labelled per section; the "brown reaction" used above to demonstrate peroxidase labelling would appear to be a conservative measure of peroxidase transport; indeed the total number of cells unambiguously identified in this study was only nine. Nonetheless, from this small amount of data it was clear that labelling was confined to deep tectal laminae (below so) but was not restricted to any particular lamina. Except for a single labelled neuron, it was detected in the colliculus contralateral to the injection site.

Discussion

The above results are generally consistent with previous reports of tectoreticular projections in a variety of species (Kawamura et al, 1974; Weber et al, 1979). In particular Kawamura et al (1974) reported that tectoreticular projections appeared to terminate in two zones, one at more rostral and one at more caudal levels of the reticular formation, contralateral to the side of the lesion.

It should be noted that from previous studies in other species (Kuypers and Lawrence, 1967; Kawamura et al, 1974) damage to cortex overlying the colliculus is unlikely to produce substantial degeneration in the brainstem. Nonetheless in the cat fibres from visual cortex, auditory cortex and inferior colliculus do terminate in the dorsolateral pons (Kawamura, 1975), a region to which the SC also sends ipsilateral projections (Kawamura et al, 1974). Thus some of the ipsilateral fibres terminating in the dorsolateral pons in the present study

Figure 1.3B, are likely to be of extracollicular origin. However, Petrovicky (1966) investigated degeneration in the reticular formation of rats following more extensive cortical lesions than those sustained by the present animals and concluded that "fibres from the visual and limbic cortex do not end in the reticular formation of the brainstem", though, as Valverde (1962) has shown, projections from frontal cortex do. Valverde reported degeneration in rpo following visual cortical lesions but Petrovicky (1966) argues that this probably arose from encroachment of the lesions upon preoccipital sensorimotor cortex. Thus it is unlikely that degeneration arising from extracollicular lesion damage would be sufficient to distort the present results; though in some animals the inferior colliculus or pretectum was damaged, comparable results were obtained for animals with damage to either structure in combination with collicular lesions.

The appearance of a small amount of ipsilateral degeneration in the ventral medulla (Figure 1.3C) is interesting, since such is not reported by other authors (Kawamura et al, 1974). This may clearly arise from ipsilateral tegmental damage, or from another extracollicular source, though notably Tasiro (1939; see Figure 1.8a, b) showed a minor tectobulbar pathway in this region. Clearly, however, the bulk of tectopontine and tectobulbar reticular projections are restricted to the side contralateral to the lesion. This is especially interesting considering the extent of lesions used in this study which approximates the size routinely used in behavioural experiments (Section 6.2).

As in the present study, sparse labelling of the ipsilateral SC following HRP injections into the brainstem has been observed previously (Greene et al, 1978); this may arise from uptake by the small ipsilateral pathway described above, or, in the present study, may result from unidentified leakage of HRP into the contralateral medulla. More data is required to decide between these alternatives. However, that cells were labelled in deeper laminae of the contralateral SC following brainstem injections is consistent with all previous reports (e.g. Kawaumura and Hashikawa, 1978), though the present results, while sparse, are inconsistent with reports of severely restricted zones of labelling. For example, Raczkowski and Diamond (1978) report that cells in deep tectal laminae (below sgi) are selectively labelled following HRP introduction directly into the predorsal bundle at its point of decussation in the caudal mesencephalon. Similarly, Graham (1977) could find little or no evidence for descending projections from lamina IV in cat. However, subsequent retrograde transport studies have demonstrated substantial projections from lamina IV to the PMRF in cat (Edwards and Henkel, 1978; Kawamura and Hashikawa, 1978) and to the spinal cord in the cat, opossum and tree shrew (Weber et al, 1978). The latter authors noted that cell populations forming the soma of origin of tectospinal tract fibres show significant interspecies variation; in particular that while neurons of a range of diameters project to spinal cord in cat, only the very large neurons do so in opossum and tree shrew. Unfortunately the paucity of data in the present experiment precluded such an analysis.

Species differ in their use of head, eye, trunk and general locomotor movements in the process of exploring and redirecting attention. Thus, as the SC and its projections have been widely implicated in the control of such behaviours (see review Chapter 3), it would seem likely that species variation in the details of descending tectal efferent pathways will be encountered. The extent of such variation and its possible functional significance would seem a fruitful area of enquiry. However, it is clear from the above results that the gross organisation of tectoreticular pathways in the rat is likely to be essentially similar to that in other mammals.

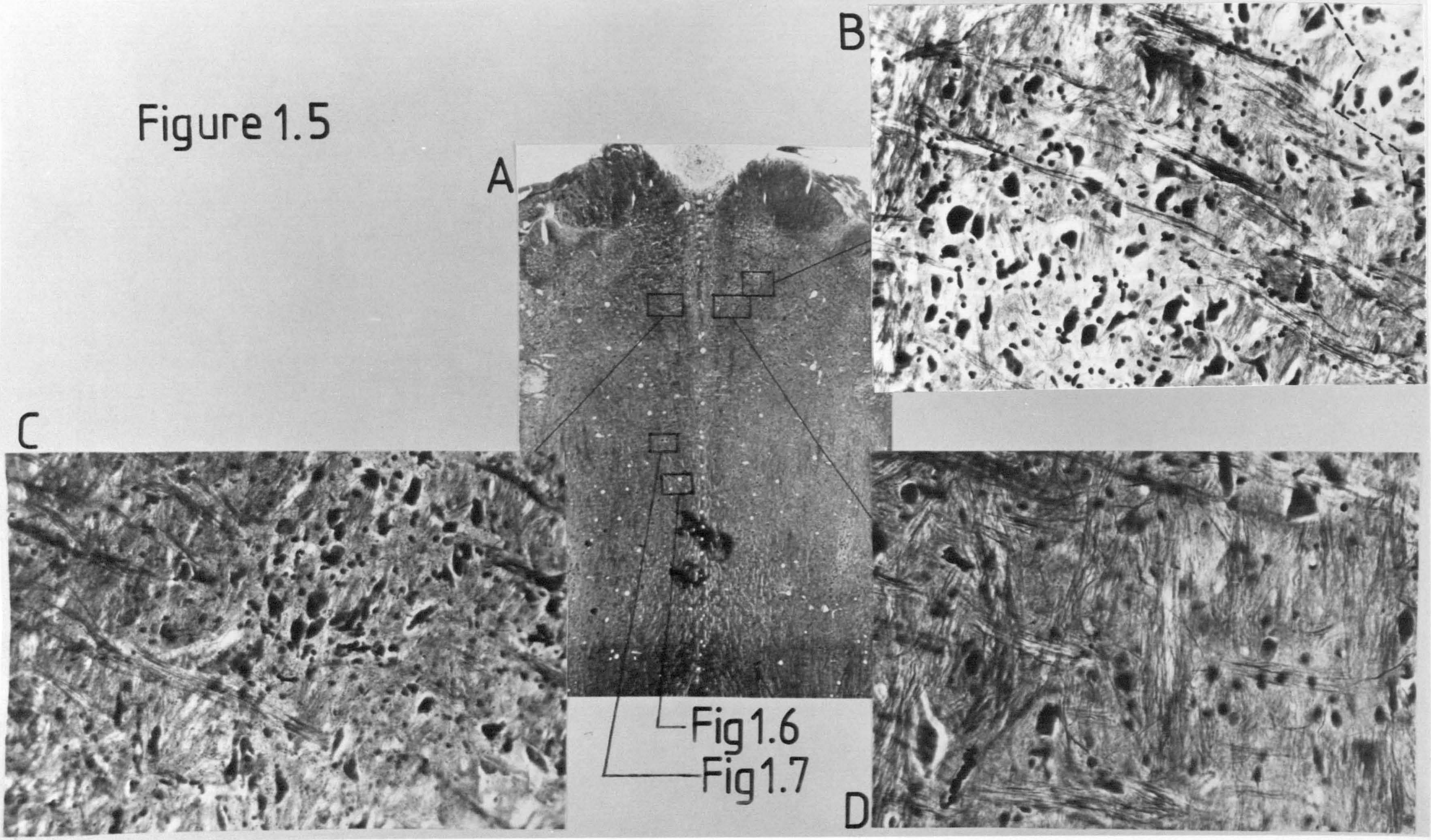
Conclusion

Examination of the pattern of degeneration in the brainstem following unilateral lesions of SC, and the labelling of collicular neurons following HRP injections into the brainstem reticular formation suggested that tectoreticular projections in the rat are essentially similar to those in other mammals.

Figure 1.5

Photomicrographs showing examples of degeneration in the pons and medulla of animal 9R (lesion of R colliculus). Photomicrograph A should be compared with the corresponding reconstruction diagram 1.5C above, and with Figure 149, p.161 in Sidman *et al*, 1962. Degeneration consisting of fine, dust-like granules may be clearly seen in B and C, often in the vicinity of large soma. Degeneration is conspicuously absent in D. The broken line in B (upper right) indicates the medial extent of the ipsilateral terminal field, in ventral nucleus rpo. Rectangles in A show the approximate region within which the corresponding photomicrographs were taken (not to scale). Magnifications: A: x20, B,C: x200, D: x300.

Figure 1.5



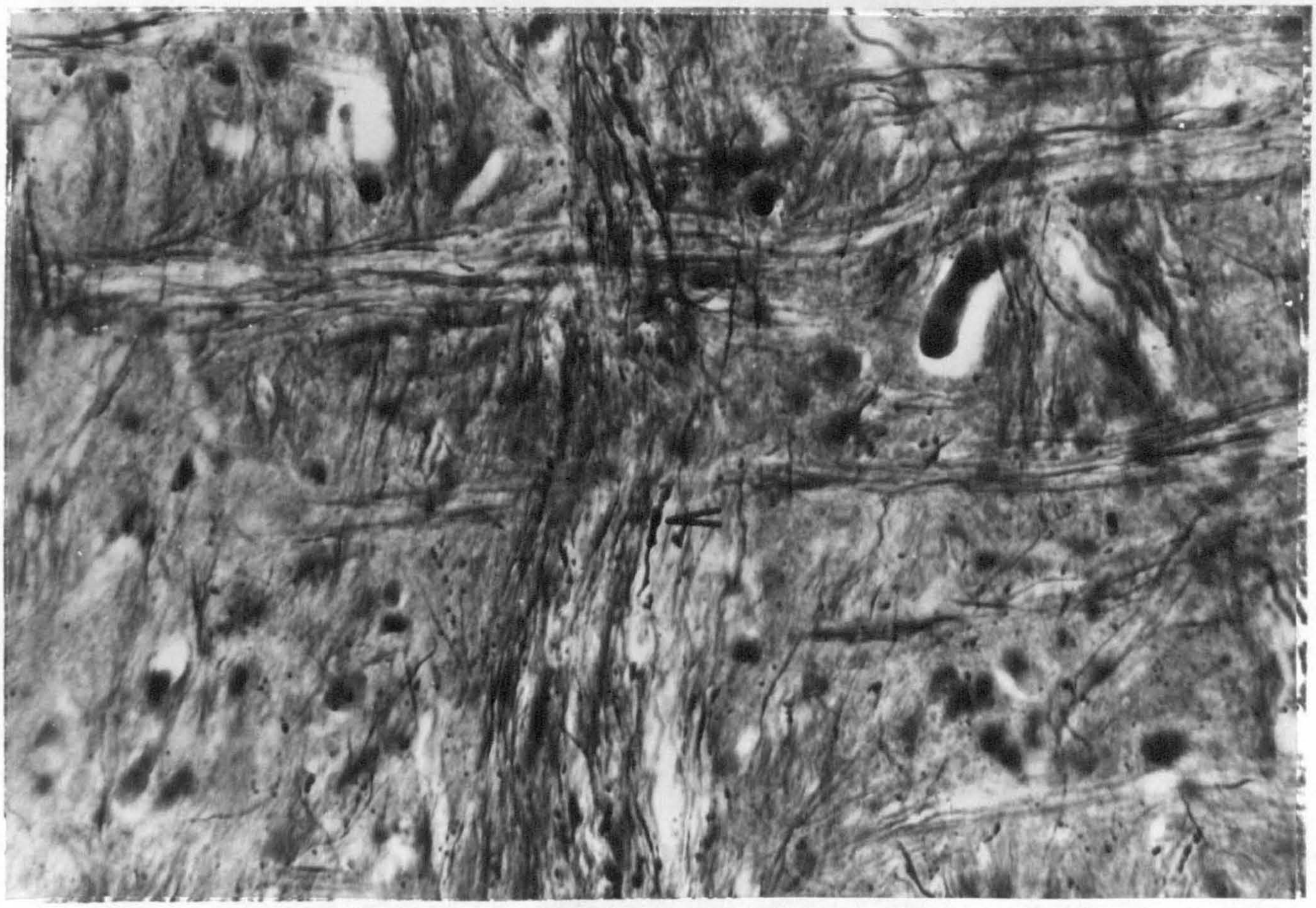


Figure 1.6. Photomicrograph showing degenerating boutons and fibres of passage (arrowed) in the caudal L brainstem (ngc) in the region indicated on Figure 1.5 for animal 9R.

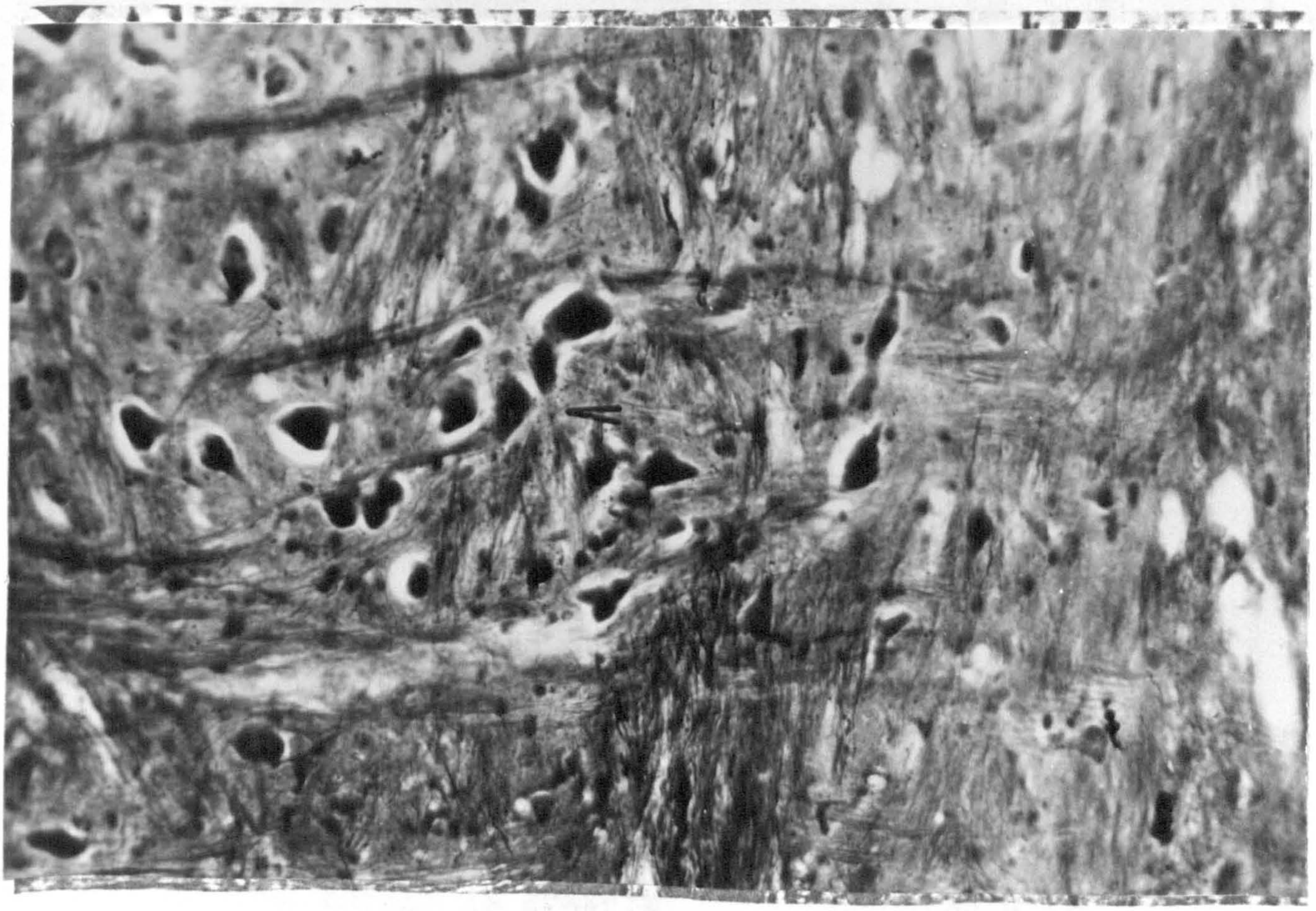


Figure 1.7. Photomicrograph showing degeneration in the L medulla of rat 9R, indicated on Figure 1.5. Degenerated boutons in the vicinity of large soma arrowed.

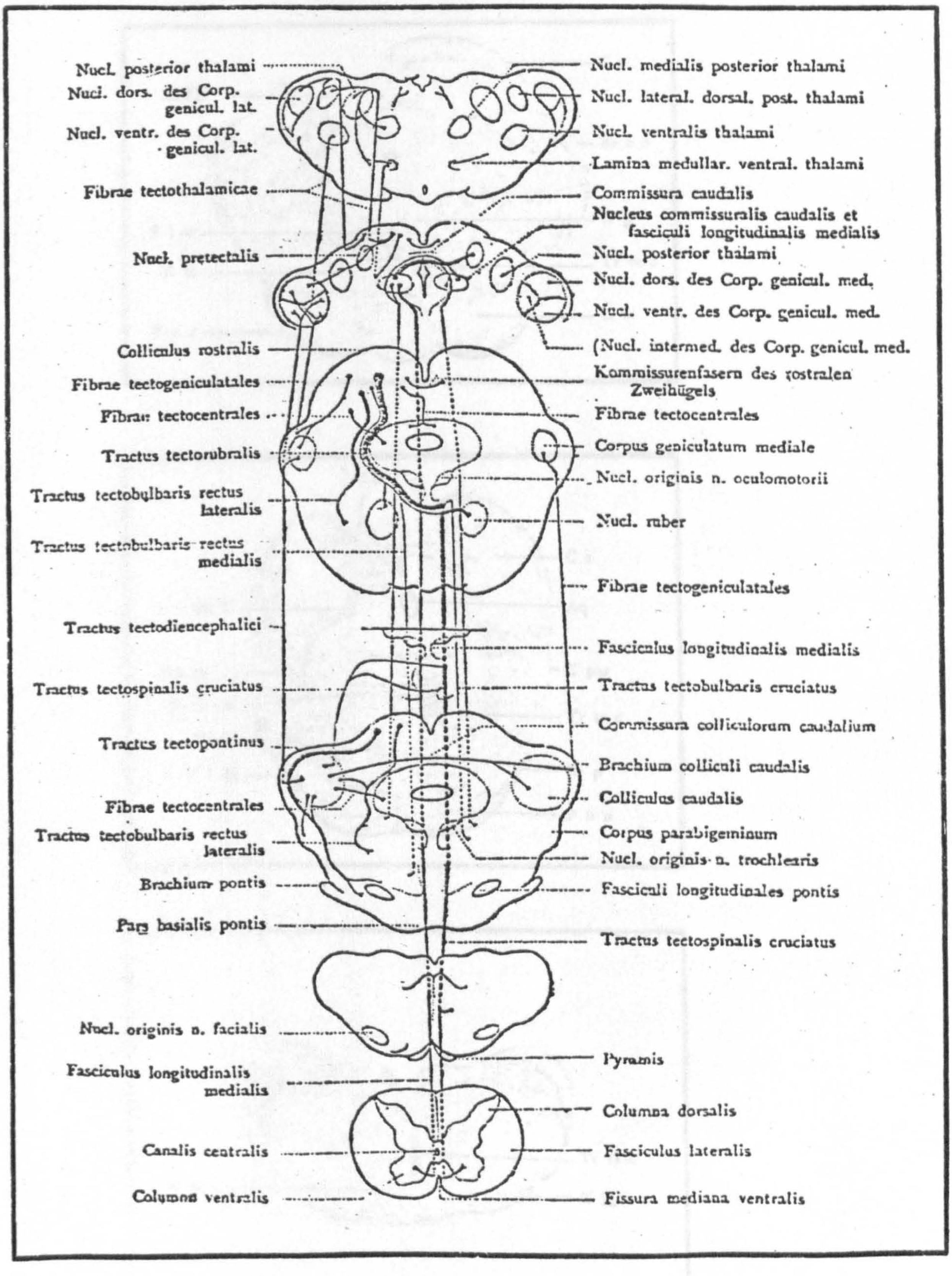


Figure 1.8a.
Summary diagram of mesencephalic and metencephalic pathways involving tectal efferents in the rat, as shown by Tasiro (1939). The author is grateful to Dr.K.Kawamura who kindly procured a copy of this paper which is unavailable in the UK.

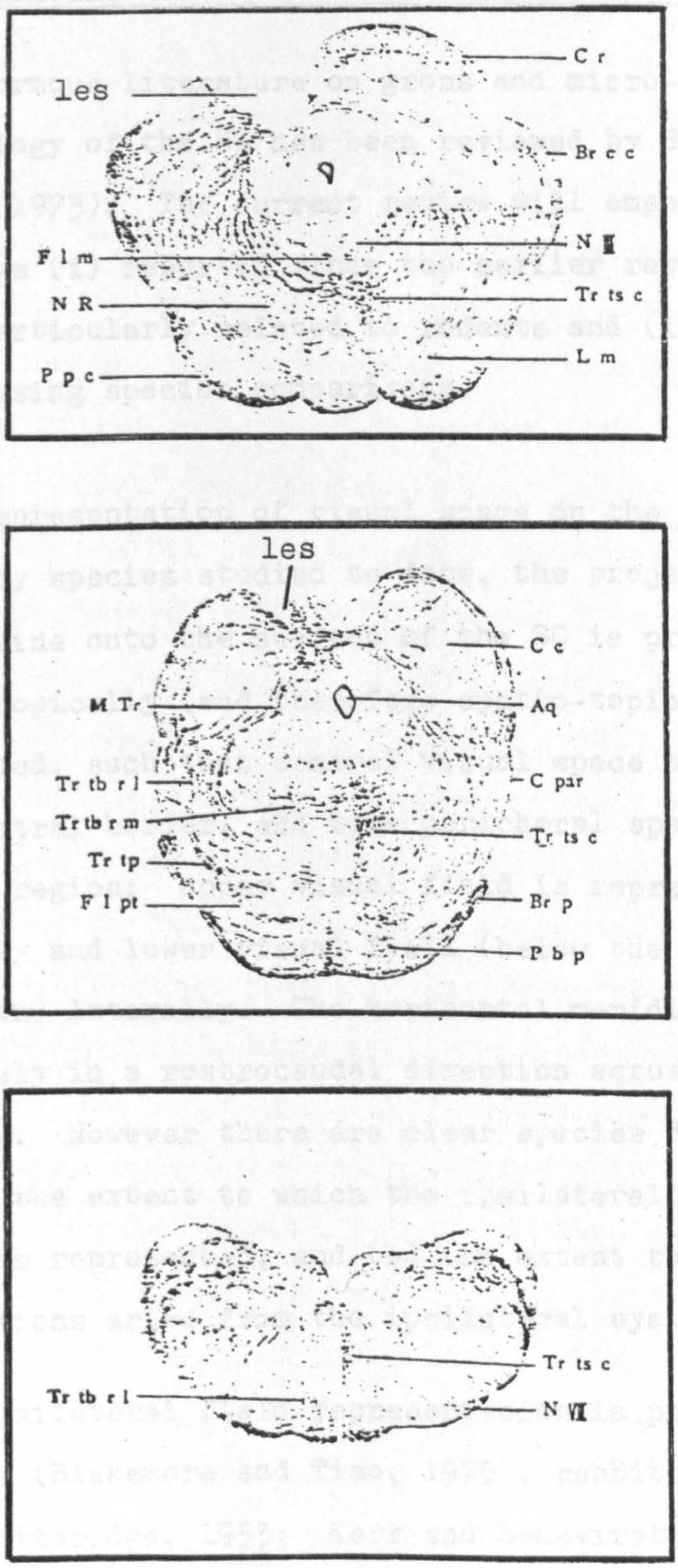


Figure 1.8b.
Degeneration of fibres in the brainstem following lesions of the superior colliculus in the rat, as shown by Tasiro (1939) (See previous figure).

CHAPTER 2

ELECTROPHYSIOLOGICAL STUDIES OF THE SC

The enormous literature on gross and micro-electrophysiology of the SC has been reviewed by Sprague *et al* (1973). The current review will emphasise findings (i) reported since the earlier review, (ii) particularly related to rodents and (iii) emphasising species comparisons.

2.1 Representation of visual space on the SC

In every species studied to date, the projection of the retina onto the surface of the SC is precisely retinotopically (and therefore spatio-topically) organised, such that central visual space occupies the rostral border, and more peripheral space the caudal region; upper visual field is represented medially and lower visual field (below the horizontal meridian) laterally. The horizontal meridian runs obliquely in a rostrocaudal direction across the surface. However there are clear species differences in (a) the extent to which the ipsilateral visual field is represented, and (b) the extent to which projections arise from the ipsilateral eye.

Some ipsilateral field representation is present in hamster (Blakemore and Tiao, 1975), rabbit (Hamdi and Whitteridge, 1953; Kerr and Seneviratne, 1963), tree shrew and grey squirrel (Lane, Allman and Kaas, 1971) but absent in the rat (Forrester and Lal, 1967; Siminoff, Schwassmann and Kruger, 1966). In the cat, a substantial ipsilateral projection has been demonstrated (Lane, Kaas and Allman, 1974) though in the monkey it is limited to a few cells whose receptive fields overlap the vertical meridian (Lane, Allman, Kaas and Miezen, 1973). Despite the presence of uncrossed fibres in a number of rodents and insectivores (rat: Hayhow, Sefton and Webb, 1962; Lund, 1966; tree shrew and ground squirrel: see Lane _et al_, 1971) and the extensive area of binocular overlap (rat: Lashley, 1932; grey squirrel: Lane _et al_, 1971), the SC of rodents receives input exclusively from the contralateral eye, as determined by electrophysiological recordings. However, in the cat (Apter, 1945; Feldon, Feldon and Kruger, 1970; Graybiel, 1975) the ipsilateral eye is well represented. In monkey the ipsilateral projection forms "clumps" of terminals which may correspond to "holes" in the sheet of terminals projecting to the contralateral SC (Hubel, Levay and Wiesel, 1975) The temporal ipsilateral retina and nasal contralateral retina project such that their representations are homonymous, except for the posterior pole region, at least in the cat (Apter, 1945). In this species the contralateral SC is occupied by more peripheral space (maximum 110^o from the vertical meridian) than the ipsilateral (maximum 90^o from the vertical meridian) and where perfect superimposition must break down. The disagreement over the existence of foveal projections to SC has been reviewed earlier (Chapter 1); it would appear that a sparse, though significant projection does exist (Hubel _et al_, 1975; Schiller, Stryker, Cynader and

Berman, 1974).

Interspecies variation is also evident in the extent to which parts of the visuospatial projections are disproportionately magnified, especially on the rostral pole which corresponds to central visual space. Animals with lateralised eyes show modest magnification (mouse: Dräger and Hubel, 1975; grey squirrel: Lane et al, 1974). Siminoff et al (1966) have suggested that retinal specialisation (rather than phyletic status) determines the geometry of reticulo-collicular projections [1]; in the rabbit magnification occurs for the "retinal streak" area of retina - a horizontal band with the densest ganglion cell distribution (Masland, Chow and Stewart, 1971; Kerr and Seneviratne, 1963). Siminoff, Schwassmann and Kruger (1966) and Forrester and Lal (1967) described the rat as having no part of the visual field magnified, though the latter authors noted that the horizontal axis was more generously displayed than the vertical. In cats, the visual field within 10° of the fovea occupies some 20% of the total SC surface (Apter, 1945), while in monkeys the central 10° occupies more than a third (Lane, Altman, Kaas and Miezin, 1973). The retinal area subtending central (midline) vision is invariably represented in rostral SC, even when the area concerned is located temporally on the retina;

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[1] Indeed magnification of part of the retinal projection occurs in fish, amphibians, reptiles and birds(see Dräger and Hubel, 1975, for discussion).

for example in the rat (Forrester and Lal, 1967; Siminoff et al, 1966) the area of retina densest in ganglion cells is located 50° out from the position where the optic nerve exits and just above the horizontal meridian (Lashley, 1932).

The projections of non visual modalities on the SC also conform to the layout of the visuospatial "map", representing contralateral receptor surfaces, and contralateral sensory space. In the mouse, for example, the point on the SC excited by each vibrissa corresponds to the area of (visual) space into which the vibrissa extends (Dräger and Hubel, 1975), and to a lesser extent the same effect is found in the cat (Gordon, 1973). Nonetheless, the generality of such correspondence is emphasised by the finding of Terashima and Goris (1975) that the tectum of the pit viper possesses a topographic map of points in space stimulating the infrared-sensitive pit.

2.2 Response characteristics of single cells

2.2.1 Visual

The optimum stimulus for generating activity in SC neurons is most often a small spot moving across the receptive field. Sprague et al (1973) have noted that mammalian SC neurons are

> "endowed with the property of being relatively insensitive to shifts in the level of diffuse illumination of the retina, and to small-sized patterns of light presented within their receptive fields." 1

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1 Though not an unreasonable generalisation, the need

Unlike visual cortical neurons, few SC neurons (for example only 11% in cat: Straschill and Taghavy, 1967; 12% in rabbit: Masland _et al_, 1971) possess concentric receptive fields with antagonistic centre-surrounds when tested with stationary stimuli. More commonly they have either an 'on' or 'off' area, generally small and circular in superficial laminae (above so) and elliptical or quadrangular in deeper laminae (Sprague _et al_, 1973). They are thus relatively insensitive to the contour or shape of a stimulus (Goldberg and Wurtz, 1972a) though size is important (cat: Sterling and Wickelgren , 1969; rat: Humphrey, 1968), smaller spots of light eliciting the most vigorous activity.

In monkeys, 87% of units sampled by Goldberg and Wurtz (1972a) responded to the onset and offset of stationary spots of light in addition to stimulus movement in any direction. About 80% of the cells encountered possessed receptive fields which included an inhibitory surround; these cells were optimally excited by a small stimulus occupying approximately 1^{o} of visual angle, thus much smaller than the area of their excitatory central receptive

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for caution is immediately evident, in that at least one study(Straschill and Hoffmann, 1969) reports that 75% of neurons in the most superficial V layer (stratum zonale) in cat respond to changes in the level of diffuse retinal illumination.

field.

Field size varies between 2° and 90° in macaques (Sprague *et al*, 1973), though Schiller and Stryker (1972) found cells in 'foveal' colliculus with RFs as small as $\frac{1}{8}^{\circ}$. Visual RF areas are approximately three times larger than those of corresponding units in visual cortex (Goldberg and Robinson, 1978). Interspecies variation in field sizes is also apparent: 6° - 167° in the opossum, 10° - 90° in rabbit, 2° - 15° in superficial SC in rats, but 30° - 90° at deeper penetrations (see Humphrey,1968), and 3° - 70° in cat (comprising two classes, one 6° - 12° and a second 30° - 45° or more). In general, cells in rostral SC have the smallest visual fields (cat: McIlwain and Buser, 1968; Sprague *et al*, 1968; monkey: Cynader and Berman, 1972; Schiller and Stryker, 1972), though in the rabbit RF size increases towards area centralis (Schaefer, 1966). Schaefer (1970) found two main classes of tectal neuron in rabbit, one activated by large spots of light which discharged during optomotor responses (including mystagmatic movements), and a second maximally responsive to small objects moving in front of a stationary background.

Fourteen per cent of units in the squirrel monkey SC show colour-coded responses (Kadoya *et al*,1971b), though in a rodent (ground squirrel: Michael, 1967) colour coding is solely restricted to the geniculostriate system, and is of course absent in the rat.

Directional selectivity is species-variable, though no overall "phylogenetic trend" is evident.
In the rhesus monkey, under a variety of recording conditions (see Goldberg and Robinson, 1978), few cells have been encountered which selectively respond to particular direction(s) of movement (Humphrey, 1968; Cynader and Berman, 1972; Schiller and Koerner, 1971; Schiller and Stryker, 1972). Goldberg and Wurtz (1972a) found only 10% of the units they examined exhibited such selectivity. In that study, most cells responded maximally to small stationary spots of light or small moving stimuli, many having inhibitory surrounds. Even fewer directionally selective cells were found by Updyke (1974) in the cebus monkey (2%), but rather more have been found in squirrel monkeys (Kadoya <u>et al</u>, 1971a).

In the cat, on the other hand, the majority of cells (75%) are directionally selective (Sterling and Wickelgren, 1969; Straschill and Taghavy, 1967), the precision of tuning increasing with depth in the SC (Sprague, Marchiafava and Rizzolatti, 1968). The preferred direction of motion is nasotemporal (Sprague <u>et al</u>, 1968; Sterling and Wickelgren, 1969) which is similar to the rabbit (Schaefer, 1966). Harutiunian-Kozak, Kozak and Dec (1968) suggest that the proportion of cells exhibiting directional selectivity in the cat may vary with degree of light-dark adaptation, whereas Arduini, Corraza and Marzollo (1974) argue that it is related to the arousal level (sleep-wake state) of the animal.

Few directionally selective cells were found in the rat by Humphrey (1968), though many have been found in other rodents (mouse: Dräger and Hubel, 1975; hamster: Rhoades and Chalupa, 1976; ground squirrel: Michael, 1972a,b; rabbit: Schaefer, 1966, 1972; Masland *et al*, 1971). In the mouse, overall preferred direction of motion was upward and nasal while in the hamster the most frequently preferred direction was nasotemporal (Rhoades and Chalupa, 1976), reminiscent of the pigeon (Jassik-Gerschenfeld and Guichard, 1972) and goldfish (Cronley-Dillon, 1964) tecta.

Michael (1972a) and Masland et al (1971) report "hypercomplex"[1] cells in the ground squirrel and rabbit respectively, similar to those in cat visual cortex (Hubel and Wiesel, 1965). Such cells are mainly found in deep laminae. No overall preferred direction was noted. Few directionally selective cells have been identified in opossum (Goodwin and Hill, 1968; Hill and Goodwin, 1968).

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[1] These respond selectively to the movement of specifically orientated bars or edges limited at each end.

Binocular convergence increases in incidence in collicular neurons with the degree of frontal vision. Despite binocular overlapping fields, no convergence occurs on neurons in rat or rabbit SC (see above), though a few units exhibit binocularity in hamster (Blakemore and Tiao, 1975). Twenty per cent of cells are binocular in opossum SC (Goodwin and Hill, 1968), whereas in the cat estimates range from 20% (Straschill and Taghavy, 1967) to 97% (Sterling and Wickelgren, 1969). Virtually all visually receptive units in the SC of rhesus monkeys receive input from both eyes according to Goldberg and Wurtz (1972a), but Marrocco and Li (1977) report only 82% to be binocularly driven. While binocular units in the cat tend to be more excited by the contralateral eye (Sterling and Wickelgren, 1969), such an imbalance does not occur in monkeys (Goldberg and Wurtz, 1972a). Hayaishi, Nagata, Tamaki and Iwama (1973) were able to demonstrate in the cat a number of different types of binocular interaction on single neurons, including facilitation, summation, occlusion, inhibition and disinhibition.

Preferred rate of stimulus movement is extremely variable between species; opossum SC neurons prefer 50° - 180°/sec displacements, cat between 0.5°/sec and 50°/sec; rat and rabbit 5° - 10°/sec (Sprague et al, 1973). Although SC cells in the rat were reported by Humphrey (1968) to discontinue responding when stimulus velocity was in excess of 25°/sec, rabbit cells continue to respond up to 80°/sec according to Masland et al (1971). Speeds of 80° - 800°/ sec were responded to by SC units in monkeys (Goldberg and Wurtz, 1972a), though Marrocco and Li found slow velocities (3° - 38°/sec) to be preferred in deep SC with cells ceasing to respond to movements faster than 70°/sec while in superficial laminae, effective velocities ranged from 45° - 612°/sec (mean: 238°/sec). Movement-sensitive cells generally have antagonistic centre-surrounds, though whether the inhibitory influence of a stimulus upon evoked response to a second stimulus is greater when the two are moving in the same direction (Sterling and Wickelgren, 1969) or not (McIlwain and Buser, 1968) remains unresolved. A possible interesting species difference was noted by Arduini et al (1974) between monkey and cat in that while 80% of movement-related neurons in monkey continued to be active in the dark, only 20% of such neurons in the cat did so (Straschill and Hoffmann, 1970).

A further source of variance in the above data was identified by Mandl (1974) who noticed that in cat, 61% of units changed response characteristics (e.g. directional and velocity preferences) when the retina was stimulated with different patterns or pattern combinations. For example, one cell gave a unidirectional response to a "dark tongue" stimulus, but a bidirectional response to a bright disc (see Mandl, 1974, Figure 3). Thus stimulus configurations which give rise to "apparent" movement illusions in human psychophysical experiments

(Duncker, 1929) also generate "apparent" effects in collicular neurons.

A comment is required at this point on the findings from recordings from the rat SC. The main findings of Humphrey (1968) have been described above. The rat SC is relatively unresponsive to stationary stimuli (except very small ones), the best response being obtained from a small (preferably black) spot moving at about 5^{o}/sec against a light background (though absolute intensity of stimulus seemed more important than figure-ground contrast). Some of these cells were especially responsive when the moving dot came to rest in their receptive field. Black-white straight edges were found to be ineffective. A columnar arrangement in SC was suggested by the finding that vertical electrode penetration encountered cells with RFs in the same region of the visual field; where cells had 'stationary' stimulus fields and 'movement' fields, these were found to be coextensive. Cells located at deeper penetrations were more likely to give after discharges (lasting 2 - 20 secs) than those at superficial levels. These cells could be maintained in a state of constant discharge by moving a stimulus back and forth in the receptive field. Deep cells generally possessed large elliptically shaped receptive fields, with the long axis oriented horizontally in the visual field. "Patchy" receptive fields were frequently seen in wide field neurons, and variability of response with time. Removal of the ipsilateral cortex had no effect upon visual RFs.

It is unfortunate that, for the rat, only a single study is available since in other more widely investigated species, results have shown considerable inter laboratory variation (for example, in terms of binocularity of cat SC neurons for which figures between 20% and 97% have been variously given; see above). Furthermore, Humphrey's (1968) study is limited since all the units examined (168) were said to be located within 1 mm of the surface, and not in deep laminae as erroneously stated by Murison (1977) and Sprague et al (1973). Moreover, there is an element of doubt, from Humphrey's own account, that depth was adequately determined since (i) marker lesions were not clearly identified in histology; (ii) the only remaining gauge to depth is distance travelled vertically following the first encountered evoked activity, resulting from the "waving (of) stimulus sticks in front of the (left) eye". It is clearly possible that such responses may not have been obtained first at the SC surface, and that depth may have been underestimated throughout, as might appear to be the case from Humphrey's report of fast-habituating, wide field cells in sgs, frequently encountered in other rodents in deeper laminae below so (Masland et al, 1971). The results of Humphrey's (1968) study are further questionable since the swiftest movement which provoked activity in monkey SC was reported to be 30^{o}/sec, while recent studies by Goldberg and

Wurtz (1972a) have put the figure at 80° - 800°/sec and Marrocco and Li (1977) report cells in superficial laminae responsive to movements of 45° - 612°/sec (mean 238°/sec). However, the latter authors found slower velocities preferred only in deeper SC (3° - 38°/sec), though some 3 - 6 mm below the area in which Humphrey (1968) claimed to have recorded. Unfortunately -as Humphrey (1968) has remarked- "adequate histology was not undertaken" in this study, and since "the surface of the SC was not distinctly marked by the beginning of visual evoked responses" it would be unwise to draw firm conclusions from it.

2.2.2 Multimodal responses

The earliest work on the electrophysiology of deep SC laminae was carried out in the course of an investigation of visual units in the reticular formation (Horn and Hill, 1966). Using rabbits, they found single units mainly located in laminae below so to have large receptive fields (often representing half of the visual field), responding to a variety of complex stimulus features. These frequently responded to more than one modality, were particularly sensitive to novel stimuli (sometimes showing inter- and intra-modal dishabituation; Horn, 1976, personal communication) also to such stimuli as the human voice and profile, or silhouettes of animals. Habituation would frequently take place rapidly, sometimes following a single stimulus presentation, rendering some cells difficult to investigate (see also Cynader and Berman, 1972). Similar experiments on rabbit (Masland et al, 1971) have shown deeper SC cells to have indistinct, large receptive fields, to respond to non visual stimuli and to habituate rapidly. Dräger and Hubel (1975a, b) described cells in deep laminae of the mouse SC which were driven by somatosensory and auditory stimuli, with visual fields arranged such that they are "in register" with visual projections to more superficial laminae. However rostral SC, containing a "magnified" topographic map of the whisker "receptive fields", has no auditory representation, perhaps suggesting that the localisation of sound is not sufficiently accurate to merit representation in a region of colliculus with fine grain topography.

In the monkey, Marrocco and Li (1977) noted that more ventrally placed deep units had high spontaneous firing rates, were particularly unresponsive to small stationary targets but were extremely excitable by large moving stimuli, habituating to iterative stimuli, and were influenced by the arousal level of the monkey. Cynader and Berman (1972), however, failed to obtain such a relationship between EEG arousal and deep cell responses in the monkey. Their investigation revealed an increase in receptive field size on passing from superficial to intermediate laminae (1^o - 70^o range), while in deeper laminae, receptive fields were "still larger" (p. 193) than in superficial or intermediate laminae. Thirty per cent of neurons in these laminae were described as "novelty" or "newness" detectors, similar to those described by Horn and Hill (1966) in the rabbit, and, as Humphrey (1970) has pointed out, similar to population of neurons in the tectum of the frog (Lettvin, Maturana, McCullogh and Pitts, 1959). "Jerk" detectors (sensitive to sudden and erratic displacements of the stimulus) and "shadow" detectors (sensitive to dark areas entering the visual field, especially if they possess a "tongue" of darkness as a leading edge), were also reported. Many cells were responsive to large dark objects, almost all were binocularly driven, 8% were multimodal and occasionally showed enhanced responses to the simultaneous presentation of auditory and visual stimuli. These same authors reported quite different results from recordings in cat SC; in particular, visual fields were larger (for units in comparable regions of colliculus), rounder in shape, fewer (only 68%) being activated by both eyes, and exhibiting more directional selectivity (67% as against 5% in monkey). A notable absence of receptors responding to "tongues of darkness" and "jerky" stimuli was reported. [1]

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[1] Though see McIlwain (discussion in Schiller, 1972) who does report 'jerk' detectors in the cat.

This represents particularly good evidence for a gross species difference since the experiments on cat and monkey were carried out in precisely the same experimental environment. The authors give a possible explanation for the discrepancy in terms of the difficult environment and habits of the two species. This point will be returned to later.

Similar results to the above were obtained for the monkey by Schiller and Koerner(1971) who described "event detectors" (sensitive to movement and size of stimulus, though not to shape, orientation or direction of movement) and "jerk detectors", located ventral to "event detectors", responding maximally to stimuli moving rapidly across the receptive field and then remaining stationary for a short period before moving rapidly again. Unfortunately it is not clear which laminae these cells are located in.

Other studies in the cat have also reinforced the results of Cynader and Berman (1972). Jassik Gerschenfeld (1965) found 72 out of 82 deeply-located somesthetically responsive cells to have visual receptive fields, and Gordon (1973) showed that 80% of visual units had acoustic and somatosensory fields, these being located paricularly in lateral SC. Both Altman and Malis (1962) and Palmer and Rosenquist (1975) report that deep SC cells respond to auditory and tactile stimuli in addition to visual. Visual responses from deep cells are less consistent than from superficial laminae; they are retinotopically organised such that visual topography coincides with that of other modalities, though non visual receptive fields tend to be larger. Straschill and Hoffmann (1969) obtained similar results, and in addition showed that most deep neurons are directionally selective, quick adapting, responsive to stimulation of either eye and activated by tactile and acoustic stimuli.

The observation by Horn and Hill (1966) that rabbit SC cells would sometimes respond to stimuli of high complexity such as silhouettes of animals, a human voice, hand, or body profile is reinforced by studies in rabbit (Schaefer, 1970, 1972) and monkey (Buchtal, Camarda and Rizzolatti, 1976). Schaefer noted that often biologically meaningful stimuli such as the experimenter's hand or body proved to be more effective in stimulating a response than movements of a uniform pattern such as a striped drum or continuously moving light spot. Buchtal et al (1976) obtained responses from cells in intermediate SC laminae in the monkey to "approaching" stimuli, 3-D stimuli and monkeys' paws and faces, reminiscent of inferotemporal cortex unit responses reported by Gross, Rocha-Miranda and Bender, (1971).

Projections of retinal ganglion cells

The three classes of ganglion cell in the retina:

W, X, Y (see Stone and Fukuda, 1974) have differential projections to the midbrain and geniculostriate visual systems. In the cat, X cells have slow conduction velocities (20 - 25 m/sec), linearly summate excitation over the receptive field area and give a sustained response to stationary stimuli. They prefer low stimulus velocities, have small receptive fields and are located mainly in central retina. Projections from X cells distribute to forebrain, many terminating in lgn_d, thence probably to simple cells in VC. A few may project to the midbrain, though none to SC (Fukuda and Stone, 1974). Y-type cells, in contrast, have wide receptive fields which lack directional selectivity, they have fast axonal conduction velocities (35 - 45 m/sec) and exhibit non linear summation across the receptive field. They respond to a wide range of stimulus velocities and have a relatively low maintained discharge rate which increases abruptly and transiently in response to high spatial frequency stimulation. Many project to lgn_d as well as the SC (Cleland et al, 1971; Hoffmann et al, 1972; Fukuda and Stone, 1974), though the latter projection comprises two pathways, one 'direct' (possibly via branching collaterals of geniculate fibres; Fukuda and Stone, 1974) and the other 'indirect' via connections with Y cells in the lgn_d and complex cells in cortex (Hoffmann, 1973). These are found in more peripheral retinal locations, and their receptive field size increases linearly with eccentricity (Stone and Fukuda, 1974).

The third group, W cells, lack an antagonistic centre-surround organisation typical of other groups, and may respond to stimulation with a tonic or phasic discharge. They have slow conduction velocities (3 - 15 m/sec); some are directionally selective and have receptive fields similar in size to those of Y cells, located in central visual field. Some W cells probably project to lgn_d, though the bulk terminate in SC (Hoffmann, 1973; Fukuda and Stone, 1974). Similar cell types have been observed in the lgn of rat, tree shrew and monkey (Fukuda and Sugitani, 1974; Sherman _et al_, 1976; Dreher _et al_, 1976). The cat SC receives input consisting of 73% W cell axons, 9% Y direct, and 18% Y indirect axons (Hoffmann and Sherman, 1974). The sharp division between X (lgn) and W (SC) projections is suggestive of a "two visual systems" dichotomy (see Chapters 1 and 3). Measurement of conduction velocities of inputs to SC in cat has revealed that nearly all pandirectional cells are driven by Y axons, while 60% of directionally selective cells receive W axon input (Hoffmann, 1973; Marrocco and Li, 1977). It is possible that, in view of the distribution of effective stimulus velocities in monkey SC (Marrocco and Li, 1977) and the increased tuning specificity of directionally selective cells with depth in SC in the cat, (Sprague _et al_, 1968) that W cells project mainly to deep SC while Y cells terminate predominantly in superficial laminae (see Marrocco and Li, 1977). This point will be returned to later.

2.2.3 Extraretinal influences

In view of the fact that visual cortical cells in layer V projecting to SC have been found to be directionally sensitive complex and hypercomplex types (Palmer and Rosenquist, 1975), there is a likelihood that directional selectivity and other receptive field characteristics of SC neurons may be "conferred" by afference from cortex. This has been examined in studies in which recordings were made from single units in SC following ablation or cooling of VC. For instance, Wickelgren and Sterling (1969) reported dramatic effects in the cat; one month after large visual cortex ablations, directional selectivity in superficial SC laminae was absent and units exhibited pandirectionality. The neurons were almost exclusively driven by the contralateral eye (clearly suggesting that, at least, ipsilateral retinal input to binocular units is conveyed via VC), and they now possessed "simpler" response characteristics, responding more vigorously to stationary lights turned on and off within their RF than prior to VC removal. Berman and Cynader (1972) reported similar findings in siamese cats, despite their aberrant visual cortical projections and lack of binocular cells in VC (Hubel and Wiesel, 1971). Rosenquist and Palmer (1971) showed that the effect is apparently exclusively due to the removal of area 17; they, however, failed to demonstrate the postoperative hyper-responsiveness to stationary stimuli. These changes are permanent, and demonstrate at least a year after the cortical ablation. However acute cooling or ablation of VC (in cat) does not appear to affect SC unit responses (Marchiafava and Pepeu, 1966), though the general level of activity is reduced (Wickelgren and Sterling, 1969; Stein and Arigbede, 1972). However, Jassik-Gerschenfeld (1965) and Jassik Gerschenfeld, Ascher and Guevera (1966) reported that long latency responses in somesthetically sensitive neurons (presumably mediated by an indirect, retino-cortico-tectal pathway) was immediately abolished on VC removal; on the other hand, stimulation of the cortex with strychnine enhanced both the long latency non visual responses and visual evoked responses in SC. Hoffmann and Straschill (1971) and Rizzolatti, Tradardi and Camarda (1973) report no changes in SC unit responses following chronic cortical removal in the cat, though in the former case cortical sparing may be responsible and in the latter case, the time interval between cortical removal and unit recording (5 days) was possibly too short to have been effective; Murison (1977) has pointed out that the dorso-lateral geniculate nucleus may have to be fully degenerated before cortico-tectal ablation effects become evident.

In awake, non paralysed cats, Richard, Thiery and Buser (1973) found a reduction in visual responsiveness of SC cells following cooling of areas 17, 18 and 19, though in only half of the cells studied, but also a selective loss of visual responsiveness in two multimodal cells in deep laminae.

Schiller et al (1974) found unresponsive patches within the usual receptive fields of cells in so and sgs in monkeys following VC removal, though binocularity, in contrast to the cat, was unchanged. The effect on directional selectivity has not been investigated, since so few collicular cells in the (rhesus) monkey exhibit this property. However, cortical cooling has been shown to abolish visual responses of cells in intermediate laminae, though these continued to discharge before eye movements in the absence of a receptive field (Schiller et al, 1974). The sparse nature of direct foveal input to SC (Hubel et al, 1975) might suggest that foveal receptive fields would be especially dependent upon cortex, yet this is not so (Schiller et al, 1974).

In rodents, the results of cortical depression have been found to be variable. For instance, Michael (1970) found that VC removal in the ground squirrel had no effect upon directional selectivity of cells in superficial laminae, accompanied by an absence of visual driving of cells in deeper laminae which are "hypercomplex" in characteristics in the intact animal. Masland et al (1971) and Stewart, Birt and Towns (1973) in chronically-lesioned, and Horn and Hill (1966) in acutely-lesioned rabbits found VC absence to have no consequences for SC unit responses. Similar findings have been reported for the rat (Humphrey, 1968; Weiss and Fifkova, 1961), though the directional selectivity parameter is uninvestigable in the rat due to the paucity

of units exhibiting this property. Rhoades and Chalupa (1977) found that removal of VC in hamsters reduces directional selectivity in SC neurons, though largely in superficial laminae in contrast to the results of Michael (1967) in ground squirrel. Subsequently (Chalupa and Rhoades, 1978) they showed that VC removal in infancy has an influence on both superficial and deeper laminal directional selectivity. Stroboscopic rearing conditions were found to exert the same effect upon SC responses as does cortical removal. Thus, the maturation of the corticotectal pathway has been suggested as responsible for the development of binocularity, directional selectivity and the corresponding reduction, with development, of hyper-responsiveness to stationary stimuli (Stein, Labos and Kruger, 1973; Norton, 1974), perhaps representing a stage prior to the development of the cortico-tectal Y-cell pathway; the remaining pandirectionality of SC neurons following adult decortication is suggestive of an intact W-input system in the absence of a superimposed Y system.
A further likely function of the visualcortico-tectal pathway is to enable the visual cortex to gain access to the oculomotor system, since Schiller (1977) and Schiller and Koerner (1971) in monkey, and Spiegel and Scala (1937) in the cat, have shown that ablation of the SC abolishes saccades elicited by stimulation of visual cortex, though not those elicited by frontal cortical stimulation. Vestibular influences on SC unit responses have also been demonstrated by Bisti, Maffei

and Piccolino (1974) who showed that 46/96 directionally sensitive units in superficial laminae systematically altered their VERs with degree of body tilt, though Rieger and Straschill (1973) have disputed this finding.

Cells responding prior to eye movements

Straschill and Hoffmann (1970) reported some SC units to be excited or suppressed by eye movements in the cat and Arduini, Corraza and Marzollo (1974) report activity in SC neurons in cat preceeding eye movements by up to 100 msecs. Schiller and colleagues (Schiller, 1972; Schiller and Stryker, 1972; Schiller and Koerner, 1971), using a monkey prepared with one eye immobilised and the other free to move, thereby enabling the simultaneous recording of visual fields and eye movements, have described SC cells discharging prior to saccades of specific size and direction, and generally independent of the position of the eye in the orbit. Wurtz and Goldberg (1972a) found that half of the cells they sampled in monkey so and sgs discharged prior to saccades whether in the light or dark, thus potentially less related to sensory input and more closely related to the oculomotor system than cells in more superficial laminae. These are likely to be cells with large soma, which are highly susceptible to anaesthesia, and which are therefore best studied in the awake animal (Straschill and Hoffmann, 1970 ; Gordon, 1972). Discharge typically begins 30 - 300 msecs (often 70 - 100 msecs) prior to first evidence of activity in the EOG, thus preceeding extraocular muscle activation by at least 10 and up to 280 msecs. Such a cell has a visual field in the same area of space as its "movement field" (ie the same region of space into which saccades are made when preceeded by activity in that cell), though the two are not coterminous. Some neurons (50%) exhibited suppression of activity [1] before or during an eye movement; these were located in deeper laminae (sgp) and were without receptive fields. Mohler and Wurtz (1976) have since identified a further type of neuron, located between "visual" and "motor" laminae which increases its discharge before saccades to visual stimuli (but not in darkness), regardless of the stimulus evoking them,perhaps reflecting the monkey's "readiness" to make an eye movement. The implications of these findings will be discussed in a later section.

Behavioural enhancement

The receptive fields of cells in superficial SC of the monkey (Goldberg and Wurtz, 1972a) have been described above. These were mapped by presenting

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[1] Reminiscent of some units in paramedian pontomedullary reticular formation reported by Luschei and Fuchs (1972) and Sparks and Travis (1971) and referred to as "pause" neurons.

'field' stimuli at various points in the animal's visual field, in monkeys which had been carefully trained to maintain fixation on a spot of light directly ahead. In a variant on this task, the fixation light was turned off and the animal was then required to fixate the field stimulus.
Thus in the first situation, the field stimulus was irrelevent while in the second it became a target for a saccade. Fifty per cent of pandirectional cells which discharged in the 1st situation were found to exhibit enhancement of their discharge in the 2nd situation; either it became brisker in response to stimulus onset (ie the "early" response) or more persistent, continuing until the start of the saccade (the "late" response). The possibility of enhanced discharge arising from a general arousal effect was investigated by presenting two field stimuli, one of which was located in the cell's receptive field. Some evidence of enhancement was obtained when the stimulus chosen for fixation was outside the cell's receptive field (Goldberg and Wurtz, 1972b, Figure 5B), though much less than when the stimulus lay within it. In four out of ten cells investigated receptive field size was increased (by about 10^{o}) in the saccade condition. Wurtz and Mohler (1976a) found that when a manual response was made in the absence of an eye movement, no such enhancement occurred. Robinson and Jarvis (1974) reported unit discharges in SC of the monkey to be much better correlated with eye movement

than with head movement; these results do suggest that the effect is particularly related to the movement of the eyes. Wurtz argues that the phenomenon of enhancement represents "a neurophysiological event related to the psychological phenomenon of attention". Thus, in addition to registering the physical parameters of a stimulus, an animal must "decide" to make an eye movement, should that stimulus merit further scrutiny. The "decision" to orient (and thus the attentional shift) is presumed to take place elsewhere in the brain: efferents to deeper SC are then likely to "enhance" activity in eye-movement related cells, producing a facilitation of eye movements to the general area of visual space in which the attractive stimulus has appeared. (This system is unlikely to direct eye movements to a specific point in space, since visual receptive fields of neurons in sgi are large). The model described a way in which "central input to the visual system ... is involved in selecting out those stimuli which the animal uses for behaviour from those which it does not use" (Goldberg and Wurtz, 1972b). Enhancement is not a universal feature of visual structures, since it is conspicuously absent in striate cortex, though 40% of cells in the frontal eye fields show enhancement similar to that in SC (Wurtz and Mohler, 1976b). This model of SC function will be returned to later (Chapter 3).

2.3 Stimulation studies

For over a hundred years, high frequency stimulation of the SC has been known to produce contraversive eye movements (Adamük, 1870), the effect being reliably obtained from a number of species (e.g. Hess, Bürgi and Bucher, 1946; Akert, 1949; Robinson, 1972). Hess was led to propose that the colliculus mediates the 'visual grasp reflex' (visuelle greifreflex), more recently renamed 'foveation' (Schiller and Koerner, 1971). Thus stimulation studies have formed the basis of the traditional view of the colliculus as an optomotor reflex centre. Apter (1946) applied strychnine sulphate crystals (which generate localised excitation of a small area of tissue) to specific points on the cat SC and noted that when a light (hand torch) was shone into the cat's face, the eyes would move to the point in space corresponding to the position of the crystal on the visuo-spatial "map" on the tectal surface (as mapped in an earlier study; Apter, 1945). Using a number of strychnine applications (0.5 mm apart), Apter was able to construct a "motor map" for the colliculus which was in accurate correspondence with the visual "map" on the collicular surface. Upward movements of the eyes thus resulted from stimulation of medial SC while lateral SC stimulation produced downward eye movements. Akert (1949) working with fish (trout) demonstrated that tectal stimulation produced coordinated orienting movements of the fish's body. These findings, taken together, suggest that the tectum/colliculus carries out similar functions in animals widely differing in orientation musculature and mechanics (Foreman, 1976).

More sophisticated studies have recently been carried out on monkeys and cats with surprisingly varied results. Robinson (1972) found SC stimulation in the monkey to produce contraversive, conjugate saccades, size and direction of movements being relatively independent of stimulus parameters (i.e. an all-or-none phenomenon) and initial eye position, though a slight tendency for saccadic amplitude to decrease with repeated stimulation was noted, suggesting either a minimal dependence of saccadic amplitude upon initial eye position, or that a purely mechanical factor intervenes once the eyes are in the 'evoked' position. Threshold of evocation decreased from about 800μA near the surface to 200μA in sgi and further to 20μA in sgp. However in the encephale isolé cat, Hyde and Eliasson (1957), Straschill (1972) and Straschill and Rieger (1973 [1]) have reported stimulation of SC to produce "goal directed" saccades, i.e. to a particular point in space, the amplitude and direction of the saccade thus depending upon the initial position of the eye in the orbit. Robinson (1972) argued that the methods used by Hyde and Eliasson (1957) may have given a

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[1] These authors also report that amplitude speed and latency of evoked eye movements to be strongly dependent upon strength of stimulating current.

misleading impression, since their photographic recording may have made a "saccadic staircase" of successive eye position-independent saccades appear to be a smooth movement to a 'goal' (this representing the mechanical limit of deflection of the eyes). Interestingly, Apter (1945) had anecdotally mentioned that repeated turning on and off of the stimulus light evoked repeated eye movements (even when in the 'evoked' position). The results of Straschill (1972) and Straschill and Rieger (1973) are contradicted by those of Schiller (1972) and Stein, Goldberg and Clamann (1976) in cat, and Wurtz and Goldberg (1972) and Stryker and Schiller (1975) in monkey. However, Roucoux and Crommelinck (1976) have shown, in cat, that goal-directed saccades result from stimulation of caudal SC while more rostral stimulation gives rise to eye-position-independent saccades. Robinson D (1972) notes that the presence of visual and auditory receptive fields in deeper SC neurons is relevant to the issue, since the latter are presumably coded in a head-centred coordinate system; thus either visual or auditory signals must undergo a coordinate transformation before they converge upon a single neuron. Interestingly, in this respect, Goldberg and Wurtz (1972a) noted that a few neurons in deep SC appeared to modify their response according to the position of the head and eyes, though the authors did not investigate them in detail. However it is possible that precise depth of stimulation in conjunction with, for example, strength of stimulating current (Robinson, 1972) might give varied results. The fact that Roucoux and Crommelinck (1976) reported maximum velocity of evoked saccades to be greater than that of spontaneous saccades while Straschill and Rieger (1973) report them to be equal suggests considerable interlaboratory variation on other measures also. Stryker and Schiller (1975) and Straschill and Rieger (1973) have indicated a possible species difference which may be important; they argue that in species whose ocular motility is extremely restricted (e.g. the owl which uses a maximum of 1.5° eye movement), head movements may be directly coded by the SC, representing a primary mode of orientation to eccentric positions in the visual field, though less so in the cat which uses (up to) 20° eye movements either side of the midline. The problems of coordinating eye movement, head turn and compensatory centering of the eyes (Bizzi and Schiller, 1970) become even less acute in animals willing to maintain an eccentric position of the eye in the orbit (monkey: Bizzi _et al_, 1972; see Stryker and Schiller, 1975). Roucoux and Crommelinck (1976) argue that the goal-directedness which they obtained in caudal SC may reflect the activity of an eye-head coordination system which is unnecessary in rostral SC (where they found eye movements to depend only upon the position of the stimulating electrode) since in the corresponding region of visual space, stimuli fall within a range of eye movement not requiring additional head orientation[1]. Hopf, Heller and Schaefer (1969) and Schaefer (1970) stimulated the SC of freely-moving decorticate cats. In addition to

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[1] See also Guitton, Roucoux and Crommelinck (1977) and Harris (1980).

contraversive movements of the head and eyes on ipsilateral stimulation, they report that stimulation of the two colliculi simultaneously (or stimulation of 2 points in one colliculus) produced synergistic and antagonistic effects which summate to produce the final eye movement, in agreement with Robinson (1972) for rhesus monkey. Defensive or attack behaviour was also elicited, depending upon the strength of stimulating current. In this and other studies, nystagmatic movements have been reported (Straschill and Rieger, 1973) especially when the electrode is in the vicinity of s.griseum centralis (Syka and Radil-Weis, 1971) and if vestibular influences on the colliculus have been interrupted (Bergman, Costin, Gutman and Chaimovitz, 1964). Half of the stimulation sites in the Syka and Radil-Weis (1971) study produced pinna responses shown elsewhere (Clamann and Stein, 1979) to parallel eye movements produced by stimulation of the same point on the tectum. Schaefer (1975) observed that whereas in the cat, stimulation of rostral SC produced forward turning of both ears, stimulation of midcolliculus only caused a forward turning of the ipsilateral ear and stimulation of posterior colliculus generated backward turning of the contralateral ear, whereas in the rabbit, pinna responses were less "forwardly" directed with rostral stimulation only producing forward turning of the contralateral ear and caudal stimulation resulting in backward turning of this ear. This finding may be significant, since in other respects, central visual field in the rabbit is less emphasised than in other species (for example in terms of SC visual receptive fields: see above), and furthermore that orientation to stimuli in the rabbit often involves moving the centre of one eye towards a stimulus rather than turning the binocular field towards it (Schaefer, 1970). Nystagmatic movements of the ear were also recorded, coupled to the nystagmatic movements of the eyes (Schaefer, 1970, 1975).

Electrophysiology: Functional considerations

The two most striking aspects of collicular electrophysiology are, apparently, somewhat contradictory. First, the structure possesses certain characteristics which are reliably present from amphibian to primate: (i) the mapping of visual space on the SC surface in a standard retinotopic fashion, irrespective of the animal's retinal organisation and ganglion cell distribution, with central sensory space occupying the rostral pole, i.e. a body-centred organisation (Trevarthen, 1968a,b). Moreover, (ii) stimulation of the SC in all species studied produces ocular and/or bodily orienting movements, in an organised way, towards the point in space corresponding to the locus of stimulation on the tectal "map", irrespective of the animal's orientation musculature and mechanics. These perceptual and motor invariants would appear to be fundamental to SC function, and invite the suggestion that some form of "standard" spatial and/or sensorimotor transformation occurs in SC, "translating" or "integrating" the sensory world into motor movement. However, in contrast, almost every other feature of SC organisation shows gross and often unsystematic variation between species and sub-species. For example, there are alarming interspecies and even intraspecies differences reported in terms of receptive field size and locations, magnification of portions of the visuospatial projection, directional selectivity, ipsilateral visual field representation, response to specific types of stimuli, goal-directedness of evoked saccades, preferred rate and direction of stimulus movement, and the degree to which unit responses are dependent upon input from VC. The relative independence of the variable and invariant features of collicular organisation is emphasised by the study of Schiller et al (1974) which demonstrated that following cooling of VC in the monkey, cells in intermediate SC laminae continued to discharge before eye movements, and overall visuospatial organisation of the SC remained unchanged, yet the receptive field characteristics of individual units were completely abolished. An obvious suggestion is that SC single unit responses reflect differences in the visual environments of the various species studied. For example, Cynader and Berman (1972) argue that the absence in cat SC of units responsive to "dark shadowy tongues" as found in monkeys may be because "the arboreal diurnal primate might be more likely to possess specific mechanisms for the detection of shadow tongues than the more nocturnal carnivore". Similarly, Cronly-Dillon (1964) argues that the temporonasal directional preference of goldfish tectal neurons may result from the need for this animal to detect its own backward movement when swimming against a watercurrent. However such post hoc reasoning is premature. In particular it is unclear why the goldfish should not need to track the 'escape' of prey from its central visual field, which is the supposed reason for the presence of naso-temporally tuned movement detectors in cat SC (Gordon, 1972), or why the mouse (an animal clearly not in danger of swimming backwards) should also have movement detectors preferring temporonasal directions; moreover why in an ostensibly similar species, the rabbit, SC neurons should prefer the opposite stimulus direction [1]. The most intuitively likely factor to influence tectal responses might be

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[1] One possibility would be that predatory (stalking) animals would prefer nasotemporal directions, while predated species might prefer temporonasal (to detect the approach of unexpected larger animals). However one might expect that in such species, large stimuli (perhaps representing predators) would be preferentially attended to when moving temporo-nasally (sic approaching), and small stimuli (perhaps representing prey) to be selectively tracked in a naso-temporal direction

the nocturnal-diurnal status of the species, though the nocturnal rat and diurnal primate (monkey) SCs have remarkable features in common, being more alike than is either to the cat or rabbit which in turn show substantial incomparability. Until specific predictions of collicular neuronal responses can be generated from a knowledge of an animal's habitat and habits, such explanations must be treated cautiously, however parsimonious and reasonable they may seem.

In many species a sharp distinction is suggested between superficial laminae (dorsal to and including so) and deeper laminae; where reported, neurons responding to more than one modality, habituating rapidly and responding to complex features are generally found in deep strata. Such a division is clearly consonant with the anatomical evidence (Chapter 1). Deeply located neurons, with large receptive fields, are thus more likely to be involved in sensory integration than in precise mapping of visual space. Humphrey (1968) noted that deep laminae appear to be capable of registering an event (i.e. that 'something has happened'), but incapable of defining its location or modality (see Foreman *et al*, 1978). Horn and Hill

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(*sic*. escaping), though such an investigation has yet to be carried out.

(1966) and others have shown that novelty is particularly well discriminated in deep colliculus. Taken together, the evidence might be interpreted as indicating a division within the colliculus into systems concerned with either (i) the physical features of stimuli - in particular visual stimuli and their relations in space, and (ii) more general, perhaps species specific (certainly highly species-variable) environmental features, which are apparently fairly dependent, for their SC coding, upon the intactness of visual cortex. It is tempting to relate this division into "two visual systems" within the SC to the two types of retinal ganglion cell projecting to the structure. In particular, the W-cell input which is not affected by VC removal is present at birth, functional even following visual deprivation, and which may, therefore, have a particular function in coding visual information on the basis of the <u>physical</u> parameters of the stimulus. On the other hand, the Y-cell input is forebrain-dependent, confers complex response characteristics upon deep SC units in many species, and is dependent upon experience for normal development. Thus the Y-cell system, and other cortical and subcortical centres projecting to the SC may confer versatility (particularly necessary for the more sophisticated mammals in whom it is especially evident) upon the species, and perhaps upon the individual. This will have significance for the discussion of orienting behaviour (Chapter 3), which will be considered after reviewing the literature on the behavioural changes which follow SC ablations.

However a further dimension of the above hypothesis follows naturally; that the W-cell system may be inwired in the neonate, thus perhaps guiding early visual responses, while the Y-system develops with experience, perhaps in part dependent upon the organising functions of the W-system. Interestingly, a virtually identical suggestion has been made by Hirsch and Leventhal (1977):

> " ... it appears that, in many cases, the invariant component of the mammalian visual system consists of retinal W cells and X cells and their central projections and terminations, while the variable component, within which the environment exerts its (still poorly understood) effect, consists of Y-cells and their central projections and terminations. Such an invariant, intrinsically-determined framework, coupled with a variable, experience-sensitive component, may provide the constancy in the organisation of the visual system that is necessary for development and function without sacrificing the flexibility of response necessary for survival in an unpredictable environment".

CHAPTER 3

ABLATION STUDIES OF THE SC

While anatomical and electrophysiological studies are often tied to a specific functional model for the structure under investigation, they can stand alone without such a theoretical framework. Hypotheses derived from behavioural experiments are, however, inevitably tied to a particular notion of the function performed by the structure in the intact animal. For example, movement selectively in SC neurons is important in its own right, independent of its functional significance, yet an experiment investigating the detection of movement by collicular-lesioned animals is inevitably bound to the theory that movement detection *per se* is in some way a collicular "function" (i.e. that an animal is able to detect movement, or a certain class of movement, by virtue of possessing a SC). Consequently, the following review will examine the evidence for and against current (behavioural) theories of SC function, drawing upon anatomical and electrophysiological investigations reviewed above, yet concentrating mainly upon reports of the behaviour of animals with collicular tissue removed or damaged.

3.1 Regulatory functions

The long phylogenetic history of the SC and its prominence, particularly in lower species, might be taken to indicate that it plays a fundamental role in some automatic or regulatory behaviours, perhaps those universally necessary among vertebrates.

Altman (1962b) showed that following SC lesions, rats exhibited increased activity in an open field apparatus divided into brightly and dimly illuminated compartments; the SC-lesioned rats appeared not to exhibit the negative phototaxis characteristic of this species. Over longer periods (24 hours) the same animals tested in their home cage showed reduced activity compared with normals (Altman, 1962a), suggesting a collicular regulation of the diurnal cycle. Histology was not provided in that study, though it is likely that the lesions invaded deep laminae (Foreman et al, 1978). In more recent studies in which such SC-lesioned rats were tested in dim (Foreman et al, 1978) or dark, and light (Murison, 1977) conditions, the level of illumination has not been shown to affect collicular hyperactivity, but Routtenberg, Strop and Jerdan (1978) have demonstrated lack of negative phototaxis in rat pups whose superior colliculi had been surgically undercut at birth. Richter (1964) in an ill-documented study with rats reported SC lesions to produce reduced reaction to restraint, and taming (especially in newly trapped wild rats); also very long cycles of spontaneous running activity (18 - 20 days in males and 30 - 35 in females), freeing the 4 or 5 day oestrous cycle from diurnal control. Marked,reflexive "tail rattling" was also reported. However histology was not provided, and there is a good chance that many of these effects were produced by extracollicular damage or general dementia. Isaac (1971) reported considerable increases in activity following SC lesions in rats (- again one assumes that the lesions involved deeper laminae in the absence of histology), though Isaac's own data provides little support for a specific effect of illumination level upon collicular hyperactivity. Injections of amphetamine were found to markedly potentiate SC activity, a finding recently replicated (Pope and Dean, 1979, personal communication). Interestingly, Isaac (1971) noted that amphetamine administration has an opposite effect upon the open field activity of rat and monkey, increasing and decreasing activity respectively. A similar differential effect occurs with large collicular lesions; in rats a threefold increase in activity results, while collicular lesioned monkeys (e.g. Denny Brown, 1962) and tree shrew (Raczkowski _et al_, 1976) show apparent hypoactivity and even immobility following SC ablation. Isaac argues that the effects of illumination on activity depend upon the nocturnal or diurnal lifestyle of the species, high illumination inhibiting activity in the former and facilitating activity in the latter, doing so via the SC (Isaac and Reed, 1961); this will be further expanded in Section 3.6 where visual control of the motor system will be reviewed in more detail. However the general hypothesis that collicular lesions in rats reduce light-aversion or light-sensitivity is not attractive; a greater overall reduction in visual stimulation would be likely to result from VC lesions than SC lesions, though rats with large visual cortical ablations (areas 17, 18, 18a) exhibit normal activity levels (Foreman et al, 1978). Whishaw (1974) was notably unsuccessful in an attempt to obtain light avoidance deficits following extremely large lesions involving all SC, or posterior neocortex; in fact simultaneous lesions of SC and VC actually increased light avoidance. In addition, lesions of superficial SC laminae which abolish the greater part of visual input to SC, nevertheless failed to result in hyperactivity (Goodale and Lister, 1974). Indeed, since cells in SC are relatively insensitive to overall level of illumination in a variety of species (Sprague et al, 1973), in particular the rat (Humphrey, 1968), it would be surprising to find a differential response to light levels depending upon the integrity of SC, though other midbrain structures which do possess single units sensitive to overall level of illumination, e.g. pretectum (Sprague et al, 1973) and accessory optic tract (Marg, 1973), are possible candidates. However, the mediation of phototaxis remains a possible function of the SC in neonates (Routtenberg et al, 1978); whether this is related to activity level in neonates is unclear. The activity level changes following SC lesions will be returned to later.

Trulson and Randall (1973) have argued that the SC is involved in the mediation of abnormal grooming behaviour in cats with pontile lesions, and rats with large dorsal midbrain lesions have been reported to groom abnormally (Pope and Dean, 1979). Grooming in rats is an infrequent behavioural category, though where measured in colliculars (Foreman et al, 1978) frequency of initiation of grooming bouts was not altered by comparison with normal animals. Rats with very deep SC lesions (Goodale et al, 1978) and with kainic acid injections in SC (Pope and Dean, 1979, personal communication) may appear to lose condition; this may in some cases be due to weight loss and general malaise following such treatments. Though it is unclear which stimuli might trigger grooming bouts, "matting" of fur or discomfort from dirt, wetness or loose fur are likely possibilities (Trulson and Randall, 1973). Since the body surface is topographically represented on the colliculus (e.g. mouse: Dräger and Hubel, 1975) and since gross inattentiveness has been reported following SC ablation in a number of behavioural settings, including inattentiveness towards objects touching the fur (Kirvel, 1975; Kirvel, Greenfield and Meyer, 1974) and to contralateral body surface following unilateral

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1 However this cannot be regarded as a behaviour universally required of vertebrates since many lower animals do not groom (e.g. amphibia and fish). At best this topic relates to mammals and birds.

injections of kainic acid (Foreman and Srebro, unpublished observations, 1979) it is likely that the disappearance of abnormal grooming in pontile-lesioned cats following collicular ablations noted by Trulson and Randall (1973) and misdirected grooming in dorsal tegmentally-lesioned rats (Pope and Dean, 1979) may reflect aspects of more general attentiveness.

3.2 Visual learning: Operant discrimination performance

Animals subjected to total striate cortex (area 17) ablations (confirmed by the complete degeneration of pars dorsalis of lgn) are capable of postoperative learning or relearning of some visual discriminations (Klüver, 1937; Bauer and Cooper, 1964; Horel et al, 1966; Weiskrantz, 1963; Weiskrantz and Passingham, 1975). Inevitably, many authors have assumed that residual visual capacities utilise the SC (see Sprague et al, 1973). Indeed it is known that in lower animals, for example some fish (Sarnat and Netsky, 1974), the optic tectum subserves pattern vision. Human patients with occipital lobe damage are capable of rudimentary, low spatial frequency vision within the visual field defect (Weiskrantz, Warrington, Sanders and Marshall, 1974). In animal studies it has been generally agreed that destriate subjects which learn a pattern discrimination preoperatively, relearn the "same" task postoperatively using flux or contour cues (e.g. Bauer and Cooper, 1964; Horel et al, 1966; Schilder et al, 1967; Weiskrantz, 1973; Weiskrantz and Passingham, 1975) and that genuine form discrimination is not possible following posterior neocortical ablation, even with 2-stage removal and with interoperative retraining (rat: Gray, Lavond, Meyer and Meyer, 1979). Theoretically, it is unlikely that the SC is involved in pattern processing in view of its single unit characteristics which are unlike those in VC and have a strong preference for movement. However, Sprague et al (1973) argue that this does not preclude the discrimination of pattern via the integration of spatio-temporal input generated by self-induced movement in the awake, freely-moving animal (see also Ingle, 1978). However, in addition to the SC there are clearly other subcortical candidates for 'residual' visual processing, in particular pretectum, lgn (dorsal and ventral), the accessory optic system and posterior thalamus (Horel, 1968). In fact Ghiselli (1938) reported that in rats, combined damage to SC and VC had no greater effect upon postoperative performance of a brightness discrimination than VC removal alone, though admittedly the SC lesions were subtotal.

Although Layman (1936) and Dyer, Marino, Johnson and Kruggel (1976) have reported normal learning of brightness and pattern discrimination in collicular rats, Papez and Freeman (1930) found an apparent deficit in postoperative retention of a brightness discrimination, a result also obtained by Goodale and Murison (1975) and Thompson (1976). Other authors have suggested that the pretectum, which is inadvertantly damaged in some SC lesions, is the principle subcortical structure responsible for visual learning (Thompson and Rich, 1963; Horel, 1968; Blochert, Ferrier and Cooper, 1976; Gray et al, 1979).

Also Horel (1968) showed that rats trained following VC removal and subsequently given SC lesions were minimally impaired on retest (62.2% savings against 86.5% in control animals) but lgn_V lesions in that instance caused a substantial impairment (3.4% savings). In the Thompson (1976) study, damage to areas of the brainstem (including areas receiving input from SC via predorsal bundle, e.g. pontomedullary reticular formation) was associated with negative savings scores. The greatest deficits after SC lesions in rats probably occur in situations where the discriminanda do not appear in a predictable region of visual space, for example where they surround the animal in a circular jumping stand (Barnes, Smith and Latto, 1970; Weinberg and Stein, 1978), though these studies may have exaggerated the deficit since few postoperative trials (30 per condition) are reported. With more prolonged training, the collicular deficit rapidly disappears (Murison, 1977). Schneider (1967, 1969) reported hamsters with bilateral undercutting of SC to engage in 'disoriented', meandering approach behaviour towards goaldoors in a 2-choice runway, nonetheless doorpush-responding correctly. Dyer et al (1976) obtained such meandering behaviour from VC rats, though conspicuously not from SCs. Thus, unfortunately, in all rodent test situations, visual discrimination performance is to varying degrees confounded with motor response, spatial localisation and bodily orientation, though where they occur, impairments in SC-lesioned rodents are temporary and mild. In cat, Berlucchi, Sprague, Levy and DiBernardo (1972) demonstrated postoperative, initial learning of upright v inverted triangles, circle v cross, and light v dark discriminations to be slowed by SC ablation, though postoperative retention of preoperatively learned habits was unimpaired. (As in the rat, additional damage to pretectum gave rise to more permanent and severe deficits). Wood (1975) found that after optic chasm section, cats were unable to perform a light v dark discrimination with the eye contralateral to a SC and VC removal though strong ipsiversive turning tendencies may have been responsible for the impairment. Where the two lesions were made in separate hemispheres, more trials were required to learn with the eye contralateral to the VC lesion than the SC lesion. Urbaitis and Meikle (1968) trained cats on a simultaneous light v dark discrimination in a Y maze and found bilateral SC lesions to produce significant retention deficits in animals which had suffered posterior cortical ablation prior to initial learning, though relearning did eventually occur. Voneida (1970) obtained deficits in pattern discrimination in cats with midline knife cuts in the caudal midbrain which would, among other things, have severed efferents from the SC to the brainstem and spinal cord; the result is similar to that obtained by Thompson (1976) with rats. Blake (1959) claimed to have demonstrated deficits in brightness and form discrimination following SC lesions, though animals were removed from 'incorrect' alleys before making a doorpush response. It might be suggested that discrimination would not have been impaired had they been trained to a door push error criterion. (cf Schneider, 1968). Winterkorn (1975) reported apparent deficits on horizontal and vertical stripes and light v dark discriminations in SC cats, independent of the spatial separation of the stimuli, though, as in the Schneider (1967, 1968) study with hamsters, only in terms of "approach" errors to incorrect goaldoors. On the other hand, other authors using cats with bilateral SC lesions have obtained deficits (training to "doorpush" criterion) on similar tasks (Sprague _et al_, 1973; Alder and Meikle, 1975). Thus, while initial learning of visual discriminations is perhaps more affected by SC lesions in cats than in rats, studies in both species have confounded several variables including spatial localisation and motor control with discriminative ability. The one important exception to this is the experiment by Tunkl and Berkley (1974) which provides arguably the best evidence for a direct involvement of the SC in pattern perception. Using a situation in which minimum (solely ocular) localisation was required, they showed that cats with bilateral SC lesions (and split-brain cats using the eye contralateral to collicular removal) required five times as many trials as normals (control eye) to solve a circle v cross discrimination. They argue that deficient oculomotor scanning of the figure is likely to be responsible.

Tree shrew

Casagrande _et al_ (1972) and Casagrande and Diamond (1974) have shown that SC lesions in tree shrews cause a major disruption in their pattern discrimination; for instance, no animal with SC ablated was able to learn to discriminate between upright and inverted triangles, though they could discriminate between vertical and horizontal stripes. Striate-lesioned animals failed the latter but were able to discriminate between triangles (except when surrounding annulae were added to the discriminanda; Killackey and Diamond,1974). This result suggests a double-dissociation between cortex and subcortex. Jane _et al_ (1972) also obtained this effect but further showed that the tree shrew with a unilateral ablation of SC could learn the triangles discrimination with the ipsilateral but not the contralateral eye.

It is not clear why the tree shrew should be so uniquely dependent upon the SC for this particular discrimination; cats and primates with SC lesions have no more difficulty on this than any other discrimination. Descending fibres in the predorsal bundle werenotably not involved in pattern discrimination in the tree shrew (Raczkowski _et al_, 1976).

Primates

Though Denny Brown (1962) reported major disruption of behaviour consequent upon midbrain lesions, subsequent studies using more restricted damage have reported minimal deficits. An extensive investigation of visual capacities of colliculectomised monkeys was carried out by Anderson and Symmes (1969) who found no deficit in form, colour, flicker fusion and movement discrimination, though simultaneous discrimination of 2 rates of rotational stimulus movement was impaired. Vetter (1975) reported no deficiency in SC squirrel monkeys on brightness discrimination, though their elevated error scores on pattern discrimination prompted Vetter to propose that they were impaired in "fine detail" perception. Marzi and Latto (1977) report small deficits on a number of visual discriminations, including horizontal v vertical stripes, and upright v inverted triangles (though the latter was no more impaired than other stimuli, in contrast to the tree shrew). Particular difficulty was experienced by SC monkeys when detailed visual scanning of the discriminanda was required; for example, to search for the presence of a gap in an outline black circle. Keating (1974, 1976) using a situation in which the monkey had to press the dimmer of 2 lights simultaneously presented for 200 msecs randomly in any 2 of 24 spatial positions, and MacKinnon, Gross and Bender (1976) and Butter, Weinstein Bender and Gross (1978) using a task requiring the animal to reach to one of a number of horizontal spatial positions signalled by a brief light flash, have identified a particular difficulty which colliculars experience in dealing with briefly presented stimuli occurring in unpredictable spatial positions. Their responses to stimuli in more peripheral areas of the visual field are subject to most frequent error. Butter (1974) has obtained a mild impairment in a colour discrimination task when response site is separate from the site of the stimulus, though not when the two are close together. Pasik and Pasik (1971) have shown that unless the (lateral) pretectum is damaged, SC lesions superimposed upon VC (areas 17, 18, 19) lesions have little additional effect upon preoperatively-learned light v dark discrimination, and suggest that "residual capacities" depend upon the accessory optic system. Denny Brown and Fisher (1976) have, however, provided evidence for a specific, pattern-perception role for the SC, in keeping with an earlier suggestion by Pribram (1958) that the SC may function as a 'pattern analyser', organising feature information in VC into percepts. Though such a model is at first glance reasonable, considering the large cortico-tectal projection and early reports (e.g. chimpanzees: Porter and McRioch, 1962) of SC lesions in primates producing "object blindness", it is not consistent with other findings (see above) which, though suggesting a role for the SC in pattern perception, do not ascribe it a central position if only because removal of the colliculus produces pattern perception deficits which are usually mild and transient. As in the cat, however, pattern discrimination deficits where they occur, would appear to arise from poor control of "neural mechanisms responsible for a detailed spatial analysis of the visual stimuli" (Marzi and Latto,1977).

3.3 Spatial behaviour

Since visual space is precisely topographically represented in SC, it is not surprising that the structure has been implicated in behaviours which have a 'spatial' component, notwithstanding that visual field representations occur elsewhere in the brain (Cowey, 1979) - or indeed that topography *per se* has functional significance is an unproven assumption (Sprague *et al*, 1973).

Schneider (1967, 1966, 1969) has proposed that within the mammalian brain there exist 2 visual systems, corresponding to the two major visual pathways (Diamond and Hall, 1969)[1]. Schneider argues that the first system, the geniculostriate pathway mediates feature analysis and thus object identification (i.e. a "what?" system) while the second, the retinotectal-prestriate, or midbrain, visual system discriminates the positions of objects in space (i.e. a "where?" system), though the two systems will inevitably be functionally dependent to some extent. Weiskrantz (1977) has observed that in terms of phylogenetic history, the SC system should properly be considered the "first" visual system. Schneider (1967, 1969) tested syrian golden hamsters (*mesocritus auralis*) with surgically-undercut colliculi

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[1] Indeed these authors now argue for a third subdivision, subdividing the tectopulvinar projection into (i) a tecto-pulvino-middle temporal cortical projection subserving visuospatial localisation and (ii) a tecto-superior pulvino-extrastriate pathway responsible for visual learning (Glendenning, Hall and Hall, 1972).

(2 with cuts beneath superficial laminae, 5 with more ventral sections) in a 2-choice discrimination apparatus and found that while the animals were capable of good discrimination between horizontal and vertical stripes and light v dark in terms of a 'doorpush' criterion, en route to the final response they tended to make erratic approaches to goaldoors, frequently running to the incorrect goaldoor (an "approach" error) before correcting the response. This was particularly noticeable when, in order to correct an approach response, the animal was required to run round a barrier separating goaldoors. Simple myopia was ruled out as an explanation by appropriate controls. Schneider concluded that the hamsters were unable to localise the discriminanda in space. However, a number of criticisms might be made of this experiment. Firstly, the animals were initially trained without an interposed barrier; its introduction may have differentially affected the control and SC groups (Dyer et al, 1976). Should this be the case, it would be interesting, though not necessarily in terms of group differences in spatial behaviour. Secondly, other strategies than visual might have been used by some or all animals, for example olfactory cues on goaldoors; this was not specifically tested for. Third, the SC group did eventually learn the discrimination to both approach and doorpush error criteria (Schneider, 1966) demonstrating their ability to localise goaldoors after further training. Fourth, Cowey (cited in Collin, 1977) has pointed out that

although SC hamsters showed a greater increase in approach errors than discrimination error in absolute terms, proportionately they are impaired equally according to either criterion. Five, approach errors were obtained from normal hamsters in a very similar situation (see Schneider, 1968, note 17) and thus the effect is not very robust. Finally, the erratic approach behaviour reported by Schneider was stimulus-specific for one animal (M7), occurring to stripe- but not light v dark discrimination. Hamsters are perhaps not ideal subjects for visual experiments since their visual abilities are limited (Rosinski and Keselica, 1977). Dyer et al (1976), Goodale and Murison (1975) and Goodale et al (1978) have been unable to replicate Schneider's results using rats; indeed in the latter studies, striate cortex-ablated rats, and not SCs, were found to localise stimuli poorly while SCs in contrast tended to run more accurately than normal rats. However the SC group showed no orienting responses to novel stimuli (Goodale and Murison, 1975)[1] unless they were presented in the direction in which the animal was running (Goodale, Foreman and Milner, 1978). Thus Goodale reinterprets Schneider's hypothesis, making a distinction between locomotor orientation, and the "orienting reflex" to peripheral novel stimuli, only the latter being subserved by the SC (Goodale et al, 1978).

However, persuasive evidence in favour of the spatial hypothesis of Schneider (1967, 1968) has been provided

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[1] This work has recently been replicated using hamsters, with similar results; lack of stimulus scanning movements of the head in collicular hamsters is also reported (Mort et al, 1980).

by Barnes et al (1970). Using a circular jumping stand, they demonstrated an apparently severe deficit in postoperative retention of the ability to jump towards the one darkened of 6 goaldoors, though 4 out of 6 SC rats were capable of discriminating light from dark stimuli when presented in a straight runway, go - no go task. A tendency was noted for the animals to jump towards goaldoors immediately adjacent to the correct one, suggestive of a specific deficit in localising. The four animals capable of go - no go discrimination were then tested on locomotor approach to goaldoors in a modified 6-choice situation in which goaldoors were approachable directly from a larger diameter centre platform. Vicarious trial-and-error behaviour was noted in SCs, though criterion doorpush performance was reached after only 18 trials for most animals. Two animals (E1, E6) showed erratic, disinhibited running, attributed by the authors to pretectal invasion. These results are surprising in some ways; lesions similar to those of animals E2, E3, E5 have been shown elsewhere to produce excessive activity (see Section 3.6), though such a change was not noted by the authors. Furthermore, poor performance on the 6 choice stand initially (Barnes et al, 1970; Figure 2) might be exaggerated by the inclusion of the erratic animals (E1, E6) dropped from later studies. As Goodale and Murison (1975) observed, animals in Barnes et al (1970) study did not collide with partitions between goaldoors, thus showing at least some form of position discrimination. Furthermore, the SC group would probably have improved with prolonged training. Indeed, using a similar situation to the modified 6-choice task of Barnes et al (1970), but with the brighter stimulus positive, Murison (1977) has shown that after 80 trials animals with very extensive SC ablations attain criterion performance. On the other hand, Weinberg and Stein (1978)[1] have obtained similar results to Barnes et al (1970), demonstrating that SC rats are incapable of jumping to the positive (illuminated) goaldoor, even when the distance between stand and goaldoor was as little as 10 cm. Vicarious trial and error behaviour was again observed for SCs, and one was reported to run erratically towards the facing goaldoor when placed on the stand. However, these authors also used a small number of trials. Animals frequently failed to jump from the small platform, the mean jump latency for 1-stage bilateral SCs being 150.6 sec (maximum allowed: 180 sec), compared with 6.8 sec for controls. Thus, while it is clear that the performance of rats with SC lesions in jumping stand localization tasks is at least temporarily disturbed, the nature of the deficit remains unclear. The jumping stand apparatus must impose different requirements from the apparatus used by Goodale et al

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[1] Though from their lesion reconstructions it is unclear to what extent the SC was removed.

(1978) in that in the former, no region of central space is identified as containing stimuli required for discrimination performance, which may be particularly confusing for animals with deficits in shifting attention to peripheral space. The "stretching" to goaldoors in vicarious trial-and-error behaviour may represent a compensation for the loss of peripheral vision, or inability to suppress the prepotent species specific "step down" response (Dyer et al, 1976). Some vicarious trial-and-error was noted in one SC rat in the apparatus used by Goodale et al (1978) (personal observations, 1976), though this was a temporary phenomenon. While Goodale et al (1978) tested animals automatically for 40 trials per day, less opportunity for recovery was allowed the animals in jumping stand studies; for example in the Weinberg and Stein (1978) study only 30 trials were reported (6 trials per day for 5 days).

Collin (1977) reported that SC-lesioned rats were impaired on a spatial task which required them to investigate a large area and rear up to obtain rewards from the tops of 16 vertical wooden pedestals arranged in a lattice array, suggesting a 'spatial' deficit similar to that described by Keselica and Rosinski (1976) who found SC-undercut hamsters to exhibit disorganised behaviour in picking up sunflower seeds arranged on the floor of an arena. Collin (1977) was inclined to attribute the deficit to hyperactivity in the former study. Nonetheless, this does potentially represent a genuinely 'spatial' deficit in SC animals, using the term 'spatial' in the sense recently adopted by O'Keefe and Nadel (1978). However, O'Keefe and Nadel (1978) and Olton (1977) have implicated the hippocampal formation, and not the SC, in 'cognitive spatial mapping', i.e. the construction of a spatial map which enables the animal to determine his own position in space relative to environmental objects. The possible relationship between spatial coding in this sense and the 'spatial' hypothesis as related to SC-lesioned animals (Schneider, 1969; Trevarthen, 1968; Ingle, 1970) will be explored in a later section, though it is worth pointing out that one test of a rat's spatial abilities which reliably produces deficits in HPC rats, the Hebb-Williams Maze (Kviem, Setekleiv and Kaada, 1964; Kimble, 1976) also identifies deficits in SCs (Weldon and Smith, 1976).

In the cat, Winterkorn (1975a,b) could find only indirect evidence for Schneider's (1969) hypothesis; cats with SC lesions successfully achieved criterion performance (on both approach and doorpush errors) on horizontal v vertical stripe and light v dark discriminations, irrespective of the spatial separation of the stimuli, though SC-, FEF- and VC- (Winterkorn, 1977) lesioned cats tended to make more "approach" errors than controls, particularly when nearing criterion. Winterkorn used a titration training procedure which may well have encouraged "approach" errors since control cats also made many of them. Winterkorn (1975a,b) evidently felt that the SC deficit was not spatial per se, in commenting that it may "reflect an animal's inability to inhibit or withold incorrect (unreinforced, 1977) responses".

Trevarthen (1968, 1970) working with monkeys and patients with the corpus callosum sectioned has arrived at similar conclusions to Ingle (1971) in postulating a "functional" division between central 'identifying' visual space and 'ambient' space, the latter providing information about movement of the environment, thus enabling the distinguishing of self-produced movement from environmental movements (Walls, 1962). This will not be further discussed here to avoid repetition since it will be considered in Section 3.5 in relation to 'peripheral' and 'central' attention.

The inability of primates to reach to brief visual targets, especially when presented in peripheral vision space (Keating, 1974, 1976; MacKinnon et al, 1976; Butter et al, 1978) might clearly represent a 'spatial' deficit, though potentially one of either (a) discriminating, (b) remembering, or (c) reaching toward the visual target.

Marks and Jane (1974) tested cats and monkeys in a situation similar to that used by Goodale et al (1978) requiring the animal to emerge from a startbox and cross an arena towards one (illuminated) of 2 goaldoors. Animals with large VC lesions exhibited a response strategy which involved halting periodically, reorienting to the correct goaldoor and then continuing. The authors argue that, as with the auditory system (Masterton, Jane and Diamond, 1967), a division of labour exists between the cortical visual system which organises "ambulatory localisation" (or "locomotor orientation"; Goodale *et al*, 1978) while the collicular system subserves "static localisation" (or the "orienting reflex"; Goodale and Murison, 1975). Thus the destriate animal converts an ambulatory localising task into a static localising task by ceasing ambulation and "statically" reorienting. It might be argued that an animal which uses a "stop-go" type of ambulation (e.g. the "hopping" of a rabbit) might use more static localising than a "continuously" running animal such as a rat. Such a model might explain three anomalous findings:

(i) The superior performance of SC rats on a continuous runway task (Goodale *et al*, 1975, 1978) compared with a jumping task (Barnes *et al*, 1970; Weinberg and Stein, 1978; Murison, 1977), the latter requiring arguably more 'static' localisation prior to jumping.

(ii) the finding of De Vos-Korthals and Van Hof (1977) that a destriate rabbit is apparently capable [1] of ambulatory

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[1] Note however that the measure of the animals' progress was more gross than that of Goodale *et al* (1975, 1978) and Marks and Jane (1974). The runway was smaller relative to the animals' body size, and lesions were made in 2 stages. Nonetheless, one might have expected

localisation in a 3-choice continuous runway. The paw-on-paw running style of the rat might require more "ambulatory localisation", i.e. continuous moment-to-moment recalibration of position relative to stimulus position, than the discontinuous style of the rabbit. Masland et al (1971) have pointed out that the relationship between SC and VC in rabbits is unlike other species, SC being more autonomous. It would not be surprising to find a re-organisation of function in this animal, especially since lower species, when jumping towards prey are guided in doing so by the tectum (e.g. frog: Ingle, 1970).

(iii) Ferrier and Cooper (1976) have shown that rats with striate ablations are capable of reliably jumping towards illuminated goaldoors. This is also consistent with the above formulation, since jumping tasks may impose greater need for static localisation. Such a hypothesis has implications for the Barnes et al (1970) and Weinberg and Stein (1978) experiments. In the latter case animals were trained postoperatively on a large central platform prior to training on a small platform, thus perhaps inducing an "ambulatory localising" habit prior to switching to a phase requiring static localisation 30 trials later; this may conceivably have exacerbated the jumping deficit.

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a clear visual guidance deficit according to Marks and Jane (1974) and Goodale et al (1978).

Thus in summary, it might be profitable to consider the visual system to be divided into 2 subsystems, though not as in Schneider's original model (1969). It would appear that for orienting behaviour, the geniculostriate system may be involved in gross spatial organisation and locomotor guidance in relation to environmental objects ("ambulatory localisation") while the SC may have a much greater role in attentional shifts ("static orientation"). It is argued that in the initial stages of operant training or relearning, particularly where discriminanda surround the animal and where jumping responses are required, performance will be especially dependent upon "static" orientation, and thus the integrity of the SC.

3.4 Attention I. Eye movements

The traditional role ascribed to the SC is that of an oculomotor reflex centre whose function is to move the eyes conjugately to a particular point in space; not surprisingly, perhaps, in view of the longstanding knowledge that electrical stimulation of the structure gives rise to contraversive eye movements (Adamük, 1870), and, in addition, that the residual visual capacities of cortically blind patients include the ability to move the eyes towards moving stimuli and flashes of light (Riddoch, 1917; Holmes, 1938; Teuber Battersby and Bender, 1960; Pöppel, Held and Frost, 1973; Weiskrantz _et al_, 1974), a result also seen in monkeys (Humphrey and Weiskrantz, 1967). In addition paralysis of gaze has been reported when pressure is applied to SC by adjacent tumours (Crosby, Humphrey and Lauer, 1962), and collicular tumours have been said to result in lack of spontaneous eye movements (Hyndman and Dulin, 1939; Denny-Brown, 1962).

As noted earlier (Chapter 2), the SC has been implicated in the "foveation of visual targets by the "visual grasp reflex" by Hess et al (1946), and Humphrey (1970), drawing an analogy between the tectum of lower vertebrates and the colliculus of higher ones, has argued that the "catching" of a prey object via tectal mechanisms in frog represents the evolutionary antecedent of the "visual grasping" of stimuli in the primate. Robinson (1972) and Schiller (1972) have tended to view the SC as a precise topographically-organised mechanism for computing the direction and distance of a saccade required to centre the eyes on a visual target (though how and why such a target is "chosen" is unclear). Robinson (1972) states that in the SC

> "a delightful correlation between sensory input and motor output was established and the tectum was shown to be a major link in the orderly transformation of sensory into motor activity",

and that a

> "visual stimulus creates neuronal activity, via the retinotectal projection, in a localised region of the superior colliculus ... That electrical activity descends to the deep layers by ... columnar organisation ... and from there descends to the pons, probably the medial pontine reticular formation ... where it is translated into the temporal motoneuron activity needed to create a saccade ... This saccade brings the original visual stimulus onto the fovea" (p. 1803).

Robinson (1975) is careful to point out that the much discussed putative direct connections between SC and the oculomotor nuclei are unnecessary for the above model, since output from the SC is inevitably temporally integrated elsewhere prior to actual saccade initiation. Precht, Schwindt and Magherini (1974) have emphasised the polysynaptic nature of the tecto-abducens pathway.

However the SC is clearly not the only structure potentially involved in eye movement control since stimulation of the cerebellum (Ron and Robinson, 1973), visual cortex (Schiller, 1977), frontal cortex (Robinson and Fuchs, 1969) and other areas (see Pasik and Pasik, 1966) produces eye movements, though the relationship between stimulus parameters and evoked saccadic parameters may vary between structures.

Pasik, Pasik and Bender (1966) and Pasik and Pasik (1971) have specifically criticised the concept of the SC as an eye movement "centre" [1] since the full range of eye movements are available to a monkey whose colliculi have been totally ablated (Anderson and Symmes, 1969; Pasik and Pasik, 1971; Wurtz and Goldberg, 1972d), though admittedly such animals do adopt a "fixed stare" expression, particularly in the homecage. Wurtz and Goldberg (1972b) and Mohler and Wurtz (1977) report an increase in saccadic latency (of the order of 100 msec) resulting from SC ablation in monkeys, in additon to reduced

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[1] They define "centre" as a structure which uniquely controls a specific behaviour

ability to accurately fixate targets with a corresponding tendency to make small 'corrective' saccades in doing so. This effect lasted about six weeks. In a very recent study, Albano and Wurtz (1978) have reported that visual scanning and saccadic investigation of a complex visual array and response to sudden unexpected stimuli is grossly reduced by collicular removal in agreement with Milner, Foreman and Goodale (1978). Interestingly, increased (contralateral) saccadic latency has been reported by Heywood and Ratcliffe (1975) in a human subject who underwent unilateral SC removal.

Removal of the SC has been recommended as beneficial to patients suffering from mystagmus (Neverov and Kuleshova, 1976), though the evidence for a significant role for the SC in mystagmatic eye movements is at best sparse (however see Bergmann et al, 1964 and Schaefer, 1970, 1972). Other types of eye movement associated with the SC have been discussed earlier (see Chapter 2).

Thus it would appear that the SC is not vital for the control or initiation of all eye movements. However, as Wurtz and Goldberg (1972b) have pointed out, even a 100 msec increase in saccadic latency which they report to be produced by SC lesions in monkey may, in the natural environment, prejudice survival in numerous situations.

3.5 Attention II. Wider conceptions

A number of authors, while not disputing the strong association between the SC and eye movement control have argued that this relationship may be one manifestation of more elaborate collicular functions, and that intrinsic processes may form the neural substrate of wider "attentional" and "stimulus selection" mechanisms. Rizzolatti et al (1974) have shown that the responses of a cell in superficial SC may be modified by the introduction of a novel stimulus distant from the receptive field of the first cell, suggestive of an "attentional shift" at neural level, or alternatively perhaps an attempt to make an eye movement in the direction of the second stimulus (Robinson and Wurtz, 1976). Wurtz and associates (Goldberg and Wurtz, 1972b; Mohler and Wurtz, 1976) have rejected the "simple" concept of foveation of eye movement initiation by descending flow from perceptual (superficial) to motor (deeper) collicular laminae, arguing that behavioural enhancement of activity in deep SC cells represents the means by which a stimulus, having been evaluated as worthy of a saccade, is attended to by the facilitation of eye movements to the area of space in which it appears. This theory of collicular function is unquestionably the most elaborate and comprehensive to date, but it is questionable whether it can be applied to all species. This point will be returned to later. Mohler, Goldberg and Wurtz (1973) and Wurtz and Mohler (1976b) have pointed out that a functional link may exist between the FEF and SC, since behavioural enhancement occurs in both. Such a link might be responsible for "corollary discharge" i.e. a suppression of activity in SC movement-sensitive cells during a saccade which would have the function of maintaining stability in the visual world and prevent self generated movement from being confused with external movements in the environment (Robinson and Wurtz, 1976).

Latto and Cowey (1971b)reported a temporary amblyopia lasting about ten days in the contralateral visual field to a lesion of the SC (superimposed upon bilateral FEF lesions) in rhesus monkeys. More recent work has shown a slight threshold increase in central vision following SC lesions, though recovering in six weeks (Latto, 1978). Singer, Zihl and Pöppel (1977) also suggested a role for the SC in visual threshold control, particularly in relation to the resetting of visual thresholds elevated by the repetitive presentation of a stimulus, in a particular locus in space, to human subjects within the visual field defect produced by occipital cortical ablations. It might be deduced from this result that one aspect of differential control of attention by the SC may be in terms of the elevation of thresholds to repetitive stimulation. Interesting in this respect is a population of neurons reported by Sprague _et al_ (1973) which increase their discharge on repeated stimulus presentation. These are located in deep SC.

The above theories make no fundamental distinction between central and peripheral visual space, except insofar as the ultimate result of SC activity is often seen as the redirecting of central (foveal) retina towards more peripheral locations. However it has been argued that central visual space (i.e. the region of space towards which the animal's attention is currently directed) is treated differently from peripheral space. Trevarthen (1968a) has put forward an alternative "two visual systems" hypothesis, arguing that while cortical mechanisms subserve central visual space (the "manipulating and identifying" form of vision), the midbrain may have special responsibility for (less acuitous) vision in peripheral or "ambient" (cf Gibson, 1966; Lee and Aronson, 1974) space, witnessed by the fact that matching of objects on simple criteria (brightness, or what Trevarthen terms "thingness") between peripheral areas of the two hemifields is possible in patients with corpus callosum and other forebrain commisures sectioned (Trevarthen and Sperry, 1973).[1] Similarly Humphrey (1970) spoke of the visual decorticate monkey as having a "visual field" but not a "visual world" thus orienting to stimuli but not "perceiving" them. A similar type of hypothesis has been put forward by Goodale and associates (Goodale and Lister, 1974; Goodale and Murison, 1975; Goodale et al, 1976; Milner et al, 1978; Goodale et al, 1978; Milner et al, 1979) who have also recognised the likelihood of a functional dissociation between

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[1] However, no specific prediction about the nature and severity of visuomotor deficits following collicular ablation have been made from the model, particularly for lower animals. For references see Trevarthen's contribution to Ingle and Sprague (1975).

'central' (i.e. currently attended) and peripheral visual space, suggesting that the SC is involved in shifting the locus of attention to novel, peripherally located stimuli, while the geniculostriate system is involved in ambulatory localisation and the identification of objects and cues in central space. Since it is peripheral space which might contain potentially dangerous (predators) or informative (food) cues, it would seem vital for an animal to have a means of monitoring or 'interrogating' peripheral space with a view to orienting towards (Goodale et al, 1978) or away from (Ingle, 1970) stimuli as appropriate. In support of the theory, Goodale and Lister (1973) showed that SC rats were inattentive to novel peripherally-presented lights, sounds and tactile stimuli while engaged in a barpressing task. Goodale and Murison (1975) extended the finding of inattentiveness in SCs to runway behaviour and Goodale et al (1976) to the startle response, the amplitude of which was reduced in SCs when the animal was engaged in an "ongoing" behaviour during stimulus presentation. Goodale et al (1978) found that the orientation to "central" distractor stimuli was unimpaired in SCs in a runway task, while Milner et al (1978) obtained results in primates which concur with the above; Stumptailed macaques (fascicularis) were trained to make L or R responses depending upon the colour (red/green) of a central fixation light. On certain trials, the fixation light was immediately preceded by onset of a peripheral distractor light. It was found that SC-lesioned monkeys failed to redirect their attention to the peripheral light when it occurred within a part of the visual field falling within the "scotoma" produced by the SC lesion. A similar result has since been obtained by Albano and Wurtz (1978). Goodale summarises this theoretical position by saying that prey catching in anurans

> "Could perhaps be regarded as an evolutionary antecedent of the behavioural components of the visual orienting reflex in mammals",

and that

> "it could be argued that during the course of vertebrate evolution the principle neural systems underlying visuospatial control of locomotion and the orienting reflex may have remained anatomically distinct despite the growth of extensive interconnections".
>
> (Goodale <u>et al</u>, 1978)

Pharmacological stimulation of deep SC and the MRF with micro injections of cholinergic substances (Grossman, 1968) produced an extreme form of "hyperattentiveness" consistent with the above theory; a similar syndrome occurs during recovery from electrolytic SC lesions (personal observations: Murison, 1977; Pope and Dean, 1979)consisting of extreme "hyperreactivity" to suprathreshold stimuli, possibly due to irratitive deposits of iron from the lesion electrode in remaining remnants of collicular tissue (see Section 5.1.6.2).

3.6 Motor control

The SC has been termed a sensori-motor structure (Ingle and Sprague, 1975) responsible for visuomotor coordination:

> "The tectum ... is not only intimately associated with the retina and cortex, but, in "speaking" directly to the motor system, it constitutes a major link in the transformation of visual information into adaptive motor patterns." (Ingle and Sprague, 1975, p.173).

However, such terminology is clearly descriptive rather than explanatory, inferring that sensory and motor functions somehow interface or integrate within SC without specifying the nature of the relationship. Following the most debilitating lesion of SC (including destruction of deep laminae), tree shrews (Casagrande and Diamond, 1974; Casagrande, 1975) and cats (Sprague et al, 1973) were notably able to manoeuvre round barriers and obstacles; rats with deep lesions may fail to notice novel objects, yet do not collide with them (Marshall, 1978) while cats with similar lesions are able to swat accurately at pieces of food suspended before them (Myers, 1964).

Possible collicular influences upon motor behaviour will be considered under two headings: (i) fine control of movement and coordination, and (ii) control of gross movement and activity [1].

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[1] Oculomotor influences have been dealt with in a previous section (see Section 3.4) and will not be reconsidered here.

(i) Fine control

When required to reach towards briefly-presented peripheral stimuli, SC-lesioned primates frequently misreach, though they are capable of accurate reaching when the stimulus is of longer (500 msec) duration (Gross et al, 1974), though it is not clear whether in the former situation, the deficit is one of registering stimulus position, remembering stimulus position, or of guiding the limb(s) to the correct spatial location in the absence of a present visual cue. Collin (1977) reported that SC-lesioned monkeys show a preference for using their ipsilateral hand, particularly when deeper laminae were invaded by the lesion. In FEF-lesioned monkeys Kennard (1939) noted a similar effect which was especially pronounced for fine manipulations. Whether SC-lesioned animals show subtle manipulatory deficits, or tactile identification deficits is unknown.

(ii) Gross control

In addition to inattentiveness towards novel stimuli, rats with SC lesions have also been reported to exhibit hyperactivity when tested in a variety of situations. This has been independently observed by a number of experimenters (Isaac, 1971; Murison, 1977; Marshall, 1978; Foreman et al, 1978; Weldon and Smith, 1979; Pope and Dean, 1979). Isaac (1971) argued that the effect is confined to nocturnal species. Indeed, Cooper, Bland, Gillespie and Whittacker (1970) have argued (as a general principle) for the inhibitory, rather than excitatory, influence of visual stimulation upon motor activity. However Isaac's (1971) hypothesis predicts that the SC deficit would disappear when testing is carried out in darkness. But, from his own report, this is manifestly not the case; on the basis of separate studies, it is clear that illumination level does not modulate SC hyperactivity (Murison, 1977).

Nonetheless it is curious and perhaps significant that hyperactivity follows both SC lesions and amphetamine administration in nocturnal species like the rat (the latter treatment mimicking the inhibitory effect of high illumination on activity according to Isaac, 1971) while in diurnal species such as tree shrew (Casagrande et al, 1972) and monkey (Anderson and Symmes, 1969; Wurtz and Goldberg, 1972b) SC lesions result in hypoactivity and even immobility. Moreover, amphetamine administration also results in hypoactivity in the monkey, apparently supporting Isaac's (1971) argument. However the cat is an enigma since amphetamine administration (Kallman and Isaac, 1976) and placement in darkness (Isaac and Reed, 1961) result in increased activity, but SC lesions produce immobility and listlessness (Myers, 1964). Voneida (1970) using cats with lesions of tecto-reticular and tecto-spinal pathways reported inactivity, immobility and lethargic operant responding. However the "inability to withold responses" reported by Winterkorn (1975a,b) in cats suggests some degree of locomotor 'release', and Berlucchi (1974: informal personal communication to M A Goodale) has suggested that SC cats might give the impression of being overactive in some cases.

Furthermore, all animals with unilateral lesions of SC show marked ipsiversive circling postoperatively irrespective of their diurnal or nocturnal lifestyle (monkey: Denny-Brown, 1962; Pasik, Pasik and Bender, 1966; cat: Sprague and Meikle, 1965; Wood, 1975; rat: Kirvel, Greenfield and Meyer, 1974; Kirvel, 1975; Collin, 1977). This behaviour might reflect a unilateral motor effect similar to that observed (bilaterally) following bilateral lesions, and is perhaps dependent upon the same mechanism. However some doubt is cast on this assumption, since it is clear from the above that the direction of change in activity level following bilateral colliculectomy in a species does not dictate direction of turning produced by unilateral SC ablation. Ipsiversive turning was obtained in both light and dark conditions in unilateral SC-lesioned rats by Collin (1977), and in enucleated rats with unilateral SC lesions by Cooper <u>et al</u> (1970), demonstrating that like the hyperactivity seen in bilaterally lesioned SCs this is also independent of visual stimulation.

Though hyperactive, the bilaterally lesioned SC rat is not hyper-exploratory, since Marshall (1978) noted that colliculars rarely investigated novel objects which they encountered and Foreman <u>et al</u> (1978), recording the frequency and duration of a range of behaviours, found that investigatory behaviours such as sniffing and headraising (both of which frequently accompany locomotion

in control and VC-lesioned animals) were less frequently recorded for SCs; thus the increased activity was solely due to an increase in "unaccompanied" running. In contrast, however, an earlier study (Goodale and Lister, 1974) has reported unchanged activity levels in SC animals which were nonetheless inattentive in another behavioural setting. The lesions in this study were probably restricted largely to superficial laminae, suggesting that deep laminae damage was responsible for the hyperactivity observed by other authors. Thus it has been proposed by Foreman et al (1978) that for the rat, as for the tree shrew (Casagrande et al, 1972) a division of function exists between deep and superficial laminae, though in the rat the latter appear to be particularly involved in attentional shifts to novel stimuli, while deeper laminae exert control over the motor system.
The latter influence is presumed to be (at least in part) inhibitory, and may represent a further contribution of the SC to the orienting response, in that a total, coordinated orienting sequence to a point in peripheral sensory space requires not only orientation of receptor surfaces towards the point of stimulation but also an instant cessation of ongoing behaviour (i.e. behavioural arrest). This applies particularly to locomotor activity, since post-stimulus continuation of running would require successive recalculations of the amplitude of body/eye movement required to fixate the stimulus; by ceasing to run (and ceasing all other activity) a 'postural

baseline' is established enabling a single orienting movement sequence to be calculated. The SC is ideally situated to organise orientation of this kind. In addition to locomotor inhibition, an increase in cortical arousal occurs as the orienting response is initiated, perhaps preparing the animal for information processing and/or sudden action. It will be argued later that projections from the SC to brainstem nuclei and motor systems are involved in controlling such behavioural inhibition. In addition, deep collicular laminae also project rostrally to intralaminar nuclei which are thought to influence cortical arousal via the diffuse thalamic projection system; when stimulated, a cortical recruiting response ensues, further suggesting an arousal-related function (Starzl and Whitlock, 1952; see also Pearce, 1953, cited Altman and Carpenter, 1961, p.163).

Moreover, the electrophysiology of deep and superficial SC laminae is consistent with the above hypothesis, since cells in superficial laminae have small receptive fields and habituate slowly to repeated stimulus presentations, thus receiving precise information which defines points in space sufficiently accurately to define specific orienting movements, i.e. the amplitude of movement required for "tonic" orienting of the head and eyes. On the other hand, cells in deeper SC respond to the <u>presence</u> of objects (Humphrey, 1968), irrespective of their modality, or position in space, and habituate rapidly to repeated stimulus presentation; they may, therefore, subserve the "general" aspects of the orienting response namely the inhibition of ongoing movement and increasing of cortical arousal level. Thus according to this model a rat deprived of a SC, placed in a novel environment (a) fails to attend to novel features of the environment and (b) thus ceases locomotion less often. Moreover, such disinhibited behaviour in the rat might account for observations in other settings. Dean (1978) and Collin (1977) suggested that mild deficits in SC rats which appear to be perceptual in nature may be due to disruption of motor activity. Goodale et al (1978, Experiment 3), videorecorded in a large arena the behaviour of rats trained to run from a tunnel on one wall to the one illuminated of 5 goaldoors on the opposite wall, 91 cm from the tunnel exit. Good locomotor control was reported for SCs, in fact better than the controls, since the SC rats' runpaths approximated the least distance between tunnel and goaldoor. However when the situation was suddenly changed such that the rats now emerged from the tunnel at only half the distance from the goaldoors, SC rats (though not deficient in doorpress accuracy) exhibited erratic responses, running at great speed in a straight line from the tunnel and finally modifying their direction when in the vicinity of the goaldoors[1] clearly indicative of some lack of motor control. However such a result could conceivably have arisen from

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[1] Identical results have recently been obtained with gerbils (Goodale and Milner, 1980. Fig. 9.)

a simple tendency to run faster which had hitherto been controlled in the full sized runway, after prolonged training. This possibility was investigated by Murison and Mayes (1980) who found that SCs ran at the same speed as control animals when no discriminative response was required, but considerably faster in a 4-choice runway, on inital exit from the startbox, in agreement with the findings of Goodale et al (1978). Thus the SC animal would appear to be unable to inhibit running on occasions when it is necessary to stop and process information prior to redirecting or reorganising a response. Such erratic locomotion, particularly following changes in the test situation may explain both the findings of Schneider (1967, 1969) with hamsters, particularly since Schneider (1969) reported animals with lesions deep in SC to exhibit the most pronounced "approach error" behaviour, and perhaps the apparently erratic approach responses of SC cats in the studies by Winterkorn (1975a,b).

Whether a similar division of function exists in other species is unclear. In tree shrew (on which other models of functional dissociation are based), superficial laminae are mainly involved in pattern discrimination, while deeper lesions produce additional changes which are, indeed, motor in nature, though producing immobility in the homecage, and an inability to track moving objects, suggesting severe inattentiveness or even blindness (Casagrande et al, 1972; Raczkowski et al, 1976). However most behavioural testing has consisted of object and food perimetry. Thus in the absence of experiments on the tree shrew similar to those of Goodale et al (1978), it is not possible to make full comparisons, but simply to note that there may be important species differences in the effects of ablation, and thus that the SC may have differing functional roles depending upon the locomotor and attentional behaviour of individual species. For example, the erratic, highly aroused insect-seeking behaviour of the tree shrew might be under different neural control from investigation in the continually foraging rat.

Anatomical substrates

Isaac (1971) argued that the inhibitory influence of the SC upon locomotor activity is exerted via projections to the midbrain reticular formation. Indeed large lesions in the MRF were reported to result in elevated activity levels (Kesner, Fiedler and Thomas, 1967; Capps and Stockwell, 1968) though these lesions also invaded large parts of deep SC and destroyed most of the descending tectal efferents. Other authors (Foreman et al, 1978) have suggested that these crossed fibres of the predorsal bundle might have an inhibitory influence on the motor system via connections to brainstem reticular sites, in particular nuclei po, ngc and pc. Such a suggestion is well supported electrophysiologically in cat (Peterson, Anderson, Filion and Wilson, 1971) and by other studies which have shown the caudal brainstem reticular nuclei to have a general inhibitory influence on behaviour (Magoun and Rhines, 1946). In a recent study in rat, Lynch and Crain (1972) made electrolytic lesions in ngc and pc and found the animals to exhibit 3-fold activity increases. Conceivably the hyperactivity resulting from SC and brainstem nuclei (to which the SC projects) which are of a similar order of magnitude may arise from assault to different parts of an interconnected system. Unfortunately, attentional measures were not taken in the Lynch and Crain (1972) study, so it is unclear whether attentional and activity changes are independent or related. Interesting in this respect are some recent unpublished results (Pope, Dean and Redgrave, 1979, personal communication) suggesting that the activity elevation following SC lesions is reproducible by introducing small quantities of kainic acid into the SC in rats. Large cells in intermediate SC are selectively destroyed by this procedure (see also Merker, 1978, who reports identical findings for the hamster), suggesting that the large stellate neurons in sgi and sai are particularly related to motor activity. However, the same kainic acid injections failed to abolish attentional behaviours (eg attention paid to holes in the floor of an apparatus). It would at this stage be unwise to assume a sharp functional distinction between ascending (attentional) and descending (motor) projections, since Voneida (1970), Thompson (1976) and Raczkowski *et al* (1976) have all suggested that perceptual or attentional deficits may ensue following lesions of predorsal bundle and brainstem reticular sites (thus due, possibly, to damage inflicted upon tectal efferents).

The effects of unilateral lesions of SC are also consistent with the "locomotor inhibition" model; predorsal bundle fibres project exclusively contralaterally, thus unilateral lesions might be predicted to result in the removal of an inhibitory influence on contralateral motor structures, giving rise to ipsiversive turning in addition to contralateral sensory neglect; indeed such has been found (Pasik and Pasik, 1966; Cooper _et al_, 1970; Sprague _et al_, 1973; Kirvel _et al_, 1974; Kirvel, 1975; Wood, 1975; Collin, 1977). However, unilateral lesions may present a more complex problem, in view of the inhibitory influence of the intertectal commisural pathway (Goodale, 1973; Sprague, 1973) and the interacting ipsilateral cortico-tectal facilitation (Sherman, 1974; Sprague, 1973; Wood, 1975). Thus a complex intehemispheric imbalance might be produced by such a lesion. This is emphasised by the work of Wirtshafter _et al_, (1978) who argue that apomorphine-induced turning after unilateral substantia nigra (sn) lesions is the result of nigral influence on the SC. Turning was greatly reduced following unilateral sn lesion when coupled with a simultaneous lesion of the predorsal bundle. (The influence of the sn must be assumed to be inhibitory on the SC since a unilateral sn lesion produces contraversive turning while a unilateral SC lesion produces ipsiversive turning). However histology is currently unavailable. Since the percentage of predorsal bundle fibres transected may be crucial this hypothesis cannot be fully evaluated.

Additional support for the 'behavioural inhibition' model of descending tectal efferents comes from electrophysiological stimulation and recording. The above model predicts that circuitry in the pontomedullary RF will have general inhibitory functions related to the onset of attentional behaviours. Mirsky, Bakay Pragay and Harris (1977) stimulated the brainstem RF of an animal (rhesus monkey) engaged in an attentional (colour discrimination go- no-go) task. They found that a number of responses could be elicited from brainstem stimulation, including "omission errors in the attention task, decreased amplitude of the VER and an 'arrest' reaction", further that "of all the effects produced by stimulation, the arrest reaction was the most durable" (p. 252). Though indirect evidence, it is perhaps significant that the SC projects to loci which, when stimulated, produce cessation of ongoing behaviour. Raybourn and Keller (1977) investigated the response of functionally-identified medial PRF neurons to stimulation of the SC and found that 50% of eye movement-related cells received synaptic input from SC, but 83% of the non-eye-movement related class (the latter showing longer latencies; 3.8 msec against 2.0 msec for the former).

Thus the "PRF is thought to contain the immediate supranuclear neuronal networks for the control of all types of conjugate horizontal eye movements" (p. 862). It is surprising that though stimulation of (deep: see p.863) SC produces activity in 67% of PMRF neurons, only half discharge in relation to eye movements. Indeed, Raybourn and Keller (1977) report neuron populations responding selectively to distal limb movement, or to "any type of alerting stimulus - sudden noise, light flash, object moved towards the animal, or light tactile touch on the face", and that "repetitive application of the same stimulus resulted in habituation of their response." (p. 873).

Furthermore Raybourn and Keller (1977) summarise their findings by saying that,

> "Our findings that the colliculus possesses extensive input into PMRF neurons not functionally related directly to eye movements, but closely related to attention, also lends some support to the idea that the role of the colliculus in oculomotor control is that of alerting other neural circuits of significant visual targets ..."

However the idea that the sole function of PMRF neurons relates to "attentional" behaviour and excitatory processes cannot be upheld in view of Mirsky et al's (1977) results of stimulation, and indeed, since the region of reticular formation concerned has long been recognised as a general inhibitory locus (Magoun and Rhines, 1946; Sauerland, Nakamura and Clemente, 1967), it is distinctly unlikely.

3.7 Models of intrinsic SC organisation

From the foregoing it is clear that at least three possible modes of internal organisation are possible for the SC; these have been discussed by Mohler and Wurtz (1976).

(1) According to "The classical model", (so named by Mohler and Wurtz, 1976) visual information entering superficial laminae passes down or 'cascades' through the SC to intermediate and deep laminae, undergoing some form of coding. It leaves the SC from intermediate and deep laminae to project to brainstem eye movement and 'orientation' centres (see Schiller, 1972; Robinson, 1972).

(2) Casagrande et al (1972) have argued that each of the SC laminae may operate as separate input and output channels. The model is based on anatomical findings in tree shrew and bushbaby which do indeed suggest afferent and efferent segregation with regard to 'independent' laminae.

(3) The 'convergence' model of Wurtz and Goldberg (1972a) and Mohler and Wurtz (1976) is based wholly on primate (rhesus monkey) work which has shown that cells in deep SC (a) show 'enhanced' discharges prior to saccades to their visual fields, and (b) fire before superficially located cells, suggesting that deep cells (which receive input from extrastriate regions of the brain) are involved in 'enhancing' (or increasing the probability of evocation of) saccades to salient (or biologically significant) stimuli within

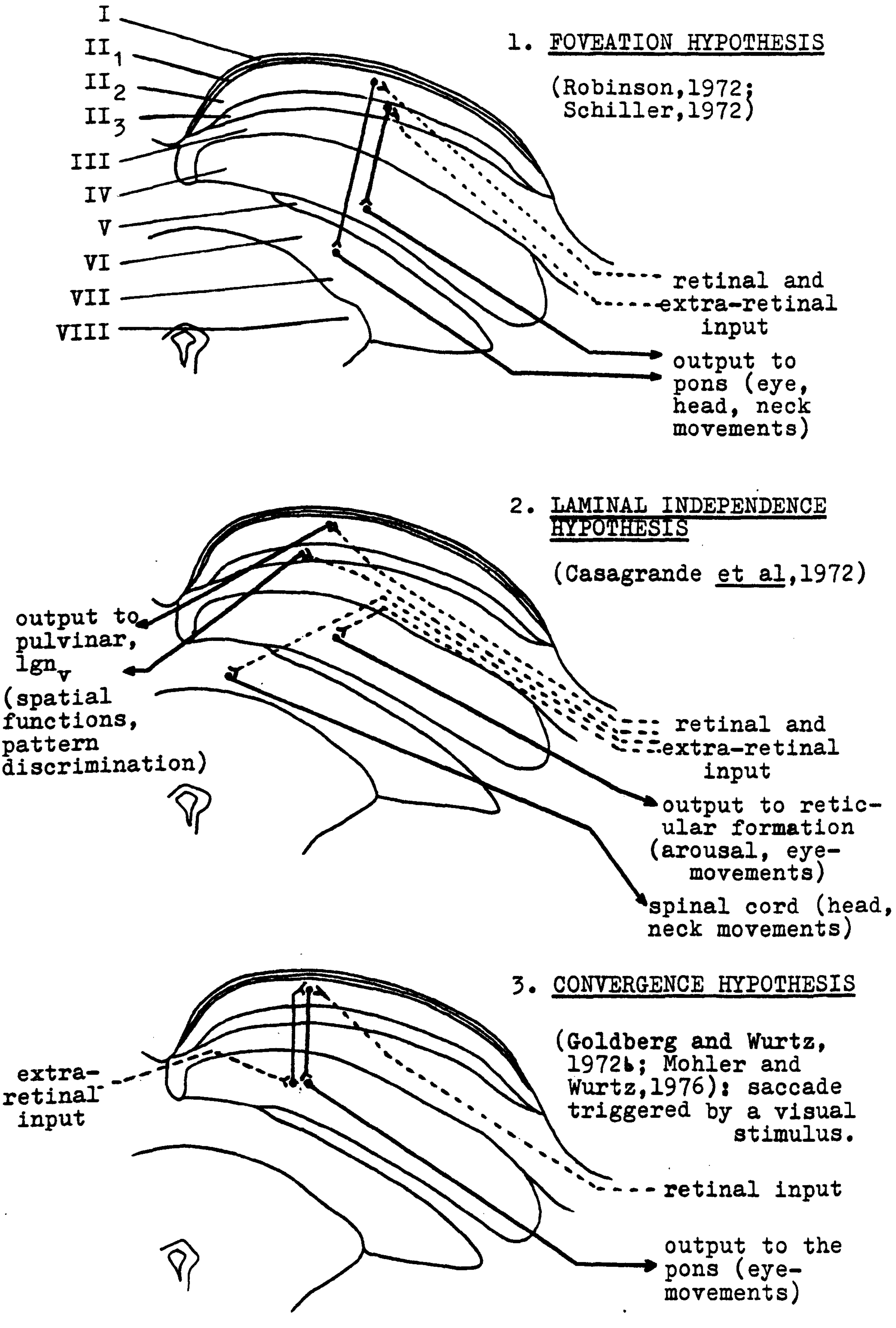

Figure 3.1
Diagramatic representation of 3 possible modes of collicular organisation. (These are not anatomically accurate, and show only the afferent, efferent and intracollicular pathways emphasised, or suggested, by each model).

the cell's receptive field. Wurtz argues that this process may enable an animal to separate "those stimuli ... used for behaviour from those which are not". Although this is an attractive model, certain reservations must be held since

(i) Only 51% of (pandirectional) cells in SC show the "enhancement" effect, and within this population, some show 'early' while others show 'late' enhancement, suggesting separate functional roles,

(ii) If the "attentional status" or "value" of a stimulus is determined elsewhere in the brain and projected to SC, it might be expected that "habituation" to novelty (one aspect of selective attention at a neuronal level according to Horn, 1970) would cease to be a characteristic of deep SC units, following cortical cooling or ablation, and this is clearly not the case (cat: Horn and Hill, 1966; rabbit: Masland <u>et al</u>, 1971), suggesting that the SC possesses <u>intrinsic</u> 'novelty detecting' functions, a deduction which might be made from other studies (frog: Lettvin <u>et al</u> 1961; cat: Rizzolatti <u>et al</u>, 1974; see Ingle, 1975).

(iii) If, as Wurtz (Mohler and Wurtz, 1976) suggests, the function of the SC is to facilitate eye movements towards a "general area" of visual space, it would not seem necessary for the superficial SC laminae to possess precise retino-topography, and the regional differences in grain of topography would appear to have no functional purpose.

(iv) The model does not account for the anatomical findings of Casagrande's group (Casagrande <u>et al</u>, 1972;

Weber et al, 1979; see above). However Wurtz (Mohler and Wurtz, 1976) recognises that his results are not inconsistent with the "independent laminae" hypothesis; indeed both systems may coexist.

(v) Since the model is wholly based on primates, a quite different model may be required for other species. In the rat for example, where few eye movements are observed, orientation consists largely of re-aligning the head and body, yet the latter are apparently poorly coded in SC at least in primates (Robinson, 1972). It is not clear whether the "enhancement" effect reported in primates in relation to eye movements occurs in the SC in lower animals prior to head and body movements which orient the animal towards a stimulus.

(vi) The effect of SC lesions in monkeys is consistent with the "convergence" hypothesis, since they lead to decreased saccadic accuracy and increase in 'corrective' saccades. However, since the effect lasts only six weeks, and other, perhaps related, SC-lesion deficits also last 10 days - 3 weeks (Latto and Cowey, 1971b) or less than 6 weeks (Latto, 1977) it is surprising that a supposedly "unique" function of such a prominent brain structure can be so readily compensated by functional reorganisation.

(vii) Following from point (vi) it is perhaps significant that the only permanent deficit found in animals with SC lesions is lack of attention to novel stimuli (i.e. 'unexpected' stimuli) (Milner et al, 1978) which, as Ingle (1975) has pointed out, remain uninvestigated vis à vis the enhancement effect.

(viii) While the model attributes major eye movement efferent output to cells in intermediate laminae, it is clear that cells in deepest SC laminae have larger visual fields than in intermediate laminae (cat: Cynader and Berman, 1972) and have extremely low eye movement thresholds, often 50% of those in intermediate laminae, suggesting that deep cells have particularly strong and direct associations with saccadic mechanisms (Robinson, 1972).

(ix) Those cortical regions which have been studied to date have response latencies to visual stimuli which are longer than those in SC (FEFs: Robinson and Fuchs, 1969; ITC: Buchtal, 1976, personal communication), thus where does the activity originate from which presaccadic enhancement is generated?

(x) It is unclear from the model why (deep but not superficial) bilateral damage to SC should produce motor effects, for example activity changes in many species (see above), and unilateral lesion a shift in hand preference (Collin, 1977).

(xi) Raybourn and Keller (1977) have argued from electrophysiological data that

> "these two 'descending' and 'convergence' hypotheses concerning collicular function are not mutually exclusive. Indeed our data seems to suggest that the SC may be involved in both roles."

Thus the problem might be summarised by asking "How much processing related to attentional/foveational/orienting behaviours is intrinsic to SC, and how much is "programmed" from outside?" The difficulty with attributing too much autonomy to a particular structure is that the rest of the cerebrum begins to appear superfluous (cf early theories of reticular arousal functions: Milner, 1970).

A possible resolution of the problem emerges if one makes the plausible assumption that a certain class of stimulus is processed by SC "intrinsically" (for example on the basis of stimulus parameters; intensity, position, etc.) [1], output from which is transmitted immediately to attentional and oculomotor systems [2], while other classes of stimuli (complex stimuli of biological significance) require 'enhancement', or otherwise the involvement of more sophisticated forebrain mechanisms.[3] Such a hypothesis is clearly testable since it predicts that the cortically-damaged animal will exhibit orienting deficits specifically to "higher order" classes of stimuli but not to "simple" stimuli, while the SC-lesioned animal will be equally inattentive to both. In addition, it is necessary to postulate substantial species variation in (a) the type of stimulus which will be of high "attentional status" to the SC and (b) the type of orientational behaviour controlled by the SC, depending upon the animal's vulnerability, habits and style of locomotion and exploration.

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[1] i.e. that the SC "self-enhances" or "self-depresses" for this class of stimulus.

[2] cf amphibians (Karten, 1975).

[3] It is perhaps worth noting in this respect that orienting evoked by "stimulus meaning" is slow by comparison with that evoked by "stimulus parameters" (eg. intensity, etc.,); see Lynn, (1966).

CHAPTER 4

THE RELATIONSHIP BETWEEN THE SUPERIOR COLLICULUS AND OTHER BRAIN STRUCTURES

4.1 Superior Colliculus and Hippocampus: A comparison

Almost without exception, prominent theories of SC function can be matched by corresponding theories attributing similar or identical functions to the hippocampus (HPC), for example both have been implicated in attentional, spatial and (inhibitory) motor behaviour. This may arise from coincidence, a genuine functional similarity or relationship between the two structures, or alternatively from the gross nature of the tests used to identify the consequences of brain damage in animals; if the latter, it follows that close inspection of the behavioural data might uncover subtle behavioural differences between animals with SC and HPC lesions. On the other hand, because of the early phylogenetic appearance of both (Kappers, Huber and Crosby, 1960), their close anatomical proximity, and prominent acetylcholinesterase (AChE) activity (e.g. HPC: Mellgren and Srebro, 1973; SC: Foreman and Srebro, 1979, unpublished) it might be inferred that they are functionally related, perhaps via ancient neural circuitry. They share similarities in single unit responses, both possessing a population of multimodal, fast-habituating neurons (HPC: Vinogradova, 1970), others discharging in relation to orienting movements (HPC: Ranck, 1973), and the results of damage in either structure in humans suggests that the functions of both are unavailable to conscious awareness (Weiskrantz, 1977).

The anatomy and physiology of the HPC will not be described here, since ample reviews have recently appeared (Altman, Brunner and Bayer, 1973; Isaacson and Pribram, 1975; O'Keefe and Nadel, 1978 [1]). It is important to note, however, that no direct projections between SC and HPC have been identified (Raisman, Cowan and Powell, 1965, 1966), though connections do potentially exist via cortical relays, via collicular projections to the midbrain reticular formation or hypothalamus (Kappers et al, 1960; see review in Trulson and Randall, 1973). Indeed some authors have gone as far as suggesting that the SC represents a "limbosomatic convergence centre" (Powell and Hoelle, 1967).

A further important reason for comparing the two structures is that lesions of SC are traditionally made using a dorsal approach and therefore invariably encroach upon the cingulate/subicular region where damage may result either from electrode passage or from dorsolateral spread of the lesion. Such is the case in both rat (see Experiment 1.4) and monkey (Wurtz and Goldberg, 1972a); in cat this is rarely the case, since lesions of SC are usually made under visual guidence using an aspirator. Unlike the SC, behavioural studies of HPC have most frequently involved rats, and cross-species comparisons are more limited.

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[1] Statements hereafter not specifically referenced are covered at length in O'Keefe and Nadel (1978).

4.1.1 Motor Control

The HPC has never been credited with responsibility for fine movement control, though the appearance of characteristic high voltage, slow wave activity (θ) has been associated with the initiation and/or control of "voluntary" motor movements (Vanderwolf, 1971). However a number of authors have viewed the structure as exerting a predominantly inhibitory influence upon behaviour (Douglas, 1967; Kimble, 1968, 1976; Altman et al, 1973), evidenced by the findings that HPC-lesioned animals are (i) hyperactive, (unable to inhibit prepotent investigatory tendencies, according to Douglas, 1967), (ii) perseverative in extinction, and unable to "withold" a response when required to do so, (iii) inflexible in their use of response strategies (e.g. 'reversing' slowly and spontaneously alternating at chance level), and (iv) are unaffected by "external inhibitory" influences (i.e. distracting stimuli) while engaged in an ongoing task (see also Crowne and Radcliffe, 1975, p. 188). This has resulted in the characterisation of the HPC animal as "reckless, exuberant and unobservant", as if behaving in a "juvenile" fashion; indeed, in contrast to SC, postnatal development of HPC is substantial, and development of dentate granule cells has been held responsible for the development of "adult", restrained behaviour in rats at about 25 days of age (Altman et al, 1973).

In discrimination learning tasks, animals with HPC lesions show normal acquisition performance but slow extinction and reversal learning. They tend to leave a startbox faster and run at greater speed than controls in runways (Riddell, Rothblatt and Wilson, 1969, Cohen, 1970; though see Means, Leander and Isaacson, 1971). Indeed when HPCs are selectively rewarded for running slowly in a runway, they are incapable of doing so (Rickert and Bennett, 1972). Such behaviour could clearly be viewed superficially as resembling the erratic running of cats with SC lesions in a discrimination task (Winterkorn, 1975a,b) particularly as SCs also fail to commit more doorpress errors than controls, though in contrast to hippocampectomised animals, rats with SC lesions are unimpaired on light v dark reversal learning (Murison, 1977).

Increased general activity has been recorded for hippocampals in a number of experiments (O'Keefe and Nadel, 1978; see Table 4.1), and has been considered by some (Blanchard, 1976; personal communication to J Watts) to be "diagnostic" of HPC damage. Blanchard, Blanchard and Fial (1970) have argued that the hippocampal rat is unable to maintain an "arrested" (defensive, immobile) posture, and Teitelbaum and Milner (1963) suggest more strongly that they are unable to inhibit movement. Indeed, stimulation of the HPC has been reported to bring about behavioural arrest (Maclean, 1957) and to slow goal-directed running (Correll, 1957) suggesting that HPC removal may represent "motor release" from inhibitory influence. However, the appearance and extent of hyperactivity shows marked variation between laboratories, dependent upon species, lesion size, apparatus size, design and illumination, test session length, age and level of deprivation of subjects and postoperative recovery period which are confounded within Table A14 shown in O'Keefe and Nadel (1978). Other variables also cloud the issue. For example, some authors have pre-habituated animals to the postoperative test environment, which Table 4.1 shows to be a potentially significant variable.

To summarise, large lesions of dorsal and ventral HPC give rise to increased activity when testing is carried out over a sufficiently long interval. However, from the majority of studies it is clear that (in marked contrast to rats with SC lesions) hippocampals are no more active than controls upon initial placement in an apparatus, and that the apparent increase in activity arises from "delayed or absent habituation" (Jarrard, 1973; see also Means, Leander and Isaacson, 1971; Douglas and Isaacson, 1964; Gray, 1971b, p.205). O'Keefe and Nadel (1978) write that

> " ... the failure of all hippocampal animals to respond immediately in novel situations means that activity measures must not be too brief if they are to reveal differences between normals and hippocampals.",

and note that certain experimenters (referring to Hostetter and Thomas, 1967) may have failed to find such differences since they

> "observed their animals for only four minutes in the open field" (p.256)

On the other hand, it should be noted that in certain instances, hippocampals have been reported to display immediate hyperactivity (Roberts, Dember and Brodwick, 1962, Experiment 1; Kimble, 1963; Altman et al, 1973; Köhler, 1976).

STUDY	POSTOP RECOVERY TIME (days)	LESION	SESSION LENGTH (mins)	% INCR'SD ACT'Y IN HPCs v CONTROLS	PREOP EXPOSURE TO APP.
A. Studies reporting increased activity					
Teitelbaum and Milner, 1963	42	d+v	60	500	yes
Lanier and Isaacson, 1975	>14	lge d	5,15	400	yes
	>14	lge d+v	5,15	700	yes
Roberts et al, 1962 (Ex.1)	30	mod. lge	5,15	50	no
Glickman et al, 1976 (gerbils)	17	lge d+v	10	700	yes
Kimble, 1963	8	d+v	10	200	yes
Kimble, 1976	2-16	lge d	10	50	yes
Kimble, 1978	2-9	lge d	5	50	yes
Iuvone and van Hartesfeldt, 1976	20	lge d	5	70	yes
Means et al, 1971	19+	lge post.v	5	450	no
B. Studies reporting mildly increased activity					
Nadel, 1968	?	d , v	60	25	no
Köhler, 1976	13	d	15	mild	no
Roberts et al, 1962 (Ex.2)	130	mod.lge.d	5,15	20-30*	no
C. Studies reporting no change					
Rabe and Haddad, 1969	10-14	a-d+p	5,15	**	no
	10-14	lge a	5,15		no
	10-14	lge p	5,15		no
Strong and Jackson, 1970	30	lge d	15	**	no
Venables, 1978	6-12	d+v	5		no
Hostetter and Thomas, 1967	14	d	4		no
Greene and Stauff, 1976	7	lge.fx	10		no
Myhrer and Kaada, 1975	?	fx	2		no
Boitano et al, 1968	150	lge	?		no

Table 4.1

Summary of experiments investigating open field activity in hippocampal rodents (max. session length 60 minutes).

Notes

See also Table A14 in O'Keefe and Nadel (1978), from which references to studies cited in the above table, but which are not given in the present bibliography, may be obtained.

* indicates that in the study by Roberts et al (1962), increased activity was only significant in the hippocampal group (Ex.2) when spontaneously alternating hippocampal rats were removed from the analysis.

** indicates that hippocampals were no more active than cortical controls but slightly more active than sham operates.

HIPPOCAMPAL LESION KEY: d - dorsal, v - ventral, a - anterior, p - posterior, fx - fornix, mod.lge - moderately large.

As with the SC (Foreman et al, 1978; Pope and Dean, 1979), size of hippocampal lesion is a significant factor in determining postoperative activity. Lesions simultaneously damaging dorsal and ventral HPC produce the most prominent and persistent hyperactivity while "recovery" of normal activity levels occurs with smaller lesions (Kimble, 1976; Lanier and Isaacson, 1975).

Not all authors agree upon the extent of hippocampal hyperactivity; among those reporting the phenomenon estimates range from a 20 - 30% increase (Roberts et al, 1962) to 500% (Teitelbaum and Milner, 1963; Lanier and Isaacson, 1975). Updyke (1968) and Venables (1978), the latter reporting the results of 5 min test sessions on postoperative days 6 and 12, notably failed to obtain hyperactivity from animals with lesions comparable to those used in studies in which extreme activity was observed. Roberts et al (1962) obtained group differences only when spontaneously alternating hippocampals were selectively removed from the activity analysis, even though these animals had sustained damage to hippocampal tissue.

Green and Stauff (1974) failed to obtain increased activity from animals with large fornix lesions, or with damage to cingulum and subiculum, over 10 minutes of testing. This is particularly significant, since fornix lesions virtually abolish cholinergic activity in the HPC (Olton and Werz, 1978), and it is this transmitter which is generally related to inhibitory functions (Carlton, 1963), paricularly in the HPC (see Isaacson and Pribram, 1975).

It is interesting to note that even in cases where elevation of activity level has not been observed, the lesion has been seen to promote other behavioural changes; for example Hostetter and Thomas (1967) found HPCs to spend a larger proportion of their time near the perimeter of the apparatus than controls (see also Kimble, 1963). This "enhanced thigmotaxis" corresponds to a similar behaviour in rats with deep SC lesions (Foreman et al, 1978; Pope and Dean, 1976, personal communication).

Marshall (1978) and Foreman et al (1978) have reported that SC rats show reduced levels of investigatory behaviours such as sniffing and headraising, and almost never rear up on their hind legs. Running, which in control animals is almost always accompanied by investigatory behaviour is rarely so in SCs. Though O'Keefe and Nadel (1978) argue that HPCs are "hyperactive" but "hypoexploratory", in fact a different pattern of open field behaviour is observed from that described above for colliculars. For example, Nadel (1968) reports more "walking and sniffing" in rats with dorsal HPC lesions, while rats with ventral HPC lesions "rear and sniff" more. Glickman, Higgins and Isaacson (1970) reported increased locomotion in HPC gerbils, though accompanied by increased rearing, sniffing and drinking during 10 minute test bouts; admittedly the same animals investigated novel objects less than controls. Kaplan (1968) reported increased exploratory headpoking in hippocampal rats, and Altman et al (1973) note that since environmental cues are investigated less by HPCs "they remain ... novel for a longer time" (p. 570); this may form the basis of an habituation deficit. In contrast it is unlikely that SCs ever detect a novel object or treat it as novel, and therefore the issue of habituation does not arise. Kimble (1963) reports increased activity and error rates for hippocampectomised rats on a Hebb-Williams maze, mirroring the result of Smith and Weldon (1976) for SCs, though Gross, Chorover and Cohen (1965) point out that 6/10 animals in Kimble's (1963) study had sustained lgn damage. In a separate study, however, similar results were obtained from hippocampals which do not appear to have sustained lgn damage (Kviem et al, 1964), and on other types of spatial maze (Jackson and Strong, 1969).

Vinogradova (1970), Gray (1971b) and O'Keefe and Nadel (1978) have inferred that motor control by the HPC is related to the redirecting of attention. Vinogradova (1970) draws comparisons between the "novelty detectors" of Lettvin, Maturana, McCulloch and Pitts (1959) in amphibia, and neurons in cat HPC, arguing (as do Nadel and O'Keefe, 1976) that a function (the function?) of the HPC is to detect novelty and, as appropriate, 'block' or 'deblock' the arousal system (ARAS), altering motor behaviour accordingly (see also Kimble, 1968). It is important to note that these authors have recognised the necessity for "behavioural arrest" to accompany orientation to novelty, though clearly, unless HPC and SC are both involved in a single orienting process, the model of Gray (1971b), Vinogradova (1970) and O'Keefe and Nadel (1978) contradicts that of Foreman et al (1978) who attribute such functions to the SC. Indeed as argued above it might be suspected that an animal grossly inattentive to novelty[1] would exhibit increased activity but reduced investigation upon initial placement in an apparatus, though there are few cases where this has been reported for animals with HPC lesions (see above).

Varied results have been obtained from recordings of activity over periods of 24 hours or more. Kim, Choi, Kim, Chang, Park and Kang (1970) and Jarrard (1976) report activity increases in hippocampal rats especially at night, while Kviem et al (1964) and Kaada et al (1961) failed to report elevated activity in a running wheel apparatus. By comparison, collicular rats show no increase in activity in their homecage over 24 hrs compared with normals, according to a recent study (Carson and Goodale; cited Foreman et al, 1978).

In hamsters, Jarrard and Bunnell (1968) report no increase in activity when satiated following hippocampal lesions, and in monkeys (Douglas and Pribram, 1966) and humans with medial temporal resections (Milner, 1966), depression of activity and lethargy are observed.

4.1.2 Attention

Local stimulation of the HPC gives rise to orienting, sniffing and other investigatory behaviours (Kaada,1951), suggesting a fairly direct involvement in either the

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[1] i.e. an attribute of the environment which does not find a representation within the animal's "cognitive map" of the environment, according to Nadel and O'Keefe, 1974.

switching of attention (in Sokolovian terms; see Sokolov, 1969; Gray, 1971b) or the initiation of investigation, though unlike the SC, the HPC possesses no sensorimotor "homunculus", and locus-specific eye movement-related activity has not been reported to date. Conversely Grastyan, Lissak, Madarasz and Donhoffer (1959) report that far from eliciting orientation, stimulation of the HPC produces an inhibition of the orienting response.

A general "attentional" role is suggested by the presence in the HPC of multimodal, fast-habituating neurons (Vinogradova, 1970), some firing during orientational behaviour (Ranck, 1973), and the strong connections between the HPC and reticular formation (Green and Arduini, 1954), though perhaps most strongly by the presence of cells specifically sensitive to novel stimulation (Vinogradova,1970). Thus it is possible that the HPC acts as an interface, comparing current sensory events with stored memory and eliciting orientation when novelty ("mismatch") is detected (Vinogradova, 1970; Gray, 1971b). However, it should be noted that electrophysiological studies have failed to demonstrate a strong relationship between collicular and hippocampal conduction pathways (Maclean, 1975).

A number of authors have reported HPC lesions to produce abolition or diminution of the orienting response; in particular, the introduction of a novel sandpaper floor surface in a runway increased response speed in hippocampal rats (Raphaelson, Isaacson and Douglas, 1965) and, following runway studies using various sudden visual and auditory stimuli Wickelgren and Isaacson (1963) concluded that hippocampals are "totally undistractable". This is clearly reminiscent of results obtained by Goodale and associates (1975,1978) with collicular rats. Further indirect evidence comes from Ackil, Mellgren, Halgren and Frommer (1969) who showed that preexposure to stimuli failed to retard conditioning to those stimuli (the "preexposure" effect) in HPC-lesioned rats, suggesting that they had failed to attend to the (initially irrelevent) cue.

However Crowne and Riddell (1969), using very large lesions of hippocampus and overlying cortex (often invading lgn), reported a decrease in, though not absence of, overt orientation to novel stimuli presented while the animal was traversing a runway, and heartrate abnormalities,though HPC lesions produce abnormal heart rate changes in response to other kinds of stimuli; see Jarrard and Korn, 1969; Plunkett, 1979. Thus the effect may not be related to attention <u>per se</u>. Reduced somatic response to distraction was noted in hippocampectomised cats by Rogozea and Ungher (1968). Thus the orienting response does not appear to be abolished, though it may be truncated, following lesions of HPC. Such a conclusion is also consistent with the results of Kaplan (1968) and Gustafson and Koenig (1979) using barpress situations and Riddell <u>et al</u> (1969) using a runway. Direct comparison of such experiments with those of Goodale and Murison (1975), Goodale <u>et al</u> (1978) and Collin (1977) is difficult since in hippocampal studies, animals' actual behaviour during distraction was not carefully noted or filmed. Also, studies have tended to confound habituation with novelty, distractors being presented on successive trials. No unilaterally-lesioned HPCs have been tested in such situations.

Douglas and Pribram (1969), in an important study with monkeys, showed what appeared to be a lack of attention towards novel stimuli. These consisted of unexpected digits presented among others to which the animal had been trained to respond. In terms of latency, their results show that behaviour was unaffected by novel stimulus presentation, yet the animals *did* appear to notice the stimuli, and made hasty barpress responses in the course of orienting and becoming generally disturbed. This is reminiscent of Raphaelson *et al*'s (1965) report of "acceleration" in HPC-lesioned rats on novel stimulus presentation while they traversed a runway.

Kaplan (1968) reports "perseveration" of goldoor approach in HPCs, which Jarrard (1968) is inclined to attribute to increased motivation, perhaps explaining why they are little affected by extraneous stimuli. However Cohen (1970) showed that HPC-lesioned rats explored a side alley added to a runway less than controls with cortical lesions, whether or not the animals had been trained to traverse the runway for food. However *both* hippocampals and cortical controls were less affected by the movement of the side alley to a new location on the runway than totally normal animals. This result inspires caution since (i) cortical processes may be involved in such attentional behaviour, or (ii) slight hippocampal damage in cortical controls may be sufficient to produce impairments.

Kimble (1968), Hendrickson, Kimble and Kimble (1969) and Crowne and Riddell (1969) have argued that hippocampals are only deficient when a *shift* of attention is required (ie. normal when not engaged in any form of ongoing behaviour).

Interestingly, a similar argument might be made for SC rats in that Goodale et al (1975) showed that startle response amplitude in the SC rat was attenuated when the animal was engaged in ongoing behaviour though not when sitting in an alert but inactive state.[1] Kaplan (1968) and Goodale and Lister (1974) report reduced suppression of barpress responding in HPCs and SCs respectively upon "distraction" via a peripherally located novel stimulus.

Nadel and O'Keefe (1974) argue for an attentional switching funtion for HPC:

> "When an unexpected stimulus occurs (or an expected one fails to occur), the expectation generated by the cartoon is not confirmed, and a signal is produced which arrests ongoing behaviour, directs attention towards the incongruity, and allows for its exploration. Such exploration, according to the model, is behaviour designed to incorporate the changed conditions into the cartoon for that environment." (p. 382)

However, using the same model, the same authors elsewhere (O'Keefe and Nadel, 1978) say, of animals with hippocampal lesions

> "Thus, available evidence suggests that hippocampal animals show normal startle, arrest and orienting and that their habituation of these reactions upon stimulus repetition proceeds normally as well. However little behavioural exploration of novel items is seen in these animals", (p. 250)

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[1] This result may be specific to situations in which a "startle" type of behaviour is elicited since it represents the one example of near normal orienting behaviour (in one condition) in SC rats.

and that,

> " ... 'failure of orienting' ... may have resulted from the lack of exploration, rather than orienting." (p. 251)

Thus it is unclear whether these authors regard the HPC as primarily involved in attentional shifts or not.

Leaton (1969) using a multiple-U maze trained rats to asymptotic running speed with 'blind' alleys (leading from the main runway) blocked. On removal of the blocks, HPCs ran normally (inattentively) if the 'distractor' alleyway was visibly very different from the main runway, though were distracted when main runway and blind alleys were visually homogeneous. This suggests a more subtle deficit than the "gross orientation" discussed hitherto. Indeed the result suggests that HPCs are specifically under-attentive towards highly novel stimuli but are disrupted by ambiguous, confusing stimuli which require careful 'sorting'. A similar suggestion has recently been made by Moore (1979). Other authors have emphasised the subtlety of the HPC orienting deficit, suggesting a particular difficulty with shifting attention between classes of complex stimuli, especially when in an aroused state (Altman et al, 1973; Jarrard, 1965; Silveira and Kimble, 1968; Winocur and Mills, 1970).

Perhaps ironically the possibility that HPCs suffer from inattentiveness in some situations is totally inconsistent with one prominent theory of HPC function, namely that of Douglas and Pribram (1966) who suggest that the HPC is responsible for the attenuation or "gating out" of stimuli from attention which are either irrelevant, redundant or whose reward associations have changed. The former clearly include irrelevant "distractors", thus the theory might be inferred to predict that (i) the HPC has a "damping" or inhibiting influence upon orienting mechanisms (possibly SC or the reticular formation), (ii) that orienting mechanisms may initiate the orienting response by overcoming the hippocampal "gate", (iii) that orientation to peripheral cues (whether or not they are relevant) in the hippocampal rat will (a) occur normally, perhaps in an exaggerated form, and (b) persist for longer, i.e. habituate slowly, giving an overall tendency for the HPC animal to be hyperdistractable. Hendrickson _et al_ (1969) point out that this is clearly inconsistent with their runway distraction data, though other authors have reported increased reactivity following HPC ablation. Karmos and Grastyan (1961) report "hyperactive orientation to conditioned and nonconditioned cues" in hippocampal dogs, and Glickman _et al_ (1970) reported greater and prolonged exploration in hippocampal gerbils. Sengstake (1968) suggests that activity elevation over long periods may reflect increased sensitivity to intero- and extero-ceptive cues, and in a number of studies, animals with HPC lesions have tended to make more use of peripheral cues than controls. Stevens and Cowey (1972) report enhanced alteration by the addition of light cues in HPCs, presumed to result from the hippocampals' noticing the "remote visual cues more readily than controls" predictable from the "sensory gating" model (Douglas and Pribram, 1966). The addition of cues relevant but redundant to an operant task has been shown to improve hippocampals' performance (Winocur and Bindra, 1976; see Stevens and Cowey, 1972).

In addition, increased responsiveness to intense auditory stimulation has been reported in hippocampals (Coover and Levine, 1972; Ireland and Isaacson - gerbils, 1968). At this point it is worth noting that collicular animals have similarly been reported to respond to auditory stimuli by startling and flinching though not turning the head to localise the source of the sound (Schneider, 1968; Murison, 1977). However the collicular is hyperresponsive to "click" stimuli unlike the hippocampal which apparently over-reacts to loud and frightening stimuli.

Ironically, the above studies fall into two distinct groups, suggesting completely opposite functions for the hippocampus. The first (novelty detection) model predicts decreased response to stimulation to follow hippocampal lesions,while the other (the stimulus gating model) predicts an increase. Gustafson and Koenig (1979) attempt to resolve the paradox by arguing that orientation in hippocampals is decreased in response to entirely novel stimuli (when the orienting response occurs but is followed by little post-stimulus investigation), while in response to less novel stimuli, the orienting response habituates slowly giving rise to what might be termed persistent attention. Interestingly, while this hypothesis accounts for most of the above data for hippocampectomised animals, it predicts a different pattern of response from that obtained in collicular-lesioned animals, the latter failing to pay attention to novel stimuli at any time, irrespective of degree of stimulus novelty. It should be noted that for hippocampals central and peripheral visual space are not distinguished apart within this model, yet such a distinction may be crucial in the interpretation of the effects of other (notably collicular) brain lesion effects (Goodale et al, 1978).

4.1.3 Theta (RSA) Activity

The appearance of θ in the hippocampal EEG (a characteristic, 7.5 - 8.5 Hz in the rat; Gray, 1970) has been variously related to arousal level (Green and Arduini, 1954), orientation and attention (Grastyan et al, 1959; Bennett, 1971), frustration (Gray, 1971b), memory consolidation processes (Adey, 1966), exploration and central processing of stimuli (Routtenberg, 1971; Gray, 1971a) and voluntary motor movements (Vanderwolf, 1971), based usually upon studies in which slowing of the EEG was thought to correlate reliably with the appearance of these particular classes of activity.

Radulovacky and Adey (1965) reported θ to accompany "orienting" behaviour in cats. However, close scrutiny of their test situation is revealing. Cats were trained to run down the start-arm of a T-maze on the sounding of a buzzer and the raising of a guillotine door, and to turn to the illuminated arm at the intersection. On "orienting" trials, the buzzer sounded but the guillotine door remained closed. The authors claim that the animal was "orienting" since it "was able to hear the reinforcing tone, and observe the ambient illumination in the reward area from the cue light, through narrow slots above and below the opaque starting doors". Clearly such a predicament involves more than simple "orienting" in the sense used by other authors (Ingle, 1973; Goodale et al, 1978), and θ activity here might reflect frustration, motor movement etc,.

Grastyan et al (1959) have argued that θ activity occurs when an animal initially orients to a novel stimulus, and disappears as habituation occurs. Koenig and Gustafson (1979) report intra-subject consistent enhancement or suppression of θ activity when novel stimuli are initially presented, suggesting a role for the hippocampus in phasic rather than tonic orienting.

In contrast, Kemp and Kaada (1975) have reported θ to appear most conspicuously when the animal (cat) was seen to tonically orient. Kemp (personal communication, 1977) suggests that the presence of θ during tonic orienting may reflect egocentric "encoding" processes taking place, allowing the encoding of spatial relationships in terms of oculomotor movements and vestibular processes. Clearly, species variation in the behavioural correlates of θ, and the parameters of the waveform (Bennett, 1971; Winson, 1972) render interpretation difficult. In this sense the methodological issues raised by investigations of the hippocampus and superior colliculus are similar since the involvement of eye movements, head movements and locomotion in orienting mechanisms, and the constraints imposed by each animal's particular stimulus environment will require that both structures are engaged in different "functions" in different species. (HPC: see Kemp and Kaada, 1975). It is interesting to note that HPC θ is particularly associated with vibrissal "sampling" of the environment (Gray, 1971a), since each vibrissa has a specific "projection area" on the collicular surface (mouse: Dräger and Hubel, 1975). Thus in the process of exploration, HPC and SC are likely to be related or complementary. Indeed Routtenberg (1971) argues that HPC θ is an indicator that "limbic-midbrain" attentional and stimulus processing functions are dominating behaviour while response execution mechanisms are suppressed; the opposite state of affairs is indicated by hippocampal desynchronisation.

Adey *et al* (1970) have shown that phase shifts occur in θ during the course of learning and performance of a visual discrimination, and that error commission is related to non-appearance of θ. This suggests that in the learning process, the directing of attention to relevant cues and rejection of irrelevant cues, and thus the changing attentional requirements of the task may be reflected in the parameters of θ observed. However Bennett (1971) concluded after a lengthy review of the literature, that θ occurrence in relation to attention in learning tasks is dependent upon the type of task employed, and that the most reliable correlation obtained is between θ trains and orienting responses. However Bennett reinterprets the term "orienting relex", suggesting that Grastyan's (1959) use of the term "orienting reflex" is different from that "in American Psychology", and notes that though θ may be related to attention, "A quick jerk and return of the head toward and away from a stimulus ... would not evoke a θ train", also that in Grastyan's terms (see also Vinogradova, 1970), θ-eliciting stimuli have some "meaning" or significance to the subject. This type of "orientation" is clearly not based on stimulus parameters alone. Bennett proposes that θ may represent "a correlate of functions performed by the HPC in mediating the investigatory or attentional component of exploratory behaviour", including "detailed examination of environmental stimuli", adopting Berlyne's (1960) definition of investigatory behaviour, namely the "clarification of stimulation" from objects already represented in the stimulus field. This clearly involves the application of a much wider concept of "attention" than that applied to SC functions (cf Goodale _et al_, 1978), particularly since it appears to assume the involvement of central visual analytical processes (or the "identifying" kind of vision;cf. Trevarthen, 1968). This in turn perhaps suggests a stronger relationship between the HPC and VC than between HPC and the SC.

Schaefer (1972) noted that stimulation of the SC in rabbit

> "resulted in the typical 'syndronisation' of the hippocampal EEG before the cortex was aroused. After turning of the pinna or the orienting of the head, the hippocampal EEG often became irregular, as it had been before onset of stimulation (This was observed although tectal stimulation was continued)".

Unfortunately it is unclear whether this is due to a special relationship between HPC and SC, or general activation. However, of particular significance for the present discussion is the finding of Routtenberg and Taub (1973) that, in a freely moving cat, θ appearance in the hippocampal EEG was synchronised with "θ" appearance in the SC (and likewise disappearance). Routtenberg (1976, personal communication) could not identify a relationship between θ-related activity and depth of SC recording electrode. It should be noted that stimulation of the dorsal midbrain is aversive and not simply "attentional" (Routtenberg, 1971). However caution must be exercised, as the two structures are closely situated, and volume conduction between them could give rise to the synchrony of wave-forms though such, if it were to occur, could conceivably have functional significance. Finally, an indirect relationship is likely to exist between SC and HPC via the brainstem. Hippocampal θ has been shown to be driven by brainstem nuclei and their septal projections (Redding, 1967); interestingly, these nuclei (pontis oralis and reticularis tegmenti pontis) are nuclei to which SC has strong descending projections (see Chapter 1); thus hippocampal θ could be influenced by efferent output from the SC.

4.1.4 Spatial behaviour

Both SC and HPC have been implicated in the control of behaviour which has a "spatial" component (SC: Schneider, 1969; Trevarthen, 1968; Ingle, 1970; HPC: De Castro, 1974; Mahut, 1971; Olton, 1977; O'Keefe and Nadel, 1978). However the nature of the "spatial" function would appear to be different, since the SC is generally considered to code space egocentrically (in relation to body midline, or the vertical meridian of the visual field), enabling the animal to orient, or move in relation to an object present in visual space at any one moment. The HPC, on the other hand, has been implicated by O'Keefe and Nadel (1978) in a higher order spatial encoding, involving the construction of a "cognitive spatial map", a hypothetical device (Tolman, 1948) which is required by an animal to monitor its position in space and the spatial interrelationships of other objects; it is "constructed" automatically as an animal moves through the environment, and consists of "a pre-existent framework with which all the stimuli to which an animal attends are represented", or a "cartoon" of the environment which enables the animal to make "continual predictions concerning the stimuli encountered consequent upon its movements" (O'Keefe and Nadel, 1978, p.382). Indeed Kimble and Green (1968) reported an absence of latent learning in hippocampal rats, (a measure of 'spatial map' formation; Tolman, 1948). It is, however, arguable that such a spatial framework will, to some extent, depend upon dynamic changes within the environment, and that a contribution of the SC to this process might be inferred. Indeed O'Keefe and Nadel (1978) have emphasised that the hippocampal spatial map provides the substrate of an "objective, non-egocentric view of the world", i.e. computing "place" independently of its position in relation to the animal or the direction from which the animal approaches it. Nevertheless the authors appear to concede that a cognitive map will represent a composite of many 'egocentric' representations which are " ... initially generated by experiences directly related to the organism (and are thus egocentrically inspired)", strongly suggesting that the role of the SC in accumulating novel information might be crucially necessary for the elaboration of such a "cognitive map". This possible relationship between SC and HPC may explain why similar, activity-related deficits are seen on some spatial mazes after both types of lesion (see above). It is interesting to note that while the process of cognitive mapping is seen to be innately organised (i.e. a Kantian "a priori", "absolute" spatial faculty), Trevarthen (1968) similarly regards the SC system as embryologically organised. The possibility of significant interactions between the 'egocentric' collicular, and 'absolute' hippocampal computations of certain spatial functions in neonatal life cannot be discounted.

A distinction between the two types of 'spatial' function (i.e. 'absolute' and 'egocentric') is nowhere more evident than at single unit level where units in SC are organised topographically, in relation to body- or ocular-midline, i.e. in egocentric space. However in some neurons in HPC, "higher order receptive fields", representing specific spatial locations, are encountered, which, for example, fire when an animal is in a particular location in an apparatus (O'Keefe and Dostrovsky, 1971; Olton Branch and Best, 1978). They appear to respond not only to the spatial position of stimuli, but also to particular complex arrangements of multimodal (Miller and Best, 1978) stimuli, thus to an array which specifies spatial position. In addition there is a population of "mismatch" cells which fire maximally when an object usually encountered in a particular place is moved or missing.

Thus it is predicted by the Nadel and O'Keefe (1976) model that an animal without a HPC will fail a task in which an appreciation of spatial relationships between objects is required, or when the animal is forced to discriminate his own position in relation to environmental objects.

In accordance with this prediction, a number of authors report 'spatial' deficits in HPCs; on spontaneous alternation (with brief confinement), passive avoidance and spatial reversals (O'Keefe and Nadel, 1978).
In addition persistent deficits have recently been observed in hippocampal rats in an apparatus which requires sophisticated use of 'spatial memory', the 8- or 17- arm radial maze. This consists of a central

platform from which maze arms radiate. The animal, usually a rat, is placed upon the central platform and allowed to investigate freely. With little training, the normal rat will run (randomly) to all eight arms, rarely repeating a choice by running to a previously visited arm, suggestive of a large-scale "spontaneous alternation" performance (Olton, 1977). The hippocampal rat tends to make frequent 'revisits'. Cortically-lesioned animals generally show no deficit, suggesting that the organisation of radial maze performance is a unique hippocampal responsibility. Jarrard (1979) has suggested that the CAI field of HPC is required for acquisition of the habit, while not for retention of learned performance. Jarrard (1979) and Olton and Papas (1979) have shown that when trained to run to a baited subset of maze arms HPC-lesioned rats tend to 'perseverate' previously visited arms, though notably rarely make error visits to any of the nonbaited subset of arms. This does suggest that the HPC animal retains a notion (albeit degraded) of spatial location. Furthermore, attractive though the "spatial" model is, it is arguably too eclectic.

For example

(i) DRL, extinction and reversal are explained within this model as being due to reduced exploration during non reward. However the above review cites as many experiments showing increased rearing, sniffing and general attention as reduced investigation following HPC ablation. Indeed the "spatial" model might predict more investigation in animals unable to piece together an environmental 'map' and who would thus be expected to treat familiar situations and familiar objects and events as novel (see Gaffan, 1972).

(ii) The hippocampus cannot be considered a unitary structure for anatomical, physiological and behavioural reasons (Nadel, 1968; Stevens and Cowey, 1973; Vinogradova, 1970; Jarrard, 1976); thus the return to a unitary (spatial) function might represent a retrograde step.

(iii) From (ii), it logically follows that if the HPC operates as a 'unitary' structure, damage to any part of the system would leave an animal equally (spatially) impaired. However Green and Stauff (1974) have shown, for example, that while the fornix system is involved in spatial performance, lesions in subiculum and cingulum leave spatial performance unimpaired. Many experimenters have been able to demonstrate such "behavioural dissociations" following selective destruction of components of the hippocampal formation, for example in relation to motivational behaviour and attentional behaviour, independently of oneanother (see eg. Jarrard, 1976).

(iv) The increased use of visual cues by HPCs is argued to result from the need to compensate for lack of spatial encoding. However, given increased use of cues, and the potential use of 'egocentric' frontal cortical mapping, few spatial tasks remain genuinely insoluble by an animal deprived of 'space'. Passingham (1979) has argued that O'Keefe and Nadel (1978) fail to specify the conditions under which the spatial hypothesis would be disproved.

To take the radial maze (8 arm) as an example, the task could also potentially be performed as (a) an olfactory discrimination between urine-'marked' and 'unmarked' arms (b) a visual discrimination; the animal can achieve 100% performance by running to the "half-foreshortened" arm to the L (or R, consistently) of the arm facing him on emergence from each response, (c) a spatial discrimination or body swing strategy (running through an angle of 135° to L, or R, on each choice), (d) a visual discrimination by assigning 'labels' or 'cues' to each arm, or (e) by running to successive adjacent arms. It is not to be assumed that all animals perform the radial maze task the same way. Furthermore, the "perseveration" shown by HPCs to particular maze arms (Olton, 1977) is indicative of a residual spatial ability. It should be noted that all previous theories of HPC function predict a deficit on the radial maze task; the "perseveration" hypothesis, or "rejection and selection of hypotheses"(Kimble and Kimble, 1970; Stevens, 1973) actually describes the (repetitive, prolonged) HPC deficit better than the "spatial" hypothesis.

However, the rapid development of the putative 'map' (cf. Tolman, 1948) suggests that upon placement in a novel environment, the hippocampus acquires novel information very rapidly. Thus a contribution from attentional mechanisms such as SC might be strongly suspected, though it is unclear how dynamic egocentric information might be processed into a stable 'map' (see O'Keefe and Nadel, 1978, p.383).

Summary

It has been argued that the HPC and SC share certain electrophysiological properties, in particular in terms of single unit responses and EEG synchrony. In some studies, lesion effects following HPC or SC damage appear similar, particularly in relation to attention. However close inspection of the lesion data suggests (a) a more subtle role for the HPC in attentional shifts, (b) a more 'peripheral' sensory egocentric role for the SC than the HPC, the latter apparently receiving largely pre-processed information, and (c) that increased activity in hippocampal animals occurs as a result of lack of habituation on prolonged testing, unlike colliculars whose initial response to novelty is particularly impaired. Many crucial experiments which have demonstrated "characteristic deficits" after one type of lesion have not been carried out with the other, and thus comparison is rendered difficult. A possible functional relationship might exist in terms of their respective contributions to the "spatial encoding" of the environment.

4.2 Superior Colliculus and Frontal Eye Fields: A Comparison

The 'Frontal Eye Field' (FEF) in monkey is defined as that area of prefrontal cortex in which stimulation produces conjugate contravesive eye movements. The anatomy and physiology of the FEF will not be covered in detail here since a recent review is available (Collin, 1977). In monkey, the FEF is a transitional (dysgranular) area of cortex (between granular frontal cortex anteriorly and motor cortex with characteristic layer V pyramidal cells posteriorly) comprising the superior and inferior limbs of arcuate sulcus (area 8 of Brodmann, 1909). Afferent input originates from the superior temporal gyrus and primary auditory, visual and somatosensory cortex, from motor cortex and the contralateral FEF, and from the midbrain via afferents from the medial pulvinar, to which SC projects (Trojanski and Jacobson, 1975) and pars multiformis of the dorso-medial thalamic nucleus, which in turn also receives input from (deep) SC (Benevento and Fallon, 1975). Efferents travel to the cingulate gyrus, superior temporal sulcus, striatum, dorsomedial intralaminar and internal medullary (lateral central nucleus) thalamic regions; also to the zona incerta, pretectum, central grey, paramedian pontine reticular formation, lobuli simplex and vermis of the cerebellum, and directly to the SC. The latter projections (Kuypers and Lawrence, 1967; Astruc, 1971; Künzle and Akert, 1977;

Künzle, Akert and Wurtz, 1976) are distributed throughout the rostrocaudal extent of SC, more medially than laterally, and particularly dense in strata griseum intermedium and opticum, terminating in the region of eye-movement related neurons (Guitton and Mandl, 1974). In non primates, the area of cortex corresponding to arcuate sulcus in the primate is found on the medial wall of the frontal pole, so determined by electrical stimulation in cat (Schlag and Schlag-Rey, 1970) and on the basis of anatomical projections in the rat (Leonard, 1969, 1972; Domesick, 1972). However in the latter case, opinions differ over the homology of frontal subfields. Leonard's (1969) original study showed projections from (i) a 'core' area of nMD to the dorsal lip of the rhinal sulcus (the assumed homologue of posterior orbital frontal cortex in primate [1]) and (ii) the remainder of nMD to the medial wall of the frontal pole, though the latter subdivides into (a) a lateral region (= pars multiformis in monkey?) projecting to the dorsomedial shoulder region of frontal pole and (b) a portion of nMD surrounding the 'core' area, projecting to a more ventrally situated area of medial frontal cortex. The latter

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[1] Though precise homologies are open to doubt; lesions of this region in rat do not reliably produce the extinction impairments (Kolb, 1973; Passingham and Foreman, 1973) which would be predicted from previous work with monkeys (Butter, 1969).

might be homologised with dorsolateral prefrontal cortex in primate, though since this region appears to receive input from the anteromedial thalamic nucleus (Domesick, 1972) it thus "appears to be some kind of combination of cingulate and prefrontal cortex" (Leonard, 1972) which has presumably not become fully differentiated in rodents.

Larsen and Divac (1978) argue for a functional dissociation between the most anteromedial surface of the hemisphere (pregenual cortex) and the supragenual region. These have separate dopaminergic innervation, and lesions of the former but not the latter give rise to impairments in delayed response-type behaviour (Larsen and Divac, 1978) similar to, albeit less severe than, those following lateral frontal lesions in the monkey (Divac and Warren, 1971). However, the ventral region of anteromedial cortex has been suggested as the most likely homologue in rat of dorsolateral frontal cortex in primate (Leonard, 1972) and this may be the crucial "focus" for the effect.

The efferent projections of medial frontal cortex in rat are similar to those of FEF in monkey. For example Leonard (1969) reported efferents to deep SC, Schneider and Leonard (cited Leonard, 1972) have found similar cortical projections from the paralamellar nMD in rodent and monkey, and Schneider has identified projections from parastriate cortex to nMD-projection cortex in hamster (cited Leonard, 1972).

4.2.1 Motor Control

Increased activity has been reported in running wheels and the open field following large frontal ablations in rats by Campbell and Lynch (1969) and Campbell, Ballantyne and Lynch (1971) who argued that HPC and frontal cortex share arousal control functions. Similarly, Kallman and Isaac (1976) reported that removal of MFC (plus the head of the caudate nucleus) mimicks superior collicular removal in producing amphetamine-enhanced, illumination-dependent hyperactivity. These authors claim that

> "the frontal cortex, the head of the caudate and the superior colliculus are all influential in maintaining the normal relationship of ambient illumination to activity levels" (p.643)

However, since it has been suggested that ventral MFC is homologous with dorsolateral frontal cortex in monkey (Leonard, 1972; Kolb, 1973), activity changes following large MFC lesions in rats may be the equivalent of that observed in monkeys with lateral frontal lesions (French, 1959; Gross, 1963; Warren and Akert, 1964). Kolb (1973, 1974) has investigated the proposed homology between MFC in rat and dorsolateral frontal cortex in monkey and found that MFC-lesioned rats were slower in habituating headpoking within a 30 minute session suggesting a perseverative tendency characteristic of dorsolateral frontally-lesioned primates (see Warren and Akert, 1964). (The result is also similar to that obtained by Kaplan (1968) with hippocampal rats). Activity was found to habituate slowly in the MFC group (Kolb, 1974), though no significant activity increase is seen in MFC lesioned rats when recorded as an accumulated score over a 5 minute session

(Kolb, 1973). Indeed, other authors have reported normal activity levels in frontally lesioned rats (Glickman et al, 1964; Albert and Bignami, 1968).

Winterkorn (1975a, b) in discussing the "approach error" behaviour of SC- and FEF-lesioned cats suggested that collicular lesion effects may arise not from damage to intrinsic collicular mechanisms but rather to fronto-pontine fibres passing through SC. This view, namely that SC and FEF lesions are likely to produce similar (or identical) deficits is not supported by the finding of Collin (1977) who found that while SC-lesioned rats ran about a test apparatus in a jerky unsystematic manner with frequent changes of direction, such behaviour was not evident in rats with MFC lesions. Furthermore, "blindsearch" behaviour in rats was less disrupted by MFC than SC lesions (unlike monkey where the reverse is the case; Collin, 1977), and in other situations, the consequences of FEF and SC ablations are additive; for example, Conway, Schiller and True (1979) showed that while bilateral lesions of SC or FEF alone produced small visual search deficits simultaneous lesions virtually abolished all saccadic eye movements.

Unilateral lesion of the frontal pole in rats produces, as with SC lesions, ipsiversive turning tendencies (Collin, 1977) which are potentiated by systemic injections of apomorphine, though Glick and Greenstein (1973) who observed the time course of apomorphine-induced rotation in frontal rats noted that ipsiversive turning lasts only 7 days after which the turning becomes contraversive. This latter effect has yet to be tested following SC lesions. Cowey and Bozek (1974) similarly observed ipsiversive response tendencies in unilateral MFC-lesioned rats when allowed free choice of arms in a Y-maze.

Indeed like the SC, frontal cortex does have projections to the midbrain RF and brainstem (Leonard, 1969), and frontal projections appear to be generally inhibitory upon arousal mechanisms (Sauerland *et al*, 1967) thus similar effects might be exerted by SC and MFC.

4.2.2 Eye movements and attention

The "Frontal Eye Field" is defined as the region of prefrontal cortex within which electrical stimulation produces contraversive, conjugate saccades (Ferrier, 1886; Brucher, 1966; Robinson and Fuchs, 1969; Schlag and Schlag-Rey, 1970). The resulting eye movements are similar to those made naturally by the animal and show habituation to repeated electrical stimulation (Vale, Sundberg and Ursin, 1976). They are not the result of activity in FEF-SC pathways since, unlike eye movements evoked by striate cortex stimulation (Spiegel and Scala, 1937; Dreher *et al*, 1965; Schiller, 1977) they occur following ablation of SC (Pasik and Pasik, 1964; Schiller, 1977). Schlag and Schlag-Rey, (1970, 1971) argue that the FEF gains access to the oculomotor system via the internal medullary lamina of the thalamus (central lateral nucleus); such connections have been demonstrated (Kuypers and Lawrence, 1967; Künzle and Akert, 1976; but see Avendano *et al*,1978).As with the SC, simultaneous bilateral stimulation of both FEFs results in vectorial summation of the two separate 'eye movements', (Robinson and Fuchs, 1969).

In contrast, simultaneous stimulation of preoccipital visual cortex and the FEF with threshold current gives rise to eye movements which would have occurred upon FEF stimulation alone, suggesting a 'predominance' of FEF over other oculomotor influences (Russell, 1894; Crosby, Yoss and Henderson, 1952), and further suggests elements of competition and cancellation or 'veto' between separate oculomotor pathways. Discharge from single units in FEF is closely related to eye movements though generally this occurs during the saccade unlike the SC where activity normally precedes the saccade (Bizzi and Schiller, 1970; Bizzi, 1972; Mohler, Goldberg and Wurtz, 1973).

A number of authors have suggested that FEF discharge is related to the 'stabilising' of the visual world during eye movements. Teuber (1964) has described such a mechanism as "corollary discharge". In particular Mohler, Goldberg and Wurtz (1973) argue that the SC is capable of distinguishing self generated from environmental movements by the active suppression of SC movement neurons by "corollary" output from FEF for which there is independent electrophysiological evidence (Guitton and Mandl, 1974). However, as noted earlier, Collin (1977) found that three monkeys with arcuate lesions could successfully discriminate between moving and stationary stimuli when tested in the dark, thus notably failing to confuse their own movements with that of the stimulus. An impairment was seen in collicular lesioned monkeys though this is more likely to be a result of movement detection deficiency per se than absence of corollary discharge (see Collin, 1977, Chapters 5 and 6). However it is questionable whether such a simple model is appropriate (see MacKay, 1972; Collin 1977) in particular whether the maintenance of stability in a dynamic visual environment could be achieved by a single "efferent discharge". Lower animals which lack prefrontal cortex presumably maintain such stability and it is unclear why such a fundamental mechanism should be committed to frontal neocortex in phylogeny.

The FEF and SC appear to be involved in the processing of different types of information. For instance, Rizzolatti (1977; personal communication) has been unable to find single units in the FEF similar to the 'complex' cells encountered in intermediate laminae of the SC (Buchtal et al, 1976). In addition, the study of Milner et al (1978) strongly suggests a different role for FEF and SC in the process of orientation to novel peripheral cues. While SC-lesioned monkeys showed reduced distractability to novel cues, FEF monkeys exhibited as many orienting responses as control animals, yet spent less time than controls in poststimulus fixation and exploration. This suggests a possible function for fronto-tectal projections, in that in both making a smooth saccade, and in instantly stabilising fixation on reaching the saccadic target, it might be necessary for the phylogenetically newer cortical eye field to 'suppress' lower oculomotor systems for the duration of the saccade, preventing 'competition' between oculomotor systems. Supportive evidence for this view has been reviewed above suggesting that (a) the FEF system (perhaps the 'voluntary' eye movement system; see below) has a 'predominant' control over others, and (b) that the FEF-oculomotor system may be anatomically separate from evolutionarily "lower" systems. However such a suggestion awaits experimental investigation.

Holmes (1938) proposed on the basis of clinical observations that the FEF represents a centre for the control of voluntary eye movements, and that following frontal lesions, the oculomotor system is totally governed by lower reflexes. Indeed, patients with arcuate lesions were unable to direct their eyes to left or right upon instruction (perhaps the equivalent of the 'anticipatory saccade' deficit observed in cats by Schlag-Rey & Lindsley, 1970) and, like SC-lesioned cats and primates, FEF damaged cats (Dreher and Zernicki, 1969) and human patients (Holmes, 1938) are found to engage in "fixed staring", unbroken by spontaneous eye movements. In addition, Luria,Karpov and Yarbus (1966) have shown that frontal patients fixating a picture will not utilise normal ocular scanpaths but rather exhibit unsystematic eye movements apparently unrelated to the stimulus material. A similar disorganisation is apparent when they are asked to investigate a picture using a narrow torch beam in the dark, suggesting that an 'information acquisition' system is disturbed or destroyed. However, inattentiveness and poor visual sampling is not a unique consequence of arcuate damage (Heilman and Watson, 1977). In monkeys with unilateral lesions of FEF Kennard and Ectors (1938) and Kennard (1939) noted that the head and eyes were deviated to the side of the lesion, the animal circled ipsiversively, failed to respond to objects in visual space contralateral to the lesion, and used the contralateral hand less, especially when making fine movements. The effects disappeared (at different stages) over a period of weeks; for example, after some weeks, circling only occurred on excitement. These findings have been observed by a number of authors (see Latto and Cowey, 1971 a, b; Collin, 1977, for references). Welch and Stutteville (1958) have argued that the deficit in orienting or attending to contralateral stimuli is not restricted to the visual modality but appears, like the SC deficit in rats (Kirvel et al, 1974), to be a polymodal phenomenon.

Crowne (1978) has demonstrated that while unilateral lesions give rise to contralateral neglect in monkeys (even to threatening stimuli such as laboratory 'catching' gloves), bilateral lesions fail to produce a bilateral neglect.

Such is one of the "more puzzling aspects of FEF lesions" (Collin, 1977; see Latto and Cowey, 1971b for references) and is perhaps suggestive that a more general interhemispheric disequilibrium is responsible for neglect and asymmetry following unilateral frontal lesions (see Heilman and Watson, 1977; Milner et al, 1978). Latto and Cowey (1971a, b) reported ipsiversive deviation of the head and eyes following unilateral FEF lesion in monkey, and a contralateral hemianopia which was unlikely to have been due to simple ocular deviation (Latto, 1977). In one animal (P4) Latto and Cowey (1971b) have demonstrated an apparently persistent bilateral amblyopia following bilateral FEF ablation. Such visual loss persisted for 12 weeks postoperatively. Recently, threshold changes have been examined in monkeys with bilateral FEF or SC lesions. In the former case, a twofold increase, and in the latter a fourfold increase is observed at 1 - 2 weeks postoperatively though the effect had disappeared by 6 weeks postoperatively (Latto, 1977).

If, in the rat, frontal cortex is anatomically and functionally subdivided as in monkey (Kolb, 1973), it would be predicted that the dorsomedial shoulder of the frontal lobe, which receives projections from the most lateral portion of nMD, is a 'frontal eye field' and that ocular, attentional or motor deficits would result if it were lesioned. However, MFC lesions invariably encroach upon more ventral tissue, and thus the separation of functional subfields is often difficult.

Collin (1977) reported contralateral neglect of visual, auditory and tactile distractors while unilaterally-lesioned MFC rats were running down a straight runway. Unfortunately the effect of bilateral lesions was not investigated; this would have been useful since one puzzling feature of the FEF syndrome in monkeys is the relative absence of persistent deficits in bilaterally-lesioned subjects, compared with unilaterals. Kolb (1973) mentioned en passant that bilaterally-lesioned MFC rats appeared inattentive to sudden stimulation though this was not formally tested. In a headpoke apparatus, the same animals were found to be slow in habituating to a test environment within a session, and showed virtually no habituation of headpoke investigation (Kolb, 1974).

Spatial and attentional deficits similar to those observed in cats, dogs and monkeys with dorsolateral frontal cortical lesions , for example spatial reversal, spatial alternation and delayed response (Mishkin, 1964; Lawicka, 1972; Rosenkilde, 1978) have been observed following anterior MFC lesions in rats (Divac, 1971; Kolb, 1973; Kolb, Nonneman and Singh, 1974)

4.2.3 Spatial Behaviour

A crude topography appears to exist within projections to the FEF in monkeys (Latto, 1975), and therefore the position of objects in visual space is roughly mapped vis à vis the animal's ocular midline, thus in terms of an egocentric framework. Thus, despite connections between the FEF and the HPC, the chance of a close functional link vis à vis cognitive mapping (O'Keefe and Nadel, 1978) is subject to the same considerations as for SC and HPC relationships (Section 4.1). However, the caudate-prefrontal system may be involved in spatial memory, in particular the middle third of the principle sulcus (Butters et al, 1972) , though lesions of arcuate sulcus rarely produce spatial deficits (review in Collin, 1977).

In the rat, Potegal (1969) reported egocentric localising deficits in animals with caudate lesions using single, body-turn training in a single-choice version of the radial maze task. However, using the radial maze with full investigatory training, Becker et al (1978) have shown that rats with MFC or caudate lesions are only briefly impaired in postoperative retention, while fornix lesions result in permanent impairment.

Other authors have suggested that the 'prefrontal' deficit is one of spatial-motor organisation, since FEF monkeys are impaired on tasks involving cue-response apposition (dog: Stepien, Stepien and Toeplitz, 1975; monkey: Stepien and Stamm, 1970) or spatial separation of cue and response (Latto and Cowey, 1971; Butter, 1974; Milner et al, 1978) suggesting a specific deficit in the establishment of perceptual/kinaesthetic (or kinaesthetic/kinaesthetic: Stamm, 1973) associations between the two (see also Rosenkilde, 1978). Collin (1977) found that FEF monkeys performed poorly on a visual search task when required to search for rewards hidden behind moveable coverslips arranged in a spatial array, while SCs performed well on this task, exhibiting a deficit when tested on simple localisation involving retrieval of food morsels placed at unexpected spatial locations yet clearly visible.

This is an important result, since it suggests a 'visual search' deficit in SCs, but a higher order spatial/kinaesthetic memory or patterning deficit in the FEF group.

Summary

As with studies of the hippocampus, inter-lesion comparisons between FEF and SC are difficult since few experiments have employed identical apparatus, species, method and lesions. Where primates with FEF and SC lesions have been subjected to similar testing, some subtle differences have emerged (Collin, 1977; Milner _et al_, 1978), though very similar manifestations of inattention were obtained following unilateral SC and MFC lesions in rat (Collin, 1977). Attentional tests such as those used by Keating (1973, 1976) would be valuable if employed with FEF monkeys; likewise the psychophysical studies of Latto and Cowey (1971b) and Latto (1977) would be useful if applied to MFC rats. However I am inclined to implicate the FEF in some higher (voluntary?) cortical-oculomotor functions, different in kind from functions of SC, in broad agreement with Latto (1977) who writes that

> "Since attention must be a widespread phenomenon in the visual system, ranging from the simple orienting response to the grading of information in terms of its semantic context, there is no reason why both frontal eye fields and the superior colliculus should not be involved in spatial attention".

However one wonders how much of the cerebrum such a range excludes.

CHAPTER 5

ACTIVITY AND INVESTIGATION

5.1 Activity and Investigation following lesions of the Superior Colliculus and Posterior Neocortex

5.1.1 Introduction

A number of experimenters have independently reported that lesions involving bilateral damage to deep laminae of the superior colliculus in rats produce a marked, immediate elevation of locomotor activity in a novel environment (Isaac, 1971; Smith and Weldon, 1976; Foreman *et al*, 1978; Weldon and Smith, 1979; Pope and Dean, 1979). Such hyperactivity appears to consist almost solely of increased locomotion, and not exploration, since investigatory behaviours such as rearing, sniffing and headraising (the latter two frequently accompanying locomotion in the normal rat) are reduced in frequency in colliculars (Foreman *et al*, 1978). Such decreased attention is to be expected since in other situations, Goodale and Murison (1975), Collin (1977) and Goodale *et al* (1978) have shown that SC-lesioned rats are grossly inattentive to unexpected stimuli, particularly when these appear in peripheral visual space. On the other hand, SC rats have not been reported to collide with objects (as if "blind" to their presence), but rather manoeuvre round them successfully (Casagrande *et al*, 1972; Ingle, 1973) without apparently 'extracting' the novelty of the object which would cause a normal animal to begin exploration of it (Marshall, 1978).

Foreman et al (1978) argue that the hyperactivity of colliculectomised rats is related to inattentiveness. Inhibition of ongoing behaviour, particularly locomotion in the rat, is a necessary first step in the redirecting of attention (Gray, 1970) and thus, assuming the SC to perform an attentional switching function, it would seem to be necessary for the SC to exert a predominantly inhibitory influence upon the motor system. Hyperactivity following SC ablation is thus envisaged as resulting from the "release" of lower motor systems from inhibitory tectal control. However, such an interpretation poses certain difficulties, since not all colliculectomised rats exhibit hyperactivity. Indeed lesions involving only superficial laminae, while producing inattentiveness to peripherally-located novel stimuli do not give rise to elevated activity (Goodale and Lister, 1974). This is surprising; if activity elevation is a consequence of profound and general inattentiveness, lesions of superficial laminae by removing an influence upon the activity of cells in deep (motor) laminae (Foreman et al, 1978) should be sufficient to produce elevated activity.

Thus the present experiment was designed to replicate an earlier study by Foreman et al (1978) comparing the behavioural consequences of lesions of posterior cortex and lesions of SC, though in this experiment the latter were made at various depths within the structure. Postoperative feeding behaviour and weight gain were monitored since Pope and Dean (1979) argue that motor aspects of feeding behaviour are disrupted in animals with deep SC-dorsal tegmental lesions.

5.1.2 Subjects

Thirty experimentally naive male hooded rats of the Lister strain (Olac Ltd.) were used, aged approximately 120 days at surgery. They were housed in same-lesion pairs in standard laboratory cages consisting of an opaque plastic base (measuring 42 x 25 x 21 cms) with a wire lid. They had free access to water and food (Hengate's 41B diet cubes) prior to deprivation for testing. Lighting in the colony room was controlled by automatic time switch (7.00 am - 7.00 pm light).

5.1.3 Surgery

Surgery was performed under clean but not sterile conditions. Thirteen rats received bilateral lesions of the SC and 6 had lesions of posterior neocortex (hereafter referred to as the "VC" group). Each rat was weighed and anaesthetised with Equithesin (dose: 60 mg pentobarbitone sodium/Kg body weight) and its head was shaved. The animal was placed in a Kopf stereotaxic apparatus equipped with non-rupture earbars, the upper incisor bar elevated 5.0 mms above the level of the interaural line. A drop of glycerine was applied to each eye for protective purposes. Following a medial incision the skin was retracted bilaterally with haemostats and the periosteum retracted as far as the temporal muscles. Appropriate holes were drilled in the cranium using a hand-held dental burr, thus avoiding heat generation. These were enlarged carefully where necessary using small haemostats and the dura was lifted and sectioned using the tip of a hypodermic syringe needle. Collicular lesions were all made by radiofrequency following earlier attempts to use anodal electrolytic lesions[1]. The bregmoidal suture, the midline suture and the surface of the brain were used as antero-posterior (A-P), lateral (L) and depth (D) reference points respectively. A radiofrequency electrode, diameter 0.5 mms, teflon-insulated except for 1 mm at the tip, was lowered into place at the following coordinates:

A-P : -5.0 mms
L : ±1.3 mms
D : between -2.5 and -3.8 mms

The ground electrode was attached to a haemostat retracting the skin, and good contact ensured by placing a saline-soaked swab of cotton wool between electrode and cut skin. The lesion electrode was connected to a Radionics RFG-4 radiofrequency lesionmaker. When in place, the tip of the electrode was heated to a temperature of 55°C which was maintained for 60 seconds. Afterwards the electrode was left *in situ* until tip temperature had fallen below 40°C and was carefully withdrawn.

Cortical lesions were made by aspiration under visual guidance. Bone was removed overlying posterior neocortex, the dura was cut as above and a 24 gauge sucker (made by grinding the point from a syringe needle) was introduced beneath the dura. An attempt was made to remove all tissue within Krieg's (1946) area 17 and the more posteromedial

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[1] See Section 5.1.6.2

tissue identified electrophysiologically as primary visual cortex by Montrero, Rojas and Torrealba (1973). Care was taken not to invade the hippocampus though some subcortical white matter was unavoidably removed.

The surface of the brain was well-irrigated with physiological saline throughout the procedure. Bleeding was treated by patient application of light pressure. A small piece of sterile sponge ('Sterispon' No.1) was applied to the lesion site. The skin was then reapproximated, closed with clean, strong thread and the wound sprayed with "Nobecutane"(Bofors Co., Sweden). The rat was then placed in a clean, padded recovery cage with free access to food and water, and was warmed for approximately one hour by an overhead anglepoise lamp, the light being diffused by tissue paper placed across the roof of the cage.

Control animals were subjected to the same procedure as that described above except that at the lesion stage, the dura was left uncut and no damage was inflicted upon cerebral tissue.

Four to five days postoperatively, animals were weighed and rehoused in same-lesion pairs. Food deprivation commenced after weighing on postoperative day 21, animals being gradually reduced to one hour access to food per day in stages over a 3 day period. Testing commenced on postoperative day 24.

5.1.4 <u>Apparatus</u>

The apparatus consisted of a standard-sized, circular,

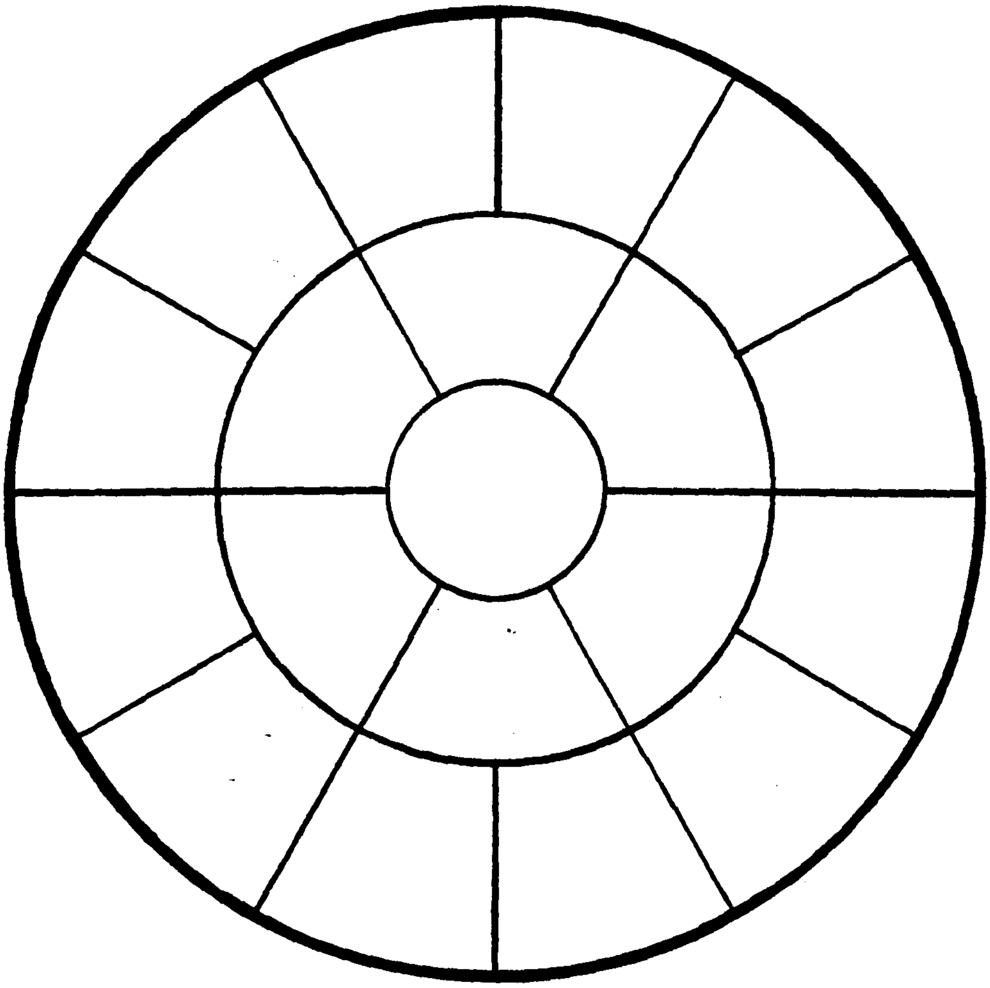

Figure 5.1
Plan view of the open field apparatus used in Experiments 5.1 - 5.3 and for preoperative testing in Experiment 5.5.

white-painted open field arena (83 cms diameter, walls 31.5 cms high). Lines on the floor of the apparatus divided it into 19 approximately equal areas (Figure 5.1). The entire arena was surrounded by a thin net drape. Overhead illumination was provided by 2 150 watt bulbs, and masking noise was supplied by a white noise generator set at 80 dbs. Temperature was maintained below 30°C at all times.

5.1.5 Procedure

Each animal in turn was removed from its homecage and transported 5 m into the testing room by hand whereupon it was placed in the centre of the apparatus. E immediately began recording the animal's behaviour by pressing the appropriate key(s) on an event recorder. The following behavioural categories were recorded:

(i) LINE CROSSINGS (whenever the animal's front paws crossed a line on the apparatus floor; otherwise referred to a "Running").

(ii) REARING (whenever the animal raised its front paws off the ground, except during grooming bouts).

(iii) GROOMING (whenever the animal indulged in a body-directed behaviour such as preening, scratching, washing).

(iv) HEADRAISING (whenever the animal's head was elevated but with the front paws on the floor; see Figure 5.2).This posture was often - but not always - accompanied by a rhythmic back-and-forth movement of the vibrissae and a pulsating, diaphragmatic breathing.

(v) SNIFFING (whenever the animal engaged in nosing the floor or walls of the apparatus).

(vi) IMMOBILITY (whenever the animal stood alert but

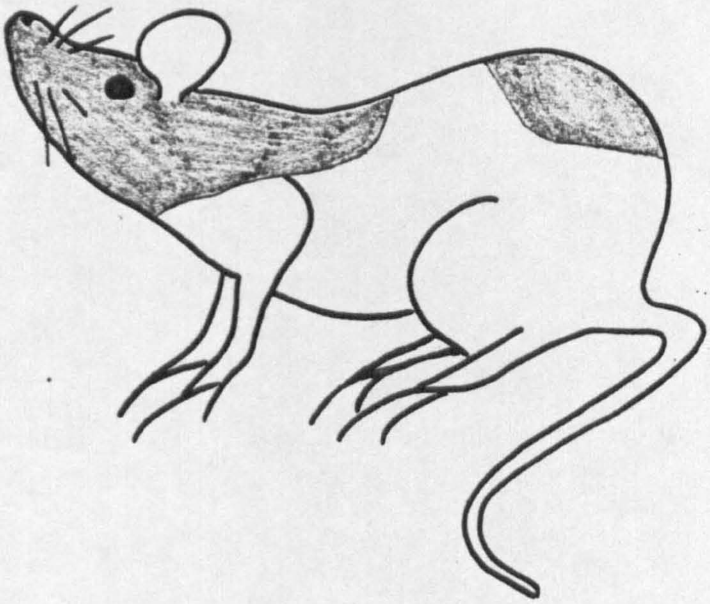

Figure 5.2
An example of the category of behaviour termed "headraising" in Experiments 5.1 - 5.3. This is frequently accompanied by rhythmical back-and-forth movements of the vibrissae.

completely immobile).

The response keys of the event recorder were "damped" with foam rubber and thus virtually silent. In the event recorder there were two sets of automatic counters, one accumulating the number of occasions on which a behaviour was initiated (hereafter termed "events"), the other responding to the continued depression of a response key (some to the continued depression of two particular keys simultaneously), thus cumulatively recording the duration of a behaviour (or co-incident behaviours), hereafter referred to as "time"s. The "time" counters were pulsed by a 0.1 sec. clock, thus providing a measure of total time engaged in each class of behaviour. All counter displays and relays were located three rooms distant from the test apparatus. A total recording period of 5 minutes was used, timed with a stopwatch. After testing the rat was removed from the apparatus, the number of faecal boli in the apparatus was noted, the scores on each event and time counter were recorded and the counters reset. The open-field was cleaned and wiped with a cloth dampened with a 2% acetic acid solution.

Throughout the study, group identity of animals was unknown to the Experimenter. Testing was carried out on 3 consecutive days; order of animals within and across days, within and between lesion groups was counterbalanced as far as possible. The animals were given their daily feed 30 minutes after the last animal had been tested. Testing always took place between 11.30am and 5.00pm.

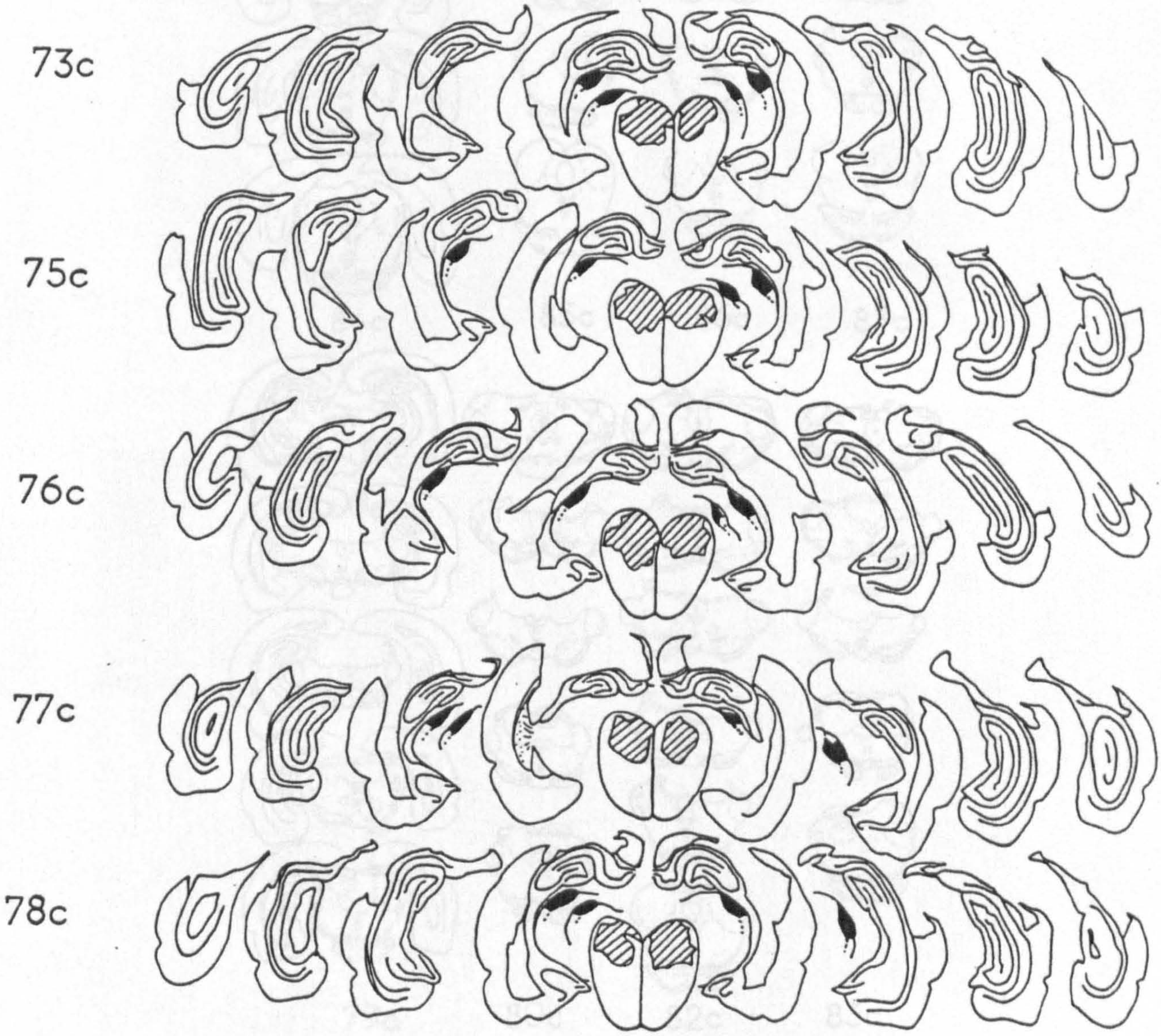

Figure 5.3a
Reconstructions of the posterior cortical (VC) lesions used in Experiment 5.1. Lgn sections are shown at two levels. Shaded areas correspond to areas of cell loss and gliosis.

Figure 5.3b (over page)
Reconstructions of collicular lesions used in Experiment 5.1.

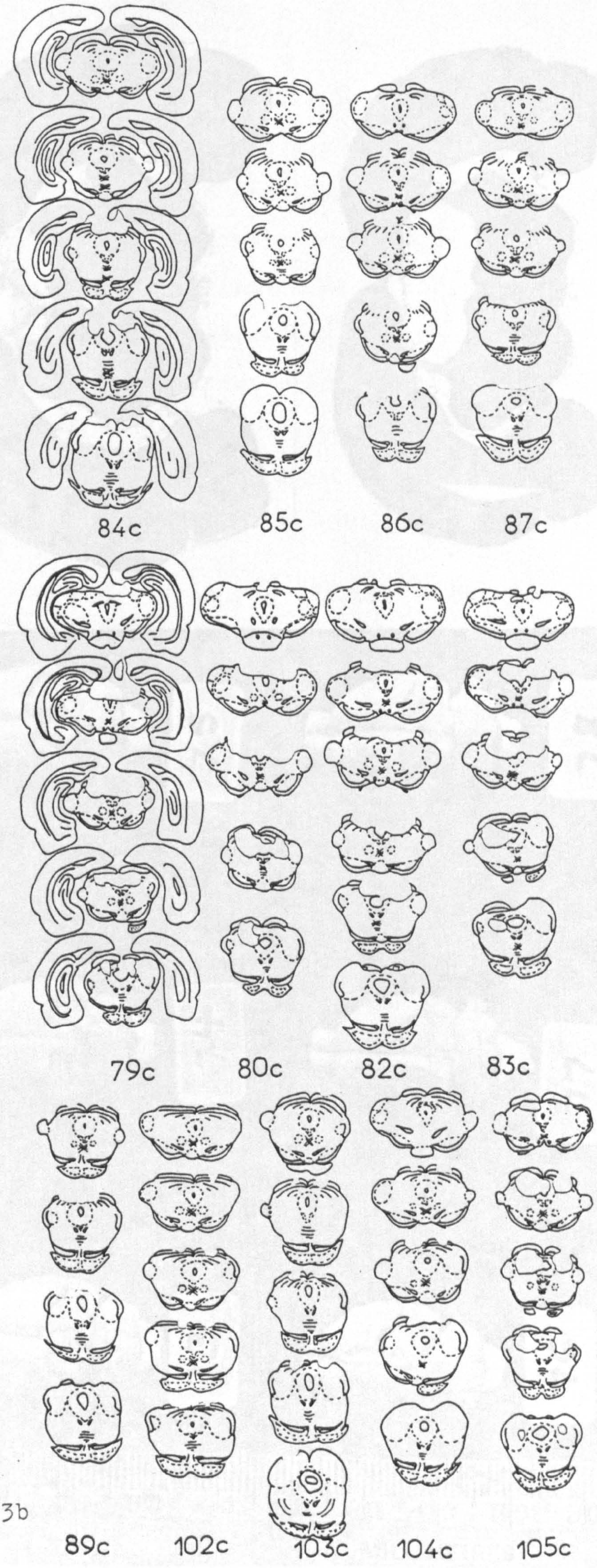

Fig. 5.3b

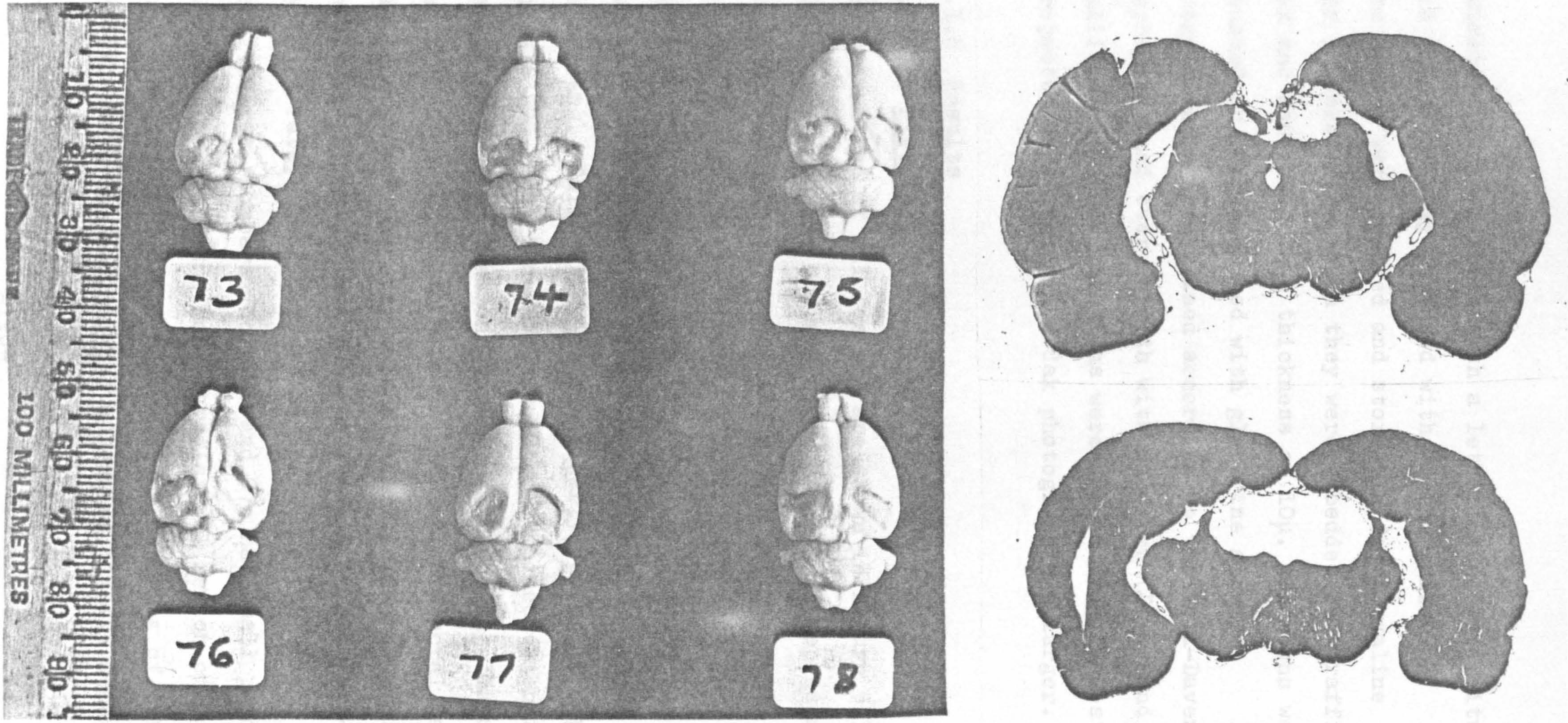

Figure 5.3c
Lesions of posterior neocortex (left) and colliculus (right; upper: 85c, lower: 79c) used in Experiments 5.1 and 7.2.

Animals were sacrificed with a lethal dose of barbiturate, and intracardially perfused with formal saline.

The brains were removed and stored in formal saline for 3 weeks after which they were embedded in paraffin wax and sectioned at a thickness of 10μ. Sections were mounted on slides coated with glycerine albumin; every seventh was stained according to the Weil-Davenport technique, and every eighth with fast red (Drury and Wallington, 1967). Sections were traced from images projected on a standard Kodak photographic enlarger.

5.1.6 Results

5.1.6.1. Histology

Reconstruction of all lesions are shown in Figure 5.3. Numbers 84c and 79c are shown in more detail representing animals with collicular lesions placed superficially and in deep laminae respectively, illustrating that the dorsal spread of the lesion into subicular areas was successfully controlled by the use of prudent lesion parameters. Collicular lesions clearly varied in depth; animals 79c, 80c, 82c, 83c and 105c sustained extensive damage to deep laminae while the rest had damage mainly restricted to the superficial 3 laminae. Pretectal damage was slight, and was only seen in animals 79c and 80c. Inferior collicular invasion was evident in all deep-lesioned rats, though always minimal. Of the visual decorticates, numbers 73c, 76c and 77c had small patches of normal cells in the most dorsolateral region of lgn corresponding to minimal rostrolateral sparing of striate cortex though the nuclei were otherwise totally degenerated, with cell loss or shrinkage and gliosis evident. The alvear region of the HPC was slightly damaged in all animals, though substantial CAI damage was only seen in animals 73c and 74c. Cingulum was removed with the cortex in all VC rats.

5.1.6.2. Postoperative recovery

Earlier attempts to use anodal electrolyte lesions in a pilot study were abandoned since in every case, these resulted in violent postoperative hyper-reactivity upon sudden stimulation. Only one animal survived, this being the only one with total bilateral ablation of the colliculi, suggesting that the effect may be due to deposition of iron during the lesion procedure irritating remaining collicular tissue.Irritative stimulation has been reported for hypothalamic lesions (Rolls, 1970). Alternatively, since lesions of periventricular grey matter can cause 'explosive' motor behaviour (Blair, Liran, Cytryniak, Shizgal and Arnit, 1978) the effect could conceivably be due to irritation of this structure.

Investigation of such animals recovering from anasthesia revealed that they were extremely hypersensitive to auditory (click) but not visual (light flash) stimuli; this could be due to the fact that superficial laminae which are predominantly "visual" (Chapter 2) were largely removed by the lesion. Cholinergic stimulation of the intact SC (Grossman, 1978) was found to elicit a similar hypersensitivity, though to both visual and nonvisual stimuli.

The violent nature of such behaviour is emphasised by the observation by Murison (1977; personal communication) that one such animal succeeded in lifting its cage roof in the course of making a violent escape. Dean and Pope (1978; personal communication) report using postoperative restraint with these animals, though where such survive, their behaviour apparently returns to normal. No hyperreactivity was seen in any animal given a radiofrequency lesion.

Weightloss was minimal in animals given collicular lesions (mean: 9.6 gms ; see Table 5.1), and no animal exhibited motor disabilities or feeding difficulty postoperatively.

5.1.6.3 Behaviour

The behavioural categories which were particularly relevant to the experimental hypotheses were extracted and subjected to statistical analysis. On the basis of previous experience (Foreman et al, 1978), the following categories were scrutinised:

	CATEGORY OF BEHAVIOUR:	MEASURE OF:
1.	Line Crossings (Running)	General Activity
2.	Rearing	Attentiveness
3.	Defaecation	Emotionality
4.	Percentage of line crossings (runs) accompanied by sniffing and/or headraising ("Accompanied Runs")	Coordination of attention and locomotion
5.	Time spent headraising or rearing ("HR/R")	Total potential visual sampling time
6.	Grooming	Attention to body surface
7.	Alert, immobile time	Time available, but not used, for exploration.

Table 5.1

Weightloss in SC, VC and Control groups on post-operative days 7 and 14, expressed as a percentage change compared with body weight at surgery.

	Postoperative Interval			
	7 days		14 days	
Group	Mean	Max[1]	Mean	Max[1]
VC (n = 6)	-5.73*	-9.30	+0.42	-2.90
SC (n = 13)	-1.90**	-6.20	+3.90	+0.90
C (n = 12)	-9.00	-15.40	+1.39	-2.80

[1] Maximum fall (-) or minimum increase (+)

** Significantly different from controls ($t(23) = 5.37$; $p<0.001$)

* Not significantly different from controls ($t(16) = 1.54$; $p<0.10$)

All event data was subjected to a $\sqrt{x+1}$ transformation since such is recommended for data which represents the probability of a particular event occurring in a limited time interval (Edwards, 1960). An Analysis of Variance between groups with repeated measures on the second (Days) factor was then carried out. Planned orthogonal comparisons were computed where these were justified by a significant Group effect in the initial analysis[1]. Comparisons between groups at levels of the second (Days) factor were made using post hoc (Scheffé) tests where these were justified by a significant interaction term in the initial analysis[2].

Figure 5.4 summarises the levels of activity and exploration in the 3 groups. Between-group differences were obtained on measures of line crossings (running) ($F(2,28) = 3.46$; $p<0.045$), rearing (t: $F = 14.0$; $p<0.006$, e: $F = 14.17$; $p<0.006$), defaecation ($F = 4.80$; $p<0.001$), HR/R ($F = 22.22$; $p<0.001$) and "accompanied runs" ($F = 94.5$; $p<0.001$). No Group effects were obtained on measures of grooming or alert inactivity.

The main effect on line crossings was due to the greater number of crossings of colliculars compared with both VC and control groups (both p's <0.01). Crossings fell in all groups across test days ($F(2,56) = 2.76$; $p<0.052$), but not

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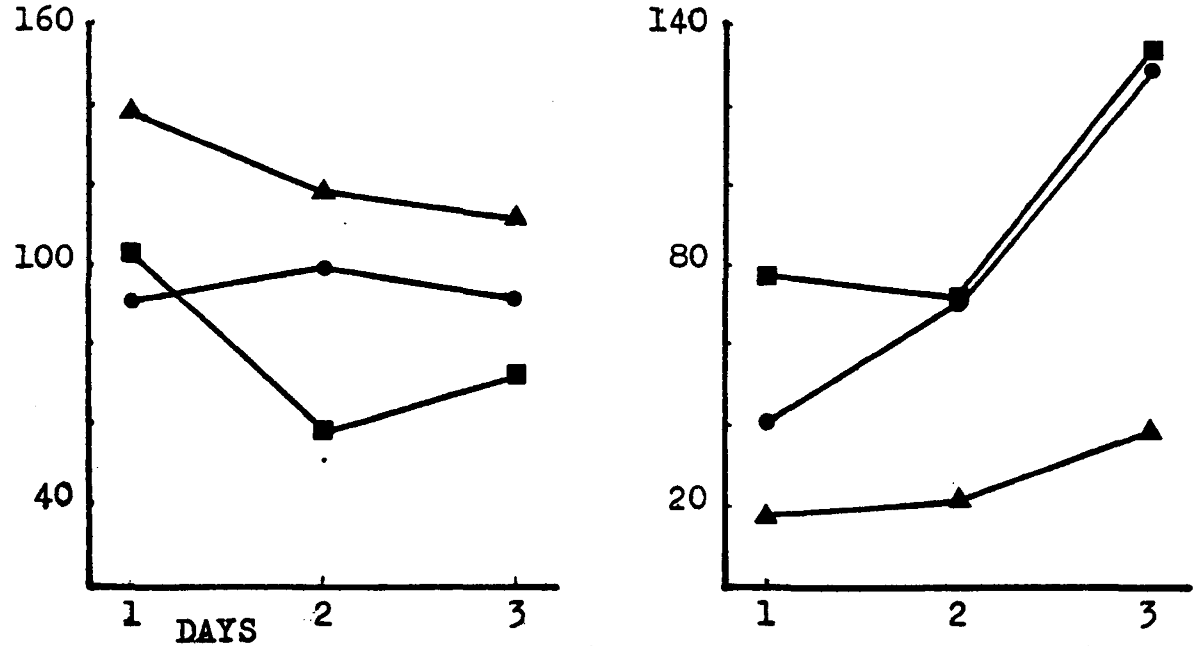
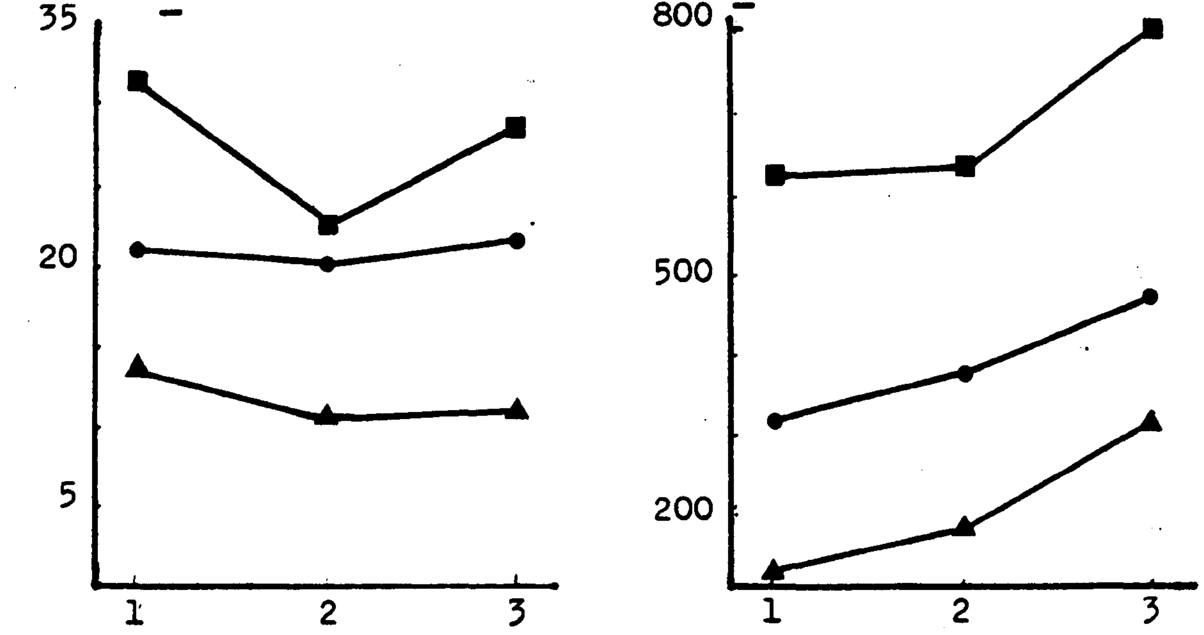
[1] Two-tailed probabilities are given througnout this thesis. Degrees of freedom are given for the first-mentioned comparison and omitted thereafter. Comparisons not mentioned may be assumed throughout to be insignificant.

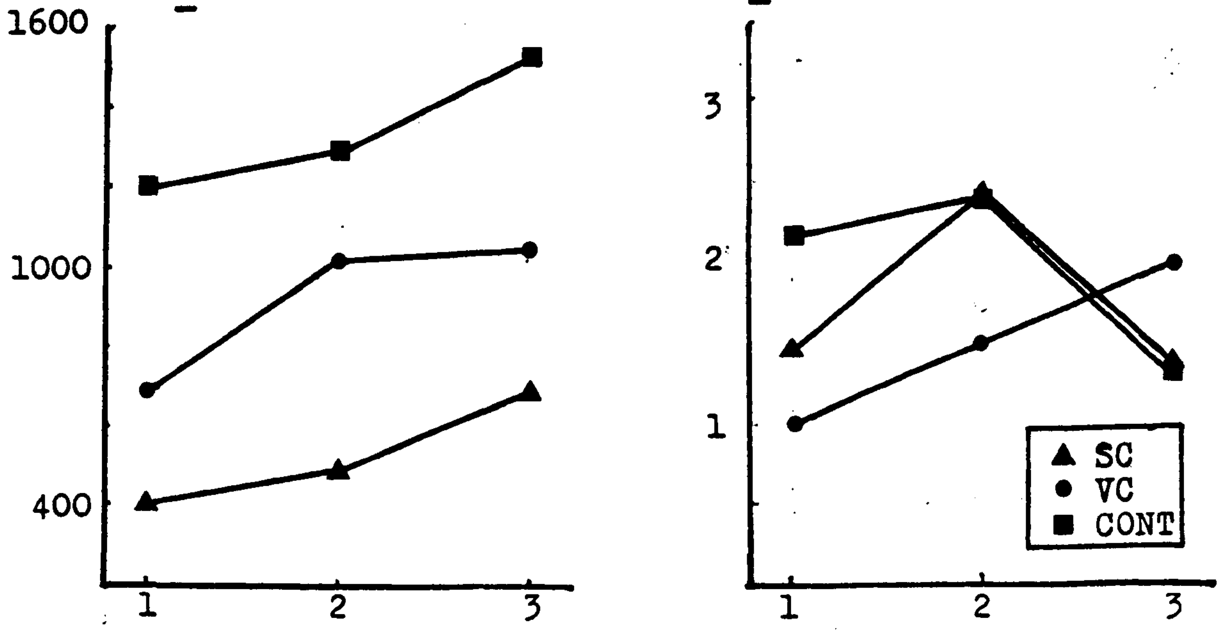
[2] Since the Scheffé test is conserv ative, significance will be assumed for $p<0.10$, as recommended by Scheffé (1959): see Winer (1971).



A.LINE CROSSINGS (RUN) B.ACCOMP.RUNNING (%)



C.REARING (e) D.REARING (t)



E.H'RAISE/REAR (t) F.GROOMING (e)

Figure 5.4
Activity and investigation recorded in Experiment 5.1.

differentially between groups. SC and VC rats spent less time engaged in rearing than controls ($p < 0.004$ and $p < 0.001$ respectively) though SCs did so significantly less than VCs ($p < 0.04$) These effects were independent of test day, though in all groups time spent rearing increased significantly with testing ($F(2,56) = 5.32$; $p < 0.008$). Similarly, where number of rears is considered, the group effect is due to the reduced number of rears in the SC group by comparison with controls ($p < 0.001$) and VCs ($p < 0.003$), though the latter groups failed to differ. No increase in rear events over days was obtained ($F = 1.41$; $p < 0.25$).

Time spent headraising and rearing (HR/R) was greater in controls than in SCs or VCs ($p < 0.001$ and $p < 0.003$ respectively) and SCs engaged in less than VCs ($p < 0.001$). The SC group showed a lower percentage of "accompanied" runs than controls ($p < 0.001$) and VCs ($p < 0.001$) on all days though the VC group tended to show less than controls, the effect almost reaching significance ($p < 0.075$). A significant Groups x Days interaction was obtained on this measure ($F(4,56) = 16.78$; $p < 0.001$). As Figure 5.4B illustrates, on day 1 the VC group engaged in relatively few "accompanied" runs, though still more than SCs ($F'(2,28) = 5.39$; $p<0.10$) but fewer than the control group ($F'(2,28) = 13.93$; $p<0.01$); no significant differences emerged between VC and control groups on days 2 or 3.

Defaecation occurred more often in both VC and SC groups than controls ($p < 0.008$ and $p < 0.035$ respectively), and a marginally significant Groups x Days interaction was obtained ($F = 2.64$; $p < 0.05$) due to the defaecation in 4 SCs on day 3 compared with 0 VCs and 1 control.

Qualitative observations

On initial placement in the apparatus on the first test day, a control rat would typically sit motionless for a few seconds before cautiously moving towards the wall of the apparatus and engaging in a repetitive cycle of running (usually remaining close to the perimeter). Locomotion was frequently punctuated with rears or bouts of sniffing and headraising, and was usually accompanied by sniffing or headraising. On later test days, stationary investigatory behaviour increased in frequency, while locomotion tended to diminish. More runs tended to encroach upon the more central areas of the apparatus and a greater percentage were combined with one or more investigatory behaviours.

In contrast, the collicular rat immediately began to run about upon initial placement in the apparatus, adopting an erratic, darting motion with frequent changes in direction. Almost all locomotion took place aroundthe perimeter of the apparatus on all test days; few instances of investigatory behaviour were recorded and locomotion was almost never combined with sniffing or headraising. However, collicular rats do occasionally stop to groom, or sit motionless though not engaging in investigation of floor or walls of the apparatus. Furthermore, when being picked up they appear unaware of E's movements and are startled by E's hand touching their fur, as though unaware of its approach.

5.1.7 Discussion

The absence of postoperative weightloss or feeding difficulties in the SC group clearly demonstrates that functional lesions of the SC can be effected without inducing extreme behaviours seen in rats with very deep, extensive ablations (Murison, 1977; Pope and Dean, 1979).

The increased locomotor activity of the SC group is consistent with previous reports (Isaac,1971; Smith and Weldon, 1976; Foreman _et al_, 1978; Pope and Dean, 1979), though by comparison with most previous studies, the degree of elevation was relatively small and varied markedly within the SC group. However, since it has been argued that deep laminal damage is especially responsible for producing hyperactivity (Foreman _et al_, 1978), the results of the present experiment are explicable, since animals exhibiting the greatest activity appeared to be those with the deeper, larger lesions. This point will be returned to following Experiment 5.3 when additional data will be considered.

Furthermore, the reduced attentiveness (_viz_.the rearing and HR/R scores) of the SC rats is consistent with previous reports (Foreman _et al_, 1978; Marshall, 1978).

Reduced attentiveness was noted in all SC rats, regardless of whether their activity was noticeably elevated. This is again in agreement with previous reports (Goodale and Lister, 1974; Marshall, 1978; Smith and Weldon, 1979), and suggests that the attentional impairment following SC ablation is less dependent upon size and locus of lesion than is the hyperactivity.

A question which inevitably arises from these results is to what extent decreased attention in SCs is likely to result directly <u>from</u> increased activity. Since some behavioural categories are mutually exclusive (e.g. running and rearing), an increase in one will reduce the animal's opportunity to engage in the other. It is unlikely that this accounts for decreased investigation in SC rats for three reasons. Firstly, SCs failed to differ from controls in terms of non-attentional behaviours which are also incompatible with locomotion (inactive time and grooming), thus SCs did have "spare" time for investigation despite their elevated score on line crossings. Secondly, attentional behaviours which are compatible with locomotion[1] and which frequently accompany running in normal rats (and which might, therefore, be expected to <u>increase</u> with increased running) were notably greatly reduced in SCs in both absolute and proportional terms. Thirdly, substantial reductions in rearing and head raising were observed in animals which failed to exhibit elevated activity. Interestingly, the

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[1] For example, in this instance, sniffing and headraising.

characteristic twisting, darting runstyle of deep-lesioned colliculars has been noted previously for both rats (Collin, 1977) and hamsters (Keselica and Rosinski, 1976).

The visual cortical lesions used in the present study were more extensive (particularly medially) than those employed by Foreman _et al_ (1978) and included area 18, cingulate cortex and the cingulum bundle. Peristriate cortex receives indirect input from the SC (Glendenning _et al_, 1975) and might be thought to be involved in visual learning and attention (Kemp _et al_, 1979). It is perhaps significant, therefore, that the behaviour of VCs in this experiment, unlike those in previous studies (Foreman _et al_, 1978) was similar to that of colliculars in terms of attentional (though notably not motor) behaviour. For example, they showed a reduced percentage of "accompanied" runs on day 1 compared with control animals, and less rearing throughout testing. The possibility that lesions of nonstriate posterior neocortex would alone reproduce some aspects of the "SC syndrome" would be worth investigating, though it should be noted that in the present study, reductions in attentional behaviour in VCs were small be comparison with SC rats.

Many theories of collicular function have emphasised the involvement of the SC in peripheral or "ambient" vision (Trevarthen, 1968, 1970; Ingle, 1973; Goodale _et al_, 1978) and from these it might be inferred that in attentional terms the SC-lesioned animal lacks a "visual field"

(Humphrey, 1970). According to Foreman et al (1978), hyperactivity in deep-lesioned SC rats results from a global deficit in novelty detection, since collicular activity is released from the modulatory influence of mechanisms which normally depress locomotion in strange environments. Implicit in this model is the assumption that the ability of a normal animal to discriminate that it is in a novel environment depends upon the simultaneous perception of numerous unexpected environmental cues. The collicular-lesioned animal, unable to do this due to a widespread "attentional scotoma", might therefore be viewed as exhibiting the type of behaviour seen in a control animal which has been partly habituated to the novel environment and for whom the environment contains fewer novel cues.

This view, however, is untenable since low levels (and not high levels) of locomotor activity are characteristically shown by control animals following adaptation and further that the trend in the activity habituation curve for SCs is similar to that of controls (Foreman et al, 1978; and above results). Thus a more plausible suggestion is that the SC rat is aroused by general environmental novelty, exhibiting elevated activity in a test environment (see above) but not in a familiar environment such as the homecage (Carson and Goodale, 1978; cited Foreman et al, 1978). Yet the SC-lesioned animal is inattentive to specific features and cues which the control subject will stop and investigate. The theoretical significance of this is that the deficiency in the use of "ambient vision" following collicular lesions (Trevarthen, 1968, 1970) is likely to amount to deficient selective attention to specific "ambient" stimuli. On intuitive grounds, it seems unlikely that a normal animal would simultaneously treat all aspects of a novel apparatus as totally and equally novel. Even in such a situation, selective attention must inevitably operate to isolate certain features ("figures") from the rest ("ground"). It is possibly this which the SC animals fail to do satisfactorily. Interesting in this respect is the comment by Blake (1959) that when live prey is introduced into the cages of cats with SC ablations, the animals showed general agitation, but not investigation of the prey object *per se*, and the report of Schneider (1968) that hamsters with undercut colliculi showed signs of general attention to movements of a checkerboard pattern above their heads but failed to turn and fixate the locus of stimulation.

A disadvantage of the present experiment was that group differences in attentiveness were inferred from the relative frequency of occurrence of behaviour such as rearing, sniffing and headraising which were assumed to have an attentional component. Behavioural categories may, however, be ambiguous. For example, rearing in rats may be regarded as an attentive behaviour (Prescott, 1970) or alternatively as an attempt to escape from the apparatus (Archer, 1973).

Pharmacological studies have shown that reduced levels of rearing may result from interruption of catecholamine pathways between brainstem and forebrain (Mason and Iversen, 1978) which may be invaded by deep lesions of SC. However, the lesions in the present study are unlikely to have encroached upon dorsal tegmentum sufficiently to interrupt such pathways; in addition Mason and Iversen (1978) report reduced rearing in tegmentally-lesioned rats to be accompanied by <u>decreased</u> and not increased locomotion. The present results suggest that damage to overlying SC laminae might be responsible for the rearing deficit observed in such experiments. Reduced rearing in the present SC-lesioned group might alternatively be due to motor disturbance; Milner (1978; personal communication) and Pope and Dean (1979) have shown that SC-lesioned rats have difficulty maintaining balance, though in the latter study this resulted in additional grooming problems notably absent in the present results.

In the following experiments, attempts will be made to examine attentiveness directly, by isolating the precise class(es) of cue to which the SC rat fails to attend and the nature of "ambient" environmental manipulation which give rise to increased activity in SCs. In addition, lesions of SC will be compared with lesions of other neural structures arguably related to the control of attention.

5.1.8. <u>Conclusions</u>

Collicular rats are more active than controls in the open field, show less "attentional" behaviour and rarely combine locomotion and attentional behaviours. However the collicular may behave differentially in novel and familiar environments and thus the SC lesion may give rise to elevated activity levels by abolishing attentional responses to specific cues.

5.2 Locomotor Investigation in Rats with Superior Collicular, Medial Frontal Cortical and Hippocampal lesions

5.2.1 Introduction

There is substantial evidence for a rather unique role for the SC in the redirecting of attention to novelty, and perhaps in the co-incident arrest of ongoing behaviour (Goodale et al, 1978; Foreman et al, 1978). However some experiments have demonstrated behavioural changes following lesions of other brain structures, for example the hippocampal formation (HPC) and medial frontal cortex (MFC), which are so strikingly similar to those following collicular lesions that either (i) functional links might be suggested between the SC and these structures (see Section 4), or (ii) functions attributed by some authors to the SC might alternatively be viewed as primarily dependent upon the HPC or MFC. For example, Altman et al (1973) suggest that the reported hyperactivity of hippocampal rats in a novel environment may be due to the removal of hippocampal "inhibition" of locomotion during investigation and shifts of attention. This, they argue, is likely to be most apparent when the animal is placed in a novel environment. Similar predictions, based on different theoretical models, have been put forward. Gaffan (1972) proposed that the hippocampal animal lacks familiarity discrimination, thus presumably continuing to treat familiar environments as novel and continuing investigation when control animals have ceased (Gray,1971b). O'Keefe and Nadel (1978) put forward a similar argument, namely that the hippocampal animal treats an environment as permanently novel since he lacks a "cognitive spatial map" within which the information in an environment may be accommodated and coded.

However, contradictions emerge in the literature on this subject (see Chapter 4). In particular, if hippocampal activity elevation is not a result of an abnormal response to novelty *per se*, but due to slow or absent habituation to an environment (Douglas and Isaacson,1964; Gray,1971b; Means, Leander and Isaacson,1971; Jarrard, 1973), it must follow that HPC-lesioned animals' hyperactivity would only become apparent after prolonged testing. Indeed O'Keefe and Nadel (1978) have themselves argued that the failure of Hostetter and Thomas (1967) to obtain increased activity from hippocampal rats may have been due to their use of short (4 minute) test sessions. However, the fundamental distinction between collicular and hippocampal lesion effects should now be clear, since, unlike HPCs, SC-lesioned animals are hyperactive upon *initial* placement in an apparatus, a behavioural change which is much more likely to arise from a genuinely abnormal response to novelty.

Recent pharmacological studies have provided evidence for an alternative connection between the HPC and SC, since SC lesions are likely to interrupt pathways from the brainstem (eg. locus coeruleus) which pass through dorsal tegmental regions (eg. the dorsal adrenergic bundle). Damage to such pathways result in a drastic reduction of forebrain noradrenaline (Mason and Iversen, 1978; Winterkorn *et al*, 1978). The behavioural consequences of such interruption may be changes in attentional behaviour and resistance to habituation (Mason and Fibiger, 1979) similar to the effects of HPC ablation (see Chapter 4); indeed such pathways may be involved in the generation of hippocampal theta activity (Redding, 1967). However, a proper comparison between SC- and HPC-lesion effects is only possible when both are investigated within a single design. Such has been undertaken for lateral hypothalamic and collicular lesions by Marshall (1978) who was able to distinguish them apart in terms of the nature and severity of postoperative attentional and motor deficits.

The reported anatomical connection between the frontal projection cortex of nMD and the SC has prompted some authors to suggest a functional link between them (see Chapter 4). Indeed, activity (Lynch, 1970; Campbell, Ballantyne and Lynch, 1970) and attentional (Latto and Cowey, 1971b ; Collin, 1977) changes have been reported following frontal lesions, reminiscent of findings with SC animals. Winterkorn (1975 a,b) observed an apparent similarity between colliculr and frontal lesions in terms of locomotor control in a discrimination runway, and suggests that the two lesions might have their effects by damaging separate parts of the same locomotor control system exerting its influence via brainstem sites. Such a suggestion is clearly consistent with a model proposed for SC by Foreman <u>et al</u> (1978).

Thus the initial section of this experiment investigated the open field behaviour of rats with SC, MFC and HPC lesions.

In Experiment 5.1 it was noted that the majority of previous studies of exploration in collicular rats required inferences to be drawn from behaviours which were assumed to be in some way "attentional" (though see Marshall, 1978). Thus in the second part of this study, the investigation by SC, MFC and HPC rats of a novel cube which was introduction into the arena was examined.

Moreover in Experiment 5.1 it was argued that the SC-lesioned rat is likely to be capable of detecting that it is in a totally novel "ambient" environment, yet inattentive to the specific features of an environment which cause a control animal to initiate investigation. Thus in the present study an attempt was made to distinguish between the colliculars' response to a specific, novel object and to novel 'ambient' cues. The animal was first placed in a novel room while in the homecage and then with a novel object inside the cage. Since it has been shown that objects placed in the homecage are very potent stimuli for eliciting a "Novel Object Reaction" in normal rats (Cowan, 1976; Mitchell, 1976), it was predicted that control animals would both exhibit attention towards the novel ambient environment (ie. the novel room) and attention towards a novel object, the latter consisting of initial avoidance followed by intense object investigation. The SC rats were expected to exhibit attention to "ambient" novelty (see Experiment 5.1), but fail to behave differentially towards the novel object. Since <u>initial</u> response to novelty was to be specifically investigated in this latter part of the study, brief exposure periods were used.

5.2.2 Subjects

Forty experimentally naive male hooded rats of the Lister strain were used. This group of animals (also used in Experiments 2.2 and 3.1) was the only group obtained from Rowatt Research Laboratories, Aberdeenshire, Scotland. They were housed as those in Experiment 1 and were approximately 110 days old at surgery.

5.2.3 Surgery

Surgery was performed essentially as in Experiment 5.1. SC lesions were made using stereotaxic coordinates previously described, except that tip temperature was maintained at only 52.5°C. Control animals in this study underwent removal of a strip of cortical tissue. These were accomplished using visually-guided aspiration as described for posterior cortical lesions in Experiment 5.1. A narrow strip of cortex (5 mm x 1 mm) was removed between 2 and 3 mm of the midline, and extending between the bregmoidal suture anteriorly and the lambdoidal suture posteriorly. Medial frontal cortical lesions were also made by aspiration. Bone overlying the frontal pole was burred and removed, including bone overlying the saggital sinus. Care was taken not to rupture the sinus or invade the bone sinuses overlying the olfactory bulbs. The medial shoulder of cortex extending from the frontal tip of cortex to a point approximately 2 mm posterior was removed, care being taken not to invade the olfactory bulbs. Bleeding tended to be extensive, and the saggital sinus was damaged in two animals, though haemorrhage was stemmed using light pressure and packing with gauze. In some cases, small amounts of topical thrombin were applied to the damaged area. Despite vascular damage, no fatalities resulted from this lesion. Hippocampal lesions were made using anodal current [1]. A stainless steel insect pin (0.01" diameter) insulated with "Insulex" except for 0.5 mm at the tip, was lowered into the HPC at the following stereotaxic coordinates:-

1,2	A-P	-3.8	L	4.7	D	3.5, 6.8
3	A-P	-2.2	L	2.0	D	3.3
4	A-P	-2.8	L	5.1	D	7.0

A second, grounded electrode was attached to the animal via skin clips and good contact ensured by liberally bathing skin and electrode with physiological saline.

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[1] In this study only, electrolytic lesions were used. They did not produce seizures or other irritant effects as in SCs (see Section 5.1.6.2). In subsequent experiments radiofrequency lesions of HPC were used, solely to maintain strict comparability with the method of lesioning used for other structures.

The lesion was made with anodal DC current, rising over 5 seconds to 0.8 milliamps which was maintained for 20 seconds and then reduced to 0 over 1 second after which the electrode was slowly withdrawn. A new electrode was used for each animal. All animals in this study were given a 0.1 ml intramuscular injection of a standard penicillin (Penbritin) immediately postoperatively because of doubts about their health (Note: this practice was not used with any other group of animals). Postoperative care proceeded as in Experiment 5.1, though animals in this study were given 60 - 90 days postoperative recovery prior to open field testing. As in the previous study, food deprivation commenced 3 days prior to the first test session. They did not undergo testing of any kind during the postoperative interval.

5.2.4 Apparatus and Method

The same apparatus, recording equipment and method were employed as in Experiment 5.1 for initial (3 day) open field testing. On the following day, all animals were tested for a further 2 minutes as on days 1 - 3 except that a novel object (see Figure 5.5) [1], consisting of a

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[1] To avoid excessive olfactory stimulation from the sudden introduction of novel objects in this and later studies (5.3, 8.2) novel objects were placed in the test apparatus and covered with used cage sawdust overnight prior to use in testing. Both object and apparatus were cleaned with dilute acetic acid solution prior to testing, thus homogenising odours within the test environment.

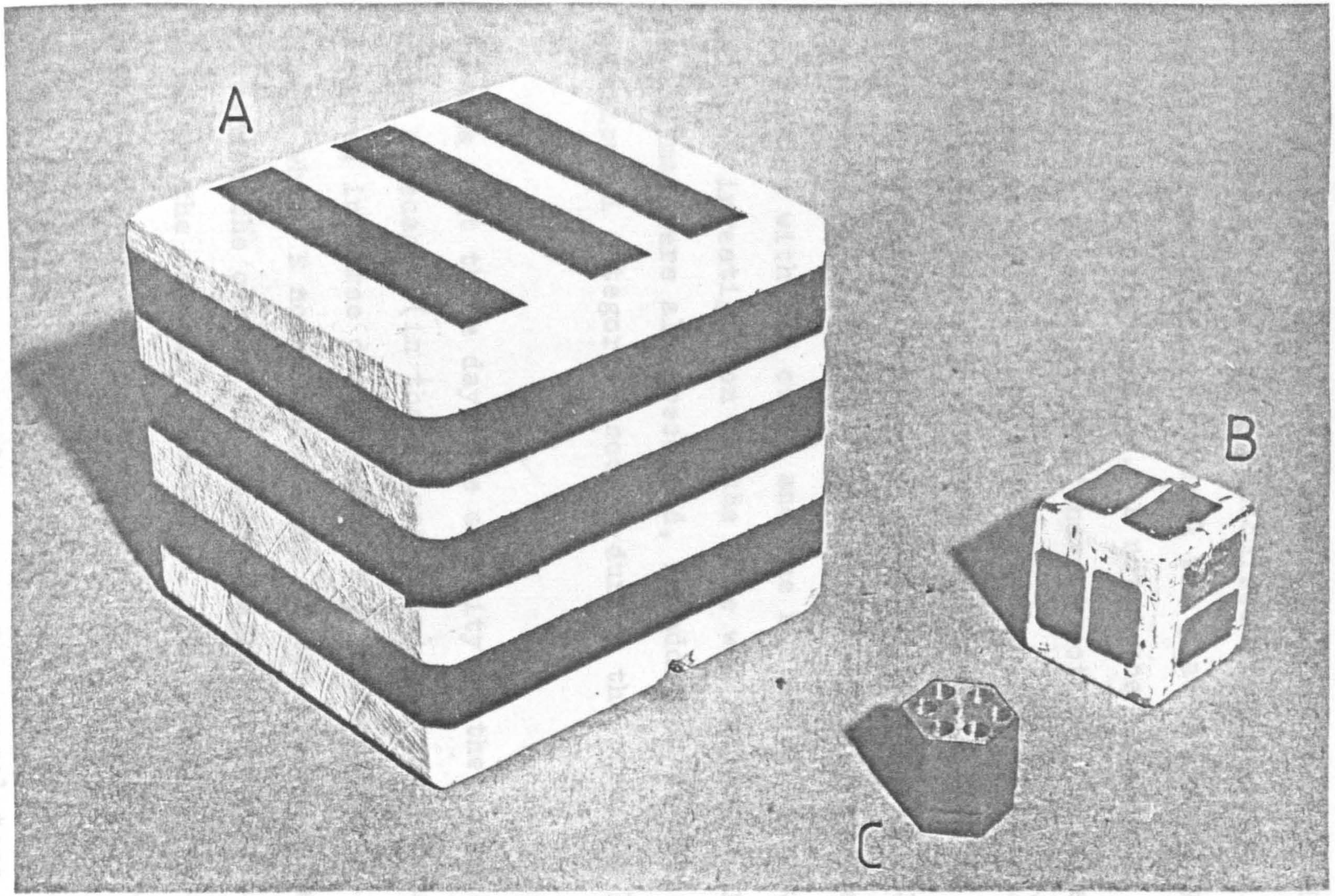


Figure 5.5
Novel objects used in Experiments 5.2 and 5.3 (actual size).

black and white striped cube of side 10 cm was placed in the apparatus prior to the animals' introduction. For half of the animals in each group, the cube was placed in the centre of the apparatus and the animal was placed at the perimeter such that the object was to its right or left side, side being randomised within groups. For the other half, the animal was placed centrally and the cube peripherally. E noted the time taken for the animal to show signs of having noticed the object. This was deemed to have occurred when the animal a) ran towards the object and began investigation or b) stood in a fixed stationary position facing the object, and within 20 cm of it. Time spent sniffing at the cube, in contact with the cube, and the number of occasions on which investigation of the cube was initiated by the animal were also recorded, in addition to the behavioural categories scored during the previous 3 days.

For the next three days the activity of the animals in their homecages (in the colony room) was semi-formally observed in three daily sessions (2 minutes per cage) during which E noted the number of times each animal traversed the centre of the homecage, and made general notes on the animals' behaviour. The homecage was as previously described in Section 5.1.2. (see Figure 5.6).

On the following day, each animal was taken, alone, in the homecage from the colony room to a novel test room (different from that in which open field testing had taken place). While one animal was being tested, the cagemate was placed, alone, in a separate cage with access to food and water. The water bottle was then removed from the test cage, which was placed on a flat, white surface. The surface had two black lines drawn one on either side of the cage perpendicular to the sides. The cage was positioned such that the imaginary continuation of the lines across the floor of the cage bisected the "observation area", this being defined as the area of cage not covered by the wire food hopper and within which the animal was able to scan the room when in a rearing position. The imaginary line bisecting the observation area served as a reference point for activity measures (Figure 5.6). The animal was observed for 2 minutes, this being timed by E with a stopwatch.

The test room was cue-rich (with various pieces of apparatus on shelves and on the floor), and illuminated by a 70 watt fluorescent light on the ceiling. A white noise source emitting approximately 50 dbs of sound was used to mask extraneous noises. E was seated on a chair overlooking the cage with a net curtain hiding E from the animal as far as possible. E recorded the following behaviours:

<u>Activity</u>:	The number of times the animal's front paws crossed the imaginary reference line on the floor of the homecage. Termed "crossings"
<u>Rearing</u>:	When the animal took up a position with the front paws off the ground (though not grooming) anywhere in the observation area.

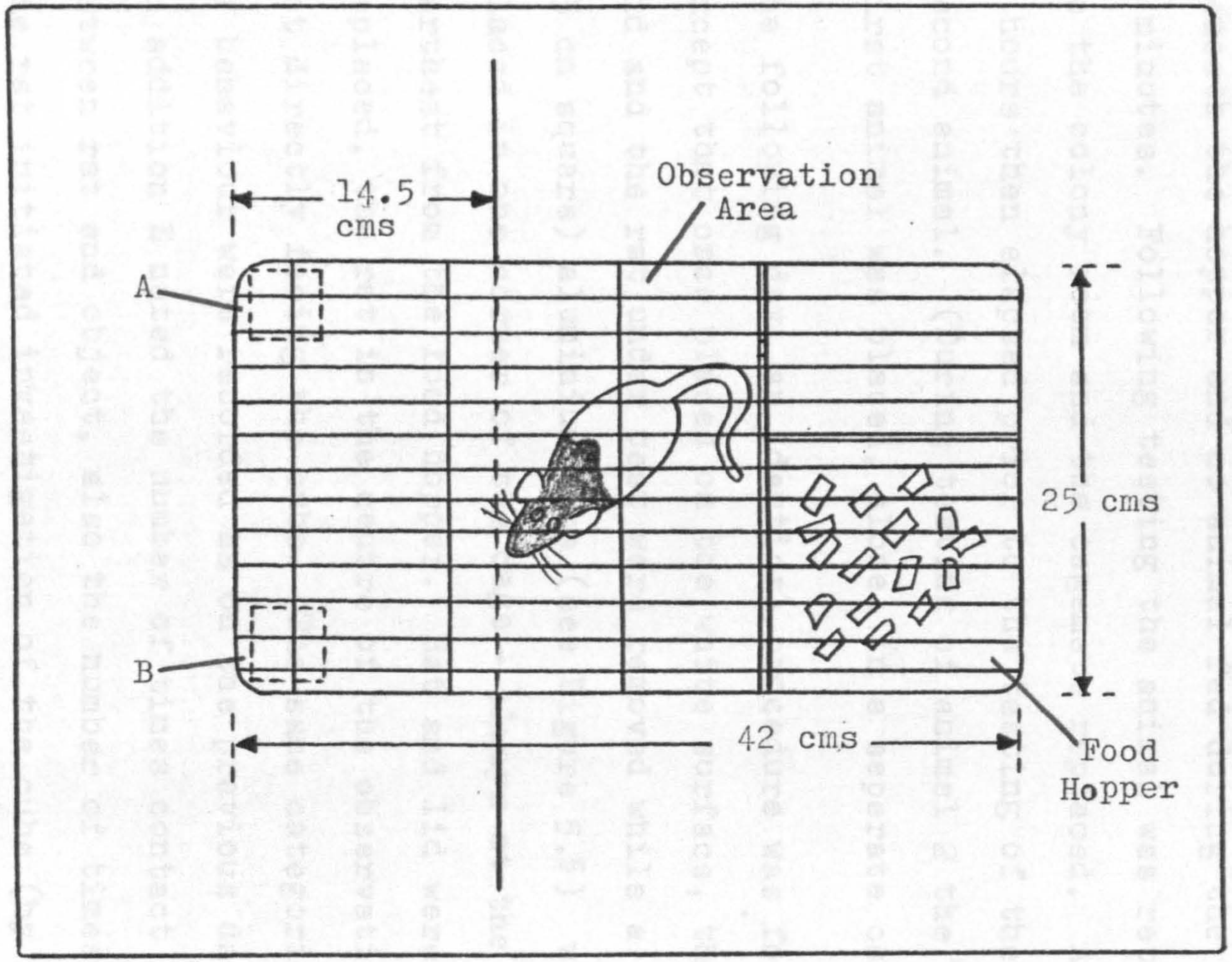


Figure 5.6
Homecage as used for observation in Experiment 5.2. Imaginary line which served as a reference for "centre crossings" is shown bisecting the observation area (see text). The two possible cube positions used on day 2 are indicated (A and B).

It was decided that periods for which the animal ran beneath the food hopper or engaged in feeding at the hopper, would not be included in the 2 minute test interval which would be extended accordingly. In practice few animals spent more than a few seconds beneath the hopper and no animal fed during the 2 minutes. Following testing the animal was returned to the colony room and the cagemate replaced. At least 2 hours then elapsed prior to the testing of the second animal. (During testing of animal 2 the first animal was placed, alone, in a separate cage).

The following day, an identical procedure was followed except that once placed on the white surface, the cage lid and the rat under test were removed while a small (3 cm square) aluminium cube (see Figure 5.5) was placed in one corner of the cage - always at the end farthest from the food hopper. Rat and lid were quickly replaced, the rat in the centre of the observation area not directly facing the cube. The same categories of behaviour were recorded as on the previous day, but in addition E noted the number of times contact occurred between rat and object, also the number of times the rat initiated investigation of the cube (by running towards it, or standing close to, and pointing towards it), plus time spent in object contact and investigation.

The animals were sacrificed and the brains processed as described in Section 5.1.5 above.

5.2.5 Results

5.2.5.1 Histology

Reconstruction of the lesions are shown in Figure 5.7. Of the control animals only one (7a) sustained substantial cortical damage, which included the medial border of striate cortex. Cell loss was evident in the dorsolateral region of the lgn of this animal. All other control animals sustained small strip lesions (represented by no's 2a, 41a, 49a in Figure 5.7) just lateral to the cingulum, but invading the corpus callosum at the deepest point in most cases. In 4 cases, cingulum was invaded unilaterally and in 2 bilaterally. No lgn cell loss was evident in these controls.

MFC lesions involved most of the projection cortex of nMD (Leonard, 1969, 1972), with some rostral sparing in rats 17a and 30a. Small areas of posterior dorsomedial (supragenual) cortex were possibly spared in animals no 1a, 10a, 13a, 19a, 23a, 30a and 46a, though the posterior extent of this subfield is not clear from previous reports and is usually arbitrarily determined (see Larsen and Divac, 1978). Most lesions approached the genu of the corpus callosum posteriorly. Minor invasion of the rostral septum occurred in no's 19a, 29a and 30a.

SC lesions were smaller than in Experiment 5.1, particularly in terms of antero-posterior extent. Some anterior, or posterior, sparing was evident in most animals except 33a, though four others (47, 18, 39, 20) sustained

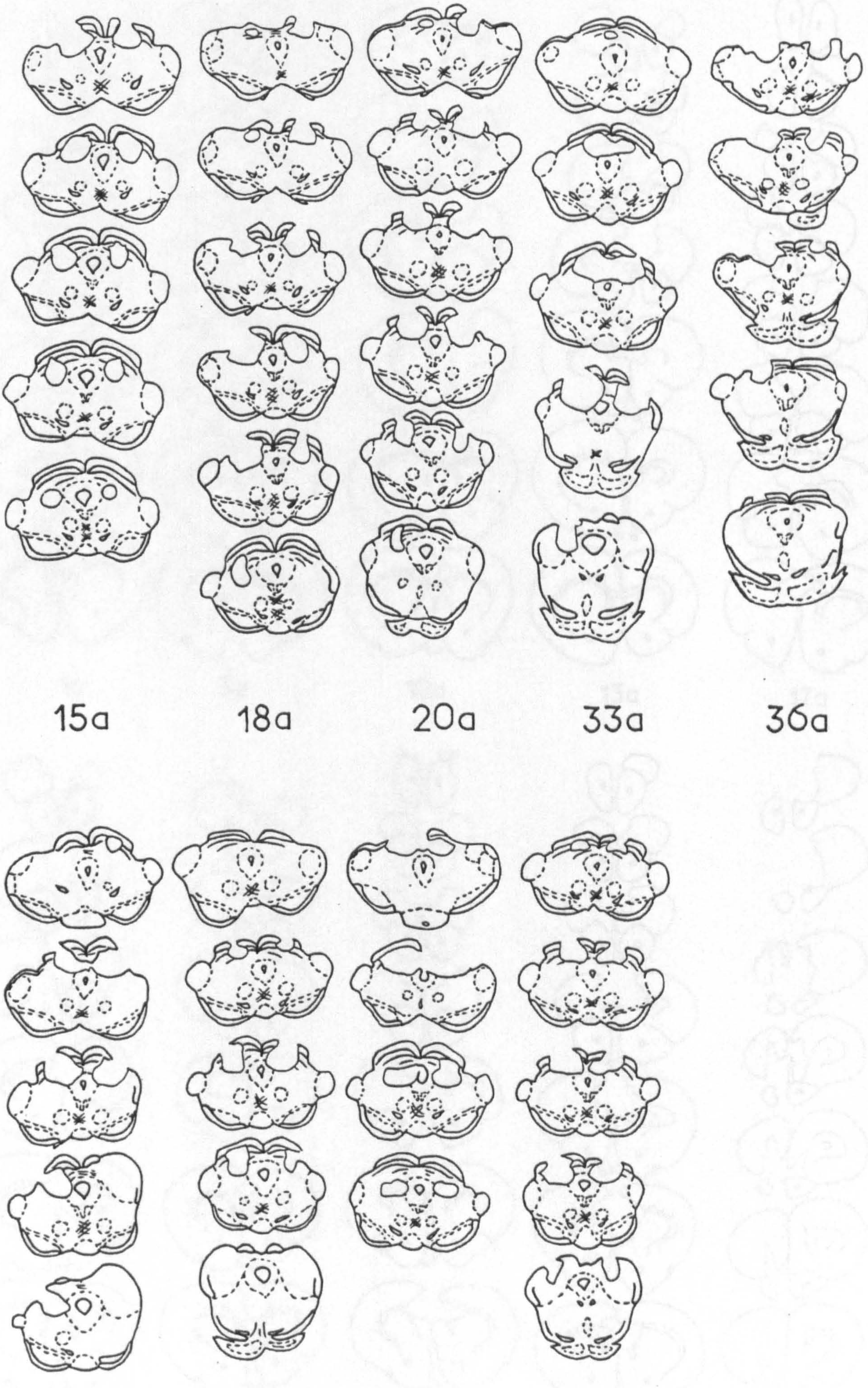


Figure 5.7a Collicular lesions used in Experiment 5.2

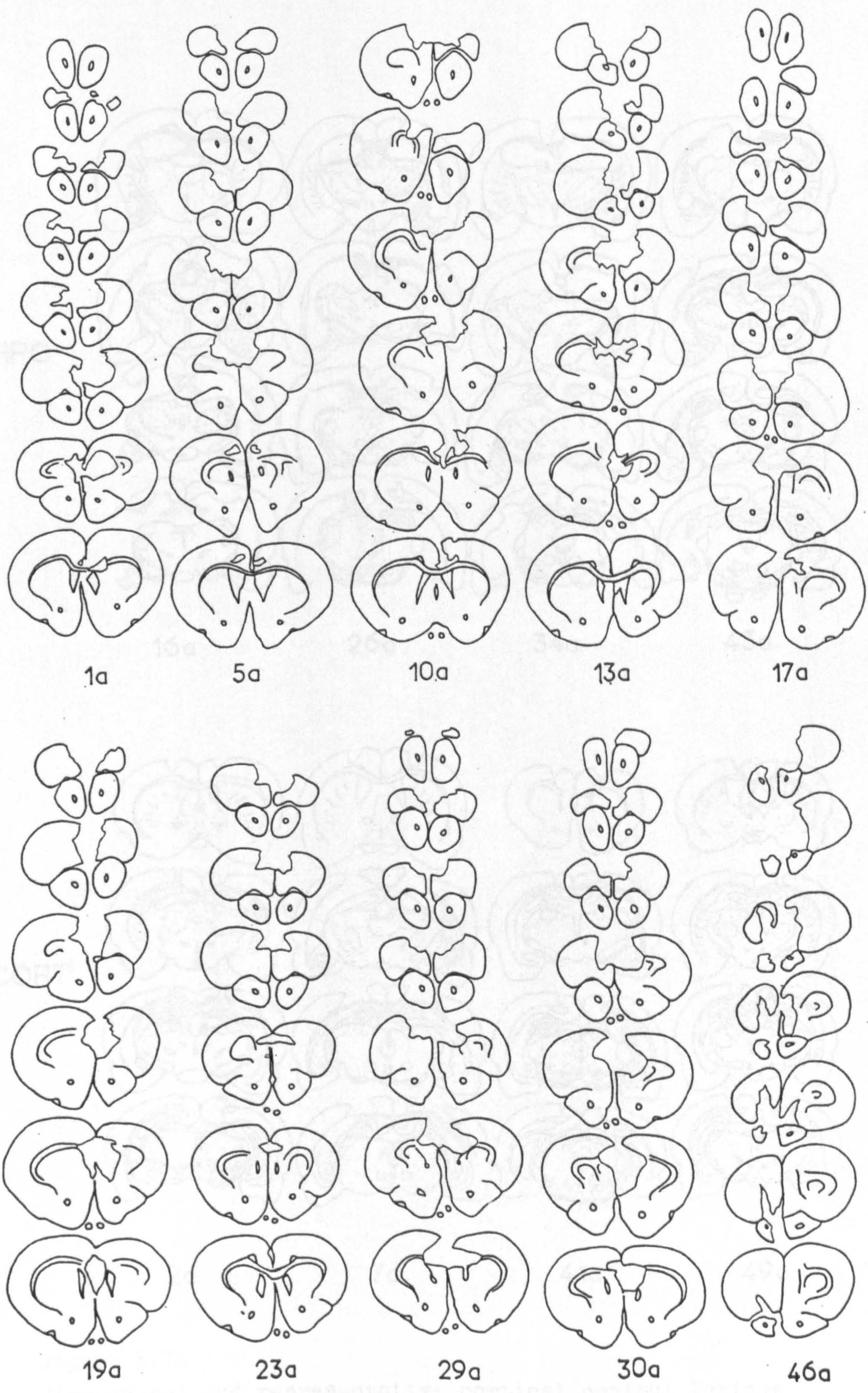


Figure 5.7b MFC lesions used in Experiment 5.2

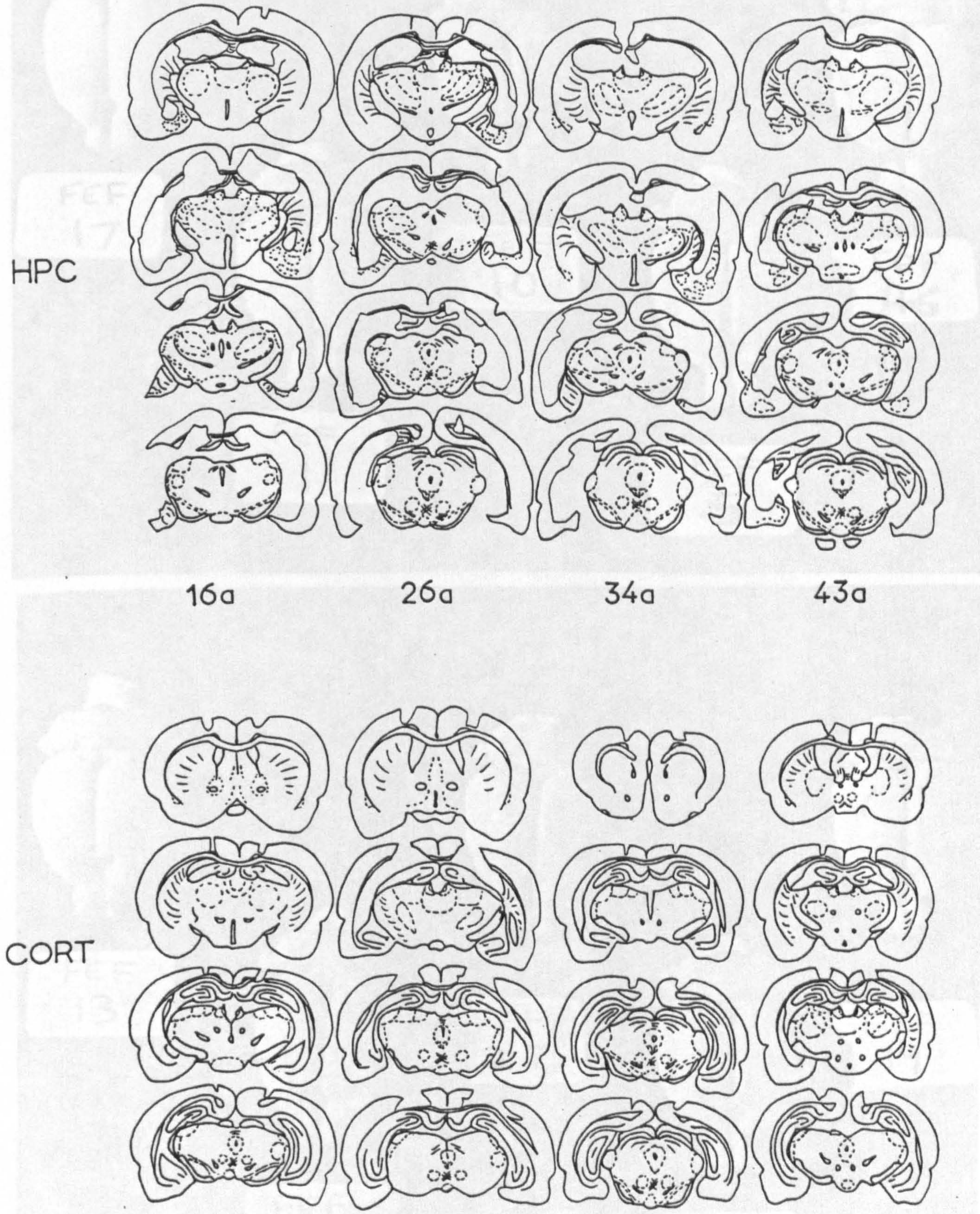


Figure 5.7c
Hippocampal and representative cortical control lesions used in Experiment 5.2

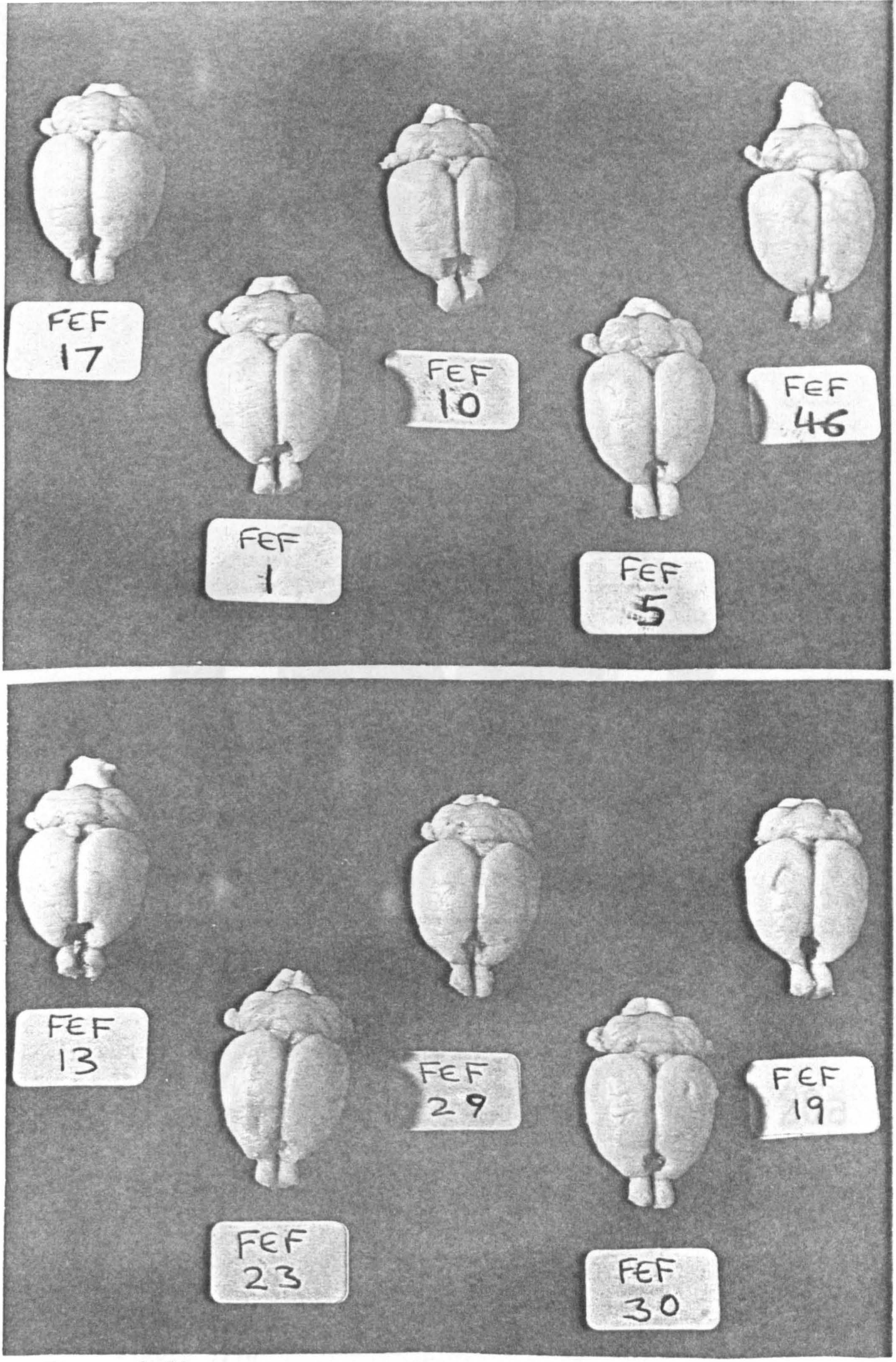


Figure 5.7d
Medial frontal cortical lesions used in Experiments 5.2 and 6.1.

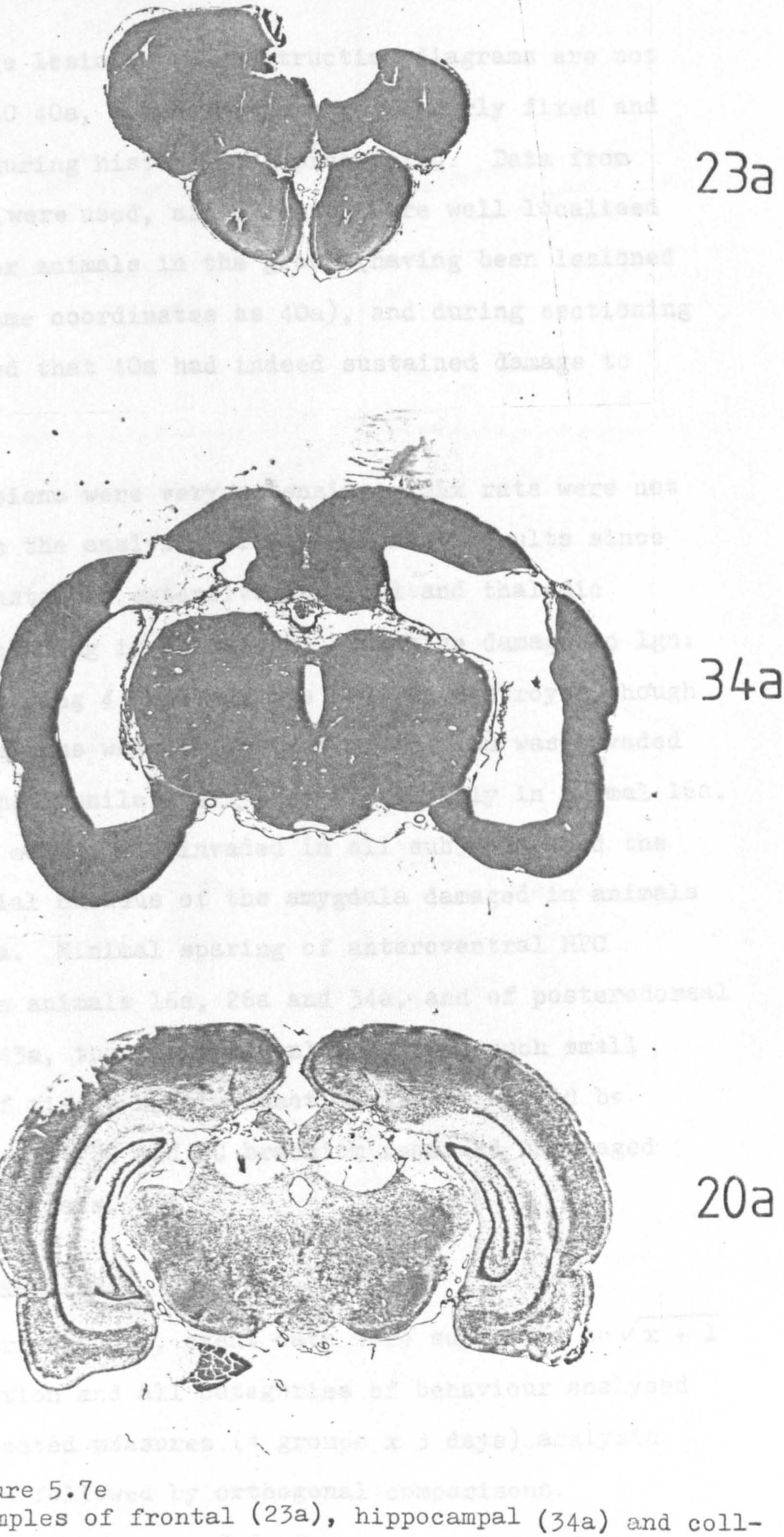


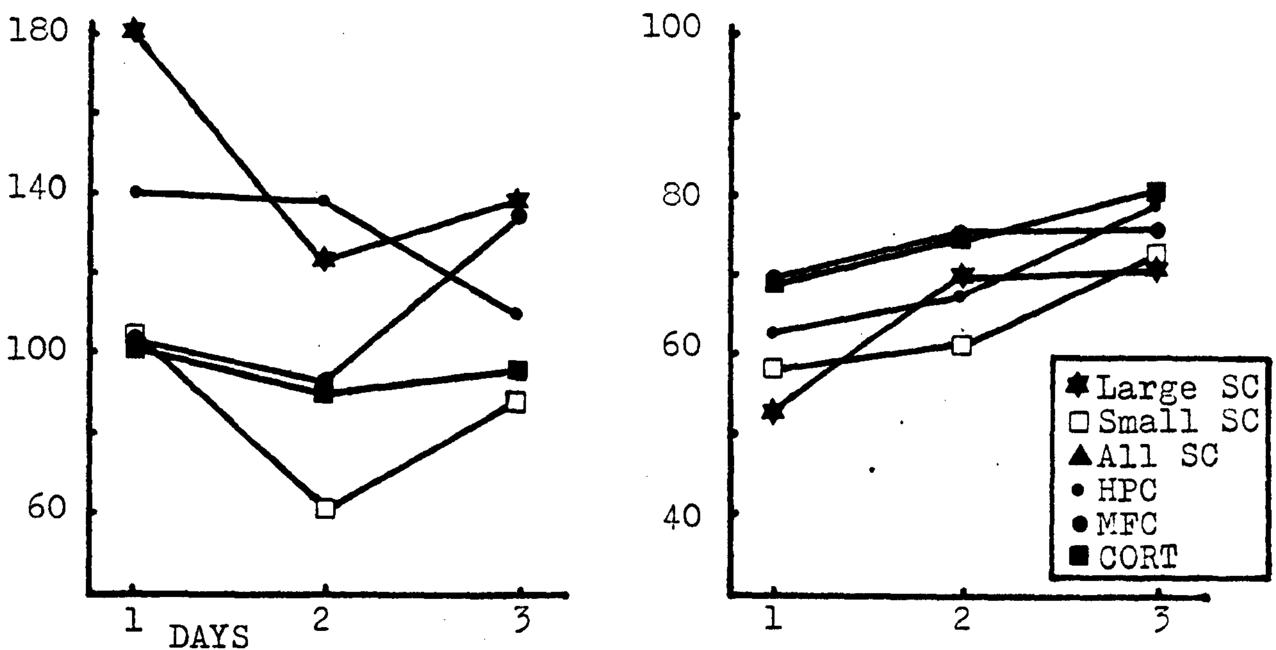
Figure 5.7e
Examples of frontal (23a), hippocampal (34a) and collicular lesions used in Experiments 5.2 and 6.1., shown in coronal section.

fairly large lesions. Reconstruction diagrams are not shown for SC 40a, since sections were poorly fixed and were lost during histological processing. Data from this animal were used, since lesions are well localised in all other animals in the group (having been lesioned with the same coordinates as 40a), and during sectioning it was noted that 40a had indeed sustained damage to the SC.

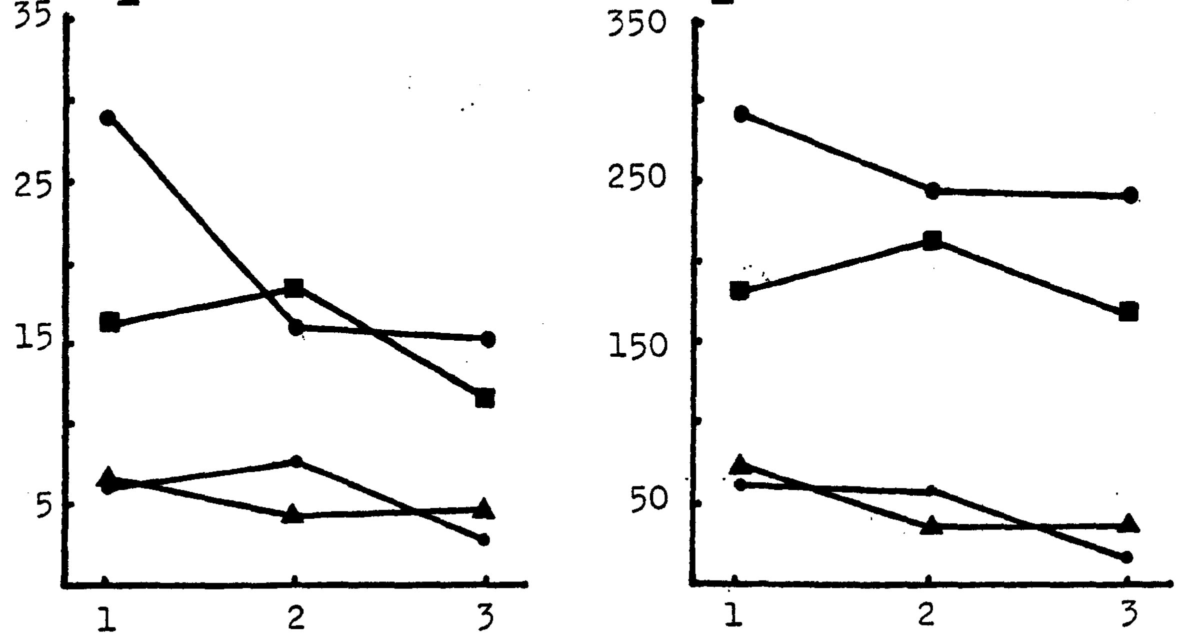
The HPC lesions were very extensive. Six rats were not included in the analysis of experimental results since they had sustained extensive cortical and thalamic damage, including in all cases, extensive damage to lgn. In the remaining 4, most of the HPC was destroyed though lateral thalamus was not damaged. Cingulum was invaded in all animals unilaterally and bilaterally in animal 16a. Entorhinal cortex was invaded in all subjects, and the corticomedial nucleus of the amygdala damaged in animals 16a and 26a. Minimal sparing of anteroventral HPC was seen in animals 16a, 26a and 34a, and of posterodorsal tissue in 43a, though it is unlikely that such small remnants of tissue remain functional. It should be emphasised that SC and SC brachium remained undamaged in all 4 HPC rats.

5.2.5.2. Behaviour

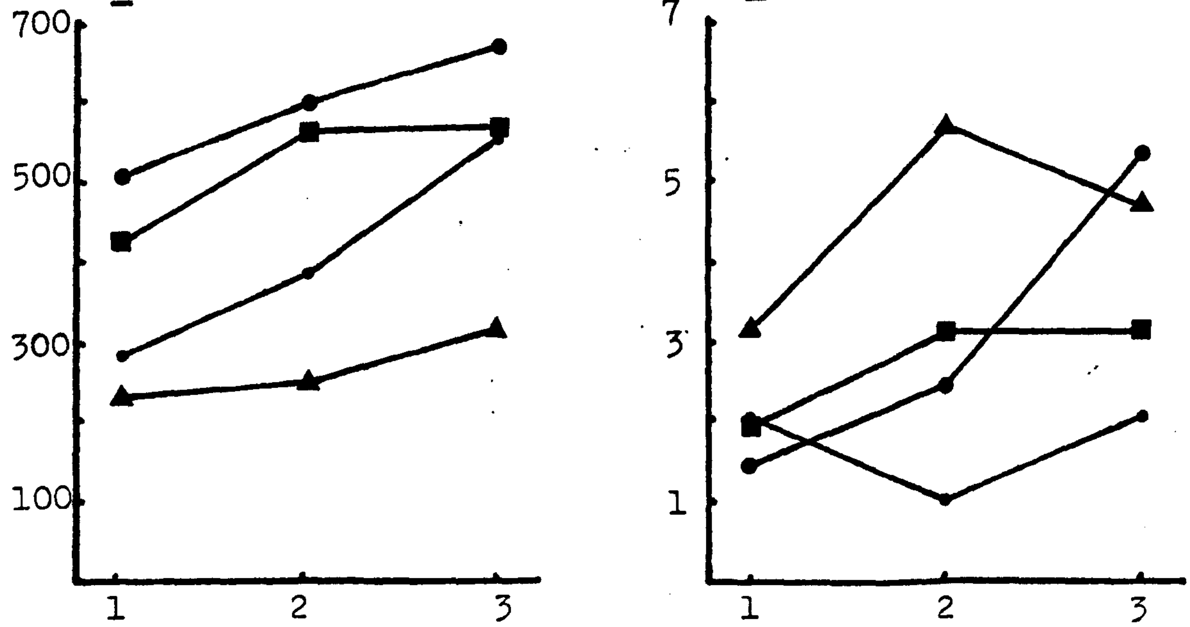
As in Experiment 5.1, event data were subjected to $\sqrt{x + 1}$ transformation and all categories of behaviour analysed with a repeated measures (4 groups x 3 days) analysis of variance followed by orthogonal comparisons.



A. LINE CROSSINGS (RUN) B. ACCOMP.RUNNING (%)



C. REARING (e) D. REARING (t)



E. H'RAISE/REAR (t) F. GROOMING (e)

Figure 5.8
Activity and Investigation recorded in Experiment 5.2

In the open field on days 1-3, the SC group was notably no more active overall than controls since no main effect of Groups was obtained ($F(3,30) = 0.75$; $p > 0.50$), and all groups failed to habituate activity significantly over days ($F(2,60) = 1.05$; $p > 0.35$). However, since size of lesion was variable within the SC group, the data was reanalysed with large and small-lesioned SCs extracted as separate groups. The large-lesioned group (33a, 47a, 18a, 39a, 20a) recorded an average of 180.8 line crossings on day 1 compared with only 105.2 and 106.3 for small-lesioned and control groups respectively. One-tailed t-tests revealed that while the large lesion group tended to be more active than the small-lesion group on day 1 ($t(8) = 1.63$; $0.05 < p < 0.10$) they were signficantly more active than controls ($t(13) = 1.93$; $p < 0.05$). Except for defaecation, where large-lesioned SCs tended to defaecate less than small-lesioned SCs (respective means = 1.53 and 2.47 boluses per animal per day), no suggestion of differential results were obtained on any other measure as a result of separating large and small SC lesioned animals, thus all subsequent results are described for the original four groups.

Main Group effects were obtained on measures of HR/R ($F = 19.12$; $p < 0.001$), rearing (time: $F = 24.15$; $p < 0.001$; events: $F = 18.04$; $p < 0.001$), "accompanied" runs ($F = 3.17$; $p < 0.04$), grooming ($F = 7.87$; $p < 0.001$) and defaecation ($F = 4.44$; $p < 0.02$). HR/R showed a significant increase in all groups over days

($F = 6.59$; $p < 0.003$) as did "accompanied" runs ($F = 9.72$; $p < 0.003$), and time spent rearing ($F = 4.66$; $p < 0.014$), though analysis of the number of rearing bouts over days just failed to reach significance ($F = 3.14$; $p < 0.051$). Defaecation decreased significantly with testing ($F = 4.85$; $p < 0.02$) and grooming tended to increase though not significantly ($F = 2.58$; $p < 0.068$). No interactions reached significance.

The Group effect on HR/R was due to the SC and HPC groups scoring lower than controls ($p < 0.001$ and $p < 0.04$ respectively) as on time spent rearing ($p < 0.001$ for both) and number of rear bouts ($p < 0.001$ for both). Only the SC group scored lower than controls on "accompanied" runs ($p < 0.003$). In contrast, the MFC group showed evidence of greater rearing than controls (time: $p < 0.05$; events: $p < 0.045$) though no more "accompanied" runs.

Grooming was more frequently observed in the SC group than in controls ($p < 0.002$), and MFC rats deposited more faecal boluses than SCs ($p < 0.004$) or controls ($p < 0.01$). As in Experiment 5.1, the latter category is somewhat unreliable due to the large number of zero scores in the raw data.

Novel object introduction

When a novel striped cube was introduced into the open field on test day 4, the behaviour of individual rats was extremely variable. Times spent in investigation of the object were subjected to reciprocal transformation and 1-way Analysis of Variance. No significant differences between groups were obtained ($F(3,30) = 0.82$; $p > 0.49$). However the criterion for "investigation" did not seem to appropriately reflect the responses of animals to the novel object. For example, animals 49a (control), 23a (MFC) and 60a (SC) scored zero, yet clearly seemed to have noticed the object since they sat in the opposite corner of the apparatus showing defaecation, piloerection and other signs of arousal. In contrast, some others, notably 43a (HPC), 41a (control) and 47a (SC), spent more than 25% of the 2 minute session in constant investigation of the cube and frequently climbed on top of it; see Figure 5.9.

As on the previous 3 days, the control group showed a great deal more (600%) rearing than SCs and HPCs in terms of both time and events, while the MFC group again engaged in (28%) more than controls. The MFC group also deposited more faecal boluses than other groups (27 compared with 6 for controls, 0 for HPCs and 6 for SCs). There was no overall group effect on locomotor activity ($F(3,30) = 1.01$; $p > 0.40$), until the SC group was divided into large and small-lesion subgroups, when a Group effect became evident upon reanalysis of the data ($F(4,29) = 7.81$; $p < 0.001$). Further comparisons revealed that the large SC group were significantly more active than all other groups (all p's < 0.002). Curiously, the small SC group were less active than controls, the effect almost reaching significance ($p < 0.07$) though no other comparisons did so.

Homecage Activity

Observation of animals inside their homecage in the colony room failed to indicate any obvious differences between groups on any measure, though the SC group appeared to be found sleeping rather often, though this was not formally measured. Activity in the colony room is subject to enormous variation and no statistical treatment of results seems appropriate. It was, however, evident that the SC animals were not hyperactive in their cages, and may, as suggested above, have been somewhat hypoactive. It was noted that SC rats appeared no slower than controls at retrieving lumps of food dropped into the cage.

Response to Novel Environment and Object in Homecage

A Note on Design

Animals were all tested in the same order of conditions; day 1, without cube; day 2, with cube, since had a counterbalanced design been used, some animals would have experienced a novel cube on day 1 followed by absence of novel cube on day 2. The latter could be considered to constitute further novelty and thus the design would have been unbalanced. However the present design is far from satisfactory since the effect of habituation between days 1 and 2 is confounded with cube introduction. Unfortunately groups were too small to be divided into treated (with cube) and untreated (no cube) split halves on day 2. Nevertheless since File and Wardill (1976) found that with 5 minute test sessions on two consecutive days, habituation of most behavioural categories is minimal, it is likely that any changes in behaviour between days 1 and 2 are largely due to cube introduction.

Data was analysed as described above for (a) crossings and (b) rearing in each case using a 4 x 2 (Groups x Days) ANOVA, the 2nd (Days) factor being a repeated measure; significant Days effects are thus likely to reflect changes due in part to cube introduction, and Groups x Days effects the differential effect of cube introduction on the four groups.

Analysis revealed a significant Group effect on crossings ($F(3,30) = 4.45$, $p < 0.02$). This was found to be due to the SC rats' traversing the cage more often than controls on both days ($p < 0.012$). It was noticeable that in the SC group, 5 animals (33a, 47a, 18a, 39a, 20a) crossed more than any control animal; it can be seen that these are the 5 SCs which exhibited elevated activity in the original open field study, and which had the largest lesions. Rearing showed no significant group differences, though rearing was greatly reduced on day 2 compared with day 1 for all groups ($F(1,30) = 22.47$; $p < 0.001$). No interaction terms reached significance. One way ANOVA was carried out on object contact and investigation data, though no significant group differences were obtained (see Figure 5.10).

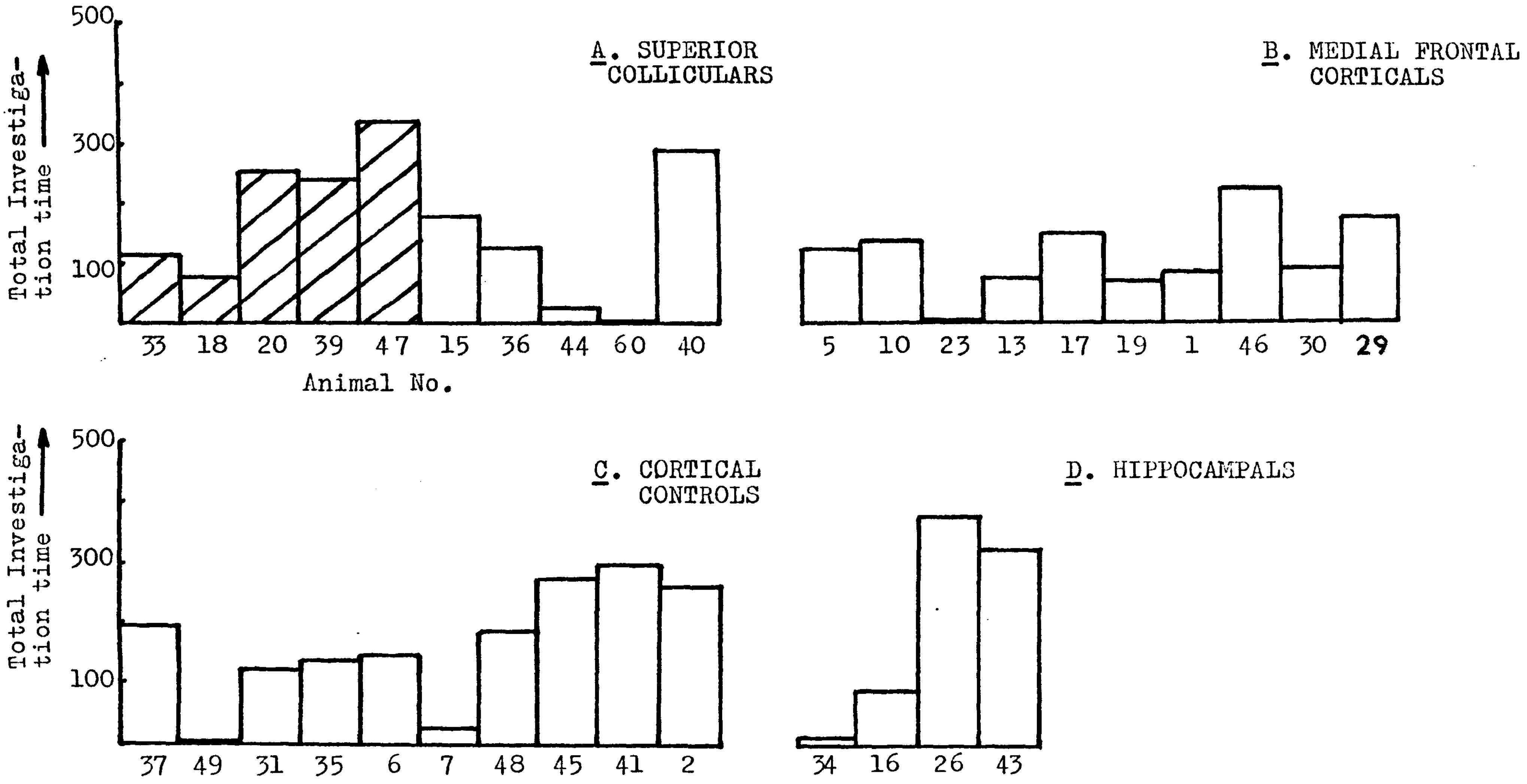


Figure 5.9

Time spent investigating novel object in the open field in Experiment 5.2 (secs x 10)
Cross-hatched bars represent colliculars with large lesions and which were hyperactive in the open field.

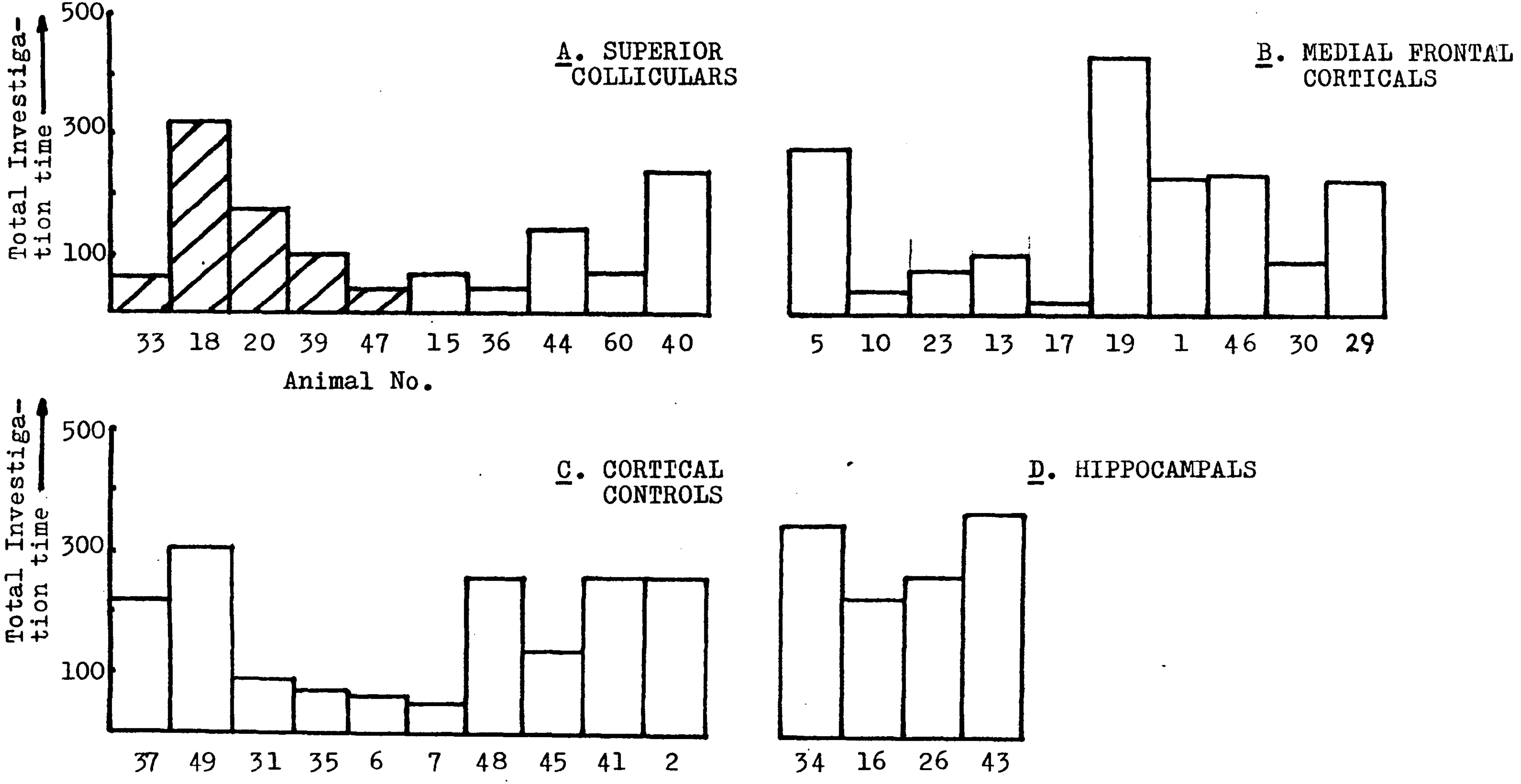


Figure 5.10

Time spent investigating novel object in the homecage in Experiment 5.2 (secs x 10)
Details as for Figure 5.9.

5.2.6 Discussion

The absence of an overall Group effect on activity in the initial open field study appears at first sight to contradict the many previous reports of elevated activity in SC rats. However size of lesion within the present SC group was variable, and, on the whole, smaller than in the previous experiment, in which collicular hyperactivity was observed. Reanalysis of the data with the SC group subdivided into those animals sustaining large, and small, lesions respectively revealed that the larger, deeper lesions (but not smaller lesions) did indeed result in hyperactivity. This crucial dependence of the activity effect upon lesion locus probably explains why some authors working with collicular rats have failed to obtain overall activity increases (Goodale and Lister, 1974), or obtained small to moderate increases (Marshall, 1978 Weldon and Smith, 1979; Experiment 5.1 above), while others, notably those routinely using very extensive ablations, have obtained substantial effects (Murison, 1977; Foreman et al, 1978; Pope and Dean, 1979).

Attentional deficits were present in all SC rats regardless of lesion size, and thus lesion size (and/or depth) would appear to be a determinant of activity level but not degree of inattentiveness. This may be so because intrinsic organisation in the SC related to attentional mechanisms, and presumably involving all laminae (Robinson, 1972; Sprague, 1975; Wurtz and Mohler, 1976a) is likely to be disrupted by moderate surgical assault mainly involving superficial laminae, while global deficits may only appear when the majority of (both superficial and deep) laminae have been destroyed. Such a proposal depends upon there existing a degree of autonomy within deep collicular laminae, which are seen as functioning (mainly in relation to non-visual stimuli) in the absence of more superficial tissue. The evidence for such a division has been reviewed previously (Casagrande et al, 1972; Sprague, 1975; see Chapters 1-3).

Though the HPC lesions employed in this study were extensive, they were comparable to those used in previous studies of hippocampal activity and attentiveness in rats (Kimble, 1963; Riddell et al, 1969; Crowne and Riddell, 1969; Lanier and Isaacson, 1975) and gerbils (Glickman et al, 1975), though notably in the present study no rat sustained damage to the lgn. Some similarities were noted between the effects of HPC and SC lesions; in particular both groups initiated rearing less frequently than controls, and spent less time engaged in headraising and rearing. Reduced rearing has been noted previously in hippocampal rats (Venables, 1978), though in some studies rearing has either been reported to increase following HPC lesion (Jarrard, 1965; Köhler, 1976) or remain unchanged (Lanier and Isaacson, 1975).

Activity was arithmetically greater in hippocampals than controls, though the effect failed to reach statistical significance possibly due to the small number of subjects in the HPC group. However, in terms of "accompanied" runs, hippocampals failed to differ from controls, but showed significantly more than colliculars. Since this category is apparently a very reliable indicator of collicular inattentiveness, it must be concluded that hippocampal lesion effects are qualitatively different from those of SC. It is unfortunate that no previous studies have measured "accompanied" running in hippocampals. That hippocampal rats successfully combine locomotion and investigation was suggested by Köhler (1976) who found them to engage in as much investigatory headpoking as controls. Such findings as these are in obvious contradiction to the view expressed by O'Keefe and Nadel (1978) that the hippocampal rat shows a total absence of investigation, though admittedly rats with very large lesions in the present study did engage in less investigation than controls. However the small number of hippocampal subjects and extensiveness of their lesions preclude reliable evaluation; thus a larger group with more restricted damage will be observed in a later study.

From the results it is clear that the effects of substantial MFC lesions are dissociable from those of the SC. In particular, the lack of hyperactivity and hyperinvestigatory behaviour of the MFC group is in direct contrast to the behaviour of colliculars. It is perhaps significant that previous authors working with cats and monkeys have reported hyperattentiveness following bilateral frontal ablations (Hagamen, Lance and Ungewitter, 1959; Miller and Orbach, 1972). Kolb (1974) while not measuring rearing, did report that rats with more extensive MFC ablations than in the present study exhibited greater headpoke investigation than controls, due to reduced intrasession habituation. Furthermore, Kolb (1973) failed to observe an overall increase in the level of locomotor activity in such rats, in agreement with the present results, though intrasession habituation was found to be reduced. Since the present data was not collected on a minute-to-minute basis it is impossible to say whether the increased attention observed in the present study was due to deficient habituation, or whether the MFC group might have differed from controls in terms of locomotor activity during the latter half of recording periods. However, the MFC animals did deposit more faecal boluses than controls (approximately twice as many as all other groups) in further agreement with Kolb's (1973) findings.

Introduction of a novel object into the open field produced such varied behaviour in the animals that no conclusions could be drawn except that, in agreement with Casagrande <u>et al</u> (1972) and Marshall (1978), the SC group failed to collide with the novel object though appearing not to notice it when running nearby. Measures of object investigation and contact failed to indicate group differences, though this was probably due to a "floor" effect, arising from the excessive fearfulness of some rats. Figure 5.9 shows time spent in object investigation by each animal.

Observation of animals in the homecage while in the colony room failed to suggest any differences between groups on any measure.. Some of the SC group with larger lesions were frequently found asleep and were on occasions difficult to rouse. Such has been previously noted by Goodale (1974: personal communction), Pope and Dean (1979) for animals with much larger lesions, and Kesner _et al_ (1967) for rats with midbrain reticular lesions. However the variability of homecage behaviour precluded meaningful statistical evaluation. Nonetheless as in previous reports (Carson and Goodale, unpublished; cited Foreman _et al_, 1978; Pope and Dean, 1979) it was clear that no gross systematic hyperactivity or other behavioural change characterised the SC rat in this situation; indeed in agreement with a study by Altman (1962) of activity in a residential maze, colliculars may have been slightly less active than controls over a long period of observation. When the animals were transported in the homecage into an unfamiliar room, however, group differences in activity were immediately noted. While all animals engaged in increased activity, the SC group did so more than any other. The result is puzzling, since it is not clear why this situation should be more effective in demonstrating elevated activity in SCs than the open field where no overall group effect was obtained. However it might be suggested that the apposition of novel and familiar visual cues, which is known to produce an extreme novel object reaction in normal rats (Cowan, 1976) is a potent novel stimulus environment within which group differences will be especially clear. It is tempting to conclude that the SC-lesioned rat is behaving differentially in a novel "ambient" visual environment and is thus attentive to gross visual environmental novelty. However the situation was clearly not exclusively visually novel and involved novel auditory cues, olfactory cues and the novelty of isolation from the cagemate, all of which might be more significant to a rat than visual novelty. However Cowan (1976) and Sheldon (1967) have demonstrated that rats tend to use visual cues in familiarity-unfamiliarity discriminations and in detecting novelty in an otherwise familiar environment.

Thus it is clear that the SC rat exhibits different behaviour in familiar and novel environments, and therefore that the SC rat may be able to detect the novelty of a peripheral "ambient" visual environment. It was noticeable that the SC group reared at the side of the cage as often as controls, in contrast to their lack of rearing in the open field. However the two cannot be directly compared, since rearing at the cage side is a very frequent and well-practiced behaviour in all laboratory rats unlike unsupported rearing in the open field, and may represent quite different aspects of behavioural organisation. Introduction of a novel cube into the homecage (in the same environment as on the previous day) produced a very clear "novel object reaction" in that almost all animals tended to avoid the cube during the first 30 seconds or so after which cautious sniffing and alert investigation of the cube ensued. However some qualitative observational data on this test is of interest. Seven animals were particularly noted as having engaged in "darting, zooming" behaviour, running erratically about the cage, frequently changing direction and rushing at the cube and retreating quickly. Of these, one (17a) was an MFC-lesioned rat while the other 6 were colliculars (33a, 36a, 18a, 39a, 15a, 40a). Of the latter, 36a was additionally noted to have bumped into the cube in the course of running and had visibly startled and jumped in the air upon doing so. It appeared to E that the SC animals lacked controlled approach behaviour, running erratically at the object in a clearly aroused state. However the 6 SCs which behaved strangely were notably not all large-lesioned animals. No particular comments were made by E on the attentional behaviour of no's 44a and 60a with small SC lesions, or on no's 20a or 47a which had larger lesions, though both of the latter animals were very active in terms of centre-crossings; the only comment made on no 47 was that this rat stood for long periods next to the object (its hind quarters in contact with it) and thus generated a substantial object contact score, while not engaging in <u>exploratory</u> contact. It was unclear whether this animal genuinely "detected the novelty" of the object or not. Such difficulties inevitably arise where observations are made of rather variable behaviours in a small area. However, it was clear that the SC group, on the whole, behaved differently from controls though not in a systematic way, and not such that the novel object was simply neglected. The result lends further support to the idea that, at least after a long postoperative recovery period, the SC rat is not totally neglectful or amblyopic but is deficient in the organisation and coordination of attentional behaviours; furthermore the degree and appearance of collicular inattentiveness may depend to some extent upon the test situation.

Rearing decreased considerably between days 1 and 2 of homecage-testing, presumably reflecting the shift of attention in all groups away from the cage side and towards the novel object. No group differences were obtained overall on object investigation or contact on day 2, though any group differences in attentiveness may have been overshadowed by individual variability and in particular the fearfulness of certain animals. Thus the above measures of cube investigation cannot necessarily be held to reflect degree of attentiveness to novelty *per se*.

5.2.7 Conclusions

The open field study has clearly shown that attentional behaviour is reduced in animals with lesions of the SC, regardless of whether the lesion is sufficiently large to produce increased activity. Lesions of MFC produced increases in attentional behaviours, while very large HPC lesions gave rise to decreased rearing and head-raising but not to a reduced incidence of "accompanied" running. This suggests a differentiation between SC, MFC and HPC lesions with respect to lesion effects. Activity in the homecage in a familiar room was not noticeably elevated in the SC rats, though in an unfamiliar room, homecage activity (with and without a novel object in the cage) was significantly elevated suggesting strongly that SC rats are differentially responsive to grossly novel and familiar environments. They are therefore not to be regarded as profoundly inattentive to all proximal and distal cues, yet their response to novelty, and organisation of investigation is grossly abnormal.

5.3 Open Field and Novel Object detection in Rats with Superior Colliculus or Medial Frontal Cortical Lesions

5.3.1 Introduction

The previous experiment showed that behaviour towards a novel object of animals previously exposed to the test apparatus for three test sessions of 5 minute duration was extremely variable; indeed marked individual variation may have obscured any group differences in attention. The animals used in Experiment 5.2 had not had previous experience of daily testing, or of transportation to a test apparatus. Thus they were observed to be resistant to handling, and were possibly unduly fearful of novel objects in the test situation. In order to reduce such variables, in the present experiment groups of animals with SC, MFC or control cortical lesions, which had been extensively tested in a previous discrimination experiment were exposed to the open field, and then to novel objects. It was predicted that the SC group would be slow to notice the novel object and possibly investigate it less than controls, yet, based on the results of Experiment 5.2 that animals with MFC lesions might be expected to engage in more exploration than controls.

5.3.2. Subjects

Twenty-one male hooded rats (general details as described in Section 5.1.2) served as subjects. They had previously been trained on a black-white simultaneous discrimination in a Grice box (see Experiment 8.1), given lesions of

SC (n = 7) (tip temperature 57.5°), MFC (n = 7) or cortical control (n = 7) lesions as described earlier (Section 5.1.3), and then retested for retention. They had thus been extensively handled for 30 - 40 days during the previous 60 days. Operations had been performed at approximately 130 days of age; participation in this experiment began at approximately 165 days of age.

5.3.3 Apparatus and Method

The open field apparatus described in Section 5.1.4 was used, and categories of behaviour recorded as in Section 5.2.4., (i.e. novel object investigation in the open field), involving 3 x 5 minute daily periods of open field testing followed by 2 days x 2 minute exposure to novel objects, different objects being used on each day to provide as much novelty as possible. The objects used are shown in Figure 5.5. On the first day of novel object testing, a small aluminium cube (object B as in Experiment 5.2) was used, while on day two, object C was used consisting of a small, hexagonal aluminium "multi-connector", bound with dark tape. The object was placed in the apparatus one quarter of the distance along a diameter, the animal being placed (facing away from the object) three-quarters of the way along the same diameter. As in the previous studies, E recorded behavioural categories described above (Section 5.1.5) and, in addition, latency to notice the novel object. The latter was based on the same behavioural criteria as used in the previous experiment and was timed by E with a stopwatch.

Sacrifice of the animals and histology was carried out as before (Section 5.1.5).

5.3.4 Results

5.3.4.1 Histology

Lesions are reconstructed in Figure 5.11. The SC lesions were well-localised with damage restricted almost entirely to SC, though removing large parts of deep laminae. Inferior collicular damage was limited and only seen in animals 16w, 19w and 23w. MFC lesions were again well placed with unilateral sparing noted rostrally for animal 27w.

5.3.4.2 Behaviour

Informal monitoring of postoperative weightloss revealed no significant group difference, and no obvious motor impairments were seen in any animal.

Analysis of open field data was carried out exactly as in the previous experiments. Main effects from the analyses of variance were obtained on measures of locomotor activity ($F(2,18) = 5.87$; $p < 0.02$), "accompanied" runs ($F = 50.62$, $p < 0.001$), HR/R time ($F = 23.24$; $p < 0.001$) and rearing (events: $F = 18.69$; $p < 0.001$; time: $F = 19.07$; $p < 0.001$).
Locomotor activity tended to fall between days 1 and 3 though not significantly ($F(2,36) = 2.31$; $p < 0.11$).
A significant increase in "accompanied" runs and HR/R were seen over test days ($F = 29.25$; $p < 0.001$, and $F = 9.71$; $p < 0.001$ respectively) though not differentially between groups. Rearing events showed no significant

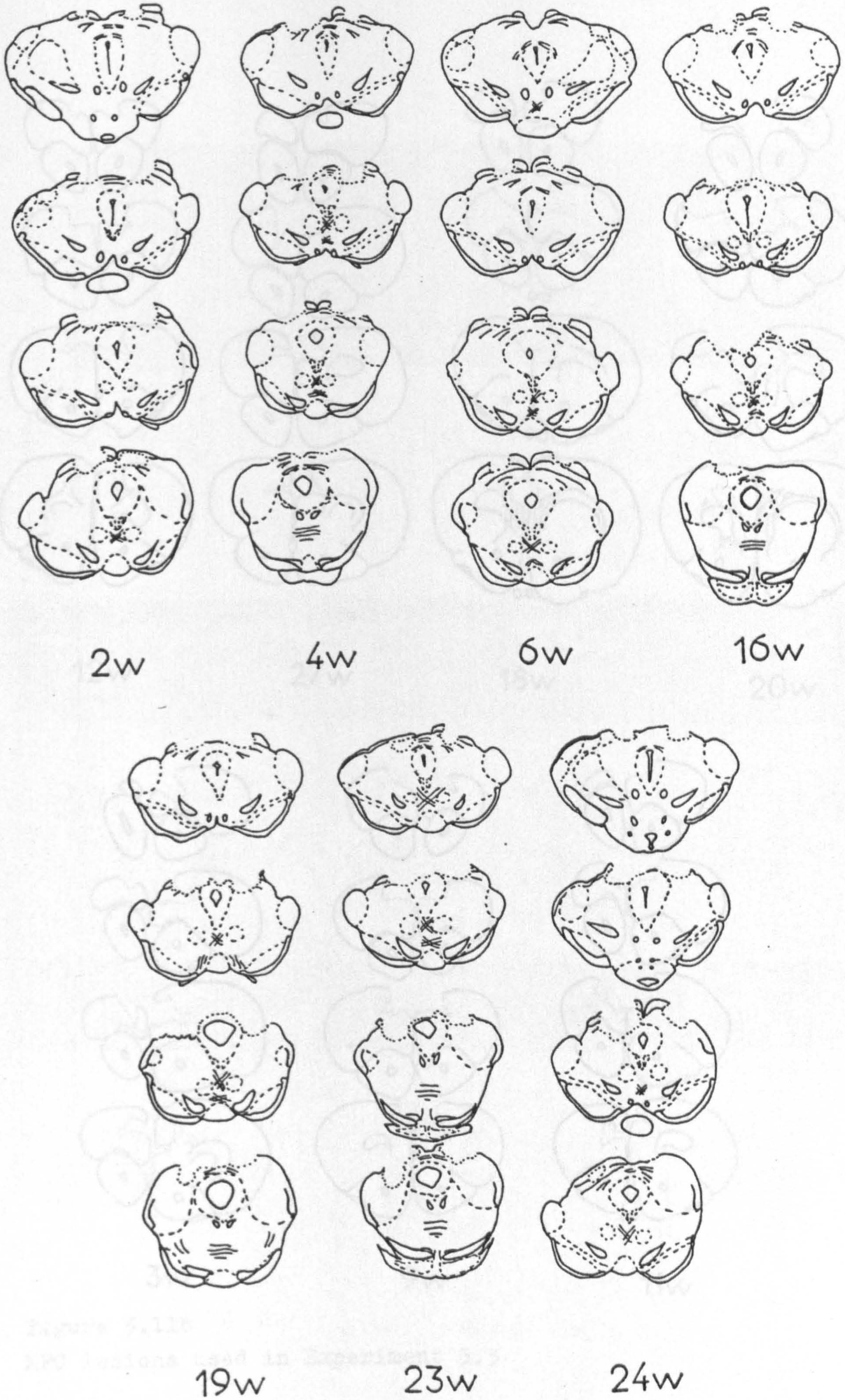


Figure 5.11a SC lesions used in Experiment 5.3

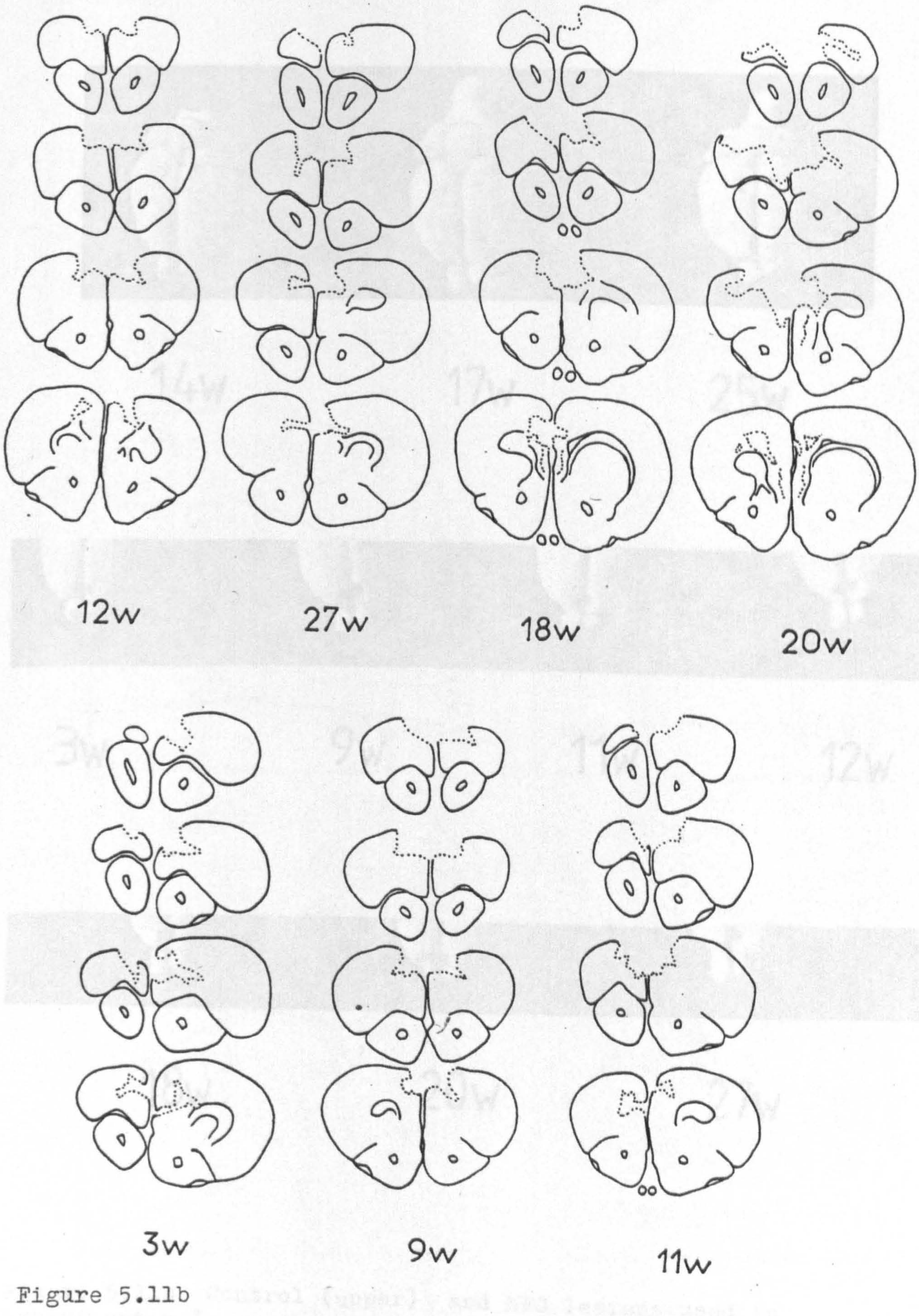


Figure 5.11b
MFC lesions used in Experiment 5.3

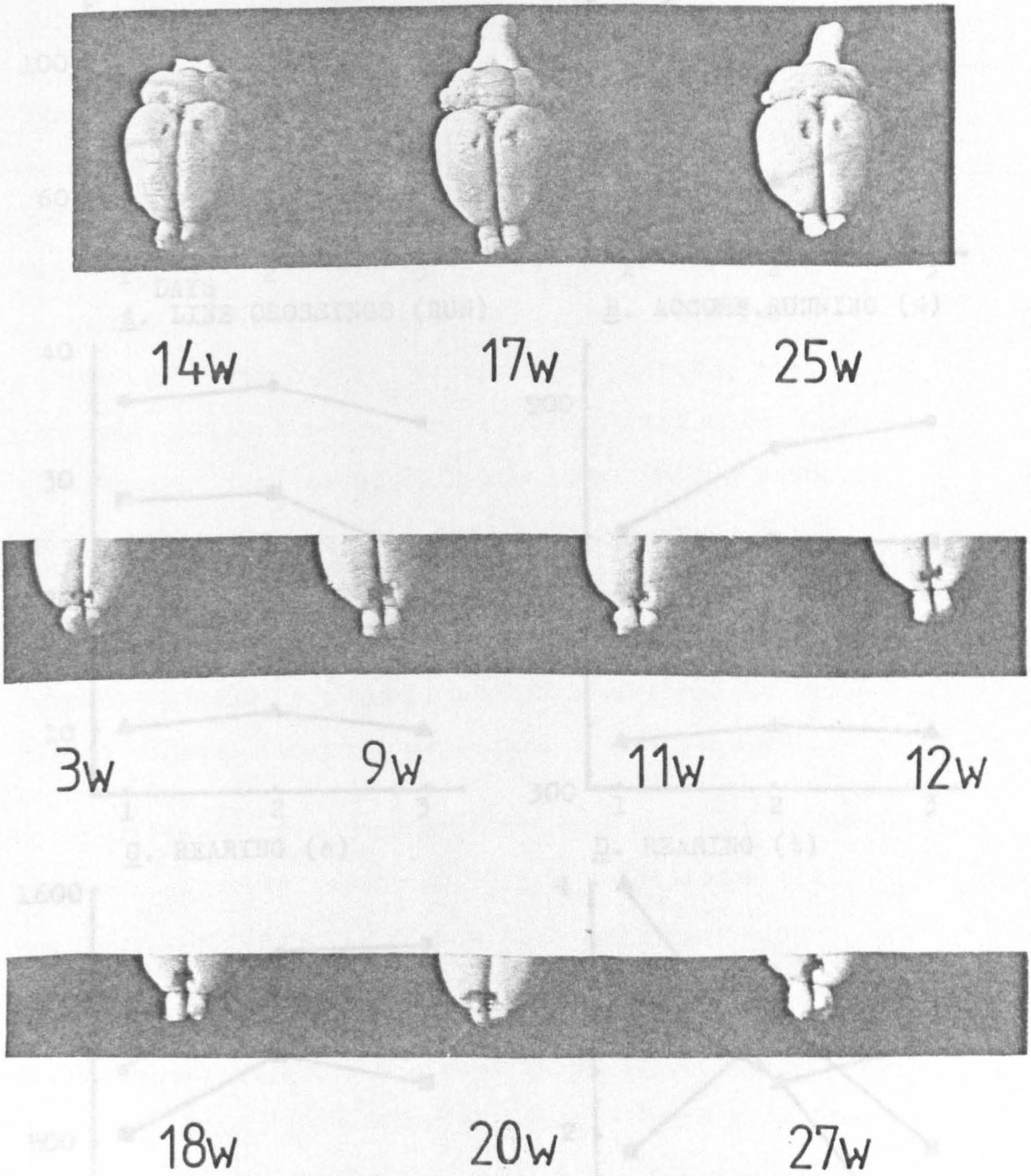


Figure 5.11c Control (upper) and MFC lesions used in Experiment 5.3.

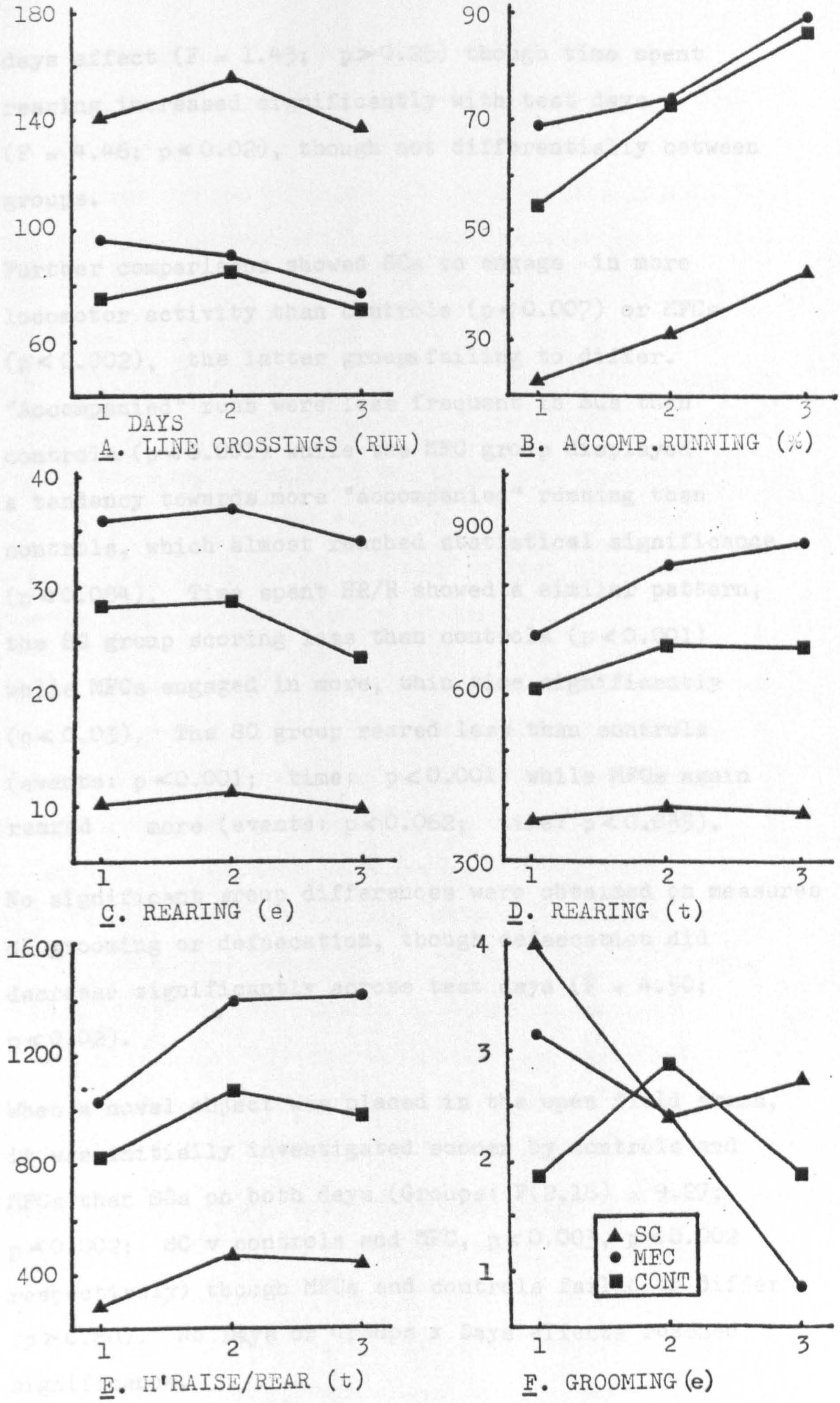


Figure 5.12
Activity and Investigation recorded in Experiment 5.3

days effect ($F = 1.43$; $p > 0.25$) though time spent rearing increased significantly with test days ($F = 4.46$; $p < 0.02$), though not differentially between groups.

Further comparisons showed SCs to engage in more locomotor activity than controls ($p < 0.007$) or MFCs ($p < 0.002$), the latter groups failing to differ. "Accompanied" runs were less frequent in SCs than controls ($p < 0.001$) while the MFC group displayed a tendency towards more "accompanied" running than controls, which almost reached statistical significance ($p < 0.084$). Time spent HR/R showed a similar pattern, the SC group scoring less than controls ($p < 0.001$) while MFCs engaged in more, this time significantly ($p < 0.03$). The SC group reared less than controls (events: $p < 0.001$; time: $p < 0.001$) while MFCs again reared more (events: $p < 0.062$; time: $p < 0.035$).

No significant group differences were obtained on measures of grooming or defaecation, though defaecation did decrease significantly across test days ($F = 4.50$; $p < 0.02$).

When a novel object was placed in the open field arena, it was initially investigated sooner by controls and MFCs than SCs on both days (Groups: $F(2,18) = 9.27$; $p < 0.002$; SC v controls and MFC, $p < 0.003$, $p < 0.002$ respectively) though MFCs and controls failed to differ ($p > 0.80$). No Days or Groups x Days effects reached significance.

Time spent in cube investigation showed significant group differences ($F(2,18) = 5.95$; $p < 0.011$) due to the greater investigation shown by the combined MFC and control groups compared with colliculars ($p < 0.006$). The MFC group showed arithmetically more object investigation ($p < 0.16$) and SCs less ($p < 0.067$) than controls. Less investigation occurred on day 2 than day 1 ($F(1.18) = 7.59$; $p < 0.014$), though the Groups x Days interaction was significant ($F = 4.99$; $p < 0.019$) due to the significance of the group difference on day 1 ($p < 0.01$) but not on day 2 ($p > 0.35$); this possibly reflects the "levelling" effect of generally reduced object investigation on day 2.

Object contact time produced a similar result; between-group differences ($F = 4.32$; $p < 0.03$) resulted from reduced contact in SCs than combined MFC and control animals ($p < 0.025$). The MFC group tended to engage in more object contact than controls though not significantly ($p > 0.13$). The Group x Days term approached significance ($F = 3.13$; $p < 0.07$) reflecting a tendency for group effects to diminish on day 2, on which less overall object contact was observed. Investigation and contact event data showed identical trends and will not be analysed separately.

While the object was present in the open field, groups differed in the amount of running ($F(2,18) = 7.51$; $p < 0.005$) and rearing (time: $F = 19.42$; $p < 0.001$; events: $F = 24.55$; $p < 0.001$) in which they indulged, and further comparisons revealed identical results to the previous open field study since colliculars engaged in more running than controls or MFCs ($p < 0.015$, and $p < 0.002$ respectively) but less rearing ($p < 0.001$ in all cases). Medial frontals and cortical controls failed to differ on running but MFCs tended to engage in more rearing than controls (time: $p < 0.09$; events: $p < 0.15$). Running increased on day 2 compared with day 1 for all groups ($p < 0.001$) while rearing decreased (time and events: $p < 0.001$). However significant Groups x Days interactions (time: $F = 9.46$; $p < 0.002$; events: $F = 4.33$; $p < 0.03$) arose from the absence of such a decrease between days 1 and 2 in the SC group.

Typically the control animal moved away from a standing position and immediately noticed the object, running warily across to it with neck outstretched and vibrissae moving rapidly back and forth. The object was often gnawed and licked; the animals often placed their paws on the object in a "walking" movement, possibly representing scent-marking. The SC group were clearly very slow in detecting the object, frequently ran past it without initiating investigation, though once the SC rat had begun investigation, sniffing and biting of the object proceeded normally. In only one case (24w), on day 1, did a collicular rat fail to "discover" the object in the allotted 120 seconds.

Mode of investigation was interesting, since in most cases the object was not continually investigated for long periods of time. Instead the rat would typically sniff and nudge it for 10 - 20 seconds and then run off, returning abruptly as if suddenly having "rediscovered" the object.

5.3.5 Discussion

The results are entirely consistent with those of Experiments 5.1 and 5.2 since increased activity was observed on all test days in the SC group, most of which had substantial lesions. In the same animals attentional behaviours such as rearing, headraising and "accompanied" runs were generally reduced by comparison with both cortical groups. Moreover, in further support of the findings of Experiment 5.2, MFC rats were again found to exhibit more investigatory behaviour (headraising and rearing) than controls.

Of particular interest in this study was the behaviour exhibited towards novel objects, which was less variable than in the previous experiment. This may be due to the smaller size of the novel objects in this study, or to the greater familiarisation of this group to handling, though the latter is probably most likely. The virtual absence of defaecation recorded on both days attests to the relative lack of fear in these animals.

It is important to note that the tendency among collicular animals to run more, and rear less, than controls in the open field is likely to cause collicular rats to encounter a novel object more quickly and frequently than controls, thus operating <u>contra hypothese</u>.

Though in the previous study, the efficacy of the criterion for "initiation of object investigation" was considered dubious, the validity of the measure was clear in this experiment. Control and MFC rats turned almost immediately towards the object and began investigation after approximately 7 seconds while the SC rats did not. These appeared to discover the object serendipitously (on average taking 17 seconds), showed surprise upon doing so. Like Marshall's (1978) collicular rats, the present SC group typically ran past the object on more than one occasion before initiating investigation. The latter occurred frequently when the animal was a short distance from the object (suggesting myopia - but see Schneider, 1968), and when the object was located directly ahead of the rat. This behaviour adds support to the view of Goodale et al (1978) that the SC rat is inattentive to all but centrally-placed cues in the visual field. In the present experiment the novel cube would tend to occupy a peripheral location in the animal's visual field, for most positions of the animal in the apparatus.

The results provide a hint as to the adaptive importance of collicular functions since without them a rat would probably be slow in detecting unexpected environmental changes, and in scrutinising potentially informative or harmful stimuli (see Ingle, 1973).

Though object detection latency was greater in colliculars than either cortical group on both days, other measures of investigation of the object failed to show differences between groups on day 2. This is probably the result of a relative lack of interest shown towards object C used on day 2. This in turn is unlikely to be due to a habituation of investigation towards novel objects in general since test periods were short, the object and rat were initially placed in different positions in the apparatus on days 1 and 2, and the second object was visually very different from the first (Figure 5.5B and C). However object C was a darker colour and smaller than B, thus probably less likely to induce investigation.

It is not clear from the results whether the investigatory behaviour of colliculars is entirely normal, particularly since time spent in object investigation by SCs is likely to be reduced as a result of the longer "object discovery" latency. However the 10 second difference in mean discovery latency between the SC and cortical groups would be responsible for only an 8% reduction in available investigation time, while the actual reduction in object investigation on day 1 in colliculars compared with control and MFC groups was of the order of 69%. The "run-away-and-return" pattern of investigation was such that further computations were not meaningful. Nonetheless, it was clear that even SC-lesioned animals which showed long "discovery" latencies would nonetheless sometimes spend substantial periods of time in object investigation, though a more detailed analysis of their investigatory behaviour might have revealed subtle abnormalities.

5.3.6 Conclusions

The results confirm that the large-lesioned collicular rat is hyperactive and shows reduced attention by comparison with control and MFC rats, the latter group showing elevated rates of investigatory behaviours. Latency to "discover" a novel object in a familiar arena was elevated by 250% in SCs compared with both control and MFC groups, though colliculars were not incapable of spontaneous investigation of novel objects once having encountered them.

5.4 Discussion of Experiments 5.1 - 5.3

The initial open field studies in the foregoing experiments are directly comparable one with another, since all were undertaken using the same apparatus and in an identical manner. A number of findings are common to all three.

It is evident that the hypothesis discussed in Chapter 3 implicating SC in the control of grooming behaviour is not supported by the results, since SCs were indistinguishable from control rats on this measure, except that they showed slightly elevated grooming in Experiment 5.2. Specific sub-categories of grooming were not investigated, and thus minor abnormalities would not have been detected (see Trulson and Randall, 1973) though grossly misdirected grooming (Pope and Dean, 1979) was not observed.

No SC animal in these studies exhibited hypophagia, ataxia, or other gross motor impairments suggesting that the findings of Murison (1977) and Pope and Dean (1979) particularly relate to extracollicular structures damaged in their large-lesioned groups.

In terms of activity and attentional behaviours, some variation was noted between studies. For example, a great deal more rearing was obtained from all animals in studies 5.1 and 5.3 compared with study 5.2 in which, unlike the aforementioned studies, incidence of rearing decreased over test days. Clearly E may have unwittingly adopted a slightly different criterion for "rearing" in study 5.2 though it is more likely that the disparity reflects differences between groups of animals since the animals in Experiment 5.2 were older than those in Experiments 5.1 and 5.3, were tested after a longer postoperative recovery period and were obtained from a different supplier. However it is reassuring to find that, despite such differences, behavioural effects of lesions (compared with control animals) are remarkably consistent. For example, the ratio of collicular : control rearing remains approximately 1 : 3.5 in each of studies 5.1 - 5.3. Similar considerations apply to other behavioural categories (for example, the HR/R category). The percentage of runs accompanied by sniffing and/or headraising was very much higher in control rats in Experiment 5.1 compared with the other two, and in Experiment 5.2, collicular rats showed a more normal level of "accompanied" running than in the other studies. Nonetheless, intergroup statistical significance remained unaffected by such variation.

Relationship between lesion size and activity

Though animals with the largest, deep SC lesions appeared to be the most active in all 3 studies, the hypothesis that extent of damage to deep collicular laminae is the crucial factor in determining postoperative activity level (Foreman et al, 1978) was tested formally. For all the animals tested in the preceding experiments (except 40a for which histology is not available; see Section 5.2.5.1), the approximate volume of deep SC removed was calculated and correlated with an activity score based on line crossings. The former was calculated using a 6-point scale: Three approximately equally-spaced anteroposterior levels of the brain were identified according to the appearance of the medial geniculate nucleus (cgm). These were (i) at the point where the lateral edge of cgm becomes continuous with the edge of the thalamus (ie. just caudal to the most posterior pole of the lgn), eg. Figure 5.7a, Section 20a, no. 1; (ii) at the point where cgm protrudes laterally from the thalamus and is approximately rounded in shape (ie. Section 20a, no. 4); and (iii) at the point where the cgm narrows just rostral to the most anterior fibres of the inferior collicular brachium (e.g. Section 20a, no. 6). At each level the extent of lesion was coded by awarding points depending upon the extent of deep laminal removal. One point was awarded if deep SC (laminae IV or below) was bilaterally invaded, but 2 points if deep tissue was invaded bilaterally to such an extent that 75% of laminae IV, V, VI and VII were absent bilaterally. Thus scores could range from 0 (where deep laminae were not invaded at any level) to 6 (where at least 75% of deep SC tissue was removed at all 3 levels). The values obtained for all animals were then correlated with number of line crossings. Since overall activity levels varied between experiments, the day 1 <u>open field</u>[1] line crossings score obtained by each collicular-lesioned rat was expressed as a multiple of the mean score for the control rats in that experiment; the resulting score was then used in the correlation. An identical

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[1] i.e. excluding novel object testing

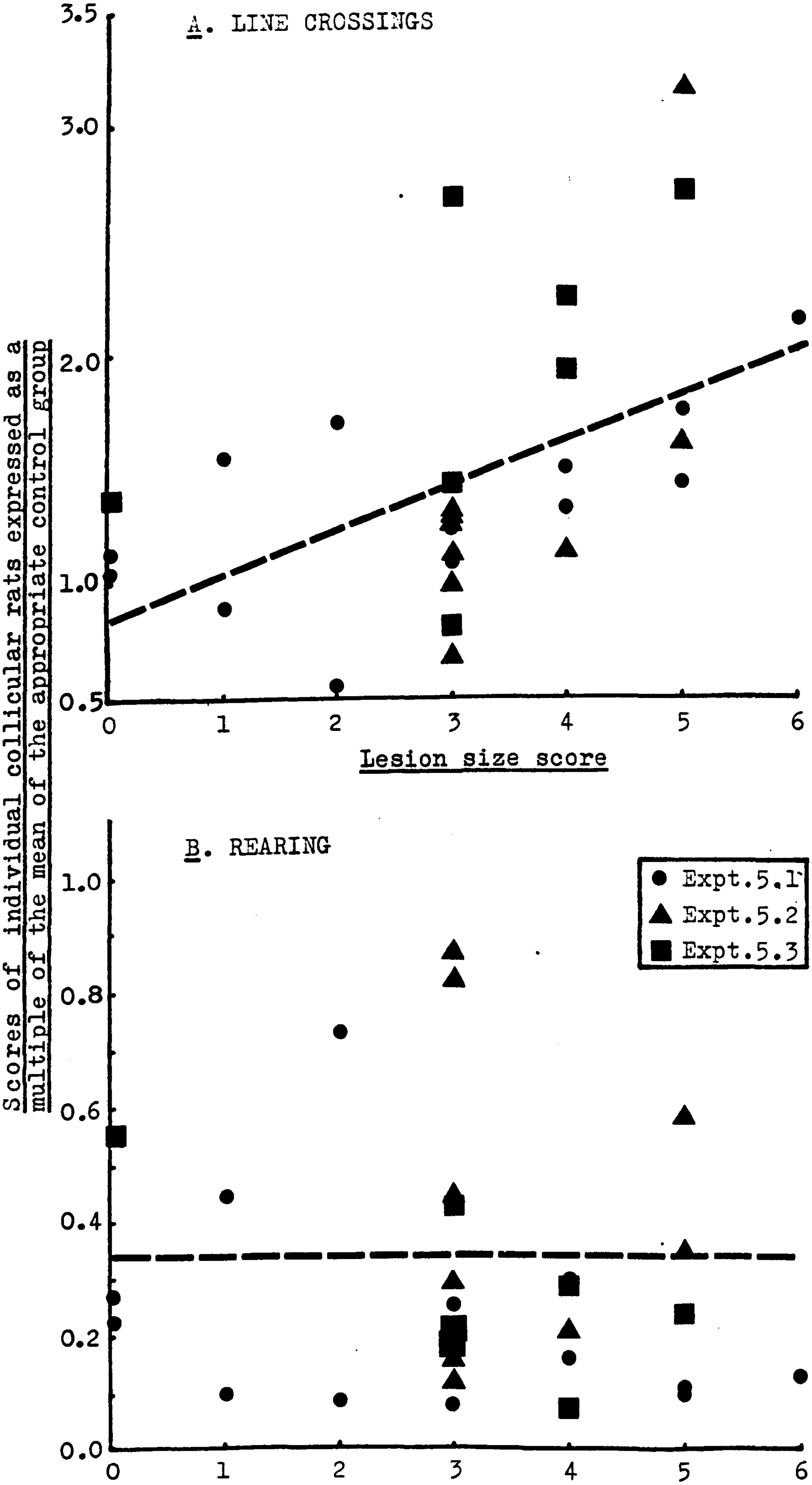


Figure 5.13. Relationship between extent of deep laminal removal and level of Locomotor (A) and Rearing (B) behaviour in the open field in collicular rats.

procedure was applied to rearing (event) data. Figure 5.13a is a scatter plot of the activity scores versus lesion size values, and 5.13b rearing versus lesions size values. Nonparametric correlation (Spearman's rho) applied to this data revealed a significant relationship between lesion size and activity ($D^2 = 1750.5$; $N = 29$; rho = 0.54; $p < 0.01$). However when the same procedure was applied to rearing scores of collicular rats (all of whom showed a substantial reduction in this behavioural category compared with controls), the corresponding coefficient of correlation failed to approach significance ($D^2 = 4064$; $N = 29$; rho = -0.01).

Thus while degree of activity elevation is highly correlated with the extent of lesion damage in deep collicular laminae, investigatory behaviour is reduced regardless of lesion extent. Since, in the case of smaller lesions, the major area of tissue damage is in superficial laminae, the result is consistent with the suggestion that in the rat superficial laminae are particularly associated with attentional behaviours while deeper laminae are more associated with motor behaviour. The results are thus consistent with reports of activity elevation in rats with lesions invading deep colliculus and dorsal tegmentum (Kesner et al, 1967; Capps and Stockwell, 1968) and with studies in a number of species reporting attentional deficits in the absence of motor involvement in animals with superficial collicular lesions, but which report greater motor involvement with depth of penetration of the lesion (Schneider, 1968; Casagrande et al, 1972; Collin, 1977).

Finally, the results of Experiment 5.3 show that the amount of testing which collicular animals undergo in separate experiments prior to open field testing is unlikely to determine their activity levels, an argument which was invoked by Murison (1977) to explain the apparently discrepant results of Goodale and Lister (1973). They found that colliculectomised rats which had undergone training in an operant (bar-press) experiment prior to open field testing failed to exhibit elevated locomotor activity in an open field arena. However, as argued above, their result is very likely to have arisen because the animals in their study had rather small, and mainly superficially located collicular lesions (Goodale, 1976; personal communication).

5.5 Holeboard Investigation in Rats with Superior Collicular, Medial Frontal Cortical and Hippocampal lesions

5.5.1 Introduction

The aim of the current series of experiments is to determine the functional "responsibilities" of the SC in the freely-moving, exploring animal, utilising situations which are relatively natural, and which hopefully provide ecologically valid measures of investigation as far as laboratory conditions permit.

Two questions have been especially confronted:
(i) What classes of stimulus does the possession of a SC enable an animal to detect or investigate?
(ii) What is the effect of losing such colliculus-mediated abilities on investigation, the negotiation of obstacles and general behavioural organisation?
The previous experiments showed that the SC-lesioned rat behaves differentially in novel and familiar surroundings, though he fails to investigate (but does not collide with) unexpected stationary objects placed on the floor of the apparatus.

Clearly, from a number of previous theories which emphasise the role of SC function in relation to certain (peripheral) areas of visual space (Trevarthen, 1968, 1970; Ingle, 1970; Goodale <u>et al</u>, 1978; Milner <u>et al</u>, 1978; Milner <u>et al</u>, 1979), it is predictable that some (central) areas of visual space would command normal investigation in the SC-lesioned animal, though no definition has ever been provided of what constitutes a "central" and "peripheral" stimulus (e.g. Goodale et al, 1978).

One class of stimulus which might be regarded as having special significance vis à vis locomotor guidance and subject to careful avoidance during locomotion is a hole or dip on the surface of the ground (in this case, surface of the apparatus). Such have been shown to elicit vigorous exploration in mice (File and Wardill, 1976) and rats (File and Wardill, 1976; Köhler, 1976), consisting of investigatory headdipping of a rather stereotyped nature. The behaviour is arguably a sensitive index of "degree of attentiveness" in rodents (File and Wardill, 1975a) and has been used in behavioural pharmacological investigations (File and Wardill, 1975b). However it is questionable whether holes in the apparatus floor would be treated by the SC-lesioned rat as "central" stimuli, and thus likely to be successfully negotiated and avoided, but not investigated (Casagrande et al, 1972; Ingle, 1973), or, alternatively whether the floor represents "peripheral" space subject to neglect by SC animals, in which case they would be likely to fall into the holes.

In an unpublished study, Pope (personal communication, 1978) tested rats with extremely large SC lesions (see Pope and Dean, 1979) on a standard 4-hole headpoke hole-board (as used by File and Wardill, 1975a), and found them to engage rarely in head-dipping compared with controls. However since holes in that apparatus were drilled 14 - 17 cm from the wall of the apparatus, thigmotactic tendencies in SC rats would result in their rarely encountering such holes. Thus in the present study a modified holeboard was used in which 2 holes were located towards the centre of the apparatus while 2 more were drilled towards the perimeter. It was predicted that SC rats would fail to encounter or investigate centrally drilled ("inner") holes though no specific prediction could be made with regard to holes drilled close to the wall ("outer" holes).

A group of HPC rats was also included in this study since previous studies have reported them to be inattentive (see Experiment 5.1), in particular to stimuli at floor level (Raphaelson et al, 1969), though Kaplan (1970) and Köhler (1976) report elevated and not reduced levels of headpoking in such animals due to slowed habituation. It is worth mentioning that the apparatus design was also particularly appropriate for this group since HPCs have also been reported to exhibit thigmotaxis (Hostetter and Thomas, 1967). Lesions of both dorsal and ventral HPC were made in all animals, since Kimble (1978) reports variable activity in partially-lesioned HPCs during the immediate postoperative period. Thus it is possible in this study to reexamine the HPC activity levels which produced inconclusive results in Experiment 5.2 (see Chapter 4 for review).

A group of rats with MFC lesions was included as

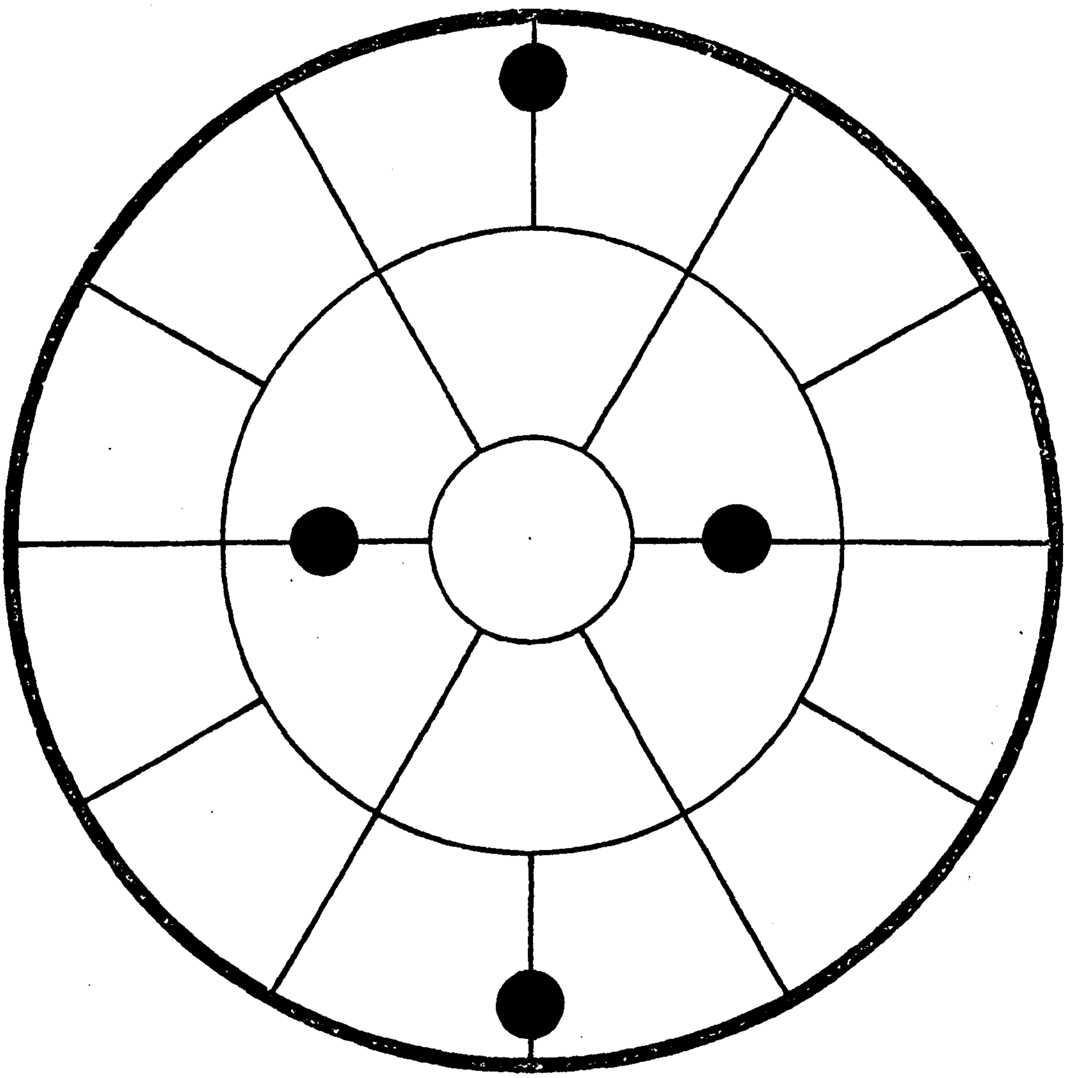


Figure 5.14
Plan view of the holeboard apparatus used (postoperatively) in Experiment 5.5, showing the positions of the two inner and two outer holes drilled through the surface.

a control group for activity levels since in the three previous studies, activity in this group was not elevated by comparison with controls; also to investigate whether the elevated levels of attentional behaviour seen in Experiments 5.2 and 5.3 extends to increased hole-exploration, especially since Kolb (1973) using very extensive MFC lesions found reduced habituation of headpoking in this group.

Unlike previous experiments, preoperative activity measures were taken in order to establish a baseline for individual animals against which to compare postoperative activity; also to maintain comparability with previous experiments reporting decreased activity habituation in HPCs (see Table 4.1).

5.5.2 Subjects

Subjects were 30 rats (as described in Section 5.1.2), experimentally naive at the start of the experiment.

5.5.3 Apparatus

For preoperative recording (see below), the apparatus was unchanged from the previous study (except that the surface was elevated approximately 8 cm from the floor by 3 brick supports) (see Section 5.1.3). Postoperatively the floor of the apparatus was replaced by an unpainted, but smooth, wooden surface marked out in the same way as the original floor, but with 4 holes (3.8 cm diameter) drilled at the positions shown in Figure 5.14, 2 at 2 cm, and 2 at 19 cm from the wall of the apparatus, which thus forced an animal to encounter two holes when only locomoting round the perimeter.

5.5.4 Method and Surgery

Animals were given access to food for one hour per day throughout the test phases of the experiment. They were each handled for 5 minutes on the day prior to initial testing which consisted of exposure for 5 minutes on each of 2 consecutive days to the original open field arena (see Sections 5.1.4, 5.1.5 above). The only categories of behaviour recorded in this study were (i) running, (ii) grooming, (iii) rearing, (iv) alert inactivity and (v) defaecations. Thirty minutes after completion of testing on day 2, all animals were placed on ad lib feed for at least 16 hr, prior to surgery (i.e. on the day following test day 2), and randomly assigned to lesion groups.

Bilateral lesions of SC (n = 12) and MFC (n = 6) were made as described in Sections 5.1.3 and 5.2.3 respectively, except that half of the SC group were given deep lesions (D: - 3.8; Temp: 55°C) and half superficial lesions (D: -2.5; Temp: 57.5°C). In 6 animals bilateral HPC lesions were made by the radiofrequency method described in Section 5.1.3, placements being made at the following coordinates:

A - P	Lat (±)	D
- 3.0 mm	2.1 mm	3.0 mm
- 4.2 mm	5.1 mm	4.3 mm
- 3.8 mm	5.6 mm	6.4 mm

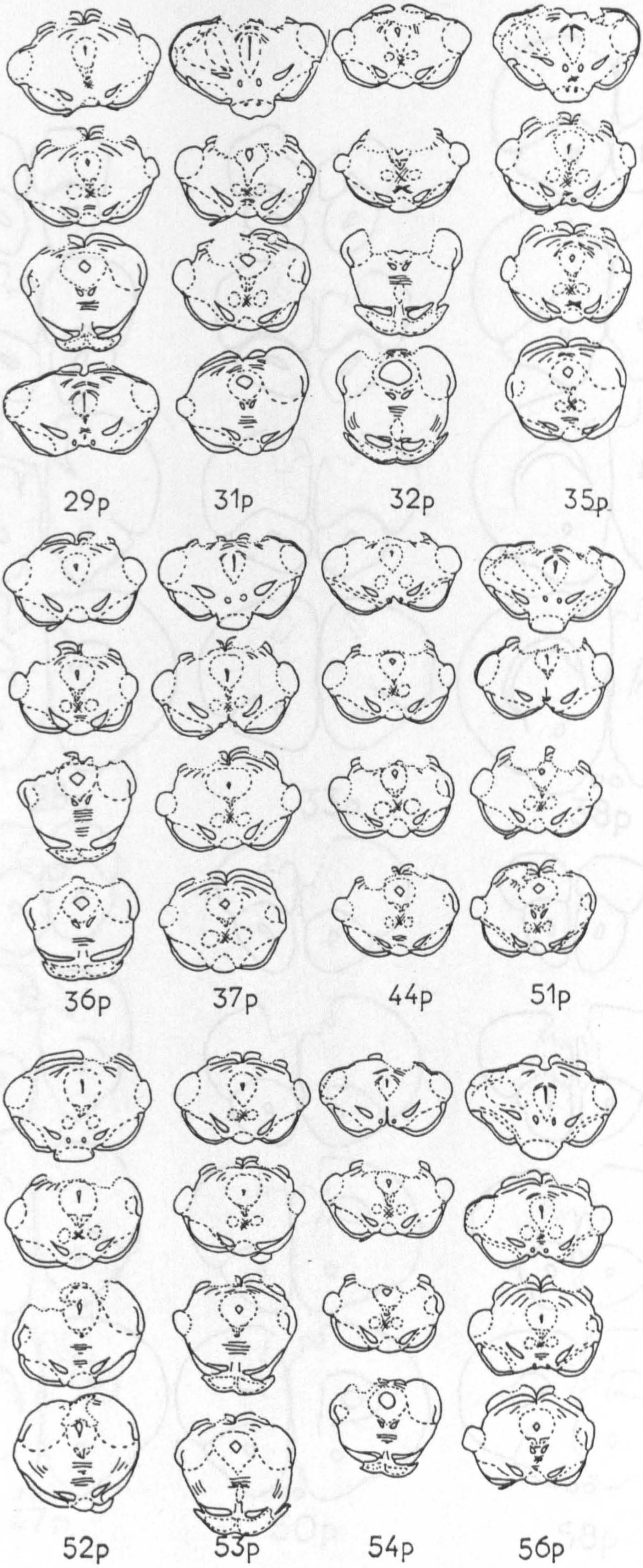
Six animals served as sham-operated controls. Following a 9 day recovery interval the rats were weighed and over the next 3 days subjected to progressive food deprivation to a one hour in 24 feeding regimen. They were then retested using the modified floor for 4 days. In addition to the categories of behaviour listed above, E also recorded (as both time and events) headpoking in holes 1 and 3 (outer) and 2 and 4 (inner) over a 5 minute period as pre-operatively. The animal was placed in the centre of the apparatus facing a random direction but not pointing directly at a hole.

5.5.5 Results

5.5.5.1 Histology

Figure 5.15 shows the reconstructed lesions of each group. The MFC group had disappointingly small lesions, tissue being spared anteriorly in all but animal 33p, while no lesion approached the genu of the corpus callosum posteriorly.

Animals in the HPC group also sustained rather small lesions. None invaded the SC, lgn, or optic tract. However all animals had substantial anterodorsal hippocampal damage, similar to that seen in animals in previous studies of attention and investigation in hippocampectomised rats (Köhler, 1976; Gustafson and Koenig, 1979). In addition, since all animals sustained some damage to posteroventral HPC it must be assumed that the HPC was substantially disrupted in all cases, though volumetrically the lesions are unlikely to have removed more than 20% of the structure. Posterior thalamus was invaded in animal 30p, and entorhinal cortex was lesioned to some extent in every rat. The SC lesions were of variable size and



29p 31p 32p 35p

36p 37p 44p 51p

52p 53p 54p 56p

Figure 5.15a SC lesions used in Experiment 5.5

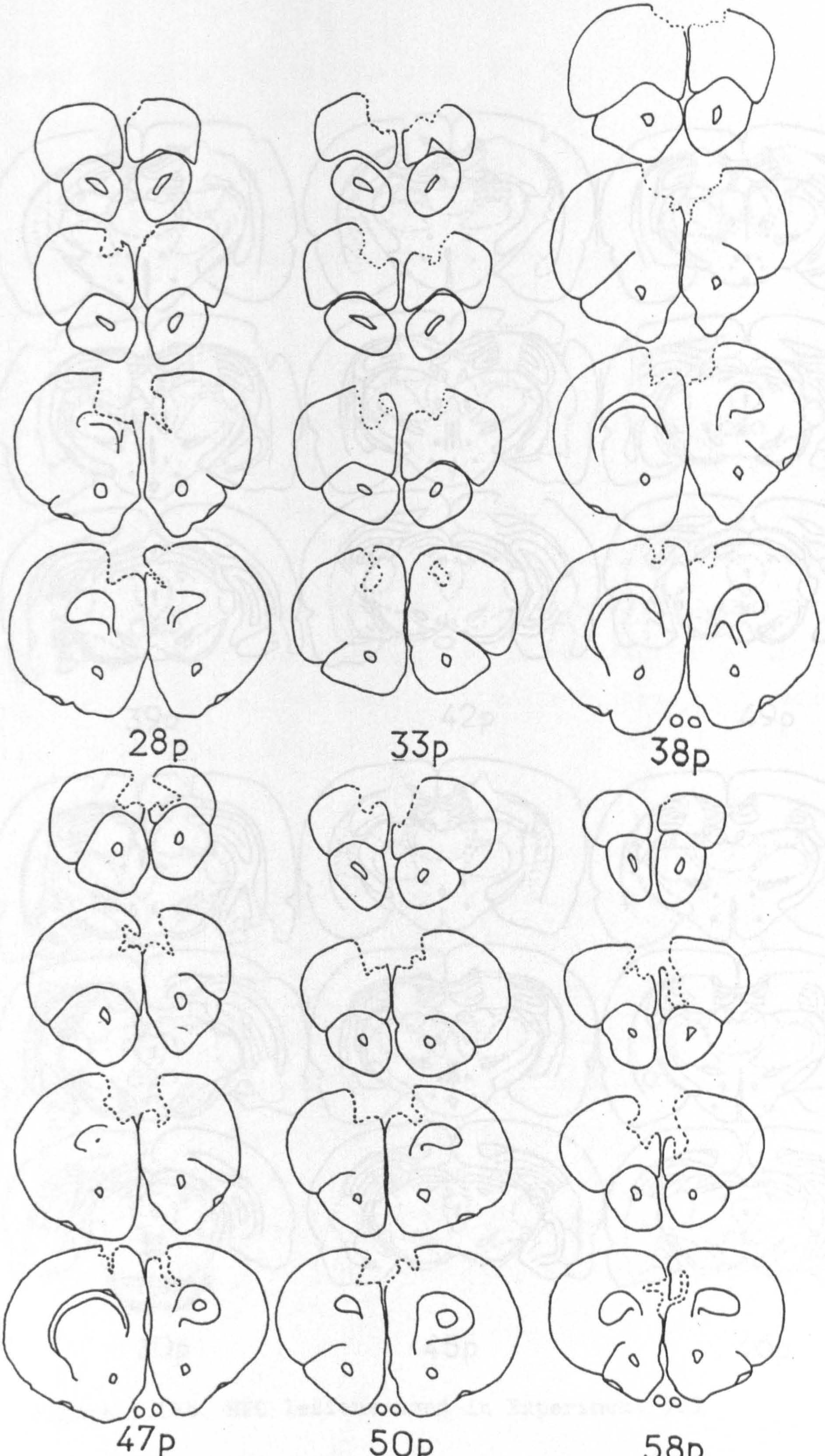


Figure 5.15b MFC lesions used in Experiment 5.5

Figure 5.15c HPC lesions used in Experiment 5.5

depth though in all but one case (No. 52p in which damage was restricted to posteromedial SC; see Figure 5.15c) groups sustained the lesions intended; animals 31p, 32p, 44p, 51p and 54p received deep lesions while in all others damage was restricted predominantly to stratum opticum and above.

5.5.5.2 Behaviour

Weight loss in colliculectomised animals was carefully monitored postoperatively, though none lost weight substantially. In the group with deep lesions, mean weight-loss (measured 7 days postoperatively, compared with weight at surgery) was 3.62% (maximum 6.0% in animal 44p) compared with a mean of 1.75% (maximum 3.6% in animal 29p) in the superficially-lesioned group. No motor or feeding impairments were noted in any animal.

Figure 5.16 shows the level of pre- and post-operative activity in each of the five groups. As in previous experiments event data was transformed using a $\sqrt{x + 1}$ transformation and both preoperative and postoperative data were subjected to (separate) analyses of variance. No significant effects were obtained on any measure preoperatively. However, significant main effects were obtained on postoperative locomotor activity both between groups ($F(4.25) = 4.41$; $p < 0.008$) and over test days ($F(3.75) = 3.01$; $p < 0.036$). The former was due to the elevated activity of the deep SC group on all days ($p < 0.01$).

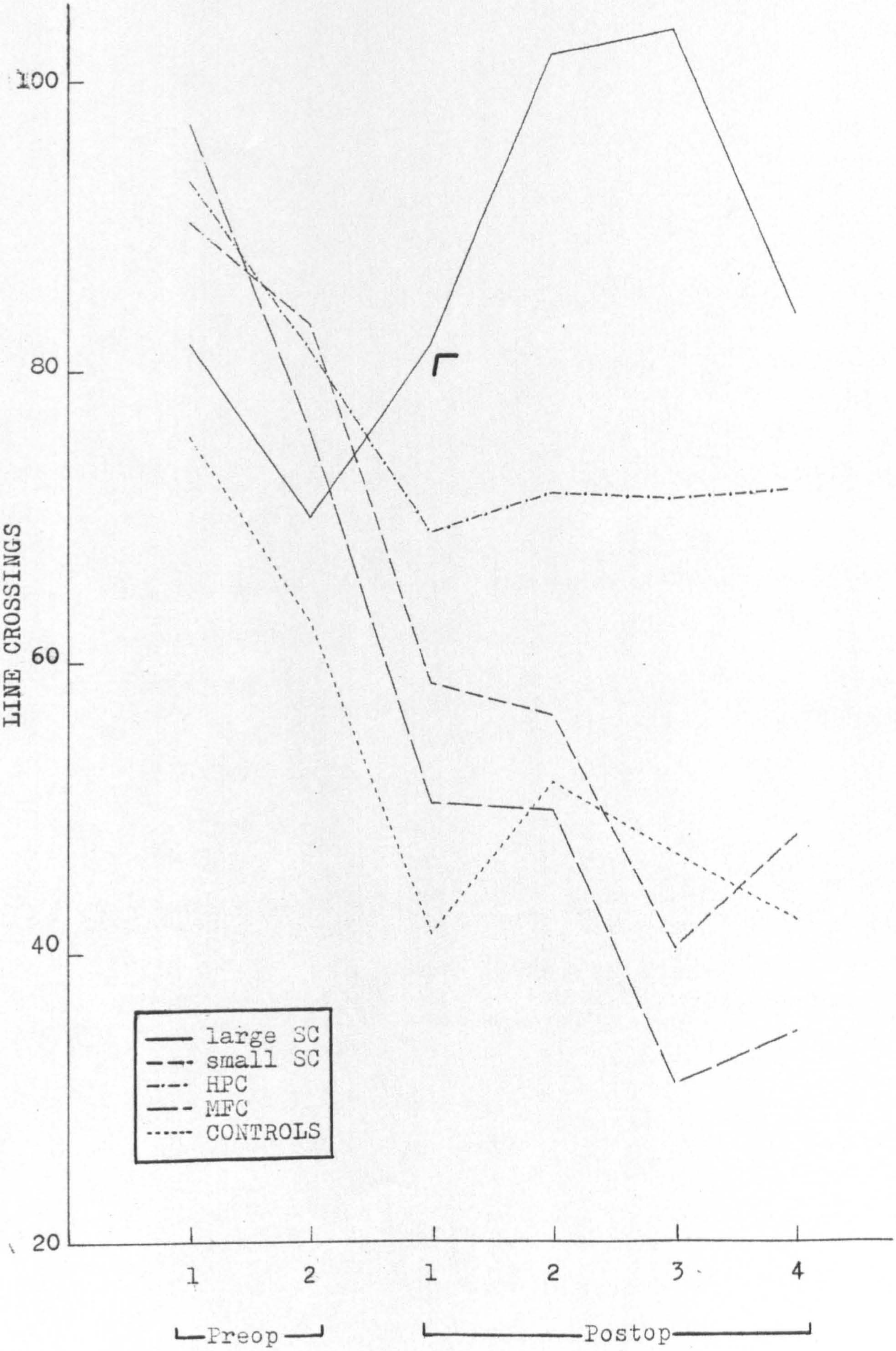


Figure 5.16
Pre- and postoperative line crossings recorded in Experiment 5.5. Depressed level of activity on postop. day 1 in the large collicular group is arrowed (see text).

In addition to the overall elevation of activity in the collicular group, the hippocampal group exhibited little evidence of habituation of activity on postoperative test days and, as predicted, the Groups x Days interaction effect reached statistical significance ($F(12,75) = 1.84$; $p < 0.028$, 1-tailed). Post hoc comparisons between experimental groups and controls on each postoperative test day were made using Dunnett's test (Winer, 1971). The HPC, small SC and MFC groups failed to differ from controls on postoperative days 1 or 2, though on all postoperative test days, deep-lesioned colliculars were significantly more active ($t(5,25) = 2.70$; $p < 0.025$ in all cases). Small-lesioned colliculars and MFCs failed to differ from controls on any day,yet on postoperative day 3, the hippocampal group was more active than controls, the effect almost reaching significance ($t = 1.795$; $p > 0.05$. Crit. $t\ (5,25) = 2.28$). On postoperative day 4, the difference was clearly significant ($t = 2.34$; $p < 0.05$).

Group differences in rearing were obtained (events: $F(4,25) = 7.62$; $p < 0.001$; time: $F = 8.80$; $p < 0.001$). Both deep- and small-lesioned SC groups reared less than control, HPC or MFC groups (time, events: all p's < 0.03) though MFC and HPC groups failed to differ from controls (time, events: all p's > 0.25). Rearing decreased over test days in all groups (events: $F(3,75) = 6.08$; $p < 0.001$; time: $F = 6.50$; $p < 0.001$). Defaecation showed no significant Group effect though in all groups decreasing over test days ($F(2,50) = 5.10$; $p < 0.06$).

The behaviour of control animals towards holes in the floor was similar to that described by File and Wardill

(1976) who used a standard apparatus in which holes were drilled towards the centre of the arena. Typically a **rat** would run about frequently bobbing its head into a hole up to the shoulders, remain in a static position for some seconds and then either proceed to raise its head and re-enter the hole in a rather stereotyped movement or alternatively to run on to another hole and repeat the head-dip procedure. As with novel object investigation (see Section 5.3.4.2) it was not uncommon for an animal to run away from a preferred hole after head-dipping, only to return almost immediately as if having "rediscovered" it. As in Experiments 5.1 - 5.3, rats typically ran round the edge of the arena, successfully avoiding holes drilled at the edge though frequently exploring them. Occasional forays were made into the centre of the apparatus where further head-dipping occurred.

Headpoke scores were initially analysed without distinguishing between inner and outer holes. Significant Group effects were evident (events: $F = 3.72$; $p < 0.017$; time: $F = 4.21$; $p < 0.01$) since the deep SC group engaged in almost no headpoking and significantly less than all other groups (all p's < 0.03). No other group difference approached significance, though the MFC group recorded 34% more headpokes than controls on days 1 and 2 combined. Amount of headpoking decreased significantly over test days (events, time: $F = 6.08$; $p < 0.001$; $F = 7.32$; $p < 0.001$ respectively).

Percentages of headpoke time devoted to outer holes were separately calculated for each animal on each day, subjected to arcsin transformation and analysis of variance which revealed significant overall Group differences ($F(4,25) = 3.57$; $p < 0.02$) and a significant Groups x Days interaction ($F(12,75) = 1.95$; $p < 0.05$). The former resulted from the deep and superficial groups both devoting a greater proportion of headpoke time to outer than inner holes than controls (deep: $p < 0.025$; superficial: $p < 0.063$) and MFCs ($p < 0.004$, 0.011). The two SC groups failed to differ ($p > 0.50$) and neither differed significantly from the HPC group (p's > 0.11). However the interaction effect was found to result from the failure of the SC group to differ from the HPC group on day 1 yet to exhibit a significantly greater proportion of headpoking at outer holes than HPCs on days 2 - 4. The HPC group was placed intermediately between deep SC and control groups throughout and failed to differ from controls on any day, though the difference almost reached significance on day 1 ($t(10) = 1.56$; $0.05 < p < 0.10$, 1-tailed). Overall percentage of total headpoke time devoted to outer holes was 89.1% in the deep SC group, 83.0% in the superficial SC group, 73.5% in HPCs, 66.3% in controls and 59.5% in MFCs. Analysis of the number of headpoke events produced identical results to the above and will not be discussed separately, though a tendency was noted for number of headpoke events to fall more sharply over days than headpoke time, suggesting that as with rearing (see

Figure 5.4), individual headpokes tend to become fewer but of longer duration on later test days.

The number of occasions on which animals fell into holes[1] was totalled over the four test days. Deep SC rats fell into holes on average 1.67 times per animal per day, the corresponding average for other groups being: superficial SCs, 0.53; MFC, 0.50; HPC, 0.72; controls, 0.44. Mann-Whitney U-tests carried out between groups failed to indicate statistically significant Group differences but suggested that deep SC rats fell into holes more frequently than all other groups ($0.05 < p < 0.1$ in all cases). However qualitative observations noted by E during testing are especially important in this respect, since "falling into holes" for animals in all groups except the deep colliculars consisted of placing or slipping a paw into a hole, while still maintaining balance and appearing relatively undisturbed by the experience. However on many occasions deep colliculars would suddenly collapse into a hole, one limb disappearing from view entirely. This was not always necessarily due to visual inattention towards the hole since it would sometimes involve a hind paw and occur as the animal was running past a hole, or moving sideways or backwards. However such animals invariably appeared surprised and disturbed. They would either run frantically to a corner, or remain standing by the hole

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[1] This almost always occurred at outer holes.

but in either case stood for some seconds defaecating, showing piloerection, diaphragmatic breathing (coupled with back-and-forth movements of the vibrissae) prior to resuming locomotion.

5.5.6 Discussion

Group differences in activity were entirely consistent with those obtained in the previous studies since deep SCs, but not superficial SCs, were hyperactive on all postoperative test days compared with each of the other groups. However it is clear that the present apparatus is not ideal for demonstrating such an effect since the deep SC group repeatedly fell into holes, and were clearly disturbed by the experience. This behaviour did not appear to result entirely from a visual attentional deficit and suggests that the SC with extensive deep laminal damage is not only extremely inattentive but probably suffers from additional motoric impairment (Foreman _et al_, 1978; Pope and Dean, 1979). The effect of falling into holes was probably to severely depress the activity of the deep SC group, particularly on postoperative test day 1 when 9/23 deep SC "fall-ins" occurred. Nonetheless the robustness of the collicular hyperactivity phenomenon is emphasised by the fact that, despite the considerably depressed activity score, the SC group was still significantly more active than any other group on all days. It is perhaps worth noting that the results of Experiments 5.1 - 5.3 (though not entirely comparable with the present design) would predict that the true level of collicular activity for animals with lesions of this size and depth might have been at a level at least twice the control group mean on postoperative day 1 (cf Figure 5.5).

Of further interest is the apparent "hyperactivity" of the HPC group. The present experimental design, in providing preoperative exposure to the test apparatus, is similar to many which have previously demonstrated elevated activity levels in hippocampal rats (see Table 4.1). Preoperative activity scores provide a baseline against which postoperative change in activity level may be compared. The drawback of the design is that the open field situation is not entirely novel postoperatively. This may be especially significant in the present study since an important distinction was drawn between HPC and SC lesion effects specifically on the basis of attention upon initial exposure to novelty (Section 4.1). Admittedly the present design involves some preoperative habituation, though postoperative testing was carried out using a novel floor surface with novel holes, 11 days following last preoperative test day.

However from Figure 5.5 it is clear that postoperative hippocampal activity level is not initially elevated above that of preoperative testing and was only significantly higher than control, MFC and superficial SC groups on day 4, following habituation by the latter 3 groups. While individual hippocampal rats showed habituation to a lesser or greater extent, it was noticeable that by postoperative test day 4, 53% of control, MFC and superficial SC animals had reduced their activity to below 50% of their individual mean preoperative levels, while no deep SC and only one HPC had done so. The result is consistent with previous reports that, in rats, HPC "hyperactivity" (in contrast to that following SC lesions) arises solely from decreased habituation over test days (Douglas and Isaacson, 1964; Means, Leander and Isaacson, 1971; Jarrard, 1973) and further demonstrates the comparitively greater magnitude of hyperactivity in SCs.

Though all animals tended to spend a large proportion of their time at the edge of the arena, close to the wall, this was found to be particularly evident in the collicular groups which spent some 80% of their time there, and the hippocampal group which also spent 80% of their time at the perimeter on postoperative test day 1, but failed to exhibit such a marked preference on subsequent test days. Clearly the measure adopted in this study cannot be said to reflect degree of "thigmotaxis" since amount of running, and time spent, at peripheral and central locations were not directly measured though it is likely that the inner-outer distribution of headpoking is an indication of the way in which the animal distributed its time generally. The result is thus indirect evidence that collicular animals show enhanced thigmotaxis and for Hostetter and Thomas' (1967) finding of such an effect in a 4 minute test session with HPCs, though the present result suggests that the effect might have diminished had Hostetter and Thomas tested their animals for longer.

In some respects the thigmotactic behaviour of SC and HPC groups is surprising, since this behaviour is generally considered to reflect fearfulness since when stressed, animals in an open field tend to run towards the wall. Clearly such a response has survival value since the small mammal is particularly vulnerable in open spaces. However both HPC (Gray, 1972) and SC (Pope and Dean, 1979) rats have been described as being less fearful than control animals and might thus be expected to leave the wall of the arena more readily. However there may be a number of reasons why such behaviour may occur, including spatial disorientation of any kind in which case the apparatus wall would provide a valuable reference point, there being few alternatives in a visually homogeneous arena.

Group differences were obtained in relation to rearing, both SC groups exhibiting less than controls, though no increase was noted in MFC animals as seen in Experiments 5.2 and 5.3, or decreased rearing in HPCs as seen in Experiment 5.2. Both MFC and HPC lesions were much smaller than in the previous studies; in addition rearing behaviour was a category particularly affected by the introduction of holes in the apparatus floor since much investigatory behaviour was directed at floor level and thus more subtle effects which, in the case of MFC lesions in earlier studies, just reached statistical significance, would have been unlikely to emerge in this study. However, as for the effects of HPC lesions on destractability, it is likely that very large lesions (with extrahippocampal involvement: see Experiment 5.2) differ from those of small, subtotal lesions (see Chapter 6). Preoperative exposure to the test apparatus failed to produce activity elevation in MFC rats, as might have been expected from previous reports (see Gross, 1968).

Headpoking was greatly reduced in deep-lesioned SCs, compared with all other groups. This is likely to reflect gross inattentiveness on the part of collicular rats, and is consistent with previous reports (Goodale and Murison, 1975; Goodale _et al_, 1978; Marshall, 1978). However an extremely puzzling aspect of the present results is that rats with smaller, superficially located lesions behaved normally in terms of head-poke investigation. This is clearly not attributable to a total sparing of function after restricted lesions, since attentional behaviour such as rearing was depressed, and other behavioural changes were observed such as a significantly greater tendency than controls to headpoke at the perimeter of the apparatus. Lesions such as these produced clear attentional deficits in studies reported above.

There is clearly no adequate explanation for the effect, though proper evaluation must await retesting with more extensive superficial lesions. One possibility is that holes at floor level are such potent stimuli that only the most severe and gross inattentiveness would abolish orientation towards them, alternatively that headpoking is a separate form of orienting behaviour from, say, peripheral attention in a runway. Since placing objects beneath the holes produces enhanced headpoking (File and Wardill, 1976), it would appear that headpoking is a behaviour not unlike "object investigation" (see Experiments 5.2 and 5.3) of which the collicular animal is not totally incapable. However in the case of headpoking, clearly detecting the presence of a hole is a prerequisite for normal hole investigation. Thus the puzzling aspect of the above result may really be that small superficially-lesioned SCs unlike deep-lesioned SCs detect the presence of holes in the first place. It would seem likely that the anomaly is best explained by assuming that since superficial lesions are small in terms of their lateral extent, stimuli in lower nasal quadrants which are represented in lateral regions of the SC occupy a "spared" area of colliculus in the case of the superficial SC lesions used in this experiment. In addition, efferent pathways appear to arise in lateral regions of SC (Tokunaga and Otani, 1976). Thus it is likely that a "Lateral Collicular Brachium → Lateral SC →

Collicular Efferent" system is intact following small lesions of superficial SC. This would provide residual function in relation to ground-level stimuli, though behaviours involving attention to other regions of space would be disrupted in such animals. However clearly such a model awaits further experimental investigation, especially since Keating (1976) was unable to identify a relationship between lateral tissue sparing and residual function in monkeys.

Rats with MFC lesions made arithmetically more headpokes than controls, and distributed their time surprisingly evenly between inner and outer holes. Thus the result is further evidence for functional dissociation between SC and MFC lesions, possibly also for elevated levels of attentional behaviour in MFC animals consistent with Experiments 5.2 and 5.3. Collection of data on a minute-to-minute basis would be valuable in indicating whether the MFC group is normal in terms of the rate at which headpoking habituates within a session, though the present study shows that intersession habituation in MFCs is not significantly slowed compared with controls.

The above study is not directly comparable with that of Köhler (1976) who used very well-handled rats for 10 minute test sessions in a 16-hole apparatus. However it was clear from Köhler's careful study that rats with HPC lesions were not inattentive to floor-level holes (and indeed tend to show an elevated level of headpoking as a result of retarded habituation). The present study only differs strongly from that of Köhler in terms of activity measures, since HPCs in this experiment were not more active than controls on initial placement in the apparatus, though the elevated activity scores on day 4 of rats in this study whose predominantly dorsal lesions were roughly comparable to those of Köhler's HPC-d group may represent a further aspect of delayed intersession habituation produced by this lesion, but which was not investigated by Köhler. However the two studies contradict the view that hippocampal rats are totally non-exploratory (O'Keefe and Nadel, 1978); indeed both suggest "that the increased activity expressed by hippocampal lesion rats ... does not relate in any simple way to alterations in exploratory behaviour" (Köhler, 1976, p. 104).

Conclusion

Rats with lesions of SC which extensively damaged deeper laminae were hyperactive, ignored holes in the floor of the apparatus and frequently fell into them. Activity and hole exploration was entirely normal in animals with small lesions of MFC; rats with HPC lesions were indistinguishable from controls in terms of hole investigation but showed slow inter-session habituation of locomotor activity. It was argued that SC, MFC and HPC lesions are dissociable on the basis of lesion effects.

Animals with restricted superficially-located

SC lesions were not hyperactive, but exhibited less attentional behaviour (e.g. rearing) than controls. Surprisingly, these animals investigated floor holes normally. There is no obvious explanation for this finding, though it was argued that degree and type of functional sparing may crucially depend upon location of lesions in the SC. Both deep and superficial SC groups tended to headpoke towards the edge of the arena; HPC-lesioned rats did so on day 1 but the effect disappeared thereafter.

5.6 General Discussion

The elevated locomotor activity of rats with deep, but not superficial, lesions of SC is consistent with a number of previous reports (e.g. Foreman et al, 1978; Weldon and Smith, 1979; see Chapter 3). The reduction in attentional behaviour, and failure to respond to specific novel features in the environment is also consistent with many previous reports (see Foreman et al, 1978; Goodale et al, 1978; Chapter 3) though interestingly the results of Experiment 5.2 (involving collicular rats which were shown to be grossly inattentive in a runway - see Experiment 6.1) suggest strongly that it would be inaccurate to describe the SC rat as totally unresponsive to gross environmental change and thus the view that the ambient environment is somehow absent in SCs is clearly unsupported. One exception to the above findings was that (Experiment 5.4) SC rats with superficial (but not deep) lesions of SC behaved normally towards holes drilled in the apparatus floor, though experiments with more extensive superficially-located lesions would be valuable in determining whether the effect is due to (i) normal attentiveness to ground-level stimuli in colliculars or (ii) functional sparing after restricted lesions. The present results are especially interesting vis à vis the depth of lesion required to produce hyperactivity. A number of possible factors may be responsible for the lesion size-activity correlation:

a) <u>A locus of hyperactivity</u>

Most experiments reporting extreme hyperactivity in collicular - lesioned rats involve lesions which extend beneath the colliculus into dorsal tegmental/cuneiformis nucleus regions (Foreman <u>et al</u>,1978; Pope and Dean,1979), and it is possible that a specific site beneath the SC is a "critical locus" which must be invaded for hyperactivity to ensue. With lesions which are largely restricted to superficial laminae either a small increase or no increase is observed (Goodale and Lister,1974; Weldon and Smith,1979). Furthermore, lesions which spare much superficial SC but extend between midcolliculus and the dorsal tegmentum have been shown to produce elevated activity (Kesner <u>et al</u>, 1967; Capps and Stockwell,1968).

However, in other studies lesions in the subcollicular tegmentum have failed to produce hyperactivity (Murison, 1977; Glickman, Sroges and Hunt,1964), only lesions in the ventral tegmentum giving rise to activity increases (Glickman <u>et al</u>,1964). Inspection of the lesions in Experiment 5.2 reveals that some (eg. 15a, 18a, 39a,60a) invaded the subcollicular tegmentum in at least one section, though the size of the lesion when estimated (see Section 5.4) was <u>volumetrically</u> small within both the colliculus and tegmentum, and no gross activity increase was seen in these animals in the open field in agreement with the results of Glickman <u>et al</u>(1964).

It would appear from the results of Pope and Dean (1979) that invasion of a specific locus beneath the SC produces deficits in motor coordination and reduced food intake (see also Kesner et al, 1967), though activity levels were raised in colliculectomised animals in which this tegmental site was not damaged.

Winterkorn and Meikle (1980) report that both antero-posterior extent of lesion within the SC and extent of dorsal tegmental invasion are factors determining the degree of ipsiversive rotation in unilaterally-lesioned cats. However, the relevence of this result for the present argument is doubtful since the effect of large bilateral collicular or tegmental lesions in cats on motor behaviour is opposite to that in rats, cats becoming slow and lethargic (Myers, 1964). Thus separate neural systems may underly rotational behaviour following unilateral lesions and activity changes following bilateral lesions. Interestingly, unilateral tegmental lesions alone in rats produce contraversive and not ipsiversive circling (Kesner et al, 1967; Pycock, 1980), though this may not be so in cats (Winterkorn, Ross and Meikle, 1978; Winterkorn and Meikle, 1980). It would, however, be surprising if, as in cats, collicular lesions in rats were to produce ipsiversive turning most effectively when in combination with invasion of the dorsal tegmentum, in view of the opposing directions of turning which unilateral lesions of the two structures produce when lesioned separately.

Central grey matter also tends to be invaded when lesions are made in deep colliculus, and indeed lesions in central grey have been reported to produce elevated activity levels (Liebman <u>et al</u>, 1970) though only when substantial damage is incurred (cf Glickman <u>et al</u>, 1964). Irritation of this area by iron deposition after anodal electrolytic SC lesions may be the cause of the "explosive motor behaviour" seen immediately postoperatively (Murison, 1977; see Section 5.1.6.2), since such is observed upon lesioning central grey matter though this is said to be a temporary phenomenon (Pope and Dean, 1979). As opiate binding sites are found in the mesencephalic central grey (Terenius, 1978) and anaesthesia results from electrical stimulation here (Reynolds, 1969) it is possibly involved in the control of fearful behaviour and response to aversive stimulation. Thus decreased fearfulness, perhaps indicated by the relative absence of defaecation in large-lesioned SC rats, may result from central grey invasion.

b) <u>Volumetric considerations: Volume of SC removed</u>

If increased activity in colliculectomised rats is wholly a result of decreased attention, in particular visual attention, large lesions in the SC will be more effective than small lesions in destroying attentional functions and intrinsic collicular organisation, increasing the area of attentional "scotoma" by removing a greater area of visual field representation. Since lesions made via a bare electrode tip are roughly circular in shape, superficial electrode placement which damages only superficial laminae will usually cause a volumetrically small lesion, severely restricted in terms of antero-posterior and medio-lateral extent. Moreover, deep electrode placements are likely to produce, in addition to deep laminal ablation, more substantial and extensive superficial damage than superficial placements. Thus depth and/or size of lesion is always confounded with extent of damage in superficial colliculus. Clearly if activity elevation results directly from inattentiveness, total lesions of superficial SC alone would be expected to produce hyperactivity. From most of the above results it is not obvious that degree of inattentiveness was related to degree of hyperactivity in the collicular groups; neither attention to novel objects nor frequency or duration of any attentional behavioural category measured was correlated with activity level, except in Experiment 5.5 where small superficial lesions failed to produce inattentiveness towards holes drilled in the floor of the apparatus. In this case, however, the effect may depend upon the surface location of the lesion rather than pure volumetric effects. Clearly it may be argued that superficial lesions are responsible for the observed inattentiveness but that additional motor deficits and hyperactivity produced by deep laminal invasion obviate and possibly exaggerate the manifestations of inattention.

c) Volumetric considerations: Volume of deep SC removed

Since the major efferent projections of the SC originate in intermediate and deep laminae, it is likely that an extensive lesion of deeper SC will be especially effective in producing behavioural effects since in that case the soma of origin of many effector systems are not simply deprived of inputs but are physically removed. It is known that such deeper cells receive input from a number of sources, including visual input from superficial laminae, plus input from a number of cortical and subcortical sites (see Section 1.2) related to visual, auditory, somatosensory and kinaesthetic senses.

Thus, although vision would appear to be the most dominant modality in the SC since superficial laminae appear to be uniquely devoted to it, deeper laminae appear to be equally concerned with input from a multitude of sources both retinal and extraretinal.

It is likely that at deeper SC level each of these inputs contributes to intracollicular mechanisms, perhaps relating to control of attentional switching, and contribute to or modify the output of deeper collicular neurons [1]. Indeed in animals with deep

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[1] It should be emphasised that no particular "flow diagram" for intracollicular mechanisms is being adopted since connections between superficial and deep SC are established and must therefore be incorporated in any functional model (see Sprague, 1975 and Chapter 1).

SC ablations, not only visual (Goodale <u>et al</u>, 1978) but also auditory (Goodale and Murison, 1975) and tactile (Kirvel, Greenfield and Meyer, 1974; Collin, 1977) neglect is observed (see Sprague and Meikle, 1967).

From the above it is predictable that lesions of superficial SC would produce inattentiveness primarily in relation to visual stimuli, since only one (visual) input is prevented from influencing effector mechanisms. Lesions in deep SC, however, would be expected to produce a more profound multimodal inattention and lead to more extreme overall behavioural changes, including such gross changes as locomotor hyperactivity (Foreman <u>et al</u>, 1978) or change of hand preference (Collin, 1977), since all structures normally receiving input via tectal projections would be rendered totally devoid of such input. However whether this inevitably reflects a sharp discontinuity between deep- and superficial lesion effects is questionable: indeed the question of whether behavioural changes following ablation are "sensory" or "motor" may turn out to be a question of semantics rather than practical experimentation.

Pope and Dean (1978: personal communication) have suggested that a region of deep SC and part of periventricular grey may represent a locus or critical site for locomotor hyperactivity in rats. However since lesions which invade periventricular grey and dorsal tegmentum are also likely to have a greater anteroposterior and mediolateral extent within colliculus, and generally a greater degree of extracollicular involvement than lesions which do not, lesion extent may be the significant factor.

d) Damage to fibres of passage

Winterkorn (1975) argued that lesions of the SC might produce behavioural changes as a result of damage to fronto-tecto-bulbar pathways. Since the results of Experiments 5.2 - 5.4 showed clear differences between SC- and frontally-lesioned rats, Winterkorn's hypothesis that the two lesions should produce comparable postoperative deficits is contradicted. However Pope and Dean's (1979) finding that incorporation of a specific, small tegmental locus in large dorsal midbrain lesions produces particularly severe motor impairments suggests (Pope and Dean, 1978; personal communication, 1979) that very deep SC ablations may interrupt an ascending neural pathway between hindbrain and forebrain. Just such a model was investigated by Winterkorn *et al* (1978), who found that degree of ipsiversive turning in collicular tegmentally lesioned cats correlated with extent of noradrenaline depletion in the forebrain, though since unilateral locus coeruleus lesions failed to reproduce the effect, lesion of the dorsal noradrenergic bundle was ruled out as being primarily responsible for the locomotor asymmetry. Clearly, if damage to underlying fibres of passage were responsible for motor effects following collicular ablations, such effects might be expected to depend crucially upon the depth/locus of lesion and not upon anteroposterior extent, since transection of a fibre bundle at any point will produce uniformly severe postoperative manifestations. However from the above discussion, this does not appear to be the case. Glickman et al (1967) reported normal activity levels in rats with bilateral lesions of the SC-tegmentum which were of small anteroposterior extent, and Winterkorn and Meikle (1980) report a lack of ipsiversive rotation in one cat (C92) with a similar, but unilateral lesion. From the above discussion, however, it is clear that comparisons between lesions in rat and cat, and between unilateral and bilateral lesion effects must be drawn cautiously. In addition Winterkorn and Meikle (1980) argue that damage to the predorsal bundle system is not responsible for turning behaviour in unilaterally colliculectomised cats. However, Wirtschafter et al (1979) have argued that in rats, the predorsal bundle is related to asymmetrical turning behaviour since it appears to mediate contraversive rotation following unilateral substantia nigra lesions. Moreover, even if tecto-reticular (predorsal bundle) projections were found not to be related to turning following unilateral SC lesions in rats, this would not lead inevitably to the conclusion that the predorsal bundle is irrelevent to other motor consequences of bilateral collicular lesions in rats , for example, open field hyperactivity (Foreman et al, 1978) and other forms of locomotor disinhibition (Murison and Mayes, 1980).

In conclusion, the most likely cause of hyper-activity and erratic locomotor responding in colliculectomised rats is the loss of control of motor functions normally exercised by deep collicular effector systems. Whether inattentiveness produced by widespread superficial collicular damage is the major cause of elevated activity in deep-lesioned rats is unclear; it is possible that SC ablation in combination with damage to dorsal tegmental tissue gives rise to particularly obvious hyperactivity. Although very large SC lesions may also encroach upon periventricular areas or nucleus cuneiformis related to fearfulness, or ascending catecholamine pathways, the view that individual "loci" within the SC may be isolated as individually responsible for particular aspects or elements of behavioural change following collicular ablation should be treated with caution. It was argued above that the lesion technique as used here is probably an inappropriate tool for further investigating division of labour within the SC and that a more profitable approach might be the employment of pharmacological techniques, alternatively the development of a lesion technique allowing the total, independent removal of superficial laminae in the rat.

Comparisons between the SC and other neural structures

The evidence for minimal functional overlap between MFC, HPC and SC has been discussed already and will not be repeated.

In view of the recent finding (Glick and Greenstein, 1975) that unilaterally frontally-lesioned rats undergo reversal (after 20 days) of the direction in which they turn following injections of apomorphine (initially ipsiversive to the lesion side) it would be interesting to investigate whether a similar reversal occurs for unilateral colliculars in view of Isaac's (1971) hypothesis that MFC and SC are co-operatively involved in control of activity level. Of further interest would be the direction of turning following unilateral lesions of SC, MFC or midbrain reticular formation made in the same, or opposite, hemispheres.

However, the above results demonstrate substantial differentiation between the behavioural effects of collicular and frontal lesions when made bilaterally. In particular, the latter failed to produce elevated activity levels in the open field, in agreement with the results of Glickman <u>et al</u> (1964) and Albert and Bignami (1968). Indeed, in further contrast to the effects of lesions in the colliculus, frontal lesions tended to give rise to elevated levels of attentional behaviours (rearing, headraising, etc.). It is worth noting that bilateral frontal ablations including the "eye fields" in monkeys (Miller and Orbach, 1972) and cats (Hagamen, Lance and Ungewitter, 1959) have been reported to result in "hyperattentiveness". The latter authors reported increased responsiveness towards visual, auditory and tactile stimuli applied ipsilateral to a unilateral frontal lesion, and increased responsiveness bilaterally upon removal of the contralateral frontal lobe. The authors were led to argue that

> "The frontal lobe normally exerts an inhibitory influence on responsiveness to ipsilateral stimuli. The decreased responsiveness to contralateral stimuli is not due to removal of structures necessary for the response but is probably secondary to the abnormal focusing of attention on ipsilateral stimuli."

However, it should be noted that elsewhere (Latto and Cowey, 1971b) bilateral visual neglect has been demonstrated in one bilaterally FEF-lesioned monkey. Thus in the following experiments, the effects of bilateral and unilateral medial frontal lesions upon other types of attentional task will be examined.

The hippocampal group in Experiment 5.2 comprised only 4 subjects, and though a tendency towards increased activity was noted, this was not significant. Like the SC group, however, the HPC rats engaged in less rearing than controls. However in Experiment 5.5 it was clear that elevation of activity in hippocampals was solely due to retarded intersession habituation unlike the SC group which was hyperactive from the first day of placement in the apparatus postoperatively. The HPC behaviour was consistent with many previous reports (see Jarrard, 1973 and discussion of Experiment 5.4).

Thus it is possible to formalise the differences between collicular and hippocampal lesions in terms of a model which makes the following assumptions:

1. A control animal initially placed in a novel apparatus is aroused by the experience in a general sense and is almost immediately active as a result of an "exploratory drive".

2. This activity is reduced by periods of orientation to novel objects which are of interest to the animal, since attention to specific stimuli is essentially a stationary activity incompatible with locomotion.

3. On subsequent placements in the same apparatus, the arousing quality of the novel environment is reduced, as information in the environment becomes incorporated in a cognitive framework and thus predictable, but voluntary attention increases and thus self-generated exploration ensues (perhaps to maintain an optimum level of arousal; see Berlyne, 1960).

Since collicular and hippocampal animals behave differentially in novel and familiar environments, it must be assumed that both are generally aroused on initial exposure to a completely novel apparatus. The SC animal, however, appears to be inattentive to *specific* environmental cues and thus gross arousal or "locomotor reactivity" (Gross, 1973) is not suppressed by the occurrence of attentional switches, though on subsequent occasions following "passive

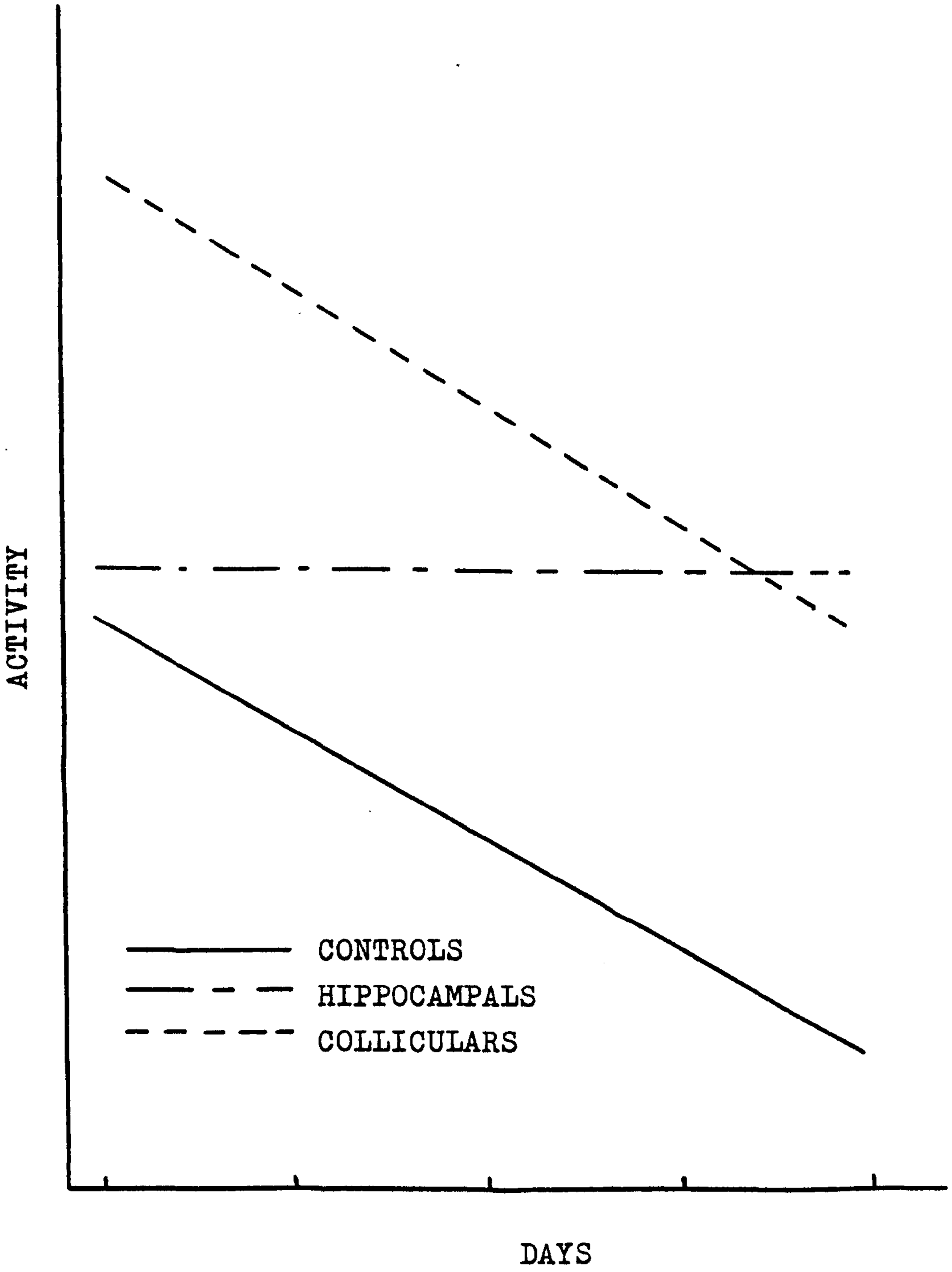

Figure 5.20
Theoretical habituation curves for control, collicular and hippocampal rats in the open field.

stimulus exposure [1] the SC animal tends to habituate overall activity from its initial very high level. The HPC on the other hand is not grossly inattentive to cues and does investigate them, but tends not to habituate to them, apparently treating the environment as novel on each subsequent exposure.

Figure 5.20 shows the activity habituation curves predicted by the above model which was based on findings of previous authors (reviewed in Chapter 4) but was specifically invoked to explain the results of Experiment 5.5 (Figure 5.16) with which the predicted curves should be compared. The model is consistent with the latter results except for the deep collicular group which on postoperative day 1 failed to show substantially elevated activity. It was pointed out above that activity on this day was particularly depressed as a result of this group's tendency to fall into holes and exhibit what can only be described as uncharacteristic behaviour (cf. Foreman et al, 1978). A much higher level of activity would have been obtained from this group in a normal open field apparatus.

A second, serious objection to the above model is that

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[1] That is, the collicular animal, with intact cortical relays, is experiencing and thus potentially habituating to environmental cues, though lacking normal exploration.

postoperative hyperactivity appears only to occur in rodents with deep SC ablations, while tree shrews (Casagrande et al, 1972), monkeys (Anderson and Symmes, 1969) and cats (Myers, 1964) appear to exhibit hypoactivity. It should be noted that in most cases the latter animals were observed in a familiar apparatus or homecage environment and data collection was informal.

The problems of species variation has been discussed earlier (Chapter 3) and the present results add nothing to the argument, though it should be mentioned that the principles of the above model are not necessarily to be abandoned for non-rodent species. The hypothesis that attentional switching and orienting mechanisms are under collicular control appears to be valid for all animals from toad (Ingle, 1973) to monkey (Albano and Wurtz, 1978); however species differ in their expression of orientation to stimuli (Ingle, 1973; Kemp and Kaada, 1975; Osborne, 1977). It is a truism to state that collicular mechanisms must be tailored to the requirements of individual species (see Section 2.3) and their idiosyncratic modes of orientation. Thus the "function" of the SC might conceivably be to modulate locomotor activity suitably in each case. The rat tends to halt ongoing locomotor foraging in response to a novel stimulus and thus the SC has a primarily inhibitory influence upon the motor system, yet in cat or monkey and possibly in insectivores, the cessation of ongoing behaviour might more frequently involve cessation of stationary acts such as manipulation of objects and visual scanning. In the insectivore, novel stimulation might frequently require instant escape. Thus the locomotor and orienting style of individual species might need to be considered in predicting the effect of deep collicular ablation.

On the other hand, the species difference may arise for anatomical reasons, since the size and position of the SC, also the size, method of lesioning and extent of extra-collicular damage incurred in different species may involve systematic variation.

CHAPTER 6

DISTRACTABILITY

6.1 An Investigation of Locomotor Orientation and Distractability in rats with lesions of SC, MFC, or HPC

6.1.1 Introduction

Evidence was reviewed above (Chapters 3 and 4) which implicates the SC, HPC and MFC in the process by which attention is redirected from an ongoing task to the locus of an unexpected stimulus. Large bilateral lesions of SC (Goodale and Murison, 1975; Goodale *et al*, 1978) and HPC (Raphaelson *et al*, 1965; Isaacson and Wickelgren, 1965; Crowne and Riddell, 1969) have been reported to abolish the orienting response to novel visual, auditory or tactile stimuli presented while the animal is engaged in a runway task.

Since hippocampal slow wave activity (θ) which may be attentionally-related (Bennett, 1971) is apparently co-incident with similar activity in the SC (Routtenberg and Taub, 1973), is evoked by SC stimulation (Schaefer 1970) and generated from sites in the brainstem (Redding, 1967) to which the SC projects (Kawamura *et al*, 1974), it might reasonably be inferred that the HPC and SC are two components of phylogenetically ancient circuitry governing the orienting response, a universally adaptive behaviour which facilitates the extraction of information from the environment in the event of any novel, potentially dangerous or informative stimulus which appears in a region of visual space to which the animal's attention is not currently directed.

A similar functional relationship might be suggested between SC and MFC on the basis of comparability of lesion-produced deficits. Unilateral lesions of both SC or MFC have been reported to produce contralateral visual neglect in rats running in a straight runway (Collin, 1977) and both SC (Kirvel, Greenfield and Meyer, 1974; Kirvel, 1975) and MFC (Cowey and Bozek, 1975; Collin, 1977) lesions produce ipsiversive progression tendencies. Similar perceptual and motor asymmetries have been reported in monkeys with unilateral lesions of SC (Latto and Cowey, 1971 a,b; Collin, 1977) or FEF (Kennard and Ectors, 1938; Kennard, 1939; Welch and Stutteville, 1958; Latto and Cowey, 1971 a,b). Furthermore, Latto (1977) has demonstrated that bilateral lesions of SC result in a temporary amblyopia which is of comparable severity and persistence to that following bilateral lesions of FEF.

In cats Winterkorn (1975 a,b) has claimed that lesions of SC and FEF (medial frontal cortex) produce a similar deficiency in the modulation of motor responses. In particular, she argues that the (motor) consequences of collicular ablation may result from damage to fibres of passage from FEF to brainstem via the SC and not from damage to mechanisms intrinsic to the colliculus itself. Such a model predicts that FEF lesions will produce identical deficits to SC lesions; however this does not always appear to be the case.

Monkeys with bilateral FEF lesions (tested 4 weeks postoperatively) have been shown by Milner et al (1978) to exhibit fairly normal visual attention to novel light flashes in contrast to SCs which were inattentive. Indeed Crowne (1977) and Collin (1977) have separately concluded that on the basis of existing reports, bilateral FEF lesions in primates appear to produce much less severe deficits than unilateral lesions.

Thus it is questionable whether unilateral FEF lesions produce a genuine contralateral inattentiveness similar to unilateral SC lesions (perhaps as a result of the removal of cells whose function is to initiate investigatory saccades) or alternatively whether the deficit is a temporary by-product of a more general interhemispheric imbalance, perhaps giving rise to deficits relating to "response requirement, rather than to visual insensitivity" (Milner et al, 1978). The presence of a finely-balanced catecholamine equilibrium between cortical and subcortical telencephalic structures mediating motor control has been demonstrated in rats by Glick and Greenstein (1973). Such a system would presumably remain in equilibrium following bilateral lesions, which would account for the absence of deficits in that case.

Thus it would seem important to ask, for example, whether bilateral lesions of FEF would give rise to the gross bilateral stimulus neglect observed in bilaterally SC-lesioned rats (Goodale and Murison, 1975;

Goodale et al, 1978). Since Collin (1977) did not include bilaterally-lesioned MFCs in his runway distraction study, the question has never been examined.

Furthermore, in the previous reports of Goodale and Murison (1975) and Goodale et al (1978), collicular rats were also noted to run significantly straighter than controls when required to traverse an arena towards an illuminated goaldoor. The animals had been trained to "shuttle" back and forth between 2 discrimination arenas connected by a tunnel. Although runpaths were determined from overhead cinefilms of selected trials, the number of frames per trial was limited. Full records of the rats' "return runs" from goaldoor to tunnel (post reward) were therefore obtained only for animals whose "outward" run had been accomplished quickly. Thus full data was almost exclusively collected for SC rats since these ran significantly faster than controls throughout. It was clear from the data (personal observations, 1975) that SC rats turned from goaldoors and ran back to the tunnel under excellent locomotor guidance, which is perhaps surprising, since it has been argued (Chapter 3) that SC-lesioned rats appear to experience locomotor orienting difficulties where a task requires them to make a localising response to a very eccentrically placed stimulus, for example, in a circular jumping stand (Barnes, Smith and Latto, 1970; Murison, 1977; Weinberg and Stein, 1978). Indeed, where errors were made postoperatively by rats in Goodale et al's (1978) study these occurred at the most eccentrically-positioned goaldoors (about 15° from the supposed centre of gaze). Thus in the present apparatus animals were required to make 180° turns between responses. The necessity for accurate spatial judgement, which this situation arguably imposes, might be expected to produce deficits in the HPC-lesioned animal, since O'Keefe and Nadel (1978) argue that the HPC rat, lacking an absolute "cognitive spatial map" is especially reliant upon egocentric localisation. This might prove to be particularly inefficient when the animal is forced to turn through such a wide angle as in the present apparatus.

Consequently, in the present study, the behaviour of bilaterally-lesioned SC, HPC and MFC rats was compared on measures of locomotor guidance and distractability.

6.1.2 Subjects and Surgery

Thirty-four rats, described in Experiment 5.2 served as subjects. Apart from open field observation, they had not participated in any previous experiment. Surgery and histological procedures are described in Sections 5.2.3/4. Training for the present experiment commenced 120 - 150 days postoperatively. The animals were maintained on a one hour per day feeding schedule throughout the experiment.

6.1.3 Apparatus and Training

6.1.3.1 Runway alternation

The apparatus consisted of a simplified version of the automated discrimination arena used by Goodale *et al* (1978), comprising a grey-painted arena designed to be slightly larger than in the Goodale *et al* (1978) study, thus measuring 100 cm square, and with walls 45 cm high. A single goaldoor was located at the midpoint of each of two opposite sides. Doors consisted of top-hinged, 4 cm squares of opaque perspex with the lower edge almost at floor level. They could be independently back-illuminated by standard 12v, 3.5 watt stimulus bulbs. Pressing a goaldoor while illuminated caused delivery of 2 x 45 mg saccharin pellets from an automated dispenser (located outside the apparatus) into a recess directly behind the goaldoor from which the animal could comfortably feed.

On day 1 of pretraining, animals were placed in cage pairs in the apparatus, both goaldoors were illuminated and food pellets were liberally scattered round the goaldoor and reward recess. On day 2, animals were placed in the arena individually with food located behind each door. During feeding, many animals spontaneously moved between the 2 goaldoors, though where strong preferences were exhibited, equal experience of goaldoors was ensured by manually transporting animals to nonpreferred doors. On day 3, only 2 pellets were located behind each door. Equal experience of the two goaldoors was again ensured. On day 4, no pellets were initially present behind the goaldoor.

When the animal had learned to press for food, it was trained to alternate between the goaldoors. After 10 presses of a door, its light was extinguished and the animal could only obtain further rewards by running to the opposite end of the arena. After each series of 10 presses, the light would extinguish, and the opposite goaldoor would become illuminated without delay. Following 10 - 12 such alternations, the schedule was automated such that, on being placed in the apparatus the rat was required to run to the one illuminated goaldoor and press it (the door initially positive was randomised within groups and alternated on successive days for individual animals), whereupon food would be delivered. The door remained illuminated for 2 seconds, during which no further rewards could be obtained by further goaldoor presses. Indeed, further rewards could then only be obtained by running to the opposite (illuminated) goaldoor. This sequence alternated for 40 trials per day, following which both door lights extinguished and no further rewards were available. The animal was immediately removed and the apparatus wiped clean with a 2% acetic acid solution.

The sequence was automatically controlled using Grason-Stadler logic modules, housed in a separate room from the apparatus. A photobeam was located as shown in figure 6.1. bisecting the arena at the midpoint between goaldoors, 2 cms above floor level. When the beam was broken by the rat's interception an automatic timer was started, which stopped only when the correct goaldoor was pressed, at which point the accumulated time was printed out and the timer reset automatically. Thus the latency of a rat's run over the second half of the appar-

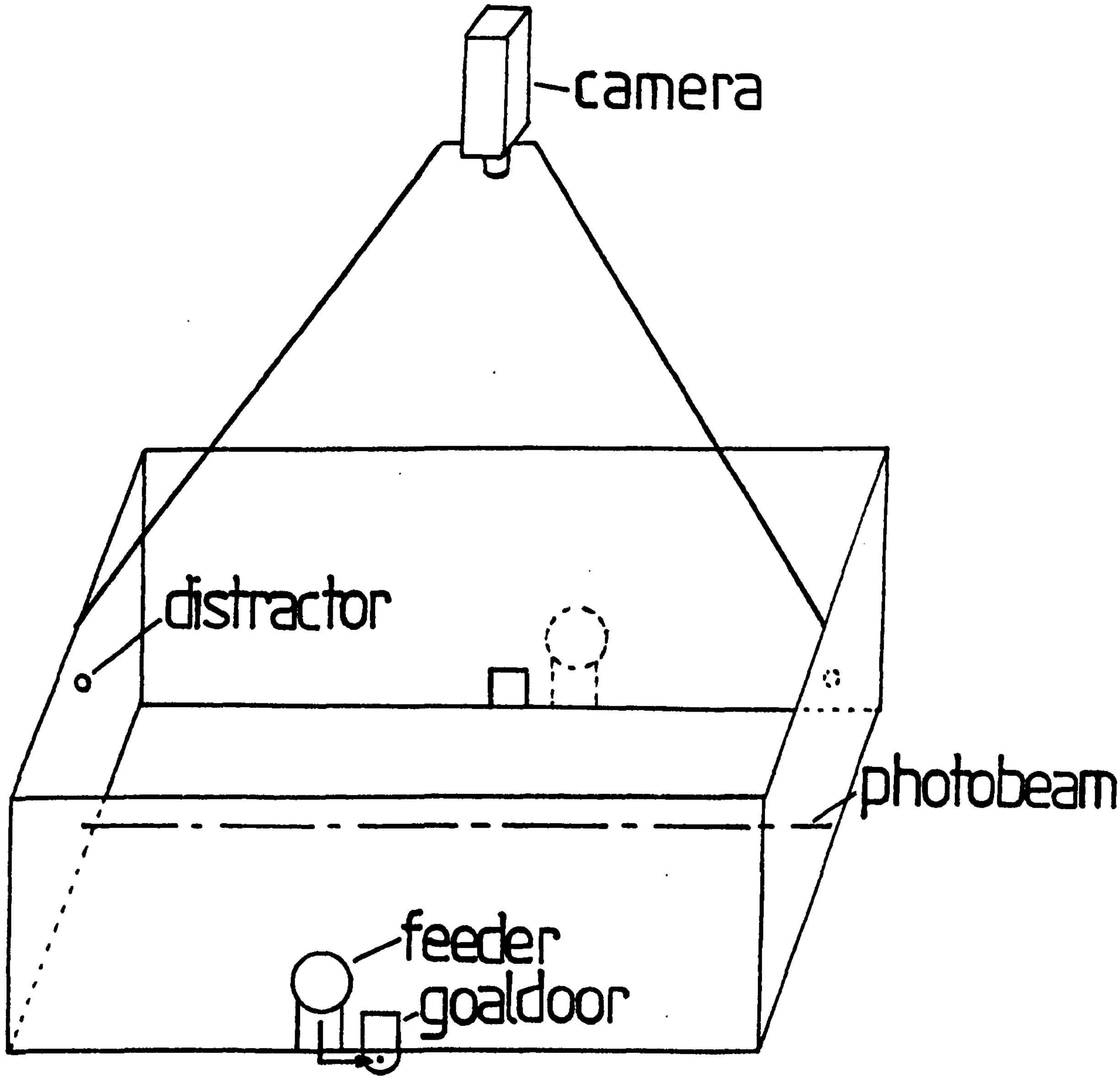

Figure 6.1
Apparatus used in Experiments 6.1 and 6.2. For dimensions see text.

atus was recorded to an accuracy of 0.1 secs. Also recorded were "repeat" doorpresses, hereafter termed "error" presses since they were made after the goaldoor light had extinguished. These were recorded for each door separately, and automatically, for each trial.

A videocamera equipped with a 4" wide angle lens was mounted on a camouflaged tripod stand 1.5m above the centre of the apparatus. Via a monitor in an adjoining room, E was able to continuously observe a rat's behaviour and record selected trials on a videotape recorder which was equipped with a 0.001 sec digital timer displayed on the screen. Trials 30 - 37 were thus recorded for all animals on selected days.

Animals' runpaths were drawn from videorecordings by tracing the progress of the animal (using the nose as a reference point) with a coloured marker pen on a transparent acetate sheet clipped to the videoscreen. Since an animal's runspeed was scaled down by the relative size of the arena and videoscreen, it was possible to follow the animal with reasonable accuracy. However it should be emphasised that replays of the videorecording were <u>always</u> used to check the accuracy of the original tracing, and frequent double-tracing of particular trials served as a monitor of accuracy, though the procedure revealed a surprising degree of consistency. Clearly such a technique is not as reliable as frame-by-frame analysis (Goodale <u>et al</u>, 1978), though the latter is only practicable for small numbers of trials, whereas the videomapping technique enabled the accumulation of data from hundreds of trials for each group. The length of individual runpaths (measured over the final two-thirds of each run) was obtained by measuring directly using a standard map measuring wheel.

Ambient illumination in the test room was provided by a 200 watt floodlight directed at the (white) ceiling. This appeared to provide a uniform level of illumination across the floor of the arena. Noises were masked by a 50 db white noise source, played via an 8" loudspeaker positioned on the camera tripod stand, and directly over the centre of the arena.

6.1.3.2 Distraction

Visual distractors consisted of standard 12 volt, 1 watt stimulus bulbs mounted, one on each side of the apparatus half way between goaldoors, 35 cm above floor level and recessed in the wall such that the glass convexity was flush with the inner facing surface of the wall.

Distraction testing lasted for 4 consecutive days, during which 4 distractor trials per day were programmed to occur on predetermined trials, embedded within the 40 daily trials. Distraction occurred on the same trials for all animals on any one day, but the sequence varied from day to day. Distraction was initiated when, on a particular, preprogrammed trial, the animal's breaking the photobeam at the midpoint of the runpath not only activated the latency timer (see above) but also initiated a sequence of flashes (2/sec for 2 secs) of one of the distractor bulbs. Note that further breaks of the photobeam did not initiate additional distractor sequences, (until the next preprogrammed distractor trial). Sequence of presentation of distractor stimuli i.e. on the left and right of the apparatus, and to the left and right of the animal was counterbalanced across days within groups. Each group was arbitrarily divided into 2 halves, the 2 subgroups beginning the alternation sequence (trial 1) at opposite ends of the apparatus thus randomising all 'side' variables.

The behaviour of animals on distraction trials was examined from the videorecordings by E. Responses were recorded as either (i) showing signs of distraction, or (ii) showing no sign of distraction, though within category (i), the incidence of (a) stopping and (b) headturning were separately noted. Where doubt arose concerning a particular response, (which only happened on days 3 and 4 when some habituation was evident), independent observers were consulted.

Histological verification of lesions proceeded as previously described in Section 5.1.5.

6.1.4 Results

6.1.4.1 Histology

The lesions sustained by these animals have been discussed in detail in a previous study (Section 5.2.5). It is sufficient to note that the SC lesions were substantial, though not very extensive anteroposteriorly except in the case of rats 33a and 47a. Moderate, situation-specific activity changes were recorded in this lesion group (Section 5.2.5). The HPC lesions were virtually total, though extra-hippocampal tissue was also invaded. Nonetheless lgn was not damaged in any animal reported here. The MFC lesions were also extensive with minimal, rostral sparing in some cases. Only control animal 7a sustained substantial cortical removal.

6.1.4.2 Behaviour

Analysis of variance was carried out on the number of repetitive (error) doorpushes made by each animal on days 1-6 prior to initiation of the distraction programme. Number of error presses decreased over test days ($F(5,150) = 134.02$; $p < 0.001$), but no Group effect was evident ($F(3,30) = 1.34$; $p < 0.27$).

However the same analysis applied to median response latencies (i.e. time between breaking the photobeam and pressing the correct goaldoor) on the last 3 days of predistraction training [1], revealed significant group

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[1] Days 1-3 were not included in the statistical analysis since behaviour on these days was extremely variable.

differences ($F(3,30) = 6.0$; $p < 0.003$) due to the slower running of the hippocampals compared with all other groups ($p < 0.05$ in all cases), and the tendency to complete trials more quickly in the collicular ($p < 0.045$) and frontal ($p < 0.053$) groups. A significant Groups x Days effect was obtained ($F(6,60) = 2.21$; $p < 0.02$) since differences between groups evident on days 4 and 5 were no longer apparent on day 6. For example while application of the Scheffé test revealed hippocampals to run slower than colliculars on day 5 ($F'(3,30) = 7.42$; $p < 0.10$) no significant differences were obtained on day 6. Colliculars tended to run faster than controls on days 4 and 5 ($0.1 < p < 0.25$), though the conservatism of the Scheffé test (Scheffé, 1959) meant that this and other comparisons on days 4 and 5 narrowly missed reaching statistical significance.

Division of the SC-lesioned animals into subgroups based on size of lesion (see Section 5.2.5) failed to indicate lesion-size dependence of any effects obtained from the initial 4-group analyses.

All groups' latencies decreased over days 4-6 ($F(2,60) = 18.10$; $p < 0.001$). This trend continued throughout distraction testing. Median non-distraction latencies (representing the median latency on all trials excluding distractor trials, the trial immediately following a distractor trial and the first trial of the day) were subjected to analysis of variance, though no significant group differences were obtained. All groups continued to reduce run latencies during this period ($F(3,90) = 11.14$; $p < 0.001$).

Figure 6.2 shows the routes taken between goaldoors on

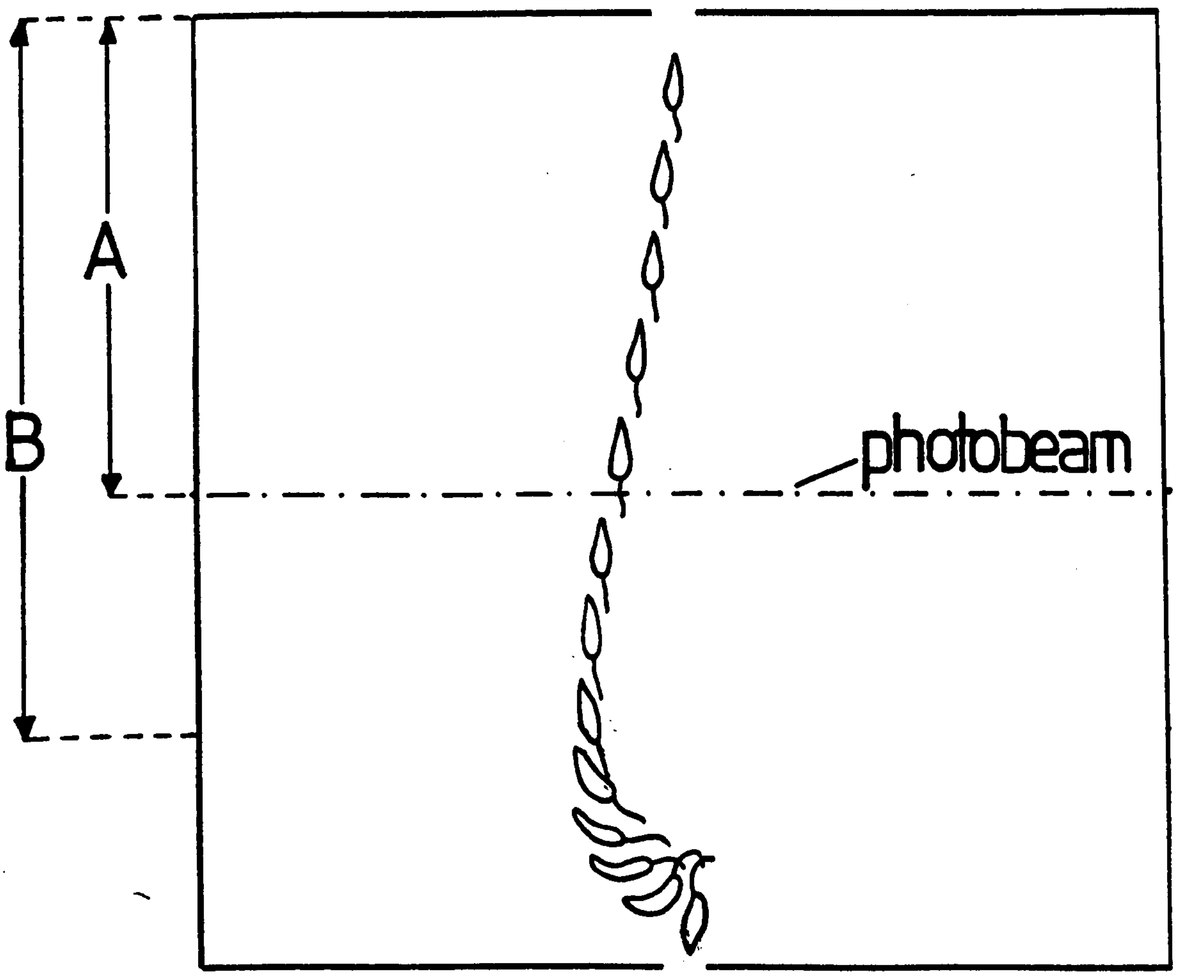

Figure 6.2
Plan view of the apparatus used in Experiments 6.1 and 6.2 showing the course of a single run between goaldoors. Response latency was measured over distance A (50 cms) and runpath length over distance B (67 cms). Note that all runpath diagrams shown in Experiments 6.1 and 6.2 represent runs from the "lower" towards the "upper" goaldoor, as depicted in this figure.

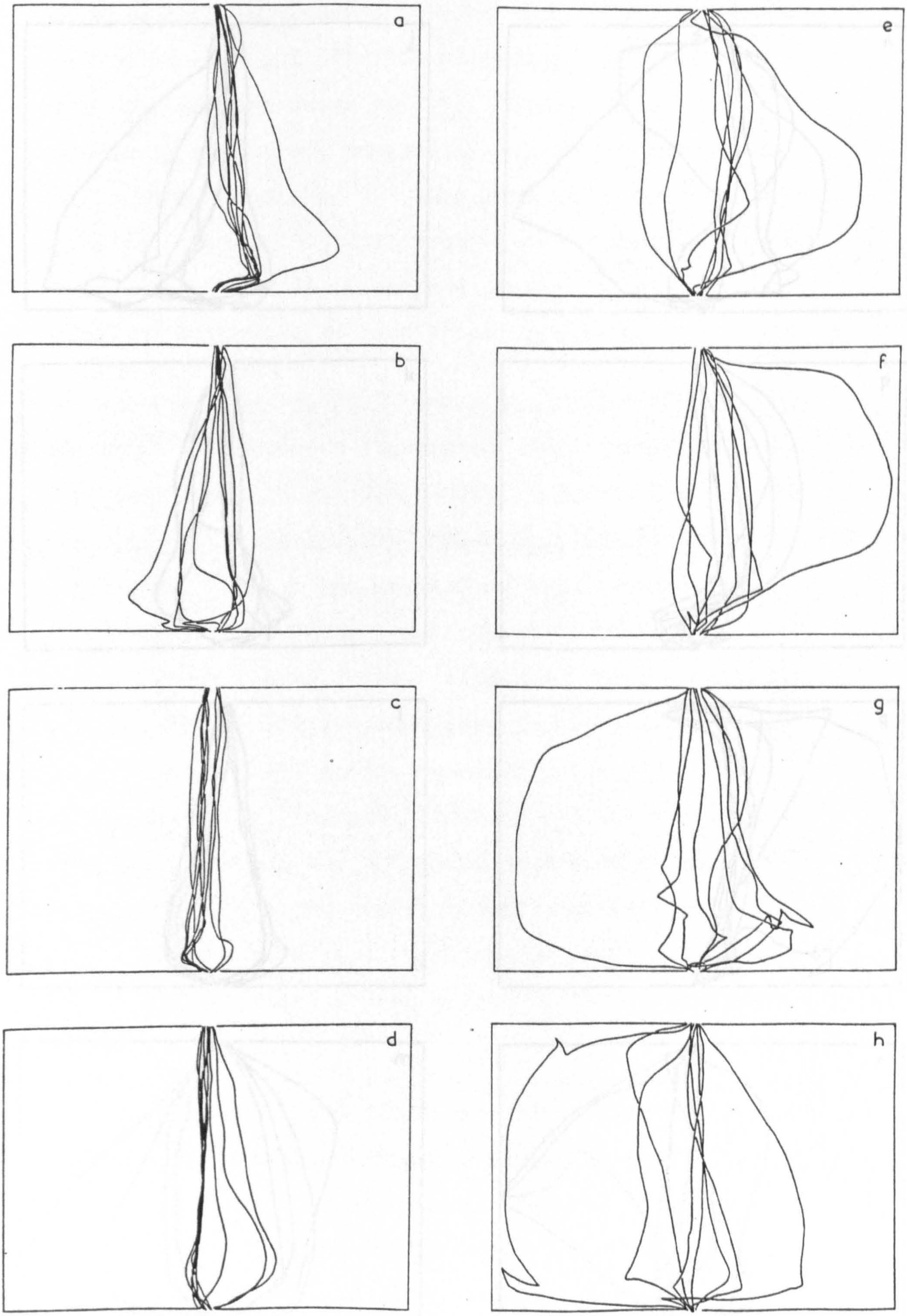

Figure 6.3a
Runpaths taken by SC rats 40a,36a,47a,60a (a-d) and Controls 7a,45a,35a,41a (e-h) on trials 30-37 inc. on test day 6.

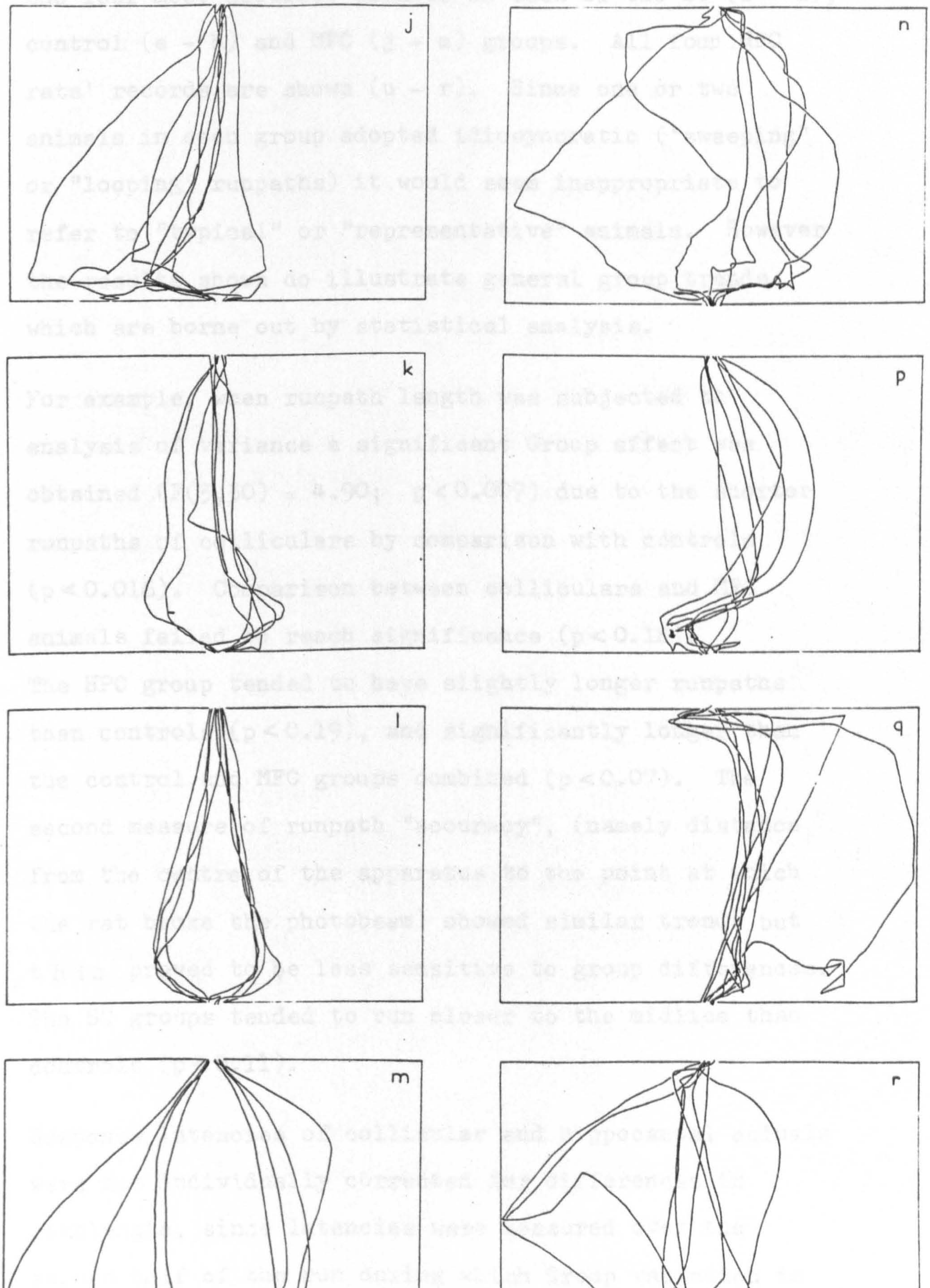

Figure 6.3b
Runpaths taken by MFC rats 17a,19a,23a,46a (j-m) and HPC rats 16a,26a,34a,43a (n-r) on trials 30-37 inc. on test day 6.

trials 30 - 37 of predistraction runway training for the four most accurate animals in each of the SC (a - d), control (e - h) and MFC (j - m) groups. All four HPC rats' records are shown (u - r). Since one or two animals in each group adopted idiosyncratic ("sweeping" or "looping" runpaths) it would seem inappropriate to refer to "typical" or "representative" animals. However the results shown do illustrate general group trends which are borne out by statistical analysis.

For example, when runpath length was subjected to analysis of variance a significant Group effect was obtained ($F(3,30) = 4.90$; $p < 0.007$) due to the shorter runpaths of colliculars by comparison with controls ($p < 0.016$). Comparison between colliculars and MFC animals failed to reach significance ($p < 0.18$). The HPC group tended to have slightly longer runpaths than controls ($p < 0.19$), and significantly longer than the control and MFC groups combined ($p < 0.07$). The second measure of runpath "accuracy", (namely distance from the centre of the apparatus to the point at which the rat broke the photobeam) showed similar trends but this proved to be less sensitive to group differences. The SC groups tended to run closer to the midline than controls ($p < 0.11$).

Response latencies of collicular and hippocampal animals were not individually corrected for differences in pathlength, since latencies were measured over the second half of the run during which Group variation in pathlength was not large in proportion to the total length of run and thus the correction factor would have been minimal.

When distractor stimuli were introduced, all control animals showed abrupt orienting responses consisting of arrest of locomotion and turning of the head in the direction of the distractor stimulus. Frequently on early presentations this was followed by the animal's running across to the distractor bulb and investigating it by rearing up and sniffing. In order to generate an index of distinction relatively independent of individual animals' idiosyncratic runspeeds, each distraction latency was expressed as a multiple of the median non-distraction latency for that day (for calculation of m.n.d.l. see above). All distraction indices so generated were entered into a 4 x 4 x 4 (Groups x Days x Distractor Presentations) Analysis of Variance.

A significant Group effect was obtained ($F(3,30) = 5.21$; $p < 0.006$) due to the SC group distracting less than controls ($p < 0.001$), MFCs ($p < 0.001$) and HPCs ($p < 0.025$), the latter groups failing to differ significantly. Distraction latencies decreased over test days ($F(3,90) = 6.23$; $p < 0.001$). No overall intrasession habituation was identified ($F(3,90) = 0.80$; $p < 0.45$). Two interaction terms reached significance, a Groups x Days effect ($F(9,90) = 7.78$; $p < 0.001$) and a Groups x Days x Distractor Presentations effect ($F(27, 270) = 1.65$; $p < 0.03$). The former was due to the tendency for group differences to disappear on day 4 when

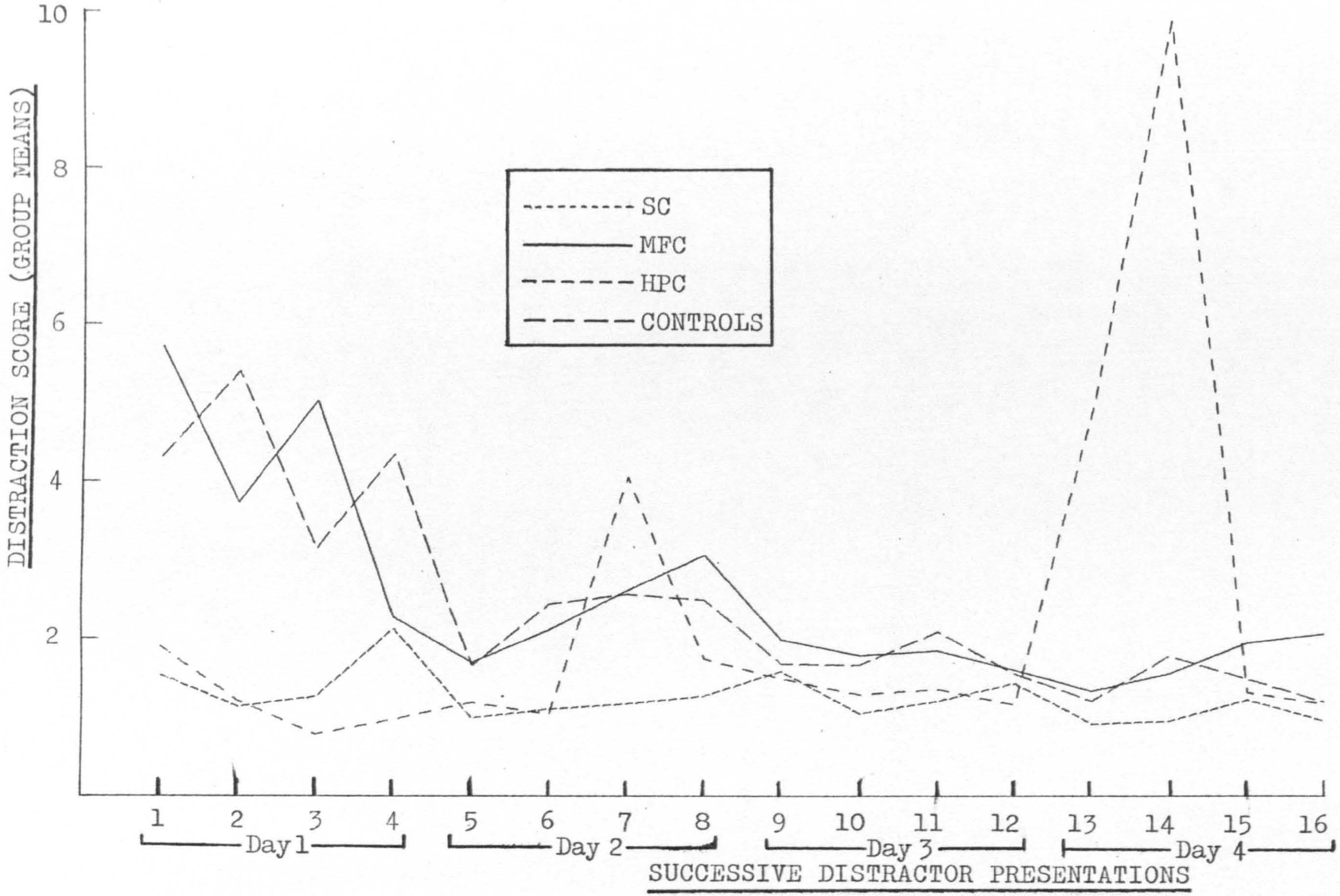

Figure 6.4
Distraction score (multiple of median non-distraction latency) on successive distractor presentations.

habituation to distractors was evident in most animals. Group differences were most evident on days 1 and 2, as expected, resulting in the significant Groups x Days interaction. The Days x Distractor Presentation interaction was almost significant ($F(9,270) = 1.82$; $p<0.065$), due to the steeper habituation gradient within days 1 and 2 than 3 and 4. The latter effect was restricted to those groups which showed distraction behaviour (ie. MFC and control groups), accounting for the significant Groups x Days x Distractor Presentation interaction.

The hippocampal group also contributed to the latter effects, since this group showed virtually no distraction to the novel stimuli on day 1 (see Figure 6.4), but were intermittently distracted on later presentations. While the control group recorded distraction latencies at least twice their m.n.d.l. on 75% of distraction trials on day 1 but only 15% on day 4, the reverse was true for hippocampals whose corresponding percentages were 6.25 and 25; this led, on occasions, to significant differences between HPC and control groups (eg. HPC<Cont: Day 1, trials 2 and 4. Scheffé test: $p<0.10$ and 0.25[1] respectively. HPC>Cont: Day 4, trials 1 and 2. $p<0.25$ and 0.10 respectively). Thus the hippocampal animals might be described as having "habituated slowly" to repeated distractor presentations, though closer examination of the data reveals this to be an oversimplification; indeed it would be more accurate to describe them as showing variable or intermittent distractability, following initial distractor presentations. The variability in this group is partly due

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[1] The Scheffé test is extremely conservative (Winer, 1971) and inappropriate for demonstrating subtle and intermittent effects; thus the most liberal criterion was adopted, using F' values for $p<0.25$ as suggestive of group differences on individual trials.

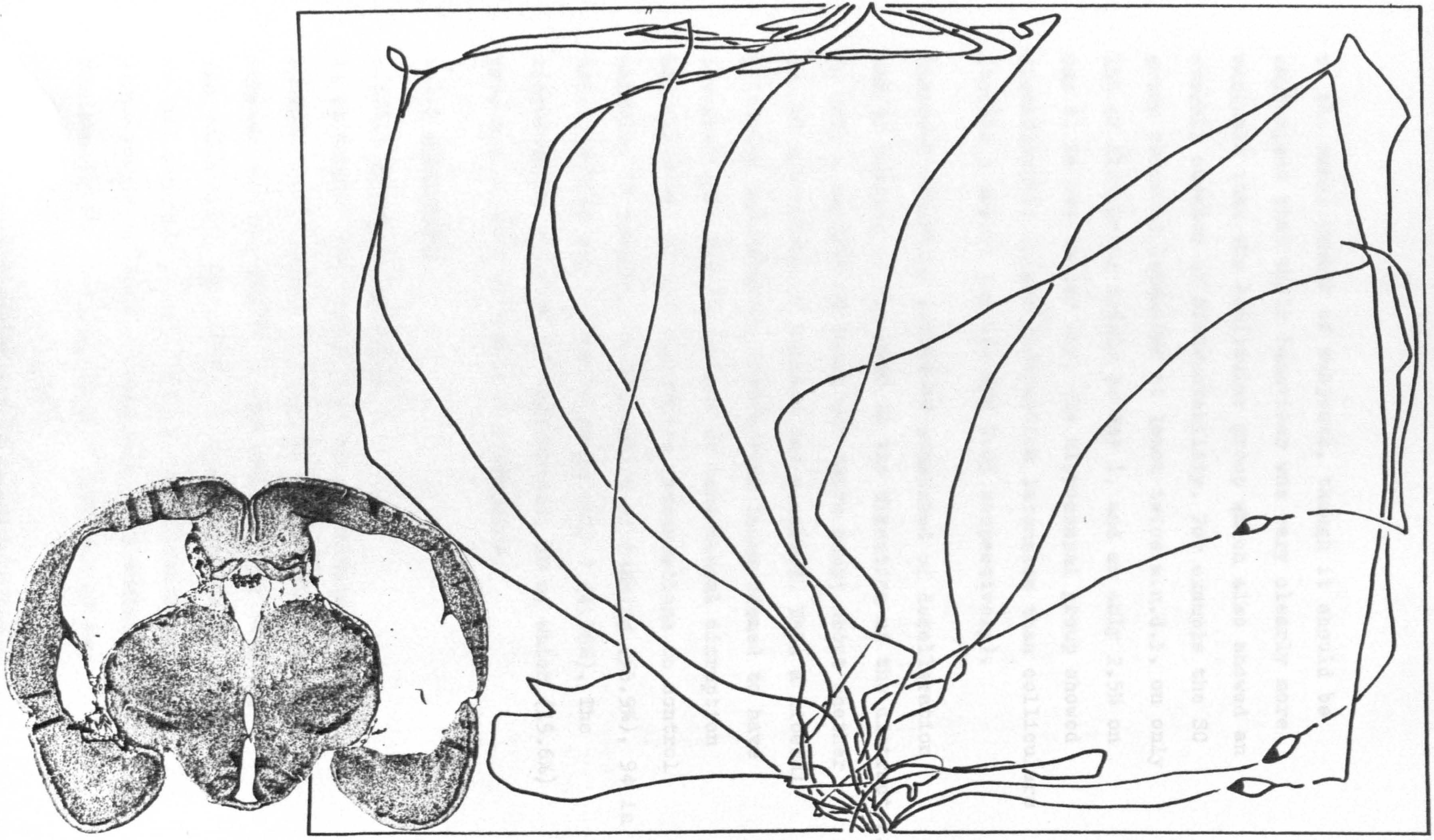

Figure 6.7. Routes taken on day 6 by rat 42a with HPC + lgn damage. Lesion shown on left.

to the small number of subjects, though it should be emphasised that their behaviour was very clearly more variable than the collicular group which also showed an overall absence of distractability. For example the SC group recorded latencies at least twice m.n.d.l. on only 15% of distractor trials on day 1, and on only 2.5% on day 4. On the latter day, the hippocampal group showed significantly longer distraction latencies than colliculars (trials 1 and 2: $p < 0.25$ and 0.05 respectively).

Observed orienting responses consisted of decelleration and/or turning of the head in the direction of the distractor. In only a handful of cases was there doubt about whether or not disruption of running had occurred. Thus a liberal criterion was adopted, distraction being deemed to have occurred when any suggestion of behavioural disruption was recorded. Of 160 distractor presentations to control animals, 91 resulted in disruption of running (56.9%), 94 in MFCs (58.75%) but in the SC group only 7 (4.38%). The hippocampals received 64 distractors, 10 of which (15.6%) produced visible evidence of disruption.

6.1.5 Discussion

6.1.5.1 Locomotor Accuracy

It is immediately clear that the prediction that SC animals would engage in misdirected and disorganised running was not upheld by the results. The SC group ran efficiently and directly between goaldoors, failed to run erratically in inappropriate directions, and surprisingly, though in agreement with Goodale and Murison (1975), Goodale et al (1978) and my own observations (1975), their runpaths were more accurate than those of controls. Their runpaths were significantly shorter, and tended to remain closer to the imaginary line joining the two goaldoors than in the case of controls. Since the target to which they were required to run was eccentrically placed in relation to the body midline when turning from a goaldoor, the evidence provides apparent support for the view that colliculectomised rats are able to localise objects in space (Goodale et al, 1978).

A possible objection to this interpretation of the results is that the present task was not exclusively visual, but might have been organised in terms of vestibular or other non-visual cues. Were this the case, the present results are still extremely interesting, since they suggest a greater "commitment" to the central task (however performed) on the part of colliculars. Clearly this style of running may represent a form of compensation for the loss of sensori-motor functions normally controlled by the SC. It is particularly significant that the colliculars failed to resort to a "pure" locomotor orienting strategy, for example by aligning the body towards the goaldoor while in the course of running, but instead tended to turn through a full 180° before setting off on each run (Figure 6.3a). Ironically, this would appear to involve the use of "static localisation", which, according to Marks and Jane (1974) should be impaired or absent after collicular ablation. Their hypothesis might be salvaged, however, if it were argued that the present task is performed using kinaesthetic or vestibular coding, independently of visual localisation. In order to examine this possibility, an analysis of variance was carried out on runway "accuracy" measures (see above) for the 10 controls and 4 HPCs described above plus the 6 HPCs which had virtually identical lesions to the previous 4 HPCs but with substantial additional bilateral damage to lgn. Clearly if the present task is performed visually by the rat, the latter group should be seriously impaired. Analysis revealed that the 'HPC + lgn' animals did indeed run less "accurately" than HPC or control groups both in terms of pathlength (Groups: $F(2,17) = 10.29$; $p < 0.002$. HPC + lgn : HPC; $p < 0.001$. HPC + lgn : controls; $p < 0.001$) and distance from the centre of the apparatus to the point at which the rat intercepted the photobeam (Groups: $F = 5.33$; $p < 0.016$. HPC + lgn : HPC; $p < 0.01$. HPC + lgn : controls; $p < 0.05$). Inspection of the HPC + lgn group data (Figure 6.7) revealed that these animals were extremely disturbed, their position in the runway bearing almost no relation to the position of the goaldoor. They tended to run to an arbitrary point on the opposite wall and then meander to left or right until they found the lighted goaldoor. In some instances they were unsuccessful and made circling tours of the apparatus before responding. From these observations it would seem reasonable to infer that the task is to some extent dependent upon visual funtion.

However it might still be argued that while non-collicular groups were using vision, the SC group alone were not. This is also unattractive as an explanation since if the SC group had resorted to a kinaesthetic, vestibular or other non-visual strategy their rate of learning the alternation sequence would certainly have been retarded, yet this group ran more accurately than any other in early training. Furthermore their responses would have been more randomly directed, since purely kinaesthetic or vestibular coding would have resulted in a precise half-circle turn on each trial. However it is difficult to see how such a strategy could have generated the extremely accurate style of running seen in colliculars since it would be crucially dependent on the animals' initial orientation while feeding at the goaldoor, whereas in fact all animals adopted various, and varying orientations while feeding. Thus the only likely hypothesis is that SC rats in this apparatus, as in previous studies (Goodale and Murison, 1975; Goodale _et al_, 1978) are capable of accurate stimulus localisation and run accurately between locations. This may be a result of their lack of attention towards extraneous irrelevant peripheral cues which might be responsible for the spontaneous variability in the runpaths of control animals. Of course this does not rule out the possibility that a non-visual orienting strategy is used by the animal to determine the approximate location of the goaldoor. This would be followed by precise visuomotor guidance of the kind seen in collicular animals in previous studies by Goodale and Murison (1975) and Goodale _et al_ (1978).

This is an attractive proposition since only for a relatively simple task like the present "shuttle" situation would such a strategy be adequate to ensure a high level of response accuracy, though in a more complex situation in which the position of the target stimulus is variable, such a strategy would not be applicable. Unfortunately it was not possible to further investigate this model by moving the relative positions of goaldoors (since they were fixed in the present apparatus), though it is clear that in other experiments where variable stimulus positions were employed, colliculars did experience particular difficulty, for example in a circular jumping stand (Barnes _et al_, 1970; Weinberg and Stein, 1978), especially immediately postoperatively (Murison, 1977). In this situation, colliculars do appear to engage eventually in a locomotor orienting strategy, running round the centre platform haphazardly (Murison, 1979; personal communication), obtaining very high latency scores prior to making a jump response (Weinberg and Stein, 1978). In this situation the collicular may initially attempt to cope with the difficulty of orienting to very peripheral stimuli by firstly adopting a non visual strategy but then eventually progressing to a locomotor orienting strategy with further training. Indeed when tested for locomotor orienting ability after initial postoperative training requiring a jump response, the collicular is relatively unimpaired (Barnes et al, 1970).

It is important to note that a priori reasons exist for believing that all 3 experimental groups in the present study would experience orientational difficulties. The SC has been implicated in locomotor (Schneider, 1968, 1970) or static (Marks and Jane, 1975; Goodale et al, 1978) localising functions, control of locomotor approach to stimuli (Barnes et al, 1970; Winterkorn, 1975) and perception in peripheral visual space (Trevarthen, 1968; Ingle, 1970), the HPC has been implicated in absolute spatial mapping (O'Keefe and Nadel, 1978) and frontal cortex has been implicated in telencephalic circuitry (Rosvold, 1972) having egocentric spatial functions (Potegal, 1969; see also Butters et al, 1972).

However as far as MFC animals are concerned, no deficit in performance was detected in the present task; speed of running was slightly elevated and though the trend was clear it failed to reach statistical significance.

Among the 4 HPC rats, one animal (43a) ran quickly while the remaining 3 ran slowly and inaccurately. By day 6 all animals had developed characteristic running styles which might be thought to involve some stereotypy (Figure 6.3).

6.1.5.2 Distraction

The introduction of distractors left the SC group almost entirely unaffected, as predicted from many previous studies using rats (Goodale and Lister, 1974; Goodale and Murison, 1975; Collin, 1977; Goodale et al, 1978), and primates (Milner et al, 1978; Albano and Wurtz, 1978). The present study extends the findings of Goodale and associates to a situation in which "central attentional load" (i.e. attentional requirements of the central runway task) was very low. Thus the argument could not be advanced that the collicular rat is inattentive to novelty as a result of being "hyperattentive" to central discrimination tasks, or having a low attentional capacity. In addition the present result emphasises the robustness of collicular neglect since the animals in the present study had more restricted collicular damage than those used by Goodale (see also Kesner and Vredenburg, 1970).

Rats with MFC lesions were indistinguishable from controls, showing normal attentiveness, though no evidence was obtained for increased attentiveness (which might have been predicted from the results of Experiments 5.2 and 5.3), reduced duration of orienting responses (predictable from the findings of Milner et al (1978) using monkeys) or neglect. Sensory neglect was reported by Collin (1977) for rats with unilateral frontal lesions, though both Collin (1977) and Crowne (1977) have pointed out that in primates bilateral frontal lesions produce less pronounced effects than unilateral lesions. The following experiment will examine this hypothesis formally. Alternatively the effect might be due to sparing of frontal tissue, though this is unlikely since the lesions used in this study were as extensive in each hemisphere as the unilateral ablations used by Collin (1977).

Hippocampectomised rats, though running less accurately than SCs were clearly more attentive, though intermittently so. The result does not provide convincing support for a functional relationship between SC and HPC in terms of the directing or redirecting of attention since the nature of the deficit was very different in each case. Specifically, SC rats showed virtually no long latencies on distraction trials, though where such did occur, they did so during early distractor presentations (when control animals were showing maximal distraction). In contrast, the HPC animals tended to show initial neglect on early distractor presentations but a stronger tendency than other groups to register long latencies on later distractor presentations. They appeared to distract towards novel stimuli but randomly and variably throughout testing giving the impression of simultaneous neglect and reduced habituation to successive stimulus presentations. Such lack of distraction on initial stimulus presentations was also observed in HPCs by Crowne and Riddell (1969) in a similar situation. This is clearly consistent with the suggestion of Gustafson and Koenig (1979) that hippocampals show deficient orientation to totally novel stimuli and decreased habituation to familiar stimuli. Such a formulation fits the present results better than the description by Raphaelson et al (1965) of hippocampal rats as exhibiting total absence of distractability; in addition, as discussed in Chapter 4, it provides an explanation for the anomaly that the HPC animal is both less (initially) and more (later) attentive to peripheral stimuli. The hippocampal would appear to distribute attention between peripheral and central stimuli differently from controls, probably explaining why in operant situations, less attention is paid to novel pre-exposure stimuli (Ackil et al, 1969), though more attention is paid by hippocampals to peripherally-located cues in a barpress alternation situation giving rise to enhanced learning (Stevens and Cowey, 1972).

These results might suggest some form of relationship between the SC and HPC, since the hippocampals' erratic orientation was directed towards stimuli which are neglected following collicular ablation. Thus the relationship between collicular and hippocampal slow wave activity (Routtenberg and Taub, 1973) may reflect the transfer of information regarding the presence or absence and visuospatial locus of novel peripheral stimuli which are subjected to some form of further analysis by the hippocampal formation (independent of visuospatial locus), perhaps relating to stimulus significance (Vinogradova, 1973). However electrophysiological evidence is probably required to substantiate this tentative hypothesis.

The present results do clearly add support to the view of Köhler (1976) that hippocampal "perseveration" is not equally applicable to all behaviours, since no hippocampal rat in this study made perseverative goaldoor presses once the cue light had been extinguished. The latter would have been predicted from more global theories of the hippocampus as a generally inhibitory structure following lesions of which an animal is unable to "inhibit" all prepotent responses (Douglas, 1967). The results also demonstrate very clearly that the effects of collicular ablation are not due to inadvertent damage to overlying hippocampus, since while the present collicular lesions were rather small, the hippocampal lesions very large, a greater, more profound deficit of qualitatively different character appeared after ablation of colliculus than of hippocampus, further emphasising (see Experiment 5.5) functional dissociation between them.

A Note on Runway Accuracy

Animals' runpaths were above discussed in terms of "accuracy" of response, though clearly "accuracy" is an inferred dimension. In a multichoice discrimination situation "accuracy" of run may be calculated by considering the correlation between position of the animal in the runway at any one time relative to the position of the correct goaldoor (see Goodale et al, 1978); clearly such a measure implies that a "good" response is the straightest response, yet in neither situation is an animal constrained to follow a particular route or routes in order to obtain reward. However evidence will be provided in Experiment6.2(below) which shows that with successive training normal rats' runpaths both become shorter and more closely approximate the imaginary line drawn between goaldoors. It would appear that straight, "economical" running is an optimal strategy which enables rewards to be most quickly and densely obtained with the minimum expenditure of locomotor effort. Therefore it is not wholly inappropriate to refer to an animal running close to the midline as having "accurate" locomotion, and further, greater variability in runpaths does probably reflect the diminution of some aspect(s) of locomotor control.

6.1.6 Conclusion

The results have shown that the bilaterally colliculectomised rat is capable of accurate spatial localisation of a goaldoor even when required to make a 180° turn towards it. Admittedly the execution of this response may involve the adoption of a simple compensatory strategy (perhaps based on vestibular or kinaesthetic cues), eliminating the need for strict visuospatial localisation but which would be inappropriate in more complex test situations. As in many previous studies, the collicular animals ran more quickly than controls and neglected novel peripheral visual stimuli presented during locomotion. Animals with bilateral medial frontal cortical ablations showed slightly elevated runspeeds compared with controls yet normal orienting behaviour. Bilaterally hippocampectomised rats showed rather poor goaldoor localisation and intermittent, slow-habituating orientation to novel distractors. The possibility of minimal functional overlap between the SC, HPC and MFC was discussed; in particular it is possible that functions of the SC and HPC, perhaps relating to the detection and evaluation of peripheral stimuli may be mutually dependent.

6.2 The Effects of Partial HPC and Unilateral SC and MFC lesions on Preoperatively-learned Locomotor Guidance and Attention to Novelty in a Runway.

6.2.1 Introduction

The foregoing experiment showed that after a long postoperative interval, rats with bilateral SC ablations ran faster and paid less attention to novel stimuli than controls. Those with MFC lesions showed a nonsignificant increase in runspeed but normal attention. Hippocampals exhibited poor locomotor guidance and a tendency to neglect novel stimuli. Thus a measure of functional overlap between the SC, MFC and HPC might be suggested.

However these findings pose a number of questions. In view of the recovery of attentional abilities in primates with SC and frontal lesions during the first few postoperative weeks (Latto, 1977), MFC lesions of the kind which failed to give rise to inattentiveness in the previous study might produce orienting deficits immediately postoperatively. Previous reports of neglect in rats with unilateral frontal lesions notably involved attentional testing soon after operation, the animals having been trained on the ongoing operant task preoperatively (Collin, 1977). On the other hand, neglect might in general be more efficiently demonstrated in unilaterally- than bilaterally-lesioned animals (Crowne, 1977; Collin, 1977). This particularly applies to frontal lesion effects. Indeed if MFC deficits are like FEF deficits in monkeys (Collin, 1977), unilateral attentional impairments may ensue following unilateral ablations even though, as the previous study demonstrated, bilateral deficits do not result from bilateral lesions.

Cowey and Bozek (1974) and Collin (1977) found that after unilateral MFC lesions, rats tended to choose the arm of a Y-maze which was ipsilateral to their lesion, and Collin (1977) reported spontaneous circling towards the lesion side. However the latter was not "forced" rotation but was argued to represent a "preference" for the ipsi- over the contralateral direction of turning. Since both ipsilateral maze arm choice and circling occurred in the dark, the behaviours are likely to result from a motor imbalance following frontal lesions. Since unilateral collicular ablations also produce ipsiversive rotation (Kirvel, Greenfield and Meyer, 1974) which persists in the absence of visual input (Cooper _et al_, 1970), a functional link between frontal cortex and colliculus might be inferred (see Chapter 4).

The present apparatus provides an appropriate situation in which to investigate postoperative turning tendencies since running behaviour can be stabilised preoperatively and should consist of relatively direct, straight running thus providing a reliable baseline against which to measure degree of postoperative asymmetry. Characteristically the asymmetry might be indicated by the tendency to turn consistently to left, or right, from a goaldoor, and also the tendency to progress ipsiversively when running between goaldoors.

Gustafson and Koenig (1979) have demonstrated abnormal attention to novelty in rats with anterodorsal HPC lesions. Indeed such lesions have an extensive influence on acetylcholinesterase activity in remaining hippocampal tissue (Olton and Werz, 1978). Thus it might be hypothesised that partial hippocampal lesions would produce all the effects of the very large lesions obtained in the previous study. In view of the suggestion that dorsal and ventral HPC may be to some extent functionally distinct (Nadel, 1968; Jarrard, 1968; Stevens and Cowey, 1973), it was decided to include groups with either dorsal or ventral HPC lesions. However, other authors have shown substantial functional recovery following such partial lesions during the immediate postoperative period (see Kimble, 1976) and thus it was deemed necessary to test these groups soon after operation.

Thus in the present study runway behaviour was preoperatively stabilised. Following bilateral lesions of dorsal or ventral hippocampus, or unilateral or bilateral lesions of SC or MFC, animals were returned to the runway and tested for locomotor guidance and distractability as in the previous experiment.

6.2.2 Subjects

Subjects were 34 experimentally naive male hooded rats. Details of their housing and treatment are as described in Section 5.1.2. They were approximately 150 days old at commencement of testing.

6.2.3 Apparatus and Method

6.2.3.1 Preoperative training

The apparatus and general training and testing procedure has been described previously (Section 6.1.3). Training was conducted for 9 days preoperatively by which time the animals appeared to have reached asymptotic running speeds. Trials 30 - 37 inclusive were videorecorded on days 5 and 9 for all animals in order to investigate the development of locomotor organisation. They were placed on <u>ad libitum</u> feed for 24 hours following testing on preoperative day 9, and all received surgery the following day, at least 16 hours since the last animal had completed testing.

6.2.3.2 Surgery

Six animals received bilateral lesions of MFC by aspiration, 3 received bilateral radiofrequency lesions of SC as described above (Section 5.1.3). Six animals received HPC lesions which were made using single placements on each side of the brain at the following coordinates:

	A - P	LAT	DEP
Dorsal (n = 3)	-2.8 mm	2.0 mm	3.0 mm
Ventral (n = 3)	-3.6 mm	5.5 mm	6.8 mm

A tip temperature of 57.5°C was maintained for 60 seconds.

Unilateral radiofrequency lesions of SC (n = 8; 4R, 4L) and unilateral aspiration lesions of MFC (n = 4; 2R, 2L) were made as described earlier (Section 5.1.3). Seven animals received small cortical control lesions. These were small bilateral lesions removing strips of cortex (1.5 mm x 1 mm) roughly overlying the posterodorsal hippocampus. Two rats received such lesions unilaterally (1R, 1L). For examples of such lesions see Figure 5.11c.[1]

Following surgery, the animals were given a 7 day recovery period on *ad libitum* feeding, followed by progressive deprivation over 3 days to a one hour in 24 regimen. On day 11, the animals resumed testing in the runway. For two days, runpaths, response latencies and repetitive goaldoor presses were recorded. Distracting stimuli were then presented as in Experiment 6.1 for two days. All other procedures were followed as in that experiment.

6.2.4 Results

6.2.4.1 Histology

As shown in Figure 6.7a unilateral SC lesions were well-localised and failed to invade the contralateral colliculus. In No's 13b, 18b, and 21b fairly extensive damage occurred throughout the anteroposterior extent of the structure, both superficial and deep laminae being substantially removed. In the remainder, damage was largely restricted to superficial laminae. The 3 bilateral SC animals (2b, 4b, 22b) had small lesions

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[1] The examples in Figure 5.11c (upper) are bilateral.

which did not extend greatly into deep laminae. Dorsal tegmentum was invaded in animals 13b and 18b; otherwise extracollicular thalamic structures were entirely spared.

Bilateral frontal lesions were similar to those used in Experiment 6.1. Most of the dorsomedial cortex identified as nMD projection cortex by Leonard (1969) was removed, though some supragenual cortex was left intact. The same applies to unilateral lesions, except that ventromedial sparing was noted in animals 30b and 31b. The unilateral lesions were well-localised and did not invade the contralateral hemisphere except very slightly in animal 29b (on the most caudal section). Rostral septum was damaged in 25b, 26b, 27b and 29b. Inevitably some damage was inflicted upon the corpus callosum and rostral cingulum bundle; the caudate nucleus was slightly invaded at its most rostral pole in most animals.

The hippocampal lesions were slightly more posteriorly located than had been intended, though in all dorsally-lesioned animals (1b, 8b, 15b), a substantial volume of anterodorsal tissue was ablated. The lesions are clearly as large as those used by Roberts <u>et al</u> (1962), Köhler (1976) and Gustafson and Koenig (1979). The ventrally placed lesions were disappointingly small particularly in the case of 19b, and entorhinal cortex was invaded in all cases. However no damage was inflicted upon the lgn or optic tract.

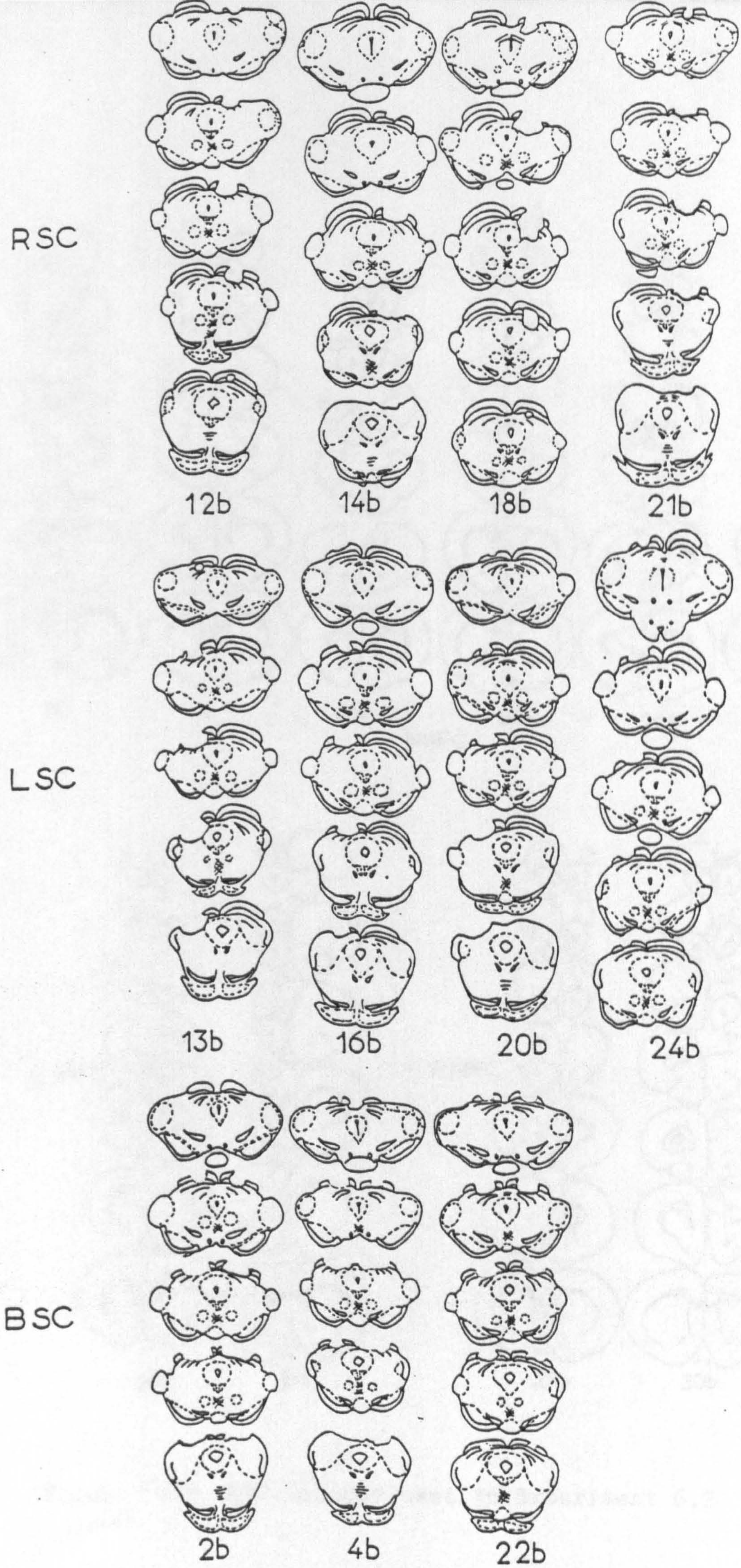

Figure 6.7a SC lesions used in Experiment 6.2

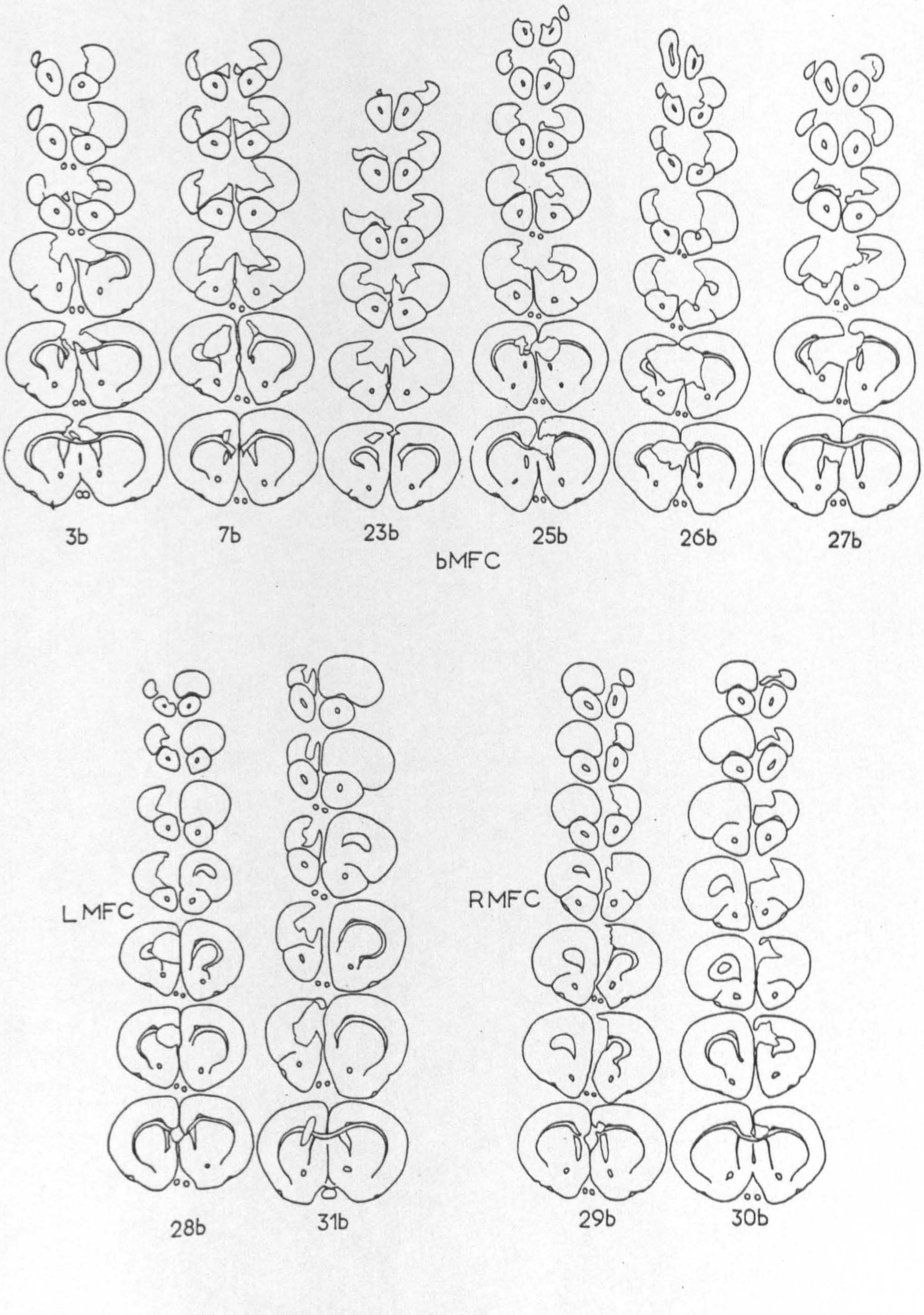

Figure 6.7b MFC lesions used in Experiment 6.2

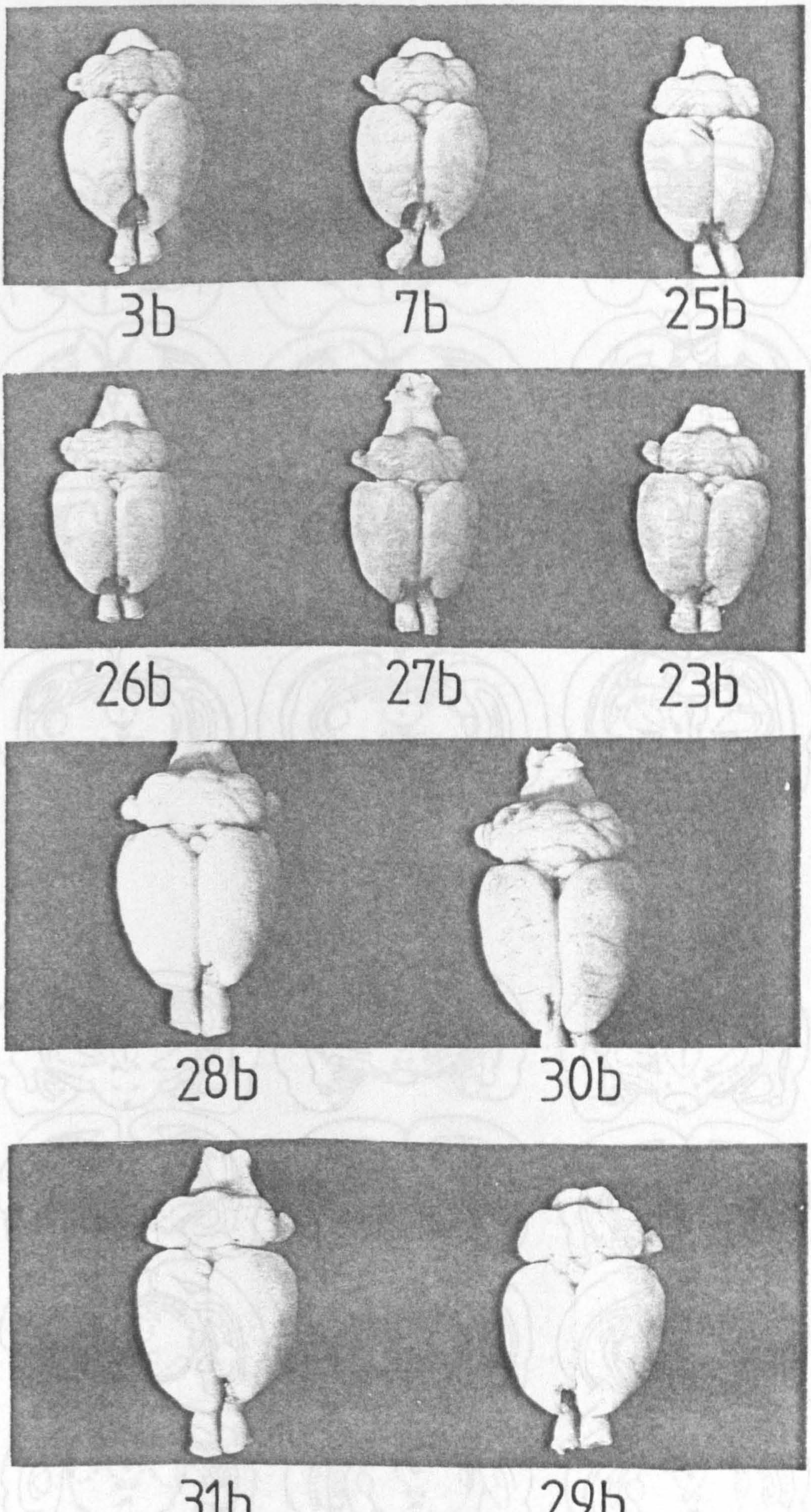

Figure 6.7d. Bilateral (above) and unilateral MFC lesions used in Experiment 6.2.

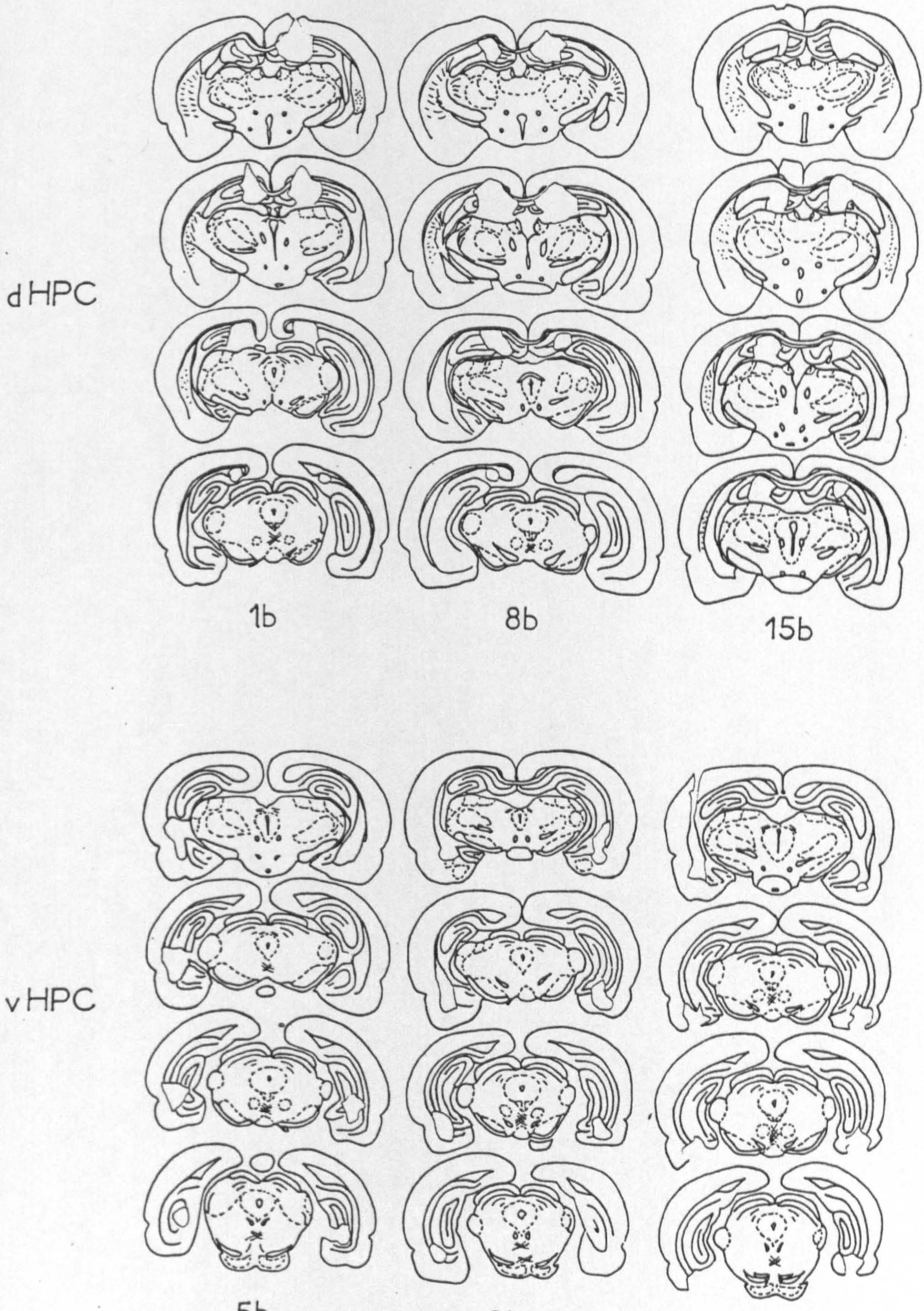

Figure 6.7c HPC lesions used in Experiment 6.2

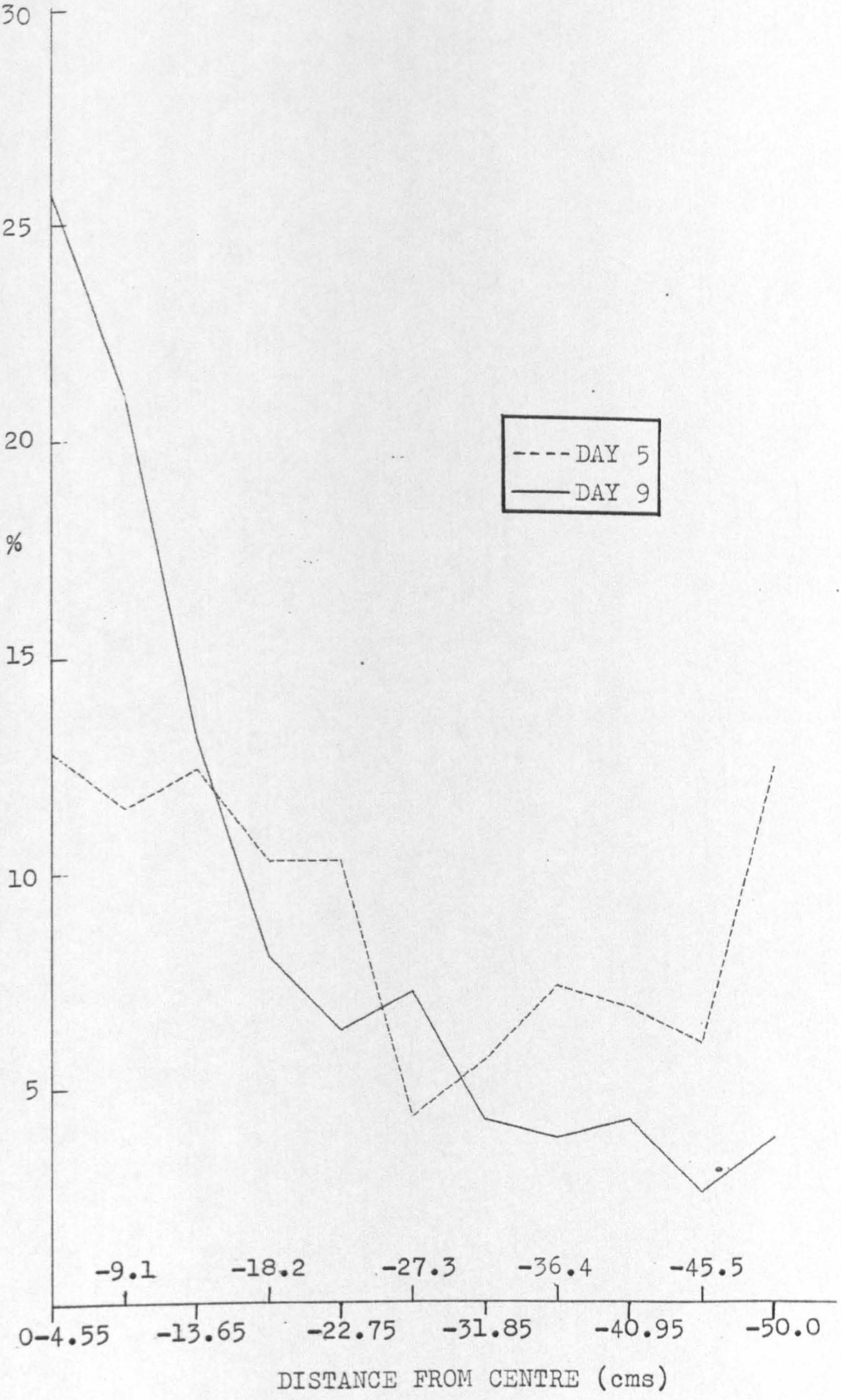

Figure 6.8
Percentages of runpaths intersecting the photobeam at various distances from the centre of the apparatus on trials 30-37 inc. for all animals on preoperative training days 5 and 9. (Note: -18.2 above = percent. of runs crossing between 13.65 and 18.2 cms from the apparatus centre).

6.2.4.2 Behaviour

Preoperative Development of Locomotor Guidance

In the foregoing study control rats' runpaths appeared to become more "accurate" on successive test days both in terms of length and distance from the centre of the apparatus. Clearly the most economical runpath would follow the imaginary line drawn between goaldoors, though this would require the animal to make an awkward turn through a full 180^{o} prior to running. Unlike a multiple-choice discrimination task the present situation does not encourage an animal to follow any particular route in relation to the "target" goaldoor.

Nonetheless it is clear from Figure 6.8 that between days 5 and 9 preoperatively, an overall trend towards more economical runpaths was observed. Since the effect (in terms of both decreased mean runpath length and shorter distance from the centre of the apparatus) occurred in all animals it was highly statistically reliable.

Postoperative Locomotor Guidance

Figures 6.9a to 6.9z show the pre (dotted lines) and postoperative (solid lines) runpaths followed by representative animals from each group. The effect of left SC ablation is shown in Figure 6.9 a,e (representing animals 16b and 24b respectively), and of right SC ablation in Figure 6.9 b, f (12b and 14b). It is clear that turning away from a goaldoor almost invariably occurred towards the side of the lesion, even in animals

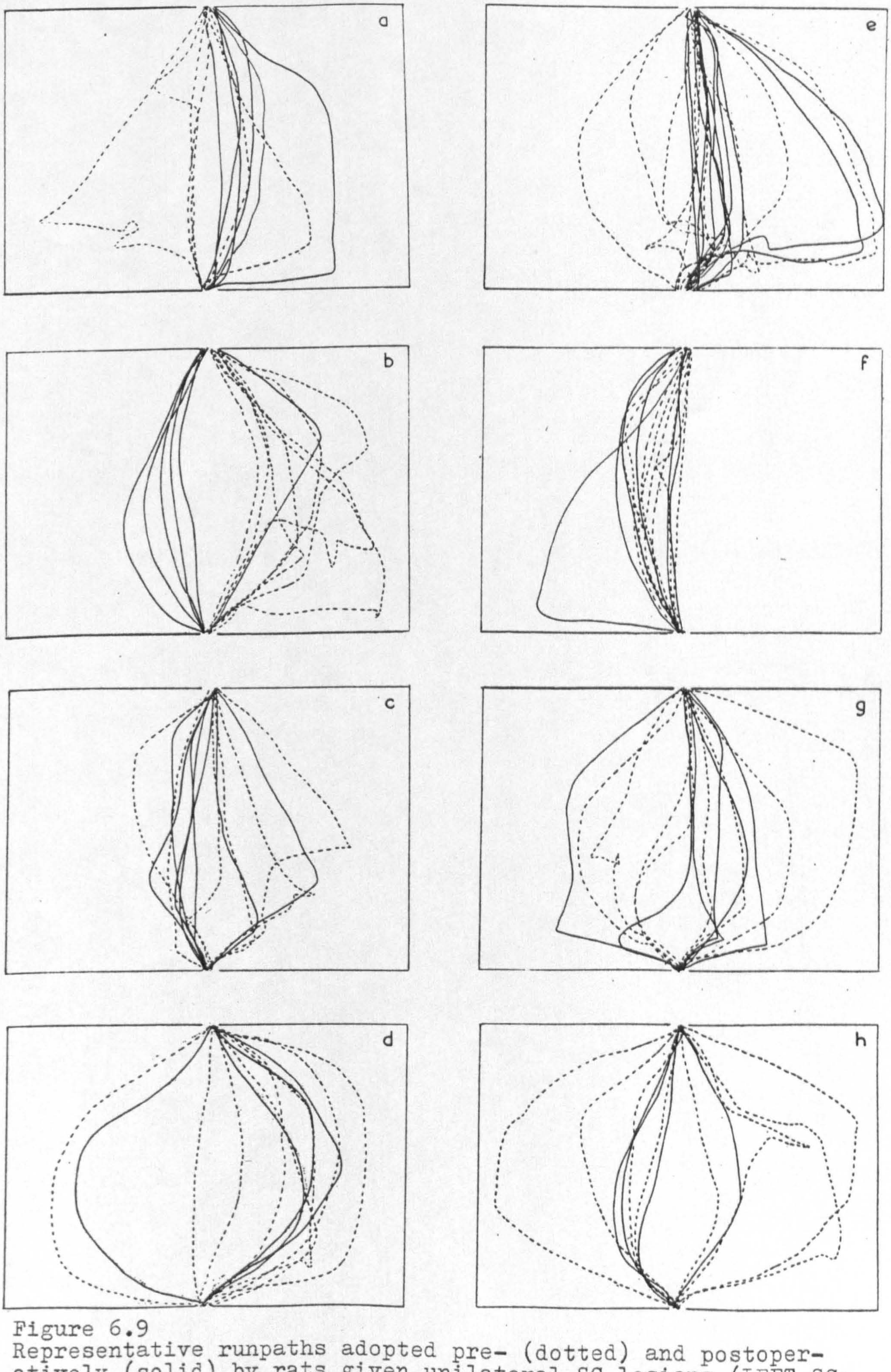

Figure 6.9
Representative runpaths adopted pre- (dotted) and postoperatively (solid) by rats given unilateral SC lesions (LEFT SC: a: 16b, e:24b; RIGHT SC: b: 12b, f: 14b), control animals (c: 6b, g: 9b) and bilateral MFCs (d: 3b, h: 7b).

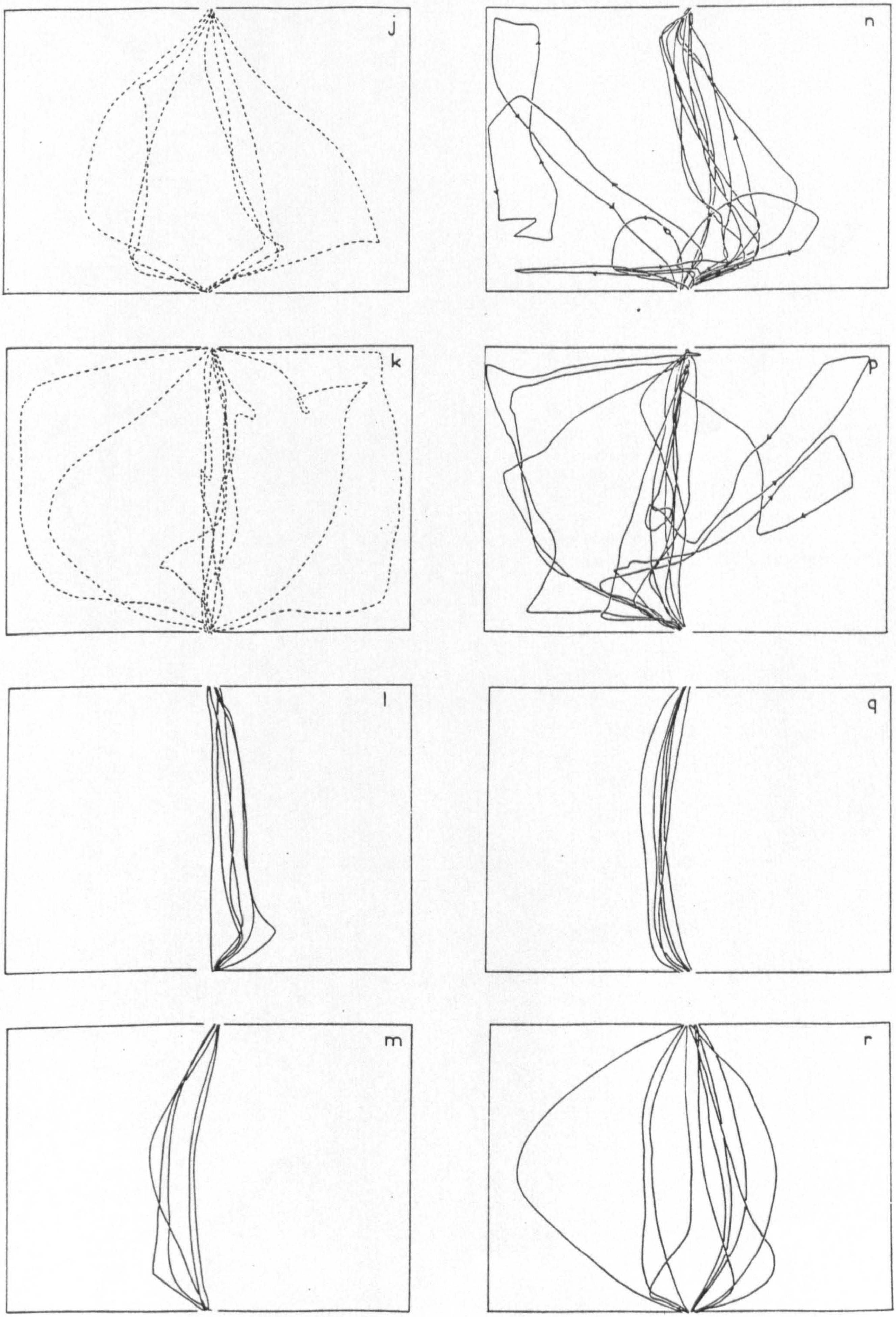

Figure 6.9
Representative runpaths adopted pre- (dotted) and postoperatively (solid)by rats given unilateral SC lesions (LEFT SC: j,n; 13b. RIGHT SC:k,p; 21b). l,m,q,r = postop. day 4 runpaths for unilateral SC rats 13b,21b,14b and 24b respectively.

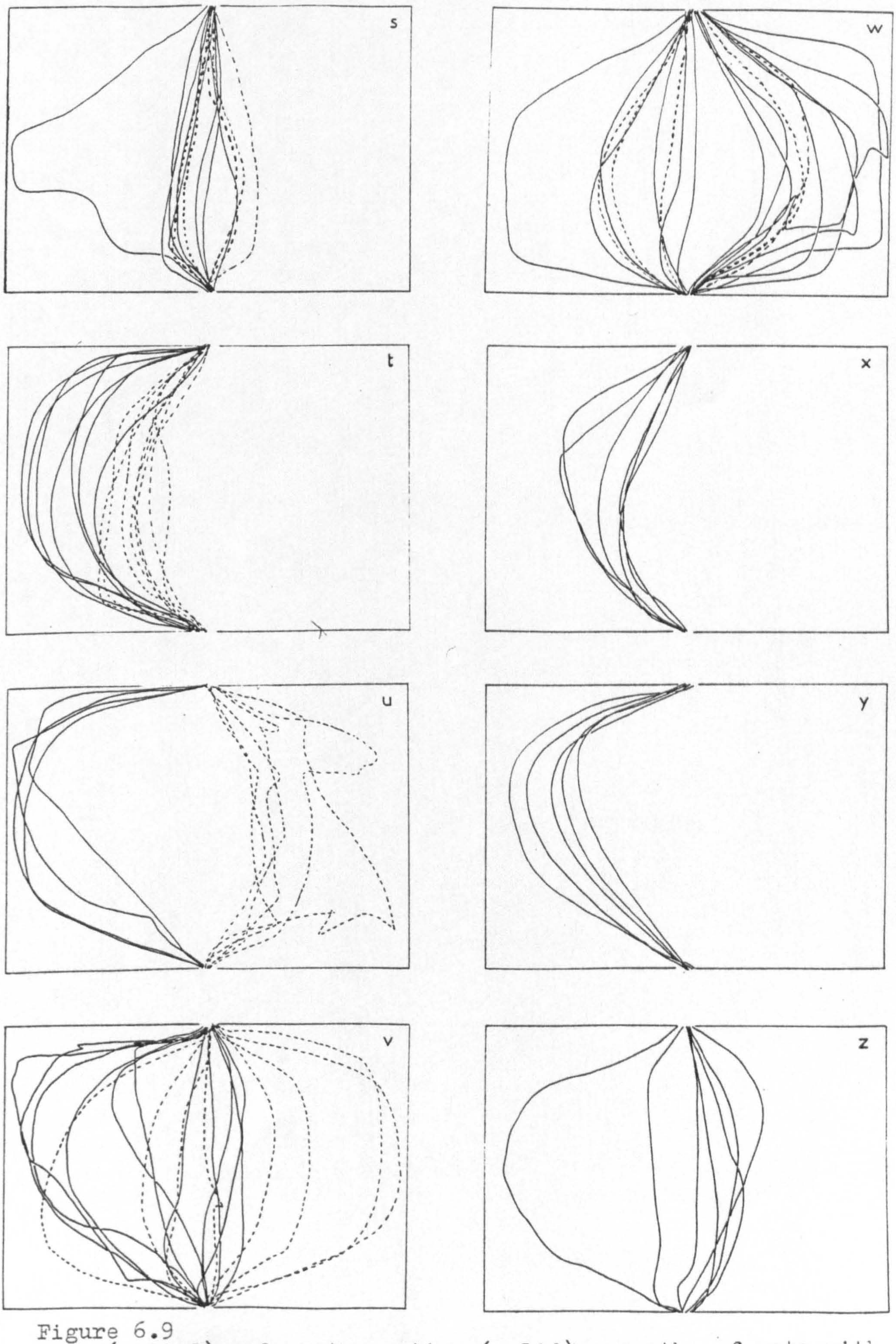

Figure 6.9
Pre- (dotted) and postoperative (solid) runpaths of rats with right MFC lesions (s: 29b; w: 30b) and bilateral SC lesions (t: 2b; u: 4b; v: 22b). x,y,z = postop. day 4 runpaths, and solid lines in t,u,v postop. day 1 runpaths.

which had exhibited a preoperative tendency to turn towards the opposite side (e.g. Figure 6.9 a,b). While 48.25% of turns were made preoperatively to the side which was later lesioned, on postoperative test day 1 (day 11 postop.), 86.6% of turns were made to this side, falling to 71.2% by the final day of distraction testing (day 14 postop.). Of the 8 unilateral SC rats 4 always turned ipsiversively (12b, 20b, 21b, 24b), 2 did so on 83.5% of trials (14b, 16b), 1 on 75% (13b) and only 1 (18b) on as few as 50% of trials.

The latter animal is especially interesting since it exhibited a very strong left-turning tendency prior to receiving a right hemisphere lesion. In particular, the animal tended to take up a stance, while feeding, at an angle to the goaldoor such that a leftward movement was facilitated. Postoperatively, strings of such left-turns were interspersed with right-turn responses (which would occur even when the animal had taken up an angled stance at the goaldoor). However by postoperative test day 4 the animal had reverted to its original leftward running which was the cause of the fall in percentage of ipsiversive turning seen in colliculars (Figure 6.10) on this day. The mean change in percentage of runs made to the side ipsiversive to the lesion (postoperative test day 1 minus preoperative) was found to be 42.7% in the collicular group.

In other respects, however, visually-guided locomotion was under good control. Only animals 13b (left SC) and 21b (right SC) were badly disrupted immediately postoperatively. Figures 6.9 j, n and k, p show the pre- (dotted lines) and postoperative (solid lines) runpaths of 13b and 21b respectively on trials 30 - 37 of postoperative test day 1. It is clear that on certain trials (notably interspersed with fairly normal runs) these animals did swerve to the lesion side and run in ipsiversive loops about the apparatus in an uncontrolled fashion. It is interesting that while all collicular lesions produced strong ipsiversive turning from goaldoors, only these two lesions which were also the deepest in the group (with the exception of 18b which was an anomalous case - see above) gave rise to such disturbed, asymmetrical running. In these animals, moreover, running had stabilised by postoperative test day 2 on which an occasional tendency was noted for most collicular animals to approach goaldoors slightly to one side (i.e. the side ipsilateral to the lesion) though on the whole visuo-spatial guidance was under good control with no "forced" circling evident. Figures 6.9 l-r demonstrate the recovery of locomotor performance on postoperative test day 4 representing animals 13b, 21b, 14b and 24b respectively.

Like the collicular animals, rats with MFC lesions showed a clear motor asymmetry throughout postoperative testing in terms of direction of turning from goal-doors. This persisted throughout postoperative testing

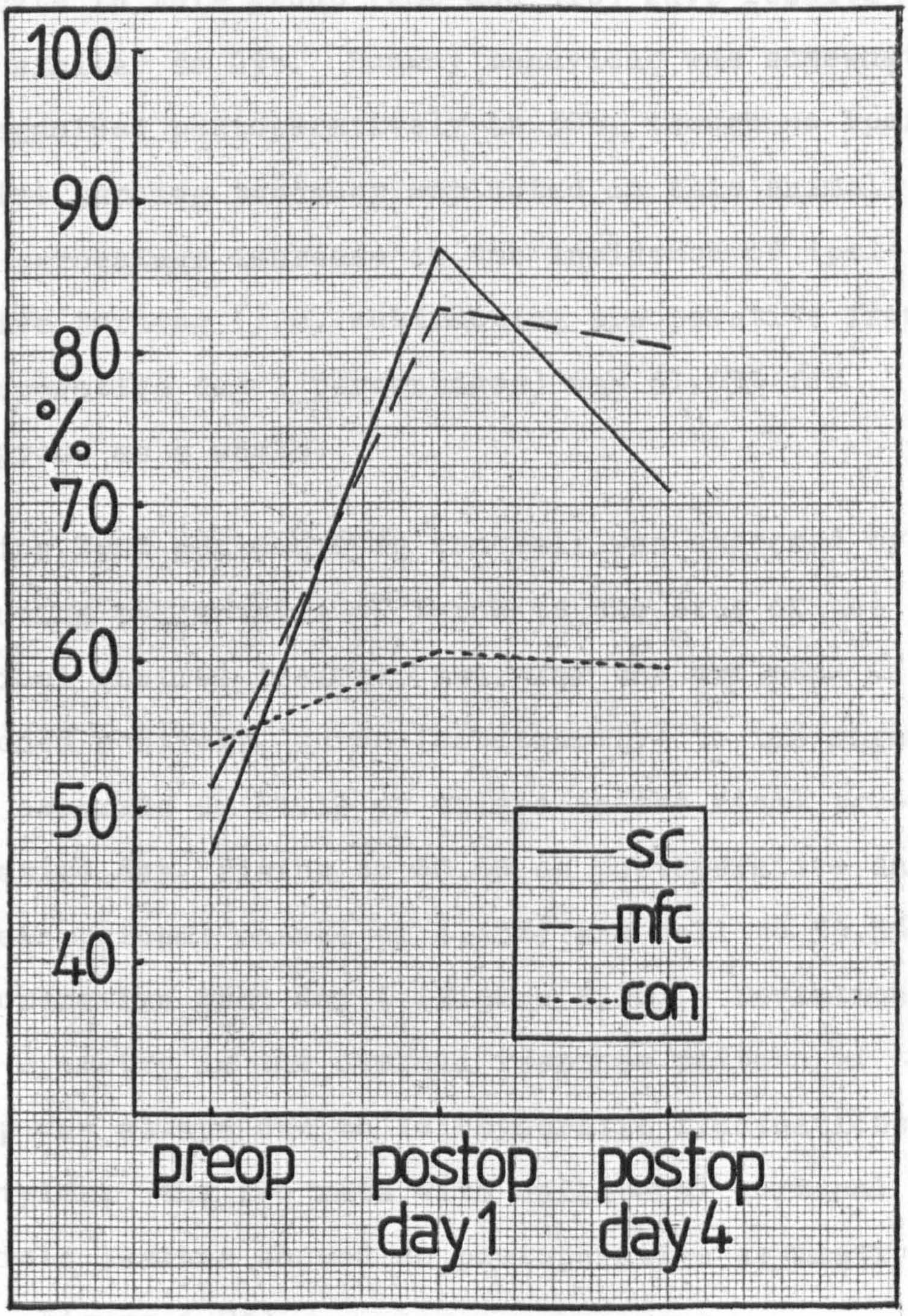

Figure 6.10
Percentage of turns from goaldoors made by unilaterally-lesioned animals towards the lesion side (or, arbitrarily, to the R in the case of unlesioned Controls).

(Figure 6.10). Figure 6.9 (s,w) shows the pre- (dotted) and postoperative (solid) runpaths of rats 29b and 30b with unilateral MFC lesions. The other two rats in this group (28b and 31b) gave results very similar to 29b. Runway behaviour was somewhat disorganised postoperatively in 30b, though no ipsiversive turning tendency was noted in this animal. Mean percentage increase in the incidence of ipsiversive turning (i.e. subtracting preoperative from postoperative day 1 percentages) was 31.03% for the group as a whole.

Turning from goaldoors in controls was assessed by computing percentages of turns to the side of the cortical control lesions, and, for the two non-lesioned controls, turns (arbitrarily) to the right. Such occurred on 54.1% of trials on the final preoperative day, rising to 60.6% on postoperative day 1 (a mean percent change of 4.43%) and fell to 59.5% by postoperative test day 4 (Figure 6.10). Deviation from symmetry in the overall response pattern of this group was always due to idiosyncratic fluctuations in runstyles; the two rats with unilateral cortical controls lesions showed no postoperative asymmetry (e.g. Figure 6.9c).

Figure 6.9 (t, u, v) show the pre- and postoperative runpaths of bilaterally colliculectomised animals 26, 46 and 22b; x, y, z show the runpaths of the same animals on non-distraction trials on test day 4. The lesions had a marked effect on running style but not in a systematic way. Initially there was a wider "sweep" to their runpaths on postoperative test day 1, though this pattern disappeared by test day 4, as is evident from Figure 6.9 (x,y,z).

Animals 4b and 22b (u,v; y,z) showed a change in turning preference which may have arisen from lesion asymmetry though gross asymmetry is not evident from the lesion reconstructions (Figure 6.7a).

Bilateral hippocampal lesions did not affect running style in any way and will not be further discussed in this context.

Repetitive doorpush errors

The number of repetitive "error" doorpresses were summed for the two goaldoors for each animal on each test day (1 and 2, predistraction; 3 and 4, during distraction). There were no group differences in the number of preoperative error presses. Postoperative scores were expressed for each test day as a multiple of the number of presses on the final preoperative day for each animal. Mann-Whitney U-tests (Siegel, 1956) showed that the bilateral MFC group committed significantly more error presses than controls on all postoperative test days ($U(6,7) = 4$; $p < 0.01$ in all cases). The unilateral MFC group also tended to press more than controls though the effect was only statistically significant on days 1 and 3 ($U(4,7) \leq 1$; $p < 0.01$).

The remaining groups tended to make few error presses, though the unilateral SC group pressed more than controls

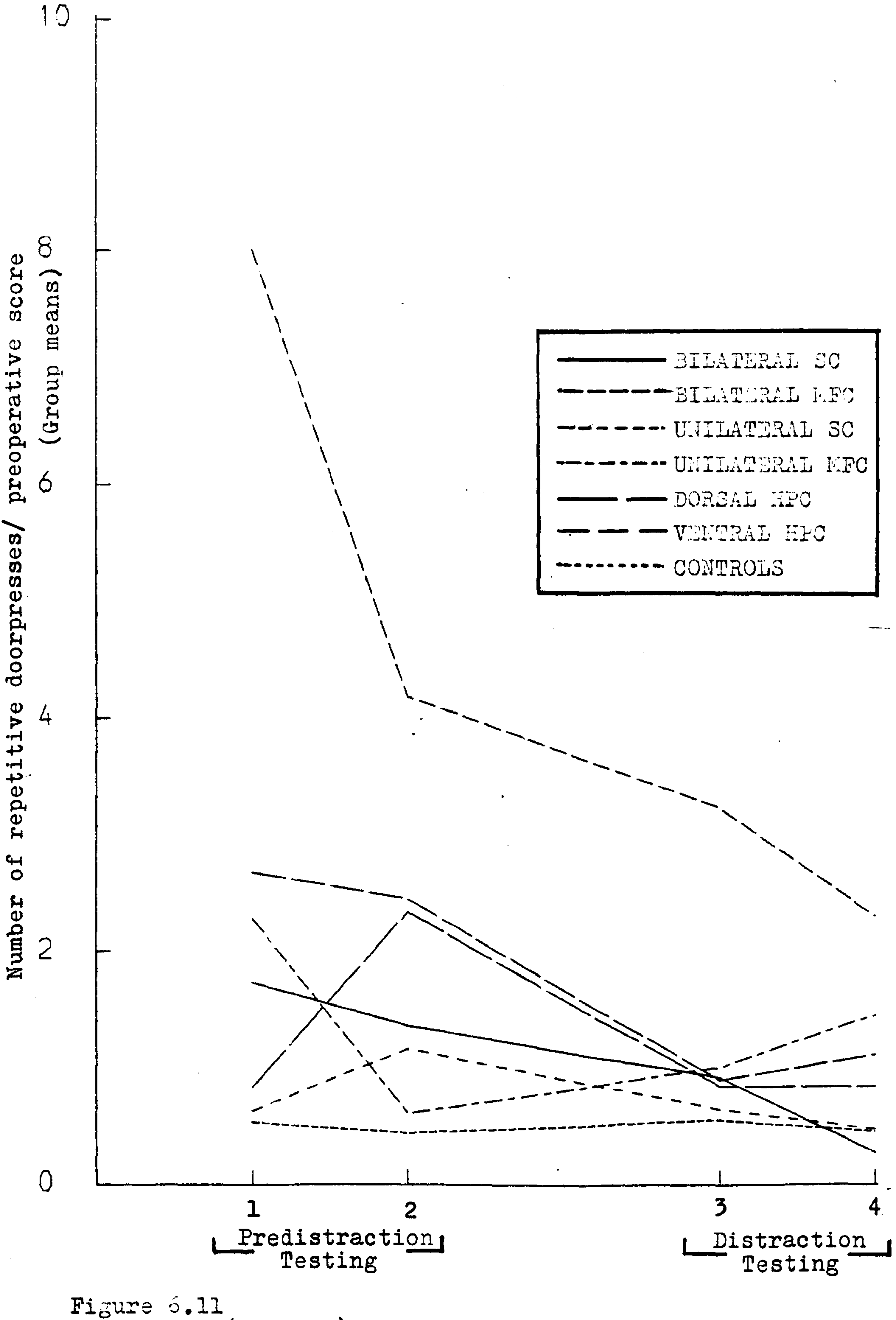

Figure 6.11
Repetitive ("error") doorpresses recorded postoperatively in Experiment 6.2, expressed as a multiple of preoperative mean.

on day 2 ($U(7,8) = 11$; $p < 0.03$). The hippocampal groups showed slightly elevated pressing; on day 2, dorsal HPCs pressed more than controls ($U(3,7) = 1$; $p < 0.02$), and on day 4, ventral HPCs did so ($U(3,7) = 0$; $p < 0.01$), pressing more than uni-and bilateral colliculars on that day (U's = 0; p's < 0.05). No other group comparisons reached significance.

Distractability

Data analysis was carried out separately for the animals with bilateral, and unilateral lesions. Distraction latencies for the former were expressed as a multiple of the median non-distraction latency (as in Experiment 6.1) and intergroup comparisons made using a 5 x 2 x 4 (Groups x Days x Distractor presentations) analysis of variance. For unilaterally-lesioned animals, mean latencies for distractor presentations in the two halves of the visual field were compared using appropriate statistical tests (see below); thus the visual field contralateral to the intact hemisphere was used as a control for the visual field contralateral to the damaged hemisphere.

Figure 6.12 shows the mean latency increase (Note: not observed incidence of overt orienting responses) for each bilaterally-lesioned group on successive distractor presentations. From this it is clear that, as in Experiment 6.1, colliculars rarely exhibited orientation to distractors, (in terms of either measure) while MFCs behaved as controls, halting, usually turning the head in the direction of distractors and sometimes running across towards them. Analysis of variance

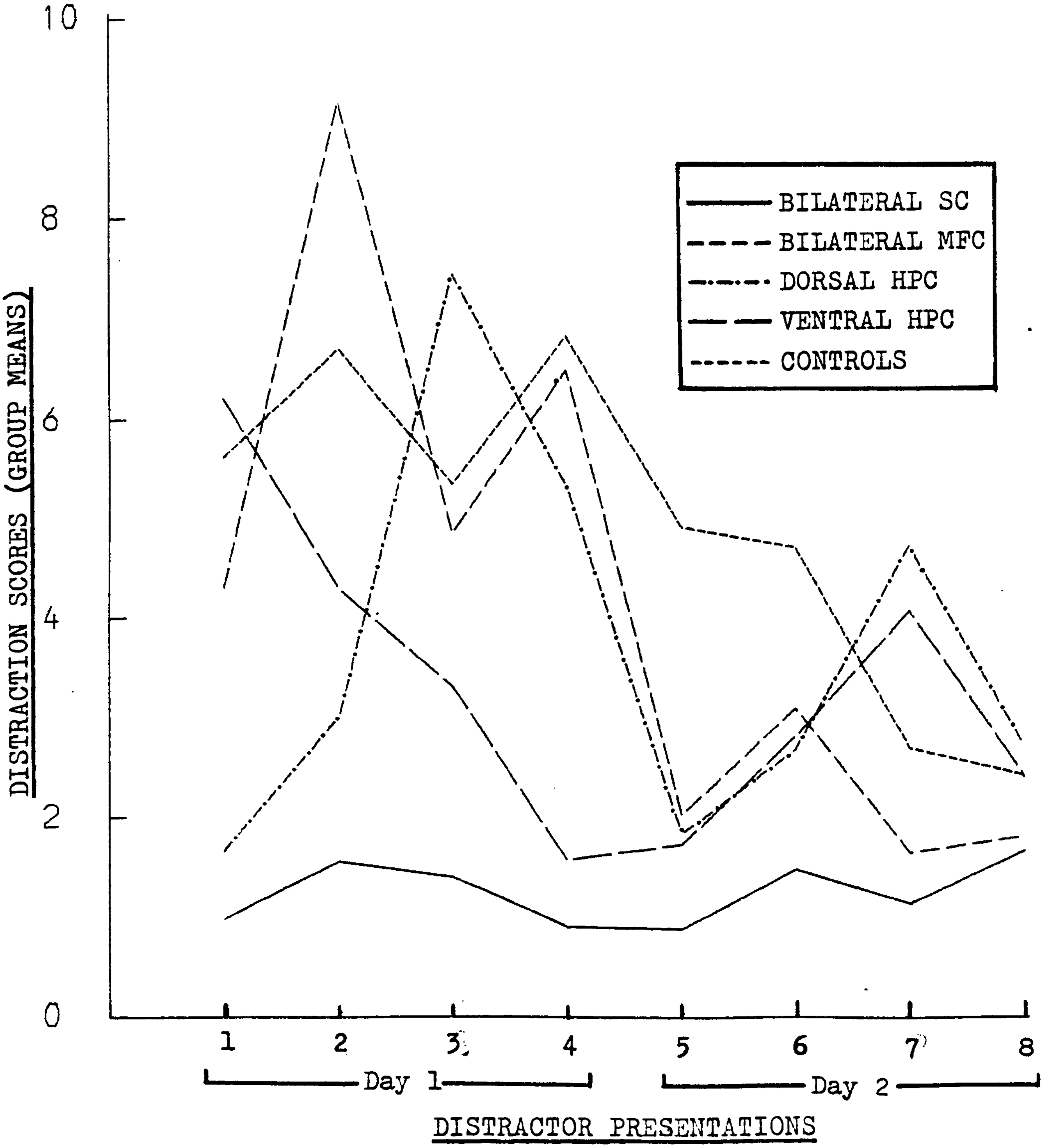

Figure 6.12
Mean distraction score for each group of rats with bilateral lesions on successive distractor presentations in Experiment 6.2 (see text).

revealed a significant Group effect ($F(4,17) = 2.69$; $p < 0.034$) due to the lower latencies of collicular animals compared with controls ($p < 0.004$), MFCs ($p < 0.05$) and the combined hippocampal groups ($p < 0.03$, 1-tailed) The latter groups' (ventral + dorsal) scores tended to be lower than those of controls, but not significantly so ($p < 0.065$, 1-tailed). Latency scores were lower on the second day of distraction testing than the first ($F(1,17) = 10.35$; $p < 0.006$) though intrasession habituation was non-significant ($F(3,51) = 0.82$; $p > 0.47$) and neither were all other comparisons and interaction terms. The near-significant difference between hippocampals and controls was not a result of lack of distractability _per se_, since distraction latencies at least twice the median non-distraction latency were obtained on 75% of distraction trials for dorsal hippocampal animals, and 58% for ventral hippocampals, compared with 73% for controls. However, few very long latencies were recorded in hippocampals. The percentage of distraction responses which gave rise to latencies exceeding 3.0 secs was only 20.8% for dorsal HPCs, 12.5% for ventral HPCs, but 39.3% in controls. Distraction was somewhat intermittent in hippocampal animals and in dorsal hippocampals failed to occur on early distraction trials (see Figure 6.12). However the small number of hippocampal subjects precludes further statistical analysis.

Distraction behaviour of animals with unilateral SC and MFC lesions is summarised in Figures 6.13 and 14. It is clear that rats with collicular lesions were neglectful towards stimuli presented contralateral to the lesion. Mean latencies for "ipsilateral" and "contralateral" [1] distraction trials were computed for each animal on each of days 1 and 2. Wilcoxon tests revealed that the mean latencies resulting from ipsilateral distractors were greater than those for contralateral presentations on both the first ($T(8) = 1$; $p < 0.01$) and second ($T(8) = 2$, $p < 0.01$) days of testing with distractors. In addition, 60 - 70% of ipsilateral distractors elicited visible orienting responses on both test days 1 and 2, though only 33.3% of contralateral distractors did so on test day 1 and none did so on test day 2.

Rats with unilateral medial frontal cortical lesions displayed a similar asymmetry, though this was not as marked as in the collicular group. Analysis of data was less reliable in view of the small number of subjects. Mean ipsilateral and contralateral distraction latencies were computed for each animal on each test day. These values were logarithmically transformed

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[1] For brevity, trials on which distractors were presented on the side contralateral to a lesion will be hereafter referred to as "contralateral distraction trials", and ipsilateral to a lesion "ipsilateral distraction trials".

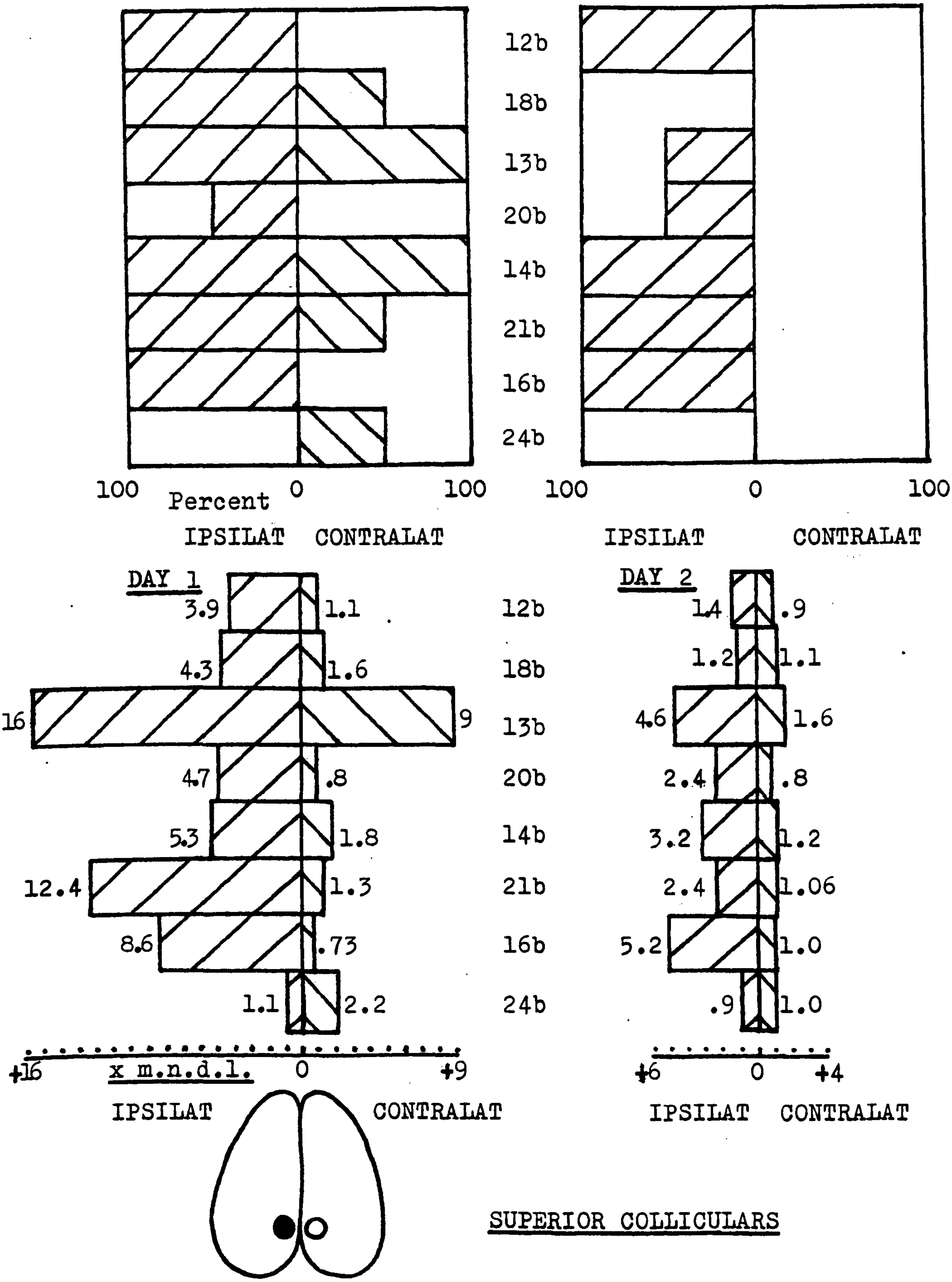


Figure 6.13

Distraction in unilaterally SC-lesioned rats. Above shows percentage of ipsi-, and contralateral distraction trials on which orienting response was observed on days 1 (left) and 2 (right). Below shows mean latency (multiple of m.n.d.l.) on ipsi-, and contralateral distraction trials.

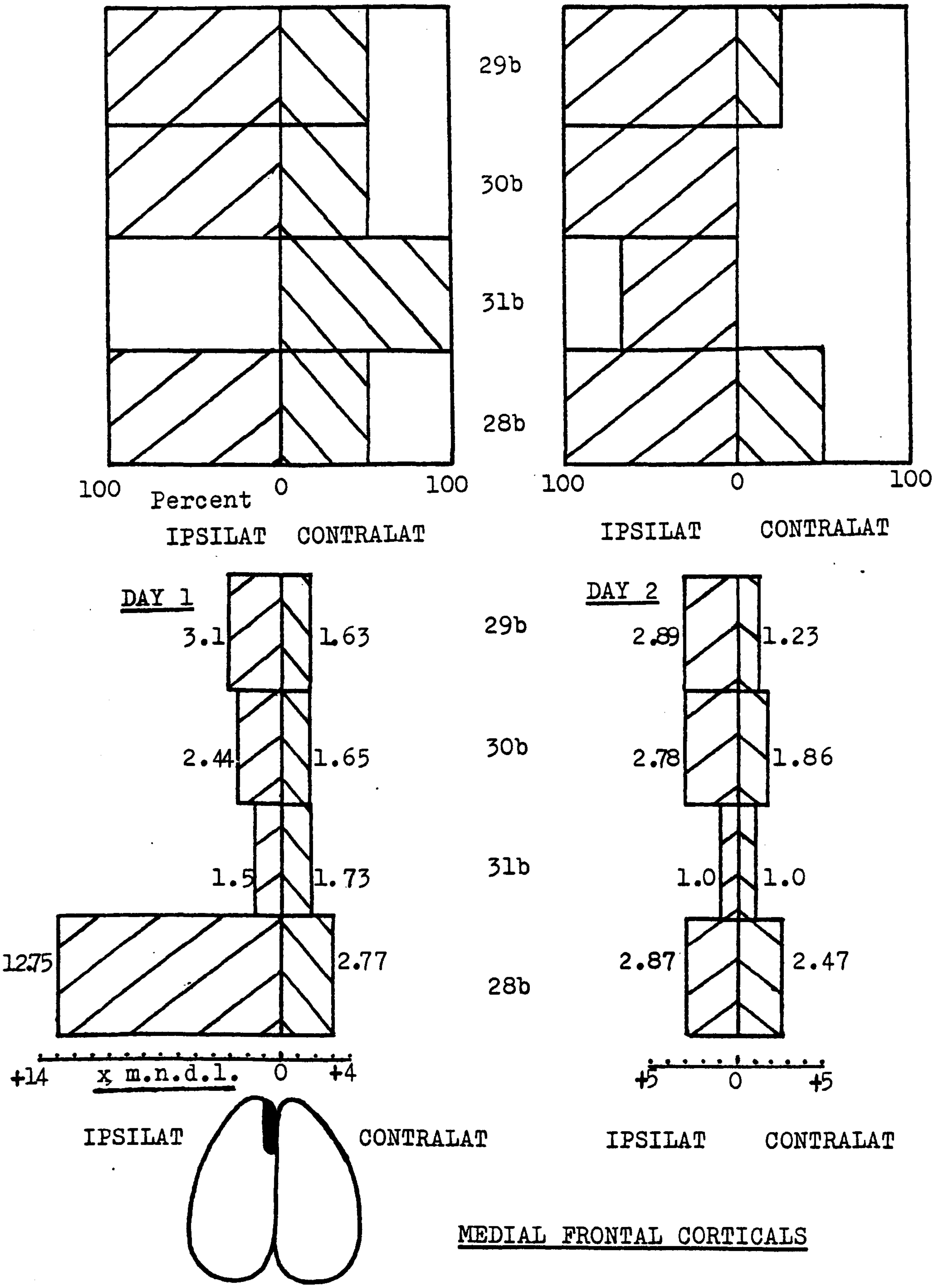


Figure 6.14

Distraction in unilaterally MFC-lesioned rats. Above shows percentage of ipsi-, and contralateral distraction trials on which orienting response was observed on days 1 and 2. Below shows mean latency (multiple of m.n.d.l.) on ipsi-, and contralateral distraction trials.

and t-tests (for related samples) were used to compare ipsi- and contralateral values. On each of test days 1 and 2, the comparison narrowly missed reaching statistical significance (day 1: $t(3) = 1.68$, day 2: $t(3) = 2.0$; $0.05 < p < 0.10$, 1-tailed, in each case). When number of visible orienting responses was considered taking test days 1 and 2 together, ipsilateral distractors elicited orientation on 81.3% of occasions, while contralateral distractors did so on 52.9%. On both measures of distraction animal 31b gave opposite results to the other three on day 1. This animal had a left MFC lesion yet responded normally to 2 stimuli on the right while neglecting 2 on the left. This animal showed asymmetrical turning from goaldoors, unlike rat 30b, though the latter animal <u>did</u> exhibit a clear asymmetry in response to distractor stimuli.

6.2.5 Discussion

Rats with unilateral collicular lesions displayed a strong tendency to turn from goaldoors towards the lesion side, though only those with very large, deep ablations showed gross, "forced" circling when attempting to run towards an illuminated goaldoor. The degree of control which collicular subjects were able to exercise over their runway behaviour is perhaps surprising. Kirvel (1975) has previously described "strong ipsiversive progression tendencies" in collicular rats with large unilateral ablations, though, as in the present study, such tendencies were most pronounced during the initial postoperative period; indeed after 10 postoperative days, the initial high degree of asymmetry had fallen by one half. It is interesting that Weinberg and Stein (1978) made no mention of motor asymmetry during (interoperative) training of unilateral colliculars on a jumping stand 11 days postoperatively. It would appear therefore that gross ipsiversive turning tendencies in colliculars are limited to the immediate postoperative period, and only severe in animals whose lesions invade dorsal tegmental regions. This is consistent with the findings of Winterkorn et al (1978). However the tendency to turn ipsiversively from goaldoors in this study persisted throughout testing, even when gross asymmetries had disappeared. Clearly degree of asymmetry may simply depend upon the extent of damage to the SC. On the other hand, current evidence alternatively suggests that collicular ablation alone gives rise to a mild (perhaps perceptual) asymmetry, upon which, in the case of very deep lesions, a more gross but temporary motor asymmetry is superimposed.

That tegmental involvement augments collicular-lesion-induced rotation in rats is surprising since when the SC and subjacent tegmentum are individually, unilaterally lesioned, the former produces ipsiversive, but the latter contraversive, turning behaviour. It is possible that, as in the case of the substantia nigra (Wirtschafter et al, 1978), the mesencephalic reticular formation (perhaps via an inhibitory influence upon the ipsilateral tectum; see Section 3.6) exerts its effect upon motor structures via the SC and the predorsal bundle system. Whether lesions of the sn augment collicular rotation, also whether predorsal bundle lesions would eliminate contraversive rotation following tegmental lesions would be worth investigating.

Unilateral MFC lesions failed to produce "forced" circling in any animal, yet, like SC lesions, did produce a strong tendency to turn from goaldoors towards the side of the lesion in the three rats with large frontal ablations. This result is consistent with the reports of Cowey and Bozek (1974) and Collin (1977) that unilateral MFC-lesioned rats tend to move ipsiversively when allowed to choose between two maze arms, and tend to move spontaneously towards the lesion side (in both patterned and unpatterned environments). Similar results were obtained for unilateral colliculars by Collin (1977), though frontally lesioned rats were slightly more likely to exhibit rotation in darkness compared with colliculars. This might suggest that the frontal animals' impairment is of a motor nature while the colliculars' might be largely perceptual. The latter is, in fact, unlikely, as Bland and Cooper (1975) have shown that unilaterally SC-lesioned rats show ipsiversive progression even after peripheral enucleation. Nonetheless, the nature of such behaviour might crucially depend upon the depth of the collicular lesion, with only deep lesions producing "forced" circling, while more superficially placed lesions like those used by Collin (1977) and in most SC animals in the above study, may give rise to a less marked effect, amounting to a "preference" for the ipsiversive turning direction.

Unlike collicular lesions, MFC lesions produced behavioural changes in addition to asymmetric turning. All frontally-lesioned rats exhibited a strong perseverative tendency in repeatedly pressing goaldoors after having received rewards. This might occur as a result of a motor difficulty in retrieving and consuming pellets (Kolb, 1973) or might otherwise represent a further aspect of the familiar frontal "perseveration" tendency seen in barpress and alternation situations (Kolb, 1974; Larsen and Divac, 1978).

Bilateral MFC and SC ablations were not noticeably disruptive of runway behaviour, though following either type of lesion runpaths were slightly more variable than preoperatively. In the case of bilateral SC lesions, it is tempting to conclude that the very fast, accurate runway performance typical of animals trained postoperatively (Experiment 6.1) does not appear in preoperatively trained rats. However such a conclusion would be premature in view of the small number of animals in the present SC group, and as they all had small lesions largely restricted to superficial collicular laminae. Similarly, the apparent normality of the HPC groups may be a consequence of the small lesion size, though it is perhaps possible that the rather poor visual guidance shown by hippocampals in Experiment 6.1 resulted primarily from damage to extrahippocampal structures.

The lack of attention to peripheral novel distractors by bilaterally colliculectomised rats is clearly consistent with a number of previous reports (see Chapter 3) and the results of the previous experiment. The contralateral neglect following unilateral lesions was strongly predicted from the previous studies of Kirvel, Greenfield and Meyer (1974), Kirvel (1975) and Collin (1977). Besides reinforcing the view that neglect in collicular animals is a genuine attentional disturbance (rather than, for example, a temporary hemispheric imbalance), the present result is particularly significant since it contradicts the argument that inattention in collicular rats reported in previous studies by Goodale and Murison (1975) and Goodale et al (1978) was due to the greater running speed of the animal. The latter is, theoretically, a distinct possibility since it might be argued that novel visual stimuli (in a fixed spatial position) to one side of an animal which is running abnormally quickly stimulate each portion of retina upon which they fall for a shorter period of time, and thus effective stimulus intensity (per unit area of receptor surface) is less, compared to that of an animal running at normal speed. Obviously such an argument cannot account for stimulus neglect in the present situation where one hemifield is used as a control for the other, and where clear asymmetry was demonstrated, since any "running speed" effect would, whatever the speed of an individual rat, produce a uniform bilateral effect. The orienting behaviour of unilateral MFC-lesioned rats was clearly asymmetrical in three out of the four subjects. Only animal 31b failed to show contralateral neglect; paradoxically, this animal exhibited a tendency towards ipsilateral neglectfulness on day 1. However, the overall result is in agreement with Collin (1977) and add support to the suggestion that the MFC in the rat is homologous with frontal eye field (arcuate sulcus) in the primate (Leonard, 1969, 1972), since monkeys with unilateral FEF ablations are neglectful towards stimuli occurring in contralateral visual space (Latto and Cowey, 1971b, 1972) and show a variety of perceptual and motor asymmetries (Kennard and Ectors, 1938; Kennard, 1939; Welch and Stutteville, 1958; Latto and Cowey, 1971a) though it should be noted that rats with unilateral MFC lesions in this and previous studies (Collin, 1977) failed to exhibit the tonic postural asymmetries reported in FEF-lesioned primates and cats. These results attest to the robustness of motor and perceptual asymmetries following MFC lesions in rats despite the variability in the effects of frontal lesions in rats, apparently leading to inconsistencies between studies on other behavioural measures (see Numan, 1978).

In both collicular and frontal rats, cross-orientations (ie. responses towards the side ipsilateral to the lesion on contralateral distraction trials; Kirvel, 1974) were rarely observed, though in deep-lesioned colliculars (but not frontals), ipsilateral distractor trials would sometimes give rise to rapid ipsiversive circling in an animal which had totally recovered from the immediate postoperative turning tendency.

As in the previous study, hippocampal animals exhibited an apparent intermittency of distraction. It should be noted that while there were few animals in the present HPC and MFC groups, a severe and reliable lack of distractability is very clearly seen in collicular groups containing only 3 or 4 animals (Goodale and Murison, 1975; Murison, 1977). As in the previous study, rats with dorsal hippocampal lesions tended to ignore initial stimulus presentations, and thus the attentional deficits seen in hippocampals in the previous study, and in the studies of Crowne and Riddell (1969) and Gustafson and Koenig (1979) which obtained similar results, are likely to be particularly due to damage to dorsal hippocampal tissue. The involvement of dorsal hippocampus in attentional mechanisms has been suggested before (Stevens and Cowey, 1973).

Very long latencies, in excess of 3 seconds (during which control animals usually engaged in examination of the distracting stimulus) were rarely observed in either dorsal- or ventral-HPC groups. Interestingly, Gustafson (1975) and Gustafson and Koenig (1979) have also reported reduced poststimulus exploration in hippocampals. Thus the present results contradict the description of hippocampals as "totally undistractable" (Wickelgren and Isaacson, 1963; Raphaelson et al, 1965) and indeed, the present study does not exclude the possibility that had distractors been presented to animals while they were not engaged in an ongoing task, entirely normal orientation might have been observed (Hendrickson et al, 1969; Gustafson, 1975). It might be suggested that the occasional, intermittent orientation seen here and in Experiment 6.1 in hippocampals occurs on trials on which the animal happens not to be devoting much attention to the central task.

In contrast, total, and not intermittent, inattentiveness has repeatedly been observed in collicular-lesioned rats; these, however, have also been shown to display normal orientation to sudden stimuli (a form of startle response) when doing absolutely nothing, but reduced orientation when engaged in any overt behaviour (Goodale et al, 1977). The result of Experiment 6.1 and the present results strongly suggest that hippocampals suffer from a more subtle attentional deficit than colliculars, perhaps producing a greater "diffusion" of attention (Stevens and Cowey, 1973, 1974), increased sensory ambiguity (see Leaton, 1969) or other stimulus sampling or selection problems (Stevens, Foreman and Venables, 1980) perhaps resulting from the absence of "high-level" gating of sensory information (Douglas and Pribram, 1966). The latter is theoretically likely since the HPC receives information which has been extensively preprocessed by prior neural mechanisms including perhaps, the SC. It would be useful to investigate the ability of HPC-lesioned rats not only to orient towards irrelevant stimuli as in the present study, but also to utilise peripheral stimuli as the basis for responding on a central task. From previous experiments (Stevens and Cowey, 1972) it would seem that hippocampals use such stimuli more readily than controls, perhaps due to the intermittent, or non-habituating tendency to sample from peripheral locations when a control animal has ceased to do so.

Summary and Conclusions

Unilateral lesions of SC, and to a lesser extent, MFC, produced inattentiveness towards distractor stimuli presented in visual space contralateral to the lesion when tested 2 weeks postoperatively. Bilaterally- and, to a lesser extent, unilaterally-lesioned MFC rats tended to make many perseverative doorpresses. Unilateral SC and MFC lesions failed to produce postural asymmetries but produced a strong, usually permanent tendency to turn towards the lesion side when leaving a goaldoor. Deeper SC lesions produced a "forced" turning(on certain trials only) during early postoperative testing, though in general, locomotor guidance was under good control and appeared to interact with prevailing idiosyncratic turning tendencies. As in the previous experiment, bilateral SC but not MFC lesions produced bilateral inattentiveness to distractors, suggesting an important functional distinction between the two structures. Dorsal HPC ablations tended to cause initial neglect of distractors; both dorsal and ventral HPC-lesioned rats tended to show less post-stimulus exploration and intermittency of distraction, but no disturbance of the runway response. Minimal functional overlap between hippocampal and collicular mechanisms is suggested.

CHAPTER 7

RADIAL MAZE PERFORMANCE

7.1 The Effects of SC, HPC and MFC lesions and Environmental Manipulations on Radial Maze Performance in Rats

7.1.1 Introduction

The inferring of functional similarities between major brain structures on the basis of similarity of lesion effects is fraught with difficulties both practical and theoretical. For example, lesion extent and volume are difficult to equate between structures differing in size and shape, while differential functional recovery and compensatory processes may exaggerate differences (or similarities) between postoperative deficits. In addition many types of brain lesion have not been directly compared within a single experimental design, or using a similar type of apparatus. For example, the view that the SC participates in spatial behaviour derives from experiments using 2-choice runways (Schneider, 1967, 1968) and jumping stands (Barnes et al, 1970; Weinberg and Stein, 1978), while studies concerned with the role of the HPC in spatial behaviour have largely been investigated using alternation, avoidance (See reviews in O'Keefe and Nadel, 1978) and the radial maze (Olton, 1977; see Chapter 4).

Indeed, the use of the term "spatial" in each case would appear to be quite different. In particular the SC animal might be expected to exhibit deficiencies in egocentric spatial localisation; i.e. to be unable to make judgements of spatial positions of objects in relation to body midline, since visual space is egocentrically coded in SC (Trevarthen, 1970) while in contrast the HPC animal is thought to be capable of (and indeed to rely heavily upon) egocentric spatial judgements, yet to be deficient in terms of his use of absolute space (O'Keefe and Nadel, 1978). The latter has been extensively investigated by Olton (1977; see Chapter 3) using a newly-designed apparatus known as the "radial arm maze", which consists of an elevated central platform from which 8 equally-spaced arms radiate (Figure 7.1). Olton has demonstrated firstly the remarkable ability of the normal rat to spontaneously investigate the apparatus in such a way that, with minimal training, return visits are rarely made to previously visited locations; secondly that an animal with damage anywhere in the fornix-hippocampal formation makes many errors by repeatedly visiting particular maze arms. These are presumed to occur because it lacks a "spatial memory" and is thus unable to discriminate visited from unvisited places.

However, since radial maze performance, and thus the development of a "cognitive spatial map" of an environment, may be "egocentrically inspired" (Nadel and O'Keefe, 1974), superior collicular involvement might be inferred in the process by which such a map is generated.

On the other hand, recent studies have cast serious doubts upon the simple, egocentric "spatial" theory of SC function, and an alternative suggestion put forward that the SC is involved in the redirection of attention to relevant peripheral cues (Goodale et al, 1978; see Chapter 3). However, the development of a cognitive spatial map is thought to be a very rapid process whereby environmental cues are quickly incorporated in a pre-existant framework (Tolman, 1948 ; Nadel and O'Keefe, 1976), following a single exposure (O'Keefe and Nadel, 1978). Since this could be viewed as requiring attentional selectivity to peripheral cues in novel surroundings, the SC might potentially be involved; in that case, the development of a "spatial map" would be slowed or eliminated by SC removal. Indeed the suggested relationship between SC and HPC (Routtenberg and Taub, 1973; see Chapter 4) might be based on just such a process of cue selection and incorporation.

Other brain structures have also been implicated in the egocentric coding of space, and are thus alternative candidates. For example, a specific frontal cortical site corresponding to the middle third of sulcus principalis in monkey has been identified as playing a major role in egocentric spatial discrimination (Butters et al, 1971), and in rats parts of the caudate nucleus functionally associated with frontal cortex (Rosvold, 1969) have been implicated in spatial judgements (Potegal, 1969). Becker, Walker, Olton and O'Connell (1978) recently investigated the effect of MFC lesions on postoperative retention of preoperatively learned radial maze performance but found only a small temporary deficit. Nonetheless, since the lesion was made after the task had been learned, the possibility still remains that initial learning of the task would have been adversely affected by MFC lesions.

Thus the present experiment investigated radial maze learning in groups of rats with bilateral SC, MFC and HPC lesions.

In addition, environmental manipulations (dark-testing and rearrangement of room cues) were used to ascertain the extent to which visual cues are utilised in radial maze performance (cf. Olton and Samuelson, 1976; Olton, 1977; Zoladek and Roberts, 1978), to attempt to identify the type of cue used, and whether particular non-visual strategies are differentially used by animals deprived of the use of one of the abovementioned neural structures. In particular, it was predicted that HPC-lesioned rats would perform extremely poorly and possibly that SC- and MFC-lesioned rats would be slower in learning when tested on the radial maze. Testing in zero illumination, or with the testroom cues grossly rearranged was expected to severely impair performance in well-trained control animals.

7.1.2 Subjects

The 33 rats used in this study were those previously described in Experiment 5.2,(but without SC 40a which had died), thus comprising 9 SC, 10 MFC, 10 Cortical Controls and 4 rats with very extensive HPC ablations. They were approximately 390 days old at testing (approx. 280 days post-operation) and had previously participated in an open field study (Experiment 5.2) and a runway distraction task (6.1), the latter finishing approximately 30 days prior to the commencement of the present study. They were given access to food for one hour per day throughout this experiment.

7.1.3 Apparatus

The radial arm maze consisted of an octagonal centre platform, width 34 cm, from which 8 arms, each 90.5 cm x 10 cm, radiated symmetrically (see Figure 7.2). The maze was constructed entirely of wood. Each arm had low hardboard walls 3 cm high along both sides only, and had a shallow, 1.2 mm diameter foodwell milled into the surface, their centre 2.8 cm from the distal end of each arm. The entire apparatus was elevated 16.5 cm from ground level, and was located in the centre of a standard testroom measuring 3 x 3.2 m (See Figure 7.2). The walls of the room were painted matt white and contained many cues such as a litter bin, sink, cupboards, shelves and pieces of spare apparatus, all of which remained in the same position for all but the last day of testing (see below). A 70 watt strip light mounted on the ceiling was the only source of light. It was positioned slightly off centre with respect to the maze. Air conditioning fans provided a mild constant background noise though no specific masking of sounds was used.

7.1.4 Method

7.1.4.1 Pretraining

Throughout the experiment animals were transported in cage pairs (in their homecage) to the test room. On day 1, both rats were placed, together, on the centre platform of the maze, both platform and arms having been liberally scattered with 45 mg saccharin pellets. Both animals remained on the maze until each had eaten at least 10 pellets. On the following day, they were removed individually from the homecage, which remained on a stool directly behind E from which position the caged animal had virtually no direct view of the room or maze. Each in turn was placed on the centre platform, only maze arms containing food pellets. The animal was allowed free exploration until at least 10 pellets had been consumed. On the following day, the foodwell at the end of each arm was baited with 2 pellets and full testing began. Testing order was alternated within cage pairs between days. On day 17, all animals were tested in complete darkness. Light was carefully excluded from the testroom and each animal, prior to testing, had a small patch of sticky paper coated with non-toxic, light-activated luminous paint ("Joy" brand) attached to the fur of its back. (Note that as a control for the general effects of this procedure, for example the unusual and possibly distracting smell of the paint ,luminous tags were attached to animals on day 16 though it is clear from the results that this had no effect upon radial maze performance). All other aspects of the testing procedure were otherwise normal.

E used a narrow 'pencil' torchbeam of red light to locate the apparatus and recording notebook, though this light was extinguished prior to the animal's placement on the maze.

E was able to visualise the maze layout via small patches of luminous paint which had been brushed onto the lower edge of each maze arm two days prior to dark testing, and no difficulty was encountered in identifying the rats' position on the maze at any time. Both animals in a cage were placed in darkness for 5 minutes prior to testing.

On days 18 and 19, rats were tested in the light as on days 1 - 15. A second manipulation was carried out on day 20, when room cues were rearranged, either by being moved to new positions in the room or masked off (in the case of immovable cues such as the sink, drain, room fittings, etc.). Figures 7.1 a and b show the normal (days 1 - 19) organisation of the room and (day 20) reorganised room. Testing was carried out exactly as on days 1 - 15, 18 and 19.

Histological procedures have been previously described (Section 5.1.5).

7.1.5 Results

Reconstruction of the lesions are shown in Figure 5.7 and discussion of histology is given in Section 5.2.5.1.

Figure 7.4 shows the performance of the four groups during learning, and during environmental manipulations. No group effect was observed in the tendency to leave food uneaten on days 1 - 3. Analysis of variance was carried out on daily scores (representing the number of different maze arms visited within the first 8 choices)

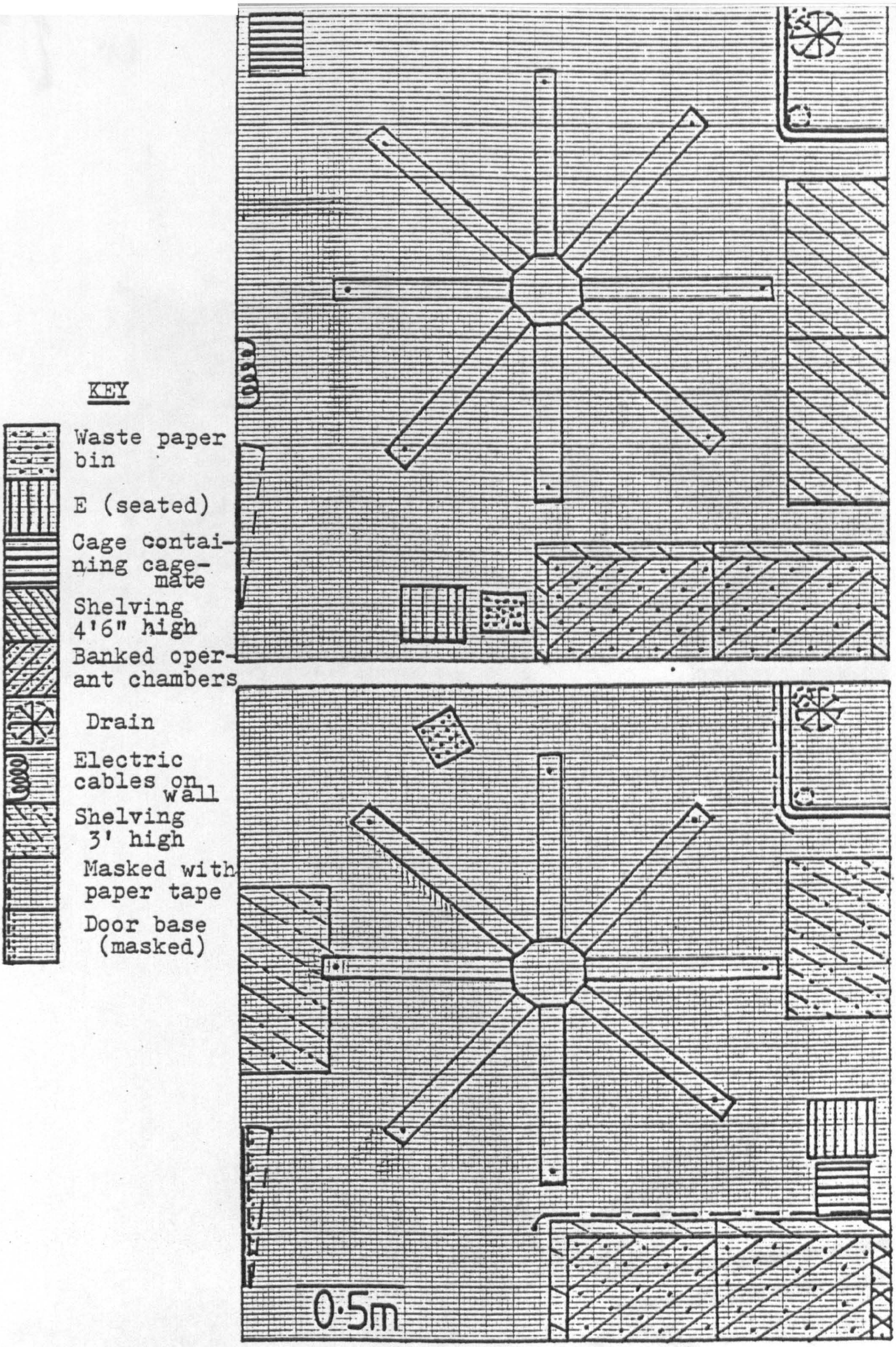
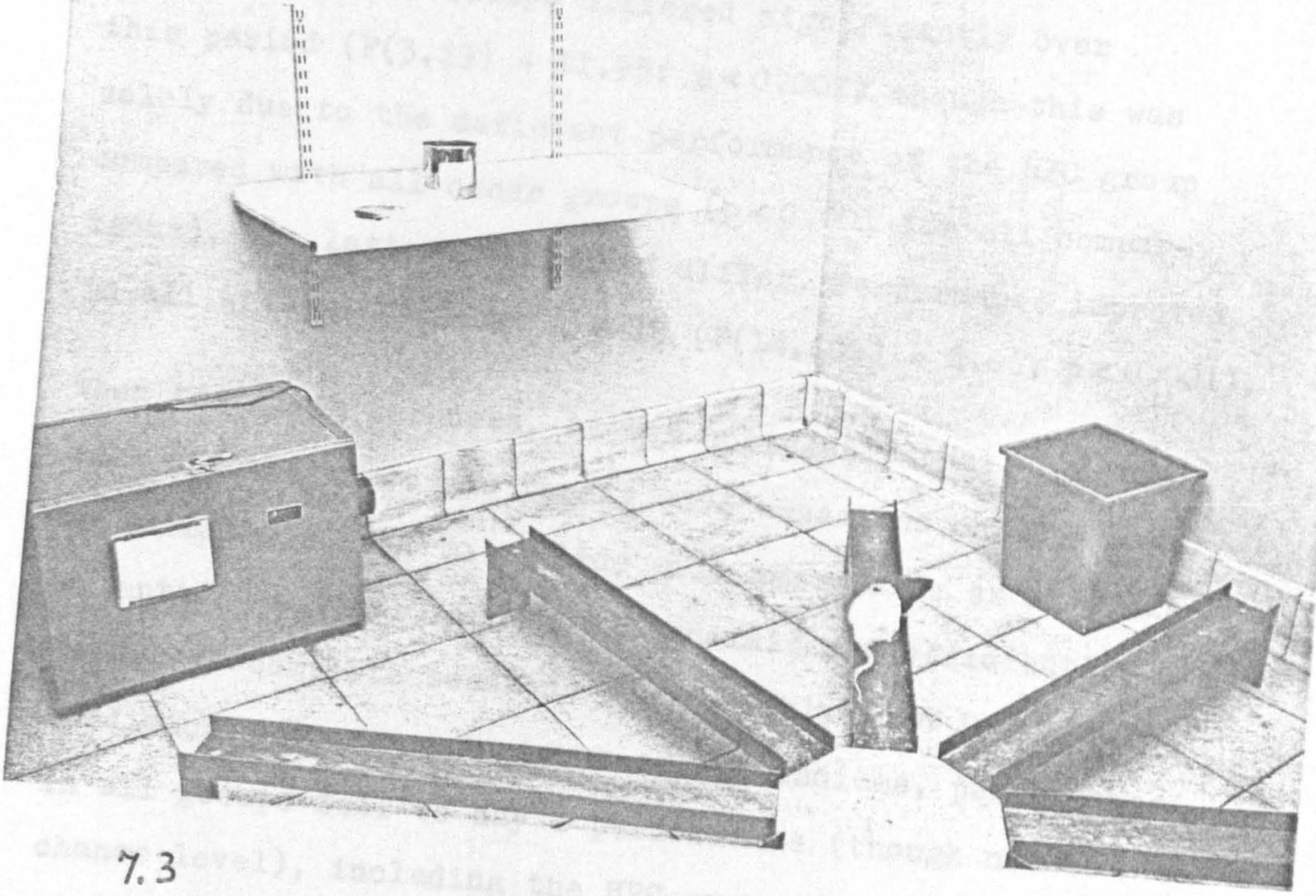


Figure 7.1a,b
Upper illustration shows plan of original room layout, and lower shows the layout following rearrangement of room cues in Experiments 7.1 and 7.3 (see text).

7.2



7.3

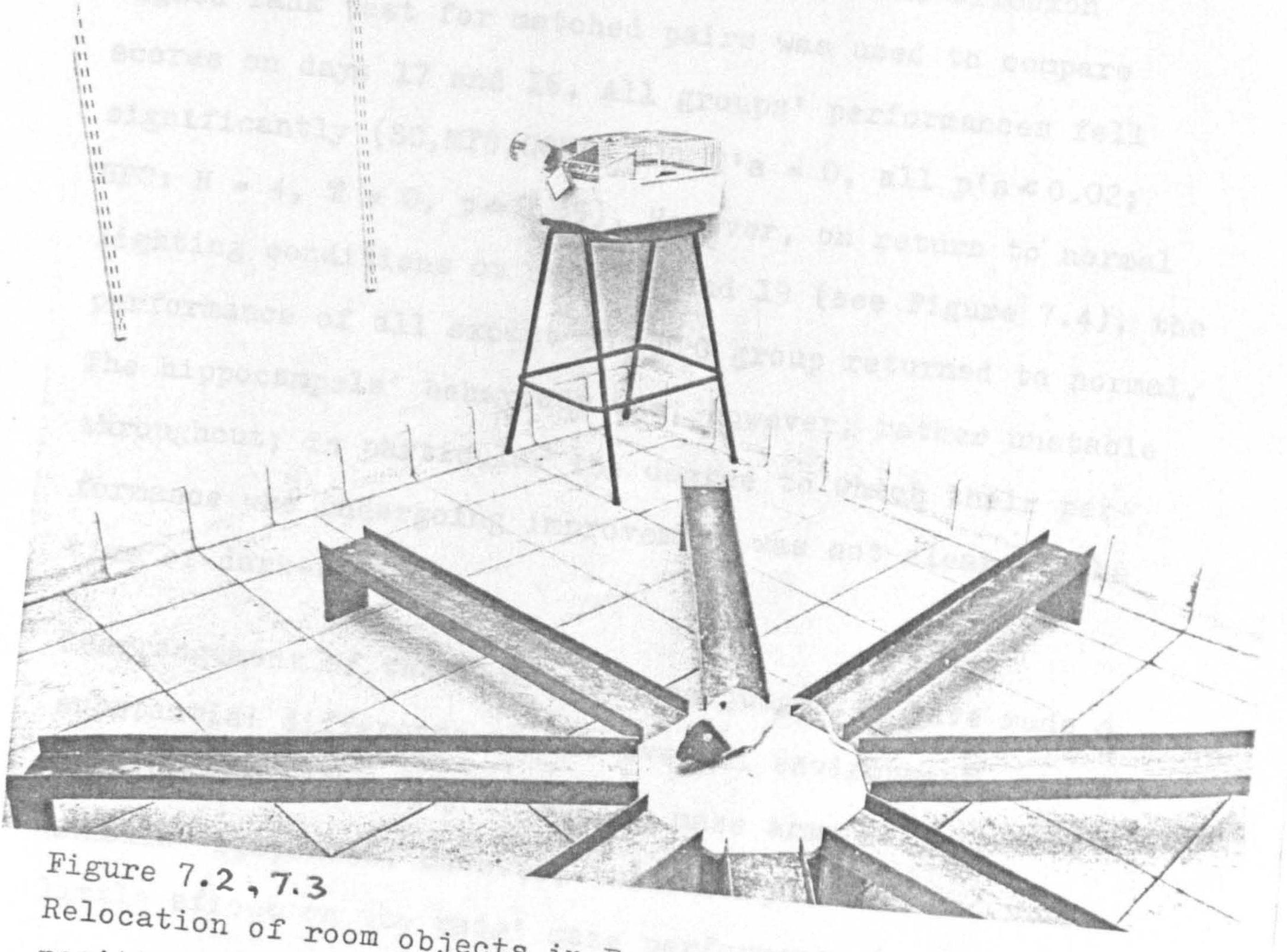


Figure 7.2 , 7.3
Relocation of room objects in Experiments 7.1 and 7.3. Initial positions of room cues are shown in the upper photograph.

for days 1 - 15. Groups differed significantly over this period ($F(3,29) = 11.95$; $p < 0.001$) though this was solely due to the deficient performance of the HPC group compared with all other groups ($p < 0.001$ for all comparisons), the latter failing to differ. Performance improved in all groups over days 1 - 15 ($F(14,406) = 6.66$; $p < 0.001$).

When tested in darkness, it was noticeable that no animal fell off the maze, and rarely were occasions noticed when an animal appeared to collide with maze walls or show disoriented behaviour. Indeed all animals ran efficiently, and seemed to complete sessions more quickly than in light conditions. However, in terms of arm choices, performance in all groups fell to day 1 performance (though not to chance level), including the HPC group. The Wilcoxon signed rank test for matched pairs was used to compare scores on days 17 and 16. All groups' performances fell significantly (SC,MFC,CONT: all T's = 0, all $p's < 0.02$; HPC: $N = 4$, $T = 0$, $p \mathrel{\hat{=}} 0.05$). However, on return to normal lighting conditions on days 18 and 19 (see Figure 7.4), the performance of all except the HPC group returned to normal. The hippocampals' behaviour was, however, rather unstable throughout; in particular the degree to which their performance was undergoing improvement was not clear at the time of dark-testing.

Rearrangement of the room cues was judged to have made a substantial difference to the overall environment, since E experienced difficulty in coding maze arms while recording animals' responses. However, this manipulation had very little effect on the rats' maze performance (see Figure 7.4).

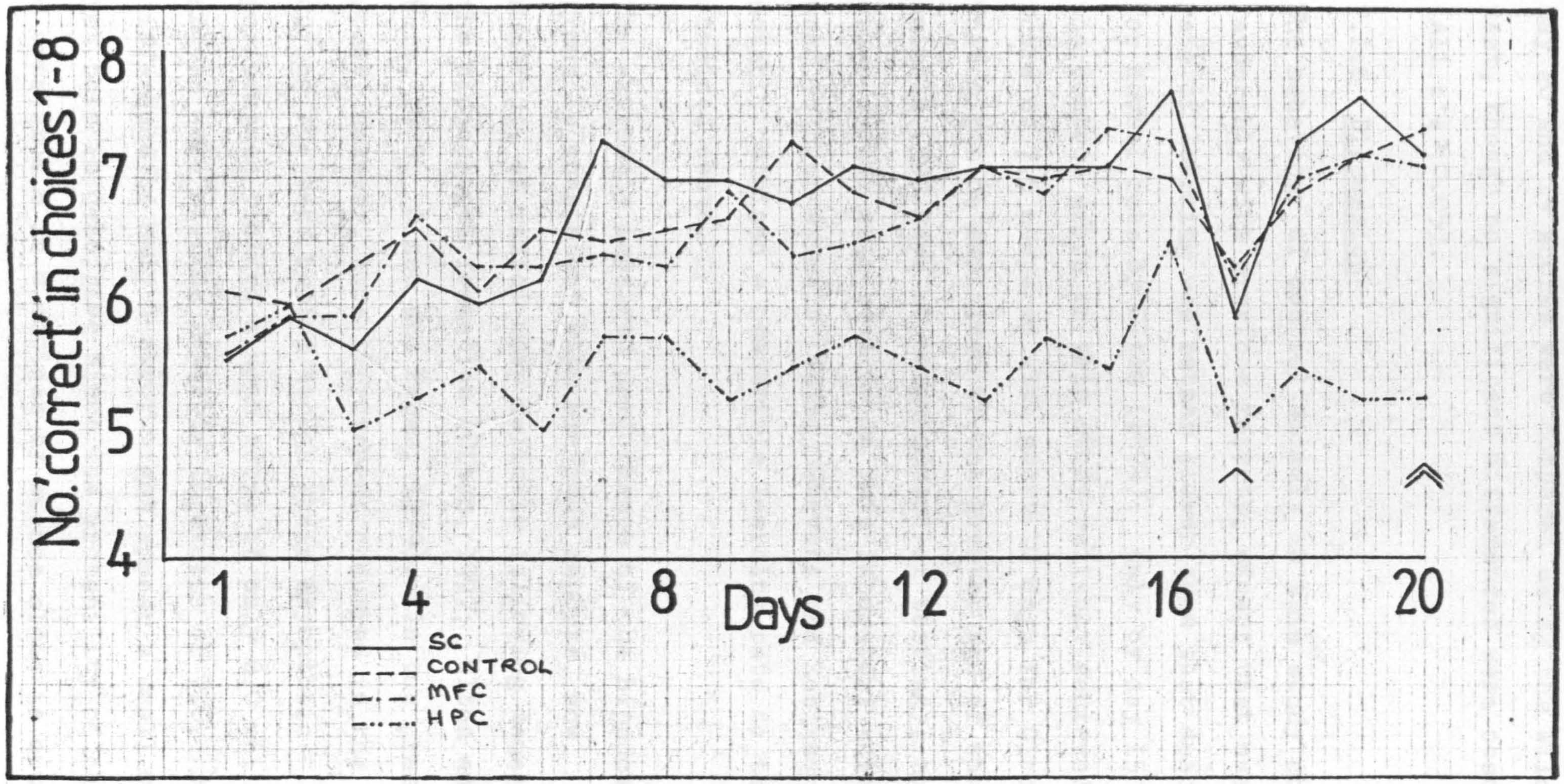


Figure 7.4
Mean number of separate arms visited in choices 1 - 8 for animals in each group in Experiment 7.1. Testing in darkness is indicated by a single arrow, testing with rearranged room cues by a double arrow.

Day 20 and 19 scores were compared using the Wilcoxon test, though no significant differences were observed (All $p's > 0.05$).

7.1.6 Discussion

The behaviour of control animals in this study compares favourably with previous reports, except that overall rate of learning was rather slower than that described for normal rats by Olton (1977); only by day 15 had the control group in this study reliably achieved a mean score of 7.5 compared with about 10 days for Olton's rats. This might be explained by the greater age of the present animals (390 days at commencement of testing), though other radial maze studies in this laboratory which used younger animals (Watts, Stevens and Robinson, 1980). notably obtained a comparable learning rate to that obtained above.

The extremely impaired performance of the hippocampal group is consistent with previous reports, now numerous, of radial maze deficits following damage to the hippocampal formation (Olton, 1977; Olton and Werz, 1978; Olton and Papas, 1979). In the present study, however, some improvement occurred in the HPC group during the test period though their asymptotic performance yielded a mean score of only 6.0 while other groups were scoring reliably in excess of 7.0. A difference of only 1 error might appear a small margin, yet this is deceptive since the probability of choosing 6 arms from 8 in 8 choices by chance alone is considerably higher than choosing 7 from 8. Thus a score of 7 reflects a vastly superior performance especially when maintained over a number of successive days (see Olton, 1977). Indeed, Zoladek and Roberts (1978, p.80) emphasise this in noting that their enucleated rats "were about an entire error lower in accuracy" than controls.

No evidence could be found to support the view that radial maze performance (and, thus, spatial map generation) is dependent upon either the SC or MFC since neither the SC or MFC group displayed deficient learning. Minimal deficits might not have emerged in this study since (a) all rats were rather old at testing, (b) controls had small strip cortical lesions which invaded cingulum bundle in some cases, thus controls may have been performing at slightly depressed levels, and (c) testing was carried out some months after surgery; since animals had gained extensive experience in the meantime, some functional recovery or reorganisation may have taken place after certain lesions.

In fact it is unlikely that small cortical lesions affect radial maze performance (Olton, 1977; Jarrard, 1979; see following experiments), and cingulum bundle is unlikely to be indispensible for spatial behaviours (Green and Stauff, 1974) though a combination of the above factors may have masked any minor differences between the non-hippocampal groups.

Nonetheless of particular significance is the total absence of "hippocampal" behaviour in the SC group. Though the collicular lesions were subtotal, they were sufficient to produce elevated levels of activity (Experiment 5.2) and profound inattentiveness towards peripheral distractor stimuli (Experiment 6.1). Thus a large proportion of the visuospatial representation on the collicular surface would have been abolished in these animals. Clearly, if egocentric spatial encoding which has been said to inspire "cognitive map" generation (O'Keefe and Nadel, 1978) is dependent upon the SC, a clear deficit would have been predicted in this group. This result casts serious doubts upon the existence of a strong functional connection between the SC and HPC in terms of spatial behaviour.

Response Style

Considerable variation in individual styles of running was noted within each group. Few choice sequences consisted of random selection (Olton, 1977) or quasi-random selection (Olton and Werz, 1978). Indeed most rats appeared to adopt specific strategies which tended to appear, disappear and variously reappear at different stages of training. As noted in Chapter 4 (Section 4.1.4). there are a number of ways in which the radial maze task may be successfully completed, only some of which require complex spatial discriminations though this has notably received little attention in previous experimental reports. By day 12, many of the above animals were apparently making choices in a systematic way. On day 15, for example, No's 5,10, 17 (MFC), 36, 18, 20, 47 (SC) tended to run to successive maze arms (1, 2, 3 or 8, 7, 6 etc) while animals 6, 2 (controls), 44, 39 (SC) and 1 (MFC) ran to successive orthogonal maze arms (1, 3, 5, 7). Such a strategy may lead to errors in cases where the sequence is wholly or partly repeated, though in many cases an apparently complex spatial discrimination was made after 4 choices, i.e. the animal would repeat the orthogonal choice sequence but using the remaining 4 (unvisitied) arms. As reported by Olton (1977), "orthogonal" runstyles are frequently adopted by hippocampal rats; for the hippocampals in the present study this was interspersed with repetitive visits to particular "preferred" arms. The "orthogonal" strategy, when used by hippocampals, never involved a complex discrimination after 4 choices, but tended to result in repetitive visits to the same 4 maze arms. A further strategy employed by animal 49 (control) on day 15, consisted of running in a consistently clockwise, or anticlockwise direction always "missing" two arms between choices. Such a choice sequence may result from the adoption of a kinaesthetic (135° "body turn") strategy or from the animals' choosing the (visually) half-foreshortened arm to the left (or right) on emergence from each arm visit. This strategy is efficient since 8 such responses represent perfect performance.

It is difficult to identify the point at which a particular strategy emerges since many appear in "partial" form at various points in the choice sequence prior to becoming the dominant choice pattern. However it would be premature to assume such strategies to be strictly non visual solutions to the radial maze task, since they almost entirely disappeared in all groups during testing in zero illumination.

Though it might be intuitively expected that animals would "mark" visited maze arms with an odour trail, Olton's (1977) studies ruled this out in well-trained animals. For example following rotation of the maze half way through a trial such that previously visited arms occupied new spatial locations, rats would run to places previously unvisited even though this involved running along arms which had previously been traversed. Indeed, animals in this study were seen to enter an arm which was littered with defaecation from previous visits. Zoladek and Roberts (1977) found that rendering rats anosmic by application of zinc sulphate to the nasal mucosa had little influence on radial maze performance. Nonetheless, it should not be assumed that all animals perform the radial maze task in the same way at all stages of learning.

When tested in darkness, behaviour was not noticeably disrupted; animals were not reluctant to run, responded briskly and gave the appearance of completing the task more speedily than when tested in the light. However many error visits were made to previously visited maze arms. This is consistent with the view that vision is in some way necessary for accurate radial maze performance (Olton and Isaacson, 1972; Zoladek and Roberts, 1977) and for spatial maze tasks generally (Beritoff, 1965; Tsang, 1934; Honzik, 1936).

Dark-testing was undertaken on one day only and thus the rats' poor performance may have arisen from a distraction effect, general disorientation, or as a result of elevated arousal level, since rats are notably hyperactive in darkness (Isaac, 1971). The former is unlikely, as animals failed to exhibit freezing, rearing or otherwise exaggerated attentional behaviour. Testing animals in complete darkness is clearly an extreme form of treatment, though no animal fell off the maze or appeared to collide with the walls.

Hippocampals were seemingly as affected by dark-testing as controls, suggesting that any improvement in hippocampals' scores over days is probably due to the use of visual information. Interesting in this respect is the distinction drawn by Honig (1978) between "working memory" (short - term memory for information relevant to the "current" trial) and "reference memory" (long - term memory for information generally applicable across many trials). By baiting a subset of radial maze arms, Jarrard (1979) and Olton and Papas (1979) were able to show that while hippocampals tend to make perseverative responses within the subset of baited arms (suggesting a disturbance of working memory), they were nonetheless largely able to successfully avoid the non-baited subset (indicating relatively unimpaired reference memory). Since the HPC group in this study was probably affected by testing in darkness, it might be argued that vision is especially significant for reference memory. This point will be amplified in a later section.

7.1.7 Conclusions

Initial learning of the 8 arm radial maze task was impaired in rats with radical hippocampal ablations but not in those with superior collicular or medial frontal cortical ablations. Testing animals in total darkness on day 16 caused performance to fall in every case to pretraining level, suggesting that vision is to some extent necessary for accurate radial maze performance in all groups. However, changing the positions of all furniture and objects in the test room had no discernable effect upon performance; thus it is unclear precisely which visual cues are utilised. Many animals developed complex response strategies, particularly in later stages of training.

7.2 Visual Lesions and Radial Arm Maze Performance

7.2.1 Introduction

It is reasonable to conclude from a number of previous studies (Olton and Samuelson, 1976; Olton, 1977; Zoladek and Roberts, 1978; Experiment 7.1) that performance on the radial maze is to some extent dependent upon the visual modality. Indeed spatial abilities, of which the radial maze is a powerful test (Olton, 1977; O'Keefe and Nadel, 1978), are thought to rely upon visual stimuli (Nadel and O'Keefe, 1976; O'Keefe and Nadel, 1978), and responses of some "spatial" units in the hippocampus which has come to be regarded as a primary structure involved in spatial behaviours (Olton, 1977; O'Keefe and Nadel, 1978), are abolished after loss of the visual modality (Hill, 1979).

Although animals may well use auditory (Riley and Rosenzweig, 1957) and olfactory (Douglas, 1966; Rosen and Stein, 1969; Southall and Long, 1969; Slotnick and Katz, 1974) cues in maze performance and orientation, visual cues are likely to be especially important in generating a precise topographical representation of space. As long ago as 1936 Honzik reported deficits on elevated ("non-inclosed") mazes in rats blinded peripherally, and Beritoff's (1965) observations of spatial orientation in dogs further demonstrate that vision provides an animal with a great deal of spatial information and guidence of locomotor investigation and orientation , even in animals not considered to use vision as their primary sense.

Within the visual system, however, there are at least two neural subsystems potentially involved in spatial behaviour, the retino-collicular system and the retino-geniculo-striate system. In view of the suggestion (Schneider, 1968, 1969) that the SC represents a "second visual system" responsible for discriminating the positions of objects in space, it might be proposed that it has special responsibility for multimodal, topographical spatial encoding, and might thus be functionally related to the hippocampal formation. However since connections between the SC and limbic system are sparse (see Randall and Trulson, 1973) and the behavioural consequences of lesions of HPC and SC are demonstrably different (see Chapters 5 and 6), a strong functional relationship would appear unlikely to exist between them. In addition, the previous study (Experiment 7.1) showed that collicular rats were unimpaired in learning the radial maze, though the lesions were subtotal and animals were tested after a long postoperative interval. Thus the possibility of some functional recovery or reorganisation having taken place cannot be discounted.

On the other hand, Marks and Jane (1974) report that lesions of striate cortex render a cat or monkey incapable of what they call "ambulatory localisation", the ability to make appropriate locomotor orientation and approaches towards relevant stimuli (see also Dyer et al, 1975). Lesions of visual cortex were reported by Tsang (1934) to produce errors on elevated mazes, and visual cortex is known to have substantial anatomical connections with the hippocampal formation (Douglas and Isaacson, 1968).

Thus the present study was aimed at determining which of these structures is least dispensible for accurate radial maze performance, both during initial learning and post acquisition. A brief report of the present findings has been presented earlier (Foreman and Stevens, 1979).

7.2.2 Subjects

The 30 male hooded rats used as subjects were described in an earlier Section (5.1.2). The 3 day open field study reported in Experiment 5.1 was the only experiment in which they had participated. They were approximately 120 days old at the time of surgery (see Section 5.1.3), at which 6 were given bilateral posterior cortical (VC) ablations and 12 bilateral lesions of SC. A further 12 were sham-operated controls.

7.2.3 Apparatus and Procedure

The apparatus and test procedure are described in Section 7.1.3. Sixteen days after operation (during which food deprivation was introduced and open field testing took place), the entire group was given 2 days of pretraining followed by 12 days of testing on the radial maze. On the following day, the control animals were divided into 3 groups, 4 receiving bilateral VC, 4 bilateral SC and 4 bilateral control lesions. The latter consisted of removal of a small circle of cortex (approximately 1 mm diameter) overlying the superior colliculus. Otherwise lesions were made following the method described previously, SC lesions being made at an electrode depth of 3.2 mm below the surface of the brain. Animals were allowed a 7 day recovery period followed by 3 days progressive food deprivation, after which they were returned to the maze and tested for a further 6 days. Following completion of testing all animals were killed, perfused and the brain removed and sectioned as described in Section 5.1.5.

7.2.4 Results

7.2.4.1 Histology

Figure 5.2 shows the lesions sustained by the pre-acquisition groups. Discussion of the lesions is to be found in Section 5.1.6. Figure 7.6 shows the reconstructed lesions of animals operated after initial acquisition. Animal 97c died during the postoperative period and 100c died after 2 days of postoperative training. These two animals appeared healthy, had been eating without difficulty and causes of death were unknown. No animal showed signs of ill-health.

7.2.4.2 Behaviour

Figure 7.7a shows the mean number of arms visited in the first 8 choices for each group across 12 days of initial acquisition training. Analysis of variance revealed significant Group differences ($F(2,26) = 69.95$; $p < 0.001$) due to the poor performance of visual decorticates compared with both C ($p < 0.001$) and SC ($p < 0.001$) groups. However the SC group also performed

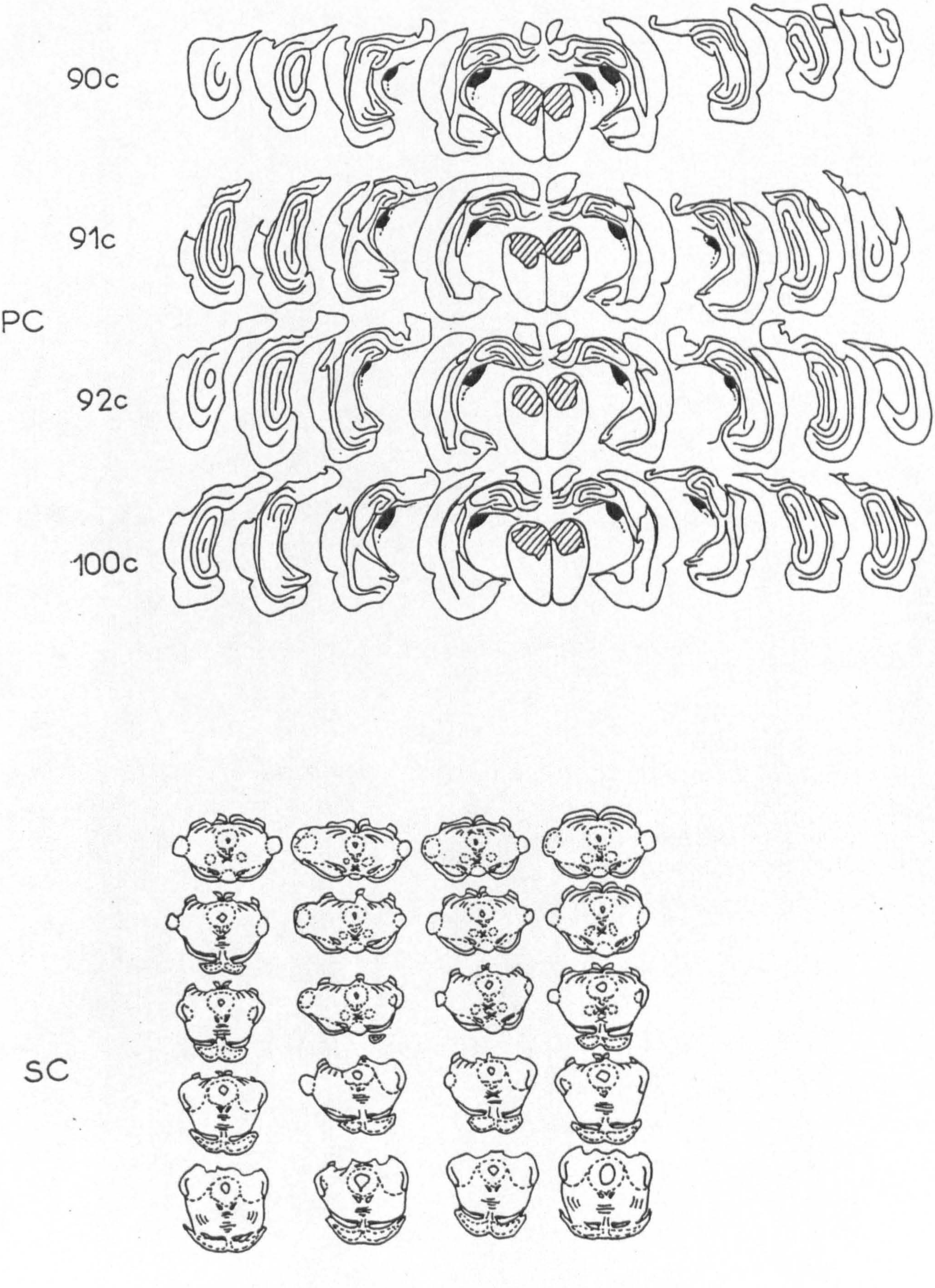


Figure 7.6
Reconstructions of posterior cortical and collicular lesions made postacquisition in Experiment 7.2

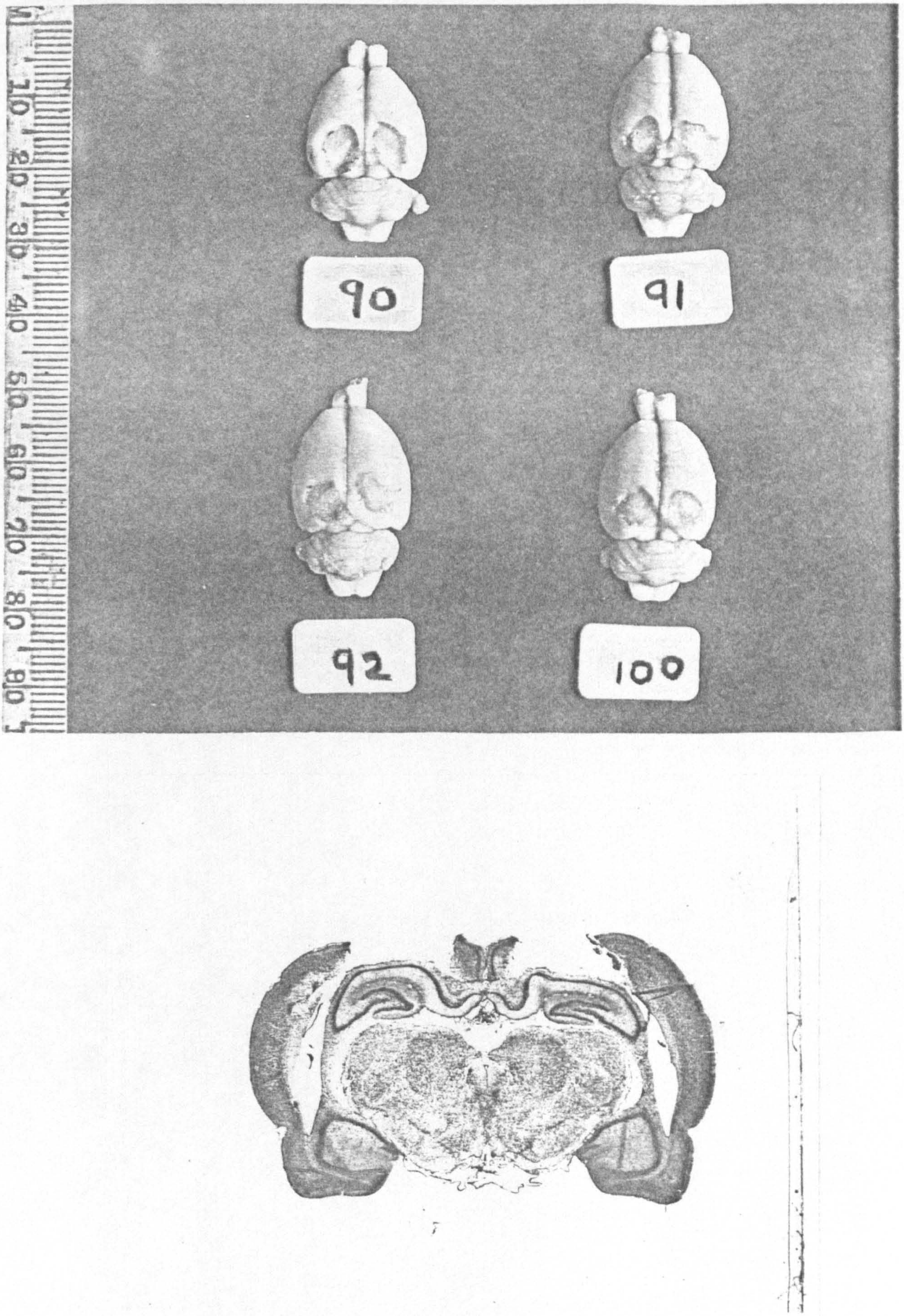


Figure 7.6b Posterior cortical lesions made postacquisition in Experiment 7.2. Below : coronal section through the brain of rat 90c.

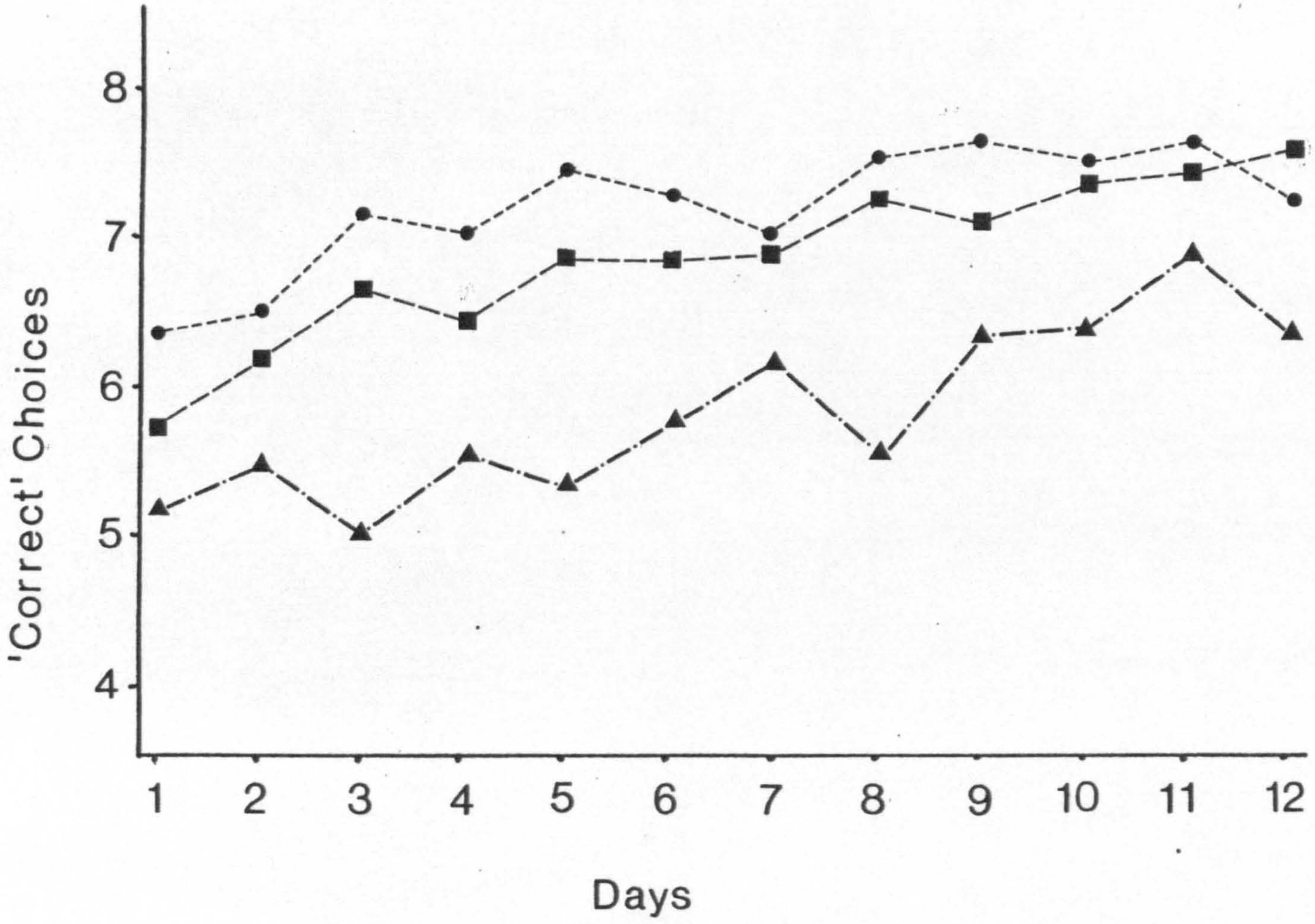


Figure 7.7a
Mean number of different arms visited in the first eight choices on test days 1 - 12 by control animals (●) and animals with lesions of visual cortex (▲) or superior colliculus (■) in Expt. 7.2. (initial learning).

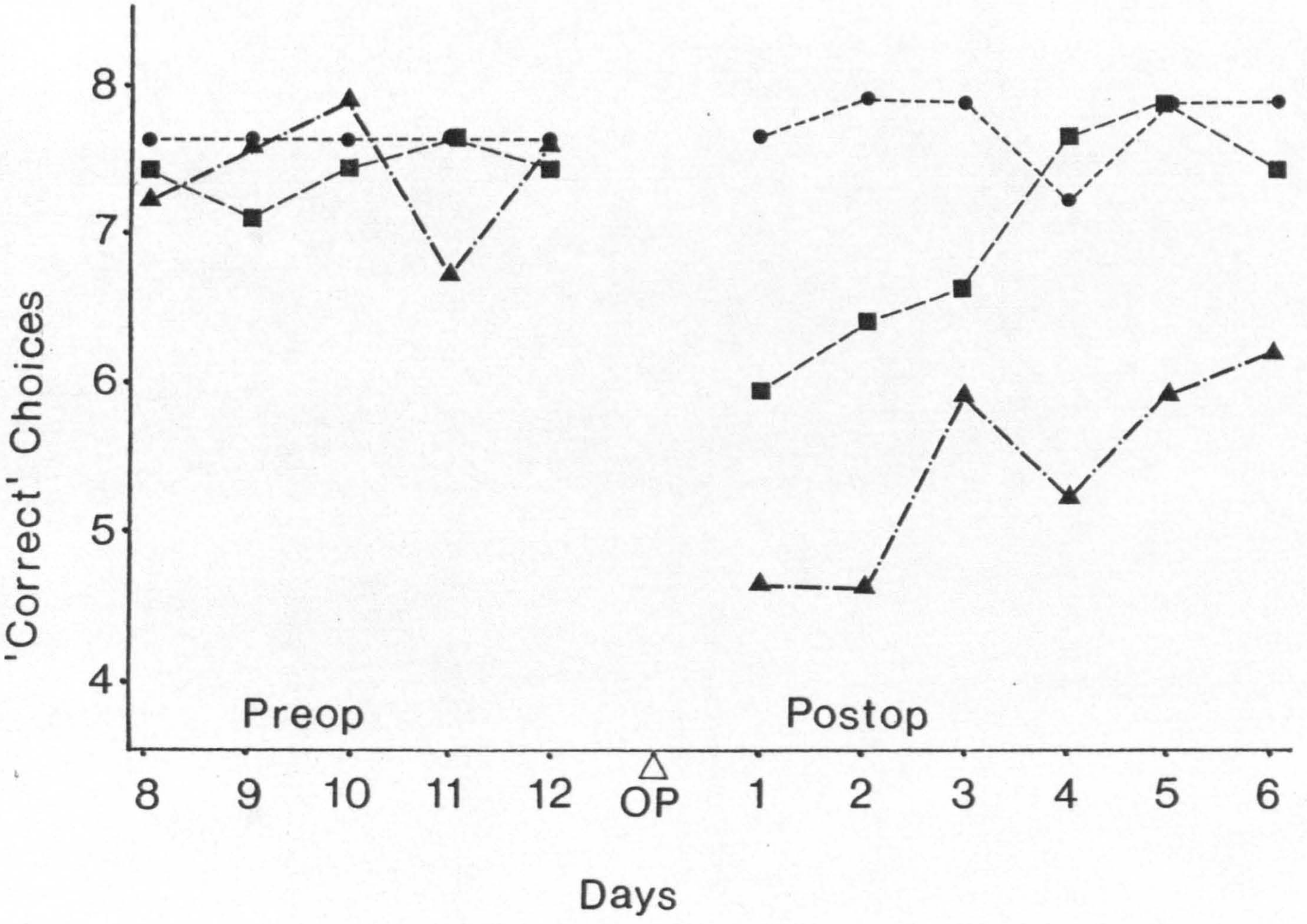


Figure 7.7b

Pre- and postoperative performances of animals given lesions of visual cortex, superior colliculus or control operations. (Symbols as for previous figure).

significantly worse than controls ($p < 0.01$). Performance improved significantly over test days ($F(11,286) = 9.84$; $p < 0.001$), though the Groups x Days term was not significant ($F(22,286) = 1.29$; $p > 0.15$) indicating that all groups improved equally with testing.

Figure 7.7b shows the pre- and postoperative performance of the original control group which received lesions following acquisition. Again the VC group was clearly deficient; analysis of variance (3 x 2 x 3; Groups x Blocks x Days, the two Blocks comprising postoperative days 1 - 3 and 4 - 6 respectively) revealed a significant effect of Groups ($F(2,7) = 35.46$; $p < 0.001$) due to the significantly poorer performance of the visual decorticates than either control or SC groups (p's < 0.001). Overall, the SC group did not perform significantly worse than controls ($p < 0.05$). Performance improved over blocks ($F(1,7) = 37.49$; $p < 0.001$) and almost significantly over days within blocks ($F(2,14) = 3.41$; $p < 0.065$). Improvement between blocks 1 and 2 was group dependent since the Groups x Blocks interaction term was significant ($F(2,7) = 14.93$; $p < 0.003$). Mann Whitney U-tests revealed that the SC group was significantly impaired by comparison with controls on postoperative test day 1 ($U = 0$, $p < 0.05$) though significantly less impaired than VCs ($U = 0$, $p < 0.05$). However collicular performance improved rapidly so that on postoperative test day 5, all colliculars and controls scored 8.0. The visual decorticates were still averaging 6.0, significantly worse than controls on each of days 4 - 6 ($U = 0$, $p < 0.05$ in each case), though SCs failed to differ from controls on any of these 3 days.

7.2.5 Discussion

The results clearly show that visual cortical destruction has a profound effect on radial maze performance while lesions of the superior colliculus produce a mild impairment. These findings are consistent with previous reports of visual cortical involvement in ambulatory localisation (Marks and Jane, 1974), locomotor approach behaviour (Dyer et al, 1976) and the learning of elevated mazes (Tsang, 1934). Though both visually-lesioned groups were impaired, the relative contribution of visual cortex to this task is likely to be much greater than the superior colliculus.

The result could be argued as evidence against Schneider's (1968) "Two Visual Systems" hypothesis; however while it is unclear which stimuli are being used and how they are used, it is not possible to claim that the visually-lesioned animals' poor performance necessarily arises from a strictly visuospatial deficit. Nonetheless, experimental manipulation of the visual environment in Experiment 7.1 (see also 7.3 below) strongly suggests that the radial maze task does depend to some extent upon visual functions. Indeed Zoladek and Roberts (1978) have shown that peripherally blinding well-trained rats produces a significant fall in performance, reducing the accuracy of "late" choices made at the end of a trial when most arms have already been visited . Thus it may be concluded that visual information (of whatever kind) used in the construction, or coding, of space is derived from visual cortex rather than the superior colliculus. Indeed, the collicular deficit may arise from disorganised locomotor behaviour previously reported by Foreman et al (1978) for colliculectomised rats, causing erratic and premature approaches to maze arms. Measurement of response latency might have been revealing, though those of the present animals which exhibited the greatest activity during Experiment 5.2 were no more impaired than those which did not. It must be concluded, therefore, that degree of "locomotor disinhibition" has a limited effect on radial maze performance.

The present results are particularly interesting in the light of Honig's (1978) distinction between "working" and "reference" memory (Jarrard, 1979; Olton and Papas, 1979). It was argued above (Section 7.1.6) that visual cues might be particularly important for reference memory, and thus radial maze deficits following lesions of visual cortex (but not, evidently, lesions of SC - see previous experiment) probably result from deficient reference memory.

Foreman and Stevens (1979) have pointed out that the radial maze task can be envisaged as comprising two stages:

(i) The tendency to spontaneously alternate

On initial introduction to the radial maze, normal animals perform at a level above that predicted by chance; indeed the apparatus might be considered to represent an enlarged version of the traditional 2-choice alternation apparatus (Olton, 1977), in which animals spontaneously locomote towards previously unvisited arms without prior training (see Douglas, 1966).

(ii) <u>The storage of information about the environment which enables an animal to discriminate apart visited from unvisited locations</u>

This stage of learning is envisaged as being superimposed upon the former and accounts for the gradual improvement of performance over successive test days.

Foreman and Stevens have argued that hippocampal and visual cortical lesions may abolish stages (i) and (ii) respectively (see Figure 7.8). Errors made by hippocampal animals occur early in the choice sequence (when the probability of making correct choices by chance is still very high). Such repetitive behaviour is characteristic of hippocampal subjects (see Chapter 4); they tend to make perseverative responses in barpress and runway (Douglas, 1967) situations, and, in particular, spontaneously alternate at chance level in massed trial conditions in a T-maze (Douglas and Isaacson, 1964; Stevens, 1973). Thus the radial maze deficit in hippocampals may result from the absence of the tendency to spontaneously alternate.

In contrast, visual decorticate rats probably retain the tendency to alternate. Peripheral blinding has been

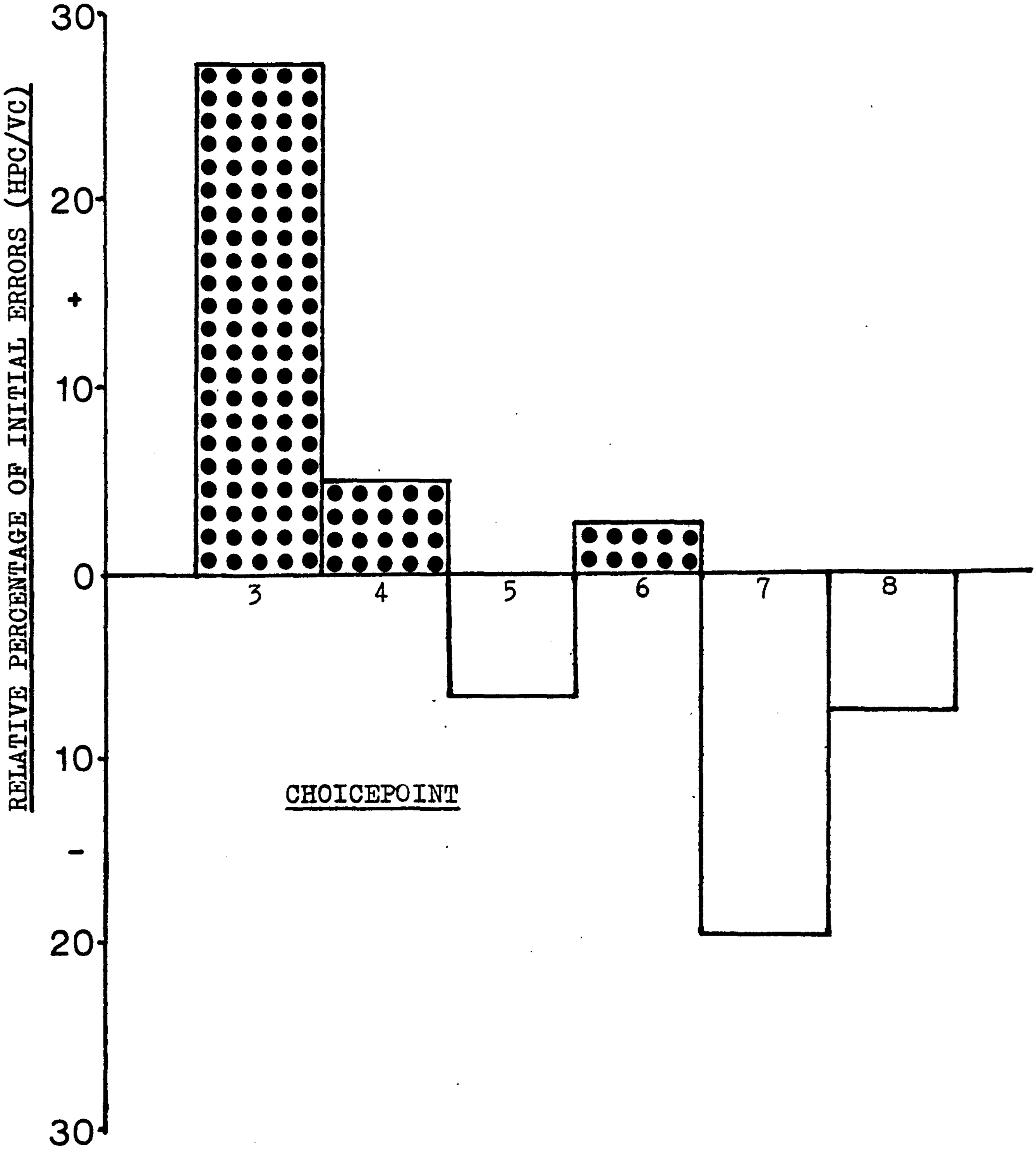


Figure 7.8
At each choicepoint (3-8, ie. successive arm choices), bar-length indicates the percentage of initial errors made by hippocampals MINUS the percentage of initial errors made by visual decorticates at that choicepoint; thus above the axis, HPC > VC; below, VC > HPC.

shown by Dember (1958) to have no effect on spontaneous alternation rates in a T-maze. Thus the late errors reported by Zoladek and Roberts (1978) for peripherally-blinded rats, and in this study for visual decorticates, may occur because animals deprived of striate cortex-pattern vision lack the fine discrimination to know "where they have been" and therefore "where to alternate to" when only a small number of locations remain unvisited.

Hippocampal animals would appear to be able to utilise visual cues particularly well (Stevens and Cowey, 1972), and they may apply visual coding strategies to the radial maze in the absence of spatial encoding; it is interesting in this respect that hippocampals will frequently adopt an "orthogonal" (but repetitive) strategy involving visits to four arms at right angles to oneanother (Olton, 1977 and previous experiment). Since orthogonal arms are visually unambiguous, this might be as good a strategy as visual coding alone will support. Furthermore, the performance of hippocampals was probably as badly affected by dark-testing as other groups' in the previous experiment. Degree of environmental enrichment in early development is one factor influencing the extent of the hippocampal radial maze deficit (Einon, Morgan and Will, 1980); such a manipulation might be expected to particularly affect reference memory and the primary use of sensory information.

The above model makes the clear prediction that increasing the number of maze arms should have particularly severe consequences for visual decorticate (or enucleated) rats, and that with a greater number of maze arms, or with a variable number of maze arms from day to day, visual cortical impairments would tend to approach the magnitude of hippocampal deficits. Surprisingly, such manipulations have not been employed to date.

The above model is roughly consistent with that of Jarrard (1978) if it is assumed that "spontaneous alternation-type" behaviour is controlled by output from working memory. Nontheless, it would be wrong to assume that working memory is not to some extent dependent upon visual cues, particularly when applied to a complex maze if not to 2-choice alternation. It would be interesting to know, for example, whether an animal trained on the radial maze in one environment but transferred to an entirely different environment (for example, a different room) would show any savings in reference memory, or whether performance would return to initial (day 1 acquisition) performance. To what extent performance on the radial maze involves the application of general, global principles, or rules specific to the species, environment or individual is clearly an area for further investigation. Moreover, it was clear from the results of the previous experiment that animals did not carry out the task in exactly the same way throughout testing, but gradually developed complex response strategies. For a rat it might be argued that in such a complex maze the animal's tendency to use nonvisual "place" strategies (O'Keefe and Nadel, 1978) is superceded first by the use of sophisticated visual (or other sensory) coding, giving rise to improved performance during the first 10 - 12 days of acquisition, followed by a tendency to seek alternative preferred, or more economical modes of response, possibly using kinaesthesis. The practical importance of this is that the effect of a lesion upon postoperative recall of preoperatively-learned performance may be crucially dependent upon the amount of preoperative testing. In particular it should not be assumed that the nature of the deficits in the initially-lesioned and post-acquisition -lesioned groups in the present study was the same. Tsang (1934), Lashley (1943) and Orbach (1959) have found that while blinded monkeys and rats are slower in learning locomotor maze tasks than controls, additional, superimposed visual cortical ablation produces a consistent further deterioration. This suggests that visual cortex "serves as a substrate for non-visual orientation involving a locomotor sequence" (Orbach, 1959). Dale and Goodale (1979) have shown that in the rat, posterior cortical removal produces both pre- and post-acquisition deficits on the 8-arm radial maze, in the former case equalling, and in the latter enhancing deficits produced by peripheral enucleation. This suggests that vision is especially required in the early stages of learning (see also Orbach, 1959) but that posterior cortex may, in a more general sense, be the repository of the hypothetical "spatial schema" once generated. Thus spatial behaviour, while dependent upon the integrity of visual cortex may become progressively less dependent upon visual input after prolonged testing. Whether this lack of dependence upon vision occurs as a result of the development of observable strategies is unclear. Consequently, the removal or rearrangement of room cues in early and late training will be examined in the following experiment, when response styles of individual animals (Eckerman, 1980) will be examined in detail.

Conclusion

Large lesions of posterior cortex including area 17, but not lesions of the superior colliculus caused rats to make many "late choice" errors on the radial maze. It was concluded that visual information utilised by spatial coding mechanisms derives from visual cortex rather than the colliculus. Furthermore, though hippocampal and visual cortical lesions produce radial maze deficits they may do so by affecting different components of the task.

7.3 The Effects of Environmental Manipulations upon Overtrained Radial Maze Performance

7.3.1 Introduction

The importance of the visual modality for radial maze performance was suggested by the above experiment, since eliminating visual cues, for example by testing in darkness,resulted in considerable response decrements- a result which has been obtained previously (O'Keefe, 1976; personal communication). However rearrangement of room objects was nondisruptive so it is unclear which stimuli the animal utilises in forming a representation or "spatial map" of the test room; the result of Experiment 7.1 argues against the use of specific room-cues as "labels" for particular locations. Thus it is important to ask whether there is any kind of environmental ambiguity which would bring about the disruption of radial maze performance in well-trained rats in normal lighting conditions.

The detrimental effect of testing in zero illumination in Experiment 7.1 may have occurred purely as a result of the generally distracting influence of such a gross environmental change. In fact this is unlikely since it was noted that in darkness all animals ran swiftly, failed to delay choice of maze arms, showed no reluctance to run initially or between choices and failed to exhibit excessive investigation, defaecation or any other behaviours which usually occur when a rat encounters a grossly novel situation. Nonetheless, to further investigate the rat's ability to perform the task in darkness, in this experiment rats were given more prolonged dark-testing; clearly, if the radial maze task is soluble in darkness, performance would improve once subjects had become familiar with the darkened environment. Since hippocampal "place units" (O'Keefe and Dostrovsky, 1971) have recently been shown to exhibit a predilection for multimodal stimulus arrays (Hill, 1979) it is entirely feasible that such spatial tasks could be carried out on the basis of non-visual cues, at least to a moderate degree of accuracy. Finally, all room cues were to be rendered ambiguous by rotation of the maze through a small angle.

The effects of small posterior cortical lesions on initial learning was also investigated in this study in order to determine whether the disruptive effects of very large ablations was due to the inflicting of nonspecific damage upon posterior neocortex, or whether the deficit arises specifically from the removal of a particular "spatial focus",eg.striate cortex. Furthermore, the present study was intended to shed light upon the nature of the deficit observed in visually-lesioned groups in the previous experiment.

7.3.2 Subjects and Surgery

Subjects were 8 experimentally naive male Lister hooded rats, maintained as described in Section 5.1.2. They weighed approximately 400 gm and were approximately 190 days old at surgery. Testing commenced 3 weeks postoperatively. In half of the subjects small posteromedial cortical lesions were made by subpial aspiration. The remaining 4 served as sham-operated controls. All treatments and procedures were as described in Section 5.1.3.

7.3.3 Apparatus and Procedure

The same apparatus and procedure was employed as in Experiment 7.1 on days 1 - 12, 16 - 22, 24, 26 - 31, 33 - 36. Testing in zero illumination occurred on days 13 - 15 and day 32, and rearrangement of room cues on day 37, exactly as in Experiment 7.1. On day 38 room cues remained in the same position as on day 37. The entire maze was rotated about its centre on days 24, 25 and 38. On day 24, it was turned through 45° (thus interchanging the positions of individual maze arms yet maintaining its overall position in the room). This procedure served as a control for day 25 when the maze was rotated through $22\frac{1}{2}^{\circ}$ (this being half of the angular separation between adjacent arms), thus rendering all room cues ambiguous with respect to arm positions. Following this, the maze was moved back to its original position for subsequent testing until day 38 when it was again rotated through $22\frac{1}{2}^{\circ}$.

7.3.4 Results

7.3.4.1 Histology

The four cortical lesions were small (Figure 7.9); only in the case of V4 was substantial damage inflicted upon striate cortex. -

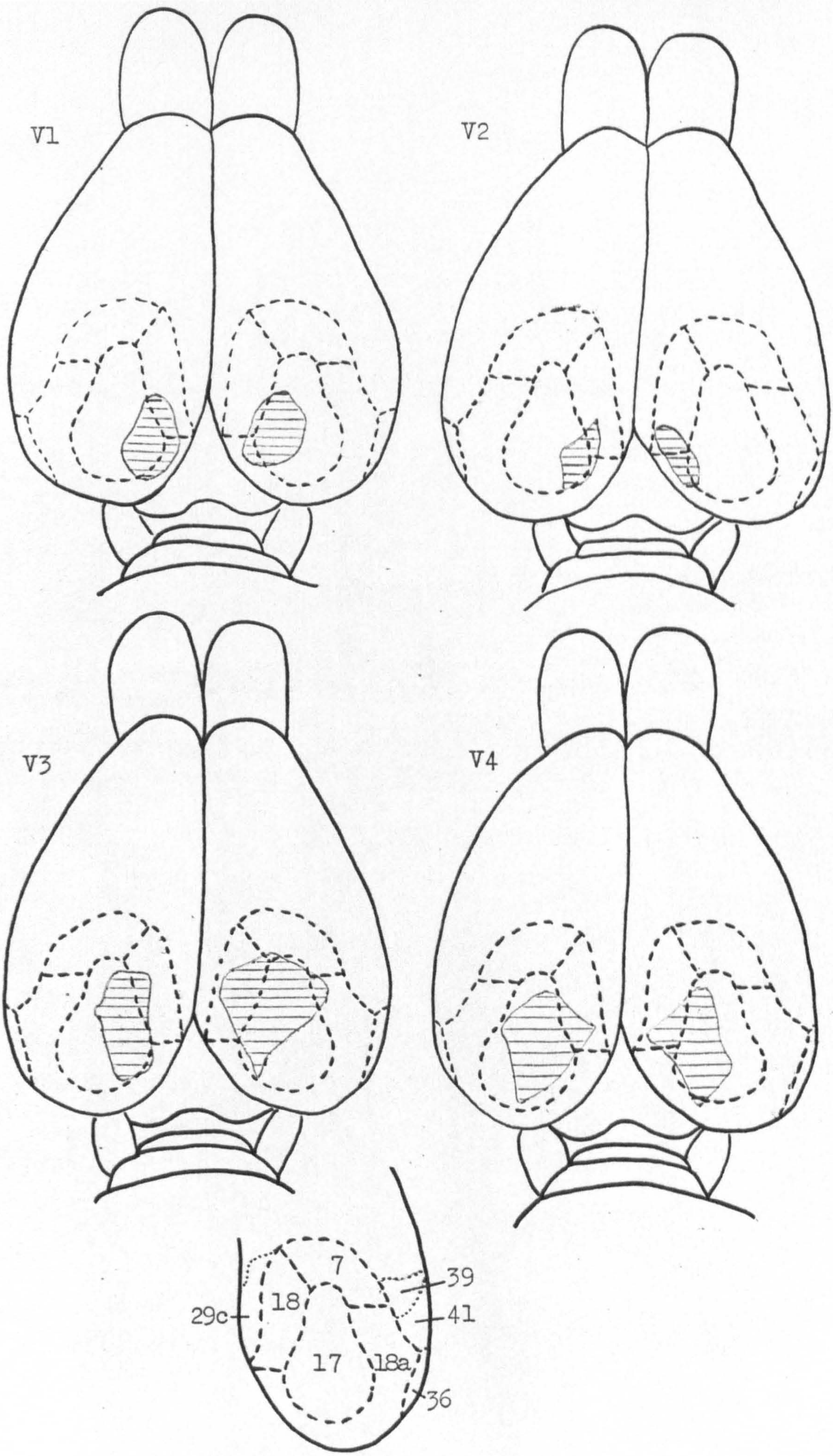


Figure 7.9
Small posterior cortical lesions used in Experiment 7.3. Extent of the lesion is indicated by hatching.

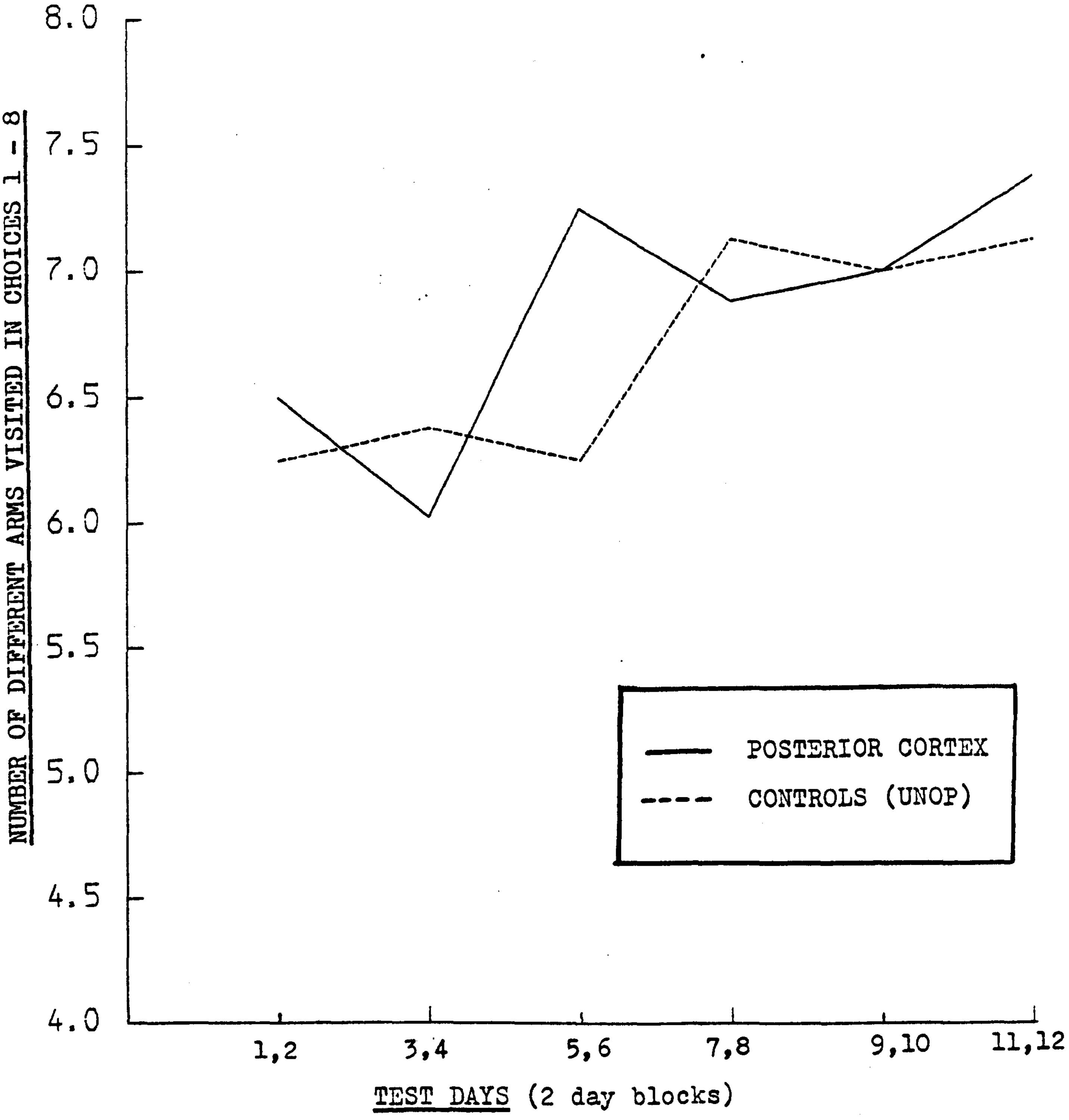


Figure 7.10
Mean radial maze scores on successive 2 day blocks for posterior cortex-lesioned and unoperated control rats in Experiment 7.3.

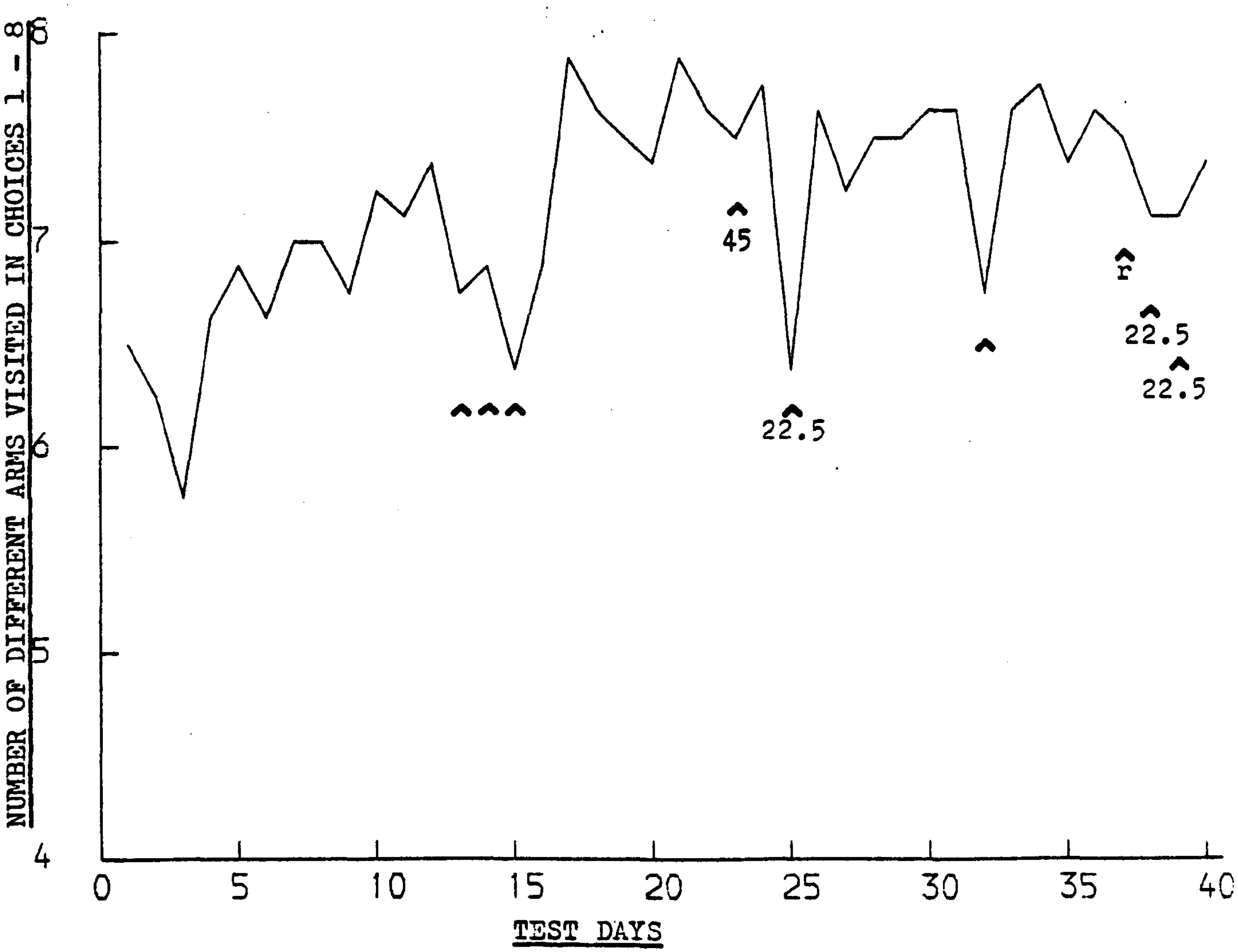
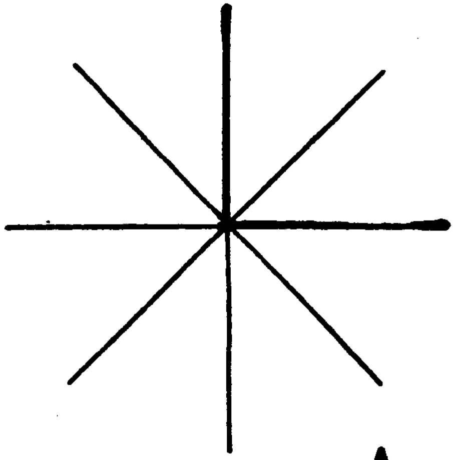
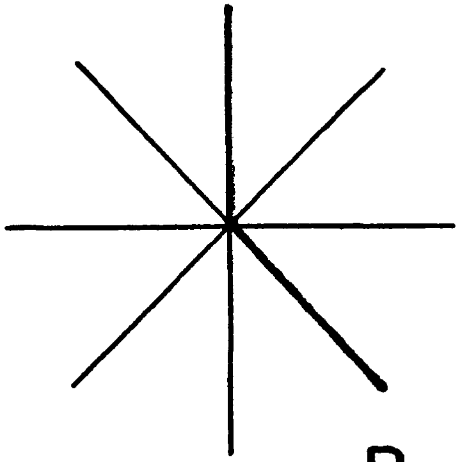


Figure 7.11
Mean score on days 1 - 40 for 8 rats in Experiment 7.3. Dark-testing is denoted by ^, room rearrangement by $\hat{r}$ and maze rotation by $\hat{n}$, where n = the number of degrees by which the maze was rotated (about its centre) from its original position.

Table 7.1a
Examples of sequences of arm choices (1 - 8) on three successive normal test days. Sequences showing algorithmic patterning are underlined. Dominant response style (DRS) is indicated by letters A - C, corresponding to the turning tendency depicted below. Brackets indicate that the sequence gave a strong suggestion of an incomplete algorithm.(Note: criterion number of successive responses required to constitute algorithmic behaviour = 4).

	Day 27			Day 28			Day 29		
Animal	Choices	Score	DRS	Choices	Score	DRS	Choices	Score	DRS
C1	25741682	7	B	64825374	7	-	24716538	8	-
2	36814782	7	-	37824617	7	A	25781467	7	-
3	21865426	6	(C)	86531847	7	-	21876542	7	C
4	63175284	8	A	73164285	8	A	63174852	8	-
V1	24683571	8	A	24713581	7	A	83614725	8	B
2	62483571	8	A	74825613	8	-	74825736	7	-
3	37147258	7	B	62748513	8	-	57136824	8	A
4	25274163	7	B	38257146	8	-	14736158	7	(B)


A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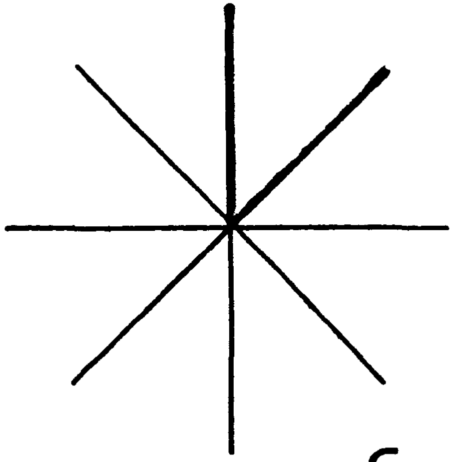
C

Table 7.1b
Sequences of arm choices (1 - 8) on 2 normal days (24 and 26) and 2 days on which the test environment was modified by maze rotation (day 25) and dark-testing (day 32). Details as for previous table.

	Day 24			Day 25			Day 26			Day 32		
	(Normal)			(Maze rotated 22.5^{0})			(Normal)			(Zero illumination)		
Animal	Choices	Score	DRS	Choices	Score	DRS	Choices	Score	DRS	Choices	Score	DRS
C1	25713486	8	A	73264173	6	-	58274163	8	B	63175284	8	A
2	63175284	8	A	24678234	6	-	25783461	8	-	15724682	7	A
3	21654378	7	C	21754248	6	-	65418731	7	-	74176348	6	-
4	85174263	8	-	63852741	8	B	84275163	8	-	73741752	6	-
V1	35714682	8	A	46824781	6	A	58246135	7	A	73615737	5	-
2	63587421	8	-	82468235	6	A	14725836	8	B	84625835	6	B
3	35782613	7	-	46782413	7	-	64825716	7	-	72485631	8	-
4	14852736	8	B	62584726	6	-	15263748	8	-	84163572	8	B

7.3.4.2 Behaviour

Analysis of variance was carried out on the number of different arms visited in choices 1 - 8 on each day for the first 12 days of testing. No suggestion of a difference in performance between the cortical and control animals was obtained ($F(1,6) = 0.53$; $p > 0.45$) though both groups improved significantly between days 1 and 12 ($F(11,66) = 2.55$; $p < 0.01$), as shown in Figure 7.10.

For all subsequent manipulations, data from both groups was combined and the Wilcoxon signed rank test used to compare scores on treatment days with those on the immediately preceding non-treatment day. Since all manipulations were expected to reduce performance, 1-tailed probabilities are given throughout.

Testing in darkness on days 13 - 15 caused a very clear depression of performance though not all animals' scores fell on any one day. However when individual mean scores on days 13 - 15 were compared with corresponding scores on the previous pretreatment day (12), the fall was found to be significant ($T(6) = 1.5$; $p < 0.05$). This is especially impressive since animals had not yet reached asymptote, and performance was still improving at this time. Performance partially returned to normal by day 16 and was significantly better on day 17 than on day 15 ($T(7) = 0$; $p < 0.01$). Rotation of the maze through 45° on day 24 produced no change in performance, though rotation through 22.5° on day 25 did produce a marked fall ($T(6) = 0$; $p < 0.025$). Performance returned to normal on the following day when the maze was returned to its original position. Further testing in darkness on day 32 again reduced the level of performance but only in 5/8 animals and the effect was not significant ($T(6) = 5.0$, $p > 0.05$. Crit. $T = 3.0$. See Table 7.1b). Rearrangement of room cues on day 37 clearly produced no change in performance, only one animal scoring lower on day 37 than on day 36, though additional rotation of the maze by 22.5° on day 38 produced a fall in performance compared with the previous pretreatment day (36) which was almost significant ($T(6) = 3$, $p > 0.05$. Crit $T = 2.0$). Closer inspection of the data failed to reveal group differences in response to environmental manipulations; nor was there any apparent relationship between lesion size and susceptibility to disruption in the cortically-lesioned rats.

As in Experiment 7.1, animals again tended to use a variety of response styles which tended to appear and disappear from day to day. The long period of training in this study provided an opportunity for runstyles to be carefully monitored. Some animals oscillated between two or more dominant response styles, while others exhibited short bursts of a particular runstyle. The behaviour is too frequent and systematic to have occurred by chance, though clearly a random pattern of choice will occasionally give rise to an apparent structuring within the response sequence. Table 7.1 shows the sequence of arms visited during choices 1 - 8 for each animal on selected days. Various forms of response patterning were adopted on day

27 by animals V1, V2, V3 and to a lesser extent V4 and C4. However, most of these styles disappeared on day 28 when only animals V1, C1 and C2 appeared to be using response patterning (on this occasion, of the orthogonal type). On day 29 substantial patterning is again evident though notably the strategies employed by individual rats on day 29 are often quite different from those employed on day 27. For example animal C3 chose consecutive arms on day 29 (having not done so previously) while animal V1, having used an "orthogonal" pattern on day 27, adopted a 135° turn pattern on day 29. Animal V3 did the reverse, choosing a 135° turn pattern on day 27 and orthogonal patterning on day 29. From Table 7.1b it is clear that some patterning occurred during testing with environmental manipulations though in only one case (C4, day 25 : maze rotation through 22.5°) was it possible that adoption of a particular response pattern throughout a trial actually generated a high score in adverse visual conditions. This case is further complicated by the fact that the 135° turn pattern adopted was uncharacteristic for that animal (see Table 7.1b); furthermore that this animal's performance was disrupted by testing in darkness on a later day (32). A number of animals obtained high scores while not using, or partially using, ostensible patterning; others (eg. animal V3, day 32 : zero illumination) achieved high scores in adverse visual conditions without using patterning.

Discussion

The first section of the experiment demonstrated that small posterior cortical lesions do not produce radial maze deficits. The result suggests that the small cortical lesions in control animals in Experiment 7.1 were probably not sufficient to have depressed the normal performance of that group; also that in other studies employing large posterior cortical ablations (Dale and Goodale, 1979; Experiment 7.2) radial maze deficits most likely arose from the specific, total removal of striate cortex (area 17) rather than nonspecific cortical loss.

The present study has also shed some light upon the cues which are used in the performance of the radial maze task. Clearly, the performance of this task is not based upon simple rules; animals use a variety of response strategies, or patterns, which are apparently adopted and discarded in a complex fashion; the use, or partial use of such patterning is surprisingly unrelated to animals' final accuracy score, even in adverse visual conditions. As noted previously, on rare occasions the adoption of patterning may apparently immunise performance from the effects of visual manipulations. In others, it may have led, during dark-testing for example, to repetition of arm visits reminiscent of choice behaviour in hippocampally-lesioned rats in normal testing conditions (Olton, 1977; Experiment 7.1). In the case of rat V2 on day 25, it would appear that the cue(s) which the animal had presumably used previously to make a complex spatial discrimination (switching between two orthogonal subsets of maze arms) were unavailable due to the 22.5° rotation of the maze and this animal (which had been reliably scoring 8) was induced to make uncharacteristic, repetitive errors, repeating part of a previously-visited orthogonal sequence of maze arms. Thus the view put forward in the previous experiment that the development of "patterning" might be responsible for the apparently reduced dependence of radial maze performance upon vision after prolonged training is clearly contradicted, in that the two are in some cases complementary. However, the role of vision may change with prolonged training. It is clearly demonstrated by the above results that accuracy of performance is not entirely dependent upon the availability of visual cues, particularly on later test days[1].

These results obviate the difficulties in classifying animals according to their idiosyncratic style (ie.response patterning), since this is unreliable both between days and within individual trials. The finding is particularly significant since Eckerman (1980) has argued that "response bias" (ie. "patterning") precludes the use of spatial encoding:

> "...an algorithm response bias, or patterning does not select arms on the basis of whether food has or has not already been removed and cannot, therefore, be taken as evidence for spatial memory".

However the present results have shown that such algorithmic responding sometimes involves complex spatial discriminations

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[1] The relative ineffectiveness of visual manipulations at later stages of testing may be attributable to animals' habituating to changes in the visual environment, though the lack of "orienting" behaviour on such test days suggests that novelty *per se* was not the primary cause of disruption,

and is rendered inefficient by the elimination of visual or visuospatial cues. Eckerman goes on to argue that statistical procedures used to evaluate radial maze performance should take response bias into consideration. He argues that following each response, still-unvisited arms should not be considered equally likely to be visited on the following choice but should be weighted by a "preference factor" based upon any response bias evident in the animal's previous responses. This is difficult to apply, particularly in the case of "orthogonal" choice patterns, and patterning was intermittent and unreliable in the present study. Furthermore, an animal's particular response style only becomes evident after about three or four arm visits. It would seem to the present author that such a statistical model is a poor approximation to an animal's choice behaviour. Such computations contribute nothing to our understanding of the strategies used by individual animals to complete the task. It would seem that (especially in the case of an animal which displays strong algorithmic behaviour) a rat's use of spatial coding or nonspatial strategies can be reasonably inferred (see above), and that careful observation and analysis of an individual animal's choice behaviour is irreplaceable.

The data powerfully point to a role for vision in performance of the task, though not equally in all animals, and not in the sense of guiding every response via specific visual "labels" which identify particular maze arms. The latter is unlikely since in Experiment 7.1, performance was unaffected by extensive rearrangement of room cues. Though all animals performed worse during a 3-day period of dark-testing, and all but one were unimpaired when extramaze cues were rendered ambiguous by 22.5^{o} maze rotation, performance did not fall to chance level, or (as in the case of some hippocampal rats) to below chance level, but rather approximated day 1 performance. Animals tended to score about 6.5 which is similar to the performance of preoperatively-trained enucleated rats (Zoladek and Roberts, 1978). The result further supports a two-tier system of organisation, with a mechanism governing high-level performance superimposed upon a more fundamental mechanism (see previous experiment). Whether normal rats are capable of initially learning the radial maze when continuously tested in darkness is clearly worthy of investigation though since enucleated rats have been shown to suffer a permanent deficiency (Dale, 1978; personal communication) it is unlikely that they would. It is unclear whether the deficit in enucleated rats, or those tested in darkness, reflects a need for specifically visuospatial coding during the initial stages of training (eg. in the organisation of memory) or a more global disorientation and inability to behave towards the apparatus in an organised fashion.

Since maze rotation through 22.5^{o} but not room cue reorganisation produces such a clear disruption of behaviour, it is likely that overall spatial layout (perhaps related to the edges and corners of the room) may be especially important for defining a spatial framework, though the criteria upon which such cues are selected remains unclear.

Though an attempt was made in the present study to rearrange the most "salient" roomcues, those which appear most salient to the human experimenter may not be the most significant cues for the rat. It is perhaps surprising that so little is known about the type of cue used by animals in spatial tasks. O'Keefe and Nadel (1978) conclude that

> "...distal cues are important for specifying directions since they do not change relative positions as the organism moves in its local environment; on the other hand, this very property means that distal cues, by themselves, cannot distinguish among places in that environment. Places would seem to be defined by extra-maze cues which are close enough to the animal for its movement to change the angles between them but not so close that movement causes changes in their spatial ordering"

In the present study, such moveable cues as the litter bin, experimenter and shelving would appear to meet these criteria yet movement of these cues such that their spatial relationships changed failed to give rise to impaired maze performance. Rats' performance in a visually homogeneous environment would be interesting in this regard.

The results of this and previous work (see Olton, 1977) suggests that spatial organisation is a very fundamental aspect of behaviour. My own observations suggest that, for example, a young child asked to give a sweet to each one of a number of people seated round a table may be capable of doing so accurately, without making repetitive donations to a single individual, will choose rather randomly between individuals and yet afterwards is unable to remember each of the people present having insufficient grasp of the concept of number to enumerate them. Such behaviour bears obvious resemblance to that shown by animals on the radial maze and suggests that working spatial memory might be a very early-developing, or even "preprogrammed" faculty. Interesting in this respect is the suggestion by Trevarthen (1972) that the superior colliculus may play a role in generating "space structuring" in neonatal (precortical - see Bronson, 1974) life, providing an integrated framework within which "higher" perceptual functions develop. Thus the relationship between collicular and limbic/spatial development in perinatal life might be especially strong. However it is clear from the present results that collicular involvement in adult spatial behaviour (at least, as measured in rats by the radial maze task) is minimal.

7.3.6 Summary and Conclusions

Rats with small posterior cortical lesions learned the radial maze task as readily as controls. All animals showed a reduction in performance when tested in darkness at a pre-asymptotic stage and 5/8 did so when the same procedure was employed on day 32. This suggests that vision is involved in radial maze performance but may become less so with prolonged training. Choice bias, or "patterning" was not static or idiosyncratic, and was surprisingly unrelated to performance in darkness or in the presence of visual-spatial ambiguity, during both of which group performances fell. Rearrangement of room cues failed to produce a drop in performance. Animals appear to differ in their performance strategy from day to day, and the use of cues may differ substantially between subjects.

CHAPTER 8

VISUAL DISCRIMINATION LEARNING

8.1 Postoperative retention of Light-Dark Discrimination in rats with SC and MFC lesions

8.1.1 Introduction

Bilateral lesions of the superior colliculus have not generally been reported to produce deficits in learning new visual discriminations in rats (Layman, 1936; Dyer *et al*, 1976) though in cats (Casagrande *et al*, 1972; Casagrande and Diamond, 1974) and monkeys (Vetter, 1975; Marzi and Latto, 1976), such have been observed. In monkeys, the deficit may result from absent or impoverished "detailed spatial analysis" of stimuli (Marzi and Latto, 1976).

However collicular rats have been reported to exhibit substantial postoperative deficits in the retention of a variety of preoperatively-learned visual habits (Barnes *et al*, 1970; Goodale and Murison, 1975; Murison, 1977; Weinberg and Stein, 1978; Milner *et al*, 1979) perhaps resulting from a degree of locomotor disinhibition (Murison, 1977). Indeed Winterkorn (1973, 1975) working with cats, and Schneider (1968) with hamsters have reported situations in which collicular animals make erratic locomotor approaches towards discriminanda. In the former case the behaviour was also shown by medial-frontally-lesioned (FEF) cats, which led Winterkorn to suggest that the SC and FEF are separate components of a descending inhibitory system operating via the brainstem to regulate motor behaviour. Indeed both FEF and SC project to the brainstem (Kuypers and Lawrence, 1967; Leonard, 1969; Künzle and Akert, 1973; Kawamura et al, 1974) though the former send fibres predominantly to non-reticular pontine nuclei and the latter to more dorsally-situated reticular nuclei in the pons and medulla. Furthermore, lesions located in the pons do give rise to visual discrimination deficits (Thompson, 1979), though it is not necessarily due to "locomotor disinhibition". It is interesting in this respect, that the clearest "approach error" behaviour in Schneider's (1968) hamsters was seen in animals which had knife cuts deep within the structure and in which fibres of the descending predorsal bundle may have been most extensively interrupted. This pathway may be especially important in mediating tecto-reticular motor control (Foreman et al, 1978).

Winterkorn (1973, 1975) found that when cats are trained in a Y-maze using a 60° spatial separation of discriminanda collicular animals showed no greater impairment than controls. However Milner et al (1979) have shown that collicular rats are more sensitive to changes in stimulus position than controls; for example when discriminanda are suddenly displaced vertically above their position during training, colliculars' discrimination performance is seriously impaired. Collicular animals are thought to be deficient in their ability to shift attention to peripheral cues (Goodale et al, 1978).

The "approach error" behaviour of SC cats observed by Winterkorn was obtained both on initial learning and postoperative retention of both light v dark and horizontal v vertical stripe discriminations, though it was most obvious on postoperative retention. It should be noted that the effect was reported to be especially evident at near-criterion performance; indeed the size of the deficit may have been exaggerated by the prodecure employed by Winterkorn which involved titration of performance at successive levels of difficulty. This may have had the effect of maintaining animals at "near criterion" performance for long periods of time. In addition, "approach errors" were numerous in control animals, perhaps reflecting their strong tendency to correct some responses at a late stage of approach, and Winterkorn's more recent finding (Winterkorn, 1978) that striate cortical ablation also gives rise to "approach error" behaviour further emphasises the generality of such behaviour. It is unfortunate that no controls were carried out by Winterkorn to test for the use of non-visual strategies, particularly since rewards consisted of meat chunks which cats may have been able to (or, at least may have attempted to) localise on the basis of olfaction. On intuitive grounds one might expect that permitting "approach error" correction enables greater sampling of, and comparison between, positive and negative cues and that this particularly invites the use of nonvisual strategies. Thus in the present study, postoperative retention of preoperatively learned light v dark discrimination was examined in rats with SC, MFC or control lesions, performance being measured in terms of approach and doorpress responses. Following retraining to criterion, controls for non-visual strategies were carried out.

8.1.2 Subjects

The 21 rats employed in this study have been described in Section 5.3.2. They were experimentally naive prior to participation in this study and were approximately 100 days old at the commencement of testing.

8.1.3 Apparatus

This consisted of a modified Grice box (Figure 8.1) comprising a startbox 28 cm x 13 cm x 36 cm separated from a choice area by a clear perspex guillotine door. The choice area which was painted matt black throughout was bounded by two side walls 36 cm high and a panel measuring 36 cm^2 facing the mouth of the startbox at a distance of 30 cm from it. On the panel were located two top-hinged clear perspex 9.5 cm^2 goaldoors with stimulus cards attached to the back magnetically.
The outer edge of each goaldoor was 4 cm from the side walls. A sheet of dark-coloured paper pasted to the perspex start box door prevented the animal from viewing the goaldoors while confined in the start box prior to the start of a trial. Pushing a goaldoor gave access to a circular foodwell (1.5 cm diameter) located

immediately behind the goaldoor when the latter was in the "closed" position. Food reward consisted of 2 x 45 mg saccharin pellets placed in a foodwell. A partition 10 cm long projected back into the choice area from the midpoint of, and perpendicular to, the panel. Thus in this apparatus, correction of an approach to an incorrect goaldoor required a substantial detour. Stimuli consisted of squares of white, and black, card which covered the entire goaldoor and which were held securely in place magnetically by aluminium plates. Illumination of the apparatus was provided by a ceiling-mounted 70 watt fluorescent strip light and a low level of masking noise was provided by air conditioning fans.

8.1.4 Method

Animals were transported to the testroom in their home-cages in squads of 6. At the start of a trial, an animal was removed from the cage and placed in the startbox facing the exit. The guillotine door was raised gently but rapidly, after which the rat was free to run to either goaldoor. Pre-training consisted of training the animal to push both goaldoors (which were at this point both fitted with neutral grey stimulus cards), equal experience of each door being ensured. The animal was removed from the apparatus immediately after consuming the reward pellets and replaced in its cage. Following 2 days of pretraining, testing commenced using black-white discriminanda previously described, the white stimulus being positive for all subjects.

E noted accuracy of the first doorpress. Animals quickly learned to run to the opposite side of the barrier on pressing an incorrect door. In addition "approach errors" were recorded when an animal ran to the incorrect side of the barrier (criterion being that head and front paws had to cross an imaginary line perpendicular to the end of the barrier), and corrected by running to the opposite side <u>without</u> pressing the incorrect goaldoor. The usual procedure for use with such an apparatus, in which both foodwells are baited and the negative stimulus door locked, could not be employed here since both approach <u>and</u> doorpress errors were to be recorded.

Following each trial, E removed urine or faeces from the apparatus which was wiped out thoroughly with a 2% acetic acid solution. Ten trials were given each day, and testing continued until all animals had reached a doorpress error criterion of 90% correct over 3 successive days [1]. The sequence in which L and R goaldoors held the positive stimulus was pseudorandomised according to the schedule of Gellerman (1933). When all animals had reached criterion, they were placed

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[1] A three day, 90% criterion was adopted by Winterkorn (1975a) though she used 40 trials per day. This was not feasible using a large group of rats. In addition, Winterkorn's animals obtained all their daily feed during testing.

on ad libitum feeding for at least 16 hours prior to surgery. They were then given bilateral lesions of the SC (n = 7), MFC (n = 7) or control cortical lesions (n = 7) as described in Section 5.3.3. Postoperatively all animals were retrained to a criterion of 18/20 correct doorpush responses. Following this each animal was given two further trials with identical grey stimulus cards on each goaldoor, but with only one door baited with food. On one trial the left door was baited and on the other the right.

8.1.5 Results

8.1.5.1 Histology

The lesions sustained by animals in this study have been described previously (Section 5.3.4.1).

8.1.5.2 Behaviour

Table 8.1 shows the number of doorpress responses and number of approach errors made by each animal during pre- and postoperative testing. Preoperatively groups failed to differ in terms of number of trials taken to reach criterion or tendency to make "approach error" responses. Postoperatively, all groups ran to incorrect goaldoors on about 40% of trials, though in half of these the incorrect approach did not lead to an error press but resulted in a corrective detour to the opposite goaldoor, i.e. an approach error [1]. All groups were thus performing at approximately 80% correct, in terms of doorpush errors, immediately postoperatively. All groups relearned swiftly, reaching doorpress criterion (18/20) in 30 - 50 trials. No group differences were evident postoperatively on any measures (t-test for independent samples; all $p's > 0.05$). In particular the SC and MFC groups failed to make more doorpress or approach errors in relearning than controls, and failed to make a greater proportion of approach than doorpress errors.

Replacing the discriminanda with identical blank goaldoors for 2 trials per animal resulted in a total of 42 choices (21 animals by 2 trials) not under guidance of the discrimination stimuli. Of these 21 resulted in responses to the food-baited side while of the remaining 21, 10 approach "errors" and 11 doorpush "errors" were recorded. Thus on 10 out of 21 occasions when animals ran to the unbaited side, they turned without responding, "corrected" their run to the opposite side whereupon they pressed the baited goaldoor without hesitation. Thus of 42 trials with blank

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[1] In Table 8.1 as elsewhere, the term "approach error" is specifically reserved for instances in which approaching a negative goaldoor did <u>not</u> result in a doorpress but instead a corrective detour to the positive goaldoor. All presses of the negative goaldoor, while clearly involving approach, are referred to as "doorpress errors". Detours from a positive to a negative goaldoor were extremely rare and do not feature in calculations.

		PREOPERATIVE		POSTOPERATIVE		
	Animal Number	No. of App'ch Err's in 30 trials prior to reaching crit'n	Trials to criterion	Doorpush Errors in (30) postop. trials	No. of App'ch Err's in (30) postop. trials	Percent App'ch Err's/ total Err's.
SC	W2	7	90	3	13	81.3
	4	4	120	1	8	88.9
	6	10	70	10	4	28.6
	16	4	70	3	7	70.0
	19	6	120	9	6	40.0
	23	5	80	5	6	54.5
	24	8	80	9	1	10.0
	ΣX	44	630	40	45	373.3
	$\bar{x}$	6.3	90	5.7	6.4	53.3
MFC	W3	7	180	5	6	54.5
	9	6	70	1	14	93.3
	11	4	160	5	4	44.4
	12	6	80	6	2	25.0
	18	7	70	5	8	61.5
	20	8	90	6	7	53.8
	27	7	80	6	5	45.5
	ΣX	45	730	34	46	378.0
	$\bar{x}$	6.4	104.3	4.9	6.6	54.0
CONT	W7	12	120	2	12	85.7
	8	9	70	10	3	23.1
	10	6	90	12	1	7.7
	14	7	80	6	1	14.3
	17	8	70	3	8	72.7
	22	6	110	3	10	76.9
	25	7	80	5	6	54.5
	ΣX	55	620	41	41	334.9
	$\bar{x}$	7.9	88.6	5.9	5.9	47.8

Table 8.1
Pre- and postoperative scores of animals in Experiment 8.1.

goaldoors, some 75% resulted in an initial press of the baited door.

8.1.6 Discussion

From the results of training to criterion and post-operative retention it appeared that the animals were learning the discrimination on the basis of vision [1], yet SC and MFC animals failed to exhibit the excessive "approach error" behaviour which would have been predicted from the results of Schneider (1968, 1969) and Winterkorn (1975a,b) with other species. However since the same animals were capable of 75% correct performance when goaldoors were blank, and indeed on 25% of occasions ran to a baited goaldoor having incorrectly approached an unbaited goaldoor, it is clear that these rats were capable of utilising odour in discriminating presence of absence of food pellets and were probably not discriminating visually between light- and dark-stimuli. On trials which resulted in "approach errors" animals would typically run to the goaldoor, sniff vigorously round the base of the door, and turn quickly away from it. Further informal investigation showed that placement of food <u>behind</u> the foodwell failed to produce a doorpress and thus the

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[1] Unfortunately this could not be tested pre-operatively without disturbing the experimental design.

animals would appear to be able to discern the presence of food specifically in the foodwell. It should be noted that since the goaldoors were always fully closed against the front panel at the start of each trial it would not have been possible for animals to view the content of the foodwell. Further evidence that olfaction was being specifically used was that when in further informal testing a foodwell was baited and left overnight, animals would fail to press that door the following morning; thus when the odour of the pellets had dispersed, the rats treated foodwells as empty. Rats could be apparently confounded by scattering crumbled pellet immediately behind a non-baited goaldoor, since this was seen to elicit door-presses in some animals though still many animals failed to press and were thus capable of detecting the absence of pellets in the actual foodwell.

The present results illustrate the extreme sensitivity of the olfactory sense in rats, and the strong tendency in this species to use olfactory cues where possible (Southall and Long, 1969; Slotnick and Katz, 1974). However the importance of this finding for the hypotheses advanced above is that, in a 2-choice runway, animals which are allowed to "correct" errors are likely to adopt nonvisual strategies. Clearly, in previous reports of the behaviour of other species in a 2-choice runway where response correction was allowed (Schneider, 1968; Winterkorn, 1975a,b) "approach error" behaviour may have occurred because animals were using, or at least attempting to use (possibly on certain trials only) some form of non-visual sampling. Just why SC animals should appear to be particularly prone to making "approach errors" and therefore, perhaps, to the adoption of non-visual strategies, is unclear since they are known to be capable of good visual discrimination (Dyer et al, 1976). One possibility is that since their visual attention is deficient (Milner et al, 1979) they may particularly favour the use of a modality like olfaction which is not represented in the SC as judged by the results of single unit electrophysiological studies (see Chapter 2). Alternatively (see Chapter 3), Murison (1977) has shown that collicular rats tend to make runway responses hurriedly before having properly sampled the discriminanda so they, more than controls, may tend to find themselves close to goaldoors prematurely. Such a response style could, of course, further exacerbate the tendency to use olfactory or other nonvisual sampling. It was particularly noticeable that in the present study, responses of all animals tended to consist of erratic "ballistic" running (often towards a preferred side of the apparatus) without any indication of visual sampling having occurred on emergence from the startbox. Winterkorn's informal observation that her SC-lesioned cats were apparently "unable to withold incorrect responses" suggests that, as with SC-lesioned rats (Murison, 1977; Goodale et al, 1978) and, seemingly, all those in the present study, her animals were probably running erratically.

Thus, to summarise, it would seem that (as Schneider, 1969, pointed out - see note 17) 2-choice runways in which response correction is allowed encourage erratic approach responses; in addition they encourage non-visual sampling, and thirdly they may particularly do so in an animal which suffers (even intermittently) from deficiencies in visual attention and motor control. The latter may apply to SC- and perhaps MFC-lesioned animals.

The apparent similarity between cat and rodent in this respect is especially interesting in view of the reported opposite effect of collicular ablation on general activity in the two species, in the former producing lethargy, in the latter, hyperactivity (see Kesner et al, 1967). It would appear, nevertheless, that in terms of runway behaviour, the consequences of the lesions are similar demonstrating one aspect of collicular control of motor behaviour which apparently shows cross-species reliability.

Conclusion

An attempt was made to demonstrate the "approach error" runway behaviour reported for collicular animals, using a light v. dark discrimination in a Grice box in which food reward was located immediately behind the goaldoor. No group differences were obtained in terms of number or proportion of postoperative discrimination (doorpush) or approach errors. Subsequent control testing revealed that the rats were probably using subtle olfactory discrimination in preference to vision. The drawbacks of this particular methodology were discussed and it was concluded that in previous such studies erratic runway behaviour in collicular animals may have led to a particularly strong tendency to attempt to use non visual cues while in the vicinity of the goaldoors.

8.2 Visual Discrimination Learning and Attention to peripherally-located cues following lesions of the SC, MFC and HPC

8.2.1 Introduction

Layman (1936) and Dyer et al (1976) reported that rats with total bilateral lesions of the SC were unimpaired in learning a vertical-horizontal stripe discrimination. However when the task is learned preoperatively, collicular rats, as in so many other operant situations (see Chapter 3)sometimes show transient postoperative retention deficits (see Milner, Goodale and Morton, 1979).

Thus while striate cortex is known to be indispensible forpattern vision (Dyer et al, 1976; Lavond et al, 1979), current evidence suggests that the SC is involved to a lesser, though demonstrable extent. Such involvement may either be in terms of control of locomotor stimulus approach behaviour (Murison, 1977) or alternatively in terms of spatial-attentional aspects of pattern perception. The latter is suggested by the findings that cats with collicular lesions are slow in learning pattern discriminations, probably as a result of deficient oculomotor scanning (Tunkl and Berkeley, 1974), and in primates, learning deficits are evident when stimulus scanning is required (Marzi and Latto, 1976) or where stimulus and response locations are separated in space (Kurtz and Butter, 1976; Butter, 1977). Furthermore, Milner et al (1979) have recently shown using well trained rats, that colliculars are more seriously impaired than controls as a result of spatial relocation of discriminanda, and are less affected by the introduction of conflicting cues directly above the discriminanda.

The latter result is a little puzzling; though stimuli which were less effective for colliculars than controls were indeed peripherally placed in relation to the central goaldoors, they were nevertheless within the "broad central area of visual space" (measured laterally about 15° either side of the midline) within which irrelevant, novel distracting stimuli were shown to elicit apparently normal orientation in collicular rats in a previous study (Goodale et al, 1978). Only to stimuli outside this area was the collicular animal grossly inattentive, Calculations based on the apparatus dimensions given by Milner et al (1979) reveal that the smallest stimulus separation which they used (and which clearly differentiated colliculars from controls) only represents a displacement of between 2° - 6.5° of visual angle (calculated over the first three quarters of the animal's approach run). Thus the "peripheral" stimuli used by Milner et al (1978) were "central" stimuli according to the definition of Goodale et al (1978). Besides degree of visual eccentricity, however, the nature of the peripheral stimuli and conditions of presentation in the two studies differ in many ways (Table 8.2); while, in one sense, the demonstration of collicular attentional impairment in both cases towards eccentrically located stimuli attests to the robustness and generality of the phenomenon, this requires the assumption that the underlying cause of the deficit is the same in each study. It is possible, however, that collicular inattention towards relocated discriminanda in Milner _et al_'s study is not a gross "orienting" deficit of the kind observed in that of Goodale _et al_. In particular, if it is assumed that the stimuli used by Milner _et al_ (1979) occurred in "central" visual space, and those used by Goodale _et al_ (1978) in "peripheral" visual space, an alternative explanation can be suggested, namely that the SC has two functions, one in peripheral vision, vis à vis low acuity vision, detection of novelty and gross bodily orientation, and a second in central visual processes, perhaps in sequential feature extraction via oculomotor "interrogation" of patterned stimuli.

This formulation would account for the reported discrimination deficits in colliculectomised cats and primates (see above) which accompany gross orienting deficits (Milner _et al_, 1978). On the other hand, it might be objected that the region of visual field which constitutes "central" visual space has never been properly defined. Milner _et al_ (1979) noted that after prolonged training, rats appear to restrict their attention to the lower edge of the discriminanda (see Lashley, 1934). Thus compared with rats in the Goodale _et al_ (1978) study which were forced to sample information from a 30° wide area of space in order to make correct runway responses, these were apparently sampling from a small area at the base of the stimulus goaldoor and thus their "central visual space" may have been correspondingly restricted. In addition, the collicular rats in the Goodale study may have mistaken distractors for goaldoors; alternatively attention towards centrally-placed distractors may not have been entirely normal. Even though no significant difference was observed between colliculars and controls in response to centrally-placed distractors, this may have been due to a ceiling effect in the control group; central visual space may (generally, or specifically in the apparatus used by Goodale *et al*) be particularly significant to an animal and unexpected stimuli suddenly appearing there may have a particularly potent and arousing quality. Thus it is possible that in the Goodale *et al* (1978) study, a collicular contribution to central visual attention may have gone undetected and the size of effective "central visual space" may have been overestimated.

Thus the present experiment was intended to incorporate features of both the visual learning paradigm used by Milner *at al* (1979) and the distraction paradigm of Goodale *et al* (1978). Though rats may attend to a restricted area of a stimulus (see Milner *et al*, 1979), it has been shown previously (Stevens, Foreman and Venables, 1980; see Mackintosh, 1974, p 585) that control animals' behaviour can be influenced by cues located very peripherally in relation to central goaldoors. Thus in the present study, animals were trained to criterion using central discriminanda which were then moved into peripheral visual space vertically, and then horizontally, for a temporary period after which they were returned to their original location. It was anticipated that control animals would exhibit orientating responses to the peripheral stimuli, and would begin to utilise peripherally located cues as the basis for responding, while the collicular group was expected to be less disturbed by the stimulus relocation and show no orientation to the peripheral stimuli.

Since MFC lesions in rats have been reported to produce attentional deficits similar to those following collicular ablation (Collin, 1977), and furthermore that hippocampally lesioned rats have been shown to extract more information than controls from peripherally-located stimuli (Stevens and Cowey, 1972), particularly in a discrimination apparatus (Stevens, Foreman and Venables, 1980) it was decided to include groups of animals with bilateral MFC or HPC lesions; the former group might be expected to exhibit neglect toward peripheral cues while the latter was expected to utilise peripheral cues more readily than controls in the performance of the discrimination.

8.2.2 Subjects and Surgery

Nineteen rats randomly extracted from the groups previously described in Section 5.5.2 were employed in this study. Five rats had bilateral collicular lesions (32p, 35p, 36p, 44p, 54p), 4 HPC lesions, (39p, 42p, 45p, 46p), 4 MFC lesions (38p, 33p, 47p, 58p) and six were sham-operated controls.

8.2.3 Apparatus and Method

The apparatus was as employed in the previous study, except that the discriminanda used for initial training consisted of aluminium squares which just covered the goaldoors, on the front of which were alternating 1.3 cm wide black and white stripes formed by mounting strips of black adhesive tape on the white-painted surface. The vertical striped pattern was the positive stimulus for all subjects. Stimuli were frequently rotated to prevent discrimination on the basis of local contour, and each stimulus card was used as frequently as a positive and negative stimulus, thus avoiding discrimination on the basis of subtle differences (e.g. olfactory) between stimulus cards. The sequence in which left and right goaldoors held the positive stimulus was determined by a Gellerman series as in the previous study.

General aspects of deprivation,transportation and familiarisation of subjects with the apparatus proceeded as in the previous study. For the first 80 trials, self-correction was allowed as in Experiment 8.1 but with "control" food pellets located behind the foodwell of the negative stimulus door. This modification was designed to reduce olfactory cueing. However after 80 trials when it was clear that animals were not learning, a rerun-correction procedure was initiated. Thus whenever an animal made an incorrect response, it was returned to the startbox immediately and rerun. If on the second attempt an error was committed, the

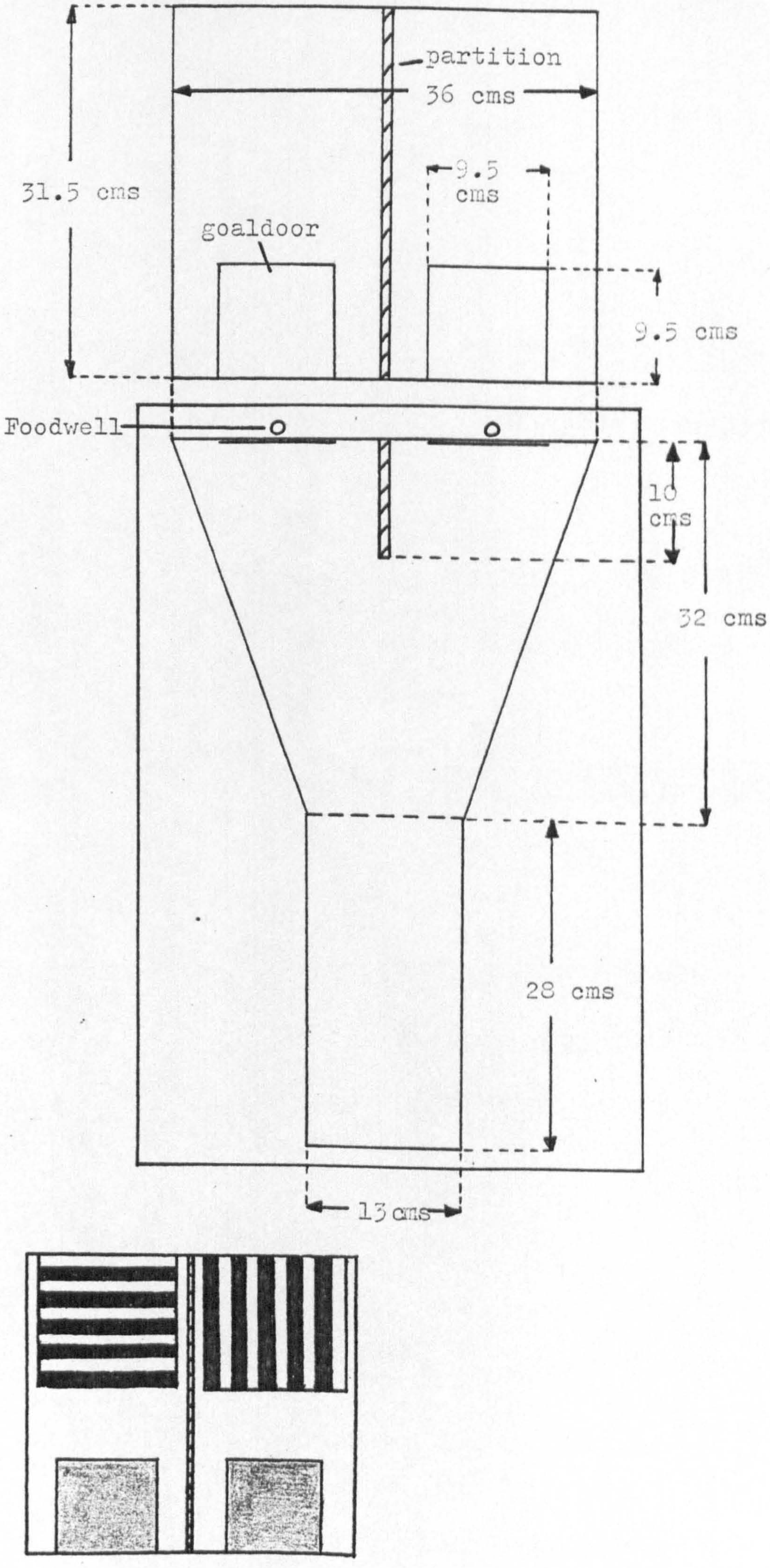

Figure 8.1 Two-choice Grice Box apparatus used in Experiments 8.1 and 8.2. Insert shows 1st position of peripherally-located stimuli (see text).

animal was rerun a third time. If a further error was made on this run, the animal was manually guided to the correct goaldoor and allowed to obtain reward. After this, or following a correct response, the animal was returned to the homecage. Thus on each trial initial response was classed as correct or incorrect and the number of (repetitive) rerun errors was also recorded. All animals were tested for 10 trials per day.

Upon reaching criterion (90% correct over 2 successive days), each animal progressed (beginning on the following day) to two successive days of training with the discriminanda placed in peripheral positions and with blank, grey goaldoors. Peripheral stimuli were placed directly above the central goaldoors on the first of these test days. For each stimulus the pattern was identical to that of the corresponding training stimulus but the surface area was larger (14 x 14 cm, i.e. just over twice as large as the original). When in place in the apparatus (see Figure 8.2) the lower edge was 17.5 cm (29^{o} of visual angle measured from the startbox exit) above the base of the goaldoor. On the following day the stimulus was identically patterned but each consisted of two portions, one of which was 14 cm high x 7 cm wide positioned 17.5 cm above the goaldoor such that its innermost edge was displaced 7 cm (about 10^{o} of visual angle measured from the startbox exit) from the innermost edge of the original goaldoor, as shown in Figure 8.1. The second portion was continuous with the first and measured 14 x 14 cm located on the side wall of the apparatus and measured 14 x 14 cm. Thus on day 2 of testing with peripheral stimuli, the total stimulus area was slightly more than 3 times that of the original goaldoors. The increased stimulus area was intended to reduce the difficulty of the task and partly to compensate for the fore-shortening effect of attaching part of the stimulus to the side wall of the apparatus. E noted for each trial whether or not the animal showed head-elevation and/or turning during the 2 days of testing with peripheral stimuli. Rerun correction was continued throughout all stages of testing. Following this, animals were tested for two further days with the original stimuli on the central goaldoors.

8.2.4 Results

Figure 8.3 shows the learning curves of each group. It is clear that little learning took place in the initial 80 trials, (during which self-correction was permitted), but was rapid upon initiation of the rerun correction procedure. The number of trials taken to reach criterion by each rat was logarithmically transformed to correct for any "skew" in the score distribution due to the occasional slow-learning animal, and groups were compared using appropriate t-tests. These revealed that both colliculars and hippocampals required more trials than controls to reach criterion ($t(9) = 2.19$; $p < 0.05$, and $t(8) = 2.24$; $p < 0.05$ respectively, 1-tailed) though no other comparison

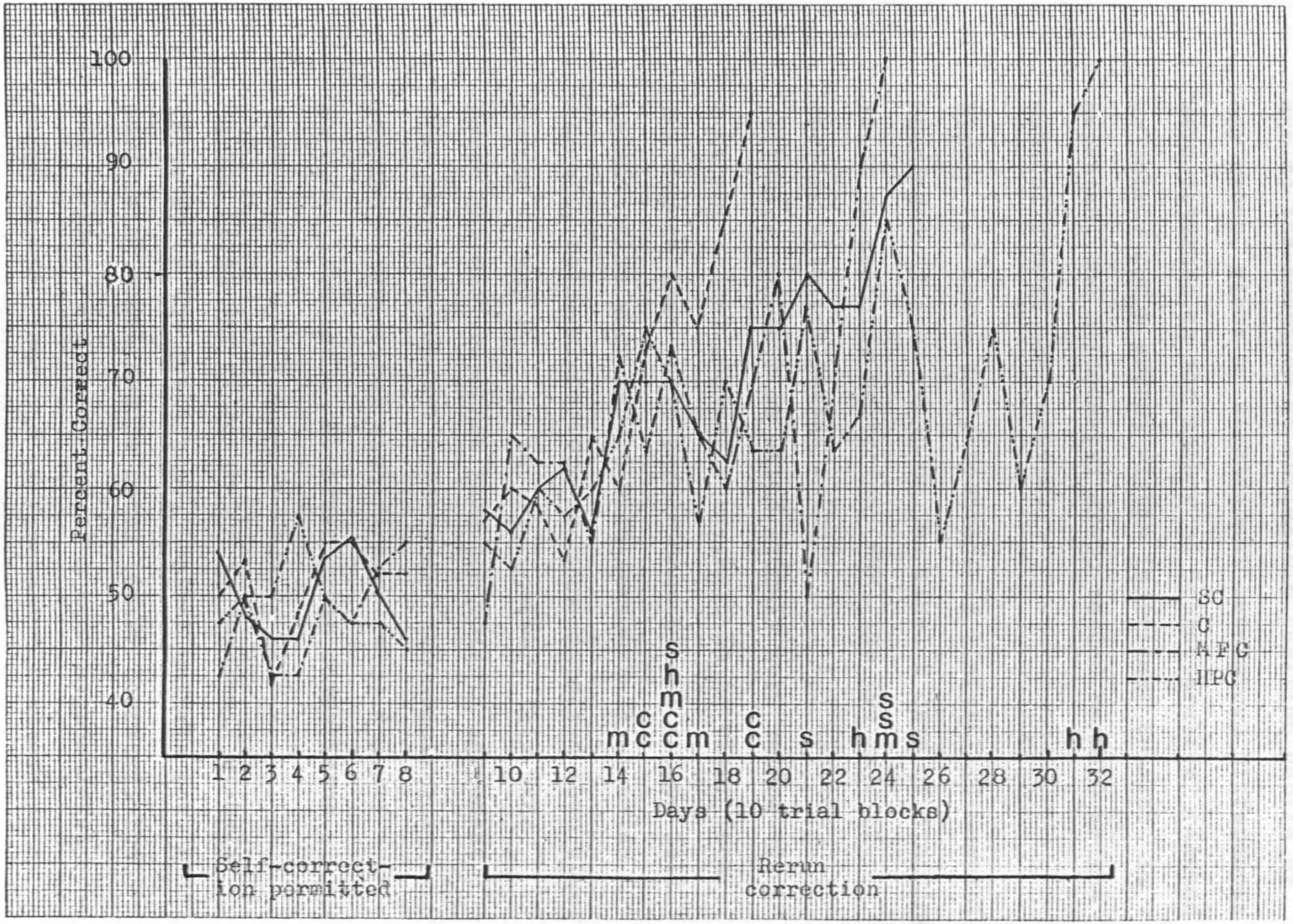

Figure 8.3 Learning curves for groups of rats in Experiment 8.2. Letters (s,m,h,c respectively) indicate that in that day a collicular, medial frontal, hippocampal or control animal reached criterion.

reached significance. Deficits were not primarily due to the adoption of inflexible position habits by any group, since no significant intergroup differences were obtained on the number of "perseverative" (second or third) rerun errors within individual trials. As expected, the hippocampal group tended to make arithmetically more than others.

Figure 8.4 shows the percentage of (initially) correct responses of each group on the final 2 days of training prior to reaching criterion (PRE) the two days of testing with peripheral stimuli (P_1, P_2) and the following two days on which stimuli were relocated upon the actual goaldoors (R_1,R_2). It is clear from the Figure that while performance of all groups fell dramatically when tested with peripherally-located stimuli, colliculars were no more impaired than other groups on day P_1. On day P_2, however, they made fewer correct responses than controls in agreement with the experimental hypothesis, the result just reaching statistical significance ($t(9) = 1.91$; $p < 0.05$, 1-tailed). No other group comparisons approached significance on days P_1 or P_2.
On the first day of returning to "central" stimuli (located on the goaldoors), control animals were still performing above chance level (66.6% correct), but the SC group was operating at a much higher level (mean 90.0%), four out of five animals attaining at least 9/10 correct on this day. Only one collicular (32p) obtained a below-criterion score making only

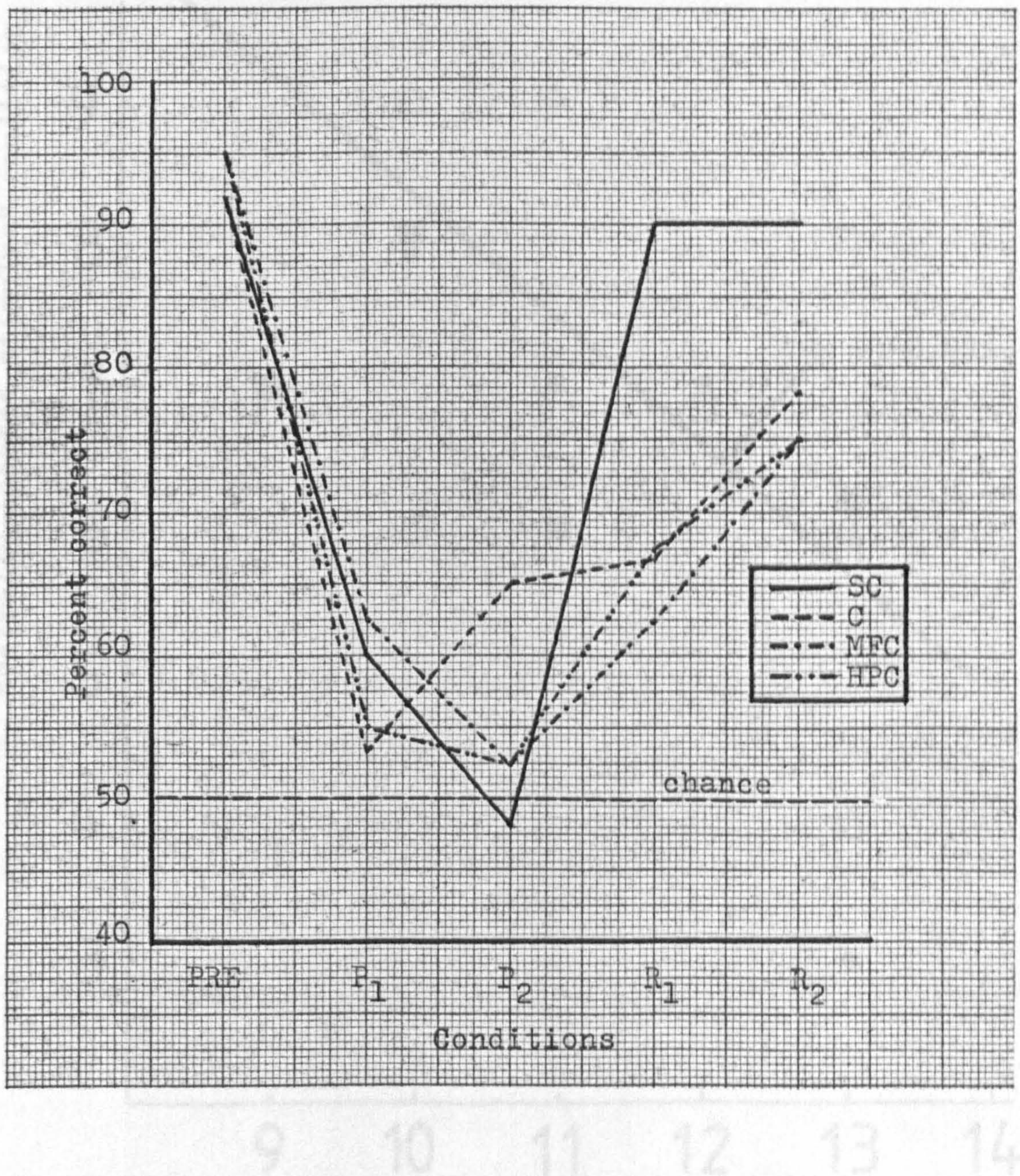

Figure 8.4
Mean percentage of correct responses for groups of animals in Experiment 8.2, at criterion prior to stimulus relocation (PRE), with stimuli relocated vertically above goaldoors (P_1), above and to one side of goaldoors (P_2), and upon returning stimuli to the central goaldoors (see text).

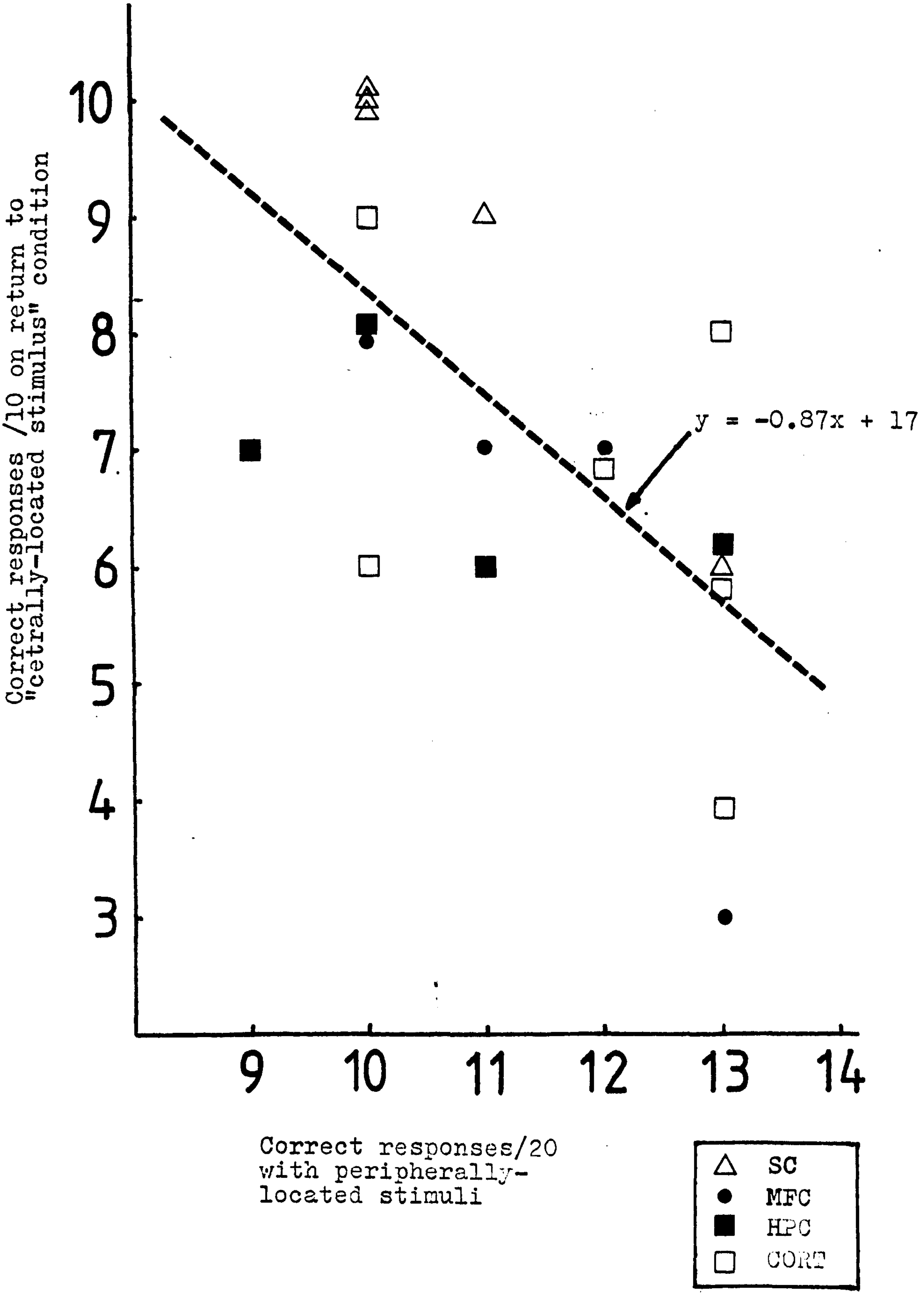

Figure 8.5
The relationship between performance with peripherally-located stimuli and performance immediately upon returning stimuli to central (goaldoor) locations in Experiment 8.2.

6/10 correct responses. It is perhaps significant that this animal was the only collicular to perform above chance during testing with peripheral stimuli (13/20 correct). Statistical comparison between SC and controls almost reached significance on the first day of retesting with centrally located stimuli ($t(9) = 1.51$, $p < 0.10$. Crit t ($p = 0.05$) $= 1.83$), while comparison between colliculars and combined control groups (control + MFC) was clearly significant ($t(13) = 2.44$, $p < 0.025$). However on the final day of testing, no significant group differences were obtained (all p's>0.05); control group performance improved to 83.5% correct on this day.

The relationship between performance using peripherally-located cues and subsequent performance on centrally located cues was investigated using Spearman's rank correlation. For all animals, the total number of correct responses during the 20 trials with peripherally located cues and the total number of correct responses on the 10 trials immediately following were correlated. This revealed a significant inverse correlation between the two scores ($D^2 = 1237.3$; rho(19) $= -0.516$; $p < 0.05$). Figure 8.5 shows the distribution of scores under the two conditions, and further illustrates that while SC animals performed poorly when required to use peripherally-located cues, they tended to perform more efficiently upon return to centrally-located discriminanda.

Overt orientation to peripherally located stimuli was not treated statistically. All animals ran fairly directly and were infrequently disrupted in any obvious way by stimulus relocation. However where orienting responses were observed these tended to be in the control and MFC groups which registered means of 4.0 and 3.0 orientations per animal during the 20 trials. Both SC and HPC groups registered means of 2.0 orientations per animal. In the HPC group only animal 42 (who totalled 6) gave more than one orientation and in the SC group only animals 36 and 44 (3 and 4 orientations respectively); tendency to orient was better distributed within the control and MFC groups. Overt orienting responses did not occur exclusively on early trials but rather intermittently and unpredictably.

8.2.5 Discussion

The small deficit in initial learning by colliculars is consistent with evidence from other species but not for rats; for this group and the hippocampal group, the result is possibly attributable to the inclusion of an initial period of training using self-correction, since perseverative, erratic behaviour has been noted in SCs(Murison, 1977) and HPCs (Kimble, 1973). The significant findings of this experiment were somewhat serendipitous, as the main experimental predictions concerned the degree of learning which was expected to take place when central stimuli were moved to peripheral locations, yet only when peripheral stimuli were very peripherally-located did a significant difference between colliculars and controls emerge. The result is further evidence, however, for the deficient use of peripheral information by collicular animals. The level of performance which occurred in this situation was low; this is to be expected from previous work which has shown that very small stimulus displacements can give rise to substantial reductions in discrimination performance (See Cowey, 1968; Milner _et al_, 1979). However other studies (Stevens and Cowey, 1972; Mackintosh, 1974; Stevens _et al_, 1980) have demonstrated that animals are capable of extracting information from relatively distant peripheral cues and that such information can influence, and even form the basis of, operant responding to "central" goaldoors. In this experiment, animals' performance fell to near chance level, yet in all except the collicular group on day P_2, a small positive saving was evident, particularly in control animals and particularly during the second day of testing with peripheral stimuli. The significant inverse correlation between scores with peripherally-located stimuli and scores upon subsequent relocation of the discriminanda strongly suggests that the animals which had attempted or begun to use peripheral cues required a period of "readjustment" before reattaining a high level of performance with stimuli located centrally.

It would appear that this task provided a situation in which redirection of attention to (potentially) significant peripheral stimuli was disadvantageous for subsequent performance, and that the poor performance of colliculars when tested with peripheral cues, and their performance on the first post-treatment day resulted from their inability or reluctance to shift attention toward a peripheral cue (Goodale and Murison, 1975; Goodale _et al_, 1978) or away from a central cue (Milner _et al_, 1979), though why a collicular deficit was not equally evident on days P_1 and P_2 is unclear in view of Milner _et al_'s findings. That colliculars were less inclined to attend to peripheral cues is suggested further by observations of their behaviour during testing, since collicular rats tended to exhibit fewer gross orienting responses than controls to the peripherally located stimuli.

The present experiment is not directly comparable with that of Milner _et al_ (1979) since these animals were not automatically tested and learned the discrimination in a relatively small number of training trials. It is likely that the rerun-correction procedure gives rise to particularly rapid learning. Furthermore, Milner _et al_'s animals were trained to a higher criterion, and variously displaced stimuli were introduced as "probes" on only half of the trials in a test session. The change in stimulus position from trial to trial may have been partly responsible for the very severe fall in performance with relatively small stimulus displacements in that study. For example, on those trials when stimuli were displaced 7 cm vertically, performance fell to chance level. In the present study, however, animals were given a full 10 trials with each stimulus location potentially allowing them to accommodate to novel stimulus positions.

Milner et al (1979) carefully ruled out an explanation of their results in terms of a non-specific collicular deficit by demonstrating that this group was less affected by the introduction of contradictory cues introduced in upper regions of the stimulus card. However it is perhaps surprising that in the present study, colliculars were unperturbed by the absence of stimuli on the central goaldoors and performed efficiently on days R_1 and R_2 having had less stimulus discrimination experience during the trials on which stimuli were located peripherally. Temporary absence of stimuli from the goaldoors might have been expected to produce a drop in animals' performance; a study of the effect of simple subtraction of central stimuli (without peripheral relocation) would be valuable in this respect [1]. From the results of the present study it would be unwise to assume that the responsiveness of collicular animals to changes in the appearance of central stimuli is entirely normal, though the results are not inconsistent with the conclusion of Milner et al (1979) that deficits in colliculars are unlikely

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[1] However it should be noted that the problem is not relevant to the present intergroup comparisons since attention in control rats may become redirected whether or not peripheral stimuli are introduced.

to be due to a "generalised impairment in looking towards novel stimuli", but rather that the collicular has special difficulty in "orienting away from the stimuli that are guiding responses, and toward potentially relevant stimuli elsewhere".

The latter is likely to be most clearly evident when the animal is required to make a well-trained response to an identifyable stimulus set in central regions of visual space. However, initial learning of a visual discrimination is also likely to involve successive changes in information processing strategy, as evidenced by the change in eye movement patterns occurring between simultaneously-presented discriminanda during learning by monkeys (Shrier and Povar, 1979), stimulus scanning movements in hamsters in a two-choice runway (Mort et al, 1980) and the apparent progressive convergence of attention in rats upon lower regions of the stimulus card (see Milner et al, 1979). Perhaps the typical visual learning situation used to test rodents is too gross, and behaviour too variable, for an initial learning deficit to occur reliably in colliculectomised animals; Dyer et al (1976) failed to obtain such a deficit, yet in the present study a small initial learning deficit was observed in colliculars, and in other species deficits have been recorded (Berlucchi et al, 1972; Tunkl and Berkley, 1974; Marzi and Latto, 1976). Milner et al (1979) employ their model to account for the frequently-observed temporary postoperative deficits in in the retention of pattern discriminations by colliculectomised animals, arguing that this has occurred in cases where animals were preoperatively trained to a low criterion. In this situation, it is likely that some degree of stimulus scanning is still required postoperatively, and that an optimal attentional strategy has yet to be attained. Since this is arguably dependent upon the integrity of the SC, the colliculectomised animal will be more likely to be impaired than a control animal. Indeed, where animals have been overtrained prior to colliculectomy, the lesion has had little effect upon postoperative level of performance (see Milner et al, 1979 for references).

Thus the role of the SC in discrimination learning is apparently twofold; in both the process whereby stimuli are initially selected prior to their guiding responses, and then in directing attention away from these when the situation demands. Clearly, the issue of whether, in any particular situation, an animal is deficient in "disattending " cue A, or shifting attention to B poses logical problems. In an earlier study of startle behaviour in collicular rats (Goodale et al, 1975) it was reported that attention to novel stimuli was normal when the animal was not engaged in an ongoing behaviour at the moment of presentation. However, as in open field studies (Chapter 5) it is clearly difficult to ascertain whether an animal is "currently engaged" in stimulus exploration or not. In addition, it is not clear why, in information processing terms, it should be necessary for attention in rats to converge upon the lower portion of a stimulus card for optimal discrimination performance, or to which class(es) of discriminandum this "rule" applies. Animals in these situations presumably sample many cues before arriving at the "relevant" stimulus dimension (Sutherland and Mackintosh, 1971), it is possible that colliculars perseverate responses in the event of initially adopting an inappropriate stimulus dimension , though such perseveration of a central "set" is not usually a characteristic of SC-lesioned animals, unlike hippocampals and frontally-lesioned rats and monkeys (see Chapter 4, and Mishkin, 1972). Moreover in the case of colliculars, inability to "shift attention away from" stimuli currently guiding behaviour is likely to apply only to shifts between spatial positions. It is perhaps worth noting that even in a situation where stimuli currently guiding behaviour disappear (e.g. in the case of a visual search task using pieces of fruit in which the stimuli are consumed), the SC has difficulty guiding eyes and hands to the locus of further pieces of fruit, though it might be significant that in a "blindsearch" situation in which responses are made within a matrix of "hidden" rewards, the collicular monkey is relatively unimpaired (Collin, 1977). On balance, therefore, the colliculectomised animal seems to suffer from a very general sluggishness in shifting attention; that is, many stimuli are less "attractive" than for a control animal.

Keating (1976) has argued that colliculectomised monkeys with foveal retinal lesions are capable of good discrimination performance, as though peripheral visual field (4^{o} from visual centre) is functional after

SC lesions, and that "geniculostriate structures can operate quite well in the periphery". Indeed in the present study, SC animals might have learned the discrimination eventually on the basis of peripherally located cues, though they would probably have required extensive training. In such a case, the function of the SC might be seen as redirecting the striate cortical feature analyser system towards the relocated stimuli (particularly as central goaldoors were blank during peripheral testing) though it should be noted that gross bodily orientation to peripheral stimuli is not necessarily required for animals to learn something about them (Mackintosh, 1974). It would clearly be of interest to determine whether cues located in areas of space separate from goaldoors would be utilised as readily by SCs as by controls; that is, whether cue acquisition in the intial stages of learning is deficient in SCs, though judging from the results of Experiment 5.3 above, which demonstrated collicular neglect of open field objects, they are likely to be deficient.

It is clear from Figure 8.5 that neither hippocampal nor medial frontal lesions produced measurably different responsiveness towards peripheral cues; both groups performed relatively poorly upon the return of cues to central goaldoors following the period of testing with peripherally located cues. This is perhaps surprising, since hippocampals might have been expected to utilise peripheral cues more readily than controls (Stevens and Cowey, 1972) and MFCs to neglect them (Collin, 1977). However, in the case of hippocampals the effect is probably too subtle to be detected with the present paradigm, and for MFCs, it was clear that bilaterally-lesioned animals were not neglectful in a runway in studies 6.1 and 6.2. Further testing using unilaterally and bilaterally-lesioned animals might be profitable.

Conclusions

Rats with SC lesions and with HPC lesions were slow in learning a horizontal-vertical stripe discrimination compared with control and medial frontal cortical rats. However the deficits may have been due to prior training on a response-correction regime. All animals' performances fell sharply when the stimuli to which they had been trained were suddenly relocated in a peripheral part of visual space. However colliculars rarely turned to fixate the novel stimulus positions and were significantly better than other groups when the stimuli were relocated on the goaldoors. Thus it would seem that the SC animal is particularly bad at shifting attention from stimuli to which it is currently attending, though it was argued that such a limited description of the SC deficit poses theoretical problems. It is likely that the SC-lesioned rat is generally inattentive in terms of initial cue acquisition, and shifting attention between cues when these appear in unexpected spatial locations.

CHAPTER 9

Conclusions and Speculations

The aims of the current series of experiments were to determine for rodents the parameters of spatial, attentional and motor changes in behaviour resulting from SC lesions, to determine the gross disadvantages of non-possession of a superior colliculus, to identify possible functional divisions within the SC and to determine to what extent collicular deficits are reproducible by lesioning other, related, brain areas. The general issues raised by the above experiments have already been discussed and will not be reiterated here; nor will I refer to many of the aspects of theories of collicular function which were discussed vis à vis the existing literature, but to which the present studies do not add new information. Nevertheless it is appropriate at this point to return to some specific "models" of collicular, hippocampal and frontal cortical functions proposed in Chapters 3 and 4 in order to draw general conclusions.

(i) Superior Colliculus and Regulatory Behaviours

Trulson and Randall (1973) argued that the SC is responsible for abnormal grooming behaviour following pontine lesions. Dean et al (1979) have found that collicular ablation abolishes motor stereotypy following apomorphine induced hyperactivity, and Pope and Dean (1979) have observed abnormal and misdirected grooming in rats with very large collicular-tegmental lesions. However in the present studies animals which had substantial collicular ablations, and which exhibited inattentiveness, were not different from controls in terms of number or duration of grooming bouts, except that incidence of grooming was slightly elevated in Experiment 5.2. Subtle abnormalities may have gone undetected, though it is clear that abnormal grooming only results from lesions involving dorsal tegmental tissue, perhaps in conjunction with extensive collicular removal. It is worth noting that Pope and Dean (1979), while apparently identifying a tegmental "locus" for abnormal motor signs (by comparing large- and small-lesion extents and assuming behavioural differences between the two sizes of lesion to be attributable to the area of non-overlap) notably failed to make specific lesions in this area of dorsal tegmentum to demonstrate that these lesions alone could give rise to the "extra" behavioural deficits.

Though (novel) stimulation of the fur does not elicit orientation in collicular rats when applied to the side of the body contralateral to a collicular lesion (Sprague et al, 1973; Kirvel, Greenfield and Meyer, 1974; Collin, 1977) or following introduction of kainic acid into the SC (Foreman and Srebro, unpublished), the gross impairment seen following deep ablations of SC probably does not represent "a more general inattentiveness" (Section 3.1) but some other motor impairment.

(ii) Visual Discrimination Learning

Experiment 8.1 was not directly comparable with the previous studies of Schneider (1968) and Winterkorn (1975a, b) for reasons of apparatus design, since the latter studies employed runways in which discrimination was required to be made at a point distant from the locus of reward. However as Experiment 8.1 showed, permitting an animal to correct error approach responses leads to the rapid use of non-visual sampling and erratic responding which might be expected to affect collicular animals more than controls. As noted in Chapter 3, Schneider's own report (1968) demonstrates that in the case of one hamster (M7) the learning deficit was stimulus-specific; furthermore animals did eventually overcome the tendency to make approach errors (Schneider, 1967). Winterkorn's (1975a, b) experiments further showed that approach error behaviour in cats was not an unsurmountable obstacle to learning, and may have been encouraged by the titration procedure she employed. In Experiment 8.2, a small learning deficit was observed in both collicular and hippocampal groups, though this may have occurred because animals were first trained using a self-correction procedure (as in Experiment 8.1). Since hippocampal (Kimble, 1963; Douglas, 1967) and collicular (Dyer et al, 1976) rats are not usually found to be deficient on visual discrimination learning, the effect of introducing a period of self-correction training may have had a particularly large influence on both groups whose visual stimulus sampling is impaired (colliculars: Milner et al, 1979), or which tend to perseverate strategies (hippocampals: Kimble, 1975).

(iii) Spatial behaviour

The hypothesis put forward by Schneider (1968) that the colliculus (and other elements of a "second visual system") is involved in defining or discriminating the spatial location of objects has been largely discredited; in particular because collicular animals in previous studies (Goodale and Murison, 1975; Dyer et al, 1976; Goodale et al, 1978) are eminently capable of localising goaldoors. Any impairment they do show is an initial postoperative period of disorientation towards stimuli in very eccentric positions in visual space (Barnes et al, 1970; Goodale et al, 1978; Weinberg and Stein, 1978). Furthermore, on the radial arm maze which is regarded as a strong test of spatial behaviour, in particular the use of extramaze cues (Olton and Collison, 1979), collicular animals in Experiments 7.1 and 7.2 were notably unimpaired at all stages of training, except for a small temporary postoperative impairment. This may result from the same underlying problem as the postoperative deficit on circular jumping stands (see above) and the temporary influence of bilateral SC lesions on control of locomotion in Experiment 6.2. Furthermore, the present results do not support the view that the colliculectomised rat "lacks an ambient visual field" (cf. Trevarthen,1974; Humphrey,1970) since it is not grossly disoriented in space and locomotes efficiently in relation to ambient spatial cues. In Experiment 7.2, for example, collicular rats (which had previously been shown to be totally inattentive to unexpected flashing lights in a runway) were nonetheless able to perform the radial maze. Moreover their fall in performance during dark-testing suggests that they were utilising visual cues to do so. It is possible that colliculars would be less affected than controls by manipulations involving maze rotation, or changes to extramaze or intramaze cues, though this requires further investigation.

(iv) Motor control

The effects of unilateral SC ablations in Experiment 6.2 strongly suggest that there exists more than one activity-related mechanism in the suprarubral midbrain. Rats with collicular ablations turned ipsiversively after responding at a goaldoor but only in the case of lesions which invaded the dorsal tegmentum were gross locomotor progression tendencies observed. Indeed other studies have noted that lesions in the reticular formation in rats produce contravesive turning in contrast to the effects of unilateral SC ablation alone. Whether hyperactivity following bilateral lesions is a result of damage predominantly located in the colliculus, or to subcollicular damage is not clear, though the results of Experiments 5.1 - 5.5 suggest that hyperactivity is obtained from animals whose lesions minimally invade dorsal tegmentum, providing that a sufficiently large volume of deep collicular tissue is removed. However it was clear in those studies that superficial lesions alone (while giving rise to a high degree of inattentiveness) failed to produce open field hyperactivity, consistent with the view of Foreman et al (1978) that deep collicular laminae and their efferents are particularly responsible for some aspect of motor control. However it is clear that activity in deep laminae is not exclusively dependent upon input from superficial SC (Chapter 1); thus the effects of deep collicular removal are likely to reflect the separation of many descending (inhibitory, or modulatory) influences from their sites of influence; thus di- and telencephalic influence upon motor (and perhaps, by the same token, attentional) behaviours is likely to be very greatly disturbed by deep, but not superficial, lesions of the colliculus. This is consistent with other studies reporting more severe, multimodal and progressively more motor-related deficits upon greater penetration of lesions into deeper collicular laminae (Schneider, 1968; Casagrande et al, 1972; Collin, 1977; Weldon and Smith, 1979). For this reason it is perhaps surprising that rats with deep collicular ablations were unimpaired on the radial maze task (Experiment 7.2), further emphasising the non-involvement of mesencephalic mechanisms in the performance of this task.

(v) Attentional Behaviour

The present results clearly support the view of Goodale (Goodale and Murison, 1975; Goodale et al, 1978; Milner et al, 1978) that the SC is involved in attentional responses towards stimuli unexpectedly occurring in spatial positions towards which the animal's attention is not currently directed. This is in accordance with the view of Marks and Jane (1974) that cortical mechanisms are primarily involved in locomotor orientation (seen, for example, to be accurately controlled in collicular animals in Experiment 6.1 above; see also Dyer et al, 1976) while tectal mechanisms are primarily concerned with static orientation (or the localisation of objects in space from a static position). However it must be admitted that Marks and Jane (1974) inferred such a rôle for the midbrain from the fact that visual decorticate animals tended to transform a locomotor orienting task into a static localising task by halting locomotion during their runway response, but did not test the prediction by using collicular lesions. Experiment 6.2 suggested (see discussion) that strategies may be employed in such tasks which do not involve strict visuospatial localisation, but perhaps require the organisation of gross, approximate localisations followed (in the case of collicular animals) by extremely accurate locomotor responses when the stimulus is located towards the centre of the visual field.

The present results and those of Goodale and associates clearly contradict the view put forward by Jane, Levey and Carlson (1972) that the collicular animal should be specifically deficient where intermodal (but not intramodal) shifts of attention are required. Many studies report attentional deficiences in colliculars required to shift attention between sets of visual stimuli, for example.

For anatomical (Chapter 1) electrophysiological (Chapter 2) and phylogenetic reasons, it would seem likely that the SC is primarily involved in the redirection of (particularly visual) attention. Since an animal has a limited attentional capacity, potentially informative or dangerous stimuli which are worthy of investigation yet not within a part of visual space being currently scrutinised, must be brought quickly into "central" scrutiny in order that information is efficiently extracted by fine-grain analysers. Experiment 5.3 clearly showed that a rat without a SC is extremely slow to detect and begin investigation of specific novel cues. The profundity of collicular neglect is an order of magnitude greater than would be predicted from experiments with primates which suggest at most a lengthening of saccadic latency and initial saccade inaccuracy (Wurtz and Goldberg, 1972a, Wurtz, 1976; personal communication).

It is clear from the above reviews that the type of stimulus which the colliculectomised animal is reported to neglect varies between studies. In particular Marzi and Latto (1976: monkey) and Milner _et al_ (1979: rat) have argued that visual search or cue localisation strategies are deficient even within areas of space which elsewhere might have been termed "central" and within which collicular attention to novel stimuli is relatively normal (Milner _et al_, 1978:

monkey; Goodale _et al_, 1978: rat). Functionally, however, these two kinds of stimulus situation (constantly present discriminanda versus unexpected peripheral events) cannot be regarded as in any way equivalent, since (see Table 8.2) in the case of an unexpected stimulus in peripheral space, a gross bodily orientation is required especially in animals which do not have a wide angle of ocular motility. Orientation to such cues is less likely to occur on the basis of stimulus _form_, more likely to be based on stimulus movement, intensity and other physical parameters and to involve reflexive, stereotyped orientation of whole body. In contrast, attention to permanently present, centrally-placed stimuli within the area of space being currently scrutinised is more likely to be based upon interrogative procedures, dependent on specific "perceptual hypotheses" or "questions" (McKay, 1970) and to involve idiosyncratic oculomotor programmes (humans: Noton and Stark, 1968) i.e. what are usually termed "voluntary saccades". In each case the SC is redirecting attention from currently sampled space (Milner _et al_, 1979) toward non-sampled space, though differently in each case. Such a model conflicts with the view of Diamond (1975) and Latto and Cowey (1972) who are inclined to draw a strong distinction between volountary and involountary saccadic mechanisms, the FEF and SC being held responsible for the former and latter respectively. However, a weaker form of this distinction would seem appropriate. Collin (1977) has shown that SC and FEF lesions in monkeys are separable in terms of their producing visual search and blindsearch strategies respectively, in the former case when stimuli were clearly visible, and "simple" localising of successive stimulus positions was required, in the latter when stimuli to be successively sampled were located behind occluding panels. This finding suggests that the FEF and SC represent complementary systems. Clearly, "volountary saccades" may occur EITHER on the basis of current visual stimulation (where stimuli are permanently and reliably placed within the visual field - this may be a collicular responsibility[1]) OR on the basis of an internal visuospatial or visuomotor schema; the latter may be particularly dependent upon the FEF.

This model may account for the following additional findings:
(a) <u>SC and FEF lesion effects are complementary</u>.
The two structures when lesioned together produce a very severe deficit compared with either lesioned separately (Conway <u>et al</u>, 1979); lesion of one structure alone presumably leaves a potentially complementary eye movement system intact, while lesions in both removes almost all saccadic generators.
(b) <u>Competition exists between the FEF and SC for control of eye movements</u>.
Since the two are visualised as competing systems, it is perhaps not surprising that stimulation of the FEF overrides or "vetos" signals generated by striate cortex stimulation (the latter passing to oculomotor systems via the SC - see

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[1] Such may be especially dependent upon rostral SC, since the stimuli concerned are likely to be located within central regions of visual space, and this kind of attention is likely to be especially dependent upon feature processing in VC.

Section 4.2.2). Clearly, the inhibitory influence of the FEF upon the SC-oculomotor system may be required to "disengage" the latter (and, thus, ongoing scanning of the visual scene) during internally-generated eye movements made on the basis of an internalised "perceptual hypothesis". Electrophysiologically, discharges related to such a function would be interpretable as "corrollary discharge". The influence of the FEF in attenuating the responses of single units in the SC has been demonstrated (Guitton and Mandl, 1974). It is interesting that in the present series of experiments, behaviours depressed by collicular ablation in rats (rearing, accompanied running) were found to be elevated in animals with frontal lesions , perhaps further suggesting an inhibitory modulation of SC mechanisms by efferent discharge from the frontal cortex (see also Hagamen et al, 1959), though why the effect should be the reverse in the case of unilateral ablations (when MFC lesions produce a neglect similar to that following collicular ablations) is puzzling.

(c) Stimulation of the FEF produces eye movements in the absence of the SC.

This finding (Spiegel and Scala, 1957; Schiller, 1979) emphasises the parallel nature of FEF and SC oculomotor influences.

(d) The deficit following FEF (MFC) lesions in cats is of an anticipatory nature.

Schlag-Rey and Lindsley (1974) have argued that a cat with a lesion in the projection cortex of the lateral nMD (FEF, or MFC) has difficulty making oculomotor movements to the anticipated locus of a visual stimulus, suggesting a deficit related to internal schemata rather than current visual stimulation(cf. Collin, 1977). Clearly, comparison of FEF and SC lesions would be valuable in this situation.

The deficit in attentional and motor control towards contralateral stimuli is, as mentioned earlier, inconsistent with the above model, yet it is important to note that in both rats (Experiment 6.2) and monkeys (Collin, 1977; Crowne, 1978; though see Kennard, 1958 and Latto and Cowey, 1971b) bilateral lesions of FEF appear to produce a much less severe deficit than that seen contralateral to a unilateral ablation. As with other telencephalic mechanisms (Glick and Greenstein, 1975), the unilateral deficit might be an exaggerated phenomenon arising from a temporary interhemispheric imbalance of motor and/or attentional processes, but not primarily from inattentiveness per se. Nontheless, the results of Experiment 6.2 add further support to the view that medial frontal cortex in the rat is (at least in part) homologous with the primate FEF (Collin, 1977).

Models of hippocampal function and comparison of HPC and SC lesion effects have been previously discussed. It was concluded that the two structures are unlikely to be strongly related (at least, in the adult) in the process of spatial encoding. Hippocampal rats failed to show the same degree of neglect of novel stimuli as colliculars, though they were clearly less distractable when traversing a runway than controls. However, learning a visual discrimination apparently involves stimulus sampling under collicular control, and successively narrowed attention to restricted cues (Milner et al, 1979; Goodale and Milner, 1980; Mort et al, 1980), a period during which systematic changes in hippocampal θ have been reported(Adey, 1966; see Bennett, 1971). Hippocampal θ is apparently co-incident with a similar waveform in the SC (Routtenberg and Taub, 1973), and, in addition, rhythmic vibrissal "sampling" in rats which has been shown to be synchronous with θ rhythm (Gray, 1971a) may be related to collicular processing since the vibrissae are known to be topographically represented on the collicular surface (Dräger and Hubel, 1975). Thus the hippocampus and colliculus are likely to be mutually interactive in the process by which information is acquired. It would be especially interesting to investigate the electrical activity of the hippocampus in response to novelty in the absence of a functional superior colliculus.

Throughout this thesis attempts have been made to provide theoretical models which not only account for findings within diverse "domains" of data (Nadel and O'Keefe, 1974), ie. anatomical, electrophysiological, behavioural, but which also possess a fundamental ecological validity, beginning with a close examination of the functional requirements of behaviours attributed to neural structures. For example, a functional division between deep and superficial colliculus was proposed, arising from anatomical, electrophysiological and behavioural data, but also from the position that, logically, attentional shifts inevitably require both specific and general components, in particular a degree of motor inhibition (behavioural arrest). In addition, the latter experiments involving visual learning suggest an additional intracollicular "division of function", viz. between rostral and caudal colliculus. The anatomical evidence for subdivisions within both afferent and efferent pathways along a rostro-caudal dimension has been reviewed above (Chapter 1), and electrophysiological evidence has been provided by Roucoux and Crommelinck (1976), Robinson (1972) and Harris (1980); goal-directedness of saccades , or absence of head involvement in orienting movements evoked by tectal stimulation appear to characterise a restricted area of rostral colliculus. Clearly, the division between rostral and caudal colliculus in these respects would be expected to depend upon the degree of ocular motility of the individual species. Rostral and caudal colliculus are further differentiated electrophysiologically, since caudal but not rostral SC contains cells with auditory receptive fields (mouse: Dräger and Hubel, 1975), and anatomically since rostral colliculus has particularly sparse retinal, but substantial visual cortical input (see Chapters 1 and 2). Rostral colliculus appears to contribute little to descending tecto-reticulo-spinal pathways (Tokunaga and Otani, 1976; see Chapter 1), but represents the most dense region of intertectal connections (Edwards, 1978). Differential neonatal development is also evident; the earliest-developing input to the SC in the neonate serves rostral colliculus (thus central vision), arising from W-type cells (see Stone and Hoffmann, 1972; Hirsch and Leventhal, 1976). Thus rostral colliculus would be well situated to organise the redirection of attention to significant, particularly novel, cues within the area of visual space being currently scrutinised, doing so in conjunction with feature-detecting mechanisms in cortex. Caudal colliculus may have a greater role in gross ocular, and bodily orientation to novel or meaningful stimuli in a region of space requiring a greater amplitude of orienting movement. In general, it is likely that "unitary hypothesis" models of collicular function are likely to be simplifications , and should be reconsidered from the functional point of view. Such may provide a resolution to a number of contemporary theoretical disputes.

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Appendix 1

Fink - Heimer staining procedure (see Hjorth - Simonsen, 1970)

Tissue stored for 3 weeks in buffered formalin. Sections mounted on glycerine - coated slides.

1. Rinse sections in H_2O
2. Soak for 5 mins. in 0.05% potassium permanganate solution
3. Rinse x2 in H_2O
4. Bleach in a 1:1 solution of 1% oxalic acid, 1% hydroquinone for 45 secs.
5. Rinse x2 in H_2O
6. Transfer to uranyl nitrate solution I for 45 mins[1]
7. Transfer to uranyl nitrate solution II for 30 mins[2]
8. Rinse x2 in H_2O
9. Transfer to silver nitrate solution (freshly prepared)[3] for 5 mins
10. Transfer without washing to Nauta-Gygax reducing solutions I[4] for 5 secs and II[4] for 2 minutes, or until sufficient (dark honey) background colouration has developed.
11. Rinse x2 in H_2O
12. Transfer to a 0.5% solution of sodium thiosulphate for 1 min.
13. Wash in H_2O
14. Dehydrate sections in a sequence of alcohols (70% - abs)
15. Clear in xylene
16. Mount using Canada balsam medium

SOLUTIONS

1 40 mls uranyl nitrate (0.5%)
50 mls silver nitrate (2.5%)
112 mls H_2O

2 80 mls uranyl nitrate (0.5%)
120 mls silver nitrate (2.5%)

3 150 mls silver nitrate (2.5%)
5 mls ammonia (conc.)
9 mls sodium hydroxide (2.5%)

(Note: pH 11+)

4 Nauta - Gygax solutions I and II:
910 mls distilled H_2O
90 mls ethyl alcohol (95%)
27 mls formalin (10%)
27 mls acetic acid (1%)

Appendix 11

Horseradish peroxidase (retrograde transport) technique

(see Kim and Strick, 1976)

1. Injection: HRP, Sigma type VI, 30% solution

2. Perfusion: (i) 100 mls 0.1M phosphate buffer (pH 7.2-7.4)
   (ii) Solution of paraformaldehyde-glutaraldehyde[1]

3. Postfixation: Perfusion medium (24 hrs, 4°C)

4. Reaction: 0.05M TRIS buffer (pH 7.2)
   0.05% DAB (3,3' diamonobenzidine) in TRIS buffer.
   (i) Incubate for 30 mins in DAB solution
   (ii) React for 30 mins in DAB solution with H_2O_2 added (about 1%)

   Note: to stop reaction return to TRIS buffer solution

5. Reaction product: Dark brown at injection site. Fine granular brown-red particles in cell bodies and proximal dendrites. Best seen under darkfield microscopy. May be lightly counterstained.

SOLUTIONS

1 1% paraformaldehyde
1% glutaraldehyde (solution in phosphate buffer)
2% sucrose