The Role of the Supramarginal Gyrus in Planning and Executing Tool Use

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Abstract

Tool use is an essential part of human day-to-day behaviour that permeates all cultures. Current neurocognitive models posit that tool use is reliant upon a left lateralised neural network, comprised of fronto-parietal circuits that separately mediate manipulation knowledge and visuomotor control. These functions must be integrated to allow effective tool grasping for functional use.

The left supramarginal gyrus (SMG) has been posited as the point of integration between these cognitive functions as a well as a locus of stored representations of tool use gestures. Damage to the left inferior parietal lobule (encompassing the SMG) results in deficits in tool grasping and manipulation (observed in apraxia); and the SMG has shown preferential activation in response to tool related stimulus. Currently, the role of the SMG during tool action execution is controversial. Some studies have posited that left ventro-dorsal structures (inclusive of the SMG) are specified for manipulation knowledge for use of tools and are integral to generating action plans for grasp and use. Bilateral visuomotor action production systems execute the grasp plan based on visual-kinaesthetic feedback, independent of tool related input from the SMG. However, imaging data has highlighted bilateral SMG activation during tool grasp execution, while planning is associated with left lateralised SMG activation. Furthermore, the basis of tool cognition input is debated between two approaches; the manipulation based approach argues that tool cognition relies on stored representations of use, whereas the technical reasoning based approach argues a reliance on technical reasoning and knowledge of the mechanical principles of tools in relation to the user and targets for action. Both approaches posit an integral role of the SMG in this integrative process.

The research questions of this thesis are threefold; (i) if the SMG is essential for planning, what function does it serve during execution of action? (ii) Are functionally salient elements of the grasp plan monitored during action execution and is this lateralised to the left SMG? (iii) What is the nature of conceptual input and tool cognition necessary for planning effective tool use?

This thesis attempts to address these research questions through use of transcranial magnetic stimulation (TMS) and kinematic data analysis. In Chapter

1, evidence establishing current models of tool use and the SMG are discussed as well as the debate between manipulation and technical reasoning based approaches concerning the basis of cognition that facilitates tool use. In Chapter 2, a methodological study examines the accuracy of TMS coil placement across two methods of stereotaxic neuro-navigation, in preparation for the upcoming experiments.

In Chapter 3, the role of the SMG during selection of functional grasp of tools for use is examined. An online correction task, in which tools were rotated rapidly during reaching (necessitating correction of grasp orientation) was conducted. This revealed a bilateral effect of SMG stimulation, resulting in delayed or erroneous grasp correction. This highlighted an integral role for the SMG in facilitating online correction of tool grasp for use. Contrary to current left lateralised models, results in this experiment are in line with a model of left SMG integration of tool grasp specific information, while the right SMG may be considered to support online correction without specific association with tool related input. However, this dissociation could not be confirmed without further control conditions.

In Chapter 4, the aforementioned paradigm was expanded to include non-rotation controls and a control site of stimulation. In the previous paradigm, each trial required an online correction; this was discussed as a potential reason for right SMG stimulation effects. The right SMG has previously been associated with tasks requiring sustained attention and detection of changes in location or motion. Inclusion of non-rotation trials aimed to ensure the task focused on tool related input integrated with motion control, and limit participant anticipation of tool rotation. Findings demonstrated delays or erroneous grasp as a result of left SMG stimulation under certain rotation conditions, regardless of hand used. This implicates a role of the left SMG in providing dynamic reintegration of tool related input in response to changes in functional elements of the established grasp plan. Furthermore, the effects of right SMG stimulation were not present with the addition of non-rotation controls.

In Chapter 5, a behavioural task was conducted to explore the nature of conceptual tool input necessary for selection of grasp; whether reliant on stored manipulation knowledge or technical reasoning (both thought to be mediated by the left SMG). Variances were examined in early movement kinematics dependent on familiarity with the tool, intention of action (transport or use) and affordance (varied orientation of the tool). This aimed to establish whether grasp actions were based on stored manipulation knowledge (which should be accessed faster for familiar tools and actions) or technical reasoning (regardless of familiarity, tools and actions should be constrained only by their structural and mechanical properties). Early movement kinematics indicated that actions were processed on the basis of structural properties and intention, as a function of affordance. While findings showed some support for the manipulation based approach, they more closely conform to the technical reasoning account.

Developing this paradigm further, the experiment in Chapter 6 integrated TMS over the left anterior supramarginal gyrus (aSMG) during action planning. This aimed to assess the role of this region as the locus of integration of either manipulation knowledge or technical reasoning, into visuomotor systems for functional tool grasp. aSMG stimulation delayed selection of grasp orientation for use, but not transport, as a function of orientation of the tool. This implicates a role of the aSMG in supporting integration of technical reasoning into affordance processing structures. However, these findings do not discount the influence of stored gestures, or manipulation knowledge.

This thesis has shown a dynamic role of the left SMG in selection of functional grasp of tools for use during action execution. This further shows that the left SMG monitors the conceptual fit between hand and tool as it pertains to the functional elements of the tool and position in relation to the user. The data indicates that this occurs when necessitated by changes to the tool orientation that affect functionally salient aspects of grasping. This is likely lateralised to the left hemisphere, however, the right SMG may serve functions such as sustained attention and location tracking that support online tool grasp selection, but are not reliant on tool related cognition. These findings support a basis in technical reasoning for selection of grasp when using familiar and novel tools, subject to constraints from the intention of action and affordances in the environment. However, these findings do not discount the role of manipulation or function knowledge for influencing online grasp selection. The methods developed in this thesis have revealed new avenues for research in the field of human tool use and could be further developed to continue exploration of this neural network.

Glossary of Abbreviations

(a)IPS	*(anterior) Intraparietal Sulcus*
(a)SMG	*(anterior) Supramarginal Gyrus*
(f)MRI	*(functional) Magnetic Resonance Imaging*
(p)MTG	*(posterior) Middle Temporal Gyrus*
(p)TC	*(posterior) Temporal Cortex*
CU	*Conventional Use*
ESC	*End State Comfort*
IPL	*Inferior Parietal Lobule*
IPS	*Intraparietal Sulcus*
LBD	*Left Brain Damage*
LOC	*Lateral Occipital Complex*
MO	*Movement Onset*
MT	*Movement Time*
NU	*Non-conventional Use*
POC	*Parietal Occipital Complex*
SPL	*Superior Parietal Lobule*
TGS%	*Percent time to Grasp Selection*
TMS	*Transcranial Magnetic Stimulation*
TPA%	*Percent Time to Peak Aperture*
TPV%	*Percent Time to Peak Velocity*

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1. Introduction

Human tool use is a fundamental and defining characteristic of the species (Beck, 1980; Johnson-Frey, 2003; Orban & Caruana, 2014; Tomasello, 1999). Humans demonstrate an understanding of tools, and their impact on the environment, that sets them apart from other tool using animals (Povinelli, 2000). This is exemplified in the frequency of tool use across a lifespan, and evidence that humans across all cultures and societies engage in the development and use of tools spontaneously as part of day to day life (Osiurak, Jarry, & Le Gall, 2010). The cognitive basis of tool use relies on knowledge of tool functionality in conjunction with the visuomotor control necessary to implement these actions (Brandi, Wohlschläger, Sorg, & Hermsdörfer, 2014; Johnson-Frey, 2004; Orban & Caruana, 2014). Brain lesions and neurodegenerative conditions have been known to cause deficits in processing one or both of these functions (Goldenberg, 2003, 2008; Sunderland, Wilkins, Dineen, & Dawson, 2013). Therefore, understanding the cognition and neural networks that facilitate tool use behaviour is a priority for research, and provides insights into this integral human behaviour (Buxbaum, 2001, 2017; Frey, 2007; Johnson-Frey, 2003; Reynaud, Lesourd, Navarro, & Osiurak, 2016).

Tool use is governed by a left lateralised network comprised of frontal, parietal and temporal regions, mediating different elements of associated tool use behaviours and knowledge (Johnson-Frey, Newman-Norlund, & Grafton, 2005; Orban & Caruana, 2014). This thesis is an investigation into the role of the supramarginal gyrus (SMG), one of the key components of this cortical network (Brandi et al., 2014; Lesourd, Osiurak, Navarro, & Reynaud, 2017; Peeters, Rizzolatti, & Orban, 2013; Reynaud et al., 2016). Using a combination of transcranial magnetic stimulation, kinematic data analysis and novel experimental paradigms involving physical, goal oriented tool use; this thesis attempts to explore three key issues within the literature regarding the SMG. Firstly; what is the role of the SMG in selection of functional grasp during action execution (Andres, Pelgrims, Olivier, & Vannuscorps, 2017; Tunik, Lo, & Adamovich, 2008a). Second; is tool use associated cognition lateralised to the left hemisphere and the left SMG(Brandi et al., 2014; Johnson-Frey et al., 2005; Kroliczak & Frey, 2009; Przybylski & Kroliczak, 2017). Third, the nature of conceptual cognition that enables effective tool use (Binkofski & Buxbaum, 2013a; Borghi, 2014; Buxbaum, 2017; Osiurak & Badets, 2016, 2017; Reynaud et al., 2016; Rizzolatti & Matelli, 2003; Thill, Caligiore, Borghi, Ziemke, & Baldassarre, 2013). This chapter will explore the definition of tools and their use in human and animal species. The current understanding of the neural network facilitating human tool use in the context of imaging and neuropsychological research is then discussed, before examining two of the leading neurocognitive accounts of tool use in humans. The current understanding of SMG functionality within these frameworks, and the methodologies being implemented to explore these issues is then discussed.

1.1. Defining Tools and Human Tool Use

Concerning tools, discourse operates under the classic interpretation of a 'tool'; referring to an object that can be held and manipulated to apply changes to other objects in the environment and achieve a specific goal (Osiurak et al., 2010). Under this definition, a nail is not a tool, but the hammer used to secure it in a surface is. It is important to note, however, that any definition of a tool compared to another object, is one of convenience rather than biological distinction (Beck, 1980). The rock that an animal might strike an egg against for the purpose of breaking (van Lawick-Goodall, 1971), might be considered a tool, but is not the object being held by the animal itself (Osiurak et al., 2010).

In developing an understanding of the cognitive basis of human tool use, a consensus of three main characteristics that define tools has emerged (Osiurak et al., 2010). Firstly, tools are unattached, manipulable environmental objects, used for specific goal oriented tasks (Frey, 2007; Ochipa, Rothi, & Heilman, 1989). Second, tools extend the sensorimotor capabilities of the user in attainment of the goal (Barber, 2003; Beck, 1980; van Lawick-Goodall, 1971). Third, the term 'tool' refers only to what is manipulated by the user, and not the object that is being acted upon (Gibson, 1979; Osiurak et al., 2010; St Amant & Horton, 2008).

Anthropologists previously considered this behaviour as a defining characteristic of the genus *Homo* (Oakley, 1949). However, under the above definition, tool use is not unique to humans. Many animals have the manual capability for using tools, and accounts report observed tool use across a number of animal species including birds (Lefebvre, Nicolakakis, & Boire, 2002), elephants (Hart, Hart, McCoy, & Sarath, 2001) and primates (van Schaik, Deaner, & Merrill, 1999). So, is human tool use behaviour special? Researchers have pointed out that observations of animal tool use in certain species arise from behaviours in captivity (Beck, 1980; van Schaik et al., 1999) or from single individuals in the wild, on a limited number of occasions (Chappell & Kacelnik, 2002). This contrasts drastically with human tool use, which is spontaneous and frequent (Osiurak et al., 2010). This behaviour is observable across all human societies, and the development of technical equipment, modified and improved over time, reflects that this a defining human characteristic (Frey, 2007). Researchers have also observed that from examining humans and chimpanzees, it becomes clear that humans understand the causal relationship between tool and the obtained results, while this understanding remains absent in chimpanzees (Vaesen, 2012).

It is true that manufacture of tools for specific functions has been observed in animal species (Hunt, 1996; van Schaik, 2003; Westergaard & Suomi, 1994), however, the purpose and manner of use highlights another differentiating feature from human tool use. These implements are mostly used for the purpose of obtaining otherwise inaccessible food items - known as extractive foraging (van Schaik et al., 1999). This behaviour has been termed as *simple* tool use; which, while still involving the use of objects for motor-to-mechanical transformations (thereby amplifying sensorimotor capabilities of the user); usually involve modest modifications of readily available objects in the surrounding environment (Frey, 2007). As noted previously, this type of tool use is limited to subgroups within species; for instance some tribes of chimpanzees have been observed cracking nuts using two stones as a hammer and anvil, but this is not a defining characteristic of the species as a whole (McGrew, Ham, White, Tutin, & Fernandez, 1997). Furthermore, the role of each stone (hammer, vs anvil) in this context is often interchangeable, with no specific features to distinguish hammer stones from anvil stones (Sakura & Matsuzawa, 1995) .

By marked contrast, humans develop and engage in the use of *complex* tools. Frey (2007) observed that the use of complex tools involves “using objects to implement transformations that convert movements of the hand into qualitatively different mechanical actions (e.g., using a knife to cut, pencil to write, or brush to clean teeth)” (p. 368). There is much evidence to suggest that the brain processes complex versus simple tool use differently; observed in the behaviour and neuro-anatomy of animal and human tool users (Peeters et al., 2013). Although humans do engage in simple tool use behaviours, there are no other animals that possess such a varied collection of complex tool use skills (Frey, 2007). Furthermore humans engage in manufacture and development of tools, a process which often involves the mechanical combining of two objects to create a single object better suited to the desired goal, or using one object to shape another to a desired purpose (Frey, 2007). Fossil records indicate that examples of this behaviour have been associated with hominids, dating back approximately 2.5 million years (e.g., shaping a rock to better sharpen wooden spears)(Ambrose, 2001). Though complex tools can be used to serve multiple purposes, they often have narrow demarcated functions for which they are designed that may not be interchangeable with others (Frey, 2007). For example, you may use a butter knife to turn a slot head screw, but it would be a challenge to prepare your morning toast with a screwdriver. Also, the distinct, refined procedures associated with skilful tool use have co-evolved alongside language, and are transmitted actively through generations (Frey, 2007). It has been suggested that the drastic differences between human and primate tool use are driven by evolutionary discontinuities in causal reasoning, hand-eye coordination, language, representation of function, social learning, executive control, teaching and social intelligence (Vaesen, 2012). This reflects the importance of cognition and the supporting brain structures, serving this integral behavioural function. However, despite renewed interest, and technological development in the field of research; the neural and cognitive basis of tool use in humans is not fully understood.

1.2. The Neural Network Facilitating Tool Use in Humans

The current understanding of the neural network and cognitive processes supporting tool use is derived from a number of methods and sources. Previously, models were developed based on observations of patients with difficulties engaging in tool related actions following brain damage. However, with the development of functional neuroimaging and cortical stimulation techniques over the last few decades, experimental paradigms have allowed exploration of cortical regions associated with tool use in healthy participants. Neuroimaging and neuropsychological research has highlighted a neural network that facilitates skilled task execution, such as tool use and other visuomotor behaviours. In this section, the neural network associated with tool use from patient observations and functional imaging methods is discussed.

1.2.1. Knowledge vs. Action: Dissociation between Conceptual and Production Systems Observed in Apraxia

Making effective use of tools requires two distinct processes: knowledge of tools, including the ability to recognise the tool itself, the associated uses, and the correct context for use; and the ability to carry out the necessary visuomotor transformations for effective use. It is well documented that brain damage can selectively impair various processes that contribute to skilful behaviours, including tool use (Goldenberg, 2003; Heilman & Rothi, 1997; Marchetti & Della Sala, 1997; Milner & Goodale, 2008). Evidence of this dissociation is observable in patients with apraxia – a disorder of higher motor cognition, characterised by deficits in learned, voluntary actions (Goldenberg, 2009; Johnson-Frey, 2004; Niessen, Fink, & Weiss, 2014). When asked to perform tool based actions, some patients present ‘errors of content’ – this refers to skilfully carrying out actions, but in the incorrect context (Johnson-Frey, 2004). For example, trying to use a toothbrush to eat (Ochipa et al., 1989). This deficit cannot be ascribed to lack of recognition (as would be expected in agnosia) as the patient could identify the object by name (Ochipa et al., 1989). These errors have been interpreted as evidence that the representations of tool use and the representations allowing identification of appropriate context for use are functionally distinct (Johnson-Frey, 2004).

The most frequent neurological correlate of apraxia is left brain damage caused by haemorrhagic or ischaemic stroke (Goldenberg, 2013). However, elements of apraxic behaviour have been associated with neurodegenerative disorders such as Alzheimer's and Parkinson's disease (Bohlhalter & Osiurak, 2013). There are three forms of apraxia as identified by researchers, ideational apraxia, ideomotor (ideo-kinetic) apraxia and limb-kinetic apraxia (Goldenberg, 2013). Ideational apraxia, highlighted in the previous example, refers to the inability to carry out use of familiar tools in the correct context (Bieńkiewicz, Brandi, Goldenberg, Hughes, & Hermsdörfer, 2014). This is manifest in selection of inappropriate tools for a required goal, and difficulty in carrying out naturalistic multi-step action (Goldenberg, 2013). Ideomotor apraxia is characterised by deficits in pantomiming actions when prompted, mimicry of tool use without the object in hand, and/or difficulty in replicating transitive and intransitive gestures (Bieńkiewicz et al., 2014; Goldenberg, 2013; Sunderland et al., 2013). Transitive gestures refer to those of object use, while intransitive gestures[1] are non-tool related, such as giving the thumbs up sign (Bieńkiewicz et al., 2014). Observations of ideomotor apraxia have also shown a milder deficit in actual use with the tool in hand (Goldenberg & Hagmann, 1998; Sunderland & Shinner, 2007). Errors associated with limb-kinetic apraxia are observable during goal oriented use of actual tools, in which patients carry out actions but in a spatiotemporally erratic manner (Hermsdörfer, Laimgruber, Kerkhoff, Mai, & Goldenberg, 1999; Poizner et al., 1995; Randerath, Goldenberg, Spijkers, Li, & Hermsdörfer, 2010). Limb-kinetic apraxia is characterised by disrupted smoothness of movements and increased hesitation, alongside deficits in fine motor movements requiring precision. However, this disorder only affects the limb contralateral to the lesion (Heilman, Meador, & Loring, 2000). Although apraxia has been used to describe a broad variety of disorders (Goldenberg, 2008), the key cognitive domains affected by apraxia encompass the use of tools (multiple and single) and gesture production (Bieńkiewicz et al., 2014). The

[1] 'Gesture(s)' are defined as a 'movement of part of the body, especially a hand or the head, to express an idea or meaning' (Gesture, n.d.) – that is to say an aspect of social communication. The use of the term in apraxia literature stems from the use of gestures in clinical assessment, as traditional apraxia theories posit an overlap in processing between tool-use and social gesture production. However, more recent interpretations focus on stored 'manipulation-knowledge' as opposed to stored gestures. For ease, and due to frequency of the terminology in the literature, the term 'stored tool use gesture' is used here interchangeably with stored manipulation knowledge.

deficits observed in apraxia provide two key elements in the current understanding of human tool use; (i) tools, their associated actions and appropriate context for use are represented distinctly from the action production systems necessary for manipulation; (ii) this is likely localised to the left hemisphere. This dissociation of manipulation function and knowledge of tools is addressed in the two streams model for perception and action.

1.2.2. Visual Pathways for Perception and Action in Tool Use

The two streams model (Goodale & Milner, 1992; Milner & Goodale, 2008; Mishkin & Ungerleider, 1982) initially proposed two separate, but interacting parallel visual pathways serving different functions pertaining to perception and action; responsible for 'what' and 'where' visual perception in the ventral and dorsal streams respectively. Regarding tool use, the dorsal stream is proposed to be involved in visual control and navigation of space, while the ventral stream is proposed to transform visual input of the tool into perceptual representations pertaining to the tools use (Milner & Goodale, 2008). More recently, researchers have proposed a further separation of the visual pathways to describe a three-stream model comprised of dorso-dorsal, ventro-dorsal and ventral visual streams (Binkofski & Buxbaum, 2013a; Buxbaum, 2017; Pisella, Binkofski, Lasek, Toni, & Rossetti, 2006; Rallis, Fercho, Bosch, & Baugh, 2018a; Rizzolatti & Matelli, 2003). These pathways are comprised of multiple neuronal circuits connecting frontal, temporal and parietal brain regions and are functionally responsible for different aspects of behaviour and knowledge in tool use (Binkofski & Buxbaum, 2013a; Brandi et al., 2014; Rallis et al., 2018a).

Evidence suggests that the dorso-dorsal stream is integral to online control of motor actions during tool use (Binkofski & Buxbaum, 2013a; Buxbaum, 2017; Rallis et al., 2018a). This pathway is specialised in processing the effector limbs in space, reaching and grasping behaviour, as well as accounting for the extension of peripersonal space afforded by the length of the tool in hand. The dorso-dorsal stream is further argued to be involved in determining whether an object affords a particular action by processing relevant object features and the capabilities of the

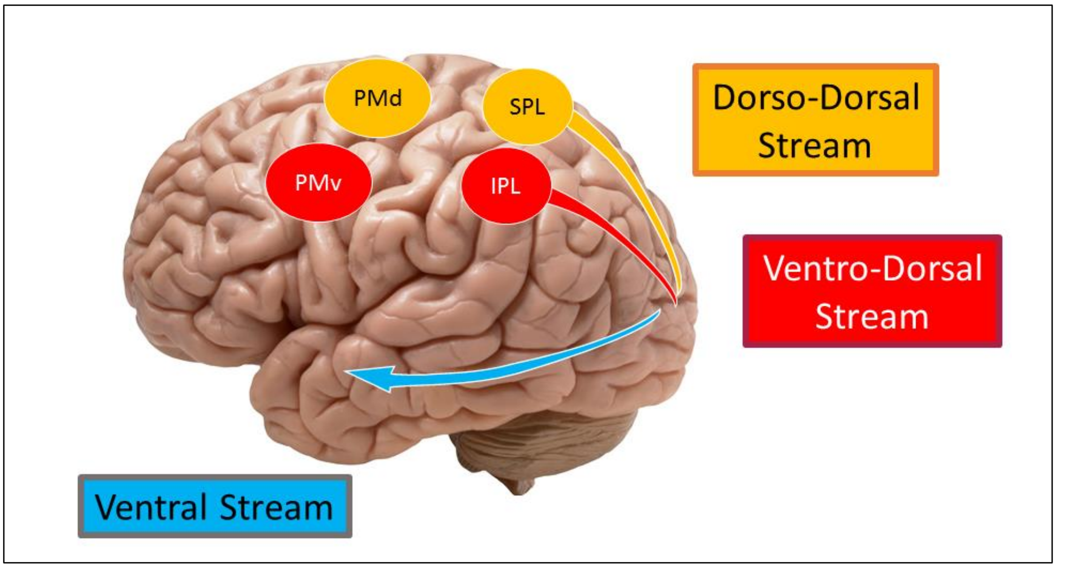

Figure 1. Variation of the two visual pathways for perception and action model (Goodale & Milner, 1992; Milner & Goodale, 2008; Mishkin & Ungerleider, 1982; Ungerleider & Mishkin, 1982). The updated model proposed two visual pathways for action, the dorso-dorsal pathway from visual cortices V3A via superior parietal lobule (SPL) and middle intraparietal sulcus (mIPS), passing information via the superior longitudinal fascilicus (SLF) (Vry et al., 2015) to the dorsal premotor cortex (PMd) for motor execution (Rizzolatti & Matelli, 2003). The ventro-dorsal Pathway projecting from visual cortices V5/MT via the inferior parietal lobule (IPL – inclusive of the SMG) to ventral pre-motor cortex (PMv) (Binkofski & Buxbaum, 2013a; Rizzolatti & Matelli, 2003; Vry et al., 2012, 2015b) – mediates input of conceptual information pertaining to tool uses and properties for functional tool use behaviours (Buxbaum & Kalénine, 2010; Rizzolatti & Matelli, 2003). Background image of human brain from https://commons.wikimedia.org/wiki/File:HumanBrain308.jpg, CC-BY-SA 2.0

user (Binkofski & Buxbaum, 2013a; Buxbaum, 2017). This pathway also mediates rapid online error correction in motor control (Rice, Tunik, Cross, & Grafton, 2007). This pathway projects from visual cortices V3A via superior parietal lobule (SPL) and middle intrapariarietal sulcus (mIPS), passing information via the superior longitudinal fascilicus (SLF) (Vry et al., 2015) to the dorsal premotor cortex (PMd) for motor execution (Rizzolatti & Matelli, 2003). The dorso-dorsal pathway is bilateral (Binkofski & Buxbaum, 2013a; van Elk, 2014) and is specialised for grasp and transport actions (see Figure 1).

The ventro-dorsal stream is proposed to mediate input of conceptual information pertaining to tool uses and properties for functional tool use behaviours (Buxbaum & Kalénine, 2010; Rizzolatti & Matelli, 2003). This pathway anatomically runs inferior to the dorso-dorsal stream, projecting from visual cortices V5/MT via the inferior parietal lobule (IPL – inclusive of the SMG) to ventral pre-motor cortex (PMv) (Binkofski & Buxbaum, 2013a; Rizzolatti & Matelli, 2003; Vry et al., 2012, 2015b). In contrast to the dorso-dorsal stream, evidence suggests that the ventro-dorsal pathway is left lateralised with regards to functionally enabling tool use behaviours (Binkofski & Buxbaum, 2013a; Brandi et al., 2014; Przybylski & Kroliczak, 2017), consistent with deficits observed in apraxia following left hemisphere damage (Goldenberg, 2013). However, exceptions have been observed in cases of right parietal damage in tasks requiring multiple step tool use in naturalistic settings such as preparing coffee (Hartmann, Goldenberg, Daumüller, & Hermsdörfer, 2005). The ventro-dorsal stream is specialised for 'use' actions (e.g. using a tool to complete a goal oriented task in the manner for its design or most suitable action for the task at hand) (Binkofski & Buxbaum, 2013a; Rallis et al., 2018a). The supramarginal gyrus (SMG) within the IPL is particularly associated with understanding tool use actions and researchers suggest that this region is functionally responsible for processing salient information about tools pertaining to use. However, there is currently a discrepancy between two key approaches in the basis of tool cognition in ventro-dorsal function (Buxbaum, 2017; Osiurak & Badets, 2017) (see 1.3).

The ventral visual stream in regards to tool use is involved in object identification and selecting appropriate associated actions (Milner & Goodale, 2008). This pathway extends from the lateral occipital complex (LOC) to inferior temporal gyrus (ITG), posterior middle temporal gyrus (pMTG), and the fusiform gyrus (FG) (Mahon et al., 2007). For tool use, this pathway is associated with semantic information pertaining to the object as well as descriptive features such as colour, texture, form and shape (Cant & Goodale, 2007, 2009, 2011; Tobia & Madan, 2017a). This pathway is regarded as a store of function knowledge relating to a tools known/learned use (e.g. a hammer is used to pound a nail) (Ishibashi, Lambon Ralph, Saito, & Pobric, 2011). However, the pMTG is also thought to process tool related motion (Beauchamp, Lee, Haxby, & Martin, 2002; Chao, Haxby, & Martin, 1999; Chao & Martin, 2000; Noppeney, Price, Penny, & Friston, 2006; Perini, Caramazza, & Peelen, 2014). There is considerable crosstalk between the ventral and ventral-dorsal pathways in the form of connections between the LOC and pMTG (ventral) and the SMG within the IPL (ventro-dorsal) (Ramayya, Glasser, & Rilling, 2010; S. Zhang & Li, 2014). The ventral pathway is associated with conceptual knowledge of tools such as typical use, and corresponding targets for action (Boronat et al., 2005; Fairhall & Caramazza, 2013; Ishibashi et al., 2011; Madan & Singhal, 2012; Perini et al., 2014). This knowledge relates to the known purpose or goal associated with a tool rather than the action of use (Garcea, Dombovy, & Mahon, 2013; Kellenbach, Brett, & Patterson, 2003; Madan & Singhal, 2012; Tobia & Madan, 2017b); a knife and a pair of scissors may both be used to cut but require different manipulation actions (Tobia & Madan, 2017b).

In summary, the ventral pathway mediates knowledge of tool function while the dorso-dorsal and ventral-dorsal pathways process action knowledge (i.e. praxis) pertaining to tools, as highlighted by their specification for grasping and use, respectively. However, as noted earlier, opinions on the nature of conceptual tool knowledge enabling tool use and the corresponding cortical structures that support these roles, are currently divided between two approaches, (i) The manipulation based approach and the 2AS+ model and (ii) the reasoning based approach, discussed below.

1.3. Two Neurocognitive Models of Tool Use

1.3.1. The Manipulation-based Approach (2AS+ model)

The manipulation-based approach posits that tool use relies upon access to stored sensorimotor knowledge about tool manipulation. This approach suggests that deficits observable in apraxia are a matter of gesture production (see below), as

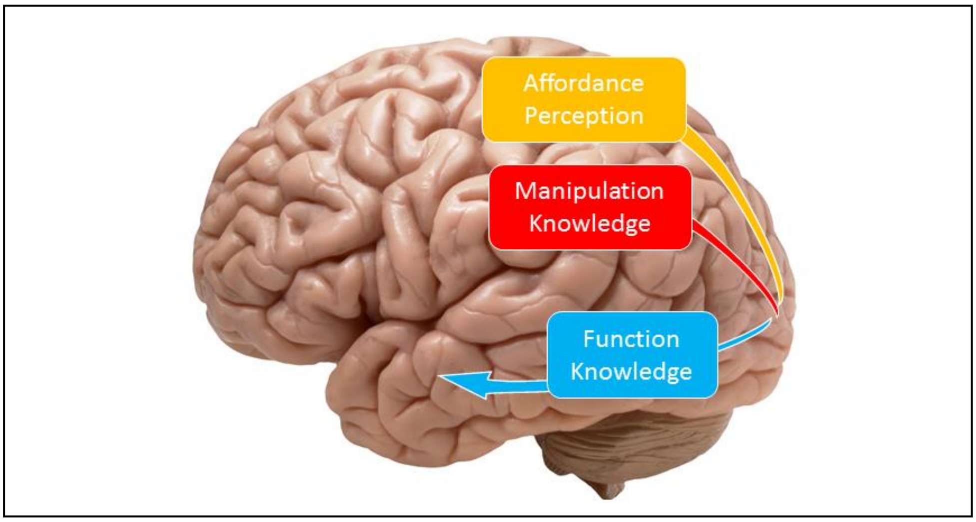

*Figure 2. Visual pathways for action as interpreted by the manipulation based approach concerning tool use. Dorso-dorsal structures process affordances in the environment and guide action **on** tools. Ventro-dorsal structures, inclusive of the SMG guide action **with** tools. This pathway is argued to be a locus of stored gesture engrams – multisensory representations of how to effectively use tools. (Buxbaum, 2017; Buxbaum & Kalénine, 2010; Buxbaum et al., 2006; Rizzolatti & Matelli, 2003). Background image of human brain from https://commons.wikimedia.org/wiki/File:HumanBrain308.jpg, CC-BY-SA 2.0.*

observed in shared deficits in production of symbolic and meaningless gestures (Binkofski & Buxbaum, 2013a; Buxbaum, 2001; Buxbaum & Kalénine, 2010; Heilman, Rothi, & Valenstein, 1982; Rothi, Ochipa, & Heilman, 1991; Thill et al., 2013; van Elk, 2014). Tool use, in this case, is reliant upon sensorimotor engrams tied to specific tool use skills (Buxbaum, 2001; Heilman et al., 1982; Johnson-Frey et al., 2005; Rothi et al., 1991).

These engrams are stored long-term and accessed upon tool interaction; encompassing the key parameters of the required gesture, amplitude of movement and posture (Buxbaum, Kyle, Grossman, & Coslett, 2007). These representations are encoded by interacting with tools and observing others interacting with tools, and occur across visual, tactile and motor modalities (Buxbaum, 2017). Access to these stored representations negates the need to reconstruct manipulation plans on each use, providing an advantage in processing (Buxbaum, 2017).

The left IPL (see Figure 2) has previously been implied as the locus of stored manipulation knowledge (Binkofski & Buxbaum, 2013a; Buxbaum & Kalénine, 2010; Daprati & Sirigu, 2006; Gainotti, 2013; Heilman et al., 1982; Rizzolatti & Matelli, 2003; Rothi et al., 1991; van Elk, 2014) and arguably accounts for activation of left IPL structures during neuroimaging studies pertaining to tool use (Boronat et al., 2005; Buxbaum, Kyle, Tang, & Detre, 2006; Grezes & Decety, 2002; Hermsdörfer, Terlinden, Mühlau, Goldenberg, & Wohlschläger, 2007; Imazu, Sugio, Tanaka, & Inui, 2007; Johnson-Frey et al., 2005; Kellenbach et al., 2003; Kroliczak & Frey, 2009; Vingerhoets, 2008; Vingerhoets, Acke, Vandemaele, & Achten, 2009). Manipulation knowledge encodes egocentric relationships; that is relationships between the user and the tool. This is specific to the action of ‘use’ and position of the tool in relation to the effector (Buxbaum, 2017; Reynaud et al., 2016). It does not consider the relationship between tools and the intended target of action (e.g. hammer and nail). Manipulation knowledge, therefore, does not facilitate selection of appropriate context for a tool’s learned use (Reynaud et al., 2016). In line with the models outlined in the previous section, allocentric relationships (i.e. between tool and objects – function knowledge) are proposed to be encoded within the ventral stream (Beauchamp et al., 2002; Chao et al., 1999; Chao & Martin, 2000;

Goodale & Milner, 1992; Milner & Goodale, 2008; Noppeney et al., 2006; Orban & Caruana, 2014).

A recent interpretation of the manipulation-based approach outlines a model consistent with the visual pathways described in the previous section. The 2AS+ model (Buxbaum, 2017) proposes that a left lateralised ventro-dorsal and bilateral dorso-dorsal pathway facilitate visually guided action for tool use, alongside an additional module for action selection (2 action systems plus additional module, see Figure 3). This model posits that the first component, the dorso-dorsal pathway, while mediating grasping and transport behaviour, is also integral in predicting the consequences of action during execution. The prediction is compared to online sensory input as movement occurs and discrepancies between the predicted and actual actions are used to guide error correction and refinement of movement (Buxbaum, 2017).

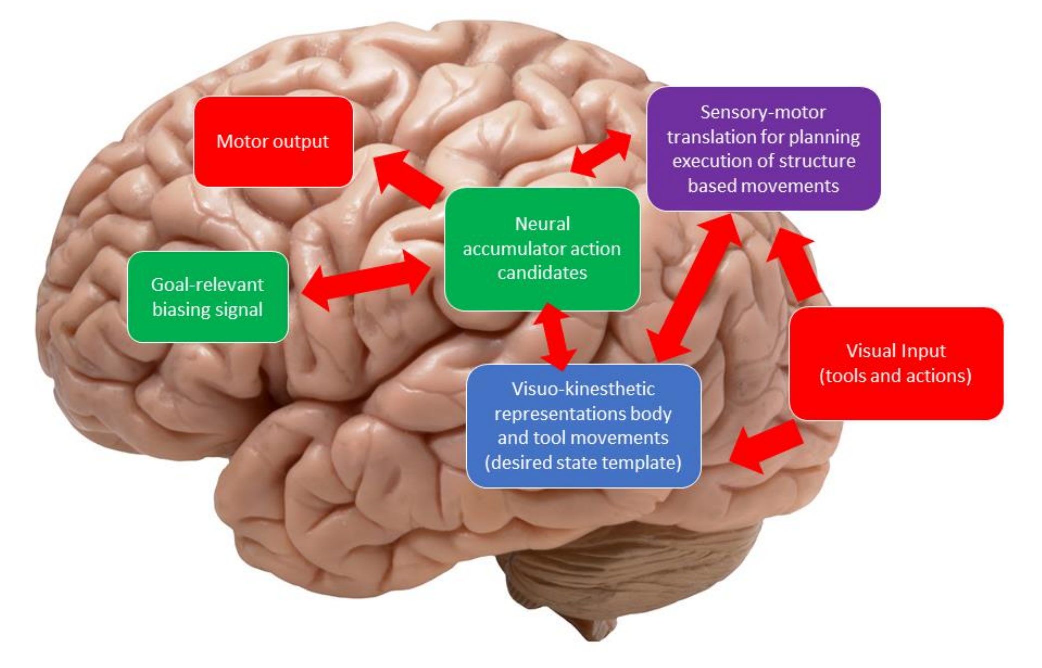

Figure 3. Illustration of the 2 Action Systems Plus (+) model of tool use. A left lateralised posterior parietal system subserves storage of abstract, multimodel manipulation knowledge (blue). This is translated into sensorimotor representations enabling tool use production via a bilateral fronto-parietal network, with additional 'fine-tuning' based on sensory motor and visual input (purple). The action selection portion of the network (green) subserves a biasing signal from the inferior frontal cortex that aids in selection of potential actions from a temporary buffer in the left SMG (Recreated from Buxbaum (2017)). Background image of human brain from https://commons.wikimedia.org/wiki/File:HumanBrain308.jpg, CC-BY-SA 2.0.

The second component, the ventral-dorsal pathway in this model encompasses the left posterior temporal lobe and supports manipulation knowledge representations in visuo-kinaesthetic format (Bracci, Cavina-Pratesi, Ietswaart, Caramazza, & Peelen, 2012; Bracci & Peelen, 2013; Buxbaum, 2017; Buxbaum & Kalénine, 2010; Tarhan, Watson, & Buxbaum, 2015). These representations act as the desired 'goal' state during action execution for how the object interaction should feel and look. This provides a template for error correction in line with constraints of the environment (Buxbaum, 2017).

The third component is necessary due to competition that can emerge between the two pathways for action (Buxbaum, 2017). Multiple potential actions may be generated by the ventro-dorsal (manipulation knowledge for goal states of tool use) and dorso-dorsal (predictions about future states of the effector, objects and environmental constraints pertaining to transport) simultaneously. Furthermore, for familiar tools with multiple uses, there may be multiple candidate actions in competition relying on manipulation knowledge (e.g. a hammer can be used to either drive or remove a nail – these actions are associated with the same object but have fundamentally different manipulation schemas and goal states). The 2AS+ model argues that these potential actions are prepared in parallel within the left SMG which acts as a neural buffer and point of connection between the two action pathways (Buxbaum, 2017). The inferior frontal gyrus (IFG) selects the action from the buffer that is most appropriate to the context of the task and environmental constraints (Buxbaum, 2017).

This model is supported across a number of neuroimaging and neuropsychological studies. Brandi et al. (2014) observed that familiar tool interaction elicited left lateralised activation of cortical regions in pMTG, SMG, intraparietal sulcus (IPS) and SPL, when compared with non-tool objects. These regions are implicated in a number of tool related neuroimaging studies (Bi et al., 2015; Gallivan, McLean, Valyear, & Culham, 2013; Lewis, 2006; Orban & Caruana, 2014). The issue of object familiarity is central to the 2AS+ model and the manipulation-based approach; familiar tools and objects should be processed differently from non-tool stimuli, as manipulation representations are based on learned schemas from previous experience (Buxbaum, 2017). However, the salience of object familiarity regarding tool use is debated within the literature (Osiurak & Badets, 2017) and will be addressed later in the chapter (see 1.3.2). Further support is shown in that co-activation of the MTG and SMG is argued to reflect access to stored contextual knowledge pertaining to familiar tools (i.e.

function knowledge) and schemas for use (i.e. praxis). Stronger left lateralised connections between MTG and SMG (relative to right hemisphere connectivity) have been observed in diffusion tensor imaging (Ramayya et al., 2010). This is consistent with the roles of the ventro-dorsal and ventral streams described by the model. Furthermore, the bilateral action production system in the dorso-dorsal stream is supported by patients with lesions to the IPS exhibiting spatiotemporal movement errors, while patients with damage to left ventral regions exhibit deficits in semantic understanding of task requirements (M. Martin et al., 2016).

The SMG, central to the 2AS+ model, has been shown in neuroimaging as responsive to a number of tool related tasks, in particular observation of tool action execution (Kroliczak & Frey, 2009; Lesourd et al., 2017; M. Martin et al., 2016; Orban & Caruana, 2014; Przybylski & Kroliczak, 2017). Co-activation of the left SMG and IPS in response to such stimuli could arguably reflect the integration of manipulation knowledge from SMG into the IPS (thought of as part of the dorso-dorsal pathway) for action production and online control of grasping (Jacobs, Danielmeier, & Frey, 2009; Orban & Caruana, 2014), in keeping with the 2AS+ model. Research has also shown that transcranial magnetic stimulation (TMS) over the IFG during planning stages of tool interaction delays the onset of movement (Tunik et al., 2008). These delays could be reflective of disruption to the selection of appropriate actions from the SMG buffer as proposed by Buxbaum (2017) and others (Bi et al., 2015; Gallivan et al., 2013; Johnson-Frey et al., 2005; Orban & Caruana, 2014).

Although prominent and well supported within the research literature, the 2AS+ model and the manipulation-based approach faces questions with regards to the cognition and processing behind tool use (Osiurak & Badets, 2016, 2017). Arguably, it cannot fully account for how humans make use of unfamiliar tools to fulfil required goals (Lesourd et al., 2017; Osiurak & Badets, 2017; Reynaud et al., 2016). An alternative approach has been proposed in recent years focussing on the influence of reasoning and mechanical knowledge (as opposed to gesture engrams) (Osiurak & Badets, 2017), as a means of addressing discrepancies in the manipulation-based approach.

1.3.2. The Technical Reasoning-based approach to Tool Use Cognition

When carrying out tool use there is a specific goal to be achieved and elements of problem solving are required (Jarry et al., 2013; Osiurak & Badets, 2017; Osiurak et al., 2010; Reynaud et al., 2016). Indeed, developmental psychologists view tool use as instances of problem solving in infants supported by mechanical knowledge (S. R. Beck, Apperly, Chappell, Guthrie, & Cutting, 2011; Mounoud, 1996). Tool use in daily life does not often rely on single gestures and schemas, but a multi-step coordination of stages that are necessary to fulfil a goal (e.g. making a sandwich may involve retrieval and use of multiple pieces of cutlery – knife, spoon – and implementation gestures – spreading, scooping, cutting) (Osiurak, 2014b; Osiurak & Badets, 2016; Osiurak, Jarry, & Le Gall, 2011). A large body of evidence has highlighted the link between tool use deficit and mechanical problem solving (Goldenberg & Hagmann, 1998; Goldenberg & Spatt, 2009; Hartmann et al., 2005; Jarry et al., 2015; Osiurak et al., 2009). This deficit cannot be attributed to executive function damage as patients with frontal lobe lesions and dysexecutive syndrome perform comparably with healthy counterparts on tool related tasks (Goldenberg & Hagmann, 1998; Goldenberg, Hartmann-Schmid, Sürer, Daumüller, & Hermsdörfer, 2007; Goldenberg & Spatt, 2009).

Another issue with the manipulation-based approach is the multiple-routes-to-action hypothesis (Buxbaum, 2017; Osiurak & Badets, 2017; Reynaud et al., 2016). This states that a patient with impaired manipulation knowledge (i.e. praxis) may still be able to make effective use of tools through intact function knowledge. However, a fundamental problem with this idea is that function knowledge encodes allocentric information regarding tools and their appropriate targets for action, whereas manipulation knowledge encodes egocentric information pertaining to the tool and user (Osiurak & Badets, 2017; Reynaud et al., 2016). The manipulation-based approach argues that deficits in manipulation knowledge can be overcome by intact function knowledge feeding into the action production system within the dorso-dorsal pathway. However, if that is the case, what need is there for manipulation knowledge in the first instance (Reynaud et al., 2016)? Furthermore, if tool use skills are facilitated by learned representations, how are humans able to interact with and make functional use of non-tools to perform goal-oriented tasks (e.g. using a particularly weighty book to hammer a nail)?

The technical reasoning-based approach[2] offers an alternative to address some of these issues by asserting human tool use is supported by the ability to technically reason how to manipulate tools to achieve the goal at hand (Lesourd et al., 2017; Osiurak & Badets, 2017; Osiurak et al., 2010, 2011; Reynaud et al., 2016). Reasoning in this instance is based on the ability to understand the mechanical principles of the surrounding environment; as well as object properties in relation to one another (Osiurak & Badets, 2017). This mechanical knowledge is abstract as it can refer to distinct physical properties of objects that may or may not be shared (e.g. wood, plastic and metal share the property of hard), and comparative properties that may make one object suitable for action on another (e.g. a knife is harder and sharper than a tomato – making it a suitable tool to carry out the task of cutting). Mechanical knowledge, therefore, encodes allocentric information based on objects (Osiurak & Badets, 2016; Reynaud et al., 2016). This abstract knowledge explains the human ability to transfer skills (Penn, Holyoak, & Povinelli, 2008) used for tools to non-tools when the conventional choice of implement is not readily available (e.g. using the heel of a shoe to pound a nail) (Osiurak & Badets, 2017; Reynaud et al., 2016). This approach argues that mechanical knowledge is supported by the IPL (Lesourd et al., 2017; Orban & Caruana, 2014; Osiurak & Badets, 2017). The role of dorso-dorsal structures in this framework is in processing the affordances of the objects in relation to the user and generating a mental simulation of the desired action for tool use, based on mechanical knowledge and technical reasoning from the SMG. This mental motor simulation acts as a goal state for how the tool and body should be positioned and moved during action. This allows for changes in orientation, force exertion and positioning during action to ensure the goal of tool use is carried out effectively (Baumard et al., 2016; Lesourd et al., 2017; Osiurak & Badets, 2016, 2017; Osiurak et al., 2011). The mental simulation is not specific

[2] 'Reasoning' is defined as 'the action of thinking about something in a logical, sensible way' (Reasoning, n.d.) – the definition in terms of tool use and the literature is discussed above, however, it is somewhat at odds with everyday parlance. In this thesis, reasoning and technical reasoning describe cognition for action that emphasises *understanding* of tool properties and the effects of action.

to tools but serves to assess the effort and constraint of any task, and allows for adaption based on changes in the environment and affordances (Osiurak & Badets, 2016).

The role of function knowledge is reinterpreted by the reasoning-based approach (Reynaud et al., 2016); in this framework, function knowledge serves to provide wider context to the accessibility and organisation of the most suitable tool objects. To return to the earlier example of making a sandwich, function knowledge allows the actor to locate the knife and chopping board, needed for cutting, while mechanical knowledge supports actual interpretation of the functional properties of tools and objects (Osiurak, 2014b). Function knowledge may also have a key role in reconstructing the appropriate use of single tools when they are presented in isolation from the corresponding task or object (e.g. a screw-driver without a screw) (Osiurak & Badets, 2017; Reynaud et al., 2016). Function knowledge is also useful for sharing tool use methods socially; allowing identification of a tools category, potential uses and associated targets for action. This allows communication of skills that define the cultural manner in which humans use tools (Reynaud et al., 2016). In support of this interpretation, patients with selective impairment to function knowledge have been shown to exhibit deficits when demonstrating the use of single familiar tools in isolation, while being able to demonstrate functional use in tool-target pairs (Hodges, Spatt, & Patterson, 1999; Osiurak, Aubin, Allain, Jarry, Richard, et al., 2008; Sirigu, Duhamel, & Poncet, 1991).

Consistent with intact mechanical knowledge, these patients can often infer uses that would not predominantly be associated with the 'common' use of the tool (e.g. making a hole with a screwdriver) (Osiurak et al., 2009, 2011; Osiurak, Aubin, Allain, Jarry, Richard, et al., 2008). From this, the reasoning-based approach suggests that manipulation actions are generated 'de-novo' based on the mental simulation of action and online information regarding the body in space, and affordances in the environment. The simulation is thought to be generated within the action production system, encompassing the anterior intraparietal sulcus (aIPS) and supported by the IPL and the SMG (Orban & Caruana, 2014; Reynaud et al., 2016).

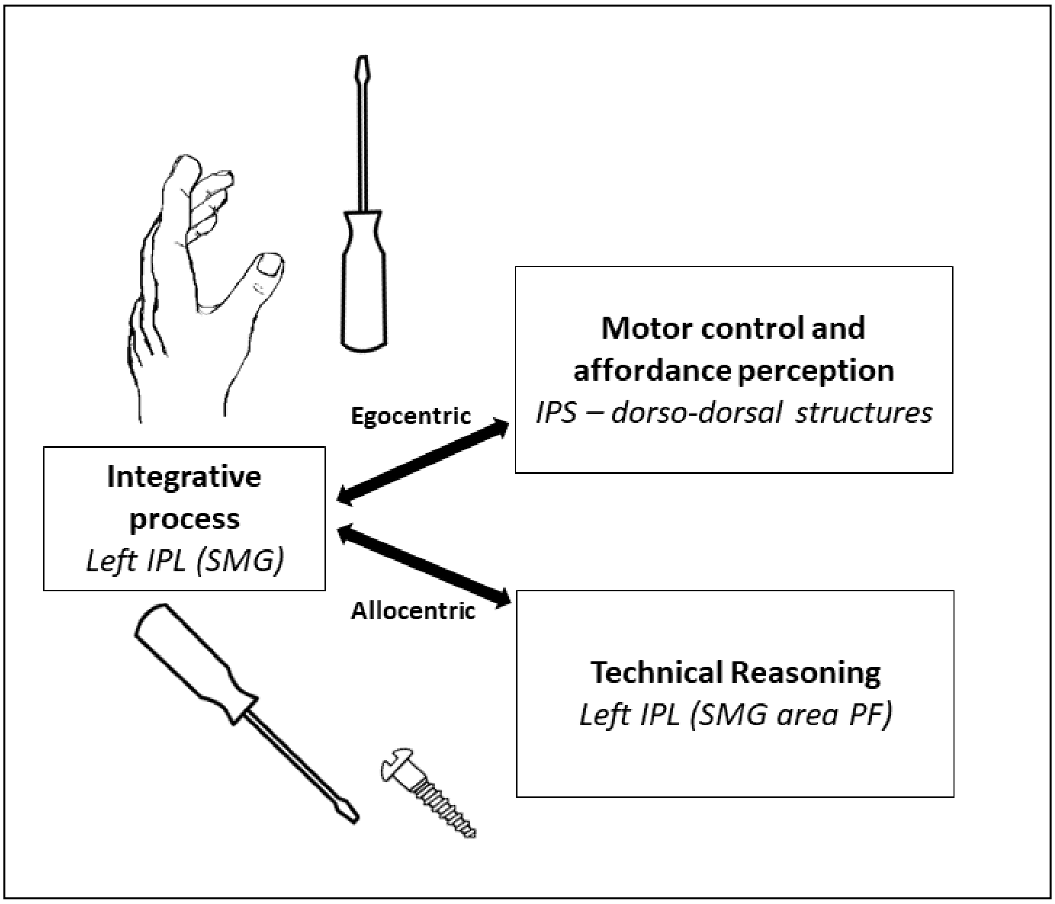

Figure 4. Illustration of the role of the left SMG in line with the technical reasoning approach (Osiurak and Badets, 2017). The SMG is both the locus of technical reasoning and integration of this knowledge into visuomotor and structural processing regions. This allows processing the Egocentric and Allocentric relationships to allow selection of functional tool grasp.

However, in contrast to the manipulation-based approach, the action production system is solely responsible for encoding egocentric relationships about tools, targets and the environment in relation to the user. But this is likely supported in terms of conceptual input from the IPL – in particular the SMG.

Recent models (Lesourd et al., 2017; Orban & Caruana, 2014; Osiurak & Badets, 2017; Peeters et al., 2009a, 2013; Reynaud et al., 2016) have suggested that the anterior SMG (aSMG) is the locus of integration for the production systems of dorso-dorsal structures (e.g. aIPS) and area PF of the left SMG, argued as essential for mechanical knowledge (see Figure 4).

The aSMG may have a role in biasing egocentric information of action production systems to favour the most appropriate orientation of hand in relation to the tool (i.e. egocentric relationships) that suits the goal oriented task of use based on mechanical knowledge (i.e. allocentric relationships) (Reynaud et al., 2016). These components of the reasoning-based approach address the issues inherent in multiple routes to action. However, the basis of transferability of tool use skills from familiar to novel objects is still prominent in the debate between manipulation and reasoning-based approaches. While the salience of familiarity in facilitating action is yet to be resolved, evidence gained from behavioural, imaging and neuropsychological tasks provides some insight into the neurocognitive basis of tool use function.

1.3.3. Are Tools and Non-tools Processed differently by the Tool Use Network?

Much of the research into the tool use network has focused on answering the question ‘are tools special?’ with regards to how they are processed in the brain. For the manipulation-based approach (Binkofski & Buxbaum, 2013b; Buxbaum, 2017; Thill et al., 2013), the answer must be yes, as tool use relies upon stored representations of action based on previous use. Therefore, familiarity with the tool is essential in order to access the appropriate representation of action for effective use (Buxbaum, 2017). Consequently, the tool use network should exhibit specificity in response to familiar tool related stimulus or actions.

A number of studies support this; planning and engaging in functional grasp and use of tool versus non-tool controls (Brandi et al., 2014) demonstrated left lateralised activation of the inferior occipital gyrus, pMTG, anterior IPS, IPL and SPL when contrasting familiar tools against a non-tool object (bar), regardless of intention of action. Activation of the MTG is considered to represent access to stored semantic representations that are to be integrated into visuomotor transformations in the IPL (Rumiati et al., 2004). Furthermore, diffusion tensor imaging has shown strong left lateralised connections between the MTG and SMG for pantomiming use of familiar tools (Ramayya et al., 2010), indicating the potential source of conceptual input to the SMG. Recent imaging has demonstrated left lateralisation of the tool use network for planning functional grasp of familiar tools, and stronger patterns of activation for familiar tools when compared to non-tool counterparts (Przybylski & Kroliczak, 2017).

Tool use regions have shown activation in response to tool naming when compared with control stimuli (Chao & Martin, 2000; A. Martin, Wiggs, Ungerleider, & Haxby, 1996; Okada et al., 2000), indicative of a specific tool representation in the brain compared to other categories of objects, and for decision making tasks about context-appropriate tool use actions or familiar skilled movements (Rumiati et al., 2004; Valyear, Cavina-Pratesi, Stiglick, & Culham, 2007).This distinction in activation for tool related stimuli has also been observed across auditory and visual modalities of presentation (Lewis, Brefczynski, Phinney, Janik, & DeYoe, 2005). Lesion and imaging studies have also shown that observation and understanding of tool use actions is associated with left regions including posterior temporal cortex and SMG (Hoeren et al., 2013, 2014; M. Martin et al., 2016; Vry et al., 2015b). Consistent with the 2AS+ model, spatiotemporal aspects of movement and environment processing are associated with a bilateral dorso-dorsal pathway and not specific for tools. This is particularly observable in left hemisphere stroke patients with SMG and posterior temporal cortex (pTC) lesions who exhibit errors of content, semantically incorrect movements for the task, whereas IPL lesions adjacent to the IPS are associated with spatiotemporal movement errors (M. Martin et al., 2016). Patients with apraxia have also displayed difficulties in reaching to grasp familiar tools but not geometric objects when barrier avoidance is required (Sunderland et al., 2013). These findings suggest specificity for familiar tools in the tool use network, in line with manipulation-based approaches (Binkofski & Buxbaum, 2013a; Buxbaum, 2017; Thill et al., 2013).

However, critics of the manipulation-based approach have argued that these findings do not provide sufficient support to justify the model (Osiurak & Badets, 2017). Contrary to the interpretation offered by the manipulation-based approach (Hoeren et al., 2013; Jax & Buxbaum, 2013; M. Martin et al., 2016; Vry et al., 2015a), the reasoning based approach posits that the deficits observed in apraxia are due to difficulty in the ability to technically reason about physical properties of tools and objects (Osiurak, Aubin, Allain, Jarry, Etcharry-Bouyx, et al., 2008; Osiurak, Aubin, Allain, Jarry, Richard, et al., 2008; Osiurak et al., 2011; Osiurak, Jarry, Lesourd, Baumard, & Le Gall, 2013).

While left brain damage (LBD) patients do exhibit difficulties in conventional use of familiar tools, the same deficits are observable when asked to use familiar tools in an unconventional manner, or solve mechanical problems (Goldenberg & Hagmann, 1998; Goldenberg & Spatt, 2009; Jarry et al., 2013; Osiurak et al., 2011). Although mechanical problem solving could be viewed as mediated by executive control, mechanical problem solving deficits are not correlated with frontal lobe damage (Goldenberg & Hagmann, 1998; Goldenberg & Spatt, 2009; Hartmann et al., 2005; Jarry et al., 2013; Osiurak, 2013; Osiurak, Jarry, et al., 2013). Furthermore, for LBD patients, real tool use performance shares a strong association with mechanical problem solving skills (Baumard, Osiurak, Lesourd, & Gall, 2014), and mechanical problem solving skills are impaired following left inferior parietal lobe lesions but not following frontal lobe lesions (Goldenberg & Hagmann, 1998; Goldenberg & Spatt, 2009). The extension of deficits to tasks not pertaining to familiar tools suggests that cognition mediating familiar tool use is not reliant on semantic representations of learned use.

Kinematic data has previously been cited in support of the importance of tool familiarity in facilitating action. The Orientation Effect (Tucker & Ellis, 1998) has previously shown that motor responses primed by familiar objects are faster when the handle of the object is oriented in the same direction as the effector hand. This has previously been interpreted as evidence of automatic activation of effector-specific motor representations associated with the tool, supporting tool familiarity and the manipulation-based approach (Borghi & Riggio, 2009; Caligiore, Borghi, Parisi, & Baldassarre, 2010; Mizelle & Wheaton, 2010; Pellicano, Iani, Borghi, Rubichi, & Nicoletti, 2010a; Thill et al., 2013).

However, the original authors have since reinterpreted these findings (Symes, Ellis, & Tucker, 2005, 2007), suggesting that this does not reflect automatic activation of stored representations associated with use. This is due to evidence showing that the orientation effect occurs even when participants respond with their feet rather than their hands (Phillips & Ward, 2002; Symes et al., 2005), meaning that the response is not effector specific and unlikely tied to manipulation knowledge (i.e. egocentric). Furthermore, when presented with a teapot, the orientation effect occurs dependent on the orientation of the spout, not the handle (Cho & Proctor, 2010, 2011). The reasoning based approach argues that this contradicts the role of familiarity, and posits that the orientation effect is due to spatial coding of stimulus response compatibility (Osiurak & Badets, 2016, 2017).

The End State Comfort (ESC) effect also provides insight into the role of familiarity. The ESC highlights that participants tend to adopt an uncomfortable initial grasp position to allow a comfortable end state when making use of the object (Rosenbaum et al., 1990). For example, when reaching for a hammer that is oriented away from them, participants will rotate their forearm to grasp the tool by the handle adopting an initially uncomfortable grasp to facilitate a comfortable, functional end state when using the hammer. This process involves identifying the functional end of the tool and the affordances of the graspable handle, and highlights that intention to achieve a particular position is factored into the planning stages of action (Hermsdörfer, Li, Randerath, Roby-Brami, & Goldenberg, 2013; Hermsdörfer et al., 2007; Short & Cauraugh, 1997; W. Zhang & Rosenbaum, 2008). In terms of familiarity, Creem and Proffitt (2001) demonstrated that the ERC occurs regardless of whether the intention of action is use or transport. This supports the role of familiarity, as grasp-to-transport actions do not require a functional grasp (e.g. by the handle with the head pointing away from the body). Based on the requirements of the task, grasping tools by the handle with the head oriented in any direction should be suitable for transport, affording a comfortable end state. Manipulation knowledge could potentially account for this, in that regardless of intention, semantic representations of the tools functional use are automatically activated prompting a functional grasp even when it is unnecessary to the task at hand. Furthermore, the effect disappeared when participants were asked to transport familiar tools while carrying out a simultaneous semantic task (Creem & Proffitt, 2001). However, research by Lindemann et al. (2006) suggests that semantic representations are not automatically activated based on visual perception of the object, but specifically depend on the intention of action (Lindemann, Stenneken, van Schie, & Bekkering, 2006).

Intention of action is also integral to mediating tool use interactions, and has been shown to vary the responsive neural regions (Buxbaum et al., 2006; Osiurak, Roche, Ramone, & Chainay, 2013) and kinematic behaviour (Jax & Buxbaum, 2013) when engaging in tool manipulation. Grasp-to-transport versus grasp-to-use actions can be independently impaired by lesions (Osiurak, Aubin, Allain, Jarry, Richard, et al., 2008; Randerath, Li, Goldenberg, & Hermsdörfer, 2009) and elicit different neural response during imaging (Brandi et al., 2014; Johnson-Frey et al., 2005). It has been posited that dependent on the intention of action either the ventro-dorsal or dorso-dorsal pathway will mediate action (Binkofski & Buxbaum, 2013b; Buxbaum, 2001; Buxbaum & Kalénine, 2010; Daprati & Sirigu, 2006; Jax & Buxbaum, 2010). Grasp-to-transport actions are based on processing the affordances of the object and the environment in space and are mediated by the dorso-dorsal pathway. Grasp-to-use actions require further conceptual input pertaining to the use of tool. Jax and Buxbaum (2010) showed support for this in demonstrating that grasp-to-use actions took longer to initiate than grasp-to-transport actions, even when the action was directed at the same object, this has further been demonstrated by others (Valyear, Chapman, Gallivan, Mark, & Culham, 2011). The manipulation-based approach argues that this is reflective of access to stored representations associated with use, delaying movement onset when compared to transport, which would require no further processing other than the affordances of the object in space.

However, the reasoning-based approach argues that this explanation is insufficient, as transport actions may also involve processing the allocentric relationship between the target to be moved and the destination for transport (Osiurak, Roche, et al., 2013). For example, when moving a pen from one surface to another, it is necessary to process the stability of the destination, the gradient of the surface (will the object roll once placed), and if it is strong enough to support the weight of the transported object (Osiurak & Badets, 2016; Osiurak, Roche, et al., 2013). Osiurak et al. (2013) demonstrated that participants initiated grasp-to-use actions quicker than grasp-to-transport actions when the goal was to hand a tool to another person. This has been cited as evidence that both grasp-to-use and grasp-to-transport actions are reliant upon goal orientated technical reasoning as opposed to stored semantic representations; the variability in initiation of movement is based on the perceived demands of the task (Osiurak & Badets, 2016, 2017).

Buxbaum (2017) proposed some reconciliation between these two models, acknowledging the important role of technical reasoning, but emphasising that it served to 'fine tune' actions rather than forming the basis of action understanding with objects. Although these two prominent models of tool use differ in terms of cognition (Buxbaum, 2017; Osiurak & Badets, 2017), both acknowledge an integral role of the SMG in mediating tool use actions.

1.3.4. The Left SMG and Tool Use Planning and Execution

The SMG in the IPL has been associated with several cognitive functions such as auditory short term memory (Buchsbaum & D'Esposito, 2009), phoneme segment sequencing (Gelfand & Bookheimer, 2003), speech repetition (Baldo, Katseff, & Dronkers, 2012) as well as gestural production and action imitation (Caspers, Zilles, Laird, & Eickhoff, 2010). As discussed throughout this chapter, the SMG plays a key role also in mediating tool use action and behaviour; this view is well supported and documented through lesion based patient studies (Goldenberg & Hagmann, 1998; Goldenberg & Spatt, 2009; Jarry et al., 2013; Osiurak et al., 2009; Sunderland et al., 2013) and meta-analysis of imaging and experimental data (Ishibashi, Pobric, Saito, & Lambon Ralph, 2016; Lesourd et al., 2017; Orban & Caruana, 2014; Reynaud et al., 2016). The SMG shows elevated activation during imaging tasks in response to tool naming (Chao & Martin, 2000; A. Martin et al., 1996), planning and execution of tool use tasks and gestures (Brandi et al., 2014; Johnson-Frey et al., 2005; Orban & Caruana, 2014; Vingerhoets, 2014; Vingerhoets, Vandamme, & Vercammen, 2009), making decisions about appropriate tool use or passive viewing of skilled actions (Rumiati et al., 2004; Valyear et al., 2007).

This pattern of activation is usually left lateralised regardless of handedness of the participant (Brandi et al., 2014; Kroliczak & Frey, 2009; Przybylski & Kroliczak, 2017). Right SMG activation has also been observed in tool grasping and gesture execution (Brandi et al., 2014; Rallis, Fercho, Bosch, & Baugh, 2018b), however the left SMG is consistently active during planning *and* execution (Brandi et al., 2014; Johnson-Frey et al., 2005). Lateralisation of tool use function to the left is consistent with current models of apraxia as a result of left hemisphere IPL damage (Goldenberg & Spatt, 2009; Hartmann et al., 2005; Sunderland & Shinner, 2007; Sunderland et al., 2013). For both the manipulation and reasoning based approaches, the SMG is the source of (or heavily involved in) processing conceptual input pertaining to the functional use of tools (based on stored manipulation representations or technical reasoning, respectively) that influences the dorso-dorsal action production systems for execution (Binkofski & Buxbaum, 2013b; Buxbaum, 2017; Osiurak & Badets, 2017). For the manipulation-based approach, the SMG has been argued as the locus of stored manipulation knowledge that is retrieved and implemented for appropriate tools during action. The 2AS+ model has further implied that the SMG acts as neural accumulator for actions coming from dorso-dorsal and ventro-dorsal pathways. From the SMG in conjunction with the inferior frontal gyrus, the most appropriate goal dependent actions are selected for execution (Bi et al., 2015; Buxbaum, 2017; Gallivan et al., 2013). According to the technical reasoning approach, the subdivisions of the SMG are involved in technical reasoning (area PF) and integration of this information into the affordance perception and motor control of dorso-dorsal structures (Osiurak & Badets, 2017; Reynaud et al., 2016) (see Figure 4) . While the nature of the cognition of the SMG is debated, the exact role of the SMG in execution is still not fully accounted for.

This has been shown using kinematic data analysis combined with TMS methods; Tunik et al. (2008) demonstrated that grasp-to-use actions and grasp-to-transport actions were significantly delayed by TMS over the SMG and inferior frontal gyrus opercularis (IFGo) when compared to a non-object-oriented stimulus response task. Despite delays to action, the execution was not impaired, suggesting that the SMG role was planning goal oriented hand-object-interaction, while aIPS monitors hand object fit during execution (Tunik et al., 2008).

Supporting this further, TMS over the aIPS during execution has been shown to delay online correction when adjustments are required in grip size or orientation (Rice et al., 2007; Tunik, Frey, & Grafton, 2005), consistent with the role proposed of dorso-dorsal structures. This suggest that the SMG provides conceptual input pertaining to tools that allows the selection of appropriate grasp for use, acting as the 'goal state' of action (Buxbaum, 2017; Lesourd et al., 2017; Orban & Caruana, 2014; Osiurak & Badets, 2017; Reynaud et al., 2016). Dorso-dorsal structures maintain this visuomotor control using this framework as a guide. However, does the SMG play a more dynamic role in monitoring the conceptual aspects of tool grasp during action? Grasping a tool for use requires processing the egocentric and allocentric relationship between the tool and effector *and* the tool and targets for use. This allows selection of a functional grasp of the tool (as demonstrated through ESC) that facilitates functional use. If the plan is established prior to use (Badets & Osiurak, 2015, 2016), does the SMG play a role in monitoring or biasing action production systems during execution? SMG activation during reaching for tools for use suggests this to be the case.

However, contralateral dorso-dorsal structures are mainly regarded as providing visuomotor control to facilitate grasp (Caligiore et al., 2010; Cohen, Cross, Tunik, Grafton, & Culham, 2009a; Rice et al., 2007; Vingerhoets, 2014). However, if the tool were to change position requiring online correction of grasp orientation, would this be facilitated by the SMG in generating a new (or modifying the current) action plan for functional grasp? The dissociation observable in apraxia and lesion studies suggest the dichotomy in function between action production cognition and salient tool knowledge for functional grasp (Buxbaum, 2001; Goldenberg & Spatt, 2009; Jax, Buxbaum, & Moll, 2006). This suggests that there may be considerable cross talk between the SMG and action production systems during action as well as execution (Orban & Caruana, 2014). Furthermore, is this activity lateralised to the left hemisphere? Online correction has been shown as associated with dorso-dorsal structures contralateral to the effector hand. However, bilateral SMG activation has been observed in executing functional tool grasp (Brandi et al., 2014; Johnson-Frey et al., 2005; Rallis et al., 2018a). If conceptual knowledge is necessary for online correction in reaching for tools, is this mediated in the right hemisphere also?

1.4. Research Aims and Hypothesis

The aim of this thesis is to address the questions regarding the role of the SMG in selection of functional grasp of tools. As has been discussed in this chapter, selection of functional grasp is an essential process in executing tool use. A functional grasp is factored into action planning prior to execution, and adoption of an uncomfortable initial grasp is accounted for to allow a comfortable functional grasp during use (Osiurak & Badets, 2016; Rosenbaum, Vaughan, Barnes, & Jorgensen, 1992; Short & Cauraugh, 1997; W. Zhang & Rosenbaum, 2008). Adopting a functional grasp involves processing the salient functional features and graspable affordances of the tool (Buxbaum, 2017; Creem & Proffitt, 2001; Osiurak & Badets, 2016, 2017). This combination requires the convergence of two functionally distinct cortical regions in the form of the SMG and dorso-dorsal structures (aIPS, SPL (Buxbaum, 2017; Orban & Caruana, 2014; Osiurak & Badets, 2017; Thill et al., 2013; van Elk, 2014)). Research implies that this occurs prior to action, generating a suitable action plan for functional grasp, which is then mediated by bilateral dorso-dorsal structures during action (Tunik et al., 2008). This presumably occurs without any further input required to assess the functional properties of the tool once action has been initiated. However, is the conceptual fit between hand and tool (and suitable posture for use) monitored during the course of reaching to ensure functional grasp. Also, is this processing susceptible to the same constraints of affordance perception in dorso-dorsal structures?

Kinematic measures coupled with TMS have already highlighted the disruption of grip size and orientation through stimulation of the contralateral aIPS during action execution (Cohen et al., 2009a; Rice et al., 2007; Tunik et al., 2005). However, this relates to the affordance perception of simple geometric shapes, not the conceptual understanding of tools and associated uses. Are conceptual elements of the action plan (i.e. processing the functional elements of tools in relation to the target for action and body position) monitored consistently during action execution, in the same manner as structural affordance perception? If so does this require consistent conceptual input for the left SMG pertaining to conceptual tool knowledge? Furthermore, online correction of grasp and hand orientation is associated with the aIPS contralateral to the effector limb (Rice et al., 2007), but if the SMG is required to provide further conceptual input, is this lateralised to the left hemisphere? Tool use neuroimaging (Orban & Caruana, 2014; Peeters et al., 2013; Vingerhoets, 2008) and lesion studies (Goldenberg & Spatt, 2009; Hermsdörfer et al., 1999; Hermsdörfer, Li, Randerath, Goldenberg, & Johannsen, 2012; Hermsdörfer et al., 2007) highlight the importance of the left hemisphere regardless of handedness of the participant (Kroliczak & Frey, 2009). However, if online correction is necessary and requires online integration of conceptual knowledge, is this still lateralised to the left hemisphere? Additionally, the nature of conceptual input provided during action execution, as previously discussed is debated within the research literature; whether this is based on technical reasoning (Osiurak & Badets, 2017) or stored manipulation knowledge (Buxbaum, 2017).

This thesis posed three key research questions:

i) What is the role of the SMG in selection of appropriate grasp of tools for use during action execution?
ii) Is the role of the SMG during action execution lateralised to the left hemisphere?
iii) What is the nature of conceptual input required to facilitate functional grasp of tools for use?

To attempt to answer these questions, a combined method of kinematic data analysis and transcranial magnetic stimulation was adopted. This method has previously been used to explore the neural network facilitating perception and action surrounding tool use and is often used in order to observe the effects of transient disruption in examination of healthy participants (Cohen et al., 2009a; Tunik et al., 2005, 2008). This method seeks to selectively disrupt the different functional pathways of the neural network allowing observation of induced deficits in action execution. This has been particularly successful in examination of early movement kinematics for online correction of reaching for geometric shapes (dorso-dorsal structures) (Cohen et al., 2009a; Tunik et al., 2005) and action intention towards functional tools (Tunik et al., 2008). TMS has also been used in examining the role of the SMG in manipulation judgement tasks and tasks involving making judgements about correct hand configuration when using tools (Lesourd et al., 2017).

Spanning 5 studies, experimental paradigms were developed to address the research questions. Experiments 1-3 explored questions 1 and 2 (Detailed in Chapter 3 and 4), examining the extent to which the SMG is active during selection of appropriate grasp orientation during action execution when reaching for familiar tools for use. This was further developed to examine left lateralisation of SMG function during online correction of grasp selection. A paradigm was developed in which participants reached to grasp familiar tools and demonstrated functional use upon grasp completion. During reaching, the orientation of the tool was rapidly perturbed, forcing an online correction of grasp orientation (Tunik et al., 2005). This was designed to force a reintegration of conceptual tool input into dorso-dorsal structures necessary to facilitate both functional grasp and visuomotor transformation of the online correction. TMS was applied over the SMG during perturbation in an attempt to disrupt this conceptual integration. This allowed examination of whether deficits observed in ideomotor apraxia (Goldenberg & Spatt, 2009; Osiurak, 2013) could be replicable in healthy participants using TMS disruption. This behaviour was examined while participants reached with the left and right hands, to explore lateralisation of this function. This methodology has the added benefit of allowing participants to fully manipulate tools in hand and apply use of the tool in a functional way. This feature is difficult to achieve in many functional imaging methods such as fMRI or EEG (with some notable exceptions, see Brandi et al., 2014) and previous research into the orientation effect has shown that perception of depth (Pappas, 2014) has important implications in processing action planning towards tools. Crucially, using TMS allows investigation of the SMG role while allowing participants to physically interact with tools and their corresponding targets.

Chapter 5 and 6 aimed to explore the nature of conceptual input provided by the SMG while planning goal-oriented actions with novel and familiar tools. As discussed, one of the key differences between the manipulation (Borghi & Riggio, 2009; Buxbaum, 2017) and reasoning-based (Osiurak & Badets, 2017) approaches relies upon learned semantic representations of use. By asking participants to complete novel tasks, with novel and familiar tools, these experiments aimed to explore the differences in early movement kinematics. This was conducted with a view to establish whether manipulation knowledge or technical reasoning is more influential on planning and executing functional tool use actions. Furthermore, these experiments explored affordance perception for tools by varying the orientation of tool presentation. The influence of action intention was examined by varying the task goal between use (e.g. using a tool to enact change on another object) and transport from one location to another; as action intention has been shown to vary early movement kinematics and provide insight into the nature of tool related conceptual input. These experiments further aimed to explore whether familiarity with tools and actions would result in lower reaction times and faster movement onset or differences in movement kinematics, indicating a learned representation for holding and using familiar tools compared to novel controls. Experiment 4 was a behavioural task, designed to pilot the novel tasks and tools, and assess differences in movement kinematics. Experiment 5 developed the paradigm further to include TMS over the SMG (and control sites of stimulation) during planning stages of action to examine whether this would offset early movement kinematics and whether this would selectively impede familiar tool actions, in line with the SMG role proposed by the manipulation-based approach. Given the previous literature, several hypotheses were developed;

i) Tool use function will be lateralised to the left hemisphere and this will be reflected in selective disruption of kinematics through stimulation of the SMG.

ii) Online correction of grasp selection will require reintegration of conceptual input from the SMG during action execution; this will be observable from delays as a result of stimulation of the SMG during correction.

iii) Left SMG function will show a preference for familiar tools; observable through differences in early movement kinematics between novel and familiar tools.

iv) The Left SMG will show selective function for actions that involve use.

2. Method Validation: Efficacy of MRI-guided Co-registration for TMS Coil Placement

Foreword

The primary aim of this thesis was to explore the role of the SMG in facilitating functional tool grasp. To do this, a TMS approach was adopted. For these purposes, it was necessary to confirm as accurate TMS coil placement as possible to ensure stimulation was targeted to the regions of interest. A methodological experiment was conducted to ensure accuracy of coil placement across experiments.

Abstract

Accurate coil placement is integral for effective use of TMS. The aim of this experiment was to assess the accuracy of the Fastrak Polhemus method of MRI guided co-registration, (which uses an electromagnetic motion sensor to co-register fiducial anatomical landmarks on the participants scalp with corresponding points on their MRI data in a single coordinate space), against the Brainsight system (using optical trackers to allow frameless stereotaxic neuronavigation for TMS coil placement). This was conducted to ensure the suitability of the Fastrak method for use in future experiments and explore accuracy of TMS coil placement over different cortical regions. Participants (n = 4) underwent 3T structural MRI with two liquid capsules placed on their scalps, one each over frontal and parietal regions. The locations were marked with MRI safe marker pen. Following scanning, participants underwent both methods of co-registration using the same fiducial landmarks. Both systems were then used to estimate the locations of the cortex beneath the liquid capsules based on the MRI data. The Euclidian distance between actual and estimated locations of the markers was then analysed for accuracy between System (Brainsight vs. Fastrak) and Region (frontal vs. parietal). Although Brainsight *(M±SE = 11.29±2.13mm)* provided closer estimations to the targets than Fastrak *(M±SE = 13.28±2.34mm),* no significant effect of System was found. Accuracy was higher for frontal *(M±SE = 11.64±1.00mm)* compared to parietal targets *(M±SE = 12.93±3.22mm),* however, Region did not significantly impact accuracy and there was no

interaction with System. It was concluded that the Fastrak method is comparable in accuracy to Brainsight and is therefore a viable method for planned experiments.

2.1. Introduction and Research Aims

Transcranial magnetic stimulation (TMS) presents researchers with the opportunity to perform controlled, localised manipulation of brain activity with observable impacts on cognition and behaviour (Hallett, 2000; Pascual-Leone, Walsh, & Rothwell, 2000; Sack, 2006; Sack et al., 2009). TMS is widely used as a research tool for non-invasively inducing transient disruption of neural activity in humans (Di Lazzaro et al., 2004; Robertson, Theoret, & Pascual-Leone, 2003; Walsh & Cowey, 2000). Providing the TMS coil is accurately placed and is maintained above the desired cortical target, participant movements are not restricted during online TMS delivery. Consequently, TMS has been implemented across a number of experiments investigating cognition for reaching and grasping tasks (Cohen, Cross, Tunik, Grafton, & Culham, 2009b; Rice et al., 2007; Tunik, Lo, & Adamovich, 2008b). Due to the many research applications of such a tool, questions have been raised regarding the best methods of localising the TMS coil to the desired cortical site of stimulation (Sack et al., 2009). Robust effects of TMS on certain cortical sites exhibit signature responses; stimulation of the motor cortex causes a twitch in the relevant contralateral appendage, most often the hand (for example, see: Premoli et al., 2017; Smith, Stinear, Alan Barber, & Stinear, 2017; Weiss et al., 2013; Ziemann, 2004) and TMS over the visual cortex can induce phosphenes (Epstein & Zangaladze, 1996; Salminen-Vaparanta et al., 2014; Schaeffner & Welchman, 2017; Stewart, Battelli, Walsh, & Cowey, 1999; Tapia, Mazzi, Savazzi, & Beck, 2014; Taylor, Walsh, & Eimer, 2010). However, areas of interest for cognition such as inferior and superior parietal regions do not produce an immediately observable response to TMS (Sack et al., 2009). These ‘silent’ regions can be problematic for localisation and positioning of the TMS coil.

A number of methods are available to compensate for this difficulty. The International 10-20 electrode scalp positioning system is arguably sufficient for certain studies (Jasper, 1958). However, this method fails to take into consideration inter-individual differences in brain structure and correspondence between surface landmarks and brain anatomy (Herwig et al., 2002; Okamoto et al., 2004). More recently, frameless stereotaxic neuronavigational systems allow the co-registration of an individual's structural MRI data and fiducial landmarks (such as the nasion and tragus), allowing accurate online targeting of cortical regions (Cohen Kadosh et al., 2007; Herwig et al., 2002; Paus, 1999; Schonfeldt-Lecuona et al., 2005). This is most commonly carried out using an explicit least-squares minimisation algorithm (Arun, Huang, & Blostein, 1987), following identification of fiducial landmarks using structural MRI and motion tracking systems. However, fiducial methods are limited in that they rely upon landmarks being robustly identifiable from structural MRI and on the participant in situ (Whalen, Maclin, Fabiani, & Gratton, 2008). Consequently, the most widely used fiducial landmarks, listed above, are few in number and limited to the front of the head. This can bias the accuracy of the co-registration toward frontal regions at the expense of occipital regions (Whalen et al., 2008).

Based on the practical requirements of the planned TMS experiments, it was necessary to examine the efficacy of two methods of MRI guided fiducial-based co-registration for TMS coil positioning; compared across frontal and parietal regions. The Brainsight frameless stereotaxic neuro-navigation *(Brainsight, Rogue-Research, Canada)* system allows accurate co-registration of fiducial landmarks to structural MRI (amongst other functions). It uses POLARIS *(Northern Digital, Inc., Waterloo, Canada)* optical tracking of the TMS coil with respect to the fiducial landmarks. Consequently, the system guides coil placement is via a frameless 3D representation of the MRI structural data in relation to the motion trackers on the coil. A number of studies have employed this system to carry out TMS coil placement (Du et al., 2017; Du, Summerfelt, Chiappelli, Holcomb, & Hong, 2014; Gooding-Williams, Wang, & Kessler, 2017; Hone-Blanchet et al., 2015; Parks et al., 2015; Randhawa, Farley, & Boyd, 2013), but to our knowledge, no published studies have validated the accuracy of the method across cortical regions.

The Fastrak/LabVIEW method (developed by Dr Alan Sunderland, University of Nottingham) makes use of the same principles and algorithms as the Brainsight system. However, this method uses Fastrak electromagnetic-based motion tracking to record fiducial landmarks and guide TMS coil placement. This system does not allow frameless stereotaxic navigation, but allows localisation of specified cortical targets based on pre-defined vectors. These vectors are generated by selecting three coordinates around the desired cortical target using the participant MRI. These coordinates are used to define a plane. A virtual vector is then projected through the centre of this plane that can be used to guide the Fastrak stylus to the location and orientation of the cortical target for stimulation (see Figure 5).

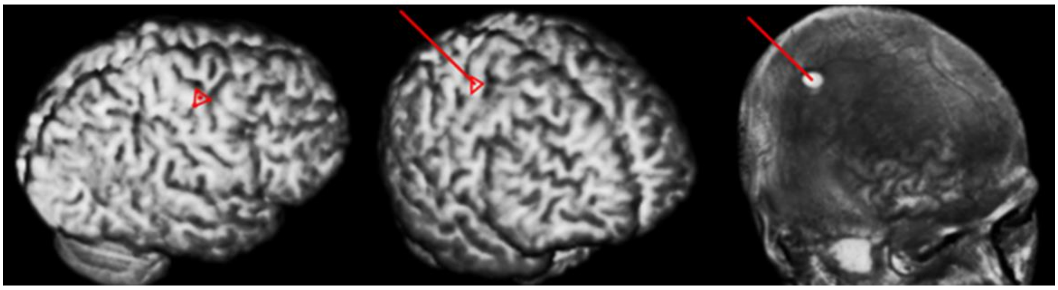

Figure 5. Illustration of the Fastrak method of target designation for TMS coil placement. A plane is defined by three points (designated by 3D coordinates) defined by the researcher. This defines a plane, through which a virtual vector is projected. The stylus of the Fastrak Polhemus allows coil placement by finding this vector and orientation.

As use of the Fastrak method was planned for upcoming experiments (for practical ease), it was necessary to ensure that it was comparable in spatial localisation to the Brainsight method and ensure that accuracy was maintained for parietal targets. To assess this, an experiment was developed in which participants would undergo structural MRI scanning with markers that could be easily identifiable in T1 weighted anatomical MRI. The brain regions corresponding to the markers could then be used as targets for coil placement for Fastrak and Brainsight. Localising the markers would then provide an indication of the spatial accuracy of both methods across cortical regions (frontal vs. parietal). This would further allow assessment of whether the distance from fiducial landmarks impacts on accuracy of the co-registration. Given that both methods used similar algorithms, it was hypothesised that there would be no significant difference between Brainsight and Fastrak methods in overall accuracy, but that accuracy may decrease for parietal compared to frontal targets.

2.2. Method

2.2.1. Participants

4 healthy participants (1 male, 3 female; age range 21 – 24, M±SD=22.25±1.25 years) were recruited from the University of Nottingham, UK. Participant eligibility to participate was determined by suitability to undergo MRI by the Sir Peter Mansfield Imaging Centre (SPMIC) magnetic resonance safety screening questionnaire. Written informed consent was obtained from all participants prior to the experiment. The study had approval from the ethics committee of the School of Psychology, University of Nottingham and was performed in accordance with the declaration of Helsinki (as of 2008).

2.2.2. Apparatus

500mg cod liver oil capsules were used to denote locations to act as cortical targets for co-registration on the two systems, as this would be easily observable under T1 weighted anatomical MRI. MR safe marker pens were used to denote the locations of the liquid capsules, and record the locations as provided by the two co-registration methods. A modified hairnet which could be tightened around specific regions of the head was used to maintain the position of the liquid capsules over their designated locations during scanning. Brainsight *(Brainsight, Rogue-Research, Canada)* neuronavigation was used to import and identify participant fiducial landmarks from the anatomical MRI data in conjunction with POLARIS *(Northern Digital, Inc., Waterloo, Canada)* used to track participant head position, record fiducial landmarks in situ and guide coil placement. For the Fastrak method, LabVIEW *(National Instruments Corporation, Austin, Texas, USA)* was used to calculate the co-registration and location of cortical target vectors in conjunction with MRIcron; *(*www.mccauslandcenter.sc.edu/mricro/mricron*)* to identify coordinate locations of fiducial landmarks and cortical targets. Fastrak Polhemus *(Polhemus Fastrak, Colchester, Vermont, USA)* was used to record coordinate locations of fiducial landmarks of participants in situ, and guide TMS coil placement over the cortical targets.

2.2.3. Design

A repeated measures 2 x 2 design was used. The independent variables were System of coil placement (Brainsight vs. Fastrak) and target Region (frontal vs. parietal). The dependent variable was the Euclidian distance between the estimated locations of the cortical targets provided by each system and the actual location of the targets as recorded when placing the liquid capsules (mm).

2.2.4. Procedure

Prior to scanning, two target locations were marked in MR safe black marker pen on the participants scalp on right frontal and left parietal areas. 500mg cod liver oil capsules were placed on the marked locations and held in place using micro pore tape and the hair net Participants then underwent MRI 3T anatomical scanning. After the scanning, cod liver oil capsules were removed, but the locations were denoted by the black marker pen.

Following data acquisition, participants were taken from the SPMIC to the School of Psychology to undergo the co-registration procedures on both Brainsight and Fastrak systems. The anatomical scans were first processed on Brainsight. 3D models were generated to assist in the identification of the fiducial landmarks (nasion, nose tip, zygomatic suture (left and right) and pre-auricular point (left and right), in conjunction with the anatomical data. The cortical surface directly under the liquid markers was designated as the targets for localisation, with a trajectory projecting through and perpendicular to the scalp (see Figure 5). Following co-registration of the participant with the anatomical data, the Brainsight POLARIS pointer tool was used to estimate the marker location. The designated locations were then marked on the participants scalp in red pen.

Participants were then taken to another lab to carry out the same procedure using the Polhemus Fastrak method. The same fiducial landmarks were used to carry out the co-registration, again identified from the anatomical scanner data and rendered 3D models. Vectors for the target markers were established as the cortical surface directly below the liquid marker. The target locations, as guided by Fastrak, were marked on the participants scalp using blue marker pen. For each method, the process was carried out three times, providing three individual estimations of the marker location on each system for each target. The Euclidian distance between an average of these three coordinate readings and the coordinates of the actual marker location was used as a measure of accuracy (see Figure 6).

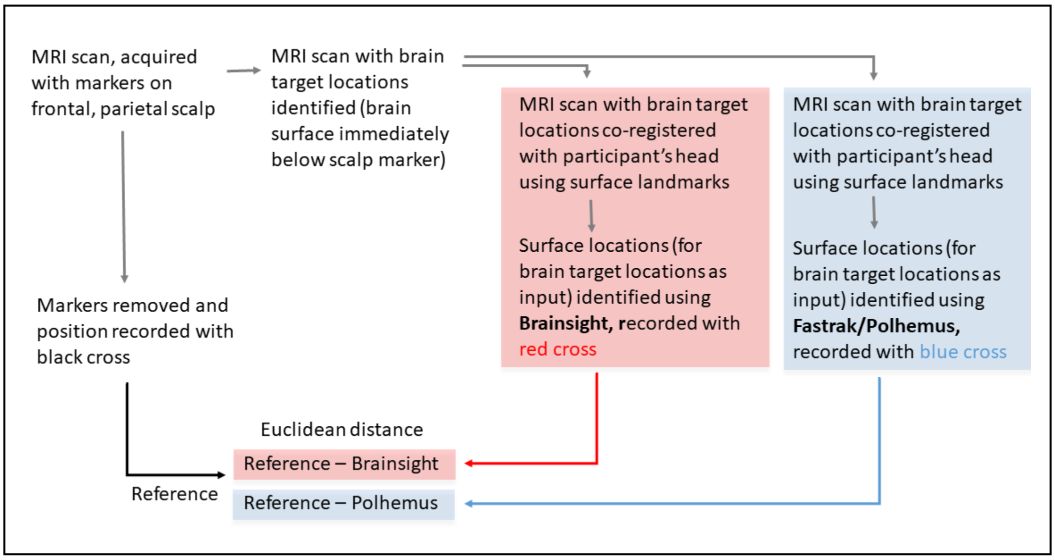

Figure 6. A flow-diagram describing the procedure for the co-registration experiment. The location of all estimations and actual locations were recorded in a single coordinate space, using Fastrak Polhemus for later analysis.

Both the Brainsight and Fastrak methods provide a validation step that assess the difference in location between the fiducial landmarks on the participant in situ and the estimated locations according to the model. This step is carried out prior to coil positioning, following the recording of fiducial landmarks of the participant. For both systems the threshold was set at <4mm. If this threshold was not met, the co-registration procedure was carried out again before localisation of the frontal and parietal target.

The positions of each of the marked locations on the scalp were then recorded in a cohesive 3D coordinate space using Fastrak Polhemus (see Figure 7 and Figure 8).

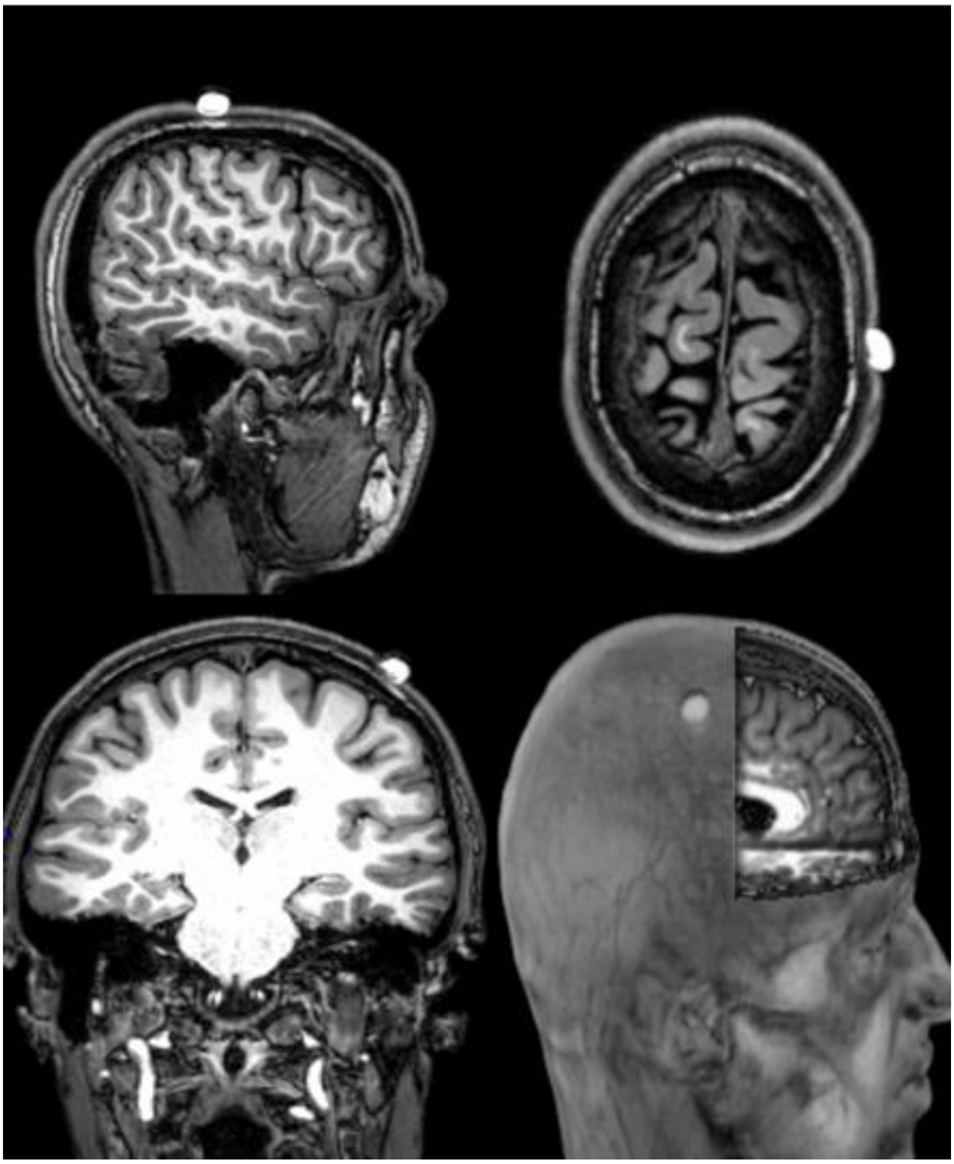

Figure 7. Anatomical MRI of Frontal liquid capsule (white) marker in Sagittal, Axial and Coronal plane and 3D rendering for 1 participant.

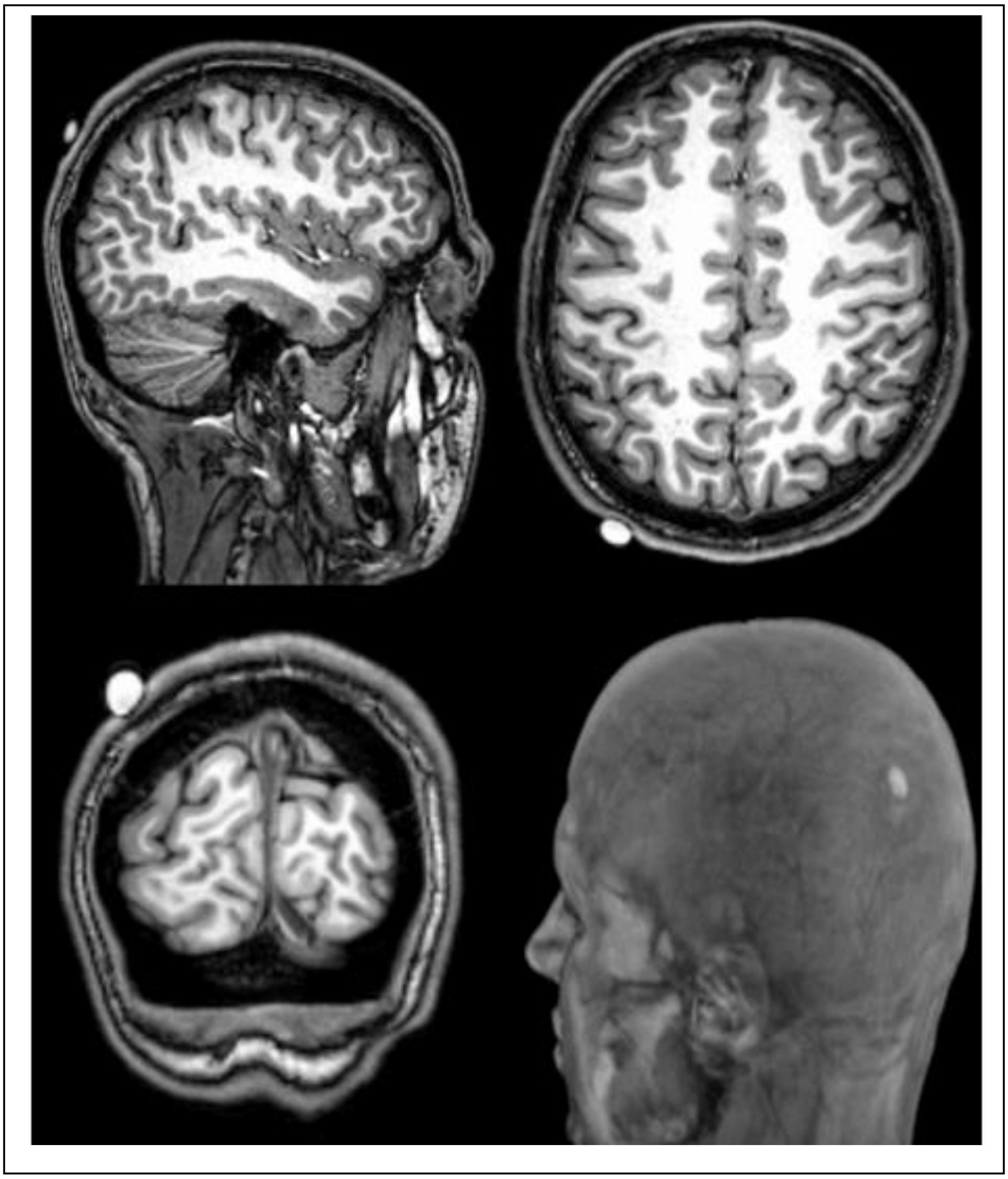

Figure 8. Anatomical MRI of Parietal liquid capsule marker in Sagittal, Axial and Coronal plane and 3D rendering for 1 participant.

2.3. Results

The Euclidian distance (mm) between the locations of cod-liver oil capsule markers and the Fastrak and Brainsight designations for the same locations were analysed in a 2 x 2 (System: Fastrak x Brainsight; Region: Frontal x Parietal) repeated measures ANOVA. Due to low number of participants (n = 4), a pertinent difference between the systems is difficult to establish, however, data collection was subject to funding and time constraints. Although Brainsight

(M±SE = 11.29±2.13mm) provided closer estimations to the targets than Fastrak *(M±SE = 13.28±2.34mm)*, no significant effect of System ($F_{(1, 3)} = 1.31, p=.36$) was found. Accuracy was higher for frontal *(M±SE = 11.64±1.00mm)* compared to parietal targets *(M±SE = 12.93±3.22mm)*, however, no effect of Region ($F_{(1, 3)} = 0.26, p=.64$) was observed and no significant interaction was observed between the variables ($F_{(1, 3)} = 0.24, p=.65$) (see Figure 9).

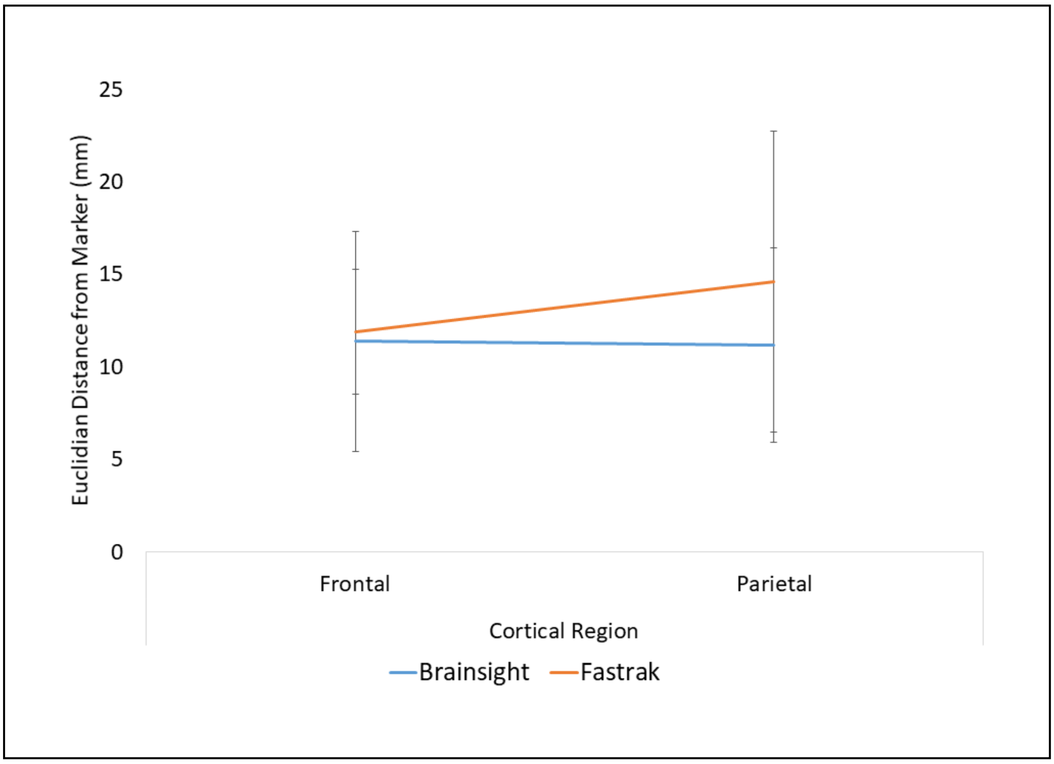

Figure 9. Mean Euclidian distance (mm) between cod-liver oil markers and cortical locations as designated for the Fastrak and Brainsight systems, for Frontal and Parietal targets.

2.4. Discussion

Consistent with the hypothesis, there were no significant differences between systems in overall accuracy. Contrary to predicted outcomes, region did not influence accuracy. From these findings, it can be inferred that the Fastrak/LabVIEW method is comparable with Brainsight for guiding TMS coil placement across frontal and parietal regions. These findings are inconsistent with previous observations of frontal bias due to proximity of the region to the fiducial landmarks (Whalen et al., 2008). However, this could be due to the small sample size and limited selection of targets. This experiment was implemented to assess the practical application of these methods for specific upcoming experiments, but this could be examined further by exploring a systematic coverage of cortical regions across a larger sample size. It might be the case that this bias may be observable with a greater variety of subject data, and systematic placement of markers, rather than the relatively arbitrary placement of two markers in this experiment. This was not possible for the present task due to time and funding limitations, but the results gained highlighted that for the planned experiments the Fastrak/LabVIEW method is viable for TMS coil placement.

It is worth noting that these methods are probabilistic, in that selection of targets is based upon previous neuroimaging or lesion based data regarding function associated with the anatomical region (Sack et al., 2009). While both Fastrak and Brainsight exhibit accuracy in guiding TMS coil placement over the desired cortical region, and this accounts for inter-individual differences in cortical structure between participants, they do *not* account for individual differences in structure-function relationships (Sack, 2006; Sack et al., 2009). An alternative approach is to use specific standardised coordinates such as Talairach (Talairach & Tournoux, 1988) based on group functional imaging analysis or meta-analysis of data associated with the function being researched, but as this is standardised across participants it can be hampered by inter-individual structural differences (Sack, 2006; Whalen et al., 2008). Alternatively, neuronavigation based on an individuals*' functional* data (fMRI), for cortical structures associated with the desired cognitive function (Andoh et al., 2006; Beauchamp, Nath, & Pasalar, 2010; Bona, Herbert, Toneatto, Silvanto, & Cattaneo, 2014; Reichenbach, Bresciani, Peer, Bülthoff, & Thielscher, 2011; Sack, 2006; Sack et al., 2009; Thiel et al., 2005), accounts for both structural and structure-function variability between volunteers. Previous research has shown this method to be accurate within the range of millimetres (Sparing, Buelte, Meister, Pauš, & Fink, 2008). However, this must be balanced with the practicality of conducting fMRI for individual participants, prior to carrying out online TMS during the planned experiments.

Due to the comparable accuracy between the Fastrak and Brainsight methods, it can be concluded that the probabilistic Fastrak method is a viable approach for guiding TMS coil placement for parietal targets. *Note; the Fastrak method was used for Experiments 1 and 2 (see Chapter 3) however, for Chapters 4 and 6, due to changes in experimental setup, Brainsight was used for TMS coil placement.*

3. TMS over the Supramarginal Gyrus Delays Selection of Appropriate Grasp Orientation during Reaching and Grasping Tools for Use – Experiments 1and 2

Foreword

These experiments aimed to explore the first two research questions, the role of the SMG in selection of grasp orientation of tools for use and left lateralisation of tool related function during execution. The experiments in this chapter were recently published (McDowell, Holmes, Sunderland, & Schürmann, 2018). The introduction and discussion sections have been altered to reflect the arguments posited in Introduction; the remaining sections appear as published.

Abstract

Tool use, a ubiquitous part of human behaviour, requires manipulation control and knowledge of tool purpose. Neuroimaging and neuropsychological research posit that these two processes are supported by separate brain regions, ventral premotor and inferior parietal for manipulation control, and posterior middle temporal cortex for tool knowledge, lateralised to the left hemisphere. Action plans for tool use need to integrate these two separate processes, which is likely supported by the left supramarginal gyrus (SMG). However, whether this integration occurs during action execution is not known. To clarify the role of the SMG two experiments were conducted in which healthy participants reached to grasp everyday tools with the explicit instruction to use them. To study the integration of manipulation control and tool knowledge within a narrow time window the orientation of the tool was mechanically perturbed to force participants to correct grasp orientation 'on-line' during the reaching movement. In experiment 1, twenty healthy participants reached with their left hand to grasp a tool. Double-pulse transcranial magnetic stimulation (TMS) was applied, in different blocks over left or right SMG at the onset of perturbation. Kinematic data revealed delayed and erroneous online correction after TMS over left and

right SMG. In Experiment 2, twelve participants reached, in different blocks, with their left or right hand and TMS was applied over SMG ipsilateral to the reaching hand. A similar effect on correction was observed for ipsilateral stimulation when reaching with the left and right hands, and no effect of or interaction with hemisphere was observed. These findings implicate a bilateral role of the SMG in correcting movements and selection of appropriate grasp orientation during reaching to grasp tools for use.

3.1. Introduction and Research Aims

In Chapter 1, the two integral visual pathways were outlined that are essential in mediating tool use behaviour and involved in the selection of appropriate grasp of tools for use. Dependent on the goal of hand-object interaction (either acting on an object or acting with it), the behaviour will be mediated by one of the two dorsal pathways (Vingerhoets, 2014). In the case of 'acting on' an object, for example, moving from one location to another, action execution will be carried out by the dorso-dorsal stream. Projecting from visual cortices V3A via superior parietal lobule (SPL) to dorsal premotor cortex (PMd) (Binkofski & Buxbaum, 2013a; Brandi et al., 2014; Vry et al., 2012); the dorso-dorsal stream is argued to place both effector limb and object into a single coordinate system. The object's intrinsic (size and shape) and extrinsic (location and orientation) visual properties guide action towards it. This system facilitates appropriate grasp to allow transportation of the object to a goal location (Johnson & Grafton, 2003), such as placing a fork in a drawer. These processes seem to be mediated by the SPL and the anterior intraparietal sulcus (aIPS) (Brandi et al., 2014; Daprati & Sirigu, 2006).

By contrast, interactions with objects that are to be 'acted with' are mediated by the ventro-dorsal stream, projecting from visual cortices (e.g. V5/MT), via inferior parietal lobule (IPL) to ventral pre-motor cortex (PMv) (Binkofski & Buxbaum, 2013a; Rizzolatti & Matelli, 2003; Vry et al., 2012, 2015b). When engaging with objects that are to be 'acted with', further conceptual input is required to carry out movements (Vingerhoets, 2014). The nature of this conceptual input varies between manipulation (Buxbaum, 2001; Buxbaum & Kalénine, 2010; Rothi et al., 1991; Thill et al., 2013), or reasoning based approaches (Badets & Osiurak, 2015; Goldenberg & Spatt, 2009; Osiurak et al., 2011; Osiurak, Roche, et al., 2013), but both indicate that this input informs selection of an appropriate grasp that allows the use of the object. For example, when reaching to use a fork, knowledge of how to use it efficiently informs the appropriate grasp orientation; by the handle with the tines facing away from the hand. Both approaches posit that the left IPL in the ventro-dorsal pathway is likely the locus of this knowledge (Osiurak & Badets, 2016) and integration of this conceptual input into the necessary motor transformations for use (Vingerhoets, 2014).

As highlighted in Chapter 1, the SMG in the left IPL is strongly associated with facilitating tool use function from findings in imaging data (Chao & Martin, 2000; Johnson-Frey et al., 2005; Kellenbach et al., 2003; Lesourd et al., 2017; Lewis et al., 2005; Okada et al., 2000; Przybylski & Kroliczak, 2017; Reynaud et al., 2016; Rumiati et al., 2004; Valyear et al., 2007) and from deficits observed in patients with damage to the left parietal lobe (Goldenberg, Hartmann, & Schlott, 2003; Goldenberg & Spatt, 2009; Sunderland & Shinner, 2007; Sunderland et al., 2013). Right SMG activation has also been observed during action execution (Brandi et al., 2014; Rallis et al., 2018a) where left SMG activation is associated with planning *and* execution (Brandi et al., 2014; Johnson-Frey et al., 2005) implicating a tool specific function of the left SMG.

Examining the role of the SMG in reaching and grasping of tools, transcranial magnetic stimulation (TMS) over the left SMG (but not aIPS) has been shown to significantly delay the onset of goal oriented actions while people reach for familiar objects to be ‘acted with’ (Tunik, Lo, & Adamovich, 2008). Tunik and colleagues (2008) inferred that the SMG may be involved in planning movements prior to engaging in action, while aIPS monitors hand-object fit during action execution. TMS over the aIPS contralateral to the hand used, results in disruption of rapid online correction of reaching and grasping behaviour when adjustments in size or orientation are required (when applied within 65ms of object perturbation) (Tunik et al., 2005). As this experiment (Tunik et al., 2005) examined reaching behaviour towards geometric objects, these hand-object interactions arguably can be carried out without access to stored semantic representations associated with the use of such objects (Vingerhoets, 2014).

Based on this, the SMG arguably provides semantic input prior to the onset of movement, that is integral to creating the action plan for use, while the aIPS monitors hand object interaction during execution. This is consistent with findings that patients with damage to left IPL show difficulty in reaching and grasping tools compared with simple geometric shapes when barrier avoidance is required (Sunderland et al., 2013). However, does the SMG play a more dynamic role in monitoring the fit between hand and object, relevant to the overall goal of movement, while reaching for a tool to perform a task? Grasping an object to be acted with requires knowledge of appropriate orientation in relation to the hand. If the SMG plays a role in establishing a plan for appropriate action prior to movement, is this plan monitored during execution?

To explore this question, an experimental paradigm was developed that required participants to reach and grasp tools with the explicit intention to use them on completion of grasp. The orientation of the tool was perturbed to force an online correction of grasp orientation and applied TMS to the SMG at the onset of perturbation. The perturbation was designed to force the integration of manipulation control and tool knowledge at a specified time point.

It was hypothesised that delivery of TMS over the SMG at the onset of this event would delay rotation of the hand to appropriate orientation for use (e.g., by the handle). In previous online correction tasks involving geometric objects (Tunik et al., 2005) stimulation to aIPS resulted in disruption of forearm rotation or grip aperture, while reaching was preserved. However, given the observed delays to onset of movement when engaging in goal oriented tool action with TMS applied to SMG (Tunik et al., 2008), an overall increase in movement time from onset to final grasp and an increased period of slowing of movement toward target is expected; as TMS over the SMG at the onset of tool perturbation may disrupt reassessment of the initial movement plan. This would indicate a role of the SMG in monitoring the conceptual fit between hand and object during reaching and grasping. This would also highlight the role of the SMG as more dynamic than previously thought, being involved in monitoring movement ‘on line’ as well as during planning stages (Tunik et al., 2008).

It is further hypothesised that effects of TMS would be significantly stronger for left SMG stimulation than for right. TMS was applied over the left and right SMG to examine the left lateralisation associated with tool use in neuropsychological and neuroimaging research. In neuropsychological studies, left-hemisphere damaged apraxic patients performed reaching and grasping tasks with the ipsilesional hand (Goldenberg, 2003; Goldenberg et al., 2003; Hermsdörfer et al., 2012, 2013). This experiment aimed to explore whether a corresponding but transient deficit would result from TMS to the left SMG. Therefore, participants carried out reaching and grasping of tools using their left hand for experiment 1. Additional right-hand trials were among conditions introduced in experiment 2.

3.2. Experiment 1

3.2.1. Methods

3.2.1.1. Participants

22 healthy right-handed participants (8 male, 14 female; age range 22 – 33, M = 25.00, SD = 4.63 years) were recruited from the University of Nottingham, UK (two participants' data were excluded from analysis due to motion tracking errors; this consisted of erroneous sampling of the hand orientation during reaching, characterised by artefacts which could not be compensated for). Participants were eligible if they were right handed and had a structural MRI scan to allow MRI guided TMS coil placement. Handedness was assessed via the 10 item version of the Edinburgh Handedness Inventory (Oldfield, 1971). Participants were identified as having a predominantly right-hand preference, with an average laterality quotient of 0.74 (SD=0.21, range 0.55-1.0). Participant safety and suitability to undergo TMS was assessed using pre-test screening (Maizey et al., 2013). Side effects or discomfort were monitored using follow up questionnaires over a 24 hour period following stimulation (Maizey et al., 2013). No side effects or discomfort attributed to TMS were reported by participants. Written informed

consent was obtained from all participants prior to the experiment. The study had approval from the ethics committee of the School of Psychology, University of Nottingham, and was performed in accordance with the declaration of Helsinki (as of 2008).

3.2.1.2. Apparatus

Eight everyday tools were used as targets during the experiment. Participant familiarity with each tool was assessed prior to testing. Tools consisted of knife, fork, spoon, peeler, wrench, hammer, screwdriver and toothbrush (all plastic, ~18cm long).

The tools were held in a cradle, connected to the axle of a stepper motor to allow rapid 90° rotation. 'Hook and loop' fabric strips, applied to each end of the tool and prongs of the cradle allowed the tool to be held in a fixed position during rotation while allowing easy removal of the tool following grasp.

Targets were presented to participants in the coronal plane, 57cm from the table edge and raised 37cm from the table top. Participants' view of the target was controlled using PLATO shutter googles *(Translucent technologies, Toronto, Canada).* Motion tracking of participants' reaching movements was recorded using a Polhemus Fastrak *(Polhemus Fastrak, Colchester, Vermont, USA)* with two sensors sampling at 60Hz. One attached to participants' index finger; used to record kinematic data and hand orientation (Roll – degrees) during reaching. The second sensor was attached to the TMS coil to monitor position over the targets. TMS was carried out using a Magstim Rapid *(Magstim Company Ltd, Whitland, Carmarthenshire, UK).*

3.2.1.3. Localisation of Cortical Sites and TMS

For both SMG sites the TMS coil was held tangentially to the surface of the head with the handle pointing upwards. TMS was delivered at 110% of participants' resting motor threshold (rMT). rMT was determined by delivering TMS pulses over the hand area of the right motor cortex at varying intensity until a visible twitch was observable in the left hand on approximately 50% of pulses. A double TMS pulse (100ms inter-pulse) was used. Ear plugs were provided to dampen the noise associated with TMS pulse discharge.

Stimulation site localisation was carried out using a Polhemus Fastrak MRI guided method of co-registration (see Method Validation: Efficacy of MRI-guided Co-registration for TMS Coil Placement) using 4 fiducial landmarks (nasion, nose tip, preauricular points) sampled from the participant using the Fastrak stylus and co-registered to the digitised anatomical landmarks from a corresponding anatomical MRI for the individual. This method used digitised trajectories projecting from the cortical target that could be tracked by the stylus. A chin rest was used to maintain head position throughout trials and coil position was monitored by the experimenter.

3.2.1.4. Design

A repeated measures 2 x 2 x 2 x 2 design was used. The independent variables were hemisphere of SMG stimulation (left vs. right), TMS (TMS vs. no TMS), final grasp position (upright vs. inverted) and congruence between tool rotation and necessary rotation of the hand to orient from initial grasp plan to corrected grasp position (congruent vs. incongruent). Dependent variables were the overall movement time from movement onset to final grasp; percentage of movement time to 3D peak velocity of movement towards target; and a combined measure of delay in the rotation of hand to correct of orientation of grasp and erroneous rotation compared to corresponding baseline performance ('miscorrection,' measured in SD – **see 3.2.1.6** Analysis**).** This measure was assessed by examining the roll data (rotation of the hand; see Figure 10 and Figure 12). Participants completed two blocks of trials, with 80 trials per block. Tool rotation varied between trials in the congruence of rotation and the final grasp position required (4 rotation conditions: Inverted Incongruent (32 trials), Inverted Congruent (16), Upright Incongruent (16) and Upright Congruent (16)) (See Figure 10). Inverted incongruent trials were identified as the most difficult during pilot testing. As it was suspected that the effects of TMS might be most observable for these trials, the number of trials for this condition was doubled for testing. TMS was delivered over either left or right SMG for each block, then was reversed for the second block (order counterbalanced between subjects). TMS was delivered on half of the trials in each block. Order of TMS and rotation conditions within blocks was pseudorandomised. TMS was delivered at the onset of object perturbation so as to delay reassessment of the action plan and selection of appropriate grasp orientation. As participants reached with their left hand, the effects of TMS to the contralateral and ipsilateral SMG could be observed. Therefore, the design negated the possibility of contralateral effects of aIPS stimulation observed by Tunik and colleagues (2005) in reaching for geometric objects being observable here.

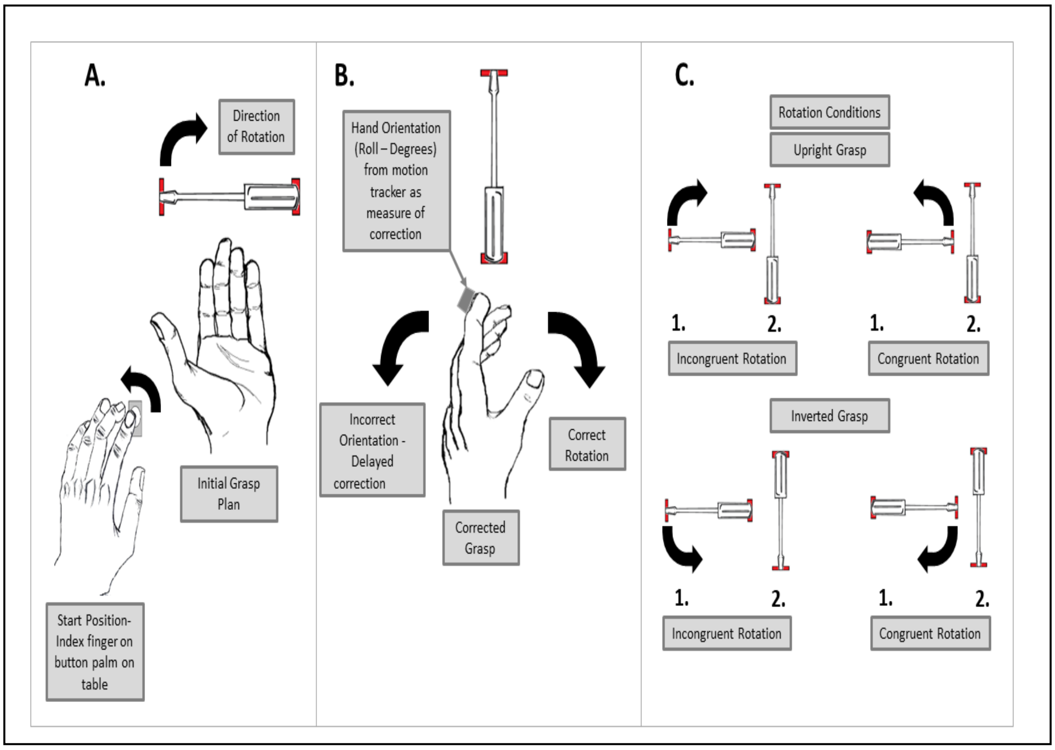

Figure 10. Panels ***A.-B.*** *describe an* ***upright incongruent*** *trial; rotation of the hand to correct grasp for tool in initial position (****A.****) is incongruent with orientation of hand for correct grasp of the target tool following perturbation (****B.****). Panel* ***C.*** *describes the 4 rotation conditions used.* ***1.*** *and* ***2.*** *indicate the start and end position of tools,* ***arrows*** *indicate direction of perturbation for each condition.*

3.2.1.5. Procedure

Participants were seated at a table with their chin positioned on the rest and the goggles positioned in front of their eyes (see Figure 11). The index and middle fingers of participants were attached together during testing. This was to prevent participants from being able to ‘twirl’ the tool should they grasp in the incorrect orientation for use; ensuring that correction should occur prior to grasping. Participants were instructed to place their left-hand index finger on a button (30cm to the left and in line with the chin rest). PLATO goggles occluded the participants' view of stimuli between trials, ensuring that the initial orientation of the tool was not visible, forcing online correction. When provided with a verbal ‘get ready’ signal from the experimenter, participants were instructed to press and hold the button until the goggles became transparent (uniform random delay of 2 – 4 seconds between Go signal and Goggles). If the button was released prior to the goggles opening the random delay was reset to ensure no reaching began prior to viewing the target tool.

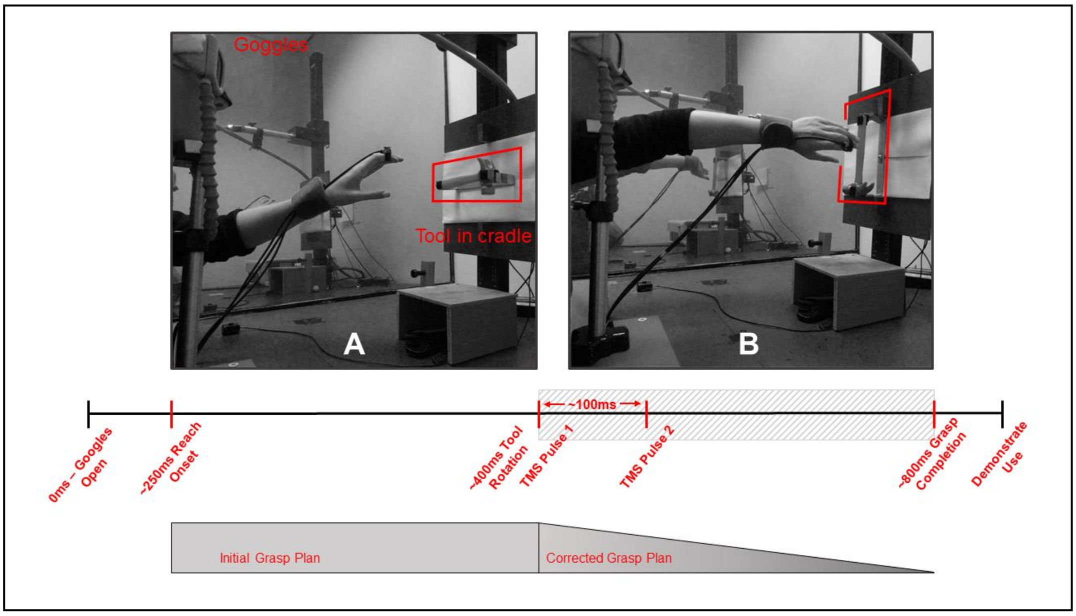

Figure 11. *Average, estimated timeline for an example trial; for an inverted grasp with a congruent rotation; rotation of the hand to grasp for tool in initial position (**A.**) is congruent with rotation of hand for correct grasp of the target tool following perturbation (**B.**). Movement and velocity data measured from **Reach Onset** to **Grasp Completion.** Hand orientation data analysed from **Tool Rotation** to **Grasp Completion** (shaded area of timeline – see Figure 12).*

Participants were instructed that as soon as the goggles became transparent they were to reach as quickly and as accurately as possible to grasp the target tool in a *manner suitable to its familiar use* while avoiding erroneous grasping. Participants were also explicitly instructed to demonstrate the use of the tool immediately after grasping.

Rotation onset of the target tool was locked to a forward movement (i.e., position) threshold of the motion sensor (30mm from start position) towards the cradle. If the threshold was not surpassed within 400ms of the goggles opening, an error tone was played, the goggles became opaque, and the trial was restarted. This was to prevent hesitation in reaching towards the target, ensuring rapid reaching and grasping. The tool completed its 90° rotation from onset to its final position within ~100ms. On TMS trials the initial TMS pulse was discharged immediately following the onset of target rotation. The second pulse occurred 100ms later, to ensure that TMS encompassed the time window of tool rotation. The TMS double-pulse was used to increase the time over which stimulation might affect function (see Figure 11) for the duration of tool rotation. Previous findings have shown that TMS over the aIPS causes deficits in reaching and grasping correction when TMS is delivered within 65ms following perturbation (Tunik et al., 2005) suggesting the aIPS has a role in detection of error. As this experiment aimed to disrupt the detection of error *and* potential re-integration of tool knowledge into the visuomotor transformation to carry out correction, the first TMS pulse was delivered at the onset of tool rotation and the second 100ms following. This was to encompass the time that this integration may occur. The efficacy of the double-pulse technique has been demonstrated in similar paradigms (Rice et al., 2007). Participants were required to provide a brief demonstration of the tool's appropriate use immediately following completion of each grasp (*e.g.,* using the knife to cut a block of plasticine). This was to ensure that participants were grasping with *the intention of use.* Testing lasted approx. 1.5 - 2 hours across a single session with breaks.

3.2.1.6. Analysis

3.2.1.6.1. Miscorrection Scores

The roll orientation of participants' wrists during reaching was examined from the onset of target rotation to the completion of grasp. Roll data was median filtered (each data point replaced with the median of 6 neighbouring data points) to remove TMS artefacts and resampled to 100 samples to allow examination of movement correction over the percentage of movement time. Baseline correction was done for each participant by averaging the roll data from baseline trials and subtracting this for each condition. A threshold of ± 1 SD was set from the baseline to define 'miscorrections' outside of this threshold. Individual trials were examined against the baseline for each condition. Data points that fell within the baseline correction were assigned a zero value. For data points that were beyond this threshold the difference between the data point and the threshold was calculated, then divided by the SD of the baseline. This provided, for each trial, a

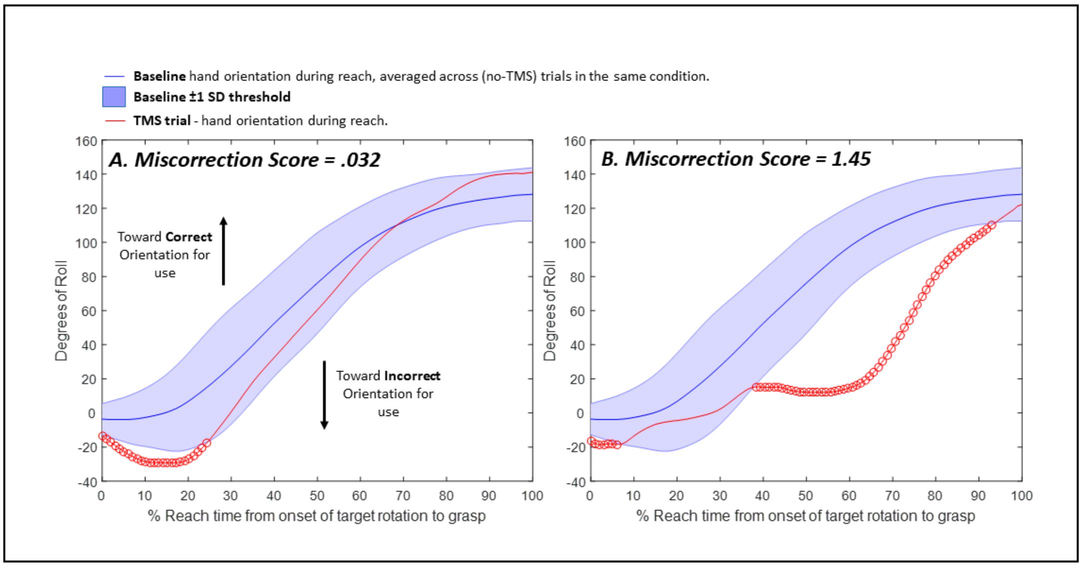

Figure 12. Reach pattern observed in hand rotation (Roll) in degrees for inverted incongruent trials sampled from 1 subject. Baseline represents averaged Roll across (no-TMS) trials. Sample ***TMS trials (A and B)*** *illustrate method of miscorrection calculation. Points during trial that fall within* ***Baseline ±1 SD threshold*** *are assigned a zero value. The difference between* ***TMS trial*** *points external to threshold in the incorrect direction* ***(circled)*** *and* ***Baseline ±1 SD threshold*** *is measured as a multiple of standard deviation from the corresponding time point from the averaged* ***Baseline****. This creates a vector of zeroes (inside* ***±1 SD threshold****) and SD values (outside* ***±1 SD threshold****). The mean of this vector provides the* ***Miscorrection Score*** *for each trial. The individual* ***Miscorrection Scores*** *are used for analysis for each of the stimulation and rotation conditions.*

vector of zeroes and SD values. An average of this vector (including zeroes) provided the miscorrection score for each trial. This measure provides a combined indication of how late the correction was and the amplitude of incorrect rotation prior to correction, as compared to baseline. These scores were quantified as a multiple of standard deviation (see Figure 12). For further explanation see Appendix A., pg. 177.

The individual miscorrection scores were averaged across trials in each condition to provide data for analysis. This process was carried out for TMS and no-TMS trials to assess miscorrection for both stimulation conditions. Trials in which the participants grasped the tool in the incorrect orientation for use were not included in the calculation of baseline performance or in the assessment of TMS trials, as this was deemed to be an incorrect reach. The percentage of these trials were analysed as error rate (% of total trials in condition).

3.2.1.6.2. Movement Time (MT)

The onset of movement was defined as the time of button release, and completion of grasp was determined by the maximum forward movement of the hand (grasp completion). Movement times (MT) were examined between these time points.

3.2.1.6.3. Percentage of movement time to peak velocity (TPV%)

TPV% was calculated as the percentage of movement time at which maximum movement velocity (cm/s) occurred between movement onset and final grasp completion. This parameter was used to determine the percentage of movement at which slowing occurred.

3.2.3. Results

All data from experiment 1 are displayed in Table 1 (pg. 58)**,** however, for the purpose of relevance, only findings pertaining to TMS will be discussed here. For a summary of the ANOVA, see Table 2 (pg. 59).

3.2.3.1. Miscorrection Scores

Data analysis revealed a significant effect of TMS ($F_{(1, 19)} = 37.1, p < .001$) with increased miscorrection when rotating the hand to grasp the tool appropriately for use during TMS trials *(M±SD miscorrection score = 0.39±0.12)* compared to no-TMS trials *(M±SD miscorrection score = 0.23±0.02,* Figure 13), indicating that TMS over the SMG impedes correction to appropriate grasp orientation for tools, consistent with the hypothesis. However, neither the main effect of Hemisphere of SMG stimulation ($F_{(1, 19)} = 0.1, p = .75$), nor the interaction between Hemisphere of SMG stimulation and TMS was present ($F_{(1, 19)} = 0.05, p = .82$), which fails to support the hypothesis of a left hemisphere bias for this function. No other significant interactions or effects were observed in miscorrection scores (for a summary of ANOVA see Table 2 pg. 59).

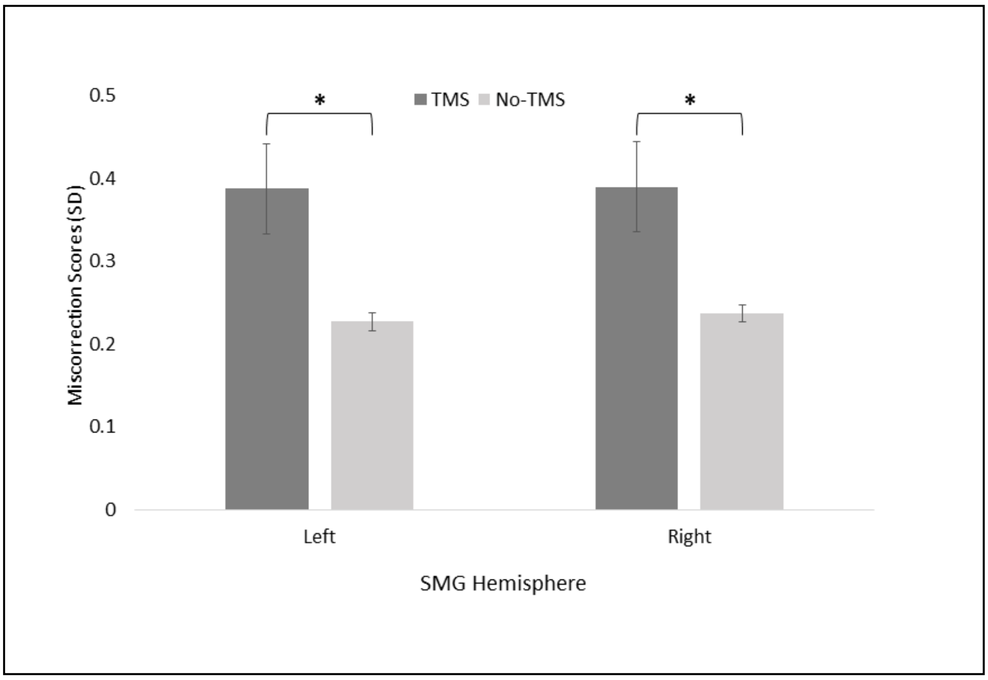

Figure 13. ***Experiment 1.*** *Significant effect of TMS on miscorrection scores (SD) for contralateral and ipsilateral SMG stimulation while reaching with the left hand. Bars indicate ±1 SE of the mean miscorrection score across subjects, *($F_{(1, 19)} = 37.1$, $p < .001$).*

3.2.3.2. Movement time and % time to peak velocity (TPV%)

An effect of TMS consistent with the hypothesis was also observed in movement time ($F_{(1, 19)} = 7.5$, $p = .01$); TMS *(M±SD = 786±215ms)* increased overall movement time compared to no-TMS trials *(M±SD = 768±221ms)*. Furthermore, an effect of Hemisphere of SMG stimulation ($F_{(1, 19)} = 4.8$, $p = .04$) was also observed, with increased movement time for right *(M±SD = 810±228ms)* compared to left SMG stimulation *(M±SD = 744±226ms)*. However, no interaction between TMS and Hemisphere of SMG simulation was found ($F_{(1, 19)} = 1.0$, $p = .32$).

Percentage of time to peak velocity (TPV %) showed a significant effect of TMS ($F_{(1, 19)} = 4.6$, $p = .04$), with lower TPV% for TMS trials *(M±SD = 31.0±10.0%)* compared to no-TMS trials *(M±SD = 32.7±10.4%)*. This partially reflects the findings in movement times, in that TMS over the SMG caused an earlier TPV%, indicating a longer period of deceleration in approaching the target. However, no significant interaction between TMS and Hemisphere of

SMG Stimulation was found *($F_{(1, 19)}$ = 0.06, p = .79)*. In summary, SMG stimulation affected movement time, velocity and selection of appropriate grasp. However, these findings failed to support the hypothesis of left lateralisation.

3.2.4. Discussion

The increase in miscorrection scores, movement time and longer period of deceleration during reach for SMG stimulation implicate this region as important for the selection of appropriate orientation of grasp when reaching for tools for use. Furthermore, due to the rapid online correction necessary in the experiment, this implies a dynamic role of the SMG in monitoring action plans and in compensating for rapid changes in goal-oriented actions pertaining to the appropriate grasp orientation for use. Research discussed earlier (Tunik et al., 2008) implicates a role of the SMG in planning stages, prior to movement execution, but not in monitoring the execution of movement. These findings do not conflict with this conclusion, but further imply that when changes in the plan are necessary the SMG plays a role in compensating for the changes to maintain the initial action plan. This observed effect could arguably be due to a role of the SMG in integrating conceptual knowledge, pertaining to a tool's use, into a suitable action plan for grasp; with TMS over the SMG delaying the integration of this conceptual input into the motor transformations for correction. This finding is consistent with proposals that objects that are to be acted with are mediated by the ventro-dorsal pathway (Brandi et al., 2014; Rizzolatti & Matelli, 2003; Vingerhoets, 2014) and that the SMG may monitor goal relevant hand orientation over the course of reaching.

Despite the significant effect of TMS over SMG, results showed this was not modulated by hemisphere. This conflicts with the left lateralisation of tool related activation observed in the literature (Johnson-Frey et al., 2005; Orban & Caruana, 2014; Peeters et al., 2013; Vingerhoets, 2014) suggesting a bilateral role of the SMG in performing online correction of actions when reaching for tools (when reaching with the left hand). Bilateral SMG activation for planning and execution of tool use gestures (Johnson-Frey et al., 2005) and appropriate grasping (Przybylski & Kroliczak, 2017) has previously been reported in imaging studies. While left SMG activation is observable during planning and execution of tool use gestures (Brandi et al., 2014; Ohgami, Matsuo, Uchida, & Nakai, 2004), right SMG is only activated during action execution. This suggests that the right SMG may serve a function pertaining to action execution that does not inherently involve the retrieval of tool knowledge, focusing instead on the spatial demands of the task. Furthermore, in a recent review of TMS based manipulation judgement tasks in the context of tool use theories, Lesourd et al (2017), posited that stimulation over the SMG may have inhibitory effects on surrounding regions that are in anatomical proximity to the SMG, but with distinct functions from the SMG (Lesourd et al., 2017).

In the case of right SMG stimulation here, the effects of TMS may have extended to the right IPS, being functionally responsible for extraction of object affordances and facilitating grasp (Buccino et al., 2004). The resulting delays to correction of grasp orientation may, therefore, be based on processing the affordances and spatial demands rather than tool related input. Online control of grasp behaviour is associated with the contralateral aIPS (Rice et al., 2007; Tunik et al., 2005) which provides a possible interpretation of the right SMG stimulation findings when reaching with the left hand, if an overlap is assumed between SMG and aIPS stimulation. However, it is difficult to dissociate the differing roles of the left and right SMG with the present data set. To address this question, Experiment 2 was performed. This experiment aimed to control for the possibility that the observed effects of right hemisphere stimulation in experiment 1 were due to similar contralateral effects pertaining to spatial or grasping functions that might facilitate tool use, while not involving tool specific knowledge. It was hypothesised that the same effects would be observed for the left hand and left SMG stimulation that were present in experiment 1. It was also predicted that effect would be smaller, if present, in the right hand right SMG stimulation condition.

Table 1. Experiment 1; Summary of mean data across stimulation and tool rotation conditions. M (±SD).

Hemisphere of Stimulation	TMS	Rotation Condition	MT(ms)	%TPV	Miscorrection Scores	Error Rates (%)
Left SMG	**TMS**	**II**	828(276)	26.92(8.43)	.38(.34)	6.25(9.06)
		IC	773(230)	30.71(12.29)	.42(.29)	4.37(7.33)
		UI	722(218)	33.34(11.01)	.33(.25)	7.50(17.33)
		UC	675(208)	33.40(11.63)	.42(.51)	5.00(8.51)
	no-TMS	**II**	793(272)	29.59(9.81)	.23(.04)	8.12(17.33)
		IC	766(238)	30.79(11.87)	.24(.04)	5.00(8.51)
		UI	717(215)	35.23(12.73)	.22(.06)	6.88(11.81)
		UC	675(214)	34.78(11.69)	.22(.07)	3.12(5.55)
Right SMG	**TMS**	**II**	897(246)	28.67(10.33)	.46(.31)	2.50(4.71)
		IC	846(230)	30.13(10.32)	.32(.31)	3.75(5.88)
		UI	733(223)	33.21(11.61)	.35(.37)	6.25(12.50)
		UC	772(214)	32.08(12.45)	.43(.33)	2.50(5.13)
	no-TMS	**II**	871(252)	29.62(10.98)	.24(.04)	7.50(13.08)
		IC	822(247)	31.73(11.04)	.24(.05)	1.87(6.12)
		UI	749(229)	35.618(14.03)	.22(.08)	4.37(10.16)
		UC	749(224)	34.35(11.72)	.25(.01)	1.25(3.85)

Mean movement times (MT) from button release to maximum forward movement towards target, % of reach time to peak velocity of movement (%TPV), Miscorrection scores (SD – see Figure 12), and Error Rates (% of total trials in condition for grasping in the incorrect orientation) for each stimulation condition and corresponding no-TMS conditions. Rotation conditions, **II:** Inverted Incongruent, **IC:** Inverted Incongruent, **UI:** Upright Incongruent, **UC:** Upright Congruent.

Table 2. Experiment 1. Summary of repeated measures ANOVA - Hemisphere of SMG Stimulation x TMS x Grasp x Congruence (2 x 2 x 2 x 2) ANOVA: carried out for movement time (MT), % of time to peak velocity (%TPV) and miscorrection scores.

	MT(ms)		%TPV		Miscorrection Scores	
	F(1,19)	p	F(1,19)	p	F(1,19)	p
Hemisphere	**4.884**	**.040**	.004	.948	.103	.751
TMS	**7.515**	**.013**	**4.640**	**.044**	**37.177**	**<.0001**
Grasp	**73.405**	**<.001**	**31.360**	**<.001**	.174	.706
Congruence	**11.853**	**.003**	1.992	.174	.237	.632
Hemisphere x TMS	1.033	.322	.069	.795	.052	.823
Hemisphere x Grasp	.063	.804	.804	.381	.059	.810
TMS x Grasp	1.663	.213	.285	.600	.003	.957
Hemisphere x TMS x Grasp	.812	.379	.227	.639	.015	.903
Hemisphere x Congruence	2.650	.120	.914	.351	.954	.341
TMS x Congruence	.902	.354	.194	.665	.012	.913
Hemisphere x TMS x Congruence	.868	.363	1.006	.328	1.132	.301
Grasp x Congruence	2.728	.115	**8.972**	**.007**	1.379	.255
Hemisphere x Grasp x Congruence	3.653	.071	.016	.901	.947	.343
TMS x Grasp x Congruence	.391	.539	.106	.749	1.016	.326
Hemisphere x TMS x Grasp x Congruence	.283	.601	.477	.498	.299	.591

3.3. Experiment 2

3.3.1. Method

Experiment 2 used the same apparatus and procedure as experiment 1 with the following changes.

3.3.1.1. Participants

13 healthy right-handed participants (8 male, 5 female, age range 22 – 33, M±SD = 25.4±3.50 years) took part. 3 subjects had taken part in experiment 1 however, there was a gap of at least 4 weeks between experiments for each subject. Participants were identified as having a predominantly right-hand preference, with an average laterality quotient of 0.67 (SD = 0.23 range 0.55-1.0, Oldfield, 1971). One participant was removed from analysis due to errors in motion tracking (see - 3.2.1.1 Participants) during testing.

3.3.1.2. Design

A repeated measures design (2 x 2 x 2 x 2) was used with one independent variable combining hemisphere of SMG stimulation and hand used for reaching (left/left or right/right). The three other independent variables were as in Experiment 1. Participants completed 64 trials, 8 per rotation condition per block, across 2 blocks of trials, one for each hemisphere of stimulation (fewer trials were implemented for brevity of testing). In contrast to experiment 1, participants performed the task with their right hand in one block, and their left in the other. Ipsilateral stimulation and reaching was used in order to establish if the ipsilateral effects of SMG stimulation observed in experiment 1 were observable for the right hemisphere and hand also (Left SMG, Left Hand vs. Right SMG, Right Hand, order counterbalanced between subjects).

3.3.2. Results

Data from experiment 2 were examined using the same methods as experiment 1 (Table 3, pg. 63 summarises the findings). Miscorrection scores, movement time (MT), and percentage of time to peak velocity were examined for left and right hand reaching with ipsilateral SMG stimulation. As with experiment 1, only findings pertaining to TMS will be discussed here. For a summary of the ANOVA results, see Table 4, pg. 64.

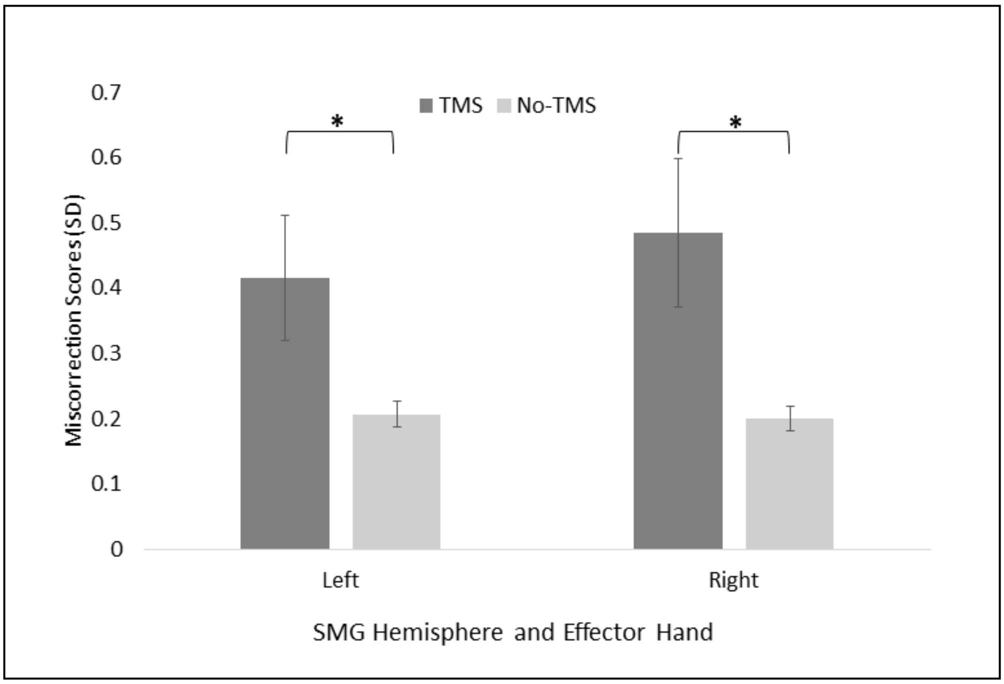

Figure 14. ***Experiment 2.*** *Significant effect of TMS on miscorrection scores (SD) for stimulation of the SMG ipsilateral to the hand used for reaching (left and right). Bars indicate ±1 SE of the mean miscorrection score across subjects, *($F_{(1, 11)} = 52.9$, $p < .001$).*

3.3.2.1. Miscorrection Scores

Analysis revealed a significant effect of TMS on miscorrection scores ($F_{(1, 11)} = 52.9$, $p < .001$), with higher miscorrection in TMS trials (*M±SD = 0.45±0.11*) compared to no-TMS trials (*M±SD = 0.20±0.02*) (see Figure 14). This is consistent with the hypothesis, however, no main effect of Hemisphere of SMG stimulation ($F_{(1, 11)} = 0.7$, $p = .39$), or interaction between Hemisphere of SMG stimulation and TMS was present ($F_{(1, 11)} = 1.5$, $p = .24$). This finding that TMS over the SMG causes a deficit in selection of appropriate grasp is consistent with the hypothesis, however, the lack of left hemisphere bias fails to support previous models.

A significant TMS x Grasp x Congruence interaction was observed ($F_{(1, 11)} = 8.1$, $p = .01$). For non-TMS upright trials, congruent (*M±SD = 0.18±0.07*) and incongruent (*M±SD =0.18±0.05*) miscorrection scores were similar, however, for inverted trials, congruent miscorrection scores (*M±SD = 0.23±0.03*) were higher than incongruent (*M±SD = 0.21±0.03*). For TMS upright trials, congruent

(*M±SD = 0.25±0.18*) miscorrection was much lower than incongruent (*M±SD = 0.48±0.31*), while for TMS inverted trials, congruent (*M±SD = 0.61±0.25*) miscorrection was much higher than incongruent (*M±SD = 0.46±0.28*). To examine this interaction further, subsequent 2 x 2 ANOVAs were carried out for the TMS and no-TMS results. For TMS data a significant Grasp x Congruence interaction was found ($F_{(1, 11)} = 5.2, p = .04$); however, this interaction was not observed in the no-TMS condition ($F_{(1, 11)} = 0.1, p = .72$), (see Figure 15).

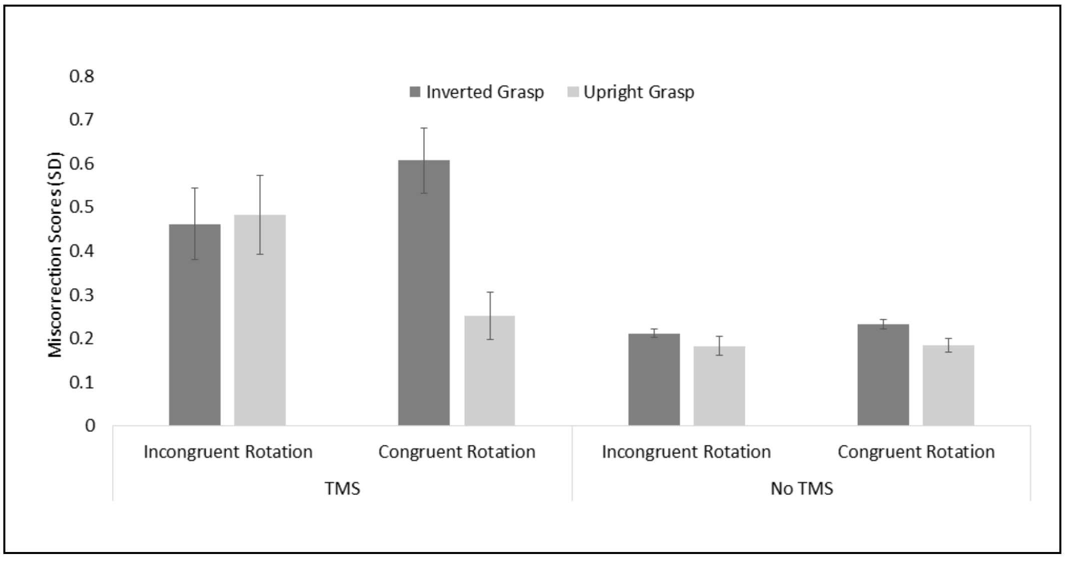

Figure 15. Miscorrection Scores, TMS x Grasp x Congruence interaction. Bars indicate ±1 SE of the mean miscorrection score across subjects, ($F_{(1, 11)} = 8.1, p = .01$).

3.3.2.2. Movement Time and Percent Time to Peak Velocity (TPV%)

No significant main effects of TMS ($F_{(1, 11)} = 2.5, p = .14$) or Hemisphere of stimulation ($F_{(1, 11)} = 2.8, p = .12$) were observed for movement time and no significant interaction between Hemisphere x TMS was observed ($F_{(1, 11)} = 0.09, p = .76$). For TPV%, no significant main effects of TMS ($F_{(1, 11)} = 0.4, p = .51$) or Hemisphere of stimulation ($F_{(1, 11)} = 3.8, p = .07$) were observed, and the interaction between Hemisphere x TMS was also not significant ($F_{(1, 11)} = 0.004, p = .94$).

Table 3. Experiment 2; Summary of mean data across stimulation and tool rotation conditions. M (±SD).

				MT(ms)	%TPV	Miscorrection Scores	Error Rates (%)
Left Hand	**Left SMG**	**TMS**	**II**	871(250)	17.18(3.81)	.41(.31)	11.45(22.27)
			IC	785(190)	21.81(7.15)	.51(.36)	7.29(14.55)
			UI	707(186)	26.16(11.22)	.44(.35)	3.12(5.65)
			UC	659(209)	25.42(10.81)	.30(.29)	3.12(5.65)
		no-TMS	**II**	805(257)	19.26(10.91)	.19(.04)	11.45(21.62)
			IC	753(212)	22.07(8.78)	.23(.06)	15.62(14.22)
			UI	682(250)	30.17(14.01)	.19(.08)	6.25(11.30)
			UC	674(220)	23.46(9.12)	.20(.08)	4.16(6.15)
Right Hand	**Right SMG**	**TMS**	**II**	989(265)	27.97(12.86)	.51(.51)	9.37(15.19)
			IC	828(269)	32.24(14.43)	.69(.39)	9.37(16.96)
			UI	811(286)	33.38(14.39)	.52(.48)	21.87(22.69)
			UC	792(253)	35.52(13.86)	.19(.08)	13.54(17.23)
		no-TMS	**II**	932(304)	29.93(11.52)	.22(.04)	10.41(15.84)
			IC	815(330)	33.53(16.39)	.22(.04)	8.33(18.71)
			UI	802(371)	35.59(14.41)	.17(.09)	27.08(29.59)
			UC	734(295)	34.03(15.69)	.16(.08)	21.87(20.03)

Mean movement times (MT) from button release to maximum forward movement towards target, % of reach time to peak velocity of movement (%TPV), Miscorrection scores (SD), and Error Rates (% of total trials in condition for grasping in the incorrect orientation) for each stimulation condition and corresponding no-TMS conditions. Rotation conditions, **II:** Inverted Incongruent, **IC:** Inverted Incongruent, **UI:** Upright Incongruent, **UC:** Upright Congruent.

Table 4. Experiment 2. Summary of repeated measures ANOVA - Hemisphere of SMG Stimulation x TMS x Grasp x Congruence (2 x 2 x 2 x 2) ANOVA: carried out for movement time (MT), % of time to peak velocity (%TPV) and miscorrection scores.

	MT(ms)		%TPV		Miscorrection Scores	
	$F_{(1,11)}$	p	$F_{(1,11)}$	p	$F_{(1,11)}$	p
Hemisphere	2.824	.121	3.818	.077	.779	.396
TMS	2.476	.144	.453	.515	**52.918**	**<.001**
Grasp	**58.497**	**<.001**	**19.394**	**.001**	**5.787**	**.035**
Congruence	**13.449**	**.004**	.931	.355	.133	.722
Hemisphere x TMS	.094	.765	.004	.949	1.509	.245
Hemisphere x Grasp	.182	.678	1.684	.221	1.061	.325
TMS x Grasp	.559	.470	.237	.636	1.988	.186
Hemisphere x TMS x Grasp	.325	.580	.399	.540	.337	.573
Hemisphere x Congruence	4.170	.066	1.419	.259	.351	.565
TMS x Congruence	.276	.610	2.421	.148	.380	.550
Hemisphere x TMS x Congruence	.593	.458	.249	.628	.049	.828
Grasp x Congruence	4.394	.060	**9.789**	**.010**	**11.341**	**.006**
Hemisphere x Grasp x Congruence	1.063	.325	1.376	.266	.774	.398
TMS x Grasp x Congruence	1.471	.251	1.278	.282	**8.191**	**.015**
Hemisphere x TMS x Grasp x Congruence	.711	.417	.024	.879	1.014	.336

3.3.2. Discussion

The findings from experiment 2 further highlight a role of the SMG in the selection of appropriate grasp orientation when reaching for tools for use when an online perturbation forces a correction of orientation. As with experiment 1, these results are consistent with the ventro-dorsal specificity for objects to be acted with; and the hypothesis that the SMG monitors goal relevant action plans during reaching toward tools for use. However, no effect of TMS was observed for increasing movement time or TPV%, inconsistent with the hypothesis and the results of experiment 1. Furthermore, there was no effect or interaction with Hemisphere of SMG stimulation for any of the kinematic measures. This indicates an absence of left hemisphere bias and a bilateral role of the SMG in selecting and monitoring an appropriate grasp orientation when reaching for familiar tools, based on the effect of SMG stimulation ipsilateral to the effector hand for both left and right hemisphere.

This effect was not unexpected provided the results from experiment 1 and previous findings of bilateral activation of the SMG for grasp execution of tools, independent of hand used (Przybylski & Kroliczak, 2017). These results also indicate that the effects of right SMG stimulation are unlikely to be accounted for by stimulation of neighbouring regions close to the right SMG when reaching with the contralateral hand (a possible interpretation discussed in Experiment 1, section 1.4.); due to similar effects for correction delay with the ipsilateral hand, observable in experiment 2. This raises questions regarding whether the role of the SMG in this process is tool specific, and what potential role the right SMG fulfils also. These questions are addressed in the next section.

3.4. General Discussion

In this task the target tool was perturbed in orientation, forcing participants to correct their grasp. Double-pulse TMS to the SMG delayed this correction of grasp orientation. TMS over the contralateral and ipsilateral SMG disrupted this process when reaching with the left hand, in experiment 1. This finding is consistent with a role of the left SMG in the online integration of information pertaining to tools into an appropriate action plan for use (Vingerhoets, 2014).

Although the results cannot provide direct insight into the nature of this conceptual information (whether reasoning or manipulation-based (Osiurak & Badets, 2016), they do indicate that the goal oriented plan is monitored throughout action during reaching to allow compensation in the event of a necessary online correction. This finding is also consistent with a role of the SMG in goal oriented planning and selection of appropriate action (Brandi et al., 2014; Tunik et al., 2008).

Furthermore, a recent meta-analysis of tool use literature (Reynaud et al., 2016) highlighted the importance of the left SMG in not only understanding relationships between hand and tool, but also between tool and target object. This function is essential to selection of appropriate grasp when planning actions (Buxbaum, 2017; Lesourd et al., 2017; Osiurak & Badets, 2016), indicating a more integral role of the left SMG over the right. These findings are consistent to an extent with prominent tool use models (Buxbaum, 2017; Osiurak & Badets, 2016, 2017), but differ in terms of the timing and duration of SMG function in generating the action plan. In line with the ideomotor principle (Greenwald, 1970; Hommel, Musseler, Aschersleben, & Prinz, 2001; Massen & Prinz, 2007; Prinz, 1997), current models posit that tool knowledge is integral to generating the action plan for functional grasp and use, but that the actual execution is mediated by motor control structures independent of conceptual input pertaining to tool use. In this case the SMG would be redundant during execution as the action plan has already been generated prior to action, therefore TMS over the SMG should not disrupt execution. However, in the present experiments, due to perturbation of the tool's orientation, integration of tool knowledge is required to correct grasp orientation for functional use. As appropriate grasp orientation is integral to effectively use the tool, following grasp, this should require input from the SMG pertaining to knowledge (Buxbaum, 2017) or reasoning about the tool's functional property (Osiurak & Badets, 2017). This does not necessarily mean that information about the tool needs to be retrieved again (following the planning of action) or that a simulation of action must be generated ‘de novo’ due to changes in the object orientation. Rather, it is posited that the SMG maintains aspects of the action plan that are functionally associated with *use* throughout the duration between motion onset and grasp completion (such as relationships between hand

and tool, and between tool and target object) to select appropriate grasp based on the goal of action (Buxbaum et al., 2007; Lesourd et al., 2017; Reynaud et al., 2016). Following object perturbation, the SMG dynamically integrates this maintained representation with visuomotor information to facilitate goal oriented rapid online correction.

How can the lack of left lateralisation observed in these findings, coupled with the effects observed for right hand reaching with stimulation of the ipsilateral SMG, be interpreted? One conceivable explanation would be that the right SMG (compared with left SMG) serves an equally important role in selection of grasp orientation of tools for use. From this explanation, it would follow that the right SMG is a locus of tool knowledge integration into bilateral visuomotor transformations for use, conflicting with current models of the tool use network (Buxbaum et al., 2007; Kroliczak & Frey, 2009; Lesourd et al., 2017; Orban & Caruana, 2014; Peeters et al., 2009b, 2013; Przybylski & Kroliczak, 2017). There are a number of reasons why this explanation is unsatisfactory. Firstly, although right SMG activation has previously been observed during execution of tool related actions (Johnson-Frey et al., 2005) and effector-independent actual grasping (Przybylski & Kroliczak, 2017), the left SMG is active during execution *and* planning (Brandi et al., 2014; Orban & Caruana, 2014; Reynaud et al., 2016); implicating a left bias for *understanding* of tool use gestures. Secondly, the left SMG shows stronger lateralised connectivity with the ipsilateral pMTG compared to the right SMG and pMTG, a region associated with stored semantic representations considered important in the planning of tool use actions (Ramayya et al., 2010). Thirdly, although cases have been reported of right hemisphere damage resulting in apraxia (Marchetti & Della Sala, 1997; Raymer et al., 1999), these are not comparable in number to those following left hemispheric damage (Sunderland et al., 2013) and not relatable to the right SMG deficits observed here. Furthermore, recent imaging data highlights a left hemisphere activation bias for grasping inclusive of wrist rotation to achieve a functional grasp (Przybylski & Kroliczak, 2017).

A more likely explanation of right SMG findings can be derived by examining the task requirements. With some notable exceptions (Brandi et al., 2014) many studies highlighting left lateralisation of function pertaining to tools require no physical visuomotor control towards tools during testing. Instead, the studies focus on planning and preparing gestures associated with tools, or on concepts pertaining to tools rather than initiation of action (Chao & Martin, 2000; Decety & Grèzes, 2001; Kellenbach et al., 2003; A. Martin et al., 1996; Okada et al., 2000). In these experiments, grasping tools for the purpose of *use* was explicitly instructed and corresponding target objects on which to demonstrate tool actions were present. This, coupled with the rapid movement and online correction, could indicate that the processes being examined may pertain to the conceptual aspects of tools; however, the additional demands of the task may require supplementary processing without specificity for tools and recruitment of the right SMG.

Given the extent of neuroimaging and neuropsychological bias towards a left lateralisation of tool function, the possibility that the right SMG is functionally distinct while still involved in the execution of the task is considered here. Structures of the right IPL have been associated with detection of salient events in the environment (Clark, Fannon, Lai, Benson, & Bauer, 2000; Gur et al., 2007; Kiehl et al., 2005; Kiehl, Laurens, Duty, Forster, & Liddle, 2001; Lagopoulos, Gordon, & Ward, 2006; Singh-Curry & Husain, 2009) and sustaining attention on goal oriented tasks (Adler et al., 2001; Häger et al., 1998; Johannsen et al., 1997; Singh-Curry & Husain, 2009; Vandenberghe, Gitelman, Parrish, & Mesulam, 2001). It could be argued that the right SMG serves functions pertaining to interactions with tools, but which are not tool specific. For example, controlling for spatial perturbations in the environment and adjusting to these demands, such as the rapid online correction during the task. The findings in miscorrection are consistent, to some extent, with the deficits shown by patients with right IPL damage, which has been linked to severe disruption of spatial functions such as keeping track of object locations, and being aware of rapid changes in location (Mannan et al., 2005; Parton et al., 2006; Pisella, Berberovic, & Mattingley, 2004). The observed right SMG effect may be due to the disruption of these functions in relation to tracking the rapid rotation of the target tool, without specifically relating to conceptual aspects of the tool itself.

However, this still does not fully account for the bilateral effect observed for both ipsilateral and contralateral stimulation in left and right hand reaching.

As discussed, it is posited here that the left and right SMG may serve different functions pertaining to tool use, but experimental dissociation of these functions needs further studies with additional control conditions. Firstly, a task including trials without tool rotation would address the difference in function suggested for the left and right SMG. As evidence suggests the right IPL is associated with tracking spatial changes (Clark et al., 2000; Gur et al., 2007; Kiehl et al., 2001; Singh-Curry & Husain, 2009) in the environment, this function should not be recruited when no online correction of movement is necessary; relying instead on the tool knowledge function of the left SMG. Secondly, TMS to control sites of parietal regions distinct from the SMG would achieve spatial specificity for the observed delays to correction, ensuring the role of the SMG pertains to tool related aspects of action rather than spatial demands of the task. Additionally, recent research implicates the importance of sub-divisions within the SMG, indicating that some areas are specialised for mechanical knowledge (area PF) while others serve to integrate this mechanical knowledge into action production systems to generate a mental simulation of action (aSMG) (Lesourd et al., 2017; Reynaud et al., 2016) and process affordances of objects in relation to grip size and location (IPS) (Przybylski & Kroliczak, 2017; Tunik et al., 2005). Further experiments should consider these divisions of function in the SMG using tasks and stimuli that selectively require understanding of mechanical function (Badets & Osiurak, 2015) (such as a judgement task between the properties of two objects in relation to one another); compared with tasks that require prediction of grasp, independent of mechanical function knowledge (Andres, Pelgrims, & Olivier, 2013). Selective disruption of sub-regions of the SMG is difficult (Ishibashi et al., 2011), requiring functional imaging with specific hypothesis testing for sub-regions (Lesourd et al., 2017). Dissociation of these functions would provide insights into the functional organisation of the IPL in regard to tool use and have wide reaching implications into the conceptual input required to execute tool use behaviour.

These experiments cannot account for the nature of conceptual input that forms the basis of the previously posited maintained action plan followed during action execution (Osiurak & Badets, 2016). Further experiments that dissociate between whether technical reasoning (Osiurak & Badets, 2017) or reliance on stored semantic representations of use (Buxbaum, 2017), are necessary to understand this input. Follow-up experiments, closely linked to the current paradigm, could explore this through having participants reach for novel tools vs familiar tools to explore whether the left SMG has an inherent bias for familiar objects. This could be further developed to vary the intention of action (Tunik et al., 2008), between use and transport to assess whether transport of objects can be carried out independent of tool or mechanical understanding.

Another interpretation of these findings is that TMS stimulation for both hemispheres may have had an overall disruptive effect on behaviour. This could be due to acoustical or tactile stimulation as a result of the pulse firing, and may not be directly due to stimulation of the SMG in this context. General disruption to behaviour and task performance has been observed and contrasted across cortical regions in previous research (Meteyard & Holmes, 2018), and the experimental controls present here cannot negate this at present. Further exploration of these factors, introducing experimental controls (such control sites of stimulation, discussed in the previous paragraph) will assist in determining the influence of a 'generic' effect of stimulation in the context of this task.

In conclusion, this study revealed a bilateral role of the SMG in mediating goal-oriented actions and shows that the SMG has a dynamic online role in the selection of appropriate grasp during reaching and grasping of tools for use.

4. Triple Pulse TMS over Left SMG Delays Online Correction of Grasp Orientation for Use of Tools – Experiment 3 (McDowell et al., 2018/in prep)

Foreword

Following the previous experiment (Chapter 3), this thesis aimed to further explore lateralisation of TMS function, with regard to the findings for bilateral SMG stimulation. In this experiment the tool rotation paradigm was developed to include controls that allowed examination of left and right SMG function while aiming to demonstrate spatial specificity for this region in facilitating functional tool grasp selection.

Abstract

In the previous experiment, it was demonstrated that TMS over the right, as well as the left SMG, significantly delayed grasp orientation selection while reaching for tools for use, conflicting with the widely reported left hemisphere bias. This experiment developed the online correction task with further controls. Twelve healthy participants reached to grasp tools with explicit instructions to use them. To study the integration of tool knowledge and visuomotor control, the orientation for the tool was perturbed during reach execution to force participants to correct their grasp on two thirds of all trials. Participants reached with their right and left hands while triple pulse TMS was applied over the left and right SMG at the onset of tool perturbation. A control site of stimulation (parieto-occipital complex, left and right) was introduced to examine spatial specificity for TMS in this region. The experiment also included a sham condition. Kinematic measures revealed a significant delay to correction of grasp orientation for left stimulation on trials requiring an inverted grasp. While right control-site stimulation elicited similar delays to correction, left SMG delays were more prominent. The present findings indicate a critical role of the left SMG in mediating selection of grasp orientation of tools for use.

4.1. Introduction and Research Aims

In the previous chapter, a bilateral effect of TMS over the SMG was demonstrated, delaying the selection of appropriate grasp orientation when grasping tools for use, during an online correction task. This finding was independent of hand used, and conflicts with a large body of work implicating the importance of the left SMG over the right (Buxbaum, 2017; Buxbaum et al., 2007; Johnson-Frey et al., 2005; Kroliczak & Frey, 2009; Lesourd et al., 2017; Peeters et al., 2013; Przybylski & Kroliczak, 2017). As discussed in TMS over the Supramarginal Gyrus Delays Selection of Appropriate Grasp Orientation during Reaching and Grasping Tools for Use neuroimaging data has previously revealed bilateral SMG activation during tool action *execution* (Brandi et al., 2014; Johnson-Frey et al., 2005) while left lateralised activation is evident during *planning* tool use (Brandi et al., 2014). It was suggested that the right SMG may have a role in mediating functions that pertain to grasping the target tool (such as controlling for the spatial perturbations of the target and error correction) but that are not inherently related to manipulation knowledge (Buxbaum, 2017) or reasoning (Osiurak & Badets, 2017). These findings were likely due to perturbation of tool orientation on every trial; which if the proposed right SMG role is accurate, would recruit the SMG bilaterally during grasp orientation selection. However, dissociation of the different roles of right and left SMG was not possible without modifications to the experimental design.

To that end, the previously used online correction paradigm (Chapter 3) was expanded, introducing further controls to develop the present model of the SMG role for tool grasp execution. Participants reached to grasp tools with the specific intention of use and the tool orientation was perturbed during reaching. As in experiment 1 and 2 (Chapter 3), this forced the integration of manipulation control and tool knowledge necessary to facilitate functional grasp which this experiment aimed to disrupt by applying TMS at the onset of perturbation. The present study aimed to replicate the findings for SMG stimulation related online correction delays, while demonstrating spatial specificity of the SMG site. To achieve this a control site of stimulation was used (parieto-occipital complex – POC). To dissociate between the function of left and right SMG and parietal regions and lateralisation (see Chapter 3 - General Discussion), participants reaching was assessed with both left and right hands and stimulation of cortical targets for both hemispheres. Previous research has indicated that online correction is mediated only by dorso-dorsal structures in the hemisphere *contralateral* to the effector hand (Rice et al., 2007), therefore any observed effects for ipsilateral reaching may be associated with additional visuomotor processes than those of error correction. Across all conditions, this experiment aimed to explore whether the previously observed effects of SMG stimulation (McDowell et al., 2018) impacted on grasp aperture also. This behaviour is largely regarded as part of the dorso-dorsal action production system, mediated by the intraparietal sulcus (IPS) (Jacobs et al., 2009; Orban & Caruana, 2014; Reynaud et al., 2016) contralateral to the effector hand. This system has previously been associated with rapid online changes to grasp size or orientation (Cohen et al., 2009b; Tunik et al., 2005). Co-activation of the IPS and SMG (Brandi et al., 2014; Orban & Caruana, 2014; Rizzolatti & Matelli, 2003) during action execution indicates potential crosstalk between these structures to facilitate tool use action. Examining grasp aperture should allow elaboration of the findings for bilateral SMG stimulation. Triple pulse TMS was implemented to examine whether grasp aperture or orientation would be impacted by TMS deliver during, and 100ms after target rotation. This stimulation paradigm has been implemented in similar motor control paradigms (Striemer, Chouinard, & Goodale, 2011). Control trials were also included in which the tool would not rotate, interspersed with those that did. This was to ensure that participants were not attempting to predict the change in orientation and would be reaching for the tool in its initial orientation. This further served to explore the proposed model of right SMG function, discussed in the previous chapter. If the right SMG mediates functions that pertain to grasping the target tool (such as controlling for the spatial perturbations of the target and error correction), then the stimulation of the right SMG during non-perturbed trials should not impact on selection of grasp orientation.

Given these changes to the experimental paradigm, the present hypotheses are threefold: (1) TMS over the left SMG (compared with TMS to control site POC and sham stimulation) will delay correction of grasp orientation. (2) TMS over right SMG should elicit similar effects, but only when spatially demanding adjustment occurs, i.e. in trials that require an inverted grasp or rotation of the hand during movement that is incongruent with the rotation of the tool. (3) All of the effects above should be observable for the hand both ipsilateral and contralateral to the SMG, while not being observable for control sites of stimulation nor for sham stimulation.

4.2. Method

4.2.1. Participants

12 healthy right-handed participants (8 female, 4 male, age range 20-28, M±SD = 23.66±2.14 years) were recruited from the University of Nottingham, UK. One participant's data was subsequently removed from analysis due to motion tracking artefacts that could not be corrected. Handedness was assessed via the 10 item version of the Edinburgh Handedness Inventory (Oldfield, 1971); participants were identified as having a right-hand preference, with an average laterality quotient of 0.82 (SD=0.15, range 0.65-1.0). Participant safety and suitability to undergo TMS was assessed using pre-test screening (Maizey et al., 2013). Side effects or discomfort were monitored using follow up questionnaires over a 24 hour period following stimulation (Maizey et al., 2013). No side effects or discomfort attributed to TMS were reported by participants. Written informed consent was obtained from all participants prior to the experiment. The study had approval from the ethics committee of the School of Psychology, University of Nottingham, and was performed in accordance with the declaration of Helsinki (as of 2008).

4.2.2. Apparatus

Eight everyday tools (all plastic ~18cm long, the same tools as in TMS over the Supramarginal Gyrus Delays Selection of Appropriate Grasp Orientation during Reaching and Grasping Tools for Use, e.g. knife, fork, spoon, hammer, screwdriver, etc.) were used as targets, consistent with the previous paradigm (McDowell et al., 2018). Participant familiarity with the tool was assessed prior to testing by asking them to demonstrate functional use of each tool. Tools were held in a cradle, connected to the axle of a stepper motor to allow rapid 90° rotation. 'Hook and loop' fabric strips were used to secure the tools in the cradle during rotation, while allowing easy removal on completion of grasp. Tool presentation was consistent with the previous experiments (coronal plane, 57cm from table edge, 37cm raised from table top, participant view controlled using PLATO shutter goggles, *Translucent technologies, Toronto, Canada).* During tool rotation and the corresponding time in non-rotation trials, a speaker played white noise to mask the sound of rotation. This was used so participants would be unable to distinguish between trials that rotated and those that did not from the sound of the stepper motor prior to rotation. On non-rotation trials, a recorded sound of the motor rotating merged with the white-noise mask was played at the same movement threshold as rotation trials.

Motion during participants' reaching and grasping was tracked using a Polhemus Fastrak *(Polhemus Fastrak, Colchester, Vermont, USA)*. As mentioned above, to further the exploration of kinematic effects of online TMS, grasp aperture was recorded during reaching. Three sensors were attached (using medical tape) to the participants thumb, index finger and wrist, sampling at 40Hz each. The thumb and index finger sensors were used to assess grasp aperture during reaching, while the wrist sensor was used to record velocity, orientation of the hand (roll) and overall movement time.

4.2.3. Localisation of Cortical Targets and TMS

Frameless stereotaxic neuro-navigation *(Brainsight, Rogue-Research, Canada)* was used to mark the cortical targets on each participants' MRI and localize coil placement. Motor threshold was determined as the stimulation intensity over M1 producing visible contraction of the hand muscles on 50% of 10 trials. Experimental stimulation was 110% of this stimulation intensity. At the experimental and control site of stimulation (SMG and POC) the TMS coil was held tangentially to the surface of the scalp with the handle oriented upwards (towards the top of the head) for both cortical sites. This handle orientation was used so that the coil could be held consistently in place by a clamp attached to a stand above the participant. For the sham (baseline) condition the coil was placed against the scalp, between the experimental and control sites of stimulation. One wing of the coil was placed against the scalp while the centre of the coil was oriented between 45° and 90° away from the head. This differed from the baseline condition in Chapter 3 for which no pulse was discharged. Participants were provided with ear plugs to dampen the noise associated with TMS pulse discharge. A chin rest was used to maintain head position throughout testing.

Triple pulse (Magstim Rapid *(Magstim Company Ltd, Whitland, Carmarthenshire, UK)*, double 70mm coil, 100ms inter-pulse interval) TMS was administered for the experimental and control stimulation blocks. Triple pulse stimulation was selected to attempt to disrupt integration of tool knowledge for the duration of target rotation (~100ms) and to examine if a further TMS pulse would disrupt online adjustment of grasp aperture during reaching. Cortical targets selected for testing were the left and right SMG (experimental) and left and right parieto-occipital complex (POC) (control site – this target was identified as a suitable control due to use as a control site in previous similar paradigms (Tunik et al., 2005)).

4.2.4. Design

A repeated measures 2 x 2 x 2 x 2 x 3 design was used. Independent variables were Effector Hand (left-handed or right-handed reaching), Hemisphere (left, right), Stimulation Site (SMG, POC – sham was used as a baseline and subtracted from all other stimulation conditions), Congruence of tool position (congruent, incongruent) and Rotation (inverted, upright, none). Out of the 6 levels of Congruence x Rotation, 4 were as in the previous experiment. These levels varied by grasp orientation (Inverted or Upright), and by congruence between hand rotation necessary for grasp of the tool in initial position and rotation of the hand necessary for grasp of the tool in the final position, resulting in conditions incongruent inverted (II), incongruent upright (IU), incongruent no-rotation (IN), congruent inverted (CI), congruent upright (CU), and congruent no-rotation (CN). The purpose of the two non-rotation conditions was to ensure participants were not planning the direction (or necessity) in adjustment of grasp orientation during reaching; but were planning to grasp the tool in its initial position.

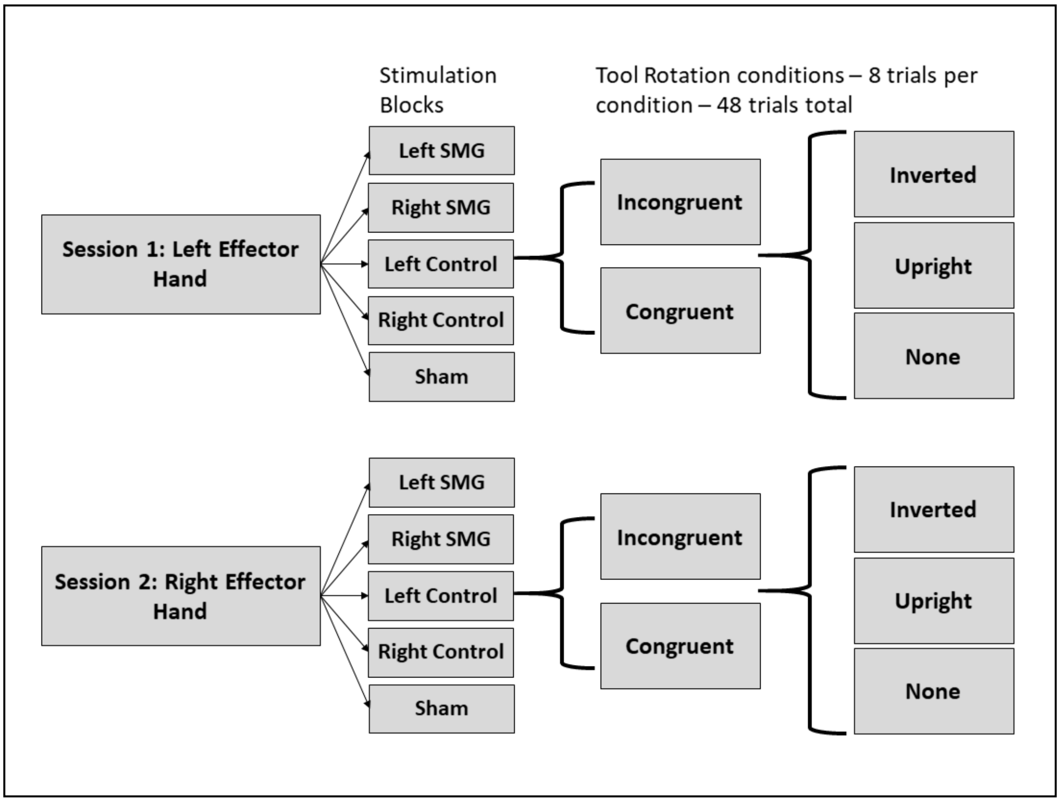

Figure 16. Example trial sequence for altogether 480 stimuli. One session for each effector hand. Within each session, one block for each of the 5 Stimulation conditions. Within each block, 8 trials were conducted for each of the 6 tool conditions varied in congruence and rotation; Incongruent Inverted, Incongruent Upright, Incongruent no-rotation, Congruent Inverted, Congruent Upright, Congruent No-rotation. Due to the length of the experiment, sessions for each hand were run on separate days.

The experiment comprised of 480 trials altogether, split into two sessions. Participants completed the first session with either left or right hand, and (after at least 24 hours) the subsequent session with the other (counterbalanced across participants).

Each session comprised 5 blocks of 48 trials each. Within each block, all trials were from one and the same out of the 5 stimulation conditions (TMS trials were not interspersed with non TMS trials, or in the current experiment sham). The order of effector hand sessions and the order of stimulation blocks within each session were counterbalanced between participants. The 48 trials were comprised of 8 per each of the 6 above listed Tool Rotation conditions, the order of which was pseudo-randomised (**see** Figure 16).

As dependent variables, several kinematic measures used to model participant reaching and grasping. Movement Time (MT) from movement onset to final grasp; percent of MT to peak velocity (TPV%); percent of MT to peak aperture of thumb and index finger (TPA%), and a combined measure of delay in the rotation of hand to correct grasp orientation and erroneous rotation to corresponding baseline performance (‘miscorrection’ score, measured in SD from baseline performance, see Chapter 3 - 3.2.1.6 Analysis). This measure was assessed via the roll data (rotation of the hand) taken from the wrist motion sensor.

For this experiment, all kinematic data measures were assessed by subtracting average Baseline (sham-TMS) data from TMS stimulation conditions (for the corresponding hand; i.e. left hand TMS – left hand Baseline; right hand with TMS – right hand Baseline). Given the increase in experimental conditions (5 TMS conditions: baseline Sham stimulation, left and right SMG and POC (control); reaching with both hands; rotation and non-rotation of tools) compared to the previous chapters; this analysis method allows use of a 2 x 2 x 2 x 2 x 3 (Hand x Hemisphere x Stimulation Site x Congruence x Rotation) repeated measures design. This method enables easier, more relevant interpretation of interactions, and enables more direct examination of lateralisation of SMG function. A potential disadvantage of this approach is that absence of an interaction could mean that there is no effect of TMS or that all variables are affected equally. Results are examined in consideration of these factors.

4.2.5. Procedure

Participants were positioned at a desk with their chin on a rest and PLATO goggles in front of their eyes. The index and middle fingers of the effector hand were secured together to prevent participants from being able to 'twirl' the tool should they grasp it in the incorrect orientation, ensuring correction occurred before grasp. Participants were instructed to place their effector hand index finger on a button (30cm to the left or right of the chin rest, for left and right hand reaching respectively). The goggles occluded the participants view between trials to ensure they could not see the initial orientation of the tool. When provided with a 'get ready' signal from the experimenter, participants were instructed to press and hold the button until the goggles became transparent (randomised delay of 2-4 sec between Go signal (verbally given by the experimenter) and Goggles opening). Participants were instructed to reach and grasp the tool as quickly and accurately as possible, in a manner suitable to its familiar use, while avoiding erroneous grasping. Participants were explicitly instructed to demonstrate use of the tool immediately after grasping (e.g. using the knife to demonstrate a cutting motion on a piece of plastecine or using the hammer to tap a plastic nail).

On tool rotation trials, rotation onset was locked to forward movement of the motion sensor from the start position (30mm) towards the target tool. The tool completed its 90° rotation within ~100ms. White noise was played via a speaker to mask the noise of the stepper motor rotating the tool, starting at the onset of rotation for 500ms. For non-rotation trials, white noise combined with the recorded sound of the stepper motor rotating a tool were played at the forward movement threshold, for the same duration. The first TMS pulse was delivered 50ms after the onset of rotation with the following two pulses delivered at 100ms intervals (see Figure 17). The triple pulse was used to explore whether the effects of TMS would impact on grasp aperture during action execution in the later stages of reaching, as well as selection of grasp orientation. Each block (comprised of 48 trials) lasted approximately 20 minutes. Participants were provided with breaks between blocks. 10 practice trials were provided prior to testing to familiarise participants with the procedure. Each session lasted approx.

2.5 hours including breaks. Sessions were conducted on separate days with at least 24 hours between sessions.

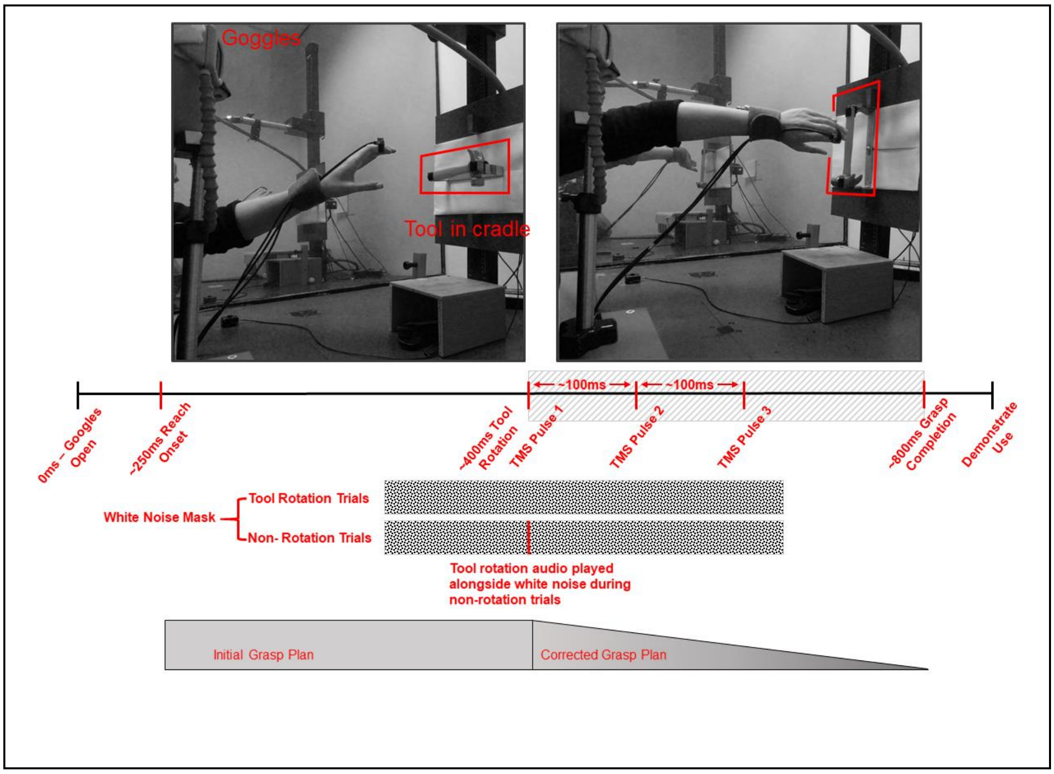

Figure 17. Average, estimated timeline for an example trial, similar to previous paradigm (McDowell et al., 2018) with the following modifications: 1. 100ms after TMS pulse 2, an additional TMS pulse 3 was applied. 2. White noise was introduced to mask the sound of rotation during trials. For non-rotation trials, a recording of the tool rotation was played, alongside the white noise, at the time at which tool rotation would be initiated on tool rotation trials.

4.3. Results

One (out of n = 12) participant's data was not suitable for analysis due to motion tracker recording error. All data from the experiment are displayed in Table 5 (see pg. 96), for a summary of the ANOVA, see Table 6 (see pg. 97). All data *(n = 11)* was analysed using 2 x 2 x 2 x 2 x 3 repeated measures ANOVA *(Hand (left, right) x Hemisphere (left, right) x Stimulation (SMG, Control) x Congruence (Incongruent, congruent) x Rotation (Inverted, Upright, None)*. Baseline (sham TMS) measures were subtracted from the Stimulation conditions and the difference in values was analysed as described above. For analysis inclusive of Rotation, Greenhouse-Geisser corrected *F* and *p* values are reported (with uncorrected *df*). For miscorrection scores, as with Chapter 3, uncorrected grasps were assigned a zero value in calculating the mean miscorrection score for each participant in each condition. The number of uncorrected trials accounted for 7.81% of all trials.

4.3.1. Miscorrection Scores

Analysis revealed a significant interaction between Hemisphere, Stimulation and Rotation ($F_{(2, 20)} = 4.75$, $p = .02$). Subsequent 2 x 3 (Hemisphere x Rotation) ANOVAs, collapsed across Hand and Congruence were conducted for both Stimulation conditions. For SMG stimulation, a significant interaction between Hemisphere and Rotation ($F_{(2, 20)} = 4.47$, $p = .03$) was identified (see Figure 19). The largest differences in miscorrection scores were observable for inverted rotation conditions; with higher miscorrection for left SMG stimulation *(M±SD miscorrection score = 0.22±0.11)* compared to right *(M±SD miscorrection score = 0.11±0.11).* Right SMG stimulation showed higher miscorrection for upright rotation *(M±SD miscorrection score = 0.15±0.19)* compared to left *(M±SD miscorrection score = 0.08±0.20),* while left SMG showed higher miscorrection for non-rotation *(M±SD miscorrection score = 0.13±0.17)* compared to right *(M±SD miscorrection score = 0.06±0.16).* This interaction was not present for control site stimulation ($F_{(2, 20)} = 0.02$, $p = .97$, see Figure 18*)*, and no effects of Hemisphere ($F_{(2, 20)} = 0.01$, $p = .90$) or Rotation ($F_{(2, 20)} = 0.10$, $p = .90$) were observable. That this interaction occurs for SMG stimulation and *not* control site is consistent with the hypothesis. Higher miscorrection scores for inverted rotation resulting from left SMG stimulation indicates disrupted integration of conceptual tool knowledge into visuomotor transformation necessary for correction of grasp. This is potentially most observable for the inverted rotation condition due to increased difficulty compared to the upright or non-rotation conditions, and preference for an upright grasp during reaching. No other main effects or interactions were observed for miscorrection scores (for summary see Table 6, see pg. 97).

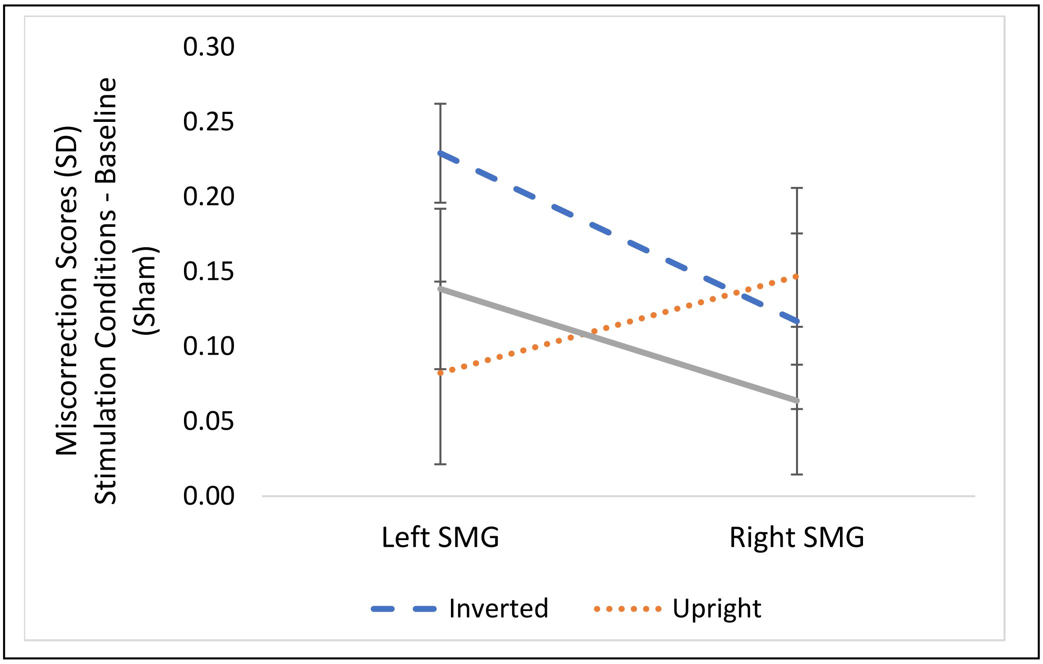

Figure 19. Interaction between Hemisphere and Rotation observed for SMG stimulation – Error bars indicate ±1 SE of the mean miscorrection score (stimulation – baseline) across subjects ($F_{(2, 20)}$ =4.47, p=.03).

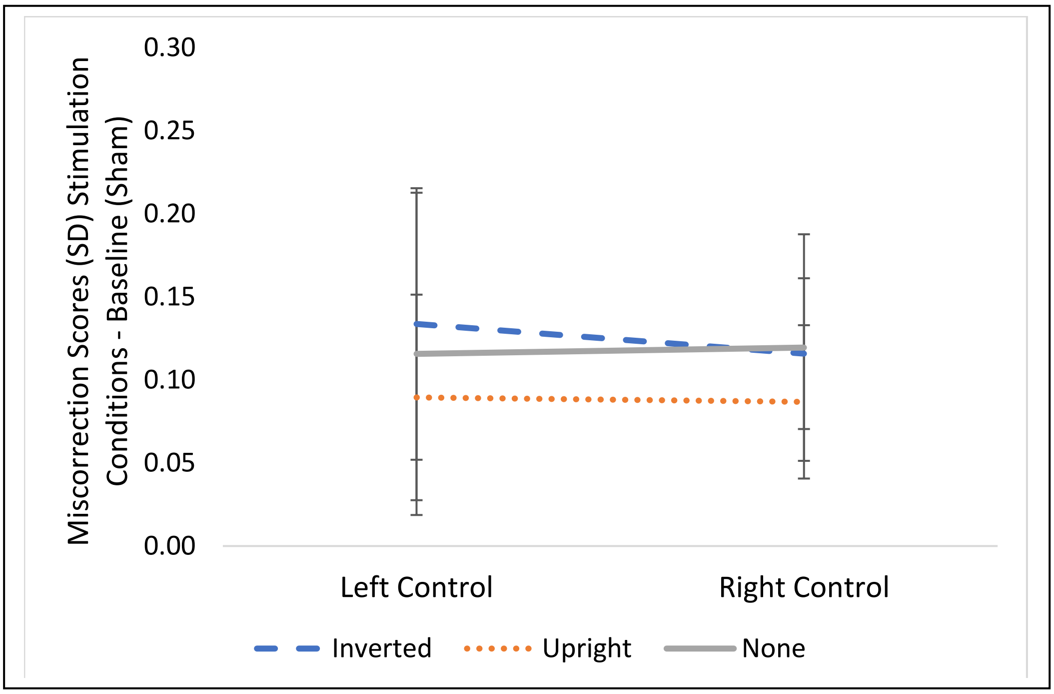

Figure 18. Interaction between Hemisphere and Rotation observed for control site stimulation – Error bars indicate ±1 SE of the mean miscorrection score (stimulation – baseline) across subjects – non-significant ($F_{(1, 10)}$ =0.02, p=.97).

4.3.2. Movement Time (MT)

A significant interaction between Hand, Hemisphere and Stimulation *($F_{(1, 10)}$ = 7.94, p=.02)* was observed for MT. Subsequent 2 x 2 (Hand x Hemisphere) ANOVAs, collapsed across Congruence and Rotation, were conducted for both Stimulation conditions to explore this interaction further. For SMG stimulation, a significant interaction between Hand and Hemisphere *($F_{(1, 10)}$ =8.72, p=.01)* showed longer left hand reaching for right SMG stimulation *(M±SD = 24±36 ms)* compared to sham TMS baseline (see Figure 20). Delays were not observable for left hand reaching with left SMG stimulation *(M±SD = -29±96 ms)* or either of the right hand reaching conditions *(Left SMG; M±SD = -12±67 ms, Right SMG; M±SD = -44±54 ms).* This pattern of results was not reflected for control site stimulation with no significant effects of Hand *($F_{(1, 10)}$ = 2.46, p=.14)* or Hemisphere *($F_{(1, 10)}$ = 0.92, p=.36),* nor interaction *($F_{(1, 10)}$ = 0.24, p=.63)* between variables (see Figure 21).

This could be reflective of contralateral disruption observed both in previous chapters here (see Chapter 3, Experiment 1) and similar TMS experiments pertaining to reaching and grasping behaviour (Rice et al., 2007). That this occurs for the SMG could be evidence of contralateral parietal control of online motion towards a target. That this is observable for the left hand but not the right and may be indicative of the non-dominant hand being more susceptible to disruption of movement as a result of TMS of the contralateral SMG, within the context of this task.

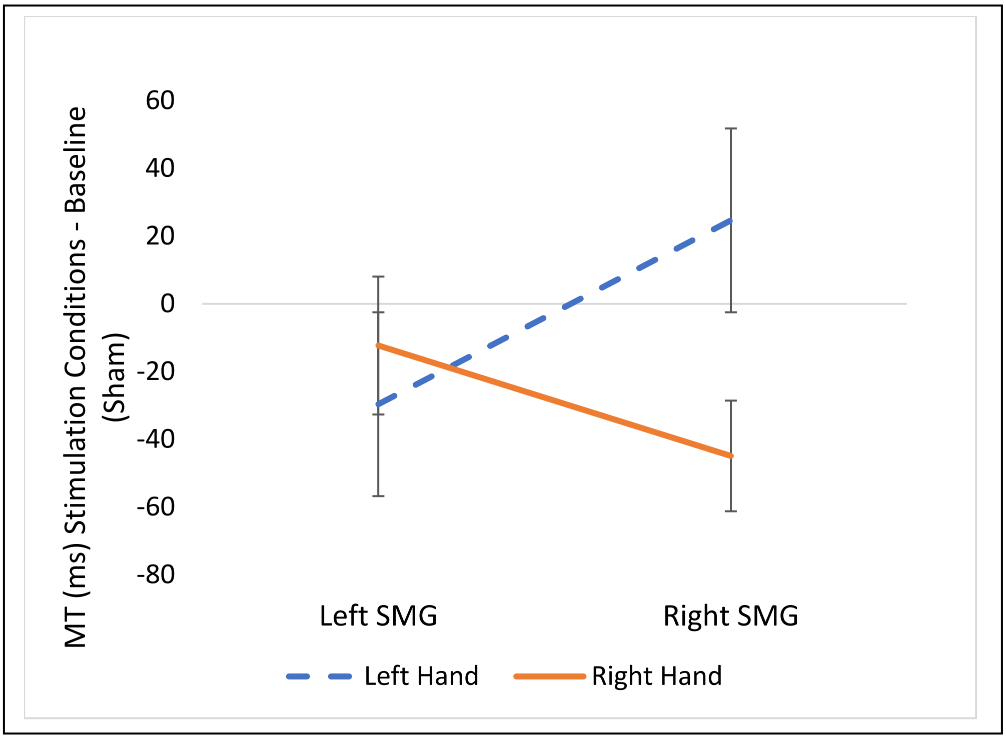

Figure 20. Interaction between Hand and Hemisphere for SMG stimulation Error bars indicate ±1 SE of the mean MT (ms, Stimulation condition – Baseline) ($F_{(1, 10)}$ =8.72, p=.01). Positive values indicate delayed MT compared to baseline, negative values indicate faster MT compared to Baseline.

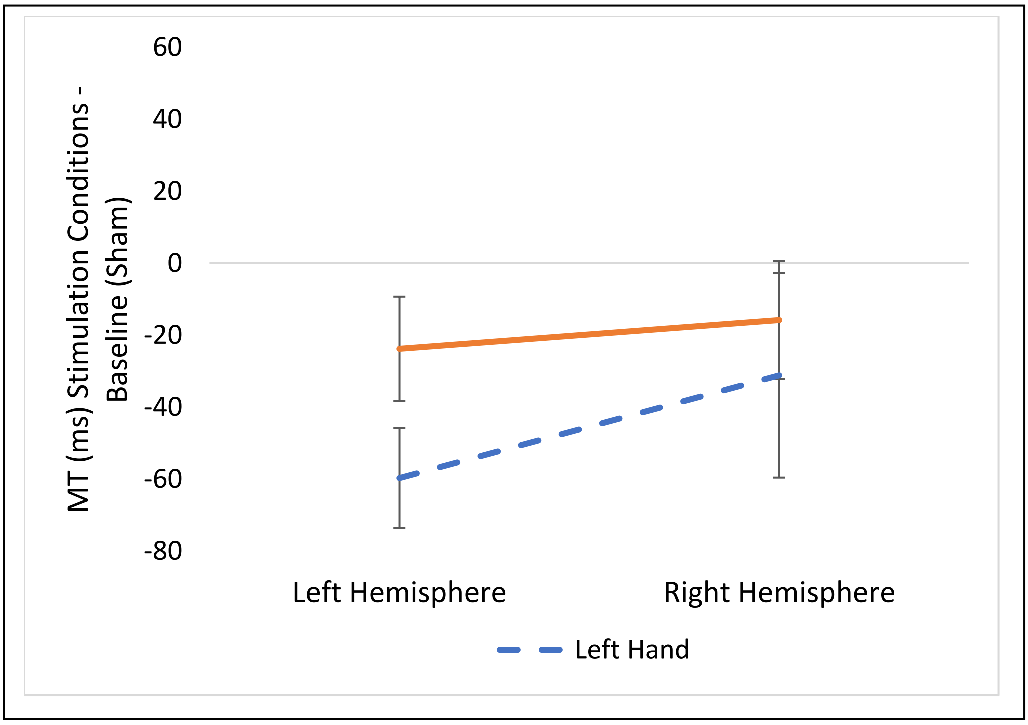

Figure 21. Interaction between Hand and Hemisphere for control site stimulation – non significant ($F_{(1, 10)}$ = 0.24, p=.63). Error bars indicate ±1 SE of the mean MT (ms, Stimulation conditions – Baseline). Positive values indicate delayed MT compared to baseline, negative values indicate faster MT compared to Baseline.

An interaction between Hand, Congruence and Rotation *($F_{(2, 20)} = 4.57$, $p=.032$)* was identified for MT. Subsequent 2 x 2 (Hand x Congruence) ANOVA collapsed across Stimulation and Hemisphere were conducted for each of the Rotation conditions.

For upright rotations, a significant interaction was observed between Hand and Congruence *($F_{(1, 10)} = 10.57$, $p=.009$)*. Right hand MT was longer for congruent rotation *(M±SD = -14±11 ms)* compared to incongruent rotation *(M±SD = -38±16 ms)*. The reverse of this pattern was observable for left hand reaching MT *(Congruent: M±SD = -49±13 ms, Incongruent: M±SD = -22±21 ms* see Figure 22*)*. This interaction was not observable for inverted *($F_{(1, 10)} = 1.89$, $p=.19$)* or non-rotation conditions *($F_{(1, 10)} = 0.001$, $p=.97$)*. That this occurs for upright rotation could be in keeping with a predisposition to an upright grasp when intending to use tools (Creem-Regehr & Lee, 2005). The differential influence of congruence on MT for each hand may be indicative of differences between reaching with the dominant and non-dominant hands.

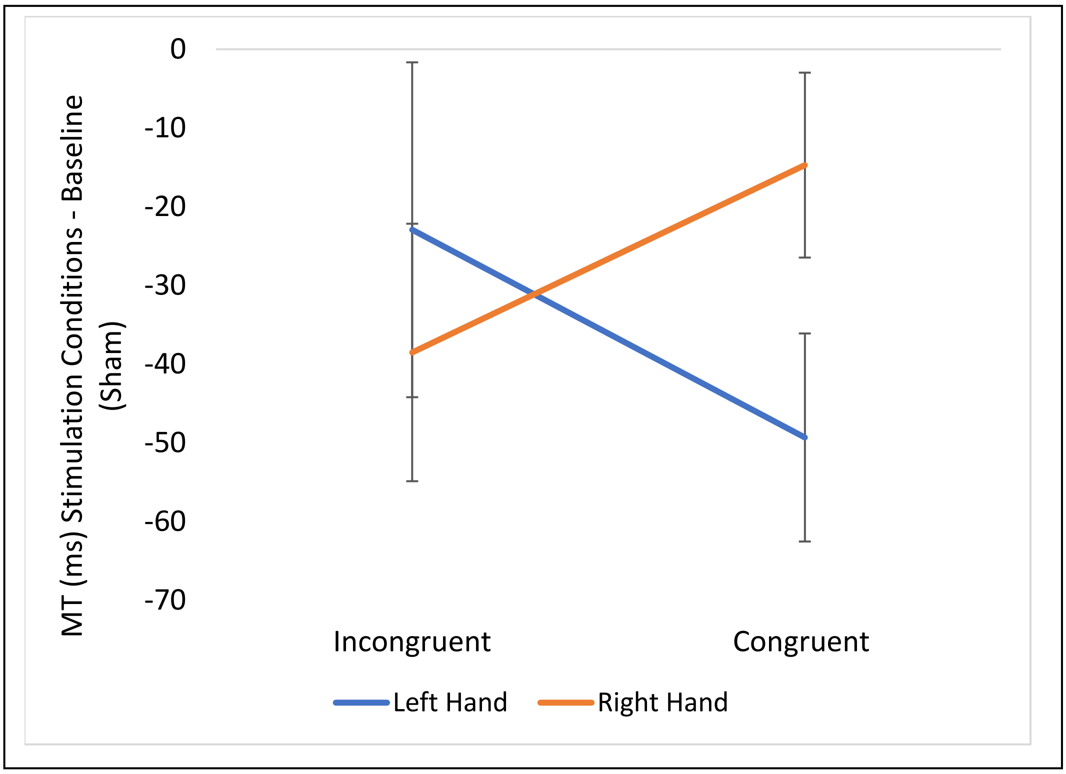

Figure 22. Interaction between Hand and Congruence for Upright rotation conditions. Error bars indicate ±1 SE of the mean MT (ms, Stimulation condition – Baseline) ($F_{(1, 10)} = 10.57$, $p=.009$). Positive values indicate delayed MT compared to baseline, negative values indicate faster MT compared to Baseline.

However, these findings are contrary to the expected outcomes as reaching for congruent rotation was slower than incongruent for the dominant hand.

Furthermore, this interaction showed no influence of Stimulation site, indicating that SMG stimulation did not observably disrupt reaching. However, results show that *all* stimulation conditions for upright rotation showed faster reaching than sham-TMS baseline (see Figure 22). While interactions in terms of hand and congruence may be reflective of the task demands and dominant/non-dominant hand reaching, faster reaching for stimulation conditions may be indicative of a general effect of stimulation sensation during action (Meteyard & Holmes, 2018).

4.3.3. Percent Time to Peak Velocity of Movement (TPV%)

A significant effect of Hemisphere *($F_{(1, 10)}$ = 6.47, p=.03)* revealed delayed TPV% for left hemisphere stimulation *(M±SD = 1.14±0.64 TPV%)* compared to earlier TPV% for right (*M±SD = -1.48±3.26 TPV%).* A significant interaction was observed between Hand and Hemisphere *($F_{(1, 10)}$ = 21.08, p=.001)* showing delays to TPV% for stimulation over the hemisphere ipsilateral to the effector hand *(left hand left hemisphere; M±SD = 2.71±1.55 TPV%, right hand right hemisphere; M±SD = 0.82±2.11 TPV%).* This was not observed for contralateral stimulation *(left hand right hemisphere; M±SD = -3.78±1.52 TPV%, right hand left hemisphere; M±SD = -0.43±1.64 TPV%).* As this effect is ipsilateral and has no interaction with Stimulation site *($F_{(2, 20)}$ = 0.42, p=.65)*, this finding could be attributed to a general disruptive effect of TMS during reaching (Meteyard & Holmes, 2018). This interaction is likely driven by below baseline (earlier) TPV% observed for right hemisphere stimulation conditions.

A interaction between Congruence and Rotation with a trend toward significance *($F_{(2, 20)}$ = 3.36, p=.055)* showed delayed TPV% for non-rotation incongruent trials *(M±SD = -0.92±2.82 TPV%)* compared to congruent trials *(M±SD = -1.03±1.24 TPV%).* For inverted rotations delays to TPV% occurred most prominently for congruent *(M±SD = -0.54±1.46 TPV%)* compared to incongruent *(M±SD = -0.30±2.27 TPV%).* Delays to TPV% were less observable for upright trials for both congruent *(M±SD = -0.99±2.80 TPV%)* and incongruent conditions *(M±SD = -0.16±3.31 TPV%*

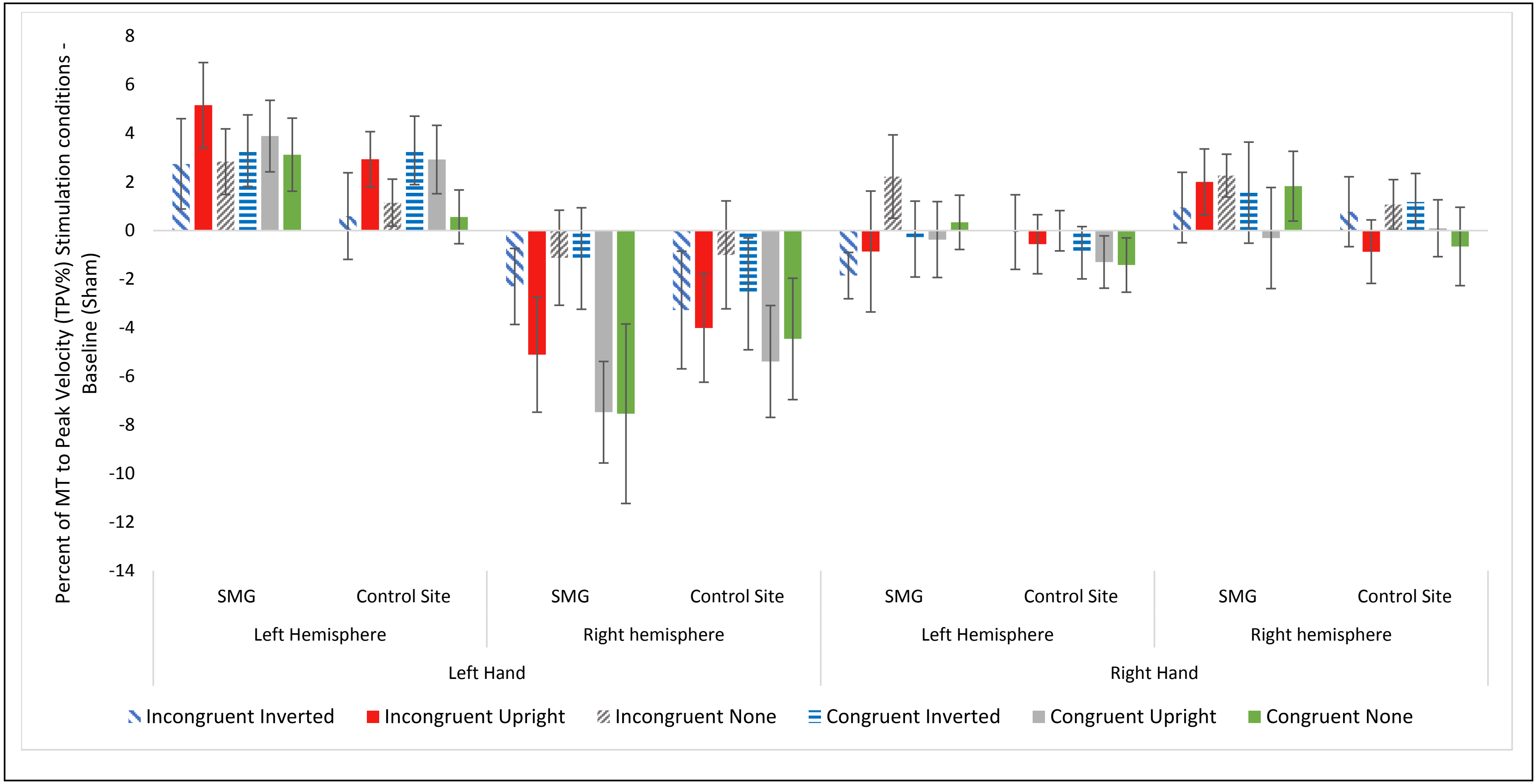

Figure 23. Bar chart summarising percent of MT to peak velocity (TPV% stimulation conditions – baseline sham TMS) across Hand, Hemisphere, Stimulation Site, Congruence and Rotation conditions. A significant effect of Hemisphere (p = .03) was observed, alongside significant interactions; Hand x Hemisphere (p<.01), Hand, Hemisphere and Rotation (p = .056), Congruence x Rotation (p = .055).

An interaction with a trend toward significance between Hand, Hemisphere and Rotation *($F_{(2, 20)}$ = 3.34, p=.056)* was also observed (see Figure 24). Subsequent Hemisphere x Rotation ANOVA collapsed across Stimulation and Congruence were conducted for each Hand condition. A main effect of Hemisphere *($F_{(1, 10)}$ = 12.99, p=.005)* for left hand reaching showed delayed TPV% for left hemisphere stimulation *(M±SD = 2.71±-1.55 TPV%)* with earlier TPV% for right *(M±SD = -3.78±5.05 TPV%)*. Right hand reaching showed an opposing effect of Hemisphere *($F_{(1, 10)}$ = 5.24, p=.045)* with delayed TPV% for right stimulation *(M±SD = 0.82±2.11 TPV%)* and earlier TPV% for left stimulation *(M±SD = -0.42±1.64 TPV%)*.

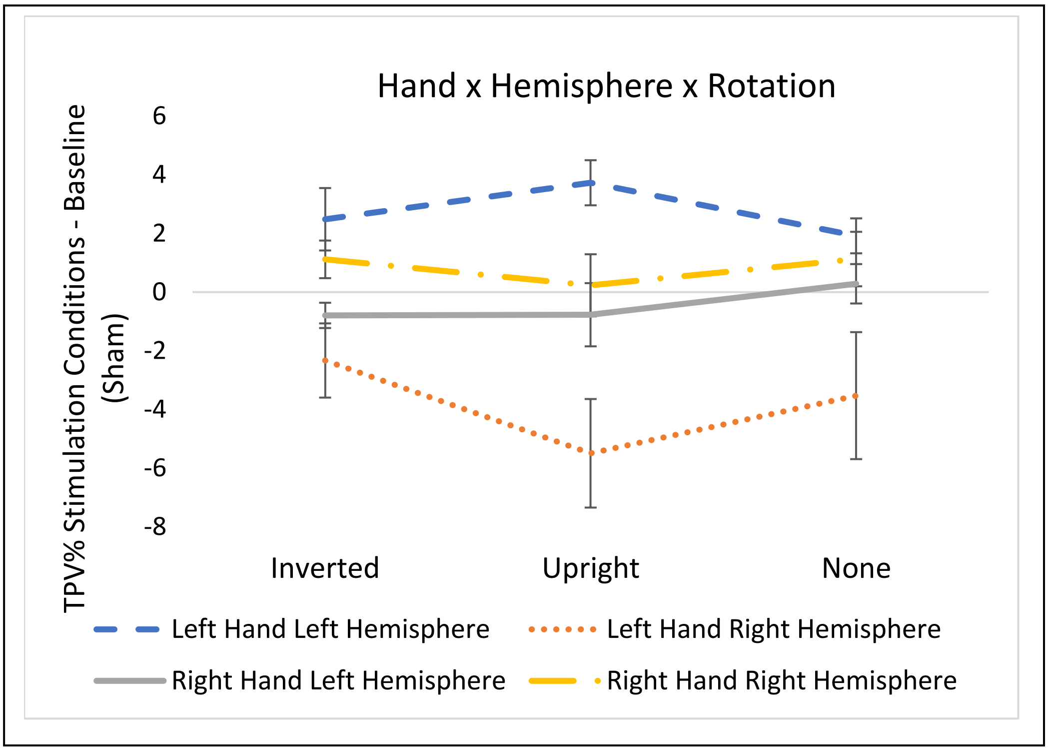

Figure 24. Interaction observed between Hand, Hemisphere and Rotation conditions. Error bars indicate ±1 SE of the mean TPV% (Stimulation condition – Baseline) ($F_{(2, 20)}$ = 3.34, p=.056). Positive values indicate delayed TPV% compared to baseline, negative values indicate earlier TPV% compared to Baseline.

For left hand reaching, a significant effect of Rotation *($F_{(2, 20)}$ = 3.73, p=.04)* showed delayed TPV% for upright trials *(M±SD = -0.58±2.59 TPV%)*, with limited delays to TPV% for both inverted *(M±SD = -2.01±2.38 TPV%)* and non-rotation trials *(M±SD = -1.79±3.32 TPV%)*. This effect was not observed for right hand reaching *($F_{(2, 20)}$ = 0.16, p=.85)*. The delay to TPV% for is consistent with ipsilateral stimulation of the effector hand and may be due to a general disruptive effect of parietal stimulation during reaching (Meteyard & Holmes, 2018). However, that the rotation interaction is present for left stimulation only and prominent in upright rotation conditions suggests potential disruption of tool behaviour, due to predisposition to an upright grasp of tools for use. Although, the lack of Stimulation site influence on TPV% makes this interpretation difficult to reconcile with these findings.

4.3.4. Percent Time to Peak Aperture (TPA%)

A significant main effect of Hemisphere *($F_{(1, 10)} = 11.94$, $p=.006$)* revealed earlier TPA% for right hemisphere stimulation *(M±SD = -2.33±4.16 TPA%)* and delayed TPA% for left hemisphere *(M±SD = 3.94±4.02 TPA%).* A main effect of Stimulation site *($F_{(1, 10)} = 8.42$, $p=.02$)* revealed delayed TPA% for SMG stimulation *(M±SD = 1.87±3.22 TPA%)* compared to control site stimulation *(M±SD = -0.26±2.83 TPA%).* A main effect of Rotation showed delays to TPA% for both inverted *(M±SD = 1.27±4.18 TPA%)* and upright *(M±SD = 2.53±4.23 TPA%)* rotation conditions that was not observable for non-rotation conditions *(M±SD = -1.39±3.45 TPA%).*

An interaction was observed between Hand, Stimulation site, Congruence and Rotation *($F_{(2, 20)} = 4.57$, $p=.038$).* This was further examined with separate 2 x 2 x 3 (Stimulation site x Congruence x Rotation) ANOVAs (collapsed across hemisphere) for each of the Hand conditions.

For left hand data, a significant interaction was observed between Stimulation site, Congruence and Rotation *($F_{(2, 20)} = 8.53$, $p=.002$,* see Figure 25*).* Control site stimulation showed delayed TPA% for inverted and non-rotation trials, with earlier TPA% for upright trials. This pattern was observable for both congruent *(Inverted: M±SD = 3.67±6.85 TPA%, Non-rotation: M±SD = 1.45±5.44 TPA%, Upright: M±SD = -4.43±6.03 TPA%)* and incongruent conditions *(Inverted: M±SD = 1.02±6.48 TPA%, Non-rotation: M±SD = -0.88±4.91 TPA%, Upright: M±SD = -4.45±7.91 TPA%)*. For SMG stimulation, congruent TPA% followed the same pattern, but with increased delays *(Inverted: M±SD = 8.46±9.83 TPA%, Non-rotation: M±SD = 7.31±6.06 TPA%, Upright: M±SD = -0.31±9.12 TPA%).* Incongruent trials, however, showed earlier TPA% for both upright *(M±SD = -0.86±8.81 TPA%)* and non-rotation conditions *(M±SD*

= -2.67±7.81 TPA%) with delayed TPA% for inverted *(M±SD = 12.63±6.86 TPA%)*. This interaction was not observable for right hand reaching *($F_{(2, 20)}$ = 0.24, p=.78).*

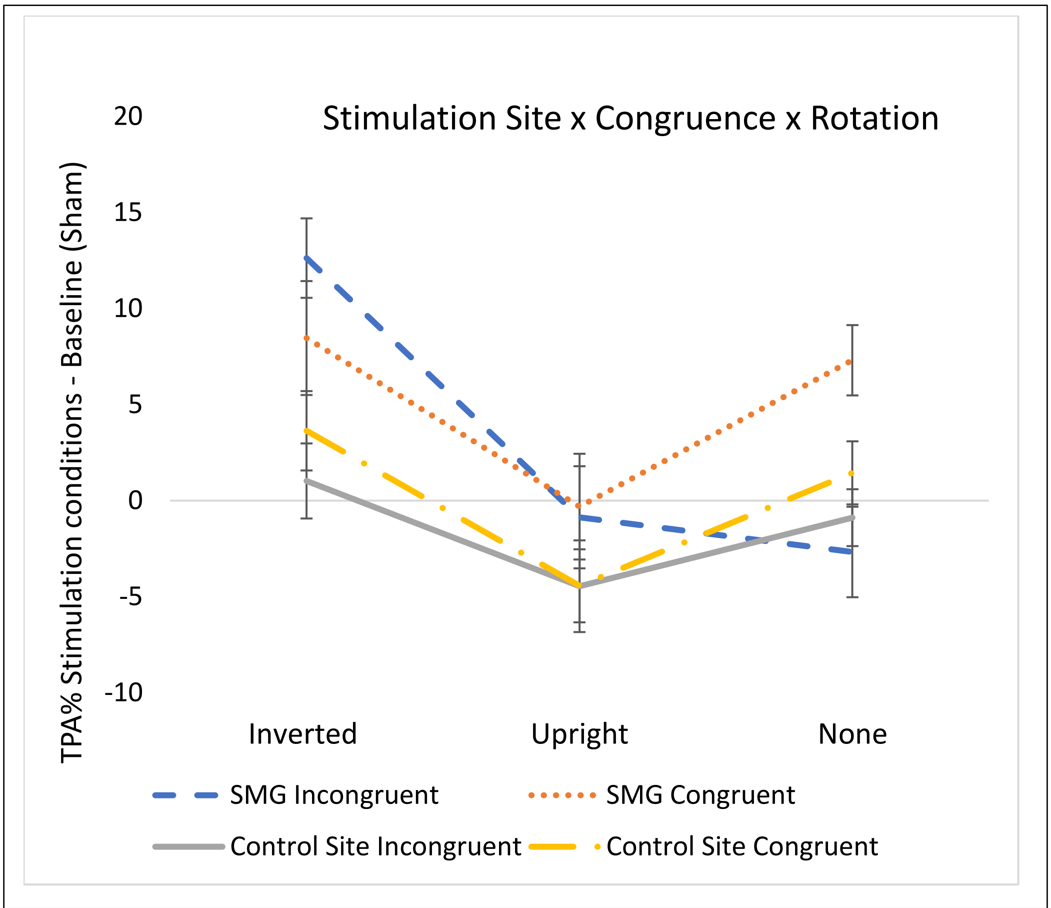

Figure 25. Interaction observed between Stimulation site, Congruence and Rotation conditions. Error bars indicate ±1 SE of the mean TPA% (Stimulation condition – Baseline) ($F_{(2, 20)}$ = 4.57, p=.038). Positive values indicate delayed TPA% compared to baseline, negative values indicate earlier TPA% compared to Baseline.

An interaction between Hand, Hemisphere, Congruence and Rotation *($F_{(2, 20)}$ = 5.56, p=.021)* was also observed for TPA%. As above, this was further explored through follow up 2 x 2 x 3 (Hemisphere x Congruence x Rotation) ANOVA for each of the Hand conditions.

For left hand reaching, a Hemisphere, Congruence and Rotation interaction *($F_{(2, 20)}$ = 7.07, p=.005)* was observed. This showed a similar pattern to the Stimulation site, Congruence and Rotation interaction observed above. Right hemisphere stimulation resulted in delayed TPA% for both inverted and non-rotation trials with earlier TPA% for upright. This was observable for both congruent *(Inverted: M±SD = -1.27±9.15 TPA%, Non-rotation: M±SD = -3.77±6.03 TPA%, Upright: M±SD = -10.16±10.39 TPA%)* and incongruent conditions *(Inverted: M±SD = 0.89±11.02 TPA%, Non-rotation: M±SD = -1.69±9.72 TPA%, Upright: M±SD = -10.19±12.10 TPA%)*. For left hemisphere stimulation, congruent trials followed a similar pattern but with larger delays to

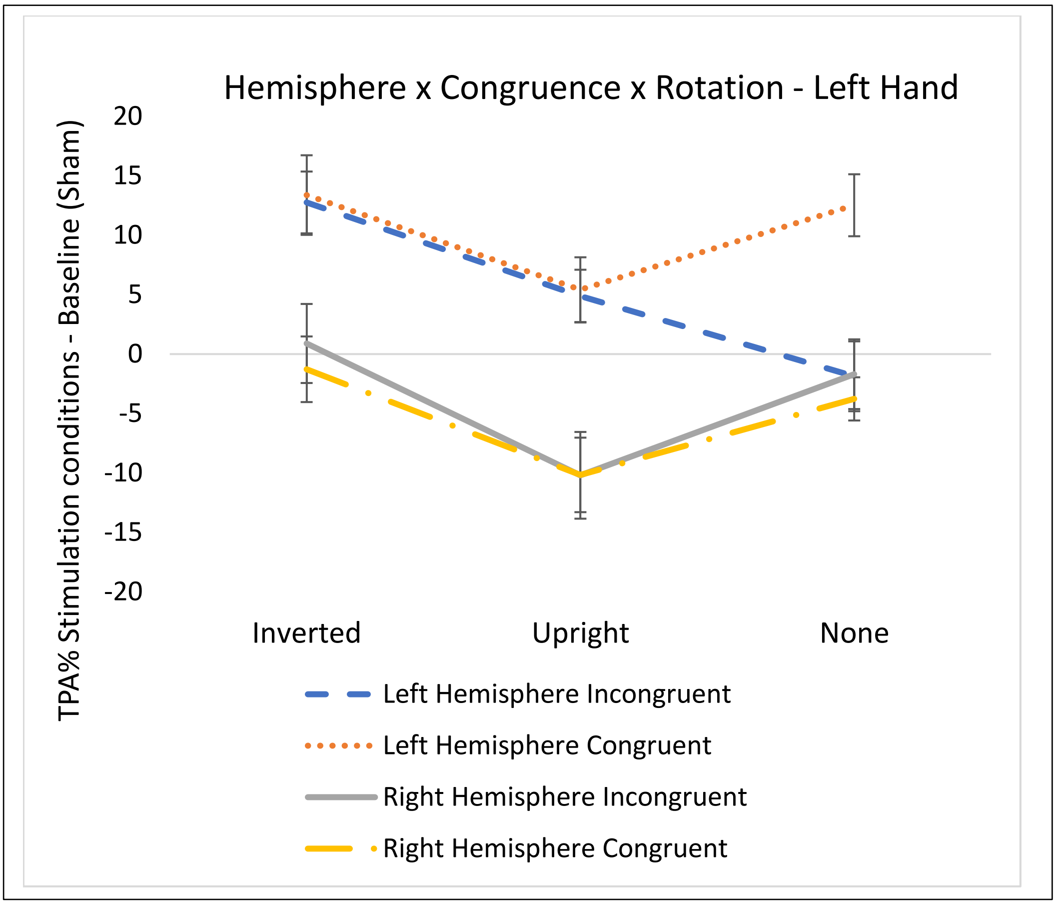

Figure 26. Interaction observed between Hemisphere, Congruence and Rotation conditions for left hand reaching. Error bars indicate ±1 SE of the mean TPA% (Stimulation condition – Baseline). This interaction was present for left hand reaching *($F_{(2, 20)}$ = 7.07, p=.005) but not for right hand ($F_{(2, 20)}$ = 0.78, p=.47). Positive values indicate delayed TPA% compared to baseline, negative values indicate earlier TPA% compared to Baseline.*

TPA% *(Inverted: M±SD = 13.38±11.10 TPA%, Non-rotation: M±SD = 12.52±8.64 TPA%, Upright: M±SD = 5.42±9.03 TPA%)*. For incongruent trials, delays were observable for inverted trials *(M±SD = 12.76±8.62 TPA%)*, with earlier TPA% for upright trials *(M±SD = 4.88±7.35 TPA%)* and limited delays for non-rotation *(M±SD = -1.87±9.74 TPA%)*. This interaction was not present for right hand reaching *($F_{(2, 20)}$ = 0.78, p=.47)*, (see Figure 26).

This follows a similar pattern to those observed in the previous interaction. This only occurred for left hand reaching with stimulation to the SMG/left hemisphere. This is consistent with the expected outcomes to an extent, with left lateralisation of mediating functional tool grasp and disruption of this process during action execution from left TMS. However, this only occurred for left hand reaching but was not apparent for the dominant right hand, inconsistent with predicted outcomes. Furthermore, delays were not present for incongruent non-rotation conditions.

An interaction between Hemisphere, Stimulation site and Congruence *($F_{(1, 10)} = 9.95$, $p=.01$)* was observed. For incongruent trials, this showed delayed TPA% for left hemisphere SMG *(M±SD = 2.64±3.11 TPA%)* and Control site stimulation *(M±SD = 1.85±4.42 TPA%)* Delays increased for both Stimulation sites for congruent conditions *(SMG: M±SD = 5.25±4.86 TPA%, Control Site: M±SD = 6.03±5.88 TPA%).* Delays were not observable for right SMG stimulation for congruent *(M±SD = -0.11±5.31 TPA%)* or incongruent trials *(M±SD = -0.27±1.52 TPA%)*. For right control site stimulation, TPA% was earlier for incongruent *(M±SD = -3.15±5.67 TPA%)* and congruent trials *(M±SD = -5.78±5.38 TPA%).*

An interaction between Hand, Hemisphere and Stimulation site *($F_{(1, 10)} = 6.00$, $p=.03$)* was also observed. TPA% was consistently delayed across Stimulation site for left hemisphere stimulation while reaching with the left hand *(SMG; M±SD = 7.81±7.13 TPA%, Control Site; M±SD = 7.88±8.74 TPA%)*. Delays were not prominent for right SMG stimulation when reaching with the left hand *(M±SD = 0.36±7.47 TPA%)* and TPA% occurred earlier for right control stimulation *(M±SD = -9.10±9.08 TPA%).* Right hand reaching was consistent across Stimulation site and hemisphere of stimulation showing small deviation from baseline *(Left SMG; M±SD = 0.06±3.41 TPA%, Right SMG; M±SD = -0.75±3.78 TPA%, Left Control; M±SD = 0.004±3.29 TPA%, Right Control; M±SD = 0.16±2.86 TPA%).*

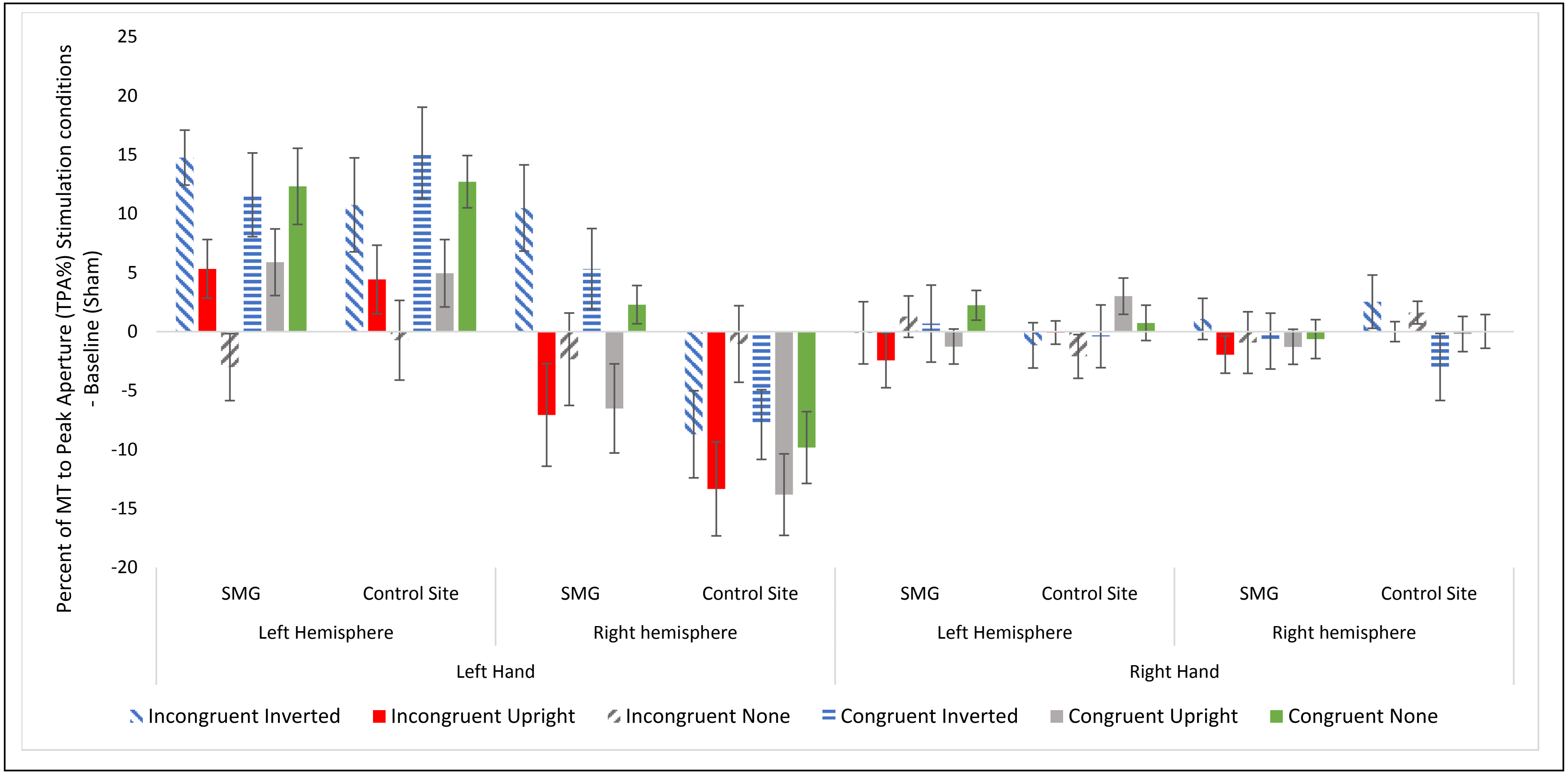

Figure 27. Bar chart summarising percent of MT to peak aperture (TPA% stimulation conditions – baseline sham TMS) across Hand, Hemisphere, Stimulation Site, Congruence and Rotation conditions. Significant main effects observed for Hemisphere (p = .01), Stimulation Site (p = .02) and Rotation (p = .04). Significant interactions observed between Hand x Hemisphere (p = .01), Hand x Stimulation Site (p = .02), Hand x Hemisphere x Stimulation Site (p = .03), Hand x Stimulation Site x Congruence (p = .03), Hemisphere x Stimulation Site x Congruence (p = .01), Hand x Hemisphere x Stimulation Site x Congruence (p = .05), Hand x Hemisphere x Rotation (p < .01), Stimulation Site x Rotation (p = .02), Hemisphere x Stimulation Site x Rotation (p = .02), Hand x Hemisphere x Stimulation Site x Rotation (p = .03), Congruence x Rotation (p = .01), Hemisphere x Congruence x Rotation (p = .05), Hand x Hemisphere x Congruence x Rotation (p = .02), Stimulation Site x Congruence x Rotation (p = .01), Hand x Stimulation Site x Congruence x Rotation (p = .01), Hemisphere x Stimulation Site x Congruence (p = .02).

Table 5. Summary of mean data across Hand, Hemisphere, Stimulation Site and Congruence and tool rotation conditions (Stimulation conditions – Baseline, Sham). M (±SD).

Hand	Hemisphere of Stimulation	Stimulation Site	Congruence	Rotation	Miscorrection Scores		MT		TPV%		TPA%	
Left Hand	**Left Hemisphere**	**SMG**	**Incongruent**	**I**	0.32	(0.25)	-29.95	(115)	2.75	(6.16)	14.76	(7.73)
				U	0.37	(0.58)	1.18	(51)	5.16	(5.83)	11.61	(11.78)
				N	0.02	(0.25)	-36.18	(97)	2.83	(4.48)	5.33	(8.23)
			Congruent	**I**	0.11	(0.33)	-73.43	(74)	3.29	(6.26)	5.89	(9.37)
				U	0.09	(0.20)	-28.67	(102)	3.89	(4.88)	12.32	(10.72)
				N	0.22	(0.49)	-10.81	(65)	3.12	(4.99)	-3.01	(9.42)
		Control Site	**Incongruent**	**I**	-0.05	(0.15)	-53.94	(113)	0.60	(5.91)	10.75	(13.22)
				U	0.25	(0.79)	-34.78	(44)	2.94	(3.76)	15.15	(12.89)
				N	0.05	(0.23)	-55.80	(85)	1.15	(3.21)	4.43	(9.64)
			Congruent	**I**	0.13	(0.43)	-58.97	(70)	3.30	(4.58)	4.95	(9.48)
				U	0.03	(0.32)	-103.88	(67)	2.92	(4.67)	12.72	(7.35)
				N	0.31	(0.97)	-50.94	(47)	0.57	(3.67)	-0.73	(11.21)
	Right Hemisphere	**SMG**	**Incongruent**	**I**	0.05	(0.26)	-12.59	(122)	-2.30	(5.19)	10.49	(12.13)
				U	0.29	(0.40)	-1.94	(152)	-5.11	(7.85)	5.33	(11.34)
				N	0.07	(0.23)	73.94	(206)	-1.12	(6.49)	-7.06	(14.43)
			Congruent	**I**	0.07	(0.30)	43.59	(151)	-1.15	(4.31)	-6.51	(12.53)
				U	0.06	(0.22)	-17.00	(73)	-7.47	(6.93)	2.29	(5.38)
				N	0.36	(0.61)	61.93	(143)	-7.54	(12.25)	-2.34	(13.00)
		Control Site	**Incongruent**	**I**	0.06	(0.24)	-20.79	(156)	-3.27	(8.03)	-8.70	(12.25)
				U	0.35	(0.51)	-56.18	(118)	-4.01	(7.40)	-7.88	(9.80)
				N	0.03	(0.22)	-19.19	(105)	-1.00	(7.37)	-13.34	(13.22)
			Congruent	**I**	0.12	(0.45)	-17.84	(138)	-2.60	(5.85)	-13.82	(11.46)
				U	0.15	(0.29)	-47.75	(69)	-5.39	(7.63)	-9.83	(10.10)
				N	0.12	(0.52)	-25.19	(108)	-4.46	(8.28)	-1.05	(10.77)
Right Hand	**Left Hemisphere**	**SMG**	**Incongruent**	**I**	0.11	(0.23)	35.30	(110)	-1.85	(3.16)	-0.10	(8.75)
				U	0.11	(0.34)	-23.49	(84)	-0.86	(8.25)	0.68	(10.83)
				N	0.06	(0.17)	-29.19	(42)	2.22	(5.69)	-2.44	(7.67)
			Congruent	**I**	0.14	(0.38)	-20.84	(163)	-0.35	(3.55)	-1.26	(4.93)
				U	0.23	(0.37)	-0.18	(106)	-0.37	(5.18)	2.24	(4.18)
				N	0.01	(0.22)	-35.48	(91)	0.34	(3.71)	1.28	(5.82)
		Control Site	**Incongruent**	**I**	0.15	(0.40)	-20.69	(104)	-0.06	(5.09)	-1.16	(6.37)
				U	0.18	(0.50)	-26.68	(64)	-0.56	(4.03)	-0.39	(8.83)
				N	0.03	(0.15)	-25.99	(44)	-0.01	(2.75)	-0.07	(3.28)
			Congruent	**I**	0.15	(0.40)	-43.33	(89)	-0.91	(2.46)	3.01	(5.10)
				U	0.05	(0.43)	-8.94	(77)	-1.29	(3.57)	0.75	(4.97)
				N	0.08	(0.31)	-17.07	(79)	-1.42	(3.71)	-2.10	(6.15)
	Right Hemisphere	**SMG**	**Incongruent**	**I**	0.00	(0.24)	-30.92	(105)	0.95	(4.81)	1.08	(5.79)
				U	0.12	(0.44)	-72.99	(82)	2.00	(4.50)	-0.80	(7.86)
				N	0.06	(0.25)	-44.68	(42)	2.26	(2.92)	-1.95	(5.24)
			Congruent	**I**	0.09	(0.28)	-65.65	(110)	1.56	(3.41)	-1.28	(4.94)
				U	0.06	(0.19)	-26.92	(51)	-0.31	(6.90)	-0.63	(5.47)
				N	0.10	(0.17)	-28.36	(65)	1.83	(4.76)	-0.92	(8.66)
		Control Site	**Incongruent**	**I**	-0.01	(0.20)	-10.25	(101)	0.78	(4.77)	2.55	(7.49)
				U	0.06	(0.27)	-30.93	(65)	-0.87	(4.34)	-2.99	(9.43)
				N	0.07	(0.25)	-3.08	(70)	1.07	(3.40)	0.00	(2.81)
			Congruent	**I**	0.13	(0.32)	-20.10	(120)	1.18	(4.44)	-0.20	(4.95)
				U	0.20	(0.35)	-22.83	(70)	0.10	(3.88)	0.02	(4.75)
				N	0.01	(0.18)	-7.64	(71)	-0.65	(5.35)	1.62	(3.18)

Mean miscorrection scores (SD), movement time (MT), percent of MT to peak velocity (TPV%), percent of MT to peak aperture of movement across Hemisphere, Stimulation Site, Congruence and Rotation (**I**) Inverted, (**U**) Upright, (**N**) No-rotation.

Table 6. Summary of Hand x Hemisphere x Stimulation Site x Congruence x Rotation (2 x 2 x 2 x 2 x 3) repeated measures ANOVA across the dependent measures (Miscorrection scores (SD), Movement Time (ms), percent of MT to peak velocity (TPV%) and peak aperture (TPA%). Conducted for Stimulation conditions – Baseline. Analysis inclusive of Rotation results are reported as Greenhouse-Geisser corrected F and p values. **Bold** values indicate significance at p< .05 level.*

	Miscorrection Score		MT		TPV%		TPA%	
	F	p	F	p	F	p	F	p
Hand	2.38	0.15	0.00	0.99	1.18	0.30	2.14	0.17
Hemisphere	0.50	0.50	0.91	0.36	**6.48**	**0.03**	**11.94**	**0.01**
Stimulation Site	0.74	0.41	1.79	0.21	0.80	0.39	**8.42**	**0.02**
Congruence	0.02	0.88	0.08	0.78	1.32	0.28	1.73	0.22
Rotation	0.87	0.43	1.18	0.33	0.32	0.73	**3.66**	**0.04**
Hand x Hemisphere	0.28	0.61	2.46	0.15	**21.08**	**0.00**	**11.48**	**0.01**
Hand x Stimulation	0.47	0.51	**10.92**	**0.01**	0.07	0.80	**7.45**	**0.02**
Hand x Hemisphere x Stimulation	0.46	0.51	0.06	0.81	0.57	0.47	**6.12**	**0.03**
Hand x Congruence	0.14	0.71	**7.94**	**0.02**	1.52	0.25	6.00	0.03
Hemisphere x Congruence	0.08	0.79	0.28	0.61	0.20	0.67	13.76	0.00
Hand x Hemisphere x Congruence	0.32	0.58	1.53	0.25	1.28	0.28	1.34	0.27
Stimulation Site x Congruence	0.08	0.78	0.57	0.47	0.94	0.35	4.64	0.06
Hand x Stimulation Site x Congruence	0.24	0.64	0.15	0.70	0.43	0.52	**5.96**	**0.03**
Hemisphere x Stimulation Site x Congruence	0.41	0.54	0.22	0.65	1.48	0.25	**11.33**	**0.01**
Hand x Hemisphere x Stimulation Site x Congruence	0.15	0.70	0.78	0.40	1.16	0.31	**4.94**	**0.05**
Hand x Rotation*	1.96	0.19	1.08	0.32	0.16	0.70	1.29	0.28
Hand x Hemisphere x Rotation*	0.23	0.75	0.80	0.44	0.81	0.44	**19.83**	**0.00**
Stimulation Site x Rotation*	1.16	0.33	1.34	0.28	**3.21**	**0.06**	**5.75**	**0.02**
Hand x Stimulation Site x Rotation*	0.16	0.72	0.31	0.64	**3.34**	**0.06**	2.08	0.16
Hemisphere x Stimulation Site x Rotation*	0.05	0.89	0.12	0.75	0.65	0.51	**4.79**	**0.02**
Hand x Hemisphere x Stimulation Site x Rotation*	0.54	0.59	2.54	0.13	2.22	0.14	**4.25**	**0.03**
Congruence x Rotation*	**4.75**	**0.03**	**2.74**	**0.09**	1.82	0.19	**5.65**	**0.01**
Hand x Congruence x Rotation*	0.85	0.41	0.57	0.49	0.43	0.61	0.95	0.40
Hemisphere x Congruence x Rotation*	1.59	0.23	0.18	0.81	**3.36**	**0.06**	**3.68**	**0.05**
Hand x Hemisphere x Congruence x Rotation*	2.61	0.12	**4.58**	**0.03**	0.64	0.51	**5.15**	**0.02**
Stimulation Site x Congruence x Rotation*	0.39	0.60	1.69	0.21	0.40	0.65	**7.54**	**0.01**
Hand x Stimulation Site x Congruence x Rotation*	0.03	0.97	1.23	0.31	1.29	0.30	**7.86**	**0.01**
Hemisphere x Stimulation Site x Congruence	0.84	0.44	0.86	0.42	0.47	0.59	**5.03**	**0.02**
Hand x Hemisphere x Stimulation Site x Congruence	0.76	0.46	0.87	0.41	0.67	0.49	1.77	0.20
Hemisphere x Stimulation Site x Congruence X Rotation	2.41	0.12	0.63	0.52	0.24	0.77	0.28	0.71
Hand x Hemisphere x Stimulation Site x Congruence x Rotation*	0.43	0.63	1.43	0.26	2.59	0.10	2.33	0.14

4.4. Discussion

In this experiment increased miscorrection was observed for left SMG stimulation under certain rotation conditions (see Figure 19 and Figure 18, pg. 83). MT appeared mainly affected by contralateral parietal stimulation (see Figure 20 and Figure 21, pg. 85), while TPV% and TPA% exhibited effects of ipsilateral stimulation (see Figure 23, pg. 89 and Figure 27, pg. 95).

This experiment demonstrated that stimulation of the left SMG delayed correction of appropriate grasp of tools for use for inverted conditions. This was observed for reaching with both the dominant and non-dominant hand. This is consistent with the hypothesis, that the left SMG serves as a point of integration between tool knowledge; relating to understanding functional use of the tool in relation to the hand and body position, and the visuomotor control necessary to facilitate correction of grasp during action execution. While control site stimulation did disrupt correction also, the most prominent delays to correction were observed for left SMG stimulation for inverted grasping. This is consistent with findings in the previous chapter, as the largest miscorrections were observed for inverted conditions. However, given the proposed role of the SMG, this should occur for upright rotation also. This may not be observable here due to an easier correction for upright rotation (as observed in Chapter 3; (McDowell et al., 2018)) and a predisposition to an upright grasp for participants in reaching for tools (Creem & Proffitt, 2001). The upright rotation in this task may not be sensitive to disruption via TMS in this context.

Left SMG stimulation did not observably disrupt correction of grasp for non-rotation trials. This finding is consistent with the hypothesis. It is posited here that prior to action onset, the SMG acts as a point of integration for conceptual tool knowledge and visuomotor affordance perception of the effector and target for grasp. Following the ideomotor principle (Greenwald, 1970; Hommel et al., 2001; Massen & Prinz, 2007), the SMG role is to integrate conceptual information pertaining to functional use, into an action plan for a functional grasp. Grasp execution is then mediated by dorso-dorsal structures to execute the grasp plan (Brandi et al., 2014; Buxbaum, 2017; Orban & Caruana, 2014; Peeters et al., 2013). However, as in this experiment, when a perturbation in tool orientation occurs the SMG must reintegrate salient information pertaining to the functional use of the tool. This online integration of tool knowledge enables a correction of grasp orientation to compensate for the change in tool orientation. Thus, allowing a grasp position that affords functional use. These findings suggest that triple-pulse TMS over the left SMG at the onset of tool rotation disrupts this integration, consistent with current models of the left SMG within the tool use network (Borghi, di Ferdinando, & Parisi, 2011; Buxbaum, 2017; Lesourd et al., 2017; Osiurak & Badets, 2016, 2017; Reynaud et al., 2016).

Alternatively, deficits in selection of grasp orientation from left SMG stimulation may be due to disruption of consistent cross talk between visuomotor production systems (dorso-dorsal structures) and the established grasp plan (defined prior to action onset with input from the SMG). In this interpretation, a suitable grasp plan is generated based on understanding of functionality within the context of the task goal and affordance perception (Buxbaum, 2017; Orban & Caruana, 2014; Osiurak & Badets, 2017). This grasp plan is consistently monitored during action execution as a ‘goal state’ for how the action should look and feel (Binkofski & Buxbaum, 2013a; Buxbaum, 2017). When the tool orientation is perturbed, cross referencing (as opposed to re-integration of tool knowledge) allows online correction of grasp orientation to maintain the established plan. Deficits in correction would therefore reflect disruption of this referencing between action production systems and a constantly monitored goal state. Considerable crosstalk during action execution has been posited by tool use models (Orban & Caruana, 2014). However, one caveat of this interpretation is that delays to grasp selection should also potentially occur when the tool remains stationary, as the plan should be consistently monitored during reach and TMS should result in delayed selection of grasp compared to baseline. This was not observable for the non-rotation conditions present here. Therefore, the initial dynamic ‘reintegration’ interpretation seems to be the most suitable account of the present findings.

In terms of lateralisation, the findings support a left hemisphere preference for tool related function consistent with current models of the tool use network (Johnson-Frey et al., 2005; Lesourd et al., 2017; Marchetti & Della Sala, 1997; Orban & Caruana, 2014; Przybylski & Kroliczak, 2017; Ramayya et al., 2010; Sunderland et al., 2013). This conflicts with the present hypothesis and observations from Chapter 3, in which both left and right SMG stimulation resulted in increased miscorrection. In Chapter 3, it was previously suggested that the right SMG may have a specialised role for identifying and controlling for spatial perturbations during visuomotor control (Clark et al., 2000; Gur et al., 2007; Hartmann et al., 2005; Kiehl et al., 2001; Singh-Curry & Husain, 2009). This function that would support functional grasp of tools (within the context of the previous experiment) but would not rely upon processing of tool use cognition. Indeed, bilateral SMG activation is observed during tool grasp and action execution (Brandi et al., 2014; Rallis et al., 2018b), while left SMG activation shows preference for both planning and execution (Brandi et al., 2014). It was hypothesised here that if TMS over the right SMG disrupted correction, it would be observable for only the most spatially demanding rotations. However, this was not the case for inverted or incongruent rotations, conflicting with the proposed role of the right SMG. This may have occurred due to methodological changes between the experimental controls in the present chapter and previous experiment. For both experiments in Chapter 3 the target tool rotated for every trial requiring an online correction. This may have resulted in the task in anticipation of a change of tool orientation and heightened spatial processing (Clark et al., 2000; Gur et al., 2007; Hartmann et al., 2005), resulting in recruitment of the right SMG and disruption of function due to TMS. As the target tool and associated demonstration of action changed for each trial also, stimulation of the left SMG elicited similar disruption to online correction, based on processing changes to functional elements of the tool. However, for the present experiment on one third of all trials the tool did not rotate, interspersed with those that did. It is posited that this control for rotation on each trial removed the anticipation of tool rotation. Thus, limiting the recruitment of right hemisphere SMG. Furthermore, this would shift the focus of the task to controlling for spatial perturbation within the context of functional aspects of the tool in relation to the effector hand. Therefore, disruption of grasp correction is predominantly observed for left SMG stimulation.

In examination of the other kinematic measures (MT, TPV% and TPA%), contralateral SMG stimulation resulted in longer movement time for right hand reaching compared to baseline. This finding is somewhat consistent with the previous observations in Chapter 3, experiments 1 and 2. For experiment 1, longer reaching times were observed for right SMG stimulation while reaching with the left hand. But for stimulation of the ipsilateral SMG for both left and right hand reaching in experiment 2, this effect was not observable. This suggests that visuomotor control of transporting the effector hand towards the target is only mediated by the contralateral hemisphere, and most observable for SMG stimulation. Research suggests that this is monitored by dorso-dorsal structures in of the contralateral hemisphere (Rice et al., 2007; Tunik et al., 2005) which may account for the observed increase in MT for right SMG stimulation. The observed ipsilateral effect of hemisphere of stimulation for peak velocity of movement is not easily attributable to cortical disruption of function. Stimulation site did not vary the impact of TMS on peak velocity suggesting this may be due to a general effect of movement disruption through twitching (Meteyard & Holmes, 2018) or noise, despite controlling for sound differences between rotation and non-rotation trials (e.g. white noise mask combined with sound recording of motor rotation). That this effect occurs for stimulation to the ipsilateral hemisphere to the effector hand suggests that TMS explanation may account for this disruption. A similar pattern is observable for peak aperture. TMS to the left hemisphere resulted in delayed TPA%, however the lack of interaction with site of stimulation indicates a general effect of TMS as mentioned above (Meteyard & Holmes, 2018).

That these kinematic measures are not observably affected in the same manner as correction of grasp orientation, suggests that they are facilitated by other cortical regions and processes than the tool related integration of the left SMG. Movement towards the target, as well as grasp aperture are likely facilitated by dorso-dorsal structures such as the aIPS and the SPL, as observed in previous similar TMS paradigms (Cohen et al., 2009b; Rice et al., 2007; Tunik et al., 2005). This further indicates that processing the conceptual aspects of tools that facilitate functional grasp are separate from processing the affordances of object size for grasping or enabling movement toward the tool for use in 3D space (Borghi, 2014; Buxbaum, 2017; Peeters et al., 2013; Rizzolatti & Matelli, 2003). This dichotomy in function is consistent with neuropsychological models of the left parietal region (Goldenberg, 2013; Goldenberg & Spatt, 2009; Hermsdörfer

& Goldenberg, 2002; Sunderland et al., 2013) and consistent with findings for grasping tools in apraxic patients (Sunderland et al., 2013). Further exploration of these movement kinematics in relation to affordance processing neural structures is necessary to fully understand this dichotomy and its impact on tool related action.

In conclusion, this experiment demonstrated a left SMG bias in selection of functional tool grasp for use. This effect was independent of the hand used and demonstrated spatial specificity for the left SMG. The left SMG likely serves as a point of integration for tool related input and visuomotor action production systems. This process is dynamic and sensitive to perturbations in tool position that might impact on goal related action plans. These effects did not extend to effector transport or grip size, suggesting task specific processing of the tool-effector posture for functional use.

5. Movement Kinematics for Acting 'With' and 'On' Familiar and Novel Tools – Exploring the Influence of Intent, Familiarity, and Orientation – Experiment 4

Foreword

This chapter aims to address the third research question, examining the nature of conceptual input required in cognition for interacting with tools for use. This experimental chapter did not employ TMS, but aimed to explore whether movement kinematics were influenced by the intention of use and familiarity as observed in other behavioural tasks in the field (Osiurak, Roche, et al., 2013; Rosenbaum et al., 1992; Tucker & Ellis, 2001). This experiment also acted as a non-TMS pilot for Chapter 6 and allowed the development of further novel tools and tasks corresponding to familiar tools. Online correction was not used in this experiment due to focussing on the factors of familiarity and intention as well as consistent orientation of affordances for action.

Abstract

In everyday life, objects can be grasped-to-use or grasped-to-transport. Comparison between these two fundamentally different modes of interaction can provide insight into the cognitive and visuomotor processes that mediate human object manipulation. However, there is currently disagreement in the research literature as to how these processes are facilitated. Arguably, grasp-to-use actions are supported by semantic representations of associated use, and transport actions with affordance perception (2AS+ model). Conversely, technical reasoning and mechanical knowledge support both grasp-to-use and grasp-to-transport actions constrained by affordances in the environment (technical reasoning model). In both models, initiation of object manipulation action is influenced by two factors, intention of action (transport versus use) and affordances of the object and environment. As a third factor, the 2AS+ model would posit familiarity with the object is important, because stored semantic representations of the object would be readily accessible. However, for the technical reasoning model, familiarity with the object would be unnecessary as technical reasoning allows mental simulation and selection of actions 'de novo' for each encounter. To assess the

impact of intent and affordance, and familiarity on movement kinematics, a task was conducted in which participants (n=12) reached for two objects; a hammer (familiar) and a cone of similar dimensions (novel). Participants completed three tasks across three separate blocks; Grasp-to-transport (Transport), grasp-for-conventional-use (CU) and grasp-for-non-conventional-use (NU). Conventional use referred to the potential action used to complete the task corresponding to the familiar object (the novel object could be used in the same way). Objects were presented in a cradle in 8 different orientations (*North, North-East, East, South-East, South, South-West, West, and North-West*) to vary the affordance of available grasp. It was hypothesised that movement onset (MO) would be faster for familiar objects in the CU condition but not in the Transport or NU, but this would be subject to the orientation of the object. A significant interaction between Intent and Familiarity was observed for MO. MO was relatively consistent across the three tasks for Novel objects. MO was faster for Familiar objects in the Transport task, comparable to Novel in the CU and slower in the NU. These findings indicate that as a function of intention of action, familiarity of tools may lead to faster processing and selection of actions. However, as this is not the case for conventional use these findings are inconsistent with the 2AS+ account, lending support to the technical reasoning approach.

5.1. Introduction and Research Aims

In the previous experimental chapters (Chapters 3 and 4), an association was established between left SMG and processing tool related stimuli while reaching for tools and grasping them for use, consistent with current models. While this supports a dynamic role of the left SMG during action execution (rather than only during planning as previous work suggests (Tunik et al., 2008)), what is actually being provided by the left SMG is not fully understood. It is likely that the SMG provides some conceptual input pertaining to the functional use of tools but as discussed in Chapter 1, the nature of this conceptual input is heavily debated within the research literature. Two leading approaches posit that conceptual tool related input is reliant upon stored representations based on previous experience (2AS+/manipulation-based approach (Buxbaum, 2017)) or reliant on reasoning the appropriate use of objects based on object and body properties in relation to the desired goal of action (Osiurak & Badets, 2017). In this experimental chapter, the nature of this conceptual input and cognition is investigated by examining the impact of action intention, object familiarity and object orientation on early movement kinematics.

When initiating movement towards a tool, action intention has been shown to vary the time to onset of movement (Jax & Buxbaum, 2013; Osiurak, Roche, et al., 2013; Valyear et al., 2011). Grasp-to-transport actions have previously been shown to be initiated quicker than grasping to use the object in a functional manner (Jax & Buxbaum, 2010). Although both tasks require object manipulation, and differ little in terms of the physical requirements of action (Osiurak, 2013), neuroimaging and lesion based studies suggest that distinct cognitive mechanisms and cortical pathways separately mediate these functions (Buxbaum et al., 2006; Osiurak, Aubin, Allain, Jarry, Etcharry-Bouyx, et al., 2008; Randerath et al., 2010). The 2AS+ model (Buxbaum, 2017) argues that this reflects the use of the dorso-dorsal pathway when carrying out transport actions, based on affordances and structural properties of objects in relation to the sensorimotor capabilities of the user. These actions do not require access to stored representations of uses of the objects (Bi et al., 2015; Binkofski & Buxbaum, 2013a; Gallivan et al., 2013), which would be provided by the slower acting ventro-dorsal stream. Thus, slower initiation of *use* actions (i.e. ventro-dorsal) reflects access of stored representations that are unnecessary for *transport* actions (i.e. dorso-dorsal) (Jax & Buxbaum, 2010). This model is arguably too simplistic (Osiurak & Badets, 2017). While it considers the egocentric relationship between actor and object (i.e. between grasping hand and object), it fails to account for the allocentric relationships between the grasped object and other objects in the environment (Osiurak et al., 2010, 2011). For example, when moving a fork from a draw to a table, the actor must identify the handle as a comfortable grasping point, which would allow transportation (i.e. egocentric relationship). However, the actor must also consider the relationship between the fork and the surface on which it is to be placed; for example, is it flat to ensure the fork won’t slide to the ground? Is it stable enough to support the weight of the fork?

The technical reasoning model accounts for this discrepancy by arguing that object manipulation (*transport* or *use*) relies upon understanding the laws of the physical world (Osiurak & Badets, 2017) based on mechanical knowledge (Osiurak, 2014b; Osiurak & Badets, 2016; Osiurak et al., 2010). Regardless of previous experience, mechanical knowledge stores abstract information about object properties that make them suitable for certain tasks (Osiurak & Badets, 2017) and allows comparative interpretation of object properties relative to one another. In the case of transport, the fork would be identified as lighter than the table, with flat aspects to its shape which would allow it to be supported by the surface and stability of the table. In the case of use, the fork has the properties of being harder and sharper than the food it is used to pierce. Understanding the comparative properties of objects is supported by mechanical knowledge which is used to facilitate a mental simulation of the action (Osiurak & Badets, 2017). The mental simulation is the outcome of reasoning and, in line with the ideomotor framework (Hommel et al., 2001) action is selected as a result of the simulation of expected perceptual effects on the physical world (Osiurak & Badets, 2017). During the execution process, the expected effects are compared to the actual effects and may be adjusted online. This approach, therefore, posits that manipulation actions are reconstructed 'de novo' on the basis of the mental simulation and online information (e.g. the physical environment and position of the body in space)(Osiurak & Badets, 2016). This accounts for why under certain circumstances, grasp-to-transport actions could take longer to initiate than grasp-to-use tasks. Furthermore, this account is arguably more suitable in explaining why humans can manipulate both familiar and novel objects for a desired purpose (Osiurak & Badets, 2017; Reynaud et al., 2016), a factor that is problematic for the 2AS+ model.

The 2AS+ model argues that stored representations of use based on previous experience enable effective use of tools (Buxbaum, 2017). In the case of unfamiliar tools or unfamiliar use of familiar objects (e.g. using the heel of a shoe to drive a nail into a surface in the absence of a hammer) the reasoning based model provides a more comprehensive account due to a basis of understanding in mechanical knowledge (Osiurak & Badets, 2016, 2017). However, Buxbaum (2017) argued that generating a mental simulation 'de novo' (based on the physical and relative properties of objects) would be more demanding than reactivation of a stored representation. Furthermore, 2AS+ posits that stored representations are multimodal and abstracted across numerous temporal instances of use (Buxbaum, 2017). Abstraction limits the computational demands of storage and retrieval and allows generalisation of action representations to similar situations (Buxbaum, 2017; Rijntjes, Weiller, Bormann, & Musso, 2012; van Elk, 2014). This provides an account for novel use of familiar tools and could potentially explain how humans can make use of unfamiliar tools to achieve a desired goal.

Although both models offer insights on the importance of familiarity of objects for action, the 2AS+ model should posit that representations for familiar tools are accessed faster than in instances of novel object use due to a lack of necessity for abstraction of a known tool use to another. For the reasoning based model, familiarity of objects for use should not impact on the ability to use or interact with them, as goal dependent mental simulations are generated 'de novo' regardless of object familiarity. Imaging studies have previously highlighted that the tool associated regions in the brain show preferential activation to tools compared with other stimuli (Bi et al., 2015; Brandi et al., 2014; Chao & Martin, 2000; Fang & He, 2005; Kroliczak & Frey, 2009; Lewis, 2006; Mahon et al., 2007; A. Martin et al., 1996) consistent with the 2AS+ model. However, further evidence suggests that this response applies to any graspable object with the potential for manual action rather than specifically for familiar tools (Vingerhoets, Vandamme, et al., 2009), consistent with the reasoning based approach. Lesion based research is no less controversial; patients with damage to the left fronto-parietal network exhibit deficits in grasping familiar tools but not novel objects (Sunderland et al., 2013). Whereas studies have shown that patients with similar injuries display intact manipulation ability for novel and familiar tools (Hodges, Bozeat, Ralph, Patterson, & Spatt, 2000; Silveri & Ciccarelli, 2009; Sirigu et al., 1991). Clearly, understanding the importance of familiarity in facilitating tool use action is integral to understanding the underlying cognitive processes.

Regardless of familiarity, both the reasoning and 2AS+ models acknowledge that environmental constraints and affordances are key in manipulation control (Buxbaum, 2017; Osiurak & Badets, 2017). The end state comfort effect (ESC) shows that people adopt an uncomfortable initial grasp (in terms of pronation or supination of the hand) that allows a comfortable end state when using the object (Rosenbaum et al., 1990). This highlights that when planning action, processing the functional (allocentric relationships) and graspable aspects (egocentric relationship) of the object are processed, and intention to achieve a comfortable functional grasp is factored into the planning of action (Randerath et al., 2009; Short & Cauraugh, 1997; W. Zhang & Rosenbaum, 2008). However, in the case of grasp-to-transport actions, Creem and Proffitt (2001) demonstrated that individuals grasp familiar tools in a manner suitable for use, even if the tool handle was oriented away from them (Creem & Proffitt, 2001). For the reasoning based approach, this is problematic, in that grasp-to-transport actions do not require a 'meaningful' grasp. Based on the physical properties of the object and destination, grasping by the handle with the head in any orientation should afford a comfortable end state for simple transport actions. Furthermore, this effect dissapeared when participants engaged in a concurrent cognitive task. This has been interpreted as disrupting access to stored representations of use, resulting in grasping objects in a non-functional grasp (Creem & Proffitt, 2001). This explanation is in keeping with the 2AS+ model, in that the influence of stored representations primes grasp of familiar objects in the most suitable manner for use, regardless of action intention. However, research by Lindemann et al. (2006) suggests that semantic representations are not automatically activated on visual perception of the associated tool, but specifically dependent on intention to act, which should not influence grasp-to-transport actions (Lindemann et al., 2006; Randerath et al., 2009).

The orientation effect (Tucker & Ellis, 1998) provides some insight into this issue. Tucker and Ellis (1998) previously highlighted that motor responses primed by familiar objects are faster when the handle of the object is oriented in the same direction as the effector hand. This has previously been interpreted as reflecting automatic activation of effector-specific motor representations associated with the tool, supporting the manipulation-based and 2AS+ approaches (Borghi & Riggio, 2009; Caligiore et al., 2010; Mizelle & Wheaton, 2010; Pellicano et al., 2010a; Thill et al., 2013). However, this has since been reinterpreted by the original authors (Symes et al., 2005, 2007), suggesting that the effect does not demonstrate activation of semantic knowledge pertaining to skillful use of tools (Osiurak & Badets, 2016). This is supported by experiments showing that the orientation effect also occurs when participants respond with feet as opposed to hands (Phillips & Ward, 2002; Symes et al., 2005). Furthermore, when presented with a teapot, the orientation effect occurs for the orientation of the spout, not the handle, indicating the spout as the most salient aspect of the object, and does not pertain to appropriate grasping for skilled use (Cho & Proctor, 2011). This suggests that the orientation effect is due to spatial-coding of stimulus response compatbility rather than sematic representations of skilled use (Osiurak & Badets, 2016).

To investigate both neurocognitive models of tool manipulation (reasoning model and AS2+ model), an experiment exploring the influence of action intention, object familiarity, and orientation on grasp planning and execution was conducted. Subjects were asked to carry out a grasp-to-transport task, and two grasp-to-use tasks (one for conventional (**CU**) and one for non-conventional use (**NU**)) to explore the effects of intention of action. The conventional and non-conventional nature of the tasks were determined in relation to the familiar tool (as there should be no intial known conventional use of the novel object). To explore familiarity, a tool that was likely to be familiar to participants, and a novel object that could be used to carry out the same tasks and was approximately the same size were presented. For orientation, the presentation of the familiar and novel object in orientation was varied in the coronal plane. For the familiar object, this should require pronation or supination of the hand during reaching to achieve a 'meaningful' grasp. The novel object was also designed to have both 'functional' and graspable aspects in shape, but would not require a pre-defined functional grasp.

In initiation of movement (movement onset – MO) it is hypothesised that grasp-to-transport actions would be initiated quicker than both grasp-to-use tasks, however, this would be subject to affordance of the object orientation (Osiurak, Roche, et al., 2013). In line with the 2AS+ model (Buxbaum, 2017), it is hypothesised that conventional use (CU) actions will be initiated quicker for familiar tools than novel tools, due to the influence of stored semantic representations pertaining to familiar use. However, this effect should not be present when matched with novel tools in the non-conventional use (NU) task or the transport task as there should be limited reliance on stored representations. Technical reasoning should play a key role in the NU task for both novel and familiar objects, as this should require an interpretation of the physical properties of both objects rather than relying on previous knowledge and experience. It is hypothesised that initiation of movement, measured as movement onset time, for both familiar and novel objects will be faster when the most spatially salient elements of the objects are congruently oriented with the participant's effector hand.

For movement time (MT) previous data suggest that reaching for objects for use is associated with longer reach times compared to transport (Tunik et al., 2008). It is hypothesised also that selection of grasp orientation will occur earlier for the transport task compared to the use task and that this will be earlier for familiar tools based on the 2AS+ model. This is expected to be reflected also in earlier peak aperture for transport, as less precision is required in the selection of grip for transport. Earlier peak velocity of movement for the use tasks are further expected, indicating a longer period of deceleration of movement towards objects for use compared to transport, reflecting additional processing of the functional properties of the object.

5.2. Method

5.2.1. Participants

12 healthy right-handed participants (6 male, 6 female; age range 23-27, M±SD = 24.83±1.64 years) were recruited from the University of Nottingham, UK. Handedness was assessed via the 10 item version of the Edinburgh Handedness Inventory (Oldfield, 1971), participants were identified as having a right-hand preference, with an average laterality quotient of 0.87 (SD=0.10, range 0.7-1.0). Written informed consent was obtained from all participants prior to the experiment. The study had approval from the ethics committee of the School of Psychology, University of Nottingham, and was performed in accordance with the declaration of Helsinki (as of 2008).

5.2.2. Apparatus

Familiar and Novel Tools and tasks

A plastic hammer was selected as the familiar tool. A wooden cone was crafted for the novel tool. It was designed to be comparable in functionality to the familiar tool for both of the 'use' tasks. Both objects were ~18cm in length and painted the same colour to negate visual discrimination between functional and graspable facets of the objects based on colour (see Figure 28). The targets for both 'use' tasks were constructed of plasticine. For CU participants were presented with a piece of plasticine, shaped to a point perpendicular to the desk (initial state). Participants were then presented with another version of this construction with the point flattened (goal state) and were instructed to use the object to change the shape of the target from initial to the altered shape. For the NU task, participants were presented with a piece of plasticine shaped into a ball (initial state). Participants were then presented with the altered shape, a ball with a rounded depression in the centre (goal state) and instructed to use the object to change the shape of the target from the initial to the altered shape (see Figure 28 and Figure 29).

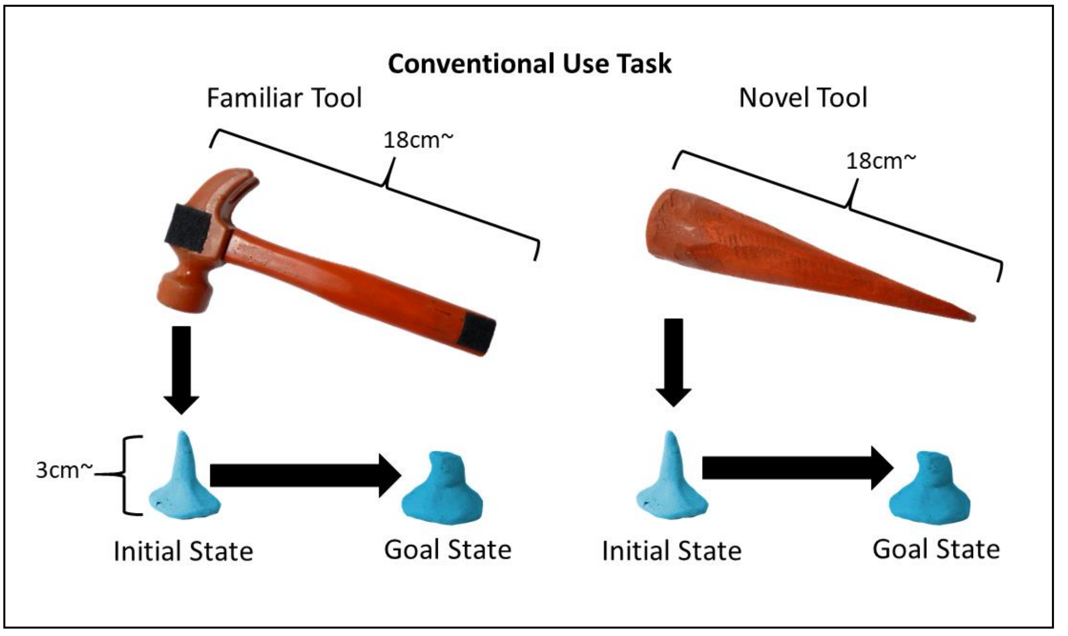

Figure 28. Conventional use (CU) task for the familiar and novel tools. Participants were shown the tools before engaging in the task. Participants were shown the 'initial' (pointed) state and 'goal' state (a flattened point forming the top of the target). Participants were not told how to use the tools, only shown the goal of action. They could interpret the best way to execute the task as long as the tool was used with one hand. The depicted use here is one example of how the tools are comparable in functionality, but other gestures of use were permitted.

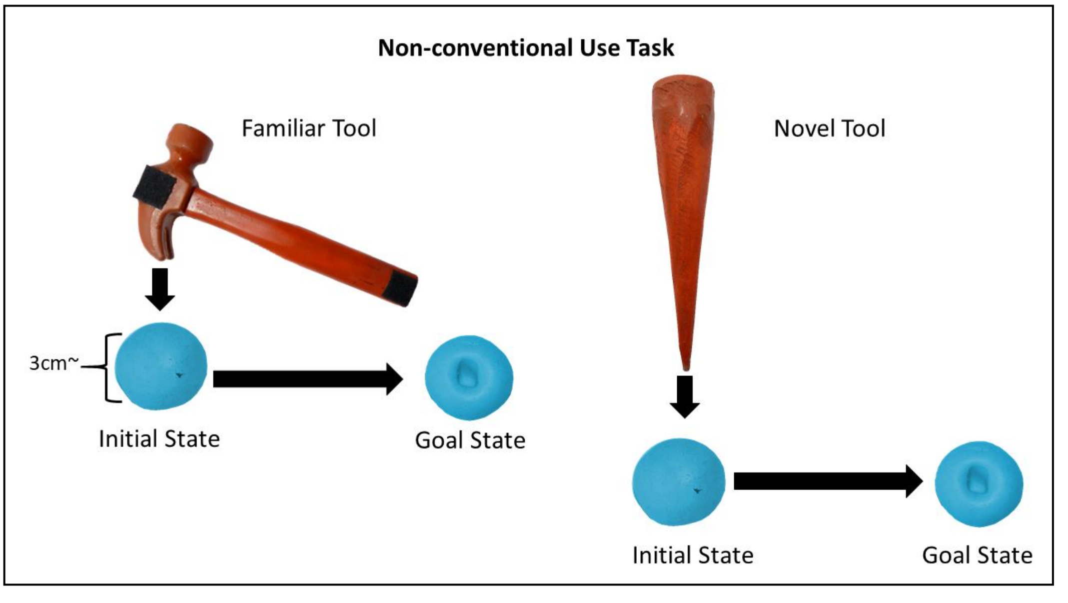

Figure 29. Non-conventional (NU) use for the familiar and novel tools. As with conventional use, participants were not advised on how to carry out the task, only the 'initial' (a sphere) and 'goal' state (a sphere with funnel shaped indentation). For the familiar tool, conventional use of the flattened hammer head would not be suitable to complete this task, therefore the claws would need to be used in a non-conventional way.

CU was designed to be similar to conventional use of the familiar tool, as participants could use the hammer in a power grip to flatten the point of the target. Participants were not instructed to use the tool in a particular way. This meant that conventional use of the hammer was not necessary as the task could be achieved with several grips or methods. Likewise, the novel tool could be used in a power grip with the same action as the hammer, but this was not necessary to complete the task. NU was designed to reflect unconventional use of the familiar object. For the hammer, this would involve using one of the claws to make a funnel-shaped depression in the target. For the novel cone tool, this would involve using the point to make the depression. Targets to be affected by the tools were designed not to be directly associated with the targets for conventional use of familiar tools. For example, the target for action of the hammer should not too closely resemble a nail, but should still be able to be enacted on with the same movement, but without driving the target into a surface. This was to offset any bias in familiarity between tool object pairs (e.g. hammer and nail) (Buxbaum, 2017) that could be mediated by function knowledge (Buxbaum, 2017; Osiurak & Badets, 2017).

5.2.3. Design

A repeated measures 3 x 2 x 8 design was used. The independent variables were Intention (Transport, CU, NU), Familiarity (Familiar, Novel) and Orientation (head of the object orientation; North, North-East, East, South-East, South, South-West, West, North-West). Participants completed three blocks of trials (1 block for each task - 32 trials per block). Block order was counterbalanced across subjects. Presentation of Orientation and Familiarity conditions were pseudorandomised within blocks.

Dependent Measures

Out of the dependent measures, three were the same as in the previous chapters (MT, TPV%, TPA%). Time to movement onset (MO) was defined as the time (ms) between goggles opening (target visible) and release of the button, indicating onset of participant movement.

Movement Time (MT) was defined as the time between MO and grasp completion, as measured from the maximum forward movement of the motion tracker towards target.

Percent of MT to peak velocity of movement (TPV%), calculated as the percentage of movement time at which maximum movement velocity (cm/s) occurred between MO and MT. This parameter was used to determine the percentage of movement at which slowing occurred, indicating a longer period of deceleration toward the target to be grasped.

Percent of MT to Peak aperture of grip (TPA%), measured as the percent of MT to maximum distance between the sensors attached the participants index finger and thumb during reaching between MO and MT.

Additionally, a fifth dependent measure was Percent of MT to Grasp selection (TGS%), defined as the percentage of MT that rotation of the forearm (degrees) was consistent ($\pm$ 10° for a minimum of 5 consecutive samples) with rotation of the forearm at the time of grasp completion. This measure quantified the percentage of reach at which the participant adopted the grasp orientation that was used for the tool. Miscorrection scores (as used in the previous chapters) were not selected for analysis here as there was no online correction during action execution and 'functional' grasp was not specified in the instructions to participants.

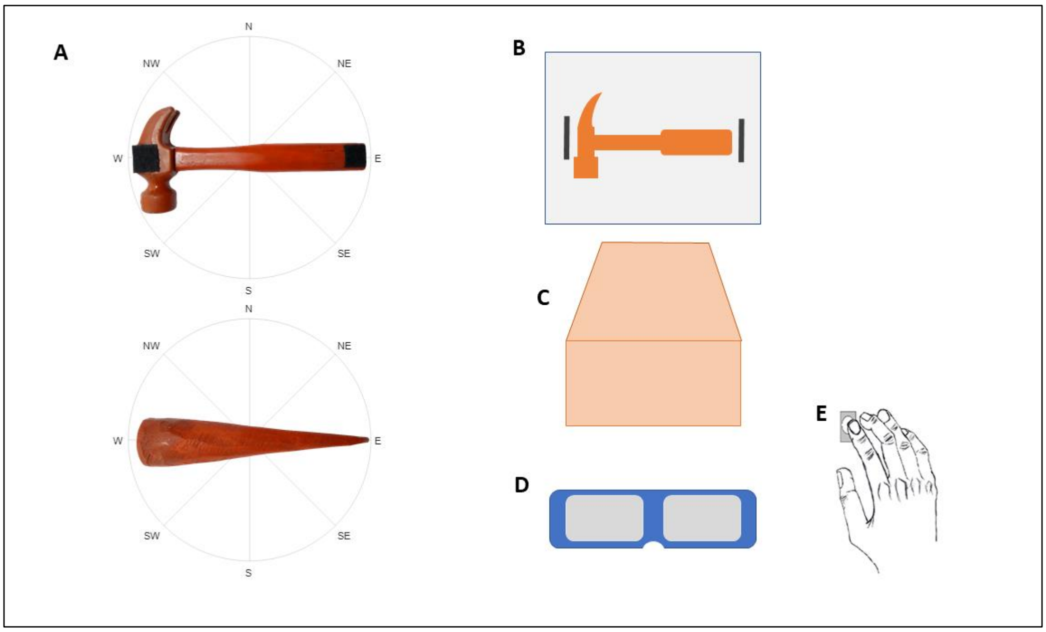

*Figure 30. Experimental set-up and apparatus for the familiar and novel tools task. (**A**) Orientations (West in this case) of the functional head for both familiar and novel tools. Although the novel tool could potentially be used in a number of ways, it was decided that the most suitable functional aspect of the tool (in this case the flattened end) should represent the functional head. (**B**) Familiar tool in cradle as would be presented to participants for the West orientation. The tool remained stationary during reaching and was oriented between trials. (**C**) Wooden plinth placed below the cradle. For the transport task, participants were required to place the tool on top of the wooden plinth. For both conventional (CU) and non-conventional use (NU) tasks, the target for action was placed on the wooden plinth in its initial state, prior to trial onset. (**D**) Occlusion goggles; between trials were blocked to ensure participants could not see which tool and which orientation was in place. Goggles were set to transparent at the onset of each trial and attached to a chin rest to maintain participant viewing distance (**E**) Button to maintain start position for participants (30cm to the right of the chin rest), if the button was not pressed down continuously by participants, the goggles would not open. This ensure participants maintained a consistent start position.*

5.2.4. Procedure

Participants were seated at the table with their chin positioned on a chin rest and the PLATO goggles positioned in front of their eyes. Prior to the onset of each block of trials, participants were briefed on the aim of the task that they would be carrying out for each trial in the block. Participants were instructed to place their right index finger on a button (30cm to the right and in line with the chin rest – see Figure 30). PLATO goggles occluded the participant’s view of target tools and orientation between trials, preventing grasp planning prior to the goggles opening.

When provided with a verbal ‘get ready’ signal from the experimenter, participants were instructed to press and hold the button until the goggles became transparent (uniform random delay of 2 – 4 seconds between Go signal and Goggles). If the button was released prior to the goggles opening, the random delay was reset to ensure no reaching began prior to viewing the target tool. Participants were instructed that as soon as the goggles became transparent, they

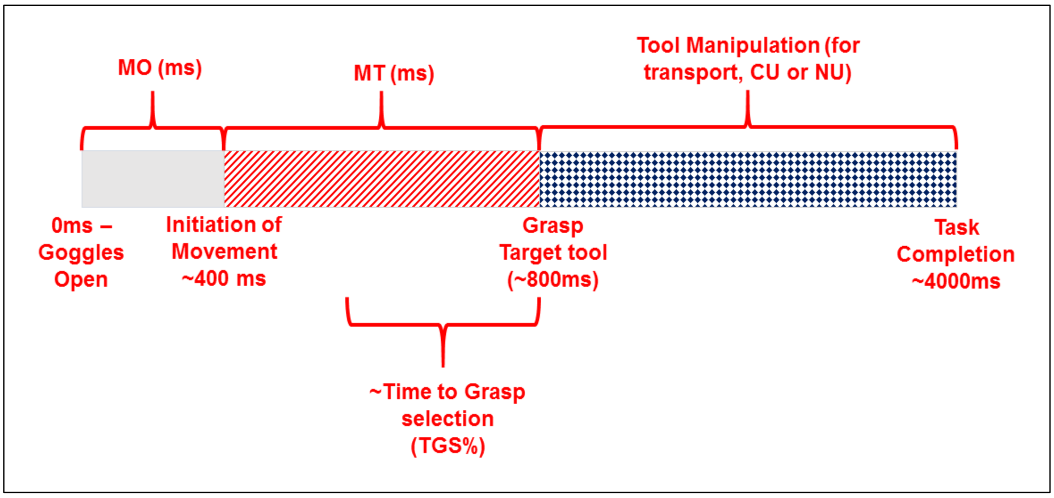

Figure 31. Average, estimated timeline for an example trial; (MO) Movement Onset, (MT) Movement Time, (TGS%) Percent of MT to Grasp Selection (TPA%) Percent of MT to peak aperture and (TPV%) Percent of MT to peak Velocity were determined within MT.

were to reach as quickly and as accurately as possible to grasp the target tool and carry out the given task (either Transport, CU or NU dependent on the block order, see Figure 31). Participants were not given specific instruction on how to grasp the object or how to carry out each individual task, outside of being instructed to use their right hand. For the Transport task participants were instructed to move the object from the cradle to the wooden plinth as quickly and as accurately as possible (see Figure 30). Participants were instructed to carry out conventional and non-conventional use as highlighted in the previous section (see 5.2.2). Following completion of the given task, participants were instructed to press the button again to end the trial. Testing lasted ~50 minutes including breaks.

5.3. Results

All data from all participants (n = 12) were processed for analysis, see Table 7, pg. 130. For transport, participants adopted a functional grasp for familiar tools for 59.9% of trials and 47% for novel. For conventional use, 80.73% for familiar and 41.15% for novel. For non-conventional use, familiar tools 82.25% and 41.67% for novel. 'Functional' in this instance refers to a power grip with the thumb oriented towards the head of the tool, however, as the task could be achieved in any way, as long as the tool was used, the present analysis will focus on early movement kinematics. A repeated measures ANOVA for Intention of action, Familiarity and Orientation (3 x 2 x 8) was conducted across the dependent measures. For analysis inclusive of Intention and Orientation Greenhouse-Geisser corrected *F* and *p* values were reported (with uncorrected *df*).

5.3.1. Movement Onset

No main effects of Familiarity ($F_{(1, 11)} = 0.001, p=.97$), Intention ($F_{(2, 22)} = 0.88, p=.42$) or Orientation ($F_{(7, 77)} = 1.85, p=.08$) were observed in movement onset. A significant Intention x Familiarity interaction ($F_{(2, 22)} = 3.31, p=.055$) showed earlier MO for familiar tools (*M±SE = 425±33ms*) compared to novel (*M±SE = 453±42ms*) for the Transport task, while both objects showed similar MO for conventional use task (*Familiar: M±SE = 452±35ms, Novel: M±SE = 455±35ms*). For the non-conventional use task, MO was later for the familiar objects (*M±SE = 484±42ms*) than for the novel (*M±SE = 452±33ms*) (Figure 32). This is somewhat inconsistent with the hypothesis, in that no difference for tool familiarity was expected when the intention was to transport the object or use it in a non-conventional manner, and familiar tools were predicted to elicit faster movement onset for familiar use.

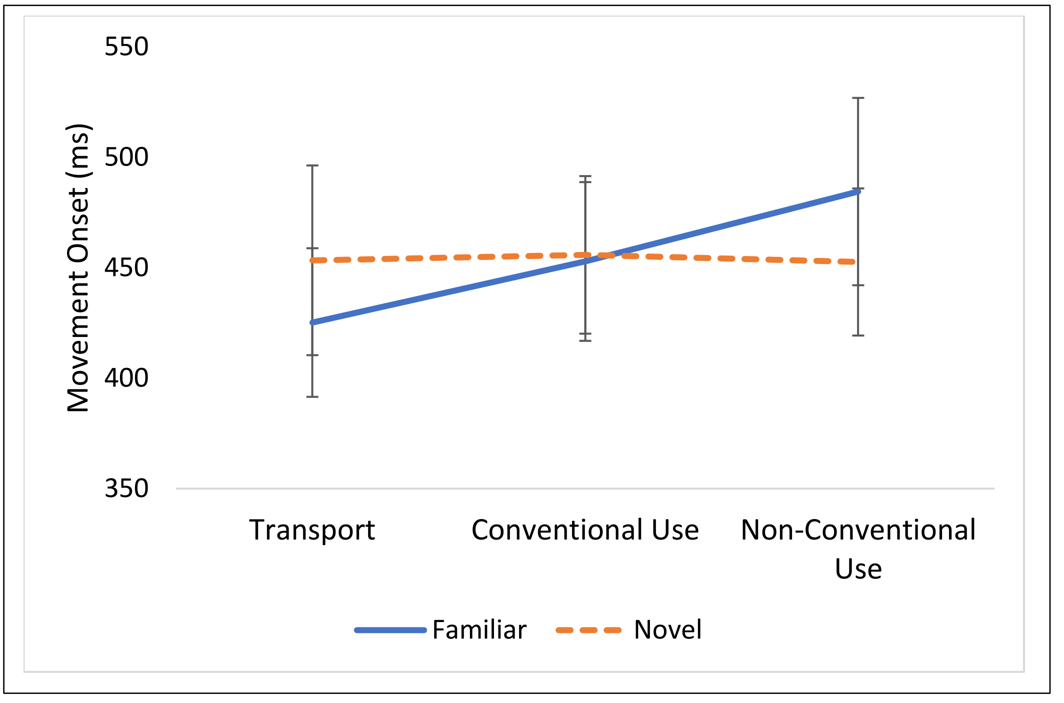

Figure 32. Interaction observed in time to movement onset (MO (ms)) between Intention and Familiarity ($F_{(2, 22)}$ = 3.31, p=.055), Error bars indicate ±1 SE of the mean.

A Familiarity x Orientation interaction *($F_{(7, 77)} = 2.61$, $p=.05$)* showed delayed MO for the familiar tool when oriented in the NW orientation *(Familiar: M±SE = 486±49ms, Novel: M±SE = 439±31ms)* while this pattern was reversed for the objects oriented in the NE direction *(Familiar: M±SE = 446±30ms, Novel: M±SE = 511±43ms)* (see Figure 33). As Intention of action does not influence this interaction, this may reflect the salience of the structural properties of the objects (most graspable aspects) within these orientations, as opposed to reliance on familiarity. No other interactions were observable for movement onset (see Table 8, pg. 131).

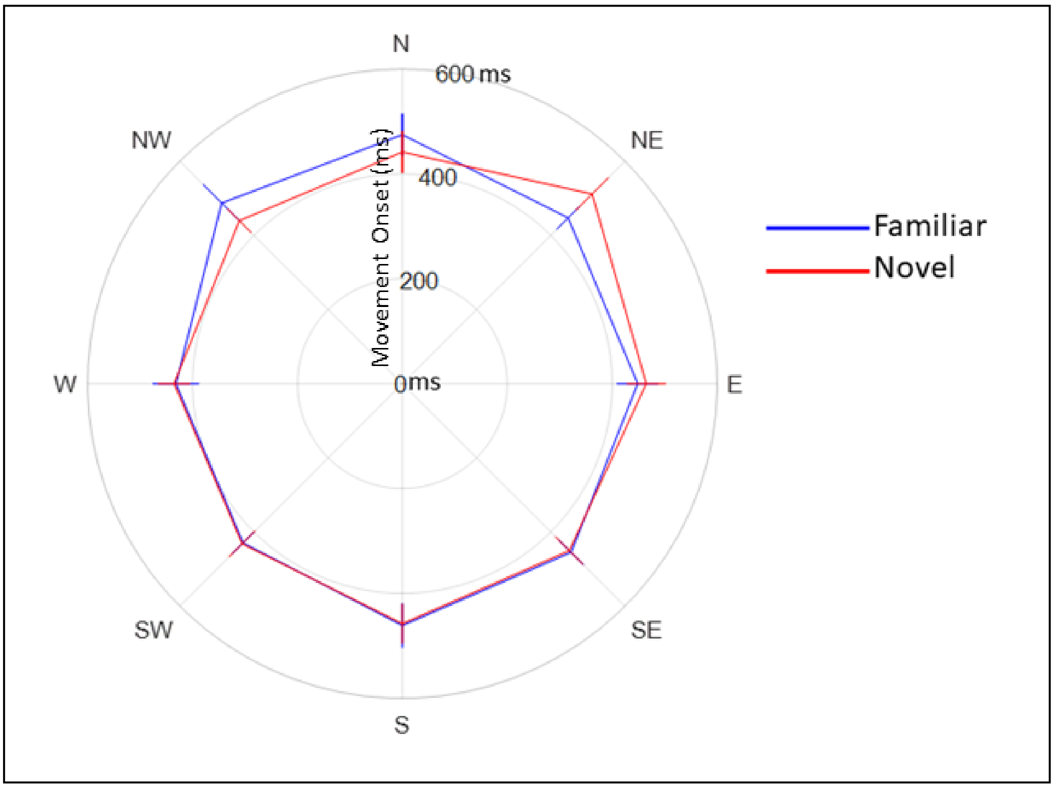

Figure 33. Polar plot for Interaction observed in Movement Onset (ms) between Familiarity and Orientation conditions ($F_{(7, 77)} = 2.61$, $p=.05$). Error bars indicate ±1 SE of the mean.

5.3.2. Movement Time

A main effect of Orientation *($F_{(7, 77)} = 3.05, p = .04$)* showed lower MT for objects oriented in the West *(M±SE = 755±59ms)* direction compared with all other orientations (North *(M±SE = 818±54ms)*, North-East *(M±SE = 836±56ms)*, East *(M±SE = 856±67ms)*, South-East *(M±SE = 833±53ms)*, South *(M±SE = 813±63ms)* South-West *(M±SE = 788±54ms)*, North-West *(M±SE = 813±63ms))*. Pairwise comparisons revealed this difference to be significant for North *($p= .01$)*, North-East *($p= .006$)*, East *($p= .006$)*, South-East *($p= .007$)* and South *($p= .008$)* orientations. This is consistent with the hypothesis and the orientation effect, as objects in that the West orientation present the most graspable aspect of the objects to the right, congruent with the effector hand position, compared to the above listed orientations which present the most graspable aspects of the objects to the left or pointing upwards. No main effects were observed for Familiarity *($F_{(1, 11)} = 2.75, p=.12$)* or Intention *($F_{(2, 22)} = 0.42, p=.66$)*.

An Intention x Orientation interaction *($F_{(14, 154)} = 2.90, p = .03$)* showed longer MT for the CU *(M±SE = 954±97ms)* and NU *(M±SE = 848±59ms)* tasks compared to the Transport task *(M±SE = 767±72ms)* for objects oriented in the East direction. This is consistent with the hypothesis and the orientation effect in that the most graspable aspects of the objects are presented incongruently with the effector hand. However, the subsequent interactions below elaborate on this finding.

A Familiarity x Orientation *($F_{(7, 77)} = 4.69, p = .01$)* interaction revealed longer MT for the familiar object oriented in the East direction *(M±SE = 939±81ms)* compared to novel *(M±SE = 773±59ms)*, but not in other orientation conditions. The east orientation presents the most graspable feature of the object to the left, incongruent with the effector hand; longer MT in this instance is, therefore, consistent with the orientation effect. However, this effect is not present for novel objects in the same orientation. This is somewhat consistent with the hypothesis, in that the incongruence between handle of the familiar object and the effector hand results in overall longer reaching time, but not for the novel object.

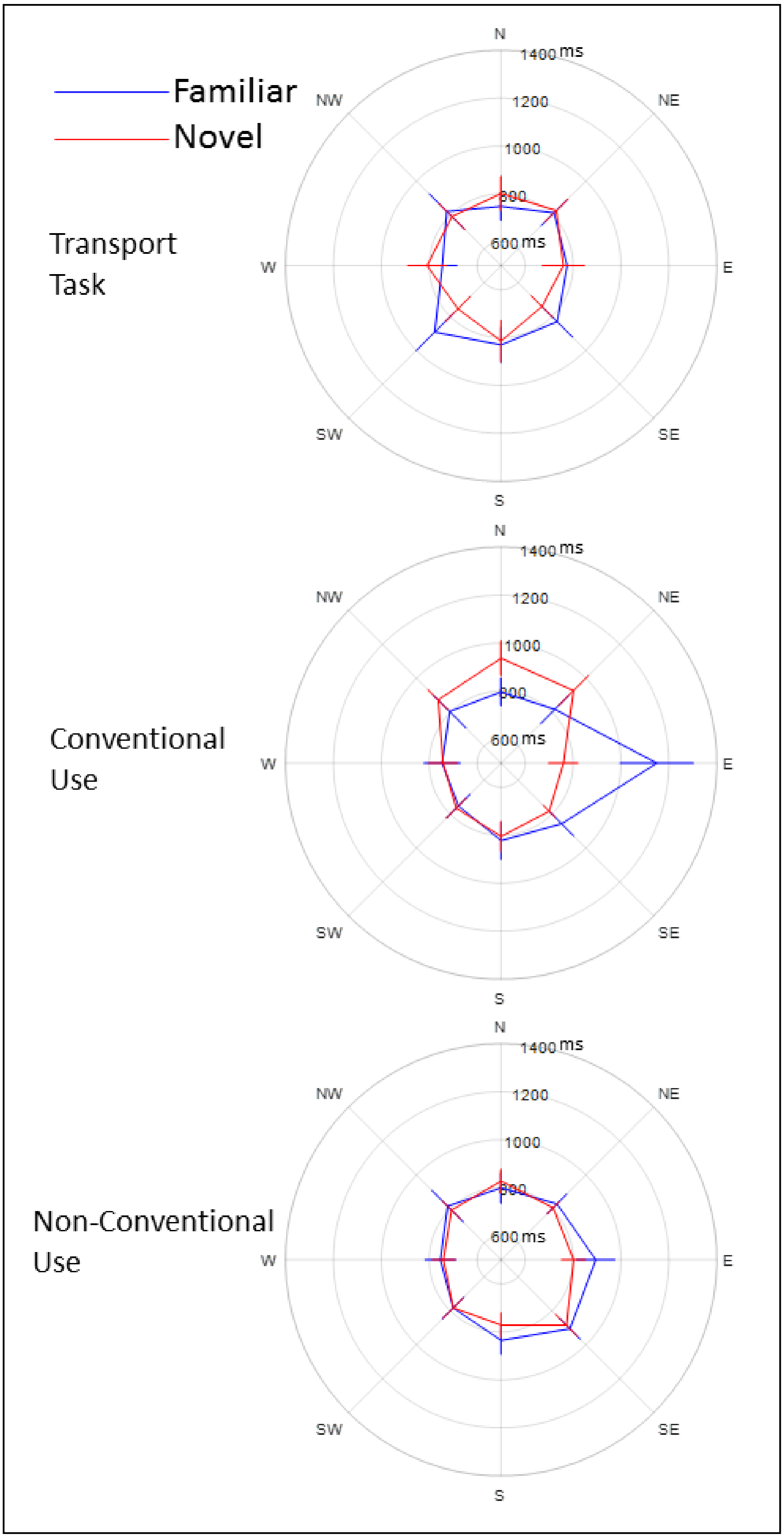

Figure 34. *Familiarity x Orientation interaction across the 3 Intention of action tasks (Transport (p = .51), Conventional Use (p < .005) and Non-conventional use (p = .47)). Error bars indicate ±1 SE of the mean.*

A trend toward significance was observed in a 3-way interaction between Intention, Familiarity and Orientation *($F_{(14, 154)} = 2.45, p = .058$)* for MT. To examine this interaction further, 2-way ANOVAs (Familiarity x Orientation) were conducted for each of the three Intention conditions. There was no significant Object x Orientation interaction for the Transport task *($F_{(7, 77)} = 0.89, p = .51$)* or NU task *($F_{(7, 77)} = 0.94, p = .47$)*.

However, this interaction was significant for CU task *($F_{(7, 77)} = 7.08, p = .005$)*, showing longer MT for familiar objects oriented in the East direction *($M \pm SE = 1149 \pm 152ms$)* compared to novel objects *($M \pm SE = 759 \pm 61ms$)* oriented in the same direction (see Figure 34). This finding suggests that the orientation effect selectively increases MT for familiar objects when used in the most conventional manner associated with them. Longer MT for familiar tools when the orientation of the handle is incongruent with the effector hand conventional use, indicates that stored representations of use may prompt a stored functional grasp of the hammer, even though this grasp has not been explicitly instructed and the task could be completed in a number of ways. That this does not occur for the novel object under the same conditions, indicates that familiarity with the object slows MT. This could be due to the flexibility of action available when reaching for the novel object, as there are no stored representations to influence selection of grasp. However, as this only occurred in the East orientation, but not the North-East or South-East orientations, this increase in reach time could be due to processing the structural properties of the object in relation to the task (in line with the technical reasoning approach) as opposed to accessing semantic associations.

5.3.3. Percent Time to Peak Velocity (TPV%)

A main effect of Orientation was observed *($F_{(7, 77)}$ = 3.98, p =.01)* revealing significantly higher TPV% for objects in the West orientation *(M±SE = 62.42±1.31 TPV%)* compared to those in the North *(M±SE = 57.75±1.92 TPV%)*, North-East *(M±SE = 57.62±2.24 TPV%)*, East *(M±SE = 57.62±2.24 TPV%)*, South-East *(M±SE = 57.11±2.31 TPV%)*, and South *(M±SE = 56.94±1.89 TPV%)* orientations. This is consistent with end state comfort (Rosenbaum et al., 1990) and the orientation effect (Symes et al., 2005, 2007; Tucker & Ellis, 1998) due to congruence between the most graspable aspects of the objects and position of the hand; higher TPV% indicates a larger period of acceleration towards the target during reaching. There were no significant effects of Intention *($F_{(2, 22)}$ = 1.88, p=.17)* or Familiarity *($F_{(1, 11)}$ = 0.07, p=.78)* (see Table 8, pg. 131).

An Intention x Orientation interaction *($F_{(14, 154)}$ = 2.31, p =.05)* was observed for TPV% (see Figure 35). This finding is inconsistent with the hypothesis, a larger period of deceleration was expected for both NU and CU compared to the transport task, as both use tasks should require increased processing of the object for use as a function of Orientation.

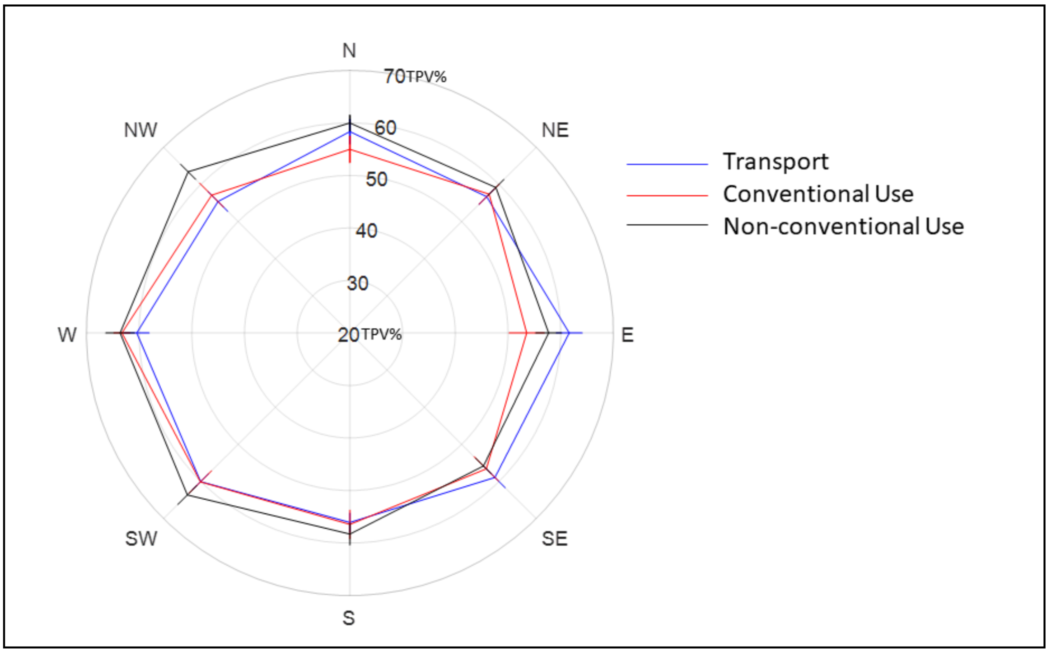

Figure 35. Interaction observed between Intention of action and Orientation ($F_{(7, 77)}$ = 3.98, p =.05) for percent of MT to peak velocity (TPV%). Error bars indicate ±1 SE of the mean.

A Familiarity x Orientation interaction *($F_{(7, 77)} = 3.04$, $p = .03$)* showed that familiar tools oriented in the West *(M±SE = 63.43±1.78TPV%)*, North West *(M±SE = 60.75±1.86TPV%)* and North *(M±SE = 68.89±1.23TPV%)* directions had higher TPV% than the novel tool in the same orientations *(West: M±SE = 61.42±1.66TPV%, North West: M±SE = 56.49±2.27TPV%, North: M±SE =56.62±2.74TPV%).* However, novel objects oriented in the East *(M±SE = 60.07±2.08 TPV%)*, South East *(M±SE = 59.15±2.31TPV%)* and South *(M±SE = 57.88±1.79TPV%)* directions showed higher TPV% than the familiar tool in the same orientation *(East: M±SE = 55.16±2.76TPV%, South East: M±SE = 55.07±2.76TPV%, South: M±SE = 56.01±2.37TPV%)*. This could be due to the influence of the structural properties of each object in these orientations, causing larger period of deceleration towards the target for familiar tools in the west direction and compared to larger deceleration for novel in the East and South-East directions. This can be further observed in that these orientations place the head of the tools in exactly opposing positions; suggesting that this difference may be influenced by the intrinsic structural properties of the object, rather than potential semantic associations.

5.3.4. Percent Time to Peak Aperture (TPA%)

A main effect of Orientation *($F_{(7, 77)} = 6.29$, $p < .0001$)* revealed earlier peak aperture for objects in the South West *(M±SE = 67.42±2.96 TPA%)* and West *(M±SE = 68.14±2.88 TPA%)* orientations compared to North *(M±SE = 80.87±1.50TPA%)*, North-East *(M±SE = 77.45±1.54 TPA%)*, South *(M±SE = 78.71±2.22 TPA%)* and North-West *(M±SE = 78.91±2.37 TPA%)* orientations (see Figure 36). Earlier hand pre-shaping for objects oriented to the West consistent with the most graspable aspect of the object being oriented to the right, congruent with the effector hand. This is consistent with the lower overall MT and later TPV% observed for these orientations (see above).

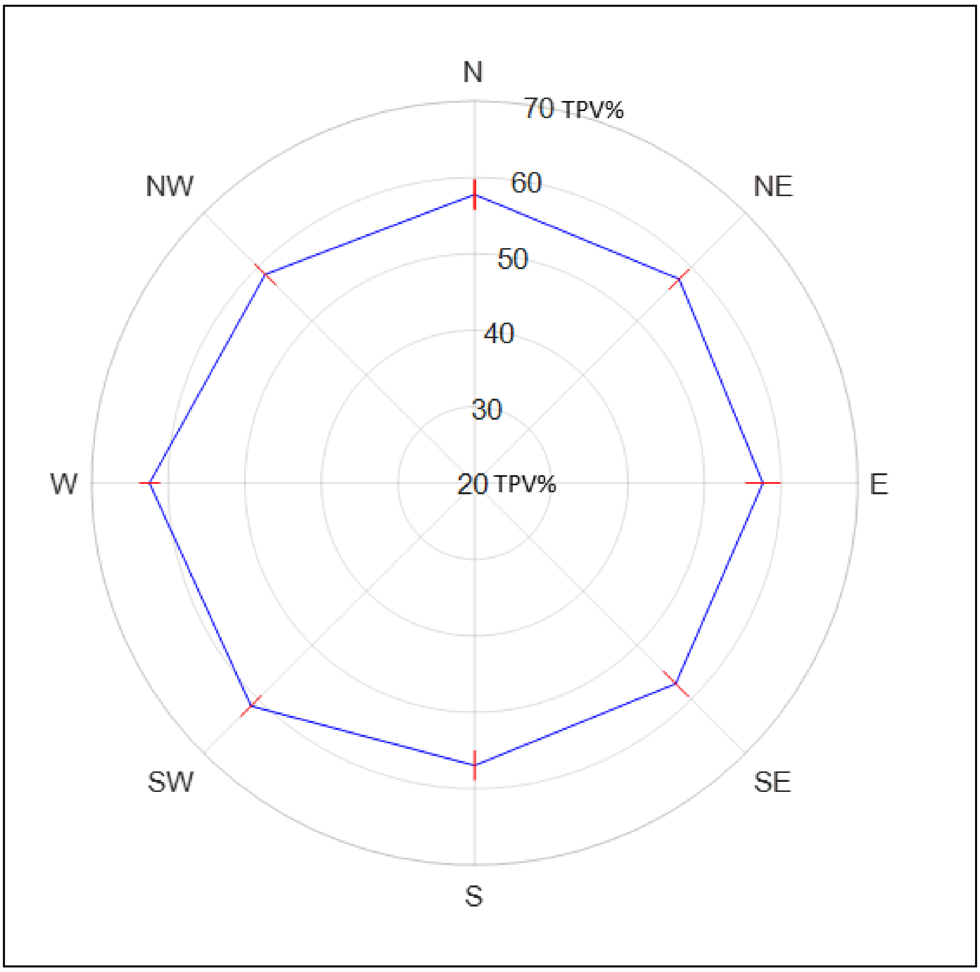

Figure 36. Main effect of Orientation observed for percent of movement time to peak aperture (TPA%) ($F_{(7, 77)} = 6.29$, $p < .0001$), Error bars indicate ±1 SE of the mean.

5.3.5. Percent Time to Grasp Selection (TGS%)

A significant main effect of Intention *($F_{(2, 22)} = 20.53$, $p<.0001$)* revealed earlier TGS% for the Transport task *(M±SE = 34.41±1.32 TGS%)* compared to both CU *(M±SE = 43.13±1.08 TGS%)* and NU *(M±SE = 41.18±0.97 TGS%)* tasks (see Figure 37). This is consistent with expected outcomes as the grasp used to move an object from one location to another would not require a specific orientation of the object in the effector hand to be transported. Therefore, grasp selection occurs earlier in reaching as for transport, providing the object affords a secure grasp, the orientation of the 'head' of the object is irrelevant to the action of moving it, in the absence of specific instructions on how to place the object. As such, for both use tasks, later occurring grasp selection is consistent with expected outcomes as grasp orientation for use requires planning of the affordance of the object in relation to the target of action, requiring a decision in terms of which grasp orientation to use.

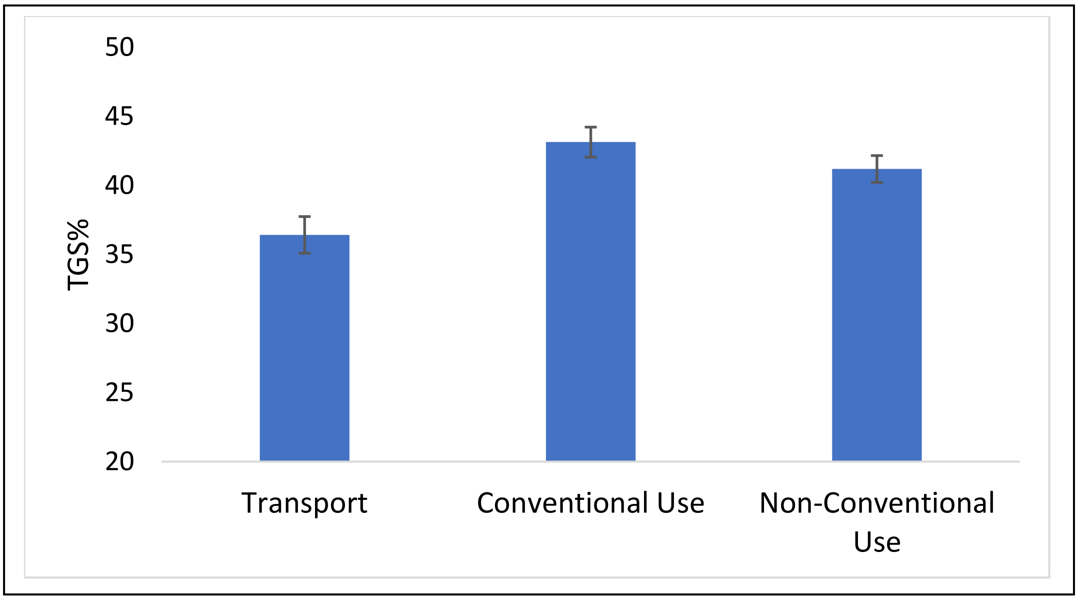

Figure 37. Main effect for Intention of action ($F_{(2, 22)} = 20.53$, $p<.0001$) observed for percent of movement time to grasp selection (TGS%).

A main effect of Orientation *($F_{(7, 77)} = 5.49$, $p = .01$)* showed significantly earlier selection of grasp in the North-West orientation *(M±SE = 30.39±2.78 TGS%)* compared to all other Orientation conditions. As with the above-mentioned findings in MT, TPV% and TPA%, this is consistent with the orientation effect, presenting the most graspable property of the object congruently to the effector hand.

An Intention x Orientation interaction *($F_{(14, 154)}$ = 4.21, p <.0001)* showed that for both CU and NU, objects oriented in the South-East quadrants (East, *CU: M±SE = 48.23±1.50 TGS%, NU: M±SE = 51.87±1.44 TGS%*, South-East, *CU: M±SE = 49.03±1.55 TGS%, NU: M±SE = 42.21±3.34 TGS%*, South, *CU: M±SE = 44.21±1.94 TGS%, NU: M±SE = 41.21±1.31 TGS%*) elicited later TGS% than for the movement task *(East: M±SE = 38.74±2.27 TGS%, South East: M±SE = 29.15±3.34 TGS%, South: M±SE = 34.55±3.47 TGS%)*. However, for objects oriented in the West orientation, later TGS% was observed for CU *(M±SE = 41.46±2.59 TGS%)* compared to NU *(M±SE = 34.28±3.31 TGS%)* and Transport *(M±SE = 34.94±2.39 TGS%)* (see Figure 38). This is consistent with the predicted outcomes and later TPV%, in that selection of grasp occurred later in reaching, for the use tasks, for orientations with the most graspable aspect of the object incongruent with the position of the hand (or requiring inversion of the hand).

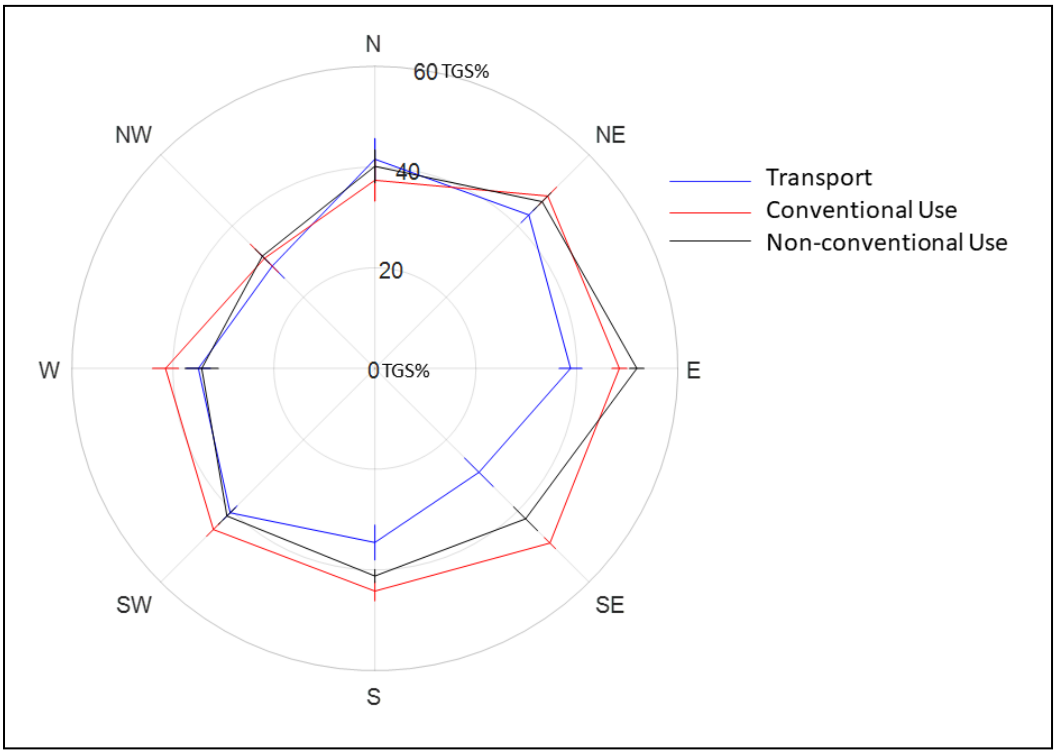

Figure 38. Interaction observed between Intention of action and Orientation ($F_{(14, 154)}$ = 4.21, p <.0001) percent of movement time to grasp selection (TGS%). Error bars indicate ±1 SE of the mean.

Processing use tasks requires consideration of both allocentric and egocentric relationships, resulting in later selection of grasp. This is not necessary when grasping for transport. Furthermore, this processing seems to impede conventional use, when objects are congruently oriented with the effector hand (west orientation), compared to transport or non-conventional use. This finding would conflict with the 2AS+ model within which appropriate grasp selection for conventional use should be readily accessible. However, absence of object Familiarity within this interaction means that this would be an invalid inference, as this pattern of results should only be observable for the familiar object in the conventional use condition, given the assumptions of the 2AS+ model.

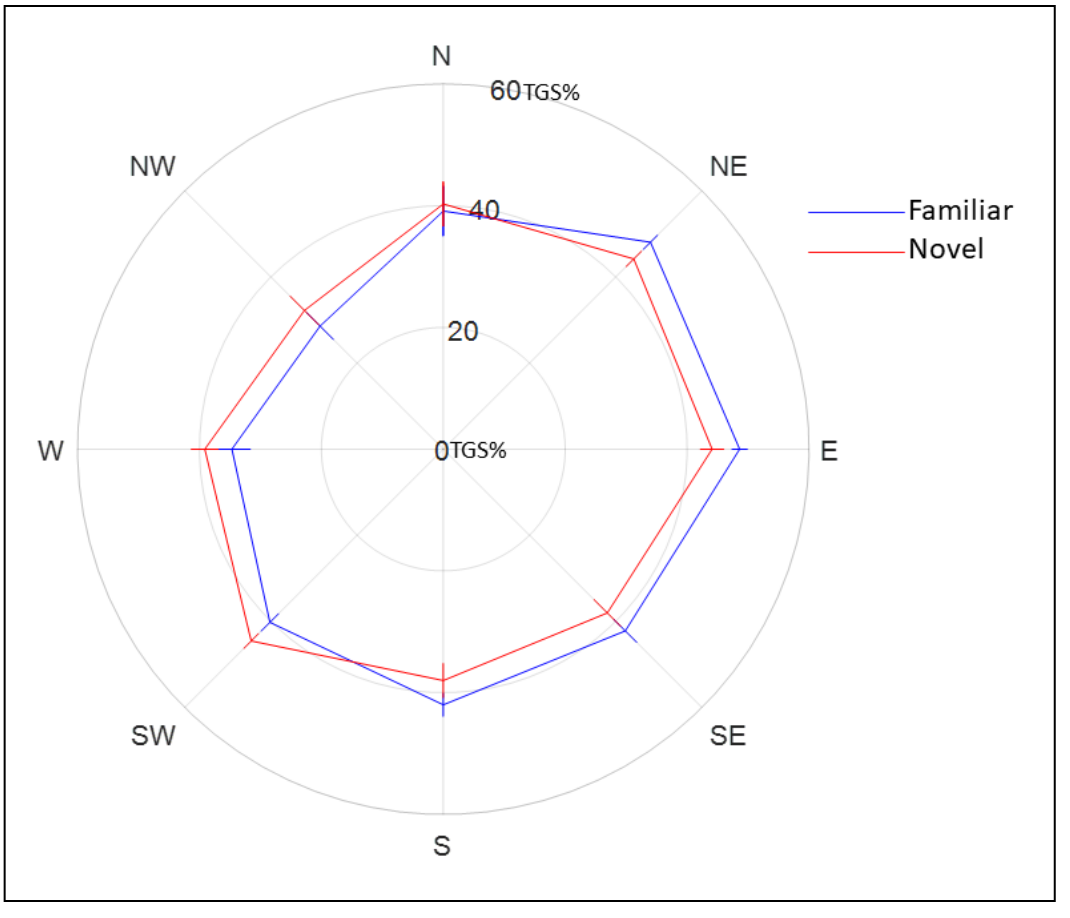

Figure 39. Interaction observed between Familiarity and Orientation ($F_{(7, 77)} = 2.44$, p=.04) percent of movement time to grasp selection (TGS%). Error bars indicate ±1 SE of the mean.

A significant Familiarity x Orientation interaction *($F_{(7, 77)} = 2.44, p=.04$)* revealed that for the familiar tool, TGS% was later in the North East *(M±SE = 48.06±1.61 TGS%)*, East *(M±SE = 48.61±1.26 TGS%)*, South-East *(M±SE = 42.21±2.63 TGS%)* and South *(M±SE = 41.98±1.89 TGS%)* orientations than for the novel tool in the same orientations *(North East: M±SE = 44.18±1.76 TGS%, East: M±SE = 44.08±1.93 TGS%, South-East: M±SE = 38.04±3.09 TGS%, South: M±SE = 37.99±2.79 TGS%)*. Whereas for North West, West and South West orientations novel tools *(North West: M±SE = 32.21±3.30 TGS%, West: M±SE = 39.12±2.22 TGS%, South West: M±SE = 44.55±1.69 TGS%)* elicited later TGS% than familiar *(North West: M±SE = 28.58±3.09 TGS%, West: M±SE = 34.67±3.02 TGS%, South West: M±SE = 40.22±1.99 TGS%)* (see Figure 39). This finding conflicts with the initial hypothesis and the 2AS+ model. These differences in TGS% seem to reflect a similar pattern of findings in TPV% and MT, in that for opposing direction of orientation for both objects results in opposing delays to selection of grasp. The lack of influence of Intention within this interaction, indicates that this occurs on the basis of the properties of the objects themselves, regardless of intention to act.

Table 7. Summary of mean data across Intention, Familiarity and Orientation conditions. M (±SD).

Intention	**Familiarity**	**Orientation**	MO (ms)		MT (ms)		TGS%		TPV%		TPA%	
Transport	**Familiar**	**N**	424	(107)	748	(200)	41.78	(16.51)	58.92	(6.68)	78.44	(7.53)
		NE	412	(108)	812	(257)	44.15	(10.35)	56.18	(6.61)	80.08	(6.05)
		E	381	(109)	775	(205)	40.00	(10.64)	59.23	(7.76)	64.98	(22.35)
		SE	451	(147)	830	(315)	29.55	(14.68)	58.42	(11.82)	77.83	(17.67)
		S	447	(162)	831	(257)	38.54	(13.21)	54.69	(10.68)	79.92	(14.13)
		SW	423	(123)	892	(375)	37.48	(9.22)	60.27	(11.14)	70.46	(16.84)
		W	460	(196)	745	(212)	33.79	(11.32)	63.38	(8.18)	63.09	(16.84)
		NW	403	(116)	821	(355)	27.70	(13.53)	55.26	(10.85)	77.69	(14.72)
	Novel	**N**	462	(202)	801	(248)	41.33	(13.84)	57.75	(10.97)	77.45	(10.24)
		NE	528	(264)	826	(233)	42.07	(7.76)	57.22	(9.92)	70.12	(15.81)
		E	445	(177)	759	(307)	37.50	(10.46)	64.00	(10.51)	67.05	(17.30)
		SE	430	(194)	741	(219)	28.75	(15.20)	59.40	(8.69)	70.23	(22.18)
		S	468	(233)	815	(298)	30.58	(14.99)	57.48	(3.40)	80.52	(12.42)
		SW	440	(153)	755	(253)	43.57	(8.79)	59.81	(8.34)	65.52	(11.44)
		W	429	(143)	809	(282)	36.09	(10.31)	57.49	(14.67)	63.57	(16.65)
		NW	425	(158)	791	(266)	29.79	(12.82)	55.52	(9.38)	79.14	(12.56)
Conventional Use	**Familiar**	**N**	499	(174)	797	(198)	35.58	(15.30)	56.99	(5.77)	79.85	(8.33)
		NE	424	(138)	817	(288)	53.05	(8.55)	59.88	(5.76)	81.22	(6.83)
		E	491	(175)	1150	(528)	53.86	(7.44)	48.98	(15.49)	69.96	(17.57)
		SE	435	(125)	857	(248)	53.20	(6.72)	53.04	(13.64)	72.61	(15.21)
		S	456	(130)	823	(272)	45.69	(8.69)	56.73	(9.94)	75.25	(19.19)
		SW	422	(105)	752	(236)	44.48	(10.32)	60.21	(11.85)	59.32	(22.10)
		W	414	(220)	746	(262)	36.07	(13.03)	65.23	(6.18)	73.55	(18.53)
		NW	481	(186)	804	(329)	28.27	(15.21)	61.22	(13.15)	85.57	(14.74)
	Novel	**N**	435	(113)	937	(245)	39.15	(15.10)	52.94	(14.19)	78.11	(16.30)
		NE	532	(242)	927	(304)	43.80	(12.89)	54.86	(14.64)	74.58	(13.09)
		E	483	(169)	760	(212)	42.99	(12.08)	58.11	(11.60)	69.14	(12.83)
		SE	438	(138)	783	(124)	44.87	(11.87)	60.15	(13.34)	83.07	(12.20)
		S	466	(146)	805	(217)	42.73	(12.27)	56.19	(10.12)	81.60	(7.99)
		SW	428	(115)	765	(199)	45.97	(7.82)	60.00	(9.88)	68.50	(15.94)
		W	444	(146)	742	(207)	46.85	(11.45)	61.28	(8.86)	73.92	(14.05)
		NW	419	(103)	872	(201)	33.57	(14.85)	52.96	(12.61)	73.94	(15.96)
Non-conventional Use	**Familiar**	**N**	501	(175)	800	(220)	39.95	(14.59)	60.76	(5.11)	84.88	(6.75)
		NE	504	(160)	829	(198)	46.98	(8.51)	60.11	(9.09)	83.07	(2.98)
		E	473	(147)	894	(281)	51.98	(7.46)	57.30	(11.27)	75.79	(9.04)
		SE	478	(130)	906	(208)	43.90	(19.51)	53.76	(9.06)	73.64	(16.49)
		S	480	(198)	835	(204)	41.73	(7.42)	56.60	(8.86)	73.58	(16.05)
		SW	442	(150)	783	(219)	38.72	(9.23)	62.62	(9.40)	62.74	(23.12)
		W	421	(87)	753	(221)	34.15	(11.58)	61.69	(13.39)	63.97	(25.38)
		NW	577	(273)	816	(323)	29.79	(12.21)	65.79	(8.02)	79.59	(17.36)
	Novel	**N**	427	(135)	828	(167)	40.32	(16.47)	59.18	(6.41)	86.53	(5.20)
		NE	474	(181)	807	(121)	46.69	(11.54)	58.23	(8.31)	75.66	(14.50)
		E	466	(112)	802	(176)	51.77	(7.08)	58.12	(9.92)	77.67	(10.16)
		SE	482	(143)	886	(221)	40.51	(12.94)	57.90	(6.98)	73.56	(10.25)
		S	439	(125)	771	(176)	40.69	(9.42)	60.00	(7.52)	81.42	(10.99)
		SW	427	(146)	782	(209)	44.13	(9.59)	64.61	(11.16)	78.01	(14.57)
		W	432	(96)	741	(167)	34.42	(13.60)	65.49	(8.17)	70.74	(22.13)
		NW	474	(131)	793	(181)	33.28	(13.13)	61.01	(8.30)	77.51	(14.63)

Mean Movement onset (**MO**), Movement time (**MT**), percent of MT to grasp selection (**TGS%**), percent of MT to peak velocity (**TPV%**) and aperture (**TPA%**) across Intention, Familiarity and Orientation conditions (**N**) North, (**NE**) North-East, (**E**) East, (**SE**) South-East, (**S**) South, (**SW**) South-west, (**W**) West, (**NW**) North-west.

Table 8. Summary of repeated measures ANOVA for Intention of action, Familiarity and Orientation across the dependent measures (Movement Onset (MO) Movement Time (MT), percent of MT to peak velocity (TPV%) and peak aperture (TPA%). Analysis inclusive of Intention and Orientation results are reported as Greenhouse-Geisser corrected F and p values. ***Bold*** *values indicate significance at p< .05 level.*

	MO		MT		TGS%		TPV%		TPA%	
	F	*p*	*F*	*p*	*F*	*p*	*F*	*p*	*F*	*p*
Intention	0.88	0.42	0.42	0.66	**20.53**	**0.00**	1.20	0.32	1.88	0.18
Familiarity	0.00	0.98	2.76	0.13	0.17	0.69	0.02	0.90	0.08	0.79
Orientation	1.86	0.13	**3.06**	**0.04**	**5.49**	**0.01**	**3.99**	**0.01**	**6.29**	**0.00**
Intention x Familiarity	**3.32**	**0.05**	0.02	0.98	0.46	0.64	0.42	0.66	2.48	0.11
Intention x Orientation	1.22	0.31	**2.90**	**0.03**	**4.21**	**0.00**	**2.31**	**0.05**	1.44	0.21
Familiarity x Orientation	**2.62**	**0.05**	**4.70**	**0.01**	**2.44**	**0.04**	**3.04**	**0.03**	1.87	0.14
Intention x Familiarity x Orientation	0.98	0.43	**2.46**	**0.06**	1.07	0.39	1.45	0.21	0.94	0.46

5.4. Discussion

In terms of action planning, delays in movement onset showed that intention of action and familiarity with the object impact upon time to initiation of movement. To an extent this is consistent with the hypothesis, due to the influence of familiarity, but not in the anticipated direction. Earlier movement onset for familiar tools in for transport could be representative of stored semantic familiarity with the graspable components of the hammer from previous experience (Buxbaum, 2017; Creem & Proffitt, 2001). This supports the role of manipulation knowledge for tool interaction as proposed by the 2AS+ model (Buxbaum, 2017). However, moving to transport an object arguably should rely *only* on processing the structural properties pertinent to the task of moving. This should not rely on accessing broader constructs about the tool, such as suitable grasp for use and should not impact on initiation of movement (Cho & Proctor, 2013; Lindemann et al., 2006; Osiurak & Badets, 2017; Osiurak et al., 2010). An alternative interpretation of this outcome, in line with the technical reasoning model, might be that processing shape and ‘graspability’ of the tool was reliant upon its intrinsic properties in relation to the target destination for transport. Osiurak et al., (2013) highlight that in transporting an object, both the properties of the object and target destination are considered in generating the mental simulation for movement. The novel object is conical in shape and rounded at the edges, with a less clearly defined handle compared to the hammer. Conversely, the hammer has a flattened edge of the head which makes it suitable for lying down flat without rolling from the target destination. The mental simulation of moving the hammer may occur faster than the novel object for these reasons, as opposed to faster access to stored representations.

Further supporting the technical reasoning interpretation, there was little difference in movement onset between familiar and novel objects for the conventional use task. The 2AS+ model argues that accessing a semantic representation of how to use the hammer effectively, should be faster and more efficient than generating a simulation based on the object and task parameters ‘de novo’ (Buxbaum, 2017). Conventional use should be the best example to observe this effect, but as this was not the case, it could be argued that this task was carried out through technical reasoning (Osiurak & Badets, 2017; Osiurak et al.,

2010) and not reliant upon stored representations. Interestingly, later movement onset was observed for the non-conventional use task for the familiar object when compared to the novel. One potential interpretation of this finding, in line with the 2AS+ model, is that when engaging in non-conventional use of a familiar tool, stored semantic representations concerning familiar use of the tool must be abstracted (Borghi, 2014; Buxbaum, 2017; Rijntjes et al., 2012; van Elk, 2014), or reinterpreted (potentially via technical reasoning) to be implemented. This may then result in longer planning prior to reaching for use. The faster movement onset for novel objects in this task may reflect the lack of interference as there are no stored semantic representations associated with use of the novel tool. However, given the findings for the other Intention conditions, the technical reasoning model may offer a better interpretation. Delayed movement onset may reflect more demanding processing of the task related properties of the familiar object compared with those of the novel. In generating a mental simulation for use, the pointed end of the novel object may offer a more easily determined plan of action for carrying out the task. The point of the cone is at the opposite end of the object when held from the flattened top (clearly unsuitable for the task) and affords use for a stabbing motion with either the thumb oriented toward or away from the functional point. The hammer would still require a grasp with the thumb oriented toward the head of the object and the claw facing away from the hand, but both the claw and flat head of the hammer are at the same end of the tool. The constraints of selecting this grasp and posture, compared with the flexibility of the novel object, could potentially lead to delayed movement onset, and an extended period of planning, without the influence of stored manipulation knowledge.

In terms of grasp execution, orientation of the object showed effects in kinematic measures, consistent with the orientation effect (Cho & Proctor, 2011, 2013; Lindemann et al., 2006; Symes et al., 2005; Tucker & Ellis, 2004) for both the novel and familiar objects across task conditions. However, the interaction showing the influence of the orientation effect for the familiar object in the conventional use task, indicates an influence of object familiarity on grasp execution. An interpretation of this finding in line with the 2AS+ model would suggest that the orientation effect occurs due to a desired grasp position based on stored semantic representations of previous use with the hammer as a function of incongruence between the position of the hand and tool handle (Borghi & Riggio, 2009; Buxbaum, 2017; Caligiore et al., 2010; Mizelle & Wheaton, 2010; Pellicano et al., 2010a; Thill et al., 2013). This is arguably not observable for the novel tool as there are no stored representations, meaning no influence of this incongruence. This finding seems to lend support to the 2AS+ model. However, there is inconsistency within the orientation conditions. For instance, if the orientation effect differentially occurs for novel and familiar objects oriented to the East, why is this pattern not also observable for objects oriented in the North East or South-East directions which present the tools in a similar direction? The technical reasoning hypothesis (Osiurak & Badets, 2017) can also provide an account of this finding; although the tools were designed to be matched in dimensions, the novel tool may afford more versatile grasp for use in the conventional task, meaning the orientation effect is not observable, when compared to the hammer. The hammer may be reasoned by participants to be most effectively used in a power grip with the thumb oriented toward the head, meaning that incongruence between effector position and graspable handle, results in longer reaching times overall. This does not occur for the novel tool in the conventional task as it affords task completion with the thumb oriented either toward or away from the cone's flat head (e.g. using a ‘hammer’ motion with the sides of the cone or a ‘squashing downward’ movement with the flattened head respectively, as observed in this experiment).

When familiar and novel objects are oriented with the heads in some opposing orientations, the significant differences between TGS% and TPV%, regardless of intention of action, suggest that these findings are due to intrinsic structural properties of the objects rather than on stored semantic representations. This main effect of Orientation provides more support for the technical reasoning account. Additionally, the orientation effects on TGS% are impacted by intention of action, showing delayed selection of appropriate grasp for use tasks (but not for transport) in those orientations which place the graspable components incongruently with initial hand position. This interaction again indicates that action intention impacts more than object familiarity, consistent with the technical reasoning approach.

There are, however, some limitations of the experimental method that have implications for the interpretation of these findings. For instance, this experiment was unable to assess order effects due to counterbalancing with a relatively small sample of participants in each counter balanced group. Meaning it is difficult to assess if grasping behaviour occurred differentially for transportation dependent on whether a participant had used the object to complete a task beforehand, or not (Osiurak, Roche, et al., 2013). Assessment of order effects would allow examination of whether a novel object became familiar dependent on the type of action carried out prior to transportation. Furthermore, this task only used one novel and one familiar object, meaning that the effects of familiarity rely upon participants being already familiar with a hammer. This means that these findings rely heavily on the intrinsic structural properties of the object. To overcome this, further novel and familiar tools (with corresponding conventional and non-conventional use tasks) should be implemented to ensure that any differences in movement kinematics can be averaged across many novel and familiar examples.

In conclusion, when planning to grasp; a combination of intention of action and the object properties significantly affect planning duration; with Orientation mainly affecting kinematic measures associated with action execution. Although object familiarity was observed as interacting significantly on some measures, an interpretation based on the 2AS+ model is irreconcilable with the pattern of results which are far better explained by the technical reasoning approach.

6. Delayed Selection of Grasp for Novel and Familiar Tool Actions Following TMS over the anterior SMG – Experiment 5

Foreword

In the previous chapter the nature of cognition involved in the planning and execution of tool use actions was explored within the context of two contemporary models of tool use (technical reasoning and 2AS+). This highlighted that the technical reasoning approach better accounts for differences in early movement kinematics observed between varying intention of action, familiarity and tool orientation conditions. The findings did not discount the role of manipulation knowledge, though, as proposed by the 2AS+ model and manipulation based approaches. However, without the use of TMS it is difficult to discern whether the anterior SMG supports this cognition during action planning or execution. This experiment sought to elaborate on these findings and overcome some of the issues in experimental design highlighted in the previous discussion, by implementing further novel and familiar tools and the introduction of TMS during action planning. This experiment focused on the anterior SMG as a region of interest due to findings cited by both the technical reasoning and manipulation based approaches positing an integral role in integration of tool related function (Orban & Caruana, 2014; Reynaud et al., 2016).

Abstract

The left anterior supramarginal gyrus (aSMG) is proposed as integral for tool manipulation for both the technical reasoning and 2AS+ neurocognitive models for visuomotor-control during tool manipulation. In line with the 2AS+ model, damage to the left aSMG would preferentially affect manipulation of familiar objects compared to novel objects, while the technical reasoning approach posits that damage to the SMG would selectively impair actions for both familiar and unfamiliar objects. In addition to tool familiarity, intention of action seems to affect left aSMG activation during action planning and execution. To examine aSMG selectivity for familiar objects and intention of action, an experiment was conducted that required participants to grasp familiar and novel objects for use

(conventional or non-conventional) or transport. TMS over the aSMG was delivered during planning stages of action. Participants (n = 8) took part under three TMS conditions (left aSMG, control site - left POC, Sham). Participants were presented with a different familiar (hammer, knife, screwdriver) and corresponding novel object for each stimulation block. It was hypothesised that TMS over the aSMG would selectively impair action planning for familiar tools with the intention of conventional use, but not transport. Movement onset did not differ across TMS conditions. Grasp selection, however, was delayed for TMS over the aSMG for conventional use of objects when oriented incongruently with the effector hand (interaction between Stimulation, Intention and Orientation). This interaction was not present for sham or control site stimulation. None of the kinematic dependent variables were influenced by familiarity. These findings indicate that the aSMG enables goal oriented manipulation of tools, constrained by affordance of the environment, supporting the technical reasoning model.

6.1. Introduction and Research Aims

As highlighted throughout this thesis, the left SMG plays a critical role in action planning and execution of tool use actions. This thesis, alongside previous research suggest that the SMG is a locus of integration for tool knowledge into the visuomotor systems that facilitate action (Baumard et al., 2014; Buxbaum, 2017; Orban & Caruana, 2014; Osiurak & Badets, 2017). This integration allows selection of contextually appropriate grasping of tools for use. In the previous chapter the current debate was highlighted between technical reasoning and manipulation-based approaches constituting the basis of this tool knowledge. Findings highlighted that effects of action intention, tool familiarity and orientation on early movement kinematics supported the technical reasoning account in grasp planning and execution. However, to elaborate on these findings, it is necessary to explore whether the aSMG supports this cognition during action planning. This experiment aimed also to overcome some limitations of the previous experiment. In the previous paradigm, due to the limited number of novel and familiar tools, differences in movement kinematics could not easily be attributed to either familiarity (i.e. activation of stored representations) or processing structural and functional aspects of the tools (i.e. technical reasoning).

In pursuit of this aim, further novel and familiar tools are implemented, alongside TMS over the aSMG during action planning.

Functional imaging and neuropsychological evidence support two models in the context of tool familiarity, action intention and affordance perception.

The first of these two models, the 2AS+ model (Buxbaum, 2017) (alongside other manipulation-based approaches (Borghi, 2014; Borghi, Flumini, Natraj, & Wheaton, 2012; Pellicano, Iani, Borghi, Rubichi, & Nicoletti, 2010b; Thill et al., 2013; van Elk, 2014)) posits that tool actions rely upon stored representations of use in the form of manipulation knowledge. Manipulation knowledge is served by the left ventro-dorsal pathway for action, supported by the posterior temporal lobe which encodes egocentric information about how hand-tool actions should look/feel (Buxbaum, 2017). This acts as a ‘goal state’ for action. The bilateral dorso-dorsal pathway is responsible for tailoring planned actions to the affordances of the environment and carrying out online adjustments to action to achieve the ‘goal state’ and complete the desired task (Brandi et al., 2014; Buxbaum, 2017; Buxbaum & Kalénine, 2010). Object manipulation actions are generated concurrently by both pathways for action converging on the SMG which acts as a ‘neural accumulator’ for candidate actions. The IFG then selects the most suitable action plan in relation to the task at hand (Cisek & Kalaska, 2010).

As highlighted in the previous chapter, this model posits that manipulation knowledge necessary for tool use actions relies upon learned gestures of familiar use (Buxbaum, 2017). Therefore, this neural network should show specificity for familiar tools and objects. Imaging data has shown preferential SMG activation during action planning and execution for tool use when compared with use of simple geometric shapes (Brandi et al., 2014). The SMG also shows activation when observing tool use actions compared to control stimuli (Kroliczak & Frey, 2009; Lesourd et al., 2017; M. Martin et al., 2016; Przybylski & Kroliczak, 2017) in particular the aSMG (Orban & Caruana, 2014). The aSMG exhibits anatomical asymmetry with a left hemisphere bias (Van Essen, Glasser, Dierker, Harwell, & Coalson, 2012). This activation has been shown as completely restricted to the left hemisphere for tool action observation (Peeters et al., 2013) and planning of tool use pantomimes (Kroliczak & Frey, 2009) in keeping with findings of apraxic patients with left brain damage (Buxbaum, 2001; Goldenberg, 2013; Sunderland & Shinner, 2007; Sunderland et al., 2013). Patient studies have also shown that left brain damaged (LBD) participants exhibit deficits in grasping familiar objects compared with geometric shapes, when barrier avoidance is required (Sunderland et al., 2013). Co-activation of the aIPS alongside the SMG in response to grasping tools (Jacobs et al., 2009; Orban & Caruana, 2014) arguably reflects the integration of manipulation knowledge that facilitates a functional grasp into the visuomotor grasping transformations mediated by the aIPS (Orban & Caruana, 2014; Rice et al., 2007; Tunik et al., 2005), in keeping with the 2AS+ model. Evidence therefore suggests specificity for familiar tools compared to controls. Furthermore, TMS over SMG and IFG during action planning delays the onset of actions for object manipulation compared with arbitrary stimulus response (Tunik et al., 2008). Object manipulation tasks involved both familiar use and transport of objects. While this does not highlight familiar object specificity, disruption of movement from TMS over IFG/SMG is in keeping with the proposed action selection module proposed by 2AS+ (Buxbaum, 2017) and other manipulation-based models (Bi et al., 2015; Gallivan et al., 2013; Johnson-Frey et al., 2005; Lewis, 2006; Orban & Caruana, 2014). Brandi et al. (2014) also highlighted that in terms of action intention, the tool use network was more active for tasks involving *use* compared to transport and activation was more prominent for use of the familiar tool versus the geometric control object, in keeping with specificity for familiar use of familiar tools; in keeping with the manipulation based approach.

A critique often levelled at this approach argues that it does not sufficiently account for human use of novel tools (Osiurak & Badets, 2016, 2017) (or novel use of familiar tools); however, as highlighted in the previous chapter, Buxbaum (2017) posits that abstraction of tool gestures (combined with fine tuning of actions, potentially through technical reasoning) supports novel tool use. With regards to orientation and affordance perception, the 2AS+ model posits that dorso-dorsal structures mediate this aspect of tool grasp planning (Buxbaum, 2017). However, evidence cited in support of the manipulation-based approach suggest that this is augmented with input from ventro-dorsal structures;

as observed in participants grasping tools in a functional manner even when use is not required (Creem & Proffitt, 2001); or responding faster to tools with handles oriented congruently with the effector hand (Tucker & Ellis, 1998). The results from the previous chapter cannot confirm this to be the case and it has been suggested that participant responses may be due to processing the most graspable aspects of objects rather, than having a preference for functional grasp due to stored tool use gestures (Osiurak & Badets, 2017; Symes et al., 2005). The findings in Chapter 3 (McDowell et al., 2018) and 4 suggest that the SMG is involved in supplementing dorso-dorsal online correction during action execution, but cannot confirm whether this is specific to familiar tools, or influenced by intention of action (as demonstration of use was required for every trial).

According to the second of the two models, the technical reasoning model (Osiurak & Badets, 2016, 2017; Reynaud et al., 2016), tool use actions are generated on a 'de novo' basis. As discussed in previous chapters, this process depends on; the action goal, the affordances of the user, environment and tool properties and is supported by technical reasoning and mechanical knowledge. The aSMG is argued to serve as a point of integration between dorso-dorsal structures (aIPS - supporting visuomotor control and affordance perception) and parietal area F (PF) (supporting technical reasoning) to guide a functional grasp of tools for use (Orban & Caruana, 2014; Osiurak & Badets, 2017; Reynaud et al., 2016). This model does not rely on stored manipulation knowledge and accounts for novel tool use, as learned representations are not required for functional use (Osiurak & Badets, 2016, 2017; Reynaud et al., 2016). Neuroimaging studies have shown that neural responses of the inferior parietal lobule (IPL) support tool use regardless of object familiarity (Orban & Caruana, 2014; Peeters et al., 2009b, 2013).

A recent meta-analysis of functional-imaging data (Reynaud et al., 2016) suggests that the aSMG responds particularly to allocentric relationships between tools (both novel and familiar) and their corresponding targets for action. This suggests the aSMG is a point of integration between the egocentric processing of dorso-dorsal structures (aIPS, superior parietal lobule (SPL)) and technical reasoning for allocentric processing in the IPL. This overcomes issues in 2AS+ in which manipulation knowledge encodes egocentric relationships, which ignores processing of the tool and target properties (Osiurak & Badets, 2017). Furthermore, this proposed role of the aSMG is in keeping with observations of patient deficits in mechanical problem solving following left IPL damage (Goldenberg & Hagmann, 1998; Goldenberg & Spatt, 2009; Jarry et al., 2015; Osiurak, 2014b; Osiurak et al., 2009; Osiurak, Aubin, Allain, Jarry, Etcharry-Bouyx, et al., 2008). This proposed aSMG role does not account for unnecessary functional grasp of tools (Creem & Proffitt, 2001) or deficits for familiar tool grasping compared with novel objects (Sunderland et al., 2013), however it can provide a clearer explanation of the orientation effect (Osiurak & Badets, 2016; Symes et al., 2005, 2007). Furthermore, the technical reasoning approach offers insight on the intention of actions, highlighting that technical reasoning and mechanical knowledge are central to object manipulation, whether the goal is use or transport. This has been shown in experiments in which movements to hand a tool to another person take longer to initiate than actions requiring use (Osiurak, Roche, et al., 2013). The findings in the previous chapter (Chapter 5) were more easily explained under the technical reasoning, due to patterns in early movement kinematics suggesting that planning and execution of actions was based on the object features as a function of orientation and affordance (as opposed to familiarity). However, those findings could not discount the influence of manipulation knowledge, requiring further exploration of cognition within this neural circuit.

This experiment aimed to further explore the role of the aSMG in the context of these two models of tool cognition and in light of the findings in the previous chapter. In pursuit of this, the replicate the experiment from the previous chapter was replicated with the addition of TMS over the aSMG and a parietal control site of stimulation (POC) during the planning stages of action. Examining the influence of aSMG TMS effects on early movement kinematics for novel and familiar tools should allow exploration of whether the aSMG shows a preference for familiar tools in initiating actions. Examining the effects of action intention (Transport, Conventional Use - CU, and Non-conventional use - NU) will highlight whether there is a bias for familiar use of tools, in line with the 2AS+ model and whether TMS over the aSMG modulates this bias. Varying the orientation of objects will allow exploration of the aSMG role in processing affordances for grasp orientation in relation to the intention of action and familiarity of the object. The previous experiment (Chapter 5) showed differing movement kinematics for opposing (East/West) orientations for novel and familiar tools, that could not clearly be attributed to the influence of either technical reasoning or manipulation knowledge and was limited to a single pair of novel and familiar tools. To overcome this limitation in the current experiment, two further novel/familiar tools and corresponding tasks will be introduced. Multiple novel/familiar tools should allow us to examine the influence of tool familiarity more clearly on movement kinematics as a function of orientation and action intention. In the following section the expected outcomes are discussed in the context of both technical reasoning and 2AS+ models. This experiment will not examine lateralisation of aSMG function (as in Chapters 4 and 5), as the aim is to examine the basis of cognition for tool use and the aSMG role in processing object manipulation. Therefore, this experiment will examine the left aSMG only with right handed participants using their dominant hand.

For object familiarity, under the 2AS+ model movement onset should be delayed for novel tools compared to familiar tools for CU, due to the influence of manipulation knowledge associated with familiar tools (Buxbaum, 2017). For transport, movement kinematics should show faster initiation of movement and grasping for novel tools as there should be no influence of a stored ‘functional’ grasp (Creem & Proffitt, 2001). NU tasks should be initiated slower than CU tasks, and there should be limited difference between novel and familiar tools for NU, as both would require technical reasoning or abstraction of known actions to achieve the desired goal (Buxbaum, 2017). With the application of aSMG stimulation during planning stages, transport and use actions would both be delayed due to the aSMG role as a buffer for both ventro-dorsal (use) and dorso-dorsal (transport) goal-oriented actions compared to sham and control stimulation. However, these differences should be more prominent for use tasks due to the necessity for integration and abstraction of manipulation knowledge (Buxbaum, 2017). Furthermore, if the aSMG is specialised for familiar objects, aSMG should most impact on movement kinematics for CU of familiar tools due to the strong association posited between familiar objects and stored gestures of use.

Alternatively, under the technical reasoning approach movement onset and early movement kinematics should not be affected by familiarity, but should differ on intention of action and orientation (Lesourd et al., 2017; Osiurak & Badets, 2016, 2017; Reynaud et al., 2016). Stimulation of the aSMG should significantly delay movement onset for objects for use (compared to sham and control site stimulation). This should potentially be more observable for use (CU and NU) than transport, due to the technical contextual requirements of each task compared to the relatively easier transport task used in the previous experiment and here (Osiurak & Badets, 2017; Reynaud et al., 2016). Differences in orientation should not be influenced by familiarity of the object, and should only occur based on the most saliently graspable aspect of the tools being congruent with the effector hand (Cho & Proctor, 2010, 2013).

Based on previous research and the findings in Chapter 5, it is hypothesised that TMS over the aSMG should delay movement onset for both *use* and *transport*. This should occur for both novel and familiar objects compared to a control site of stimulation, in keeping with the technical reasoning view of the aSMG as the locus of technical reasoning. This is also consistent with the 2AS+/manipulation based view of the aSMG as a buffer for action plans from which the most appropriate can be selected. For action execution, it is hypothesised that aSMG stimulation should not impact on early movement kinematics following the onset of movement as observed by Tunik et al. (2008). It is hypothesed that TMS over the aSMG, but not other sites will elicit stronger delays to movement onset for use tasks, due to the required integration of technical reasoning in carrying out these actions, and this should not be influenced by familiarity of the tool or task. When reaching for objects for transport, it is hypothesised that TMS over the aSMG will impair movement onset but not selectively for familiar objects in line with the technical reasoning model.

6.2. Methods

6.2.1. Participants

9 healthy, right handed participants (6 female, 3 male; age range 23-28, $M \pm SD$ = 24.55±7.82) were recruited from the University of Nottingham UK. Participants were eligible if they were right handed and had a structural MRI scan to allow accurate TMS coil placement. (One participant's data was excluded from analysis due to overt delays in Movement Onset, and Movement Time). Handedness was assessed via the 10 item version of the Edinburgh Handedness Inventory (Oldfield, 1971) participants were identified as having a right hand preference, with an average laterality quotient of 0.84 (SD = 0.28, range 0.6 - 1.0). Participant safety and suitability to undergo TMS was assessed using pre-test screening (Maizey et al., 2013). Side effects or discomfort were monitored using follow up questionnaires over a 24 hour period following stimulation (Maizey et al., 2013). No side effects or discomfort attributed to TMS were reported by participants. Written informed consent was obtained from all participants prior to the experiment. The study had approval from the ethics committee in accordance with the declaration of Helsinki (as of 2008).

6.2.2. Apparatus

6.2.2.1. Novel and Familiar Tool pairs and tasks

Three everyday tools (Hammer, Screwdriver and Knife) were used for the familiar tool condition, all plastic, ~18cm in length. The familiar tools were painted (orange) to limit distinction in colour between the functional head and handle of the tool. The novel tools were designed to be comparable in functionality for the tasks corresponding to each familiar tool. A cone, constructed of wood, was used to correspond to the Hammer. A flat length of wood with a slope at one end and rounded off at the opposite end, was used to correspond with the Knife. A tubular shaped length of wood, sloped at one end, was used to correspond to the Screwdriver. For the Intention of action conditions, Transport was the same as in Chapter 5 (grasping the tool and moving to a wooden plinth).

Two tasks involving use of the tool to affect change on an object were used for this experiment. The first task was designed to be similar to the most conventional use of the familiar tool and could be carried out in a similar movement with the novel tool. The second use task (NU) was designed to be an unconventional use of the familiar tool. Targets to be affected by the tools were designed to not be directly associated with the targets for conventional use of familiar tools, to avoid association between tool target pairs. This was to ensure that tool use was carried out based on either manipulation knowledge or technical

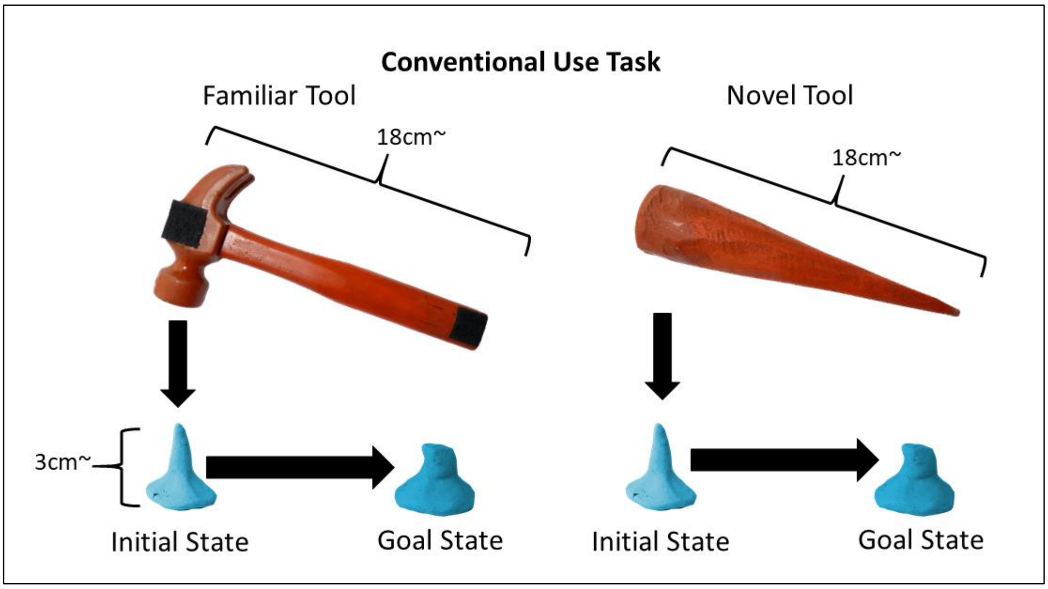

Figure 41. Conventional use task for the 'Hammer and Cone' familiar and novel tools. The tasks required here are the same as reported in Chapter 5. No specific instruction on how to achieve the task or grasp the tool was issued to participants.

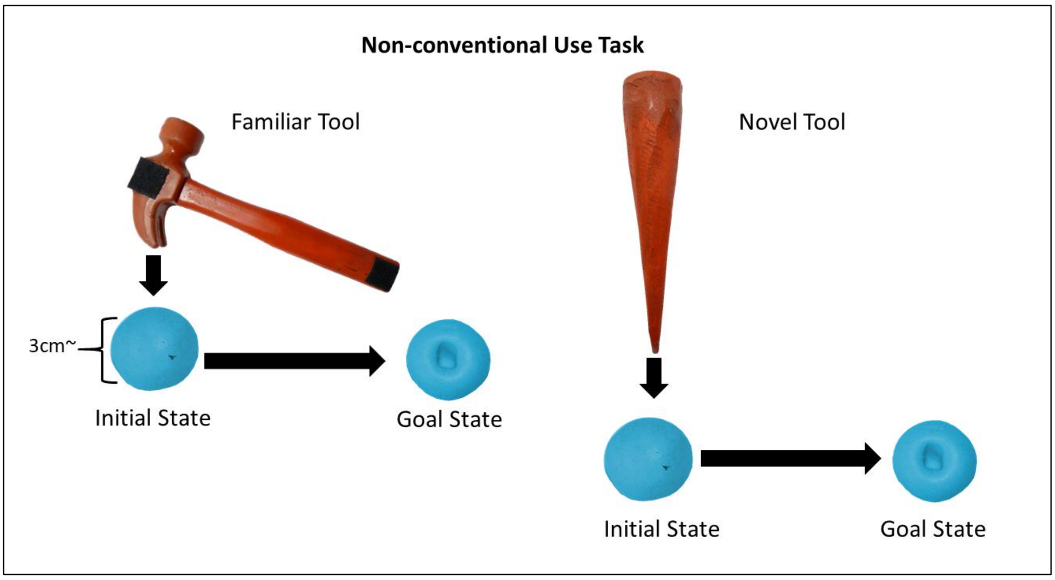

Figure 40. Non-Conventional use task for the hammer and novel comparative familiar and novel tools. The tasks required here are the same as reported in Chapter 5.

reasoning related to the tool and not the target (Osiurak & Badets, 2017). For example, the target in in the hammer condition should not too closely resemble a nail but should still be able to be enacted on with the same movement, but without driving the target into a surface.

Both *use* tasks for the hammer were the same as those reported in Chapter 5 (see Figure 41 and Figure 40). For the *conventional use* (CU) task, participants were presented with a piece of Blu-Tack™, shaped to a point perpendicular to the desk. Participants were instructed to flatten the point using the object. For the *non-conventional use* (NU) task, a piece of Blu-Tack™ was shaped into a ball and subjects were instructed to use the object to make a rounded depression in the centre of the ball.

For the knife and novel tool, for the CU task, participants were presented with a ball of Blu-Tack™ and instructed to make a lined depression in the centre (see Figure 43). This could be achieved with a cutting motion with the blade, however, other methods of use were available.

For the NU task, participants were presented with a flattened circular piece of Blu-Tack™ that was stuck to the surface of the desk (see Figure 42). Participants were instructed to use the object to remove the Blu-Tack™ from the table surface, this would need to be carried out using a scraping motion.

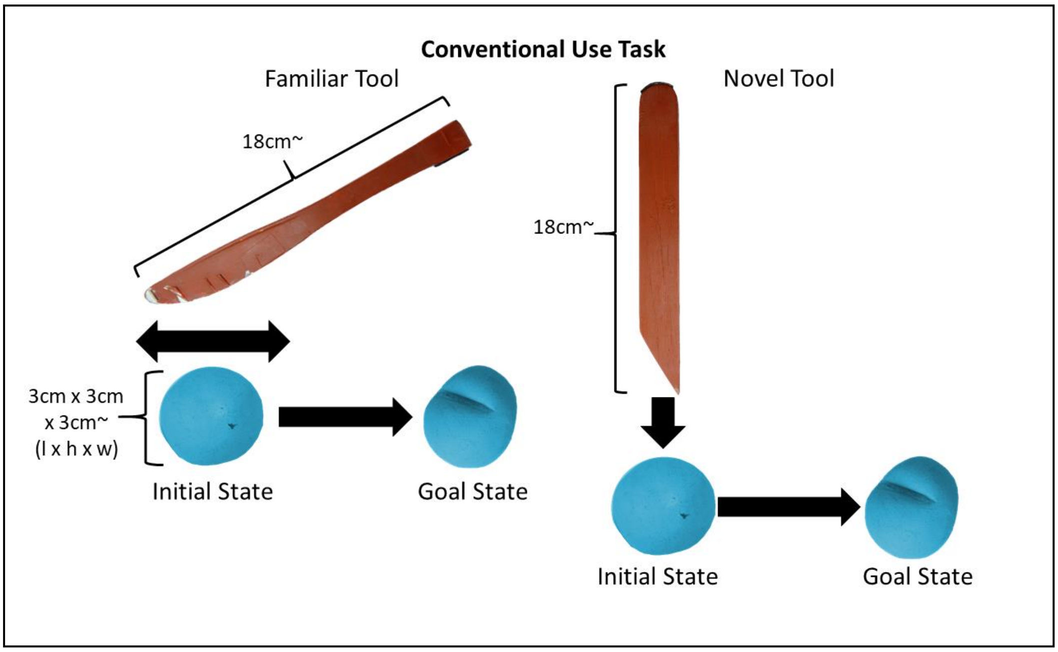

Figure 43. Conventional use task for the knife and novel comparative familiar and novel tool. Participants were instructed to change the object from 'initial' to 'goal' state, but given no specific instructions how to do so. This task allowed conventional cutting use of the knife and the novel tool could be used similarly.

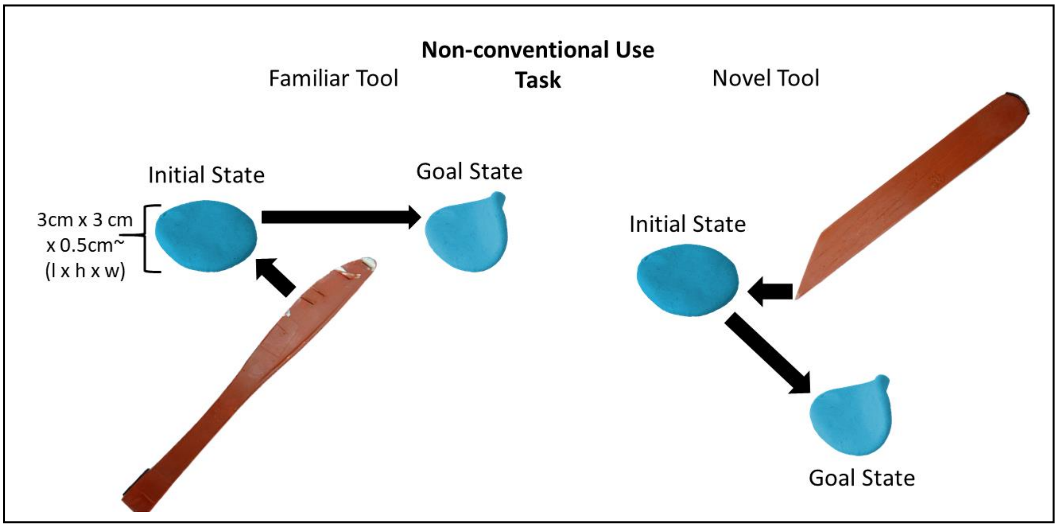

Figure 42. Non-Conventional use task for the knife and novel comparative familiar and novel tool. Participants were instructed to remove the target from its stuck position on the plinth.

For the screwdriver and novel tool, for the CU task, participants were presented with a cardboard box with a rotatable circle in the centre of the face presented horizontally towards subjects on the table (see Figure 44). Within the circle was a horizontal slot, with a black line oriented towards the edge of the circle. 90° clockwise was a corresponding black line, external to the circle on the surface of the box. Participants were instructed to use the object to rotate the circular part of the box so that the black lines formed a singular solid line. For the NU task, participants were presented with a horizontal, tubular piece of Blu-

Tack™, and instructed to bisect it medially. This could be achieved using a downward stabbing or cutting motion (Figure 45).

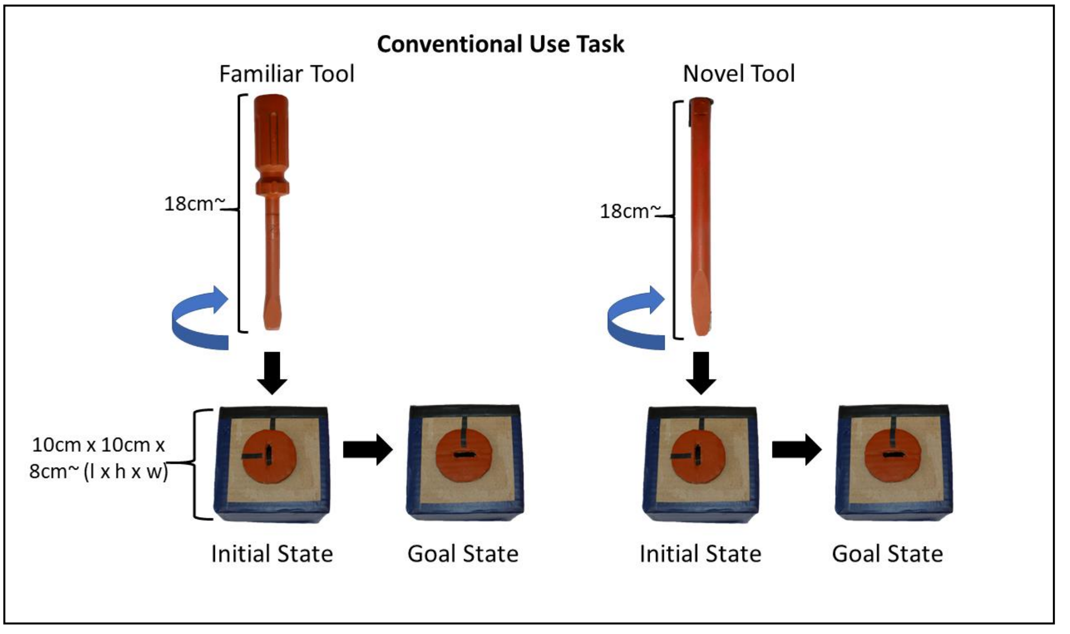

Figure 44. Conventional use task for the screwdriver and novel comparative familiar and novel tool. Participants were instructed to change the object from 'initial' to 'goal' state, but given no specific instructions how to do so. This task allowed conventional use of the screwdriver and the novel tool could be used similarly.

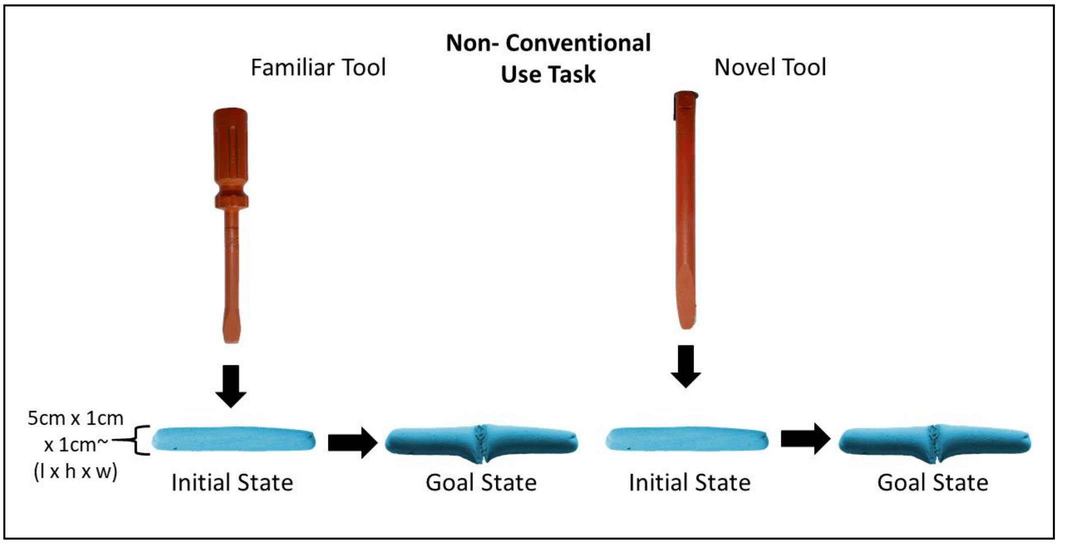

Figure 45. Non-Conventional use task for the screwdriver and novel comparative familiar and novel tool. Participants were instructed to change the object from 'initial' to 'goal' state, but given no specific instructions how to do so.

For each of the above tasks, participants were not provided a demonstration or instruction on how to use the presented object but were presented the target in its initial state followed by the end state. They were instructed to use the object to manipulate the target to the end state, with no specific instruction on how to carry out the action. This was intended to limit the preconception of how to use novel tools and explore how participants would interpret the best use of the object, or whether the influence of praxis associated with familiar tools would transfer to the use of novel objects for the same task.

For the transport task, participants were instructed to move the object from the cradle and place it on a wooden plinth placed in front of the cradle, as quickly and as accurately as possible.

6.2.2.2. Tool Presentation and Motion Tracking

Tools were presented in a cradle that could be rotated 180°, allowing presentation of the tool targets with the head in each of the 8 orientations. Participants' view of the target was controlled using PLATO shutter googles *(Translucent technologies, Toronto, Canada).* Motion tracking of participants' reaching movements was recorded using a Polhemus Fastrak *(Polhemus Fastrak, Colchester, Vermont, USA)* using three sensors sampling at 40Hz, attached to index finger, thumb and wrist, to allow examination of movement, hand orientation and grip aperture during reaching.

6.2.2.3. Localisation of Cortical Sites and TMS

Triple pulse (Magstim Rapid *(Magstim Company Ltd, Whitland, Carmarthenshire, UK)*, double 70mm coil, 100ms inter-pulse interval) TMS was administered for the experimental and control stimulation blocks. Triple pulse stimulation was applied to attempt to disrupt cognition pertaining to planning action, for the duration of planning prior to reaching. Cortical targets selected for testing were the left SMG (experimental) and anterior parieto-occipital arc (POc-a) (control site – this target was identified as a suitable control due to use as a control site in previous similar paradigms (Tunik et al., 2005)).

Frameless stereotaxic neuro-navigation *(Brainsight, Rogue-Research, Canada)* was used to mark the cortical targets on each participants' MRI and localize the coil position. The TMS coil was held tangentially to the surface of the scalp with the handle oriented upwards for both cortical sites. Motor threshold was determined as the stimulation intensity over M1 producing visible contraction of the hand muscles on 50% of 10 trials. Experimental stimulation was 110% of this stimulation intensity. As in Chapter 4, for the Sham condition the coil was placed, between the experimental and control sites of stimulation, one wing of the coil in contact with the scalp, with the centre of coil oriented between 45° and 90° away from the scalp.

Participants were provided with ear plugs to dampen the noise associated with TMS pulse discharge. A chin rest was used to maintain head position throughout testing.

6.2.3. Design

A repeated measures 3 x 3 x 2 x 8 design was used. The independent variables were Stimulation (aSMG, control site, Sham), Intention of action (Transport, CU, NU), Familiarity (Familiar, Novel) and Orientation (head of the object orientation; North, North-East, East, South-East, South, South-West, West, North-West). Participants completed altogether 9 blocks of 32 trials each (3 blocks for each of the three Stimulation conditions, 16 trials for novel and 16 for familiar tools for each block), as well as a control condition which instructed participants to lift their finger from the button and count to three before returning to initial position (10 trials). Stimulation block order was counterbalanced across subjects. For each block, participants were presented with one of the three familiar/novel tool pairings to ensure the novel object was as unfamiliar as possible on each stimulation condition. The order of tool presentation and stimulation condition was counterbalanced between participants (see Figure 46).

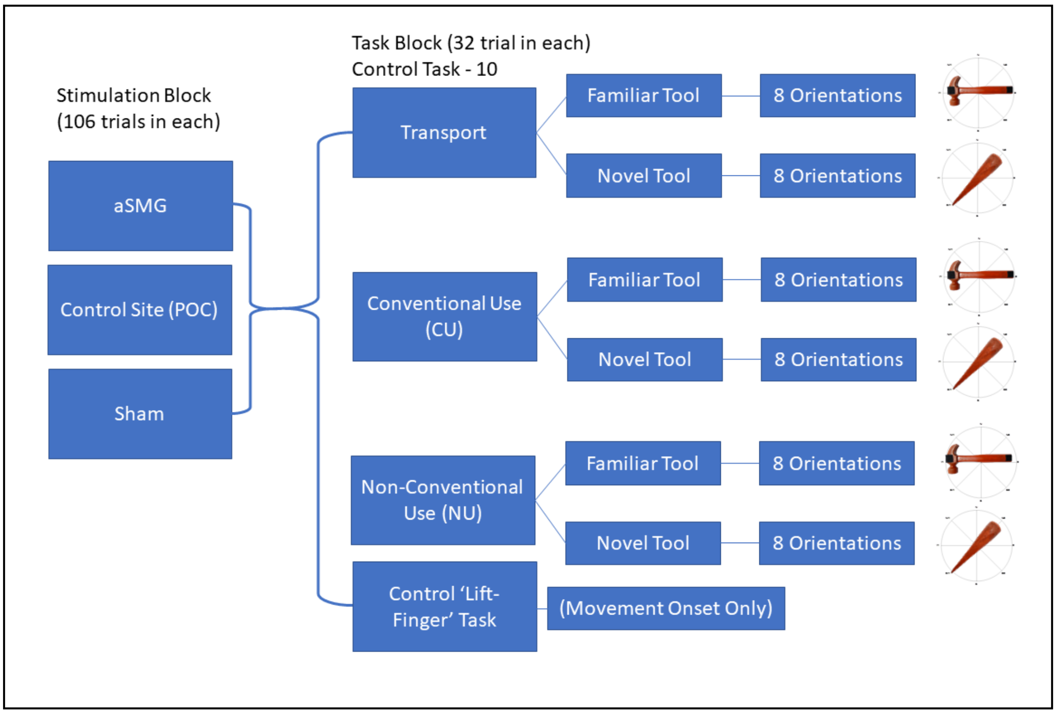

Figure 46. Diagram of blocks and conditions for the novel/familiar tool paradigm. Order of stimulation and intention task blocks was counterbalanced between participants.

6.2.3.1. *Dependent Measures*

As in the previous experiment (Chapter 5), dependent variables were the time to movement onset (MO) was defined as the time (ms) between goggles opening (target visible) and release of the button, indicating onset of participant movement. Movement Time (MT) defined as the time between MO and grasp completion, as measured from the maximum forward movement of the motion tracker towards target. Percent of MT to peak velocity of movement (TPV%), calculated as the percentage of movement time at which maximum movement velocity (cm/s) occurred between MO and MT. This parameter was used to determine the percentage of movement at which slowing occurred. Percent of MT to Peak aperture of grip (TPA%), measured as the percent of MT to maximum distance between the sensors attached the participants index finger and thumb during reaching between MO and MT. Percent of MT to Grasp selection (TGS%), defined as the percentage of MT that rotation of the forearm (degrees) was consistent ($\pm$ 10° for a minimum of three consecutive samples) with rotation of the forearm at the time of grasp completion. This measure quantified the percentage of reach at which the participant had selected the grasp orientation for the object.

6.2.4. Procedure

The experimental procedure for the current paradigm was executed in a similar manner to that reported in Chapter 5, with the addition of TMS and two further novel and familiar tool pairs and corresponding tasks. Participants were seated at a desk with their chin positioned on a chin rest and PLATO goggles in front for their eyes. The chin rest was used to maintain head position, and ease consistency in coil positioning during TMS and action execution. Participants were instructed as to the goal of action at the onset of each block of trials. For use tasks, participants were shown the target in its initial state, and instructed to use the tool to change it to the desired state, without specific instruction or demonstration on how to do this. At the onset of each trial, participants were provided a ‘get ready’ and ‘go’ signal from the researcher. At the ‘go’ signal participants were instructed to hold down the start position button and to wait for the shutter goggles to become transparent. They were instructed to carry out the task as quickly and accurately as possible following the goggles opening. At the onset of goggles opening, three TMS pulses were delivered in 100ms intervals. Participants were instructed to press the button once the action had been completed to end the trial (see Figure 47). The duration of each block was ~15mins. The whole procedures lasted ~2.5 hours including breaks.

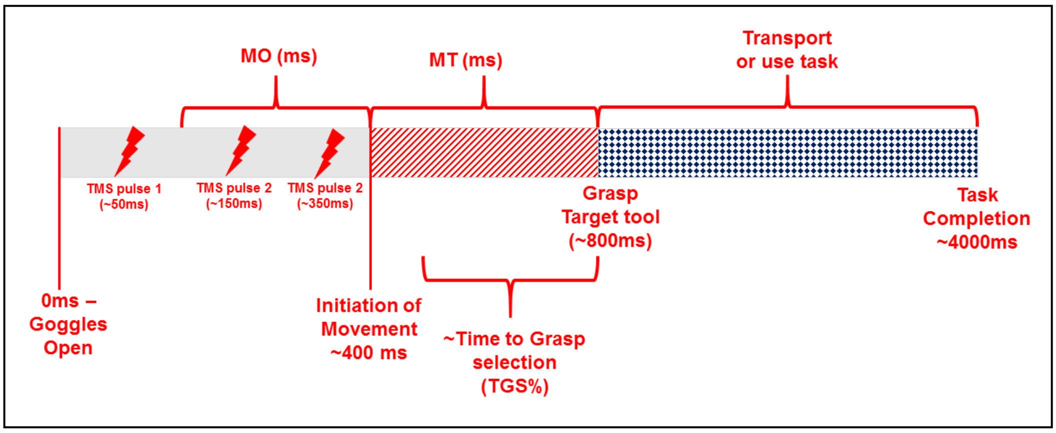

Figure 47. Estimated example trial timeline for an individual trial. Triple pulse TMS – first pulse delivered at approx. 50ms after goggles opening. This was designed to disrupt action planning prior to action execution.

6.3. Results

All data from 8 participants was processed for analysis (One participant's data was excluded from analysis due to overt delays in Movement Onset, and Movement Time). Total functional grasp (i.e. with thumb toward the head of tool) of tools are summarised in supplementary Table 11, Appendix B., pg.197. However, as with Chapter 5, no grasp was specifically instructed, and use could be accomplished in a number of ways. Therefore, analysis prioritised examination of early movement kinematics.

A repeated measures 3 (Stimulation) x 3 (Intention) x 2 (Familiarity) x 8 (Orientation) ANOVA was conducted for each of the kinematic dependent measures. For analysis inclusive of Stimulation Site, Intention and Orientation, Greenhouse-Geisser corrected F and p values were reported (with uncorrected *df*). For a full summary of mean data see appendices (Table 12, pg. 198, Table 13, pg. 199, Table 14, pg. 200).

6.3.1. Movement Onset (MO)

For MO, a 3 x 4 (Stimulation x Intention - collapsed across Familiarity and Orientation) ANOVA was conducted first to compare movement onset for Transport and Use against the control 'Finger Lift' condition across stimulation conditions. No significant effects of Stimulation $(F_{(2, 14)} = 0.36, p=.70)$ or Intention $(F_{(3, 21)} = 2.20, p=.11)$ or interaction between these factors $(F_{(6, 42)} = 1.14, p=.35)$ were observed, contrary to the hypothesis.

Table 9. Summary of Movement onset (ms) across Stimulation and Intention conditions (collapsed across Familiarity and Orientation). M (±SE).

Stimulation	Intention			
	Transport	CU	NU	Control – 'Lift'
Sham	316 (17.77)	327 (18.30)	342 (18.49)	304 (30.32)
aSMG	324 (18.91)	315 (13.55)	334 (18.07)	315 (37.70)
POC	336 (16.75)	343 (20.30)	354 (17.89)	288 (25.21)

The subsequent 3 x 3 x 2 x 8 ANOVA was carried out for participant data without the control task. An effect of Intention was observed *($F_{(2, 14)} = 5.46$, $p=.02$)*, showing significantly higher MO for the NU task *(M±SE = 343±16ms)* compared to the Transport *(M±SE = 325±15ms, p= .01)* and CU *(M±SE = 328±16ms, p = .02)* tasks, inconsistent with expected outcomes. No effect of Familiarity *($F_{(1, 7)} = 0.99$, $p=.35$)*, Stimulation *($F_{(2, 14)} = 2.72$, $p=.10$)* or Orientation *($F_{(7, 49)} = 0.76$, $p=.62$)* was observed for MO, failing to support the hypothesis. No significant interactions were observed between variables (see Table 10, pg. 162).

6.3.2. Movement Time

An effect of Intention *($F_{(2, 14)} = 5.46$, $p=.02$)* showed significantly lower MT for the Transport task *(M±SE = 553±25ms)* compared to both CU *(M±SE = 617±32ms)* and NU *(M±SE = 653±34ms)* tasks, consistent with expected outcomes as intention to *use* objects, should be more demanding in processing affordances and tool-object interactions, resulting in longer movement time.

A main effect of Orientation *($F_{(7, 49)} = 4.94$, $p<.01$)* showing significantly lower reach times for objects placed in the *West* direction *(M±SE = 564±28ms)* than any other orientation (see Appendix C., pg. 198, Table 13, Table 14), this is consistent with the orientation effect (Symes et al., 2005, 2007; Tucker & Ellis, 1998) as the *West* orientation presents the most graspable aspect of the objects congruently with the effector hand. However, there was no observed interaction between Familiarity and Orientation *($F_{(7, 49)} = 1.11$, $p=.37$)*, suggesting no influence of familiarity on the orientation effect. No main effects of Stimulation *($F_{(2, 14)} = 1.31$, $p=.30$)* or Familiarity *($F_{(1, 7)} = 0.19$, $p=.67$)* or interactions between variables were observed (Table 10, pg. 162), contrary to the expected outcomes.

6.3.4. Percent Time to Peak Velocity (TPV%)

A main effect of Intention *($F_{(2, 14)} = 16.35$, $p<.01$)* revealed significantly later TPV% for the Transport task *(M±SE = 62.06±1.38 TPV%)* than for the CU *(M±SE = 57.48±1.63 TPV%)* or NU *(M±SE = 57.51±1.69 TPV%)* tasks. This is consistent with the expected outcomes as grasping for transport does not require a functional grip or processing the functional elements of the tool resulting in a shorter period of deceleration toward the target.

An effect of Orientation *($F_{(7, 49)}$ = 12.83, p<.01)* showed significantly later TPV% for objects presented in the *West* orientation *(M±SE = 62.92±1.62 TPV%)* than for any other (*North: M±SE = 56.78±1.39 TPV%, North-East: M±SE = 58.20±1.59 TPV%, East: M±SE = 60.64±1.54 TPV%, South-East: M±SE = 55.90±2.08 TPV%, South: M±SE = 57.19±1.65 TPV%, North-West: M±SE = 58.76±1.45 TPV%*), with the exception of the *South West (M±SE = 61.77±1.51 TPV%)*. This is consistent with the observed effect in MT of congruently orienting the graspable aspects of tools with the effector hand.

A Stimulation x Intention (*$F_{(4, 28)}$ = 4.52, p=.03*) interaction revealed earlier TPV% in the CU task for aSMG stimulation (*M±SE = 55.64±2.5 TPV%)* compared to Sham (*M±SE = 58.22±1.21 TPV%*) and Control Site (*M±SE = 58.59±1.85 TPV%*) stimulation. For the Transport task Sham TPV% *(M±SE = 63.66 ±1.16 TPV%)* was higher than both aSMG (*M±SE = 61.87±1.52 TPV%*) and Control (*M±SE = 60.65±1.96 TPV%*). While for the NU task Control stimulation *(M±SE = 59.52±1.95 TPV%)* resulted in higher TPV% than aSMG (*M±SE = 56.65±1.8 TPV%*) and Sham (*M±SE = 56.37 ±1.92 TPV%*) (see Figure

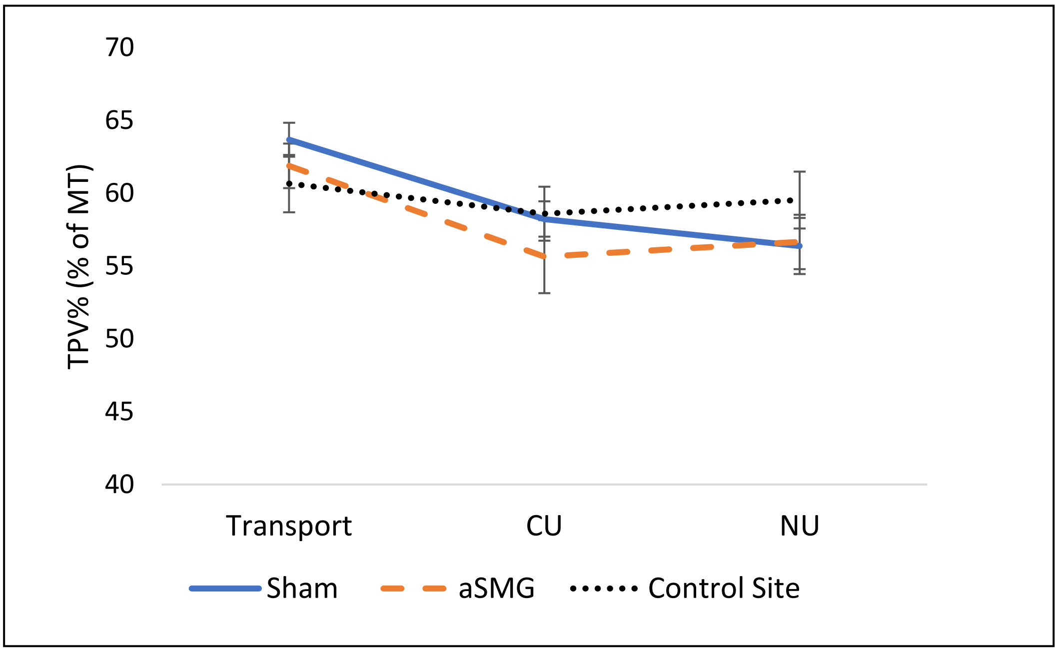

Figure 48. Interaction observed between Stimulation and Intention ($F_{(4, 28)}$ = 4.52, p=.03) of action observed for percent of MT to peak velocity (TPV%). Error bars indicate ±1 SE of the mean.

48). This is inconsistent with the hypothesis, in that aSMG stimulation for the familiar use tasks results in longer period of deceleration but not for the NU task or Transport. This may be due to disruption of access to representations of familiar use for the goal-oriented action at the onset of movement resulting in a longer period of slowed movement toward the target, however this does not account for the delay in TPV% for Control stimulation for non-conventional use.

An Intention x Orientation interaction ($F_{(14, 98)} = 2.39$, $p = .007$) showed that for the Transport task, TPV% was later for objects with the head oriented in the East (*M±SE = 65.47±1.81 TPV%*), South East (*M±SE = 60.19±2.32 TPV%*) and West (*M±SE = 66.77±1.95 TPV%*) orientations compared to the same orientations for CU (*East: M±SE = 56.93±1.77 TPV%, South East: M±SE = 53.60±2.4 TPV%, West: M±SE = 60.69±1.51 TPV%*) and NU tasks (*East: M±SE = 59.54±1.86 TPV%, South East: M±SE = 53.90±2.48 TPV%, West: M±SE = 61.29±2.14 TPV%*), (see Figure 49). This is consistent with the expected outcomes and end state comfort for use of objects (Rosenbaum et al., 1990; W. Zhang & Rosenbaum, 2008).

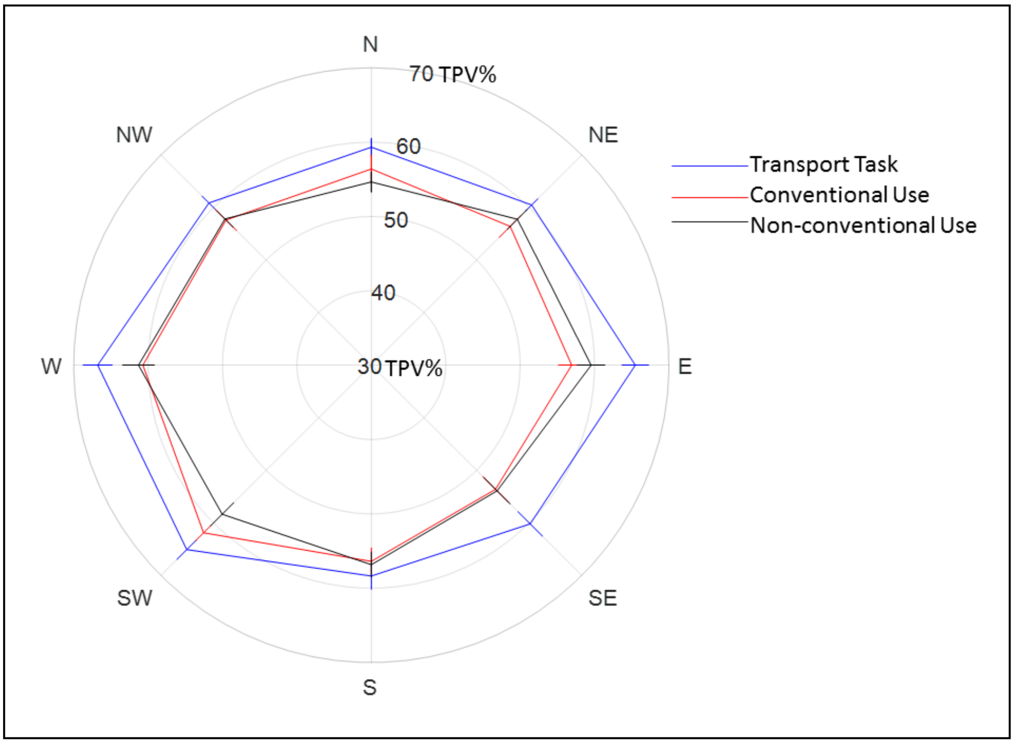

Figure 49. Interaction observed between Intention of action and Orientation ($F_{(14, 98)} = 2.39$, $p = .007$) for percent of MT to peak velocity (TPV%). Error bars indicate ±1 SE of the mean.

For the transport task, position of the head of the tool (in relation to body posture and target to be affected) is not integral to grasp planning. In both CU and

NU, it is more important to consider these factors, and as such, earlier TPV% reflects a larger period of deceleration for both *use* tasks as a function of orientation. No other main effects or interactions were observed for TPV% (see Table 10, pg. 162).

6.3.5. Percent Time to Peak Aperture (TPA%)

A main effect of Orientation ($F_{(7, 49)} = 5.53, p < .001$) showed that the objects oriented in the *East (M±SE = 71.92±0.93 TPA%)*, *West (M±SE = 72.88±1.67 TPA%)* and *South-West (M±SE = 72.91±1.32 TPA%)* reached peak aperture earlier than the other orientation conditions (*North: M±SE = 77.41±1.49 TPA%, North-East: M±SE = 75.47±1.17 TPA%, South-East: M±SE = 73.98±1.79 TPA%, South: M±SE = 78.79±1.85 TPA%, North-West: M±SE = 77.91±1.32 TPA%*) (see Figure 50). This is likely due to the horizontal presentation of the target objects in these orientations, which seems to elicit earlier aperture compared to the other orientations which require pronation or supination of the forearm. No effects of Familiarity ($F_{(1, 7)} = 0.92, p = .37$) or Intention of action ($F_{(2, 14)} = 0.95, p = .49$) were observed for TPA%. No other interactions were observable for TPA% (see Table 10, pg. 162).

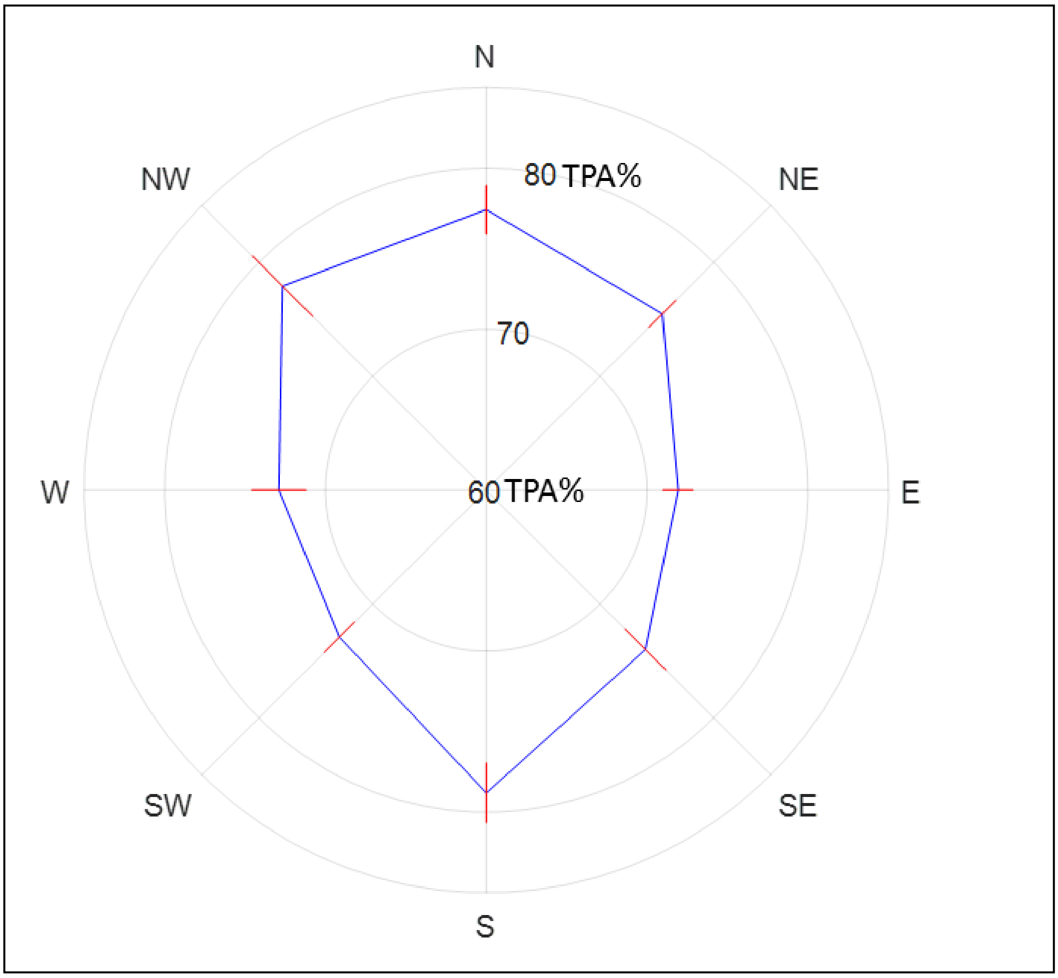

Figure 50. Main effect of Orientation observed ($F_{(7, 49)} = 5.53$, $p < .001$) for percent of MT to peak aperture (TPA%). Error bars indicate ±1 SE of the mean.

6.3.6. Percent Time to Grasp Selection (TGS%)

A main effect of Intention *($F_{(2, 14)}$ = 7.49, p=.006)* revealed significantly earlier TGS% for the Transport task *(M±SE = 36.71±1.73 TGS%)* compared to both CU *(M±SE = 41.98±1.31 TGS%)* and NU *(M±SE = 41.24±1.31 TGS%)* (see Figure 51). This is consistent with the findings in TPV% and MT and the expected outcomes. Grasp selection should occur later with the intention of *use* due to additional processing of tool-body posture in relation to the target to be affected. For Transport, the absence of this processing results in earlier selection of grasp orientation.

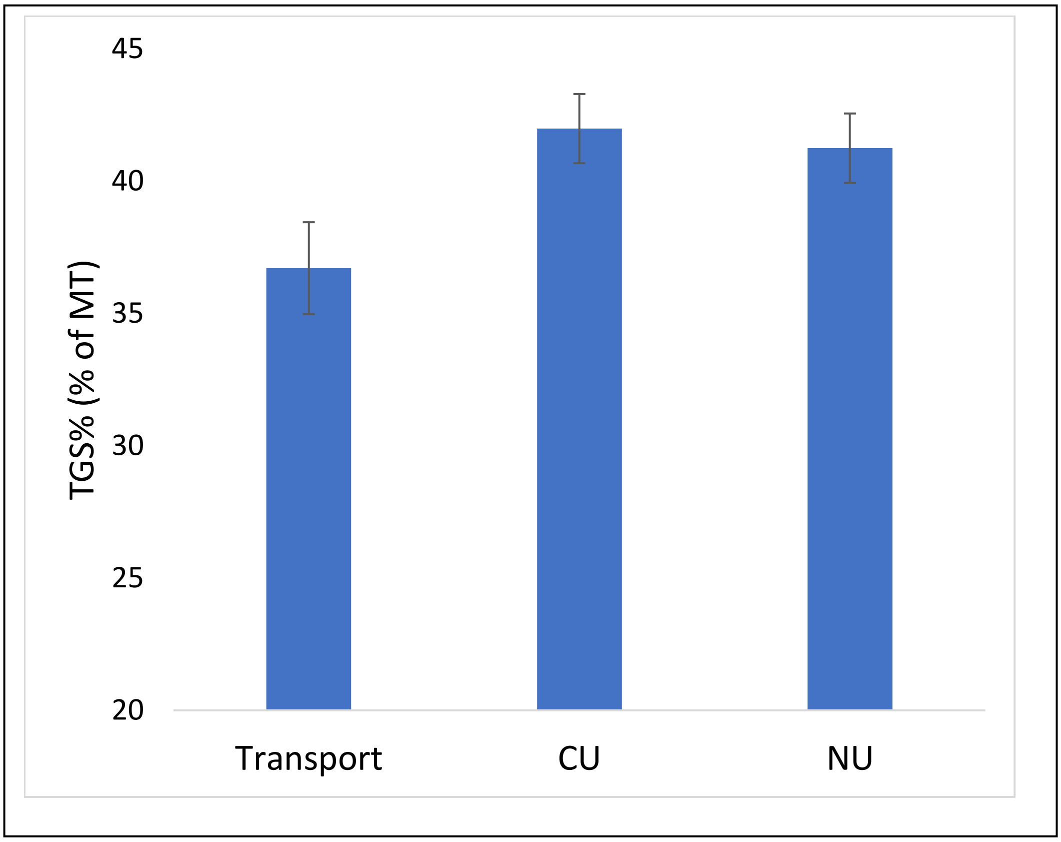

Figure 51. Main effect of action intention ($F_{(2, 14)}$ = 7.49, p=.006) observed for percent of MT to grasp selection (TGS%). Error bars indicate ±1 SE of the mean.

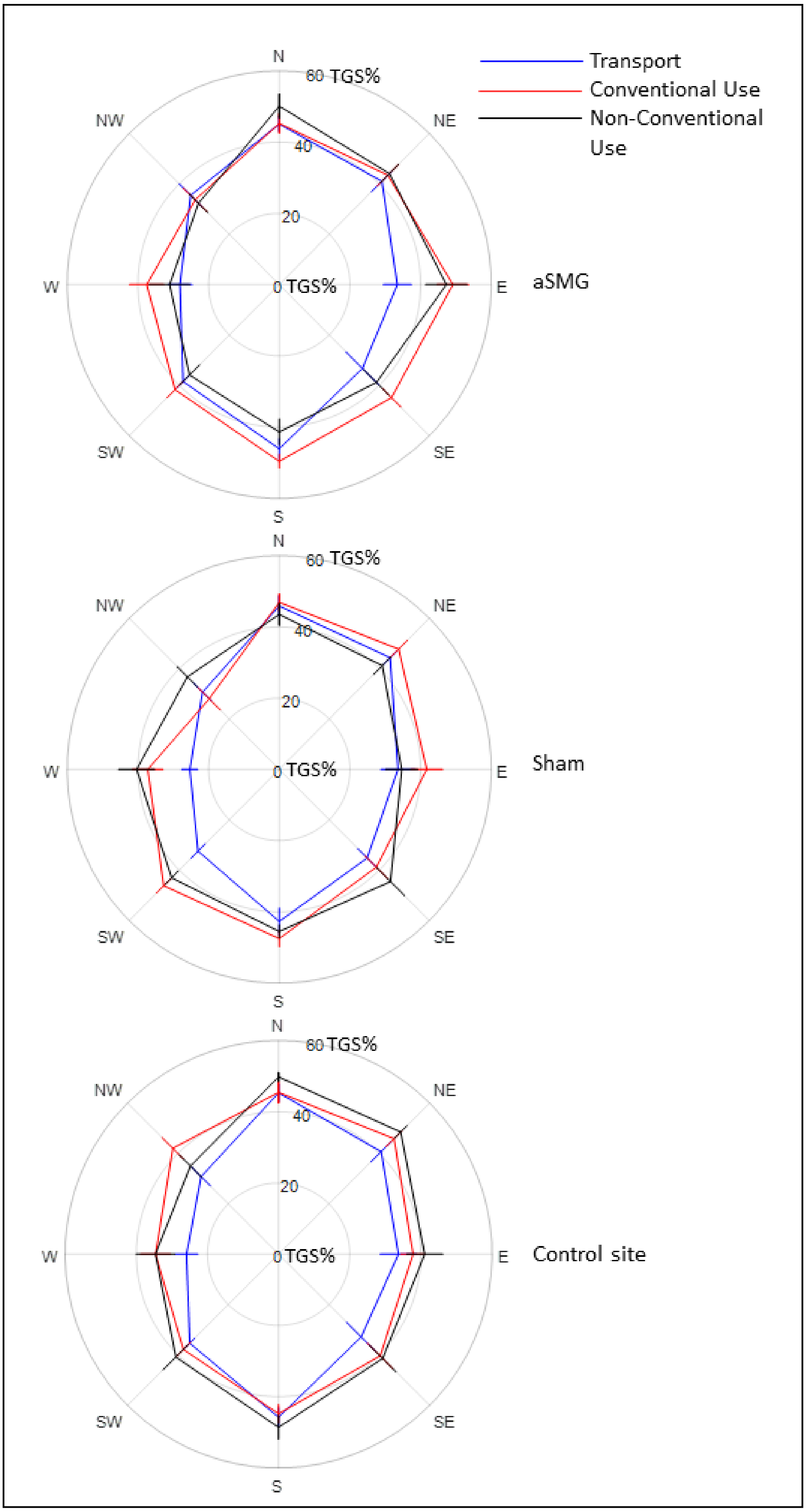

Figure 52. Interaction observed between Intention of action and Orientation conditions conducted for each Stimulation condition (collapsed across Familiarity) for TGS%; aSMG (p = .038), Sham (p= .13) or Control site (p= .81). Error bars indicate ±1 SE of the mean.

A significant main effect of orientation showed earlier TGS% for *West* *(M±SE = 33.84±1.98 TGS%)* and *North-West* orientations *(M±SE = 32.71±1.63 TGS%)* than any other orientation (*North: M±SE = 46.34±1.32 TGS%, North-East: M±SE = 44.09±1.29 TGS%, East: M±SE = 39.12 ±1.89 TGS%, South-East: M±SE = 38.88±2.30 TGS%, South: M±SE =45.76±1.52 TGS%, South-West: M±SE = 39.08±1.98 TGS%*). This is consistent with expected outcomes and findings in movement time, as grasp selection occurs earlier for orientations in which the graspable elements of the tools are oriented congruently with the effector hand.

A significant interaction between Stimulation, Intention and Orientation ($F_{(28, 196)} = 1.59, p= .038$). To explore this further, subsequent 3 x 8 (Intention x Orientation) ANOVAs for each of the individual stimulation conditions were conducted.

For aSMG stimulation, a significant Intention x Orientation interaction ($F_{(14, 98)} = 2.01, p = .038$) highlighted that for objects oriented to the *East*, CU *(M±SE = 49.07±4.51 TGS%)* and NU *(M±SE = 47.25±5.88 TGS%)*, TGS% was later than for Transport *(M±SE = 45.06±2.08 TGS%).* This was not observed in any other orientation (see Figure 52). A main effect of Orientation ($F_{(7, 49)} = 3.09, p<.01, p = .009$) was observed, but no observable effect of Intention ($F_{(2, 14)} = 2.56, p = .112$).

For sham stimulation, the Intention x Orientation interaction was not statistically significant ($F_{(2, 14)} =1.60, p=.13$, see Figure 52). However, main effects of Intention ($F_{(2, 14)} = 6.69, p = .009$) and Orientation ($F_{(7, 49)} = 5.30, p<.0001$) were observable for sham.

For control site stimulation, main effects were observed for Intention ($F_{(2, 14)} = 4.41, p = .033$) and Orientation ($F_{(7, 49)} = 4.78, p<.0001$), however no interaction was observed between these variables ($F_{(14, 98)} = 0.57, p = .81$, see Figure 52).

These findings are partly consistent with the expected outcomes, in that stimulation of the aSMG delayed selection of grasp. However, this was only observable for orientations in which the tool handle (or non-functional head of the tool) was oriented incongruently (East) with the effector hand. That this occurred for conditions requiring use, suggests that processing of the functional properties of the tool in relation to the posture required to implement use are disrupted by TMS during planning, resulting in delayed selection of grasp orientation during reaching. This is not the case for transportation of the tools as functional processing is not required for transport. This appears to affect both conventional and non-conventional use of tools as familiarity was not included within this interaction.

Table 10. Summary of repeated measures ANOVA for Stimulation Site, Intention of action, Familiarity and Orientation across the dependent measures (Movement Onset (MO) Movement Time (MT), percent of MT to peak velocity (TPV%) and peak aperture (TPA%). Analysis inclusive of Stimulation Site, Intention and Orientation results are reported as Greenhouse-Geisser corrected F and p values. ***Bold*** *values indicate significance at p< .05 level.*

	MO		MT		TGS%		TPV%		TPA%	
	F	*p*	*F*	*p*	*F*	*p*	*F*	*p*	*F*	*p*
Stimulation Site	2.73	0.11	1.31	0.30	0.07	0.90	0.89	0.42	0.27	0.71
Intention	**5.47**	**0.02**	**9.66**	**0.01**	**7.49**	**0.01**	**16.35**	**0.00**	0.95	0.39
Familiarity	1.00	0.35	0.19	0.67	0.48	0.51	0.39	0.55	0.93	0.37
Orientation	0.76	0.54	**4.94**	**0.01**	**13.54**	**0.00**	**12.84**	**0.00**	**5.53**	**0.00**
Stimulation Site x Intention	0.35	0.73	3.31	0.09	0.82	0.47	**4.53**	**0.03**	1.68	0.23
Stimulation Site x Familiarity	0.52	0.56	0.50	0.59	3.12	0.08	0.80	0.45	2.39	0.14
Intention x Familiarity	0.03	0.94	0.35	0.61	1.71	0.23	0.60	0.54	0.03	0.93
Stimulation Site x Intention x Familiarity	0.57	0.61	0.24	0.71	0.73	0.53	1.18	0.34	1.23	0.32
Stimulation Site x Orientation	0.77	0.56	0.60	0.65	0.45	0.77	0.64	0.62	0.58	0.64
Intention x Orientation	0.87	0.50	1.05	0.39	0.99	0.44	2.39	0.06	0.91	0.47
Stimulation Site x Intention x Orientation	0.63	0.69	0.68	0.59	**1.59**	**0.04**	1.47	0.22	0.97	0.44
Familiarity x Orientation	1.05	0.39	1.11	0.36	0.78	0.52	1.54	0.22	0.38	0.76
Stimulation Site x Familiarity x Orientation	0.95	0.45	0.97	0.43	0.88	0.49	0.60	0.70	1.33	0.28
Intention x Familiarity x Orientation	0.63	0.66	1.68	0.20	1.56	0.20	0.74	0.58	2.04	0.11
Stimulation Site x Intention x Familiarity x Orientation	1.16	0.35	0.96	0.42	0.99	0.44	0.77	0.58	0.71	0.61

6.4. Discussion

This experiment revealed a significant delay to selection of grasp orientation as a result of aSMG stimulation. This effect was dependent upon the goal-oriented task as a function of the tool orientation. The delay occurred for both conventional and non-conventional use of objects. This finding is consistent with the hypothesis, in that both use conditions require greater integration of technical reasoning; these tasks require processing the functional and mechanical properties of the tool, the target for action as well as the position, posture and orientation of the tool for functional use. The transport condition was not affected by TMS-related delay, likely due to limited requirement for processing allocentric relationships between tools and targets for action, as the goal was to move the tool from one location to another without affecting change on an external object. This is not to say that all transportation tasks can be achieved without processing the tool and environment factors such as weight, stability and shape (Osiurak, 2014b; Osiurak et al., 2010; Osiurak, Roche, et al., 2013), but that this is highly reliant on context. As transportation in this experiment was consistently from cradle to wooden plinth, it is likely that this allowed relatively simple processing of the structural affordances of object and destination consistently throughout the task.

These findings support the technical reasoning account of the aSMG role in tool use processing (Goldenberg & Hagmann, 1998; Hartmann et al., 2005; Lesourd et al., 2017; Osiurak & Badets, 2016, 2017; Reynaud et al., 2016). Stimulation over the aSMG delayed grasp selection for both conventional and non-conventional use, suggesting an association with technical reasoning. Furthermore, this occurred predominantly for tools oriented in the *East* orientation, for which the most saliently graspable aspects of the tools would be oriented incongruently with the participant's effector hand. This suggests that the aSMG processes egocentric relationships during action planning in consideration of the tool-hand position for selection of grasp. That this occurs for use suggests further processing of the allocentric relationships between the tools and targets for action. That both elements of tool and user relationships are considered is consistent with the technical reasoning account of aSMG integration (Orban &

Caruana, 2014; Osiurak & Badets, 2017; Reynaud et al., 2016). What is unclear is why aSMG stimulation failed to elicit delays to movement onset. This contrasts with previous object manipulation findings for SMG stimulation for similar tasks (Tunik et al., 2008). Tunik et al., (2008) showed that SMG stimulation delayed the onset of movement; tool grasping was efficient but occurred later as a result of delayed movement onset. In these findings, movement onset was not significantly delayed, but grasp selection occurred later into the reach for aSMG stimulation. TMS over the aSMG during planning stages likely delayed the integration of technical reasoning into visuomotor systems for execution (e.g. dorso-dorsal structures – aIPS and SPL). Technical reasoning in the case of use addresses the mechanical properties of the tool and target for action. The visuomotor processing necessary for moving the hand toward the target is not disrupted by aSMG TMS and allows for initiation of movement. Selection of grasp occurs later in the reach once salient information pertaining to the allocentric relationship between tools and target (i.e. technical reasoning) is available to dorso-dorsal structures which then process the necessary egocentric elements of the planned action. These structures can then alter the grasp orientation (e.g. egocentric relationship between hand and tool) to suitably fit the goal state to effectively make use of the tool. This account is consistent with the aSMG role proposed by the technical-reasoning model.

These findings fail to support a familiar tool preference for aSMG in line with the 2AS+ model (Brandi et al., 2014; Buxbaum, 2017; Grafton, Fadiga, Arbib, & Rizzolatti, 1997; Vingerhoets, 2008). The deficits in selection of grasp for use were not affected by familiarity with tools or conventional tool use, suggesting a lack of influence of stored representations, which are central to forming tool gestures for the manipulation-based approach. The 2AS+ model argues that novel tool use is facilitated by abstraction of the multisensory representations of tool use (Buxbaum, 2017; Rijntjes et al., 2012; van Elk, 2014) to the specific goal-oriented task, fine-tuned by affordance perception and technical reasoning (Buxbaum, 2017). Abstraction also allows access to the most similar (but not identical) representation that is pertinent to the task at hand (Buxbaum, 2017; Jax & Buxbaum, 2010). However, the demands of adjusting a stored representation for swinging a hammer to another object that can be used for the same purpose, should be more computationally demanding than just accessing the representation with minimal need for adjustment. This is somewhat reflected in the movement onset data, due to non-conventional use tasks being initiated later than both conventional use and transportation. This could arguably reflect stored representations of conventional use and transport being more readily accessible than non-conventional use tasks, which would require additional processing. However, there was no observable influence of familiarity with the tool itself. The manipulation-based approach has previously argued that viewing objects can prime the representations of actions associated with them (Borghi & Riggio, 2009; Caligiore et al., 2010; Mizelle & Wheaton, 2010; Pellicano et al., 2010a; Thill et al., 2013), therefore, it should be expected that familiar actions with familiar tools should be initiated quicker than for novel tools/actions. This is not observable here and is problematic for the 2AS+ interpretation.

The lack of familiarity influence in this experiment may be accounted for by the fact that tool-target pairs were not associated as strongly as they would be in common tool use activity (e.g. hammer and nail). This was designed as a control to ensure that novel tools would be comparable with the familiar, as there were no ready associated objects for action for the novel tools. It may be the case that manipulation knowledge for the hammer would be more readily accessible if the target for action was distinctly a nail. However, this arguably falls within the remit of function knowledge (Osiurak & Badets, 2017; Reynaud et al., 2016), associated with contextual knowledge about tools and limits the transferability of manipulation knowledge across tool use scenarios. Therefore, this account negates processing the functional and mechanical properties of the tool in relation to the target for action (i.e. allocentric relationship).

The kinematic data also fail to support the 2AS+ model with regards to the orientation effect (Symes et al., 2005, 2007; Symes, Tucker, Ellis, Vainio, & Ottoboni, 2008). Movement time, %TPV and %TGS all revealed a significant effect of orientation, showing that objects with the most graspable aspects oriented congruently with the effector hand elicited faster reaching, earlier selection of grasp and later peak velocity. There was no observable interaction with familiarity, which suggests that stored representations are likely not used to prime or facilitate quicker or more accurate action on familiar tools (Borghi & Riggio, 2009; Caligiore et al., 2010; Mizelle & Wheaton, 2010; Pellicano et al., 2010a). Rather, dorso-dorsal structures, in line with the technical reasoning approach (Osiurak & Badets, 2017; Reynaud et al., 2016), process the most saliently graspable structures of the object (Symes et al., 2005, 2007). That this interacts with action intention (but not familiarity) for aSMG stimulation in selection of grasp, further supports the technical reasoning interpretation of these findings. This also provides some clarity to the orientation effect observed in Chapter 5; interactions between orientation and familiarity were difficult to explain under the 2AS+ model and could not clearly be attributed to familiarity activating stored manipulation knowledge. However, given that no interaction with familiarity is observable with multiple novel and familiar tools, the findings in the previous chapter are more easily explained by processing of the structural properties of the tools in those particular orientations, in line with the technical reasoning approach.

The 2AS+ model aSMG role (a buffer for selection of object manipulation actions) (Buxbaum, 2017; Caligiore et al., 2010; van Elk, 2014) is not supported by the present findings. Delays to selection of grasp were only observed for use actions as a function of orientation, but not for transport. If the aSMG acts as a buffer for appropriate object manipulation actions, delays should also impact on transport actions as well as use. The technical reasoning model can better account for these findings as both conventional and non-conventional use require understanding of the functional and mechanical properties of the tools and target. That this occurs for tools in the *East* orientation is likely due to the functional 'head' of the tools being oriented incongruently with the effector hand. The demands of integration of allocentric and egocentric (Osiurak & Badets, 2017; Reynaud et al., 2016) processing for grasp in this orientation means this integration is more susceptible to disruption from aSMG stimulation when use is required, resulting in the delays to selection of grasp orientation. However, as stated earlier, the influence of manipulation knowledge cannot be ruled out completely due to delayed movement onset for non-conventional use of objects, implicating stored representations of grasp and use. There are further avenues for research to consider, regarding the aSMG role and cognition pertaining to familiar and novel tool use. It might be the case that technical reasoning and manipulation knowledge work in tandem to facilitate action, drawing on previous representations for movements and posture, but driven predominantly by technical reasoning dependent on the goal of the task. The findings from this experiment cannot explicitly support such a model.

In conclusion, this experiment highlights an integral role of the aSMG in selection of grasp orientation for use of both novel and familiar objects as a function of affordance and orientation. These findings implicate that the aSMG provides an integrative role between affordance and body perception and technical reasoning based on understanding of the mechanical properties of objects for use. While these findings support a technical reasoning model, the influence of manipulation knowledge cannot be ruled out.

7. Discussion, New Directions for Research and Conclusions

This thesis aimed to address three key questions regarding the role of the SMG in selection of functional tool use grasp, while developing novel research methods and experiments. Over the course of five studies, findings have been observed that both conform with and elaborate on current neurocognitive models of tool use, while also opening avenues for experimental research in this field. In this chapter, each of the research questions will be discussed within the context of the cumulative findings.

7.1. What is the Role of the SMG in Selection of Appropriate Grasp of Tools for Use during Action Execution?

The SMG acts as a locus of integration between conceptual input pertaining to functional use of tools and the visuomotor functions necessary to facilitate action towards tools (Buxbaum, 2017; Buxbaum et al., 2007; Lesourd et al., 2017; Orban & Caruana, 2014; Osiurak & Badets, 2017; Przybylski & Kroliczak, 2017). This function is essential in action planning and compensating for changes to grasp planning during action execution. As outlined in the introduction, making use of a tool requires a functional understanding of the tool properties and the actions that they afford (Buxbaum, 2001; Johnson-Frey et al., 2005; Orban & Caruana, 2014). For example, the flat head and weight of a hammer makes it suitable to strike another object. However, to select a functional grasp of the tool for use, one must also understand the affordances of the object in relation to the user’s own capabilities and body position (Osiurak, 2014a; Osiurak et al., 2010). For example, understanding that grasping a hammer by the handle, with the thumb oriented toward the head, and the head facing away from the user affords a powerful striking motion. The SMG serves to reconcile these two essential processes, facilitating accurate grasp planning for functional use (see Figure 53).

This is supported in the findings from experiments in Chapter 3, 4 and 6. In these experiments participants were instructed to grasp physical tools with the explicit instruction of demonstrating use. During reaching, the tools orientation was perturbed forcing a correction of grasp orientation to facilitate a functional grasp. Here, it is posited that this perturbation forces reintegration of the visuomotor processes (necessary to track rotation of the target tool in space and correct hand orientation) and conceptual tool knowledge (necessary to understand the functional elements of the tool that facilitate use). This reintegration, carried out within the SMG, allows adjustments to the grasp plan that factor both the rapid online correction and understanding of the tool and body posture that allows functional grasp. When TMS was applied over the SMG at the onset of tool perturbation, errors of miscorrection (delayed or erroneous correction) were observed in movement kinematics. Thus, it can be inferred that the SMG is critical in performing this integrative function.

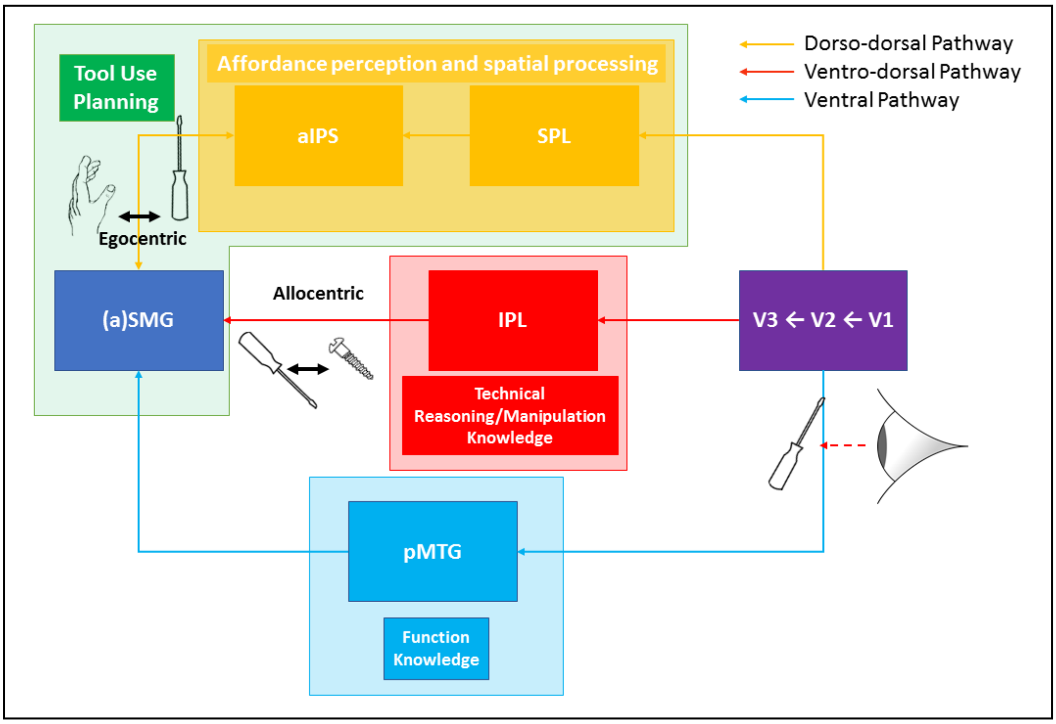

Figure 53. Flow diagram (adapted from Orban and Caruana, 2014) Depicting the role of the aSMG/SMG as supported by outcomes in this thesis. The aSMG/SMG supports integration of processing from 2 sources; (i) Dorso-dorsal structures for affordance perception and spatial processing (aIPS and SPL). (ii) Ventro-dorsal structures supporting technical reasoning/manipulation knowledge (IPL) Thus (a)SMG facilitates functional selection of grasp and use by integrating processing of egocentric and allocentric relationships. This allows accurate goal-oriented action planning, taking into account the functional elements of the tools, targets for action and the effector affordances in relation to the tool and environment. Function knowledge (likely supported by the pMTG) also shares connections with the SMG. However, the present findings are inconclusive as to whether this influences grasp selection during practical execution.

This is consistent with current models to the neural network facilitating tool use (Borghi, 2014; Buxbaum, 2017; Gallivan et al., 2013; Johnson-Frey et al., 2005; Orban & Caruana, 2014; Osiurak & Badets, 2017; Peeters et al., 2013;

Przybylski & Kroliczak, 2017; van Elk, 2014). The SMG, within the IPL is identified as part of the ventro-dorsal stream (Binkofski & Buxbaum, 2013a; Rizzolatti & Matelli, 2003), and shares connections with the pMTG (Ramayya et al., 2010), an area associated with understanding the function and contextually appropriate use of tools. It also shares cortical proximity (via the aIPS) with dorso-dorsal structures in the SPL, making it a likely point of integration between these two functions (Orban & Caruana, 2014). In functional imaging studies, the SMG is consistently highlighted as displaying heightened activation in response to tool related tasks or stimuli (Brandi et al., 2014; Chao et al., 1999; Chao & Martin, 2000; Negri, Lunardelli, Reverberi, Gigli, & Rumiati, 2007; Orban & Caruana, 2014; Peeters et al., 2013; Rumiati et al., 2004; Vingerhoets, 2014; Vingerhoets, Acke, et al., 2009). The present experimental outcomes are consistent with these findings. Furthermore, these outcomes are consistent with neuropsychological models of left parietal damage patients' deficits in tool manipulation and object grasping (Goldenberg & Spatt, 2009; Johnson-Frey, 2004; Niessen et al., 2014; Randerath et al., 2009). Disruption to grasp correction, as observed in Chapters 4 and 5 is reminiscent of deficits in barrier avoidance when grasping familiar tools in apraxic patients (Sunderland et al., 2013).

The findings in this thesis also elaborate on identifying when the SMG is involved in planning grasp actions for tools, with the explicit intention for use. Imaging research has highlighted SMG activation during planning and action execution of tool use (Brandi et al., 2014; Lesourd et al., 2017; Reynaud et al., 2016; Vingerhoets, 2014; Vingerhoets, Acke, et al., 2009). TMS research has also highlighted that the stimulation over the SMG prior to movement delays the onset of tool grasp actions suggesting a key role in action planning (Tunik et al., 2008). Following the ideomotor principle (Greenwald, 1970; Hommel et al., 2001; Massen & Prinz, 2007), the grasp plan should be established prior to action onset, in conjunction with input from the SMG relating to functional use of the tool. This ensures the motor control of action is guided by an expected perceptual effect (Badets & Osiurak, 2016; Hommel et al., 2001). The actual execution was previously argued to be monitored by dorso-dorsal structures, including compensation for online changes to the grasp plan (Cohen et al., 2009b; Osiurak & Badets, 2017; Rice et al., 2007; Tunik et al., 2005). However, findings in this

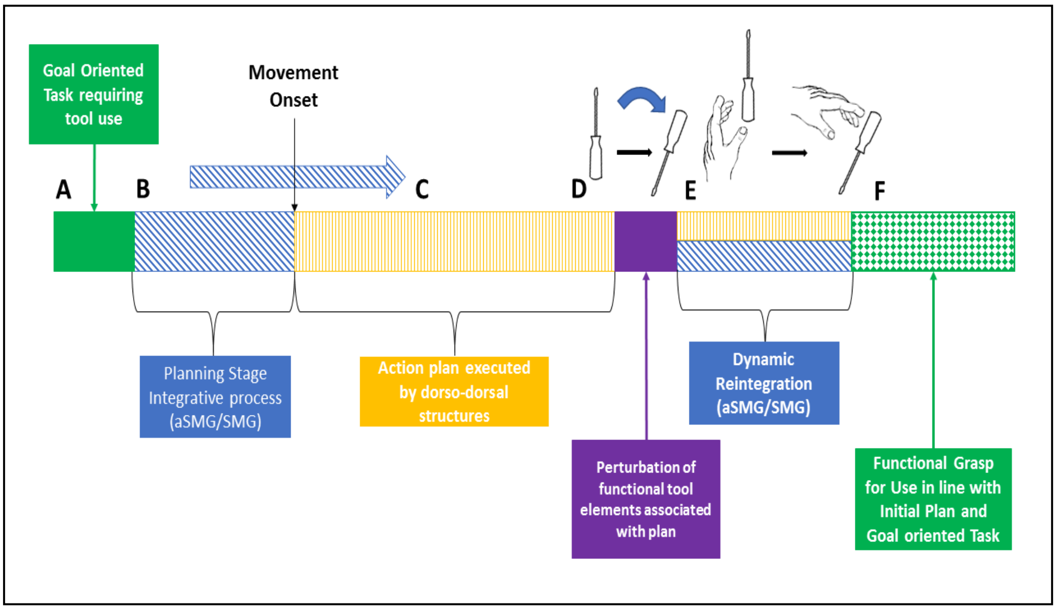

Figure 54. *A timeline of the SMG role and neurocognitive processes during selection of functional tool grasp for use. (**A**) Functional tool use is goal oriented with a specific intention to enact change on one object (e.g. a nail) with another (e.g. hammer) to fulfil a task. (**B**) The aSMG/SMG performs the integrative process between conceptual tool related knowledge (pertaining to functional elements of the tool in relation to the goal of task) into visuomotor structures that process affordances of the tool in relation to the user. This enables processing the egocentric and allocentric relationships necessary for functional use. Grasp plan is established and carried forward into execution stages of action. (**C**) Once the plan is in place, action execution is mediated by bilateral dorso-dorsal structures, processing spatial information about the position of the effector, tool and target for action, in line with the established grasp plan. (**D**) In experiments 1 to 5, perturbation of the functional elements of the tool that relate to the goal oriented action (i.e. rotation of the functional head of the tool) necessitates reassessment of the grasp plan to ensure functional use. (**E**) Dynamic reintegration from the (a)SMG into dorso-dorsal structures, processes the spatial changes and functionally salient properties of the tool to allow compensation of grasp. This ensures a grasp orientation that is consistent with the established action plan and goal of the task. (**F**) Functional grasp orientation is achieved allowing functional use of the tool, in line with the initial grasp plan.*

thesis indicate that the SMG performs dynamic reintegration of salient tool knowledge when changes to the tools orientation necessitate it. This highlights that the SMG plays a dynamic role in monitoring the conceptual fit between hand and tool target, pertaining to grasping the tool in a manner suitable for functional use, as well as understanding the tool properties in relation to the task goal (Buxbaum, 2017; Lesourd et al., 2017; Reynaud et al., 2016). Dorso-dorsal structures such as the aIPS and SPL may monitor the physical fit between hand and object, responsible for grip size in relation to the tool dimensions, as well as transport of the effector hand to the target tool (Brandi et al., 2014; Gallivan et al., 2013; Orban & Caruana, 2014; Tunik et al., 2005) (see Figure 54). However, the question remains as to whether the SMG is involved in consistently monitoring the conceptual fit between hand and tool during action execution or whether this occurs as a direct result of perturbation of salient tool features (in the case of these experiments, rapid change in orientation of the functional head of the tool).

An alternative account of these findings is that the SMG consistently monitors the conceptual fit between hand and tool during the course of reaching to ensure that the goal state of how the tool should be positioned in the hand is maintained. In this interpretation, on perturbation of the tool, cross talk between the SMG and action production systems (Orban & Caruana, 2014) facilitates rapid online correction for functional grasp. This is delayed by TMS over the SMG in the case of the present studies. However, it would be expected to see disruption of grasp orientation selection (e.g. delayed orientation of grasp) when reaching for stationary tools also, for this interpretation to be correct. As cross-talk between these two functions should be ongoing, regardless of the necessity for online correction. In Chapter 4, non-rotation conditions were implemented, and this effect was not apparent for tools that remained stationary during reaching. The currently discussed model of SMG function, therefore, favours the dynamic reintegration of SMG conceptual tool information as a necessary response to changes in orientation.

This does not negate the role of the SMG in planning tool use actions. A wealth of research implicates the SMG in planning and preparing tool use gestures across a number of tasks (Brandi et al., 2014; Hermsdörfer et al., 2007; Johnson-Frey et al., 2005; Lesourd et al., 2017; Lindemann et al., 2006; Moll et al., 2000; Ohgami et al., 2004; Reynaud et al., 2016; Valyear et al., 2011; van Elk, 2014). Rather, this interpretation suggests that as well as in planning, the SMG has a role in correcting the grasp plan online should the situation and task goal require it. Furthermore, the findings in Chapter 6 demonstrate disruption of grasp planning for use, but not for transport (Lesourd et al., 2017; Reynaud et al., 2016; Tunik et al., 2008a). For this experiment, triple pulse TMS was delivered prior to action onset in an attempt to disrupt action planning, observable in delayed movement kinematics. These findings did not show delays to movement onset (as observed in Tunik et al., 2008), but selection of grasp orientation occurred later in the reach than for baseline sham stimulation and control stimulation, as a function of tool orientation. This somewhat conflicts with the ‘dynamic reintegration’ model for SMG function, as in this experiment, no online correction of grasp was necessary during action execution. However, it is posited that TMS over the SMG prior to action onset results in delayed integration. Transport of the effector towards the target is not delayed as this is likely mediated by dorso-dorsal structures as discussed above. TMS over the SMG prevents integration of the functional properties of the tool for the desired goal-oriented task; this integration must ‘catch-up’ leading to grasp selection occurring later in the reach. The findings from Chapter 6 also seem to highlight that the SMG role has a preference for use of tools as opposed to transport (Brandi et al., 2014; Lesourd et al., 2017; Reynaud et al., 2016). This suggests that the SMG has a specificity for goal-oriented, functionally salient properties of tools for use. This is consistent with the neural network as observed by Buxbaum (2017) and others (Borghi & Riggio, 2009; Lesourd et al., 2017; Orban & Caruana, 2014; Thill et al., 2013; van Elk, 2014).This is also consistent with imaging findings suggesting an SMG activation bias for use of tools (Brandi et al., 2014; Peeters et al., 2013; Valyear et al., 2011; van Elk, 2014). This is not to say that the SMG plays no part in mediating grasp-to-transport actions under certain circumstances (Osiurak, Roche, et al., 2013), but this will be discussed further below.

To summarise findings in relation to the present question, the experimental outcomes of this thesis indicate that the SMG plays a critical role in planning functional, goal-oriented grasp of tools for use. The SMG serves as a locus of integration between action production systems and conceptual tool knowledge that allows perception and planning related to the functionally salient aspects of the tool. This integration is inherently linked to the goal of action, and subject to change dependent on the task at hand. This integration is likely dynamic when perturbation in the tools orientation require reassessment of the hand position in related to the ‘goal state’ for functional use. The SMG facilitates this integration during the planning of action to establish a functional grasp of tools for use, but this is susceptible to disruption from TMS, resulting in delayed selection of grasp.

7.2. Is the Role of the SMG during Action Execution Lateralised to the Left Hemisphere?

This thesis examined this question across three experiments, detailed in Chapters 3 and 4. Initially, findings in chapter 3 indicated a bilateral effect of SMG stimulation resulting in disruption of online correction when reaching for tools. This finding conflicted with the widely reported left hemisphere bias for tool related cognition observed in neuropsychological (Goldenberg, 2003; Goldenberg & Hagmann, 1998; Goldenberg & Spatt, 2009; Hermsdörfer et al., 2007) and neuroimaging models (Buxbaum, 2017; Buxbaum & Kalénine, 2010; Johnson-Frey, 2004; Johnson-Frey et al., 2005; Kroliczak & Frey, 2009; Orban & Caruana, 2014; Przybylski & Kroliczak, 2017). Left lateralisation of tool function to the parietal lobe is consistently reported across a number of tool related tasks (Beauchamp & Martin, 2007; Brandi et al., 2014; Chao et al., 1999; Chao & Martin, 2000; Lewis, 2006). For apraxic patients, deficits in manipulation or pantomiming tool use gestures are often observable following left hemisphere damage for the hands both contralateral and ipsilateral to the lesion (Goldenberg et al., 2003; Goldenberg & Spatt, 2009; Hermsdörfer et al., 2012; Jax et al., 2006; Sunderland et al., 2013). While findings for left hemisphere SMG stimulation conformed to these models, right SMG stimulation disruptions for both left and right hand reaching are inconsistent.

The potential role of the right SMG was then considered in facilitating functional grasp of tools, within the context of experiments 1 and 2 (see Chapter 3). Bilateral SMG activation has been observed during tool action execution (Brandi et al., 2014; Johnson-Frey et al., 2005), however the left SMG displays activation during planning *and* execution (Brandi et al., 2014). This suggests that the right SMG may serve functions that facilitate selection of appropriate grasp, but do not inherently involve retrieval or processing the functional aspects of tools. This role may pertain to processing the spatial demands of rapid online correction. This is consistent with findings that the right IPL is associated with detection of salient events in the environment (Clark et al., 2000; Gur et al., 2007; Kiehl et al., 2005, 2001; Singh-Curry & Husain, 2009) and sustaining attention for goal oriented tasks (Adler et al., 2001; Häger et al., 1998; Johannsen et al., 1997; Singh-Curry & Husain, 2009; Vandenberghe et al., 2001). Right IPL damage has also been linked to disruption of tracking object locations and awareness of rapid changes in location (Mannan et al., 2005; Parton et al., 2006; Pisella et al., 2004). Given the demands of online correction for this task, it is plausible that the right SMG, while not inherently involved in processing tool tasks, is recruited to compensate for the orientation changes during action. Given that rotation occurred on every trial (for the experiments in Chapter 3) the right SMG may be necessary to facilitate online correction. This would also account for the observed effect of stimulation to the ipsilateral right SMG on miscorrection when reaching with the right hand.

The experiments in Chapter 4 allowed investigation of this issue by including trials where no rotation occurred. It was suggested that disruption as a result of right SMG stimulation should occur prominently for the most challenging rotation conditions in terms of compensation of movement. If the right SMG is associated with motion and location tracking (Mannan et al., 2005; Parton et al., 2006; Pisella et al., 2004), this should be most observable for incongruent rotations or those requiring greater exertion in re-orienting the hand (e.g. inverted trials). This was not evident in the reported experimental outcomes. This may be due to the implementation of the non-rotation controls. As the target tool no longer rotated on every trial, this may have removed an anticipation of the target tool rotating, causing the focus of the task to be more emphatically related to processing the functional aspects of the tools in relation to the grasp orientation for functional use. This is not to say the right SMG does not support tool use, but based on current findings, it serves a secondary function to the left SMG in relation to selection of functional tool grasp. The effects observed in Chapter 4 also do not diverge between the left and right hand, in keeping with evidence from apraxic patients (Buxbaum, 2001; Goldenberg et al., 2003; Goldenberg &

Spatt, 2009) and neuroimaging findings (Johnson-Frey et al., 2005; Kroliczak & Frey, 2009; Przybylski & Kroliczak, 2017).

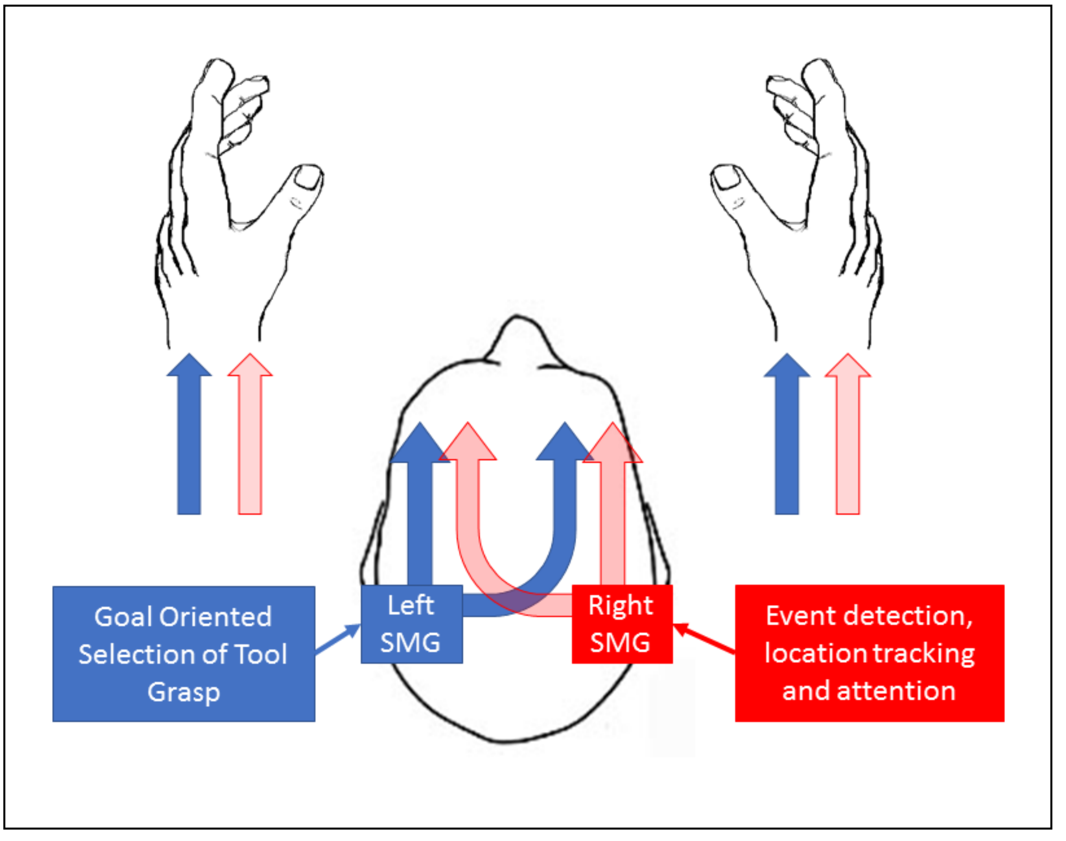

Figure 55. *Lateralisation of SMG function for left and right SMG during online correction of grasp, as observed in the experimental outcomes in this thesis. Left hemisphere SMG demonstrated specificity for online correction for tools when reaching to grasp for use regardless of hand used, consistent with current models. Right SMG effects were also observable in Chapter 3 for both left and right hands, however, this effect was not present with the addition of non-rotation control trials. There is a potential right lateralised role of the right SMG in event detection and tracking location and orientation of objects during goal directed tasks. This function would support selection of tool grasp without relying on tool related input, in the context of the reported experiments, but our findings do not confirm this and this may be task specific.*

The findings across Chapters 3 and 4 also seem to indicate that transport of the effector hand towards targets during reach execution is mediated by the contralateral hemisphere, while selection of functional grasp appears localised to the left SMG. In experiment 1 of Chapter 3, participant movement times and peak velocity were primarily affected by TMS over the right SMG, when reaching with the left hand. However, this effect was not present for ipsilateral stimulation in experiment 2, suggesting a contralateral preference for visuomotor control of the hand towards the tool target. In Chapter 4, movement times were also primarily affected by right SMG stimulation when reaching with the left hand. This finding suggests that movement kinematics associated with dorso-dorsal functioning (such as movement of the hand towards the target for grasp) are likely to be mediated preferentially by the contralateral hemisphere (Rice et al., 2007). These findings are not robust, as they are only observable for the right hand in Chapter 4 and the left in Chapter 3, but this does serve to highlight the dichotomy between online processing of effector transport and processing goal related elements of grasping. This highlights a future direction for research that may use adapted versions of the present experimental paradigm to explore further (see 7.4 Future Directions for Research).

To summarise, the findings in this thesis implicate a left hemisphere bias for the SMG in selection of functional grasp of tools for use, consistent with current models of the tool use cortical network. Findings implicate the involvement of the right SMG when contextual task demands necessitate consistent processing of spatial perturbations such as rapid changes in orientation (see Figure 55). This is consistent with present models of right SMG function associated with motion perception, online control and sustained attention. While this function supports selection of functional tool grasp, it does not specifically process the functionally salient aspects of tools for use during planning or execution.

7.3. What is the Basis of Conceptual Input Required to Enable Functional Grasp of Tools for Use?

This research question was addressed through a behavioural task in Chapter 5 and an integrated TMS and kinematic analysis expansion to this task in Chapter 6. So far, this thesis has highlighted that the SMG is a locus of integration between functional knowledge of tools and visuomotor processing necessary for executing functional grasp. This occurs during action planning and during execution when perturbation of the functional aspects of the tools require online reintegration of this salient information. The data reported here indicates that this occurs within the left SMG. However, to this point this thesis had not explored the nature of cognition that facilitates processing of the functional elements of tools in relation to their use (Buxbaum, 2017; Orban & Caruana, 2014; Osiurak & Badets, 2017; Reynaud et al., 2016).

In Chapter 1, two current models of tool use were examined; suggesting that tool use cognition is either based on stored manipulation knowledge, garnered from previous experience with tools (Borghi & Riggio, 2009; Buxbaum, 2017; Thill et al., 2013; van Elk, 2014) or processed through technical reasoning on occasion of use on a 'de novo basis'(Osiurak & Badets, 2016, 2017; Osiurak, Jarry, et al., 2013; Reynaud et al., 2016). To explore these models, a task was designed that would encompass 3 elements in each model; familiarity, action intention and orientation.

The manipulation-based approach argues that multisensory stored representations of tool use gestures form the basis for action planning and functional tool use. These gesture engrams are encoded through object interaction and observation of others and are stored long-term (Buxbaum, 2001, 2017; Heilman et al., 1982; Johnson-Frey et al., 2005; Rothi et al., 1991). These engrams encompass the parameters of the required gesture, amplitude of movement and posture for use (Buxbaum et al., 2007). This information is egocentric (i.e. pertains to the relationship between effector and tool), while structural based aspects of movement towards objects in space are mediated by dorso-dorsal structures (Buxbaum, 2017). This processing can, however, be subject to influence of stored manipulation knowledge (Creem & Proffitt, 2001). Intention to use an object should therefore be more demanding in terms of planning actions, as this requires access to stored representations of use whereas transporting a tool from one location to another would not (Jax & Buxbaum, 2010, 2013; Valyear et al., 2011). A key aspect of this model is also familiarity with the tool or gestures associated with them (Brandi et al., 2014; Buxbaum, 2017; Buxbaum et al., 2007; Dawson, Buxbaum, & Duff, 2010; Rüther, Tettamanti, Cappa, & Bellebaum, 2014). If a tool gesture is stored and retrieved, this should occur more rapidly for familiar tools when compared to novel tools that can facilitate the same action. These processes operate as a function of object orientation (Brandi et al., 2014; Creem & Proffitt, 2001). The orientation of tools during action planning has been shown to elicit faster motor responses dependent on handle orientation toward the effector limb (Song, Chen, & Proctor, 2014; Symes et al., 2007; Tucker & Ellis, 2004). Researchers have argued that this is indicative of activation of stored gestures for the tool (Buxbaum, 2017), resulting in faster action onset consistent with the manipulation-based approach.

The technical reasoning model conflicts with this interpretation arguing that object manipulation (transport and use) is supported by mechanical knowledge and technical reasoning, thereby tailoring actions to the goal-oriented task at hand (Osiurak, 2014b; Osiurak & Badets, 2016, 2017; Osiurak, Jarry, et al., 2013; Reynaud et al., 2016). Mechanical knowledge stores abstract information about object properties, which allows interpretation of the potential outcomes of interactions between objects (i.e. allocentric relationships) (Baumard et al., 2014; Goldenberg, 2013; Goldenberg & Hagmann, 1998; Goldenberg & Spatt, 2009; Osiurak et al., 2011). Within this framework, mechanical knowledge informs technical reasoning to generate a mental simulation – this forms the action plan for effective use of tools and guides a grasp that is in keeping with the plan (Orban & Caruana, 2014; Osiurak, 2014a; Osiurak & Badets, 2016). Visual and kinaesthetic feedback during action execution ensure that the body posture, grasp and movement amplitude is consistent with the mental simulation (Osiurak & Badets, 2016). This model better accounts for humans making use of novel tools or making novel use of familiar tools, due to a lack of influence of stored representations (Baumard et al., 2016; Osiurak & Badets, 2017). The role of mechanical knowledge and technical reasoning in object manipulation also highlights that transport actions can be more cognitively demanding than some tool use actions, dependent on the context of the task (Osiurak, Roche, et al., 2013). In terms of orientation, proponents of the technical reasoning approach have shown that rather than tool positions eliciting direct activation of their associated gestures, movement times are more likely to be affected by presentation of the most saliently graspable aspects of the tools (Osiurak & Badets, 2016; Symes et al., 2005, 2007).

In Chapter 5, some support was observed for the 2AS+ and the manipulation based approach, in that movement onset was affected by action intention for the familiar tool but not the novel. Delays to movement onset are associated with extended planning of action, reflecting a heightened cognitive demand in formulating the action plan prior to execution (Jax & Buxbaum, 2013; Jax et al., 2006; Osiurak, Roche, et al., 2013). Earlier movement onset was observed for familiar tools compared to novel when the goal was to transport, minimal difference for conventional use and delayed action planning for non-conventional use. This implicates the influence of stored manipulation knowledge, as this is readily accessible for transport, but must be bypassed or overcome for non-conventional use (Buxbaum, 2017; Buxbaum et al., 2006; Creem & Proffitt, 2001; Jax & Buxbaum, 2010). However, stored manipulation knowledge is not supported, as differences were not observed for conventional use for familiar and novel tools. This favours the technical reasoning model as conventional use of familiar tools should result in much faster access to stored semantic representations when compared to generating a mental simulation of action on each occasion of use (Osiurak & Badets, 2016). Differences in kinematic measures consistent with the orientation effect for familiar and novel tools were also observed, suggesting an influence of stored manipulation knowledge for the familiar. However, this was not easily reconcilable with the manipulation-based approach due to the same effect for the novel tool in the opposite orientation. This suggests that processing is likely based on saliently graspable aspects of the tools (in combination with the functional aspects), rather than on associated stored gestures for use. Furthermore, although the novel tool was designed to be comparable in use with the familiar hammer, participant behaviour showed versatility of use for the novel control, which may have influenced planning and action execution, leading to faster grasping. In other words, the possibility could not be discounted that the novel tool may have been better suited to the corresponding tasks than the hammer, resulting in the differences in movement kinematics observed here. That this occurred for novel tools suggests interpretation of tool properties and potential for action rather (in line with the technical reasoning approach (Osiurak, 2014a; Osiurak & Badets, 2016, 2017)) than abstraction of known gestures to suit the task at hand. The findings from this experiment provided interesting insights into the nature of conceptual input and support the technical reasoning model but could not discount the influence of manipulation knowledge on action planning. That only one familiar and novel tool (and corresponding conventional and non-conventional use tasks) were used in this paradigm may have been the reason for the mixed effects observable in these results.

To pursue this research question further, the paradigm was developed to include two more familiar and novel tool pairs (alongside corresponding tasks) in Chapter 6. Triple pulse TMS was integrated during the planning stages of action, over the anterior SMG (aSMG) and a control site of stimulation, alongside sham stimulation. The aSMG has been posited as the locus of integration between mechanical knowledge and technical reasoning into action production systems for visual kinaesthetic feedback in line with technical reasoning model (Orban & Caruana, 2014; Osiurak & Badets, 2017; Reynaud et al., 2016). Therefore, the region of interest was focused specifically on the aSMG for this task in contrast to earlier experiments. Results showed delayed selection of grasp for both novel and familiar tools, for both conventional and non-conventional use tasks compared to transport for stimulation of the aSMG but not for control or sham stimulation. This was observable when tools were oriented with the functional head incongruently with the effector hand. That there was no difference between use tasks and familiarity indicates that cognition pertaining to grasp selection was supported by technical reasoning and mechanical knowledge (Lesourd et al., 2017; Osiurak & Badets, 2017; Reynaud et al., 2016). As the orientation effect occurred for both novel and familiar tools, it can be inferred that rather than activating stored manipulation knowledge (Buxbaum, 2017), the aSMG integrates information pertaining to the most saliently graspable aspects of the tool in combination with the functional properties of the tool for interaction with the target object. This demonstrates processing of both the allocentric and egocentric relationships to facilitate tool action, in keeping with the technical reasoning approach (Osiurak & Badets, 2017; Reynaud et al., 2016). Furthermore, that non-conventional use of tools was delayed to a similar extent as conventional use suggests that tool use actions in this instance are generated on a 'de novo' basis. These results do not discount the role of technical reasoning or mechanical knowledge in object transport. It was suggested that this may have occurred, but due to the simplicity and consistency in transporting the object from cradle to wooden plinth on every trial the demands on technical reasoning would have been minimal. This is consistent with the technical reasoning model as technical reasoning for tasks of this nature has been shown as contextually sensitive (Osiurak, Roche, et al., 2013). The 2AS+ model should posit that stored gestures are more easily accessible, and this should be observable for conventional use of familiar tools (Buxbaum, 2017; Jax & Buxbaum, 2013). As this was not the case, the presently discussed findings better support the technical reasoning model. This contrasts with findings in Chapter 5, however this is consistent with the interpretation that the observed differences were due to the limited number of novel and familiar tools.

In response to this research question, the findings in this thesis seem to support the technical reasoning model of cognition in tool use action. These findings also support the role of the aSMG as a locus of integration that likely processes technical reasoning pertaining to the allocentric relationship between tools and their targets for action. Behavioural findings do not discount the 2AS+ model and the influence of manipulation knowledge (Buxbaum, 2017; Buxbaum & Kalénine, 2010; Thill et al., 2013; van Elk, 2014) and evidence in the behavioural tasks support some salience for object familiarity, but this requires further research. The present methods could be developed to further explore this conceptual knowledge integration in future (see 7.4. Future Directions for Research).

7.3. Updated Model for Lateralisation, Basis of Functional Tool Knowledge and Online Grasp Selection in SMG Function

Given the findings across 5 experiments, this thesis posits a role of the SMG in selection of functional tool grasp that elaborates on current models of the tool use neurocognitive network. This thesis suggests that the SMG serves an integrative role between visuomotor transformation systems and SMG processing of functional properties of tools during planning *and* action execution when contextually necessary.

Visuomotor systems guide hand position in 3D space through visual and tactile feedback and are likely supported, bilaterally, by dorso-dorsal structures such as the SPL and aIPS during action execution (Binkofski & Buxbaum, 2013a; Boronat et al., 2005; Buxbaum, 2001; Buxbaum & Kalénine, 2010; Orban & Caruana, 2014; Thill et al., 2013; van Elk, 2014). This system also likely processes egocentric relationships between effector and objects (i.e. tools). These structures receive information from the SMG during action planning that pertains to the functionally salient elements of tools and targets for action (Osiurak & Badets, 2017; Reynaud et al., 2016). This is likely based on based on technical reasoning and mechanical knowledge of the object properties supported by the IPL (Osiurak & Badets, 2016, 2017; Reynaud et al., 2016). Mechanical knowledge supports the identification and understanding of object properties based on previous experience (Goldenberg, 2013; Goldenberg & Spatt, 2009; Hartmann et al., 2005; Jarry et al., 2015; Osiurak, 2014a; Osiurak et al., 2010, 2011). Mechanical knowledge of the object properties in relation to one another (e.g. a fork is harder and sharper than a tomato, making it suitable for piercing and transporting) informs the technical reasoning process that allows production of action plans for use on a 'de novo' basis (Osiurak & Badets, 2017; Reynaud et al., 2016). Technical reasoning is likely carried out during the planning stage of action by the (a)SMG and integrates information regarding the functional properties of the tool into the visuomotor systems that encode egocentric information (Reynaud et al., 2016).

With access to functional information about the tools and task from SMG technical reasoning, dorso-dorsal structures can encode a mental simulation of how the action should look and feel during execution, which facilitates selection of the most suitable grasp orientation (i.e. egocentric processing) for tool use (Osiurak & Badets, 2016, 2017; Reynaud et al., 2016). This role is lateralised to the left SMG, consistent with observations of patients with LBD damage (Goldenberg & Hagmann, 1998; Goldenberg et al., 2003; Goldenberg & Spatt, 2009; Sunderland & Shinner, 2007; Sunderland et al., 2013) and neuroimaging findings (Brandi et al., 2014; Gallivan et al., 2013; Johnson-Frey, 2004; Johnson-Frey et al., 2005; Orban & Caruana, 2014; Peeters et al., 2013). However, in the presently discussed model the right SMG is also recruited in online control of corrections requiring sustained tracking of changes in location or orientation, dependent on the context of the task at hand (Adler et al., 2001; Clark et al., 2000; Gur et al., 2007; Kiehl et al., 2005, 2001; Singh-Curry & Husain, 2009; Vandenberghe et al., 2001). This is consistent with neuroimaging findings revealing bilateral SMG activation during tool action execution, but left hemisphere bias for tool action planning *and* execution (Brandi et al., 2014; Johnson-Frey et al., 2005).

This integration predominantly occurs during the planning stages of action (Brandi et al., 2014; Lesourd et al., 2017; Tunik et al., 2008a). Dorso-dorsal structures mediate action execution once the plan is in place (Buxbaum, 2017; Osiurak & Badets, 2017; Reynaud et al., 2016; Tunik et al., 2008a). However, if perturbations to objects or environment occur that impact on the functionally salient aspects of tool grasping and use (e.g. rapid changes in orientation of the functional elements of the tool) left SMG integration is required to compensate for these changes. This implicates an online, dynamic reintegration of technical reasoning processes into dorso-dorsal structures to allow compensation in selection of grasp orientation. This ensures that functional grasp is in keeping with the relative properties of the tool and target for action and planned action execution (Osiurak & Badets, 2016, 2017). Thereby processing both the allocentric and egocentric relationships necessary to facilitate functional use.

This model is consistent with left lateralisation of tool use related function observed across a number of neuropsychological (Goldenberg & Hagmann, 1998;

Goldenberg & Spatt, 2009; Hermsdörfer et al., 2007; Sunderland et al., 2013) and neuroimaging studies (Borghi, 2014; Brandi et al., 2014; Gallivan et al., 2013; Johnson-Frey, 2004; Johnson-Frey et al., 2005; Kroliczak & Frey, 2009; Orban & Caruana, 2014; Przybylski & Kroliczak, 2017; van Elk, 2014; Vingerhoets, 2014, 2008; Vingerhoets, Acke, et al., 2009). However, the model is not comprehensive of the tool use network and there are some discrepancies in function that require further exploration. The technical reasoning model best accounts for the present findings, but there are patterns of findings in similar studies that this model cannot account for easily. Apraxic patients have been observed as being able to match hand postures to novel objects without impairment but show deficits in identifying the appropriate hand posture for grasping familiar tools (Dawson et al., 2010). This pattern was also observed in abnormal lifting kinematics for familiar tools but not novel tools within the same experiment, implicating an explicit role of manipulation knowledge and stored gestures (Dawson et al., 2010). Furthermore, researchers have observed increased activation in the SMG when observing a set of functional novel objects after observing an experimenter manipulating them compared to observing them without manipulation (Rüther et al., 2014). This finding indicates changes in the representation of objects potentially based on stored manipulation knowledge as a result of observing the objects in use (Buxbaum, 2017).

The currently discussed model also does not factor the influence or role of function knowledge, which is considered as integral by both the technical reasoning (Reynaud et al., 2016) and 2AS+ models for day-to-day tool use (Buxbaum, 2017). For 2AS+ and the manipulation-based approach, function knowledge encodes information pertaining to the contextually appropriate use of tools and the objects that they are used in conjunction with (e.g. a screwdriver and a screw) (Boronat et al., 2005; Buxbaum, 2017; Hodges et al., 2000; Negri et al., 2007). This may be misconstrued as similar to understanding allocentric relationships between objects. However, allocentric processing pertains to understanding the interactions and potential for action between objects and tools; as well as the potential impact of tool action on a target object *regardless* of previous experience with them (Osiurak & Badets, 2017; Reynaud et al., 2016). Function knowledge is associated with the temporal cortex, in particular the pMTG (Beauchamp et al., 2002; Chao et al., 1999; Chao & Martin, 2000; Noppeney et al., 2006; Orban & Caruana, 2014; Perini et al., 2014; Ramayya et al., 2010). The manipulation-based approach argues that this influences selection of tool grasp even when use is not required (Buxbaum, 2017; Creem & Proffitt, 2001) and can compensate for deficits in use in the absence of intact manipulation knowledge (Buxbaum, 2001; Buxbaum, Schwartz, & Carew, 1997; Sirigu et al., 1991). This is carried out through inference of the object use (i.e. manipulation knowledge) from knowledge of the appropriate context and targets associated with the tool (i.e. function knowledge), this is referred to as the multiple routes to action hypothesis (Buxbaum, 2001; Buxbaum et al., 1997; Sirigu et al., 1991; Yoon, Heinke, & Humphreys, 2002; Yoon & Humphreys, 2005).

The potential theoretical issues with this model have been discussed (see 1.3.2. The Technical Reasoning-based approach to Tool Use Cognition), however, the potential influence of function knowledge was observed in Chapter 5. Behavioural data showed non-conventional action planning was delayed for familiar tools. This could be interpreted as the influence of function knowledge on grasp behaviour, as familiar tools have associated functional uses. Bypassing this associated knowledge to plan for non-conventional use results in delayed movement onset due to extended and more demanding planning (Boronat et al., 2005; Buxbaum, 2017; Buxbaum & Kalénine, 2010; Creem & Proffitt, 2001). However, this effect was not observable when further familiar and novel tool pairs were introduced, suggesting that this may have been related to processing functional properties of the tools (i.e. based on technical reasoning and mechanical knowledge of the tools intrinsic size, shape and functionality in relation to the target for action) rather than the influence of function knowledge (i.e. previously learned association between a tool and a target for action, or contextually appropriate use).

For the technical reasoning-based model, function knowledge serves to organize searching of memory in order to get tools and objects that are not directly at hand (Osiurak & Badets, 2016). Tool use is often a multi-stage process, therefore function knowledge can be essential in mediating the overarching process of pulling tools and items together, whereas technical reasoning mediates actual tool use to affect change and achieve a goal-oriented task (Goldenberg & Spatt, 2009; Osiurak & Badets, 2016). Function knowledge is also arguably useful in single tool use, when required to demonstrate use of a single tool in isolation from a target for action and participants have to form a representation of an experimenter's expectations (Reynaud et al., 2016). Function knowledge in this manner facilitates socially knowledge that can be culturally shared (Reynaud et al., 2016) (as is often proposed as an important element of human tool use). As with the manipulation-based approach, the technical reasoning model posits that the left temporal cortex (in particular pMTG) is likely the locus of function knowledge. Research using diffusion tensor imaging (DTI) to explore the tool use network has revealed stronger left lateralised connectivity between the left SMG and pMTG (Ramayya et al., 2010). This could be consistent with the explanation offered by the technical reasoning approach. Performing tool gestures with no tool in hand (or target for action) relies not on technical reasoning but a combination of gesture production and contextual understanding of the expected action from another's point of view (Reynaud et al., 2016). This is arguably mediated by function knowledge input from the pMTG into the SMG.

Although function knowledge is clearly an important part of the tool use, it was not the primary focus of this research investigation. As stated in both the manipulation and technical reasoning approaches, function knowledge operates independently from manipulation knowledge or technical reasoning (Buxbaum, 2017; Osiurak & Badets, 2016). While this may still involve processing tool related information that can facilitate use under certain circumstances, the primary focus was in action planning of g*oal-oriented tool use* with physical tools to hand and *explicit intention of use*. Therefore, the experiments reported here controlled for factors that may be influenced by function knowledge. In Chapters 5 and 6, to remove the associations between familiar tools and targets for action, control targets that could be interacted with in the same way were developed (e.g. for the hammer, subjects were required to flatten a pointed piece of Blu-tack™ – this could be carried out with a hammering motion). This was to ensure that novel tools (which should have no associated tool targets in function knowledge) were comparable at this level with familiar. However, the influence of function knowledge is clearly still debateable within the research literature and potentially apparent in the presently discussed findings. As stated previously, the findings in this thesis do not discount the existence or the role of stored manipulation knowledge or function knowledge. But the present findings are better accounted for by the technical reasoning model. Further development of research is necessary to explore this discrepancy between models, however, Buxbaum (2017) has posited that technical reasoning may serve to tailor stored gestures to the specific requirements of the task and environment, working in tandem with one another. This does, however, fundamentally conflict with the 'de novo' processing of salient functional features of tools in relation to other objects, making the two theoretical models difficult to reconcile.

7.4. Future Directions for Research

Over the course of this thesis, novel experimental methods were developed that have been useful in elaborating on the role of the SMG in selection of functional tool grasps, but also may be adapted further to explore some of the unanswered research questions detailed in the previous section.

When examining the nature of conceptual input pertaining to tool use, whether technical reasoning based (Osiurak & Badets, 2016) as the current findings suggest or manipulation-based (Buxbaum, 2017), adaption of the current paradigm could elaborate on whether manipulation knowledge is encoded for novel tools following observation of their use. In Chapter 6, participants were presented with novel tools and asked to either transport or use them. Due to the small number of participants, it was beyond the scope of this experiment to examine order effects and grasp selection to establish whether participants adopted a consistent grasp behaviour with tools before or after they had implemented functional use of them. Therefore, in a future experiment it would be pertinent to elaborate the existing paradigm to include more tools and vary the presentation of task conditions; asking participants to grasp tools for transport either before or following engaging in functional use of the tool. Proponents of the manipulation-based approach suggest that when grasping a tool for transport that has an associated use, a functional grasp is often adopted even when use is not required (Creem & Proffitt, 2001). If this is the case, then in grasping novel tools, participants should adopt an unnecessary functional grasp for the purpose of transport following observation of another person making functional use of the object (Creem & Proffitt, 2001). This experiment could be varied in terms of tool orientation in presentation to examine whether participants would adopt an uncomfortable initial reach to facilitate functional grasp even when the task does not explicitly require this (Rosenbaum et al., 1992; Short & Cauraugh, 1997; W. Zhang & Rosenbaum, 2008). Furthermore, the amount of exposure to the functional use of the tools could be varied between participants to assess the requirements of encoding a functional gesture. This could take the form of; no observation of functional use, observing functional use, or carrying out functional use after observing a demonstration. Analysis of early movement kinematics and grasp orientation would allow examination of preference for action and whether or not a functional grasp has been encoded on the basis of interaction or observation.

Furthermore, the current TMS methodology applied during the previous experiments could be implemented in an attempt to disrupt encoding of gestures, encoding of function knowledge and action execution. Granted, the triple pulse TMS method used during action planning and tool perturbation (used across experiments in this thesis) may not be sufficient to disrupt action encoding during observation of novel tool manipulation, due to the duration of time it may take to demonstrate functional use and the (potentially) transient nature of TMS. A more efficient method may be to apply repetitive TMS (rTMS) during observation of function (or varied between observation conditions) in an attempt to disrupt this process. Any impact of rTMS could then be examined in early movement kinematics and grasp preference during a transport task. Target location for disruption could be varied between the left SMG and pMTG. rTMS over the SMG has demonstrated disruption of gesture production when carrying out meaningless and meaningful gestures (Reader, P Royce, Marsh, Chivers, & Holmes, 2018). The SMG has also shown heightened activation in response to novel objects after viewing them being manipulated by an experimenter (Rüther et al., 2014). This suggests that encoding functional use changes the representation of the object, potentially developing associated manipulation knowledge (Rüther et al., 2014). Whereas, pMTG is associated with encoding of function knowledge and understanding learned contextual appropriate use of tools

(Beauchamp et al., 2002; Chao et al., 1999; Orban & Caruana, 2014; Ramayya et al., 2010). Understanding functional use of the novel tool in context may lead this information to be encoded as function knowledge, therefore rTMS over the pMTG may disrupt encoding or action execution. Observation of functional grasping (consistent with the demonstration provided before grasping) would provide insight into the role of function knowledge as it applies to both technical reasoning and manipulation knowledge in action. Further controls could be added by using novel objects with multiple functions and varying the function demonstrated between subjects.

Further research should also be implemented to explore the lateralisation of SMG function during tool grasp execution and the potential supportive role of the right SMG that was observed under certain conditions in this thesis. As discussed, bilateral effects of SMG stimulation during action execution may be attributed to a role for compensation in spatial changes and detection of salient events (Clark et al., 2000; Gur et al., 2007; Kiehl et al., 2005, 2001; Lagopoulos et al., 2006; Singh-Curry & Husain, 2009). This appeared to be the case for the rapid online correction necessary to correct grasp in Chapter 3, but whether or not this is consistent in supporting tool grasping or simply relies on processing spatially salient events is unclear. To explore this further, modification of the current paradigm could be implemented to dissociate these functions during action execution. This would require implementation of spatial correction tasks that involve changes in dimensions of non-tool objects for grasping or changes in orientation of non-tool objects that do not rely upon processing functionally salient elements for use. This could be conducted in a similar manner to Tunik et al., (2005) in which geometric objects were perturbed in orientation and task demands required grasping at the horizontal or vertical axis. With the implementation of TMS at perturbation onset over the left and right SMG and contrasting the outcomes with those observed for functional tool rotation, dissociation of the proposed left and right SMG roles would provide insight into the lateralisation of these functions. Alternatively, making use of virtual and/or altered reality systems (Rallis et al., 2018a) would allow changes to the perceived physical properties of virtual tools during action execution. This could be varied in terms of functional elements (i.e. changes in orientation of the functional head) or structural elements (changes in dimensions for the graspable elements of tools). By selective application of TMS over the left and right SMG during action execution, this dissociation could be further explored.

7.5. Conclusions

This thesis set out to explore the functional role of the left SMG in facilitating tool use. Over 5 experiments, this project has developed novel experimental paradigms integrating TMS, kinematic data analysis and actual tool use behavioural paradigms. These findings implicate a left lateralised role of the SMG in integration of conceptual tool knowledge pertaining to functional tool properties, into visuomotor control processes to enable functional grasping and functional use. This thesis has highlighted that the SMG can process and integrate this salient tool information dynamically to allow rapid online correction and maintenance of grasp and use plans during action execution. These findings also implicate an integral role of technical reasoning, as opposed to manipulation knowledge in providing the conceptual understanding tool properties and simulating interactions between tools and objects. These findings have demonstrated that this is not specific to familiar tools and support the view that tool use is based on technically reasoning and goal oriented understanding of mechanical properties of tools and targets for action. These results do not discount the role of manipulation knowledge or function knowledge in influencing tool behaviour and the dissociation between these conceptual models requires further research. The research methods developed here will be useful in following this line of enquiry in future projects.

Appendices

Appendix A.

Experiments 1 – 3; Roll data calculation and preparation for miscorrection scores.

Data collection was carried out using LabVIEW, connected via national instruments to Polhemus Fastrak. Analysis was conducted primarily in MATLAB.

For experiments 1 – 3, miscoretion was the primary measure of erroneous and delayed correction of grasp orientation for the online correction task. The data for each trial underwent several stages of processing before calculation of miscorrection.

The trials were trimmed from onset of tool rotation to the maximum forward movement of the hand towards the tool, indicating that participants had grasped the tool and were moving their hand away from the cradle to demonstrate use. The data was zeroed to allow comparison of correction across trials. Trial roll data was then filtered using median filtering to remove any artefacts. This

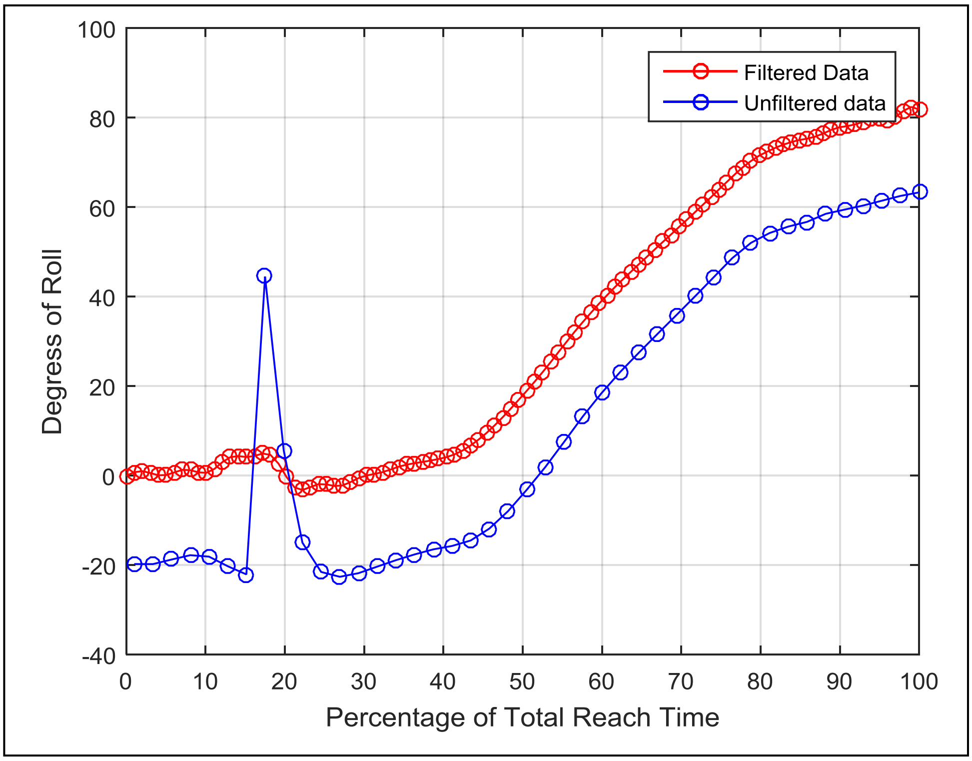

Figure 56. Roll data in degrees over percent of reach from movement onset to maximum forward movement - preparation for a single trial – median filtered, zeroed and resampled to 100 data points to allow comparison across trials.

was carried out for each data point in a trial which was replaced with the median of 6 (3 each side) neighbouring data points. Roll data was then resampled to 100 data points to allow even comparison across trials (see Figure 56).

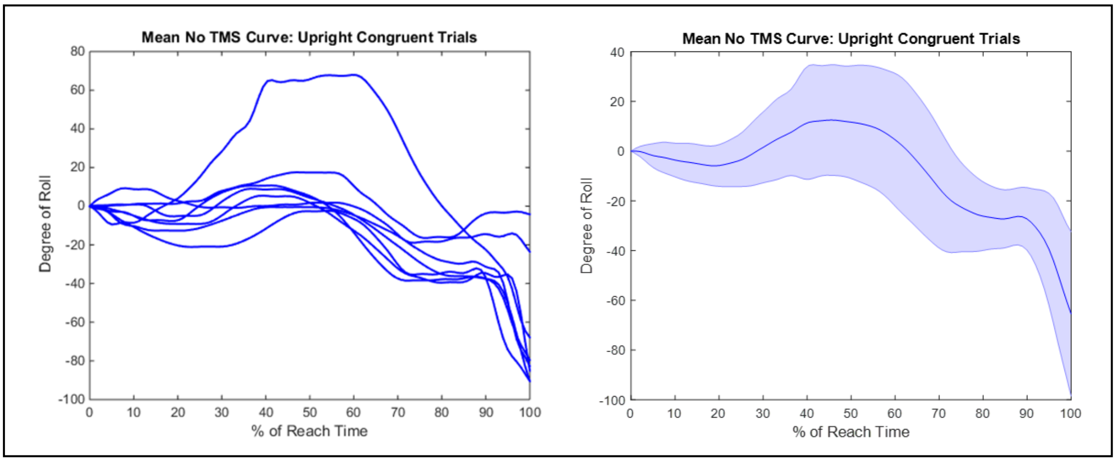

Figure 57. Non-TMS trials are used to form the baseline for miscorrection analysis. An average of the roll data over percentage of reach time, and ± 1 SD from the mean from the upper and lower thresholds for comparison against TMS trials.

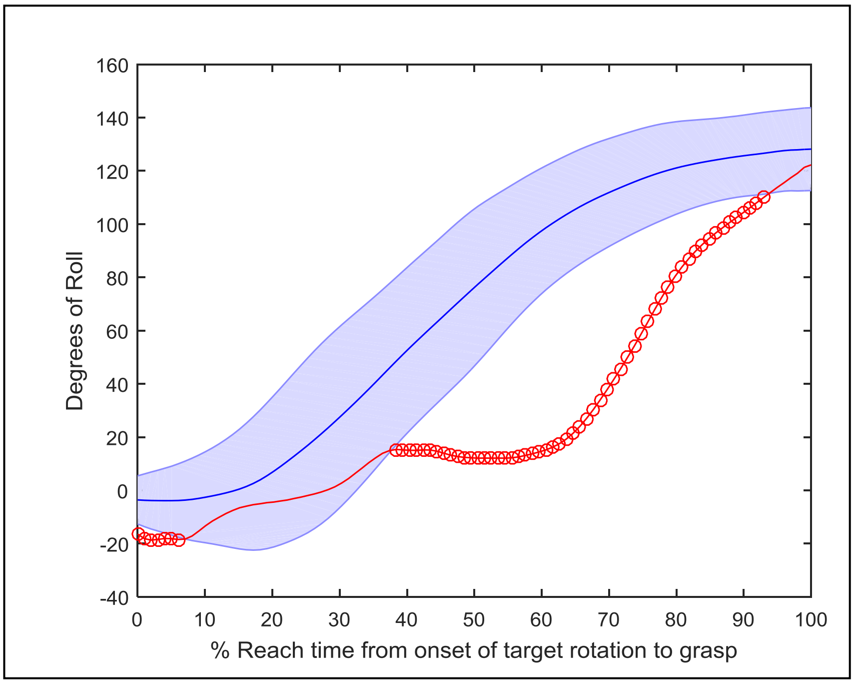

Figure 58. Example of analysis, 1 resampled test trial over the corresponding baseline average. Circled values indicate delayed or erroneous correction. Time points that fall within the threshold (~10-40%) are given a zero value.

The baseline correction was calculated by averaging the non-TMS trial roll data in each rotation condition (e.g. inverted incongruent, inverted congruent, upright incongruent, upright congruent) over percentage of reach time, with upper and lower threshold set as ± 1 SD from the mean (see Figure 57).

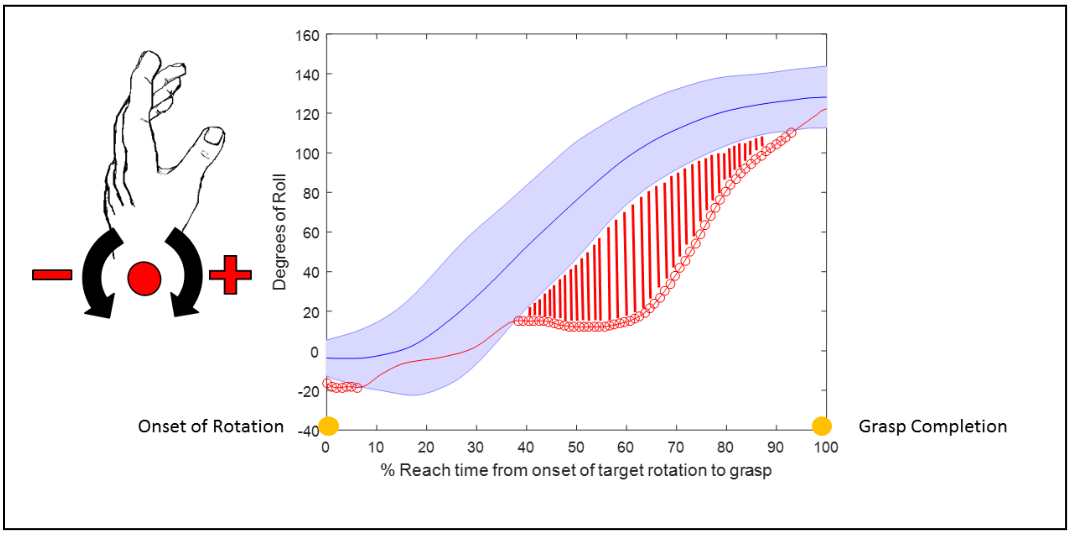

Figure 59. The difference between roll data time points external to the threshold and the threshold itself (highlighted here by red lines) is calculated as a fraction of standard deviation of the corresponding baseline time point. Combined with the zero scores for values that fall inside the threshold, this produces a vector of zeroes and standard deviations from the baseline performance. An average of this vector provides the miscorrection score for each trial. Consequently, higher miscorrection scores describe correction that was later or oriented in the incorrect direction for a longer period of the reach when compared to baseline.

Test trials for each condition were then compared against baseline performance (see Figure 58). Roll time points that fell within the ± 1SD range of the threshold were assigned a zero value. For roll data points that were outside of this threshold, the difference in roll between the data point and threshold was calculated as a fraction of SD from the mean baseline time point (Figure 59). For each trial, this formed a vector of zeroes and SD values. The average of this vector provided the miscorrection score for each trial in each condition. Trials that were identified as incorrect grasps were assigned zero values when calculating the average miscorrection for each rotation condition in Experiments 1, 2 and 3.

Appendix B.

Table 11. Summary of Functional grasp – i.e. with thumb oriented toward the functional end of the tool (%) for grasp and use of novel and familiar tools in Chapter 6. Functional grasp here is defined as a power grip with the thumb oriented toward the functional head of the tool. As noted earlier, the tasks could be carried out a number of ways and does not require this grasp orientation.

		Stimulation		
Intention	Familiarity	Sham	aSMG	Control
Transport	Familiar	61.72	57.03	58.59
	Novel	60.16	55.47	57.03
Conventional Use	Familiar	63.28	72.66	68.75
	Novel	56.25	60.94	50.78
Non-conventional Use	Familiar	46.88	71.88	65.63
	Novel	46.09	66.41	51.56

Appendix C.

Table 12. Summary of mean data for Sham stimulation (Chapter 6) across movement onset (MO), movement time (MT), percent of MT to grasp selection (TGS%), peak velocity (TPV%) and peak aperture (TPA%). M ± (SD)

Intention	Familiarity	Orientation	MO(ms)		MT(ms)		TGS%		TPV%		TPA%	
Transport	**Familiar**	**N**	350	(122)	565	(86)	45.33	(9.87)	61.54	(4.75)	75.14	(9.96)
		NE	320	(50)	542	(55)	45.63	(7.03)	60.72	(3.26)	76.02	(3.91)
		E	334	(81)	525	(90)	31.06	(15.02)	66.82	(10.02)	65.69	(9.74)
		SE	312	(83)	534	(67)	34.86	(10.54)	65.93	(5.88)	76.31	(15.32)
		S	314	(53)	575	(104)	43.29	(10.14)	60.13	(6.85)	82.34	(5.38)
		SW	299	(42)	516	(56)	36.84	(10.52)	65.64	(6.34)	76.41	(10.19)
		W	303	(32)	475	(67)	24.67	(7.01)	71.41	(7.91)	62.68	(14.71)
		NW	302	(88)	560	(44)	29.45	(13.02)	63.36	(7.03)	77.76	(14.23)
	Novel	**N**	320	(62)	554	(57)	46.41	(8.41)	58.61	(7.40)	77.08	(5.73)
		NE	285	(41)	560	(83)	43.04	(9.48)	62.27	(4.33)	80.49	(9.21)
		E	332	(77)	562	(102)	36.05	(18.63)	62.94	(10.02)	74.26	(10.77)
		SE	314	(147)	578	(96)	35.50	(12.18)	64.56	(7.93)	83.45	(10.48)
		S	317	(56)	570	(62)	42.05	(12.86)	59.02	(5.55)	76.49	(11.84)
		SW	360	(129)	503	(60)	28.10	(10.93)	68.40	(7.08)	72.37	(12.58)
		W	319	(59)	564	(153)	25.94	(6.60)	66.24	(5.96)	77.99	(18.81)
		NW	289	(41)	558	(62)	31.88	(14.83)	61.12	(6.14)	76.09	(11.57)
CU	**Familiar**	**N**	330	(49)	627	(71)	42.55	(10.74)	56.30	(4.38)	77.49	(7.63)
		NE	334	(72)	596	(133)	44.42	(9.34)	58.69	(6.73)	77.41	(6.77)
		E	359	(98)	598	(95)	41.98	(14.56)	62.75	(8.99)	75.11	(6.01)
		SE	319	(75)	639	(109)	39.61	(17.28)	54.72	(9.98)	72.23	(11.88)
		S	342	(46)	654	(133)	44.28	(10.79)	55.41	(9.05)	80.79	(7.98)
		SW	311	(55)	596	(103)	43.13	(11.17)	63.17	(2.18)	72.24	(10.76)
		W	310	(39)	532	(67)	35.72	(14.52)	63.68	(9.09)	81.09	(15.12)
		NW	333	(64)	584	(63)	26.57	(13.00)	58.70	(5.93)	73.78	(18.24)
	Novel	**N**	314	(47)	630	(136)	51.27	(5.04)	56.15	(7.62)	76.94	(4.32)
		NE	319	(58)	614	(84)	51.06	(11.88)	55.45	(6.83)	74.79	(9.98)
		E	323	(49)	606	(91)	41.46	(14.54)	58.00	(5.79)	73.69	(10.05)
		SE	349	(82)	649	(110)	38.01	(12.76)	55.54	(4.50)	70.52	(8.05)
		S	323	(65)	601	(86)	50.69	(8.46)	56.29	(8.43)	83.87	(9.02)
		SW	326	(71)	619	(171)	49.25	(8.42)	57.99	(7.33)	77.20	(9.57)
		W	334	(67)	571	(76)	38.64	(11.62)	59.24	(6.95)	72.23	(13.47)
		NW	310	(50)	571	(54)	29.44	(14.00)	59.59	(5.30)	79.48	(6.83)
NU	**Familiar**	**N**	364	(93)	883	(474)	41.69	(9.42)	52.54	(12.51)	69.58	(17.54)
		NE	333	(65)	861	(465)	40.11	(13.48)	51.49	(9.15)	71.14	(18.02)
		E	353	(70)	634	(219)	37.92	(15.31)	60.46	(10.48)	73.84	(13.20)
		SE	361	(95)	669	(170)	42.17	(19.06)	53.11	(7.45)	70.04	(17.12)
		S	337	(64)	635	(140)	46.94	(5.81)	58.03	(6.37)	83.77	(4.39)
		SW	335	(76)	738	(356)	43.42	(9.33)	55.45	(13.66)	69.95	(14.77)
		W	346	(102)	675	(248)	44.03	(15.74)	58.11	(11.40)	73.99	(12.30)
		NW	316	(49)	629	(139)	33.44	(13.30)	58.41	(9.12)	81.25	(13.90)
	Novel	**N**	346	(62)	600	(93)	45.32	(10.91)	56.82	(5.81)	80.30	(4.65)
		NE	326	(52)	622	(122)	42.25	(14.01)	58.54	(8.73)	74.04	(10.25)
		E	349	(63)	689	(301)	31.34	(14.33)	59.34	(8.97)	65.40	(13.21)
		SE	341	(75)	792	(397)	46.84	(14.78)	52.63	(12.23)	76.68	(12.12)
		S	329	(45)	751	(367)	44.04	(9.32)	56.78	(10.85)	75.32	(14.78)
		SW	340	(43)	729	(386)	42.65	(12.05)	57.83	(11.97)	74.73	(9.53)
		W	347	(104)	640	(250)	36.64	(15.04)	55.99	(9.85)	72.99	(16.28)
		NW	360	(80)	779	(549)	40.02	(16.60)	56.46	(10.53)	74.51	(9.00)

Table 13. Summary of mean data for aSMG stimulation (Chapter 6) across movement onset (MO), movement time (MT), percent of MT to grasp selection (TGS%), peak velocity (TPV%) and peak aperture (TPA%). M ± (SD)

Intention	Familiarity	Orientation	MO(ms)		MT(ms)		TGS%		TPV%		TPA%	
Transport	**Familiar**	**N**	322	(57)	554	(66)	45.71	(8.40)	59.86	(3.69)	76.20	(13.49)
		NE	314	(55)	550	(66)	42.50	(12.01)	59.07	(4.42)	73.95	(16.23)
		E	331	(92)	520	(79)	30.58	(13.27)	65.05	(7.66)	65.66	(7.66)
		SE	310	(64)	629	(250)	32.54	(18.86)	58.31	(12.05)	76.47	(20.83)
		S	313	(52)	572	(78)	47.70	(8.21)	56.78	(6.54)	80.57	(4.78)
		SW	351	(105)	535	(82)	41.19	(10.18)	66.00	(9.37)	75.67	(11.93)
		W	299	(53)	482	(87)	26.98	(8.42)	69.72	(9.08)	69.50	(8.69)
		NW	318	(76)	526	(49)	38.24	(11.76)	62.02	(6.12)	74.08	(14.94)
	Novel	**N**	339	(67)	565	(70)	44.40	(4.56)	59.50	(5.77)	80.66	(7.66)
		NE	333	(45)	553	(85)	39.54	(13.98)	61.62	(4.47)	67.65	(18.35)
		E	331	(57)	511	(83)	36.21	(15.33)	69.08	(8.13)	74.97	(11.08)
		SE	307	(43)	591	(115)	34.02	(18.78)	57.37	(6.94)	64.64	(14.56)
		S	352	(85)	562	(39)	44.47	(9.94)	62.26	(3.96)	80.42	(4.87)
		SW	315	(60)	541	(98)	35.77	(8.76)	62.61	(7.36)	72.34	(10.81)
		W	329	(65)	631	(256)	29.10	(13.58)	61.16	(9.69)	75.50	(14.82)
		NW	323	(56)	573	(71)	32.59	(17.58)	59.61	(5.63)	76.77	(17.55)
CU	**Familiar**	**N**	317	(42)	624	(100)	46.16	(7.38)	55.38	(10.56)	74.77	(16.02)
		NE	315	(20)	641	(111)	45.68	(14.71)	54.89	(8.23)	75.30	(10.39)
		E	303	(62)	705	(164)	51.27	(11.51)	51.35	(9.26)	66.50	(19.42)
		SE	327	(48)	694	(115)	47.15	(14.46)	50.79	(5.80)	68.10	(13.70)
		S	303	(41)	642	(118)	49.17	(7.38)	56.70	(5.52)	77.56	(12.53)
		SW	305	(68)	597	(137)	38.50	(13.10)	64.41	(8.45)	67.98	(7.04)
		W	322	(78)	621	(119)	36.93	(13.31)	58.08	(7.24)	71.26	(20.13)
		NW	314	(43)	602	(88)	29.43	(14.61)	56.43	(10.73)	78.67	(14.09)
	Novel	**N**	309	(47)	648	(106)	44.28	(13.62)	55.37	(6.92)	80.78	(7.72)
		NE	319	(61)	659	(168)	41.17	(13.50)	52.81	(12.01)	74.76	(14.27)
		E	342	(138)	783	(407)	46.87	(14.54)	50.43	(8.68)	67.83	(21.19)
		SE	311	(58)	736	(202)	42.61	(9.35)	50.18	(10.47)	68.05	(16.13)
		S	290	(32)	678	(165)	50.05	(6.13)	53.87	(11.69)	80.46	(8.70)
		SW	360	(109)	695	(267)	44.87	(9.15)	62.33	(10.46)	72.63	(10.21)
		W	323	(58)	577	(101)	38.02	(14.67)	59.62	(11.69)	72.79	(23.14)
		NW	291	(52)	598	(112)	37.85	(13.65)	57.66	(10.51)	86.43	(11.29)
NU	**Familiar**	**N**	310	(41)	647	(78)	48.37	(12.50)	53.54	(8.07)	80.23	(3.88)
		NE	325	(42)	717	(310)	43.98	(14.54)	54.94	(7.61)	73.88	(15.98)
		E	312	(45)	637	(121)	48.17	(19.34)	60.21	(8.05)	78.12	(9.91)
		SE	343	(56)	631	(73)	42.11	(19.70)	57.68	(5.17)	80.30	(9.59)
		S	347	(81)	638	(113)	41.70	(13.21)	54.30	(6.36)	81.19	(9.16)
		SW	326	(54)	633	(122)	36.68	(10.67)	56.61	(9.60)	73.70	(10.71)
		W	351	(90)	578	(74)	32.85	(18.84)	62.67	(9.43)	78.18	(14.34)
		NW	354	(62)	612	(67)	26.25	(12.01)	55.88	(6.81)	77.59	(13.78)
	Novel	**N**	323	(67)	612	(77)	51.81	(8.00)	53.88	(6.35)	81.05	(5.20)
		NE	313	(39)	656	(121)	44.12	(7.69)	57.22	(6.88)	83.12	(5.39)
		E	354	(104)	619	(93)	46.34	(16.04)	57.01	(4.96)	78.11	(6.78)
		SE	338	(56)	734	(262)	35.56	(14.52)	51.44	(11.64)	81.72	(10.57)
		S	341	(98)	656	(107)	41.07	(10.91)	55.09	(4.36)	80.14	(7.95)
		SW	346	(73)	606	(101)	35.09	(14.70)	57.19	(7.89)	70.13	(21.17)
		W	336	(77)	595	(89)	29.22	(14.82)	61.37	(9.88)	77.12	(15.91)
		NW	329	(56)	609	(91)	38.32	(14.91)	57.39	(7.17)	79.91	(10.37)

Table 14. Summary of mean data for Control stimulation (Chapter 6) across movement onset (MO), movement time (MT), percent of MT to grasp selection (TGS%), peak velocity (TPV%) and peak aperture (TPA%). M ± (SD)

Intention	Familiarity	Orientation	MO(ms)		MT(ms)		TGS%		TPV%		TPA%	
Transport	**Familiar**	**N**	325	(67)	585	(101)	45.11	(12.86)	55.83	(6.78)	76.88	(8.39)
		NE	320	(71)	561	(89)	40.50	(13.37)	58.28	(6.81)	77.14	(8.72)
		E	344	(64)	552	(113)	35.95	(16.68)	63.73	(12.81)	76.62	(10.88)
		SE	345	(96)	588	(188)	33.14	(17.18)	58.39	(13.06)	79.69	(13.33)
		S	349	(70)	611	(129)	46.12	(7.83)	53.74	(8.39)	70.88	(14.45)
		SW	333	(54)	535	(80)	35.73	(8.84)	64.51	(5.79)	77.77	(13.24)
		W	348	(65)	489	(65)	29.67	(10.91)	68.51	(5.50)	75.05	(15.12)
		NW	336	(37)	538	(54)	32.41	(10.07)	59.62	(4.83)	83.39	(14.08)
	Novel	**N**	365	(71)	562	(82)	45.50	(6.80)	60.56	(5.50)	80.58	(10.92)
		NE	326	(53)	555	(98)	40.92	(11.32)	60.88	(7.40)	77.08	(9.20)
		E	327	(51)	550	(130)	31.38	(15.32)	65.22	(8.07)	73.07	(6.21)
		SE	332	(46)	582	(129)	32.52	(17.85)	56.60	(8.93)	74.74	(12.46)
		S	338	(36)	573	(86)	45.44	(8.64)	58.24	(5.69)	76.14	(9.52)
		SW	342	(67)	537	(88)	34.92	(11.47)	63.36	(7.35)	74.33	(9.09)
		W	335	(76)	540	(79)	22.10	(7.76)	63.60	(6.26)	68.44	(10.00)
		NW	315	(74)	577	(80)	29.18	(11.51)	59.43	(3.91)	72.17	(16.28)
CU	**Familiar**	**N**	355	(70)	580	(98)	43.75	(10.03)	58.69	(5.97)	80.03	(5.35)
		NE	374	(100)	575	(91)	45.92	(9.64)	58.68	(5.67)	74.58	(5.58)
		E	333	(40)	616	(100)	40.28	(16.06)	57.25	(8.83)	68.12	(13.43)
		SE	344	(68)	645	(173)	41.01	(20.86)	55.05	(13.48)	74.15	(8.53)
		S	312	(58)	620	(182)	47.72	(9.11)	56.78	(12.39)	73.43	(18.67)
		SW	313	(49)	553	(105)	34.44	(6.50)	61.21	(4.73)	65.36	(14.28)
		W	339	(82)	526	(135)	34.50	(15.63)	64.49	(9.72)	68.49	(10.66)
		NW	346	(80)	600	(137)	43.92	(13.36)	57.45	(7.67)	80.67	(10.87)
	Novel	**N**	354	(75)	605	(150)	47.11	(10.20)	56.42	(9.93)	72.69	(13.45)
		NE	359	(83)	627	(146)	45.81	(10.16)	57.83	(9.90)	71.40	(10.00)
		E	356	(83)	531	(79)	35.26	(13.19)	61.82	(6.89)	71.29	(18.05)
		SE	343	(77)	624	(144)	39.67	(14.44)	55.37	(8.91)	70.09	(10.42)
		S	351	(88)	574	(121)	41.81	(10.38)	59.25	(7.19)	81.74	(6.25)
		SW	329	(72)	571	(123)	41.22	(12.95)	62.21	(11.18)	71.81	(11.11)
		W	341	(70)	581	(146)	34.63	(14.56)	59.07	(9.35)	66.24	(15.02)
		NW	348	(79)	606	(140)	40.16	(14.25)	55.89	(6.63)	72.11	(16.80)
NU	**Familiar**	**N**	365	(80)	678	(179)	48.46	(10.13)	56.13	(10.54)	73.42	(12.78)
		NE	339	(53)	607	(60)	50.17	(6.29)	60.92	(8.96)	78.76	(3.12)
		E	319	(81)	652	(123)	49.18	(17.31)	57.43	(10.95)	74.07	(10.41)
		SE	357	(71)	672	(180)	38.91	(15.18)	53.09	(11.67)	65.62	(25.41)
		S	356	(66)	604	(104)	50.18	(8.44)	57.85	(6.86)	75.65	(14.23)
		SW	349	(70)	564	(123)	43.74	(15.67)	63.72	(10.48)	73.64	(8.18)
		W	331	(86)	522	(97)	32.90	(18.45)	65.68	(7.59)	77.36	(10.98)
		NW	372	(95)	615	(78)	39.44	(14.58)	60.01	(11.24)	84.62	(10.91)
	Novel	**N**	316	(81)	637	(82)	51.06	(7.20)	54.93	(3.92)	79.68	(3.80)
		NE	396	(112)	603	(117)	46.84	(10.90)	63.47	(10.55)	77.09	(11.88)
		E	388	(69)	554	(98)	32.94	(15.95)	62.79	(9.18)	72.24	(11.52)
		SE	338	(51)	663	(110)	43.78	(18.23)	55.50	(8.94)	79.03	(11.14)
		S	361	(85)	609	(127)	47.01	(12.22)	58.95	(6.58)	77.62	(10.00)
		SW	367	(67)	736	(371)	37.93	(14.06)	59.30	(11.45)	74.08	(15.81)
		W	368	(86)	558	(122)	36.29	(14.43)	63.93	(11.39)	71.11	(14.26)
		NW	355	(69)	582	(88)	30.57	(15.55)	58.77	(3.08)	73.11	(6.90)

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