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Assessment of Executive Functions in people with Human-Immunodeficiency Virus (HIV) Infection using the Behavioural Assessment of the Dysexecutive Syndrome: A Pilot Study

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Doctorate in Clinical Psychology

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Thesis Abstract

Objective: Recent improvements in the treatment of Human-Immunodeficiency Virus-1 (HIV) (Highly Active Anti-Retroviral Therapy [HAART]) have dramatically reduced mortality rates. However, improved survival has led to more people with HIV experiencing mild-moderate cognitive impairment. Impairments in executive functions (EF), for example planning and impulsivity, are often identified in people with HIV, with wide-ranging and complex implications, including employment and medication adherence. Previous research has predominantly used 'traditional tests' such as the Stroop, which do not have good ecological validity (Bennett et al., 2005). The main aim of this study was to assess EF in people with HIV using a battery approach with good ecological validity, the Behavioural Assessment of the Dysexecutive Syndrome (BADS) (Wilson et al., 1996). Secondary aims were: *i.* to compare BADS performance to functional outcomes associated with EF as measured by self- and other-report on the Dysexecutive Questionnaire (DEX) (Wilson et al., 1996), and *ii.* to assess potential mediating factors for EF impairment.

Design: The study used a cross-sectional comparison pilot design to compare performance on the BADS of a sample of participants with HIV relative to the published normative data.

Method: A total of 20 participants (13 men; 7 women) with HIV were assessed on the BADS and completed the DEX self-report. An identified proxy for each participant also completed the DEX. Demographic, medical and cognitive, emotional and behavioural information was also collected.

Results: On average, participants scored significantly lower on the BADS relative to normative data. However, performance on the BADS did not relate to self- or other-report of everyday functioning as measured by the DEX. EF impairment on the BADS was present despite the majority of participants taking HAART and having maximally suppressed plasma viral loads. BADS performance was significantly associated with demographic

factors: gender and ethnicity, where female and Black African/Caribbean participants were more impaired.

Conclusions: EF impairment, particularly impulsivity, planning and self-monitoring, is evident in this sample of people with HIV relative to normative data published in the BADS manual. This suggests the value of using a battery approach with good ecological validity and converges with previous research suggesting EF impairment in people with HIV. The lack of significant association between the BADS and DEX-S and DEX-O might suggest potential limitations in insight, where participants are less able to accurately predict performance on the BADS or other people's perceptions. Further research should develop the use of neuropsychological batteries with good ecological validity to consider EF impairment in people with HIV in larger representative samples to improve external validity of the results. Clinical implications include the potential of EF screening for people with HIV and raised awareness in health service staff.

Statement of Contribution

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Assessment of Executive Functions in Human-Immunodeficiency Virus-1 (HIV) Infection using the Behavioural Assessment of the Dysexecutive Syndrome: A Pilot Study

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(For Journal Guidelines see Appendix A)

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Abstract

Impairments in executive functions (EF), for example planning and impulsivity, are often identified in people with Human-Immunodeficiency Virus-1 (HIV). Previous research has predominantly used 'traditional tests' such as the Stroop, which do not have good ecological validity (Bennett et al., 2005). The main aim of this study was to assess EF in people with HIV using a battery approach with good ecological validity, the Behavioural Assessment of the Dysexecutive Syndrome (BADS) (Wilson et al., 1996). The study used a comparison pilot design to compare performance on the BADS within a sample of participants with HIV to the published normative data. A total of 20 participants with HIV were assessed (13 men; 7 women). On average, participants scored significantly lower on the BADS relative to normative data. Further research should develop the use of neuropsychological batteries with good ecological validity to consider EF impairment in people with HIV. Clinical implications include the potential of EF screening for people with HIV.

Keywords: HIV/AIDS; Neuropsychological impairment; BADS; Dysexecutive syndrome; Ecological validity; Everyday functioning

Assessment of Executive Functions in Human-Immunodeficiency
Virus-1 (HIV) Infection using the Behavioural Assessment of the
Dysexecutive Syndrome: A pilot study

Introduction

Since the 1980s HIV has affected more than 40 million people worldwide
(Manji & Miller, 2004) with 77,400 people living with HIV infection in the UK
at the end of 2007 (Health Protection Agency [HPA], 2008). The
introduction in the mid-1990s of Highly Active Anti-Retroviral Therapy
(HAART) revolutionised the treatment of HIV by blocking viral replication
and restoring immune function. This has dramatically improved survival
rates, physical health, resistance to opportunistic infections and reduced the
prevalence of HIV-Associated Dementia (HAD) (Lawrence & Major, 2002).
Despite these improvements, up to 60% of people with HIV still present
with mild-moderate HIV-related cognitive impairments, which significantly
impact daily functioning (Ghafouri et al., 2006). In fact, the actual overall
prevalence of cognitive impairment in HIV has increased, possibly due to
increased survival rates and limited ability of some anti-retrovirals to cross
the blood-brain-barrier, leaving the brain to act as a sanctuary for the HIV
virus (Starace et al., 2002).

HAART may have a non-uniform effect on neuropsychological functioning
(Cysique et al., 2004) where participants on HAART regimes continue to
experience deficits in cognitive abilities such as working memory and
mental flexibility (Gibbie et al., 2006). Further still Starace et al. (2002)
demonstrated individuals on HAART regimes were more likely to show
cognitive impairment than those not taking HAART (Starace et al., 2002)
(see extended paper). Cognitive impairments are most often observed in
the symptomatic stages of HIV, but are often still detectable in
asymptomatic stages when compared to the non-clinical population (Reger
et al., 2002). As well as stage of HIV, the expression of cognitive
impairment is thought to be predicted by other factors, such as low CD_4

count, high plasma viral load, older age, intravenous drug use and female gender (DeRonchi et al., 2002) (see extended paper).

Executive functions (EF) are associated with the frontal brain regions and describe abilities such as planning, mental flexibility, impulsivity, insight, decision-making and inhibition (Verdejo-Garcia & Perez-Garcia, 2007). These skills have been theoretically 'fractionated' into a heterogeneous group of dissociable but interdependent skills necessary for socially appropriate behaviour (Jurado & Rosselli, 2007) (see extended paper). Even subtle deficits in EF can impact on quality of life (Heaton et al., 2004), medication adherence (Hinkin et al., 2002) and employment (Hoffman, 1997). Consequently, research into EF may have wide-ranging implications for people with HIV, particularly for social and interpersonal relationships.

Response inhibition (Hinkin et al., 1999), impulsivity (Hardy et al., 2006) and decision-making (Sahakian et al., 1995) have been shown to be impaired in people with HIV. However, EF has been predominantly assessed using 'traditional measures', for example, Trail Making Test (Reitan & Wolfson, 1985) or the Stroop (Stroop, 1935) which are brief, abstract and laboratory-based. These traditional measures are often insensitive to EF problems and not representative or predictive of real-world problems (Alvarez & Emory, 2006). In other words, they have poor ecological validity (Chaytor & Schmitter-Edgecombe, 2003) (see extended paper). Hardy et al. (2006) used the Iowa Gambling Task (IGT), a measure with suggested good ecological validity which examines decision-making to assess people with HIV and found increased levels of impulsive behaviour compared to HIV-negative controls. However, the relationship between the IGT and real-world behaviour remains largely unexplored (Tranel et al., 2007). Moreover, no single test is sensitive to all aspects of the fractionated EF, so a battery approach has been indicated to better examine EF (Woods et al., 2009). Sahakian et al. (1995) used the Cambridge Neuropsychological Test Automated Battery (CANTAB) (Sahakian & Owen, 1992) and found EF to be particularly affected in people with HIV, especially planning. However, this study took place before the widespread introduction of HAART.

Comprehensive reviews of neuropsychological effects of HIV (Grant, 2008; Woods et al., 2009) have pointed to the remarkable lack of further research robustly exploring executive function in-depth, with participant selection heavily biased towards white homosexual men allowing for little generalisation to further populations (Pereda et al., 2000).

The Behavioural Assessment of the Dysexecutive Syndrome (BADS) (Wilson et al., 1996) is a battery approach to EF assessment which has good ecological validity, simulating aspects of everyday living. The BADS is supplemented by the Dysexecutive Questionnaire (DEX), with versions for self- and other-report, providing evidence of functional outcomes associated with EF. There is a significant evidence base supporting the validity, reliability and superiority of the BADS over traditional tests of executive function (Norris & Tate, 2000) (see extended paper). The BADS has been used with many neurological populations such as Parkinson's Disease (Kamei et al., 2008), and people with risk factors for HIV, such as injecting drug-users (Verdejo-Garcia & Perez-Garcia, 2007).

Therefore, the research problem is that previous empirical studies have identified EF impairment in people who are HIV-positive compared to the non-clinical sample using traditional measures. However, these traditional measures are limited as they do not easily reflect everyday experiences and are rarely comprehensive. This study therefore questions to what extent, and in what way, does EF impairment still exist when using a battery measure with good ecological validity which more accurately reflects real-world experience. On this basis EF in with people with HIV was assessed using the BADS in a cross-sectional descriptive pilot study to explore broad aims within a small sample and determine trends and patterns, before investing resources into larger studies (Van Gorp et al., 1993). This group difference comparison design (Coolican, 2004; Cook & Campbell, 1979; Fraker & Maynard, 1987) used independent samples to compare existing groups (see Extended Paper). This primary aim of the study was to:

- Explore executive function in people with HIV-infection using the BADS relative to published norms (Wilson et al., 1996).

This reflects the real-life experience of clinical neuropsychologists who do not have the benefit of a control group and rely on normative data to interpret scores (Muir-Broaddus et al., 2002). This aimed to make the study findings more clinically relevant.

The study had two secondary aims:

i. To triangulate quantitative measurement of executive deficits on the BADS to self- and proxy-report questionnaires on day-to-day experience of executive functioning

ii. To explore risk factors that might contribute to expression of executive deficits in people with HIV.

Method

Research Participants

A sample of 20 participants with HIV participated in the study. Sample characteristics are presented in Table 1. This sample size is similar to previous pilot studies employing comparable methodologies (Jovanovski et al., 2007; Moriyama et al., 2002). Participants were recruited from local Genito-Urinary (GU) clinics and Infectious Diseases (ID) departments. Staff from these departments identified and approached potential participants according to the inclusion/exclusion criteria. If participants were interested in taking part staff took consent for participant details to be passed to the researcher using the referral form (Appendix B) and gave potential participants a copy of the study information sheet (Appendix C). The principal investigator also liaised with local charitable organisations to advertise (Appendix D) and enable self-referral to the study through the distribution of information sheets and referral forms via these agencies. Participants were not recruited on the basis of known/suspected neurological deficits.

Table 1.
Characteristics of the Study Sample

Characteristic	Frequency	Mean (SD)	Range
Demographic Factors			
Age (years)		43.47 (8.26)	28-59
Gender			
Male	13		
Female	7		
Ethnicity			
White British	15		
Black African/ Caribbean	5		
Sexual Orientation			
Heterosexual	11		
Homosexual	8		
Bisexual	1		
Employment			
Employed	6		
Unemployed	14		
Living Arrangements			
Alone	12		
With Others	8		
HIV Medical Factors			
Time since Diagnosis (years)		9.78 (5.76)	3-24
CD_4 count (cells per mm^3)		493.26 (151.83)	259-715
Medication Regime			
None	4		
Duo-therapy	1		
HAART	14		
Unknown	1		
Months on Current Medication		39.73 (33.59)	1-104
HIV Stage			
Asymptomatic	10		
Symptomatic/ AIDS	9		
Unknown	1		
Cognitive, Behavioural and Emotional Factors			
Education			
5-11 years	8		
12-13 years	6		
14-16 years	5		
17+ years	1		

Monthly alcohol use (units)	4.60 (8.68)	0-30
Pre-morbid IQ (WTAR)	96.50 (20.98)	50-120
Mood (HADS)		
Anxiety	7.95 (3.41)	3-18
Depression		1-11
	5.35(2.41)	

Note. WTAR=Wechsler Test of Adult Reading; HADS=Hospital Anxiety and Depression Scale; HAART= Highly Active AntiRetroviral Therapy

Once referral details were received by the principle investigator, participants were contacted to arrange the assessment. Participants meeting the following inclusion criteria were selected for participation: a positive HIV-1 diagnosis and aged between 18 and 60 years old.

Exclusion criteria were: having received a HIV-positive diagnosis in the last three months; fluctuating medical status (more than one night stay in hospital for any illness or infection in the last two weeks/change in HIV medication regime in the last two weeks); major psychiatric disorders (current episode of psychosis, mania or severe depression); significant substance misuse (self-reported intravenous drug use in the last week); severe neurological deficits (history of head injury/cerebral incident requiring hospital admission for more than 24 hours/degenerative neurological disease, e.g. Multiple Sclerosis/brain tumours). Also excluded were people who were unable to complete the assessment due to: visual impairments (unable to read font size 28 with corrected vision), hearing impairments (unable to hear the researcher in a quiet room with corrected hearing), unable to understand and consent to the research process based on the principles set out in the Mental Capacity Act (2005), insufficient language ability (score of less than 15 on the Sheffield Screening Test for Acquired Language [SST]) (Syder et al., 1993). The SST is a brief screening measure to identify communication problems (Blake et al., 2002). It assesses receptive and expressive language and has been widely used in other neurological samples such as dementia (Potkins et al., 2003).

Procedure and Measures

The assessment duration was 1-1½ hours. This took place either at local clinics, drop-in centres, participants' homes or university, depending on the participant's preference and which environment was most conducive to assessment (quiet, distraction-free and confidential). After sight, hearing and language ability were checked, other exclusion criteria were assessed using participant self-report. Participants who did not meet the criteria to be included in the study were excluded at this point with an opportunity to discuss reasons for exclusion with the researcher. Participants who were eligible to participate had the opportunity to discuss the benefits and possible inconveniences of participation. Sufficient understanding of the implications and requirements of participation in the study was checked verbally and all participants who were included signed an informed consent form confirming their voluntary participation (Appendix E).

Socio-demographic and behavioural information (age, ethnicity, sexual orientation employment status, living arrangements, years of education and monthly drug and alcohol use) were collected via an interview with multiple-choice options (Appendix F). To control for confounding variables brief questionnaires were used to assess: mood (Hospital Anxiety and Depression Scale [HADS]; Snaith & Zigmond, 1994) and pre-morbid IQ (Wechsler Test of Adult Reading [WTAR]; Wechsler, 2001). The HADS is a 14-item self-report screening measure for anxiety and depression specifically developed for use with people with physical illnesses. The HADS has been favourably compared to structured clinical interviews for mental health problems (Whelan-Goodison et al., 2009). The WTAR is a commonly used measure to estimate pre-morbid IQ by relying on previous knowledge (word pronunciation) rather than current cognitive functioning (Franzen et al., 1997). The WTAR displays high correlation with comprehensive measures of IQ which suggests the WTAR has good construct validity (Wechsler, 2001) (see extended paper).

To assess EF, participants completed the self-report version of the DEX and the BADS neuropsychological battery. The DEX (Wilson et al., 1996) is a 20-

item questionnaire which provides information around activities of daily living associated with executive functions, particularly interpersonal interactions (Shinagawa et al., 2007). Each item is measured on a 5-point Likert scale ranging from 'never' to 'very often'. Scores are summed to an overall score with high scores indicating more problems with executive functions in everyday life (see extended paper). The BADS take approximately 40 minutes to administer by a trained professional and consists of six sub-tests:

1 – Card Sort

Participants are required to respond to a series of playing cards with 'yes' or 'no' according to certain rules. It is scored on number of errors made and completion time. This particularly examines inhibition and mental flexibility.

2 – Action Program Test

Participants are required to solve a novel problem practically: how to get a small cork out of a long thin tube using a beaker of water, a wire hook, a bottomless tube and a screw top. Structured prompts are given if the participant gets stuck although for each prompt given a point is deducted (from a starting point of 4). This considers problem-solving and sequencing.

3 – Key Search Test

Participants are asked to imagine they have lost their keys in a field (represented by a square on a piece of paper). They are directed to search the field drawing a line to show where they would walk. Participants are scored on completion time and efficiency of search strategies. This especially focuses on planning and impulsivity.

4 – Temporal Judgement

Participants estimate time to do four common activities. One point is awarded for each answer within a specified range. This measures ability to self-monitor and select an appropriate cognitive plan.

5 – Zoo Map Test

Participants plan a route around a zoo visiting pre-identified locations following certain rules. In the 'high-demand' trial, participants are responsible for planning the route and ensuring they do not break rules. In the 'low-demand' trial with the route specified so participants are only responsible for ensuring they do not break the rules. Participants are scored on route taken, planning and completion times with points deducted for rules broken. This assesses planning and inhibition.

6 – Modified Six Elements Test

Participants have 10 minutes to attempt three tasks, each with two parts, (dictation, picture naming and arithmetic). The instructions make it clear the participant cannot complete all tasks within the time and should plan their time to attempt *some* of each subtask, whilst following the rule that two parts of the same task cannot be attempted immediately after one another. The test is scored on number of subtasks attempted, time spent on each subtask, with points deducted for rule breaks. This explores strategy application, planning, perseveration and self-monitoring.

Each subtest raw score is converted to a standard score between 0 and 4. Subtest standard scores are summed and converted to a Total Profile standard score (mean 100, SD 15). Higher scores on the BADS represent better performance and less impairment. The BADS has normative data derived from 216 participants from a non-clinical sample (Wilson et al., 1996) (see extended paper).

The participant designated someone who knew them well (a proxy/other) (family/friend/healthcare professional) to complete the DEX. Proxies were unaware of how participants rated themselves. As the same questionnaire is used with participants (DEX-S) and proxies (DEX-O) it has been suggested that a comparison between the two scores may give an idea of participants' insight (Bogod et al., 2003).

In addition to this information, with participant consent, staff from GU or ID departments collected medical information pertaining to HIV from participants' medical notes (time since diagnosis, most recent CD_4 count and viral load, medication regime, length of current medication regime, HIV Stage as measured by the Center for Disease Classification [CDC],1993) (Appendix G). Participants were offered a £10 gift voucher as a goodwill gesture for participating in the research. Feedback on test performance in the form of a brief neuropsychological report or face-to-face feedback was optional. The study was approved by a NHS Research Ethics Committee (Appendix H-I).

Statistical Analysis

Statistical procedures were conducted using Statistical Package for the Social Sciences (SPSS) v16.0. An independent samples *t*-test was used to compare the sample mean BADS Total score with the normative average, as provided in the BADS manual. Bivariate correlations (one-tailed) were used to calculate Spearman's rank coefficients to explore the association between the BADS Total score, DEX-O and DEX-S. Spearman's correlations (one-tailed) were conducted to explore associations between executive measures (BADS Total score, DEX-S and DEX-O) and demographic, medical and cognitive, behavioural and emotional variables which have been previously identified to influence performance. Black African and Black Caribbean participants were grouped together for ethnicity analyses as subgroup numbers were small. A Bonferroni correction could have been used to correct for multiple comparisons and reduce the resultant Type I error. However, this reduces statistical power and increases the risk of a Type II error (Perneger, 1998) and was therefore omitted. An alpha level of .05 was used for all statistical tests.

Results

Of the 30 potential participants identified through recruitment (24 self-referrals, 6 staff-referrals) 20 participants went on to complete the assessment (see Figure 1).

```
┌─────────────────────────┐        ┌─────────────────────────┐
│  30 participants referred │  ===>  │  7 potential participants │
│      or self-referred     │        │    non-contactable        │
└─────────────────────────┘        └─────────────────────────┘
              │
              ▼
┌─────────────────────────┐        ┌─────────────────────────┐
│     23 participants       │  ===>  │  3 participants excluded: │
│   contacted and met for   │        │ Current severe depression │
│        assessment         │        │ (1) Insufficient language │
│                           │        │ ability to complete       │
│                           │        │ assessment (2)            │
└─────────────────────────┘        └─────────────────────────┘
              │
              ▼
┌─────────────────────────┐
│      20 participants      │
│         assessed          │
└─────────────────────────┘
```
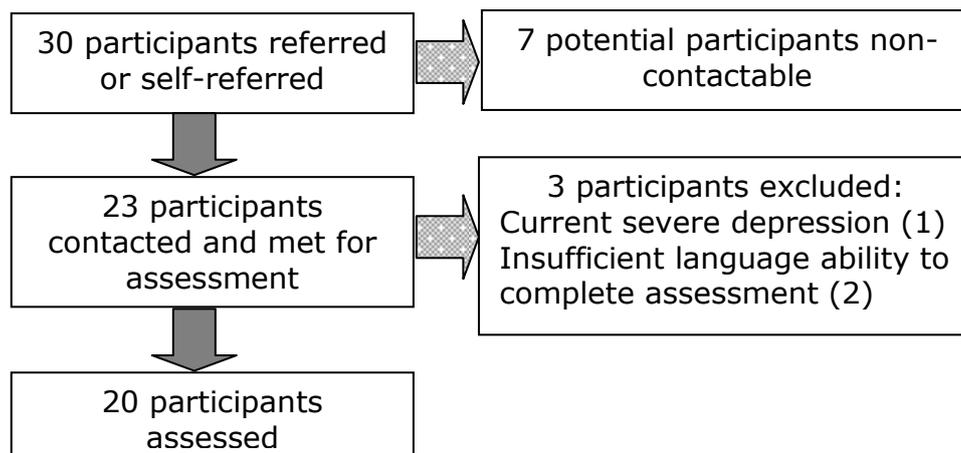
Figure 1. Flow of participants through the study

Relationship between the BADS and Normative data

Table 2 describes participants' means and SDs of BADS performance and scores on the DEX-O and DEX-S. Overall BADS performance classification categorisation is presented in Figure 2 and demonstrates that 20% of participants fell into the 'impaired' range on the BADS Total score but no participants were classified as 'superior'.

Table 2.
BADS and DEX scores for the sample

Characteristic	Number (%)	Mean (SD)	Range
BADS Total Profile Score		85.30 (23.67)	33-113
DEX-S		22.80 (10.07)	4-46
DEX-O		29.76 (13.31)	9-60
DEX-O Rater			
Family/Friend	11 (65)		
Healthcare Professional	6 (35)		
Not Completed	3		

Note. BADS=Behavioural Assessment of the Dysexecutive Syndrome; DEX-S=Dysexecutive Questionnaire-Self Report; DEX-O=Dysexecutive Questionnaire-Other Report

40.0%

30.0%

20.0%

10.0%

0.0%

Percentage of participants

Impaired   Borderline   Low Average   Average   High Average   Superior   Very Superior

BADS Classification Category
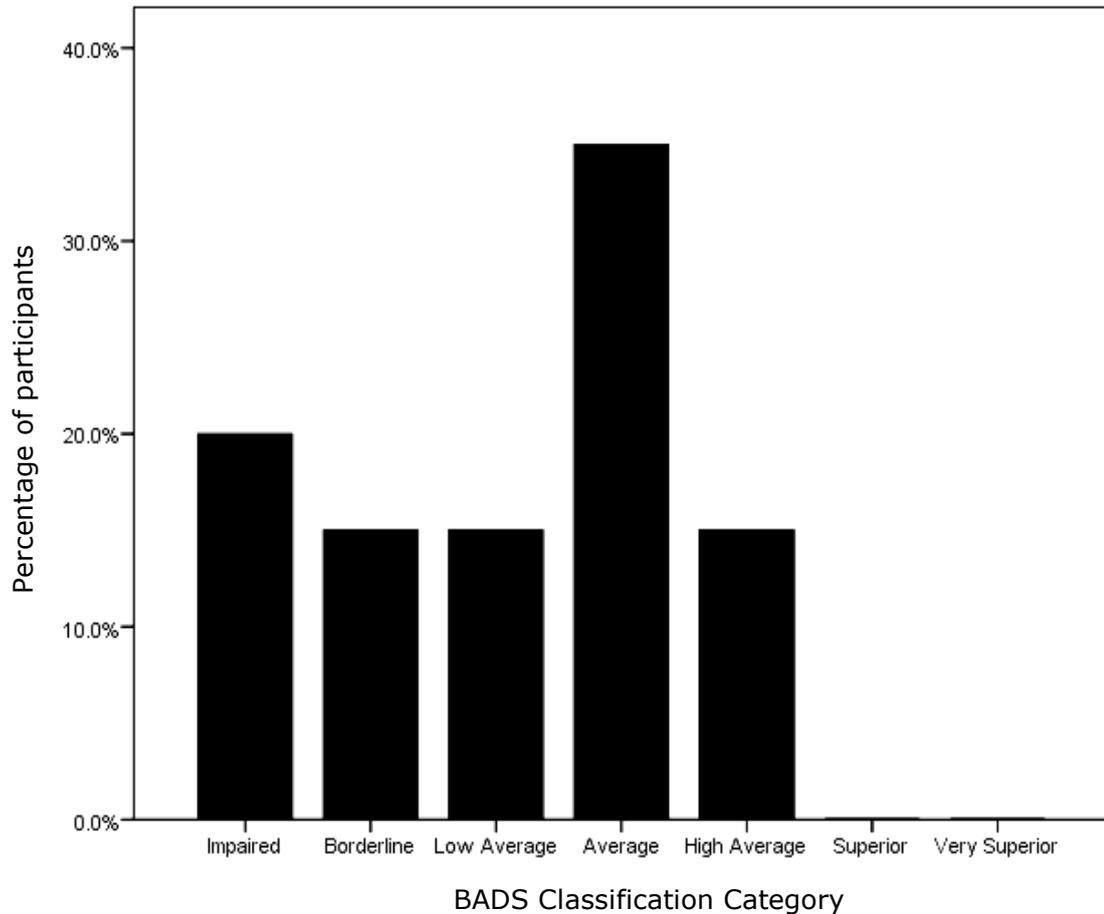
Note. BADS=Behavioural Assessment of the Dysexecutive Syndrome

Figure 2. Percentage of participants by BADS performance category

The average score for the BADS Total score was lower for the study sample (*M* = 85.30, *SE* = 5.29) than the BADS normative sample (*M* = 100.00, *SD* = 15.00). This difference was statistically significant *t*(234) = 3.96, *p*<.001, with a small-moderate effect size *r* = .25 (Cohen, 1988). A one-sample *t*-test showed that the BADS total score mean for this sample was significantly different to the population mean *t*(19) = 2.78, *p*=.01, *r* = .54.

The means and standard errors of participants' subtest scores on the BADS are displayed in Figure 3. From Figure 3 it is possible to see that, on average participants performed less well on the Zoo Map test, with relatively preserved performance on the Action Program test (see extended paper).
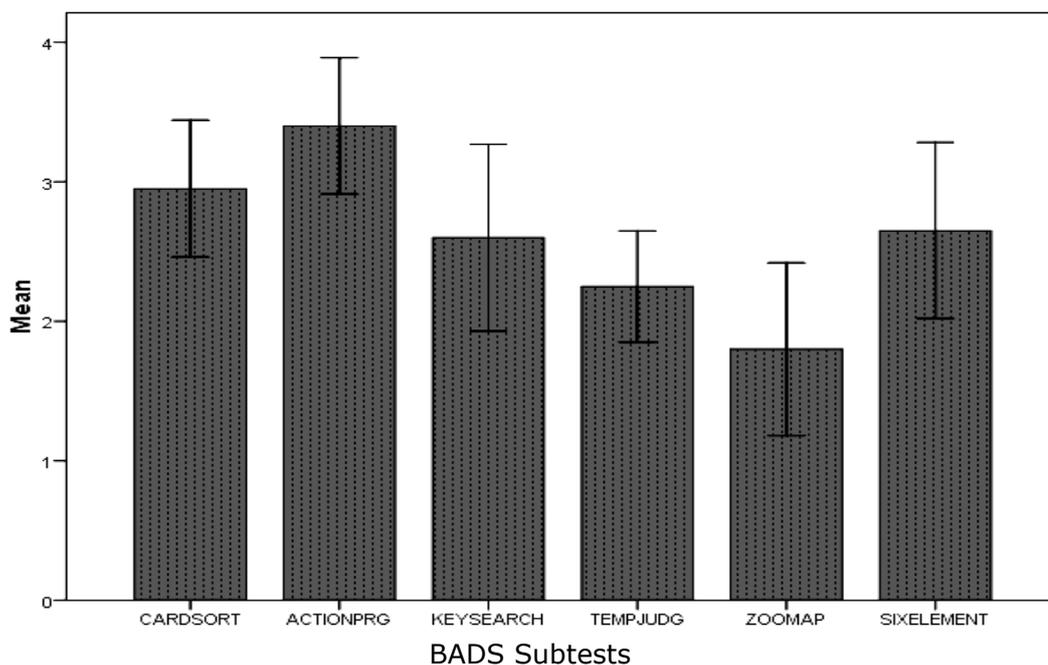
Note. BADS=Behavioural Assessment of Dysexecutive Syndrome

Figure 3. Mean BADS subtest score

Relationship between the BADS, DEX-S and DEX-O

The BADS Total Profile Score was not statistically significantly correlated with the DEX-S (r_s = .11, p=.33, one-tailed) or the DEX-O (r_s = -.33, p=.10, one-tailed). However, the negative association between the DEX-O and the BADS approaches significance and suggests that 'others' report more everyday problems when more impairment was found on the BADS. On the other hand, the lack of association between self-report (DEX-S) and BADS suggests participants are not accurately reporting their performance as demonstrated by the BAD. The DEX-S and DEX-O were not statistically significantly associated with any of the BADS subtests, nor were they significantly correlated with one another (r_s = .26, p=.15, one-tailed). It is not possible to statistically consider whether the DEX scores are comparable to the non-clinical population due to lack of normative data reported in the manual (see extended paper).

Relationship between measures of EF and mediating variables

Table 3 displays the coefficients of the correlational analyses between the medical, demographic and cognitive, emotional and behavioural variables and the BADS, DEX-S and DEX-O.

Table 3.
Correlation coefficients for comparison between variables and the BADS, DEX-S and DEX-O (one-tailed)

	BADS Total Score	DEX-S	DEX-O
Medical Factors	Correlation coefficient r_s (*p*-value)		
Time since diagnosis	.21 (.20)	-.07 (.40)	-.32 (.13)
HIV stage (CDC)	.31 (.10)	.47 (.02)[*]	.07 (.40)
CD_4 count	.09 (.36)	.01 (.49)	-.14 (.30)
Medication Regime	.14 (.29)	.41 (.04)[*]	-.01 (.49)
Months on medication regime	-.24 (.20)	.27 (.17)	-.09 (.38)
Demographic Factors			
Gender	-.48 (.02)[*]	-.23 (.16)	.17 (.26)
Ethnicity	-.52 (.01)[**]	-.42 (.03)[*]	-.22 (.20)
Age	.34 (.07)	-.09 (.35)	-.04 (.44)
Referral Source	.20 (.20)	.54 (.01)[**]	-.22 (.20)
Cognitive, Emotional and Behavioural Factors			
Average alcohol use	.26 (.13)	.27 (.12)	-.07 (.39)
Years of education	-.07 (.39)	-.22 (.18)	.34 (.09)
WTAR	.23 (.16)	-.01 (.48)	.08 (.39)
HADS-A	-.15 (.26)	.39 (.04)[*]	-.06 (.41)
HADS-D	-.11 (.33)	.16 (.25)	.02 (.47)

Note. HIV=Human Immunodeficiency Virus; WTAR=Wechsler Test of Adult Reading; HADS-A=Hospital Anxiety and Depression Scale-Anxiety Subscale; HADS-D=Hospital Anxiety and Depression Scale-Depression Subscale [*]=p<.05, [**]=p<.01

Medical Factors

It was not possible to determine the association between the measures of EF and plasma viral load as 85% participants had undetectable viral loads. The BADS Total Score and DEX-O were not associated with any HIV medical factors. The DEX-S was statistically significantly positively correlated with CDC HIV stage (r_{pb} = .47, p=.02, one-tailed) in the expected direction. The DEX-S was also positively correlated with medication regime (r_{pb} = .41, p=.04, one-tailed) although this was not in the anticipated direction. Overall, those in later stages of HIV and on more medications were more likely to report more problems with executive function (see extended paper).

Demographic Factors

The BADS Total Score was significantly correlated in the predicted directions with gender (r_{pb} = -.48, p=.01, one-tailed) and ethnicity (r_{pb} = -.52, p=.01, one-tailed) on point biserial correlations (Male=0, Female=1; White British=0, Black African/Caribbean=1). Women and Black African/Caribbean participants performed less well on the BADS than the male or White British participants. The DEX-S was also significantly correlated with ethnicity (r_{pb} = -.42, p=.03, one-tailed) where Black African/Caribbean participants reported fewer problems than White British which was not in the expected direction. The DEX-S was also associated with referral source in the anticipated direction (r_{pb} = .54, p=.01, one-tailed) (Self-referral=0, Staff-referral=1) so staff-referred participants reported more problems than self-referred participants. The DEX-O was not associated with demographic variables (see extended paper).

Cognitive and Emotional Factors

The BADS and DEX-O were not significantly associated with cognitive, behavioural or emotional measures. There was significant positive correlation in the expected direction between the DEX-S and anxiety as measured by the HADS (r_s = .39, p=.04, one-tailed) so more anxious participants reported more EF problems in their day-to-day life (see extended paper).

Discussion

The main aim of the study was to assess executive function in people with HIV-infection using a measure with good ecological validity (BADS) compared to normative data. Despite 75% of the sample being on HAART regimes and 85% having undetectable viral load levels which are thought to protect against neuropsychological impairment (Ferrando et al., 1998), this study still found difficulties with EF in this sample. The results showed the EF ability in this sample was below that which was predicted by normative data for the BADS. This is consistent with previous research demonstrating EF impairment in people with HIV (e.g. Sahakian et al., 1995). The present study adds to these findings by using a battery, measuring more than one aspect of EF, which is reported to have superior ecological validity to traditional laboratory tests such as the Trail Making Test or the Stroop (Norris & Tate, 2000) (see extended paper).

Participants performed on average most poorly on the Zoo Map, with relatively preserved performance on the Action Program. This suggests decreases in ability to plan and self-monitor and increases in impulsivity are evident in participants with HIV in this sample. This is consistent with Hardy et al. (2006) who found increased impulsivity in people with HIV. Sequencing and approaches to novel tasks are less affected aspects of EF in participants in this sample as shown by normal performance on the Action Program. However, these conclusions are only tentative because although subtest may be weighted more on particular skills, all the subtests are multi-faceted in nature to reflect the complexity of everyday tasks.

Seventy percent of the sample was unemployed and 45% cited disability related to HIV as the reason for their unemployment. This may be, in part, due to executive function difficulties and would support previous findings, which reported that those with cognitive impairment were more likely to be unemployed than those without (Heaton et al., 1995). Further research is needed to explore this relationship.

The study had two additional aims:

i. To triangulate quantitative measurement of executive deficits on the BADS to self- and proxy-report questionnaires on day-to-day experience of executive functioning (DEX).

The results showed the BADS, DEX-S and DEX-O were not significantly related to each other. Although this finding does not support previous research (e.g. Wilson et al., 1998), which found strong relationships between the BADS and DEX (especially DEX-O), it is consistent with Norris and Tate (2000) and Woods and Liossi (2006), who also found limited or no association between the DEX and BADS. This lack of significant association may be due to differing levels of demand in each individual's environment, leading to different relative importance of EF skills.

Proxies more closely reported problems similar to BADS performance than participants themselves, although the association between the BADS and DEX-O only approached significance. Participants self-report (DEX-S) was not statistically significantly associated with the BADS or the DEX-O which suggests they could not accurately predict their performance or how others saw them. , This converges with previous research which suggests a lack of insight is associated with EF difficulties (Jovanoski et al., 2006) (see extended paper).

ii. To examine factors that might contribute to expression of executive deficits in people with HIV.

Medical Factors (see extended paper)
Factors relating to HIV and disease progression were not significantly associated with the BADS or DEX-O. This presence of EF problems in this study, even whilst on HAART regimes, adds weight to previous studies which found minimal benefit of HAART for mild-moderate cognitive problems (Cysique et al., 2004). This may initially seem contrary to research which has pointed to the benefit of HAART for memory and

psychomotor speed (e.g. Ferrando et al., 1998) but these studies did not demonstrate benefits for EF. Although medication adherence was not directly measured in the current study, these findings cannot be attributed to insufficient adherence or ineffective HAART regimes as higher CD_4 counts were associated with longer length of medication regimes. Maximum viral suppression was evident in most participants which is noted as the gold standard outcome for HAART.

Participants in symptomatic stages of HIV reported more EF problems on the DEX-S than asymptomatic participants. Likewise, participants taking HAART reported more problems than those taking fewer or no medications. This indicates that disease progression is associated with increased reporting of EF difficulties in everyday life, although disease progression is not associated with BADS performance. Therefore, it may be that the BADS is not picking up subtle difficulties, although a floor effect was not evident in the data. Alternatively, progression of the disease may lead to increase environmental demand, for example medications for physical health problems and increased anxiety, which affect the importance of EF in their day-to-day life. However, as HAART is not a homogenous regime but involves various antiretroviral combinations, different regimes may vary in ability to cross the blood-brain-barrier. This might lead to different regimes affecting cognitive abilities differently.

Demographic Factors (see extended paper)
Women performed less well on the BADS than men, although this difference was not found on self- or other-report of everyday functioning. This poorer BADS performance suggests HIV may affect the frontal regions of women more than men. This corresponds to Failde-Garrido and colleagues (2008) who also found women were likely to experience more cognitive impairment in HIV than men. There may be differences in history of drug use/abuse (Failde-Garrido et al., 2008), or education level (Stern et al., 1996) between men and women which may influence EF ability. However, no significant differences between men and women were found on these variables in this study. Alternatively, there may be differences in brain

structure (Cahill, 2006) and hormone receptors in the brain (Hafner et al., 1994; Kimura, 1992) between men and women. Whichever mechanism, this has implications for the tendency for women to be under-represented in HIV research.

Black African/Caribbean participants tended to perform less well on the BADS than White British participants. This is consistent with previous research where people from non-Western backgrounds performed less well on neuropsychological tests (Rivera Mindt et al., 2008). As participants from Black African/Caribbean backgrounds did not speak English as a first language they may have been at a disadvantage when completing the BADS. However, all participants scored above the cut-off on a basic language ability test. There were also no differences between groups on pre-morbid IQ levels. However, there may be other risk factors in people from BME backgrounds which either affects their EF ability or their ability to perform on the BADS (Rivera Mindt et al., 2008). For example, there may be differences in access to education (Kaufman, Cooper & McGee, 1997), acculturation (Lucas, 1998) or literacy (Manly, Touradji, Tang & Stern, 2003). Socio-economic status may also restrict access to services such as healthcare, and influence brain development (Brickman Cabo & Manly, 2006). Additionally EF might be more 'culturally mediated' than other cognitive skills (Rivera Mindt et al., 2008). Tests such as the BADS developed and normed within Western countries, may be 'euro-centric' and have less validity for black and minority ethnic (BME) groups living with HIV, in keeping with previous research (Proctor & Zhang, 2002). It is not possible to further speculate as no data is recorded in the BADS manual on the ethnicity of the non-clinical normative sample. Moreover, 85% of the Black African/Caribbean participants were women so there may be combined effects of gender on poorer EF outcome for this group.

Black African/Caribbean participants reported fewer everyday EF problems despite more difficulties being found on the BADS score for these participants. This might provide some support for reduced insight into EF impairment (Hart et al., 2005) but in contrast several authors have not

found the connection between executive functions and insight (Sanz et al., 1998). Instead self-report may offer a realistic representation of everyday experience where Black African/Caribbean participants experienced fewer problems pertaining to EF. This may be due to low level of environmental demands which influences the importance placed on EF skills but needs further exploration.

Cognitive, Emotional & Behavioural Factors (see extended paper)
Participants with higher levels of anxiety reported more problems on the DEX-S. However, problems with EF may cause more anxiety and increased hypervigilance to difficulties. This would support previous research on the detrimental effects of anxiety on cognitive performance (Kizilbash et al., 2002).

Strengths and Limitations
The study did not include a matched control group with which to directly compare participants' performance on the BADS. A matched control group might have provided a more accurate estimation of expected performance by controlling for a number of participant variables, such as fatigue (Coolican, 2004). However, comparison of the sample to the normative data was felt to be important as this reflects real-world experience of neuropsychologists. Neuropsychologists rarely have the ability to compare patient data to a matched control and rely on the normative data available (Muir-Broaddus et al., 2002) so this method should enhance the clinical utility of the findings. The study sample and BADS normative sample were not significantly different in age or IQ, so the two groups were matched to some extent making comparisons appropriate (see extended paper).

The large number of statistical analyses on a small heterogeneous sample in the current study may statistically increase the likelihood of false positive findings over multiple comparisons. The small sample may also have led the study to be under-powered and the effect sizes were within the small-moderate range. However, the intention of this study was to be explorative

and promote effective allocation of resources in future research to further explore the trends found in this study.

Despite the small sample size, one of the strengths of the study is the larger proportions of females, heterosexuals and BME groups than previous research and the minimal exclusion criteria to allow for greater representativeness in the sample than in previous research and thus achieve more clinically useful findings. However, it is important to bear in mind the limitations of using a measure developed and normed in a Western country and English language when considering the performance of participants who have a different cultural heritage (see extended paper).

Future Research

This pilot study has suggested the value of using a battery approach with good ecological validity to explore the fractionated EF construct. A longitudinal study of EF in people with HIV within a larger cohort of participants might allow for identification of patterns of impairment or compensation and factors that facilitate or inhibit this process. Other measures with good ecological validity that gather additional qualitative information such as the Multiple Errands Test (Shallice & Burgess, 1991), might allow for detailed analysis of strategies used by participants and analysis of common errors made. Future research should also incorporate functional and meaningful outcomes related to EF and look to explore individual environmental demands, for example, the burden of medication adherence, as a potential predictor of the impact of EF in everyday life (see extended paper).

Clinical Implications

Screening for EF difficulties in people with HIV, even early in the course of the infection, or when there is maximum viral suppression, may be particularly useful, especially in women and people from BME communities. The BADS might be a useful tool for this purpose due to its focus on ecological validity. In comparison with traditional tests the BADS clearly resembles everyday activities more accurately and the close

approaching significance of the association between the BADS and DEX-O might suggest this is a useful approach. However, it would be important to supplement this with both self- and other-report, to determine the functional impact and environmental demands, being mindful of potential difficulties with insight.

The support of future research, considering compensation strategies might lead to the improvement of rehabilitation strategies and/or rehabilitation programs for people with HIV who might benefit (see extended paper). As EF difficulties often present most evidently in social interactions, it might be useful to have information on executive function difficulties available to patients and their families to develop awareness of potential difficulties. A comprehensive understanding of EF might also benefit staff working with people with HIV, with implications for staff training in providing effective support strategies.

Conclusions

Previous research with people with HIV has used traditional measures such as the Trail Making Test, which might be insensitive to real-world implications of EF difficulties. Using a neuropsychological battery with renowned ecological validity, EF difficulties were found in people with HIV, especially women and people from BME communities. These difficulties are evident even in maximal viral suppression, which suggests HAART may not have universal protective side-effects. Further research needs to consider these provisional findings in larger samples, incorporating not only functional outcome assessment but exploration of individual environmental demands.

<div align="center">References</div>

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Extended Background

This extended background provides a comprehensive critical review of the literature relating to Human-Immunodeficiency Virus (HIV) and executive function. First, HIV and the general cognitive impact for individuals, including the influence Highly Active Anti-Retroviral Therapy (HAART), is discussed before a brief exploration of the implications of cognitive difficulties and some of the factors which might influence expression of cognitive impairment. Executive functions are theoretically discussed and literature on HIV and executive functions specifically is explored. The review considers measurement issues in executive function, in particular ecological validity. A particular measurement tool, with good ecological validity, the Behavioural Assessment of the Dysexecutive Syndrome (BADS) is discussed. Finally the review finishes with an extension of the aims and research question of the study.

Search Strategy

Research studies and theoretical articles were identified using electronic databases such as PsycINFO, Web of Science and Ovid, using key words such as 'HIV', 'AIDS', 'dementia', 'executive function', 'neuropsychology', 'cognitive impairment', 'BADS' and 'ecological validity'. The reference list and citing articles for these articles were also searched and relevant articles obtained. All studies were considered for inclusion and critically appraised for methodological quality using guidelines, such as the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) (Vandenbroucke et al., 2007). Most research has examined the aetiology of neuropsychological impairment in HIV, rather than treatment, often therefore using observational cross-sectional case-control methodologies. This methodology is not high in the hierarchy of rigorous evidence and can only offer speculations on associations, not causality (Greenhalgh, 2001). Although attempts have been made to be comprehensive, this review does not aim to be a systematic review. Therefore, only the most important previous research articles have been presented to highlight and identify strengths and gaps in the evidence base.

Epidemiology & Overview

It is valuable to have a basic understanding of the HIV infection, the course of the disease and psychopharmaceutical effects of commonly used treatment as these may interact in complex ways with cognitive functioning.

HIV is a systemic viral infection identified by testing for antibodies to HIV (seroconversion) (Enzyme Linked Immuno-Sorbent Assay [ELISA]). As a retrovirus, HIV contains an enzyme which replicates HIV cells using the DNA of the cell it has infected. High levels of infection in the blood (plasma viral load) weaken the immune system by destroying CD_4 cells. This lowers CD_4 count and the immune system cannot function effectively, increasing susceptibility to infections (for details on structure and mechanism of HIV see National Institute of Allergy and Infection Diseases [NIAID]).

Lowered CD4 and consequent infections affect all organs, including the brain, causing progressive changes (Kopinsky, Bao & Lin, 2007). HIV affects nearly 33 million people worldwide (Woods, Moore, Weber & Grant, 2009). Unlinked anonymous methods calculate the number of individuals unaware of their HIV-positive status through analysis of blood samples collected from the general population gathered for reasons other than HIV testing. It is currently estimated that 27% of those with HIV in the UK are unaware of their serostatus (McGarrigle et al., 2006). There have been dramatic changes in prevalence from predominantly homosexual men to 40% of all new infections being in young adults (aged 15-24) (Knoll, Lassmann & Temesgen, 2007) and 30-35% of those infected with HIV in Europe being women (Maki & Martin-Thormeyer, 2009). HIV is transmitted through contact with the blood or bodily fluids (such as plasma/semen) of an individual infected with HIV. The main exposure to these fluids is through:

- Unprotected sexual contact
- Sharing needles (intravenous drug use)
- Mother-baby transmission
- Recipient of blood products

Types

There are two recognised types of HIV infection: HIV-1 and HIV-2. HIV-1 accounts for the vast majority of cases, whereas HIV-2 is predominantly found in West Africa (Oster, 2000). Both infections lead to Auto-Immune Deficiency Syndrome (AIDS) with little differences in CD_4 counts (Grand et al., 1997) and are nearly indistinguishable in autopsy (Ndour et al., 2000). The main difference is that HIV-2 is less easily transmissible and, with lower viral load levels, is thought to have a longer duration between infection and illness (Ndour et al., 2000). However, due to environmental differences comparisons between HIV-1 and HIV-2 are limited (Ndour et al., 2000). Due to the location of the current study in the United Kingdom and its predominance in Western countries, HIV-1 is the focus of this research study. In HIV-1 there are genetically distinct subtypes thought to affect transmissibility and medication response, however, research in this area is inconclusive (Oster, 2000).

Stages and Course of Infection

Both the World Health Organisation (WHO) (2007) and the Center for Disease Classification (CDC) (1993) have suggested staging models for HIV which classify severity and progression of the infection. The CDC model, outlined in Table 4, has been used in the present study as it integrates both disease indicator factors and infections, compared to the WHO which focuses on solely clinical manifestations. The CDC model describes three main stages in HIV infection: asymptomatic, symptomatic and AIDS (Table 4). Although this model is a helpful guide to severity of HIV, it has been criticised by clinicians as in this model patient cannot return to previous stages irrespective of whether the AIDS-defining illnesses resolve or CD_4 count improves.

Table 4

Simplified Version of CDC Classification of Stage of HIV infection

CDC Classification Stage	Corresponding Infection Level	Details
1	Asymptomatic	No serious illness CD_4 above $200mm^3$
2	Symptomatic	Non-AIDS defining illnesses CD_4 above $200mm^3$
3	AIDS	AIDS-defining opportunistic infection Current or previous CD_4 below $200mm^3$

Note. CDC=Center for Disease Classification

Treatment

Pre-1996 HIV was treated with single anti-retroviral drugs (mono-therapy). Since 1996, HIV has been treated with Highly Active Anti-Retroviral Therapy (HAART). HAART is a combination of at least three anti-retroviral drugs from the finite number of anti-retrovirals available. HAART combinations usually include two nucleoside reverse-transcriptase inhibitors and one protease inhibitor (Ellis, Langford & Masliah, 2007). As HAART aims to suppress viral replication it cannot cure HIV, so once individuals start on these medications most may remain on them for the rest of their lives, although they may change the specific regimes (Panel on Clinical Practices for Treatment of HIV Infection, 2001). The maximum success of HAART is a viral load which is undetectable using conventional assays, associated with restoration of the immune system (Burgoyne, 2005). As a result, HAART has reduced the incidence of AIDS-defining illnesses from 30% to 10% (Lawrence & Major, 2002) and increased survival rates from 64% to 85% of people surviving for more than 2 years post positive diagnosis (Knoll et al., 2007). As a result of its success in prolonging life, HAART is recommended for all patients with HIV (Knoll et al., 2007).

Despite its successes, maintaining viral suppression requires high levels of adherence to medication regime, which involve managing complex and

frequent dosing and unpleasant side-effects (Burgoyne, 2005). For HAART to be effective 90% adherence to the regime is required and poor adherence can lead to medication resistance (Bangsberg et al., 2000). Resistance is problematic because there are only a finite number of anti-retrovirals available. Indeed, increasing numbers of individuals *are* developing medication resistance (Robertson et al., 2007). Furthermore, although some anti-retroviral medication, such as zidovudine, may have neuro-protective effects (Baldeweg et al., 1995), there is a question over the ability of other anti-retroviral to blood-brain-barrier (BBB) and act directly on the brain (neuroactive). Research is currently inconclusive as some authors have found the BBB becomes compromised as HIV progresses, making it easier for HAART to cross (Robertson et al., 2007).

As a result of the change in HIV from a fatal disease to a chronic infection (Robertson et al., 2007), clinical management issues have shifted towards issues of daily functioning and the potential neurotoxic side-effects of HAART (Melrose, Tinaz, Castelo, Courtney & Stern, 2008). Accordingly the prevalence of other difficulties such as mild-moderate cognitive impairment has increased and become a key quality of life issue (Ghafouri, Amini, Khalili & Sawaya, 2006).

Neurobiology
HIV is known to affect the brain even early in the course of the infection (Ghafouri et al., 2006), and, after the lungs, the brain is the most affected organ (Masliah, DeTeresa, Mallory & Hansen, 2000). HIV viral agents, proteins and free radicals as well as by-products of HIV replication may directly damage neurones (Antony & Bell, 2008; Hult, Chana, Masliah & Everall, 2008). However, the presence of HIV in the brain may also cause chronic inflammation of the macrophages and microgilia (immune cells in the brain tissue) or set off disturbances in astrogilia (which maintain neurone viability) that ultimately leads to neuronal cell death (Grant, Marcotte & Heaton, 1999). There may also be additive/multiplicative effects of polypharmacy, high levels of stress hormones, opportunistic infections and normal ageing (Kopinsky et al., 2007). For further discussion on the

mechanisms of HIV in the brain see Brew, Crowe, Landay, Cysique and Guillemin (2009). An understanding of the underlying neural systems affected by HIV may help understand the neuropsychological consequences.

The main structural brain changes are shrinkage enlarged ventricles and sulci (Sahakian et al., 1995) and thinning of the prefrontal cortex (Thompson et al., 2005). The fronto-striatal circuits, linking the prefrontal cortex to the striatum and basal ganglia, have been identified as the most affected areas of the brain (Castelo, Sherman, Courtney, Melrose, & Stern, 2006; Ellis et al., 2007). This is particularly relevant to the present study as the prefrontal cortex is closely associated with executive functions. Functional magnetic resonance imaging (fMRI) of 11 people with HIV showed that, compared to HIV-negative controls, functional changes in the prefrontal cortex may occur before the structural changes and there is some suggestion of a re-organisation of function and compensatory brain mechanisms such as activation of the parietal region (Melrose et al., 2008).

Cognitive Impact of HIV Infection
The neurobiology described and resultant cognitive impairment encompasses a range of cognitive domains for people with HIV including memory, attention, and executive functioning (planning and problem-solving). Global cognitive disturbances are described as HIV-Associated Neurocognitive Disturbances (HAND). Cognitive deficits within HAND can range from subtle minor motor/cognitive disorder (MCMD) to severe and disabling HIV-Associated Dementia (HAD) (Woods et al., 2009). Figure 4 outlines terminology used to describe HIV-associated cognitive impairment.

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                    ┌─────────────────────┐
                    │   HIV-Associated    │
                    │   Neurocognitive    │
                    │   Disorder (HAND)   │
                    └─────────────────────┘
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| Subsyndromic neurocognitive impairment (SNI) | Mild Motor/Cognitive Disorder (MCMD) | HIV-Associated Dementia (HAD) | Previous Terminology |

| Asymptomatic neurocognitive impairment (ANI) | HIV-Associated Mild Neurocognitive Deficits (MND) | HIV-Associated Dementia (HAD) | Newest Terminology |

| Mild neurocognitive impairment Does not interfere with activities of daily living (ADL) | Marked impairment in at least two cognitive domains Decline in ADLs | Severe impairment in at least two cognitive domains Considerable impairment in ADLs | Details |

Note. Adapted from Grant & Atkinson, 1995; Woods et al., 2009; Antinori et al., 2007)

Figure 4. Definitions and classification of HAND

Despite limited research, most researchers consider the milder forms (MCMD) as distinct from dementia (HAD) and not necessarily linked to one another (Heaton et al., 1995). Unlike other neurodegenerative disorders such as Alzheimer's, HAND is not invariably progressive and individuals may recover, worsen or experience static (Cole et al., 2007) or fluctuating courses (Robertson et al., 2007).The inconsistent use of terminology used in HIV research however, hinders the research in cognitive impairments in HIV as it makes different study findings difficult to compare (Grant, 2008). For further definition of the terms see Woods et al. (2009).

History of cognitive impairment in people with HIV

Although it is no longer the case, before the introduction of HAART, cognitive impairment was often a sign of imminent mortality in people with HIV (Woods et al., 2009). An integrated global cognitive assessment battery was suggested (Butters et al., 1990), which included tests such as the Trail Making Test (TMT) (Reitan, 1958) and the Grooved Pegboard test (Trites, 1977). This recommendation has been highly influential and this battery is still commonly used today, despite being nearly 20 years old. This approach is also used to categorically determine whether individuals with HIV have a cognitive impairment or not. Cognitive impairment is 'diagnosed' when an individual scores below two standard deviations on two or more tests. This black/white categorisation is a significant weakness of previous studies as it does not consider everyday function or specific cognitive domains. Although some authors have moved away from this model of assessment, most of the research outlined below is based on the Butters et al. (1990) battery, with focus on biomedical rather than psychosocial aspects of cognitive impairment (Rivera Mindt et al., 2008). For this reason this study will also use the term 'cognitive difficulties' to denote the idea that cognitive abilities lie on a spectrum. The research body has also been greatly affected by the use of HAART, with studies divided into 'pre-HAART' and 'post-HAART' depending on whether they were conducted with people prior to (pre-) the introduction of HAART or since then (post-). This review focuses on the post-HAART era, as most useful to place the current study within a context.

Prevalence of cognitive impairment in HIV

Most research suggests between 30-60% of people with HIV show at least mild cognitive impairments (Grant, 2008) with the prevalence of cognitive difficulties increasing as CDC disease stage progresses (Reger, Welsh, Razani, Martin & Boone, 2002). Goodkin et al. (2001) reported that 5-14% of asymptomatic individuals showed signs of MCMD/MND compared to 25% of people with AIDS. However, even asymptomatic individuals show nearly double the rate of cognitive impairment (35.3%) compared to matched HIV-negative controls (17.0%) (Grant et al., 1999). Reger et al. (2002) used

rigorous methodological inclusion criteria (interval/ratio level data, matched control group and use of well-known standardised tests) to identify 41 primary studies of cognitive impairment in people with HIV to be included in a meta-analysis. The analysis found effect sizes for global cognitive impairment increased with disease progression, from .05 to .21 in asymptomatic individuals to .42 to .82 in individuals with AIDS, with significant impairments in motor and executive functions. However, there was considerable overlap between the CDC stages, especially between symptomatic and AIDS categories, and the system used to classify effect size is arbitrary and may not be clinically meaningful (McGrath & Meyer, 2006). There is a considerable lack of consistency between the studies in terms of populations sampled, definition of impairment, methodology and outcome measures which limits the ability to compare findings across studies, potentially undermining conclusions made by Reger et al. (2002). Moreover, little research has included the impact on activities of daily living when determining cognitive impairment, despite this being a defining feature of MND or HAD.

Impact of HAART

In an 18-month longitudinal prospective study including 130 homosexual or bisexual men Ferrando et al. (1998) demonstrated the superior effects of HAART on reversing cognitive deficits in attention, learning, memory and psychomotor speed. This benefit was less evident in measures of executive function (as measured by the TMT and Stroop). Unfortunately, the authors do not comment on this discrepancy in their interpretation and conclude that HAART may traverse a compromised BBB or that low concentrations are sufficient to help neuropsychological function. Tozzi et al. (1999) and Letendre et al. (2004) also found that individuals who achieve viral suppression through HAART showed a significant improvement in neuropsychological test performance, although the samples used were small so results have limited power. However, this finding does agree with large cohort studies where HAART has been found to reduce the relative risk of HAD (Bhaskaran et al., 2008), although these authors did not distinguish

between cognitive domains or randomise participants to treatment groups due to the complex nature of HAART regimens.

Although there are reduced rates or even reversal of severe forms of cognitive impairment, the prevalence of individuals experiencing milder forms of cognitive problems is still substantial (Baldewicz et al., 2004). It has been suggested that people on HAART may reach a sub-optimal plateau (Ellis et al., 2007). Research also reveals that not all individuals or cognitive domains benefit uniformly as a result of HAART. Cysique, Maruff and Brew (2004a) compared two cohort studies and found individuals on monotherapy showed deficits in attention, verbal fluency and visuospatial skills, whereas individuals on HAART showed deficits in learning and complex attention. Overall the authors found no statistically significant difference between prevalence rates of cognitive impairment in participants on mono-therapy compared with HAART, 41.1% and 28.8% respectively, although this does seem like a large difference. Moreover, this study compared two different cross-sectional studies which used different outcome measures so results are not directly comparable. Nonetheless, the results do agree with other research studies, such as Tozzi et al. (2007) who found that 62.8% of 26 patients persistently showed abnormal neuropsychological performance over 65 months despite HAART, using a prospective observational cohort. However, medication adherence was not accounted for, so participants may not have been taking HAART as instructed, which may reduce viral suppression and influence neuropsychological impairment (Tozzi et al., 2007).

Cysique, Maruff and Brew (2004b) investigated the impact of neuroactive HAART on neuropsychological function in 97 individuals with advanced HIV (exclusions: previous psychiatric disorders, neurologic disease or drug use). Individuals were assessed on the measures recommended by Butters et al. (1990) and found individuals on neuroactive drugs did not perform better on neuropsychological tests than those on less neuroactive combinations. However, the post-hoc quasi-experimental design may mean individuals

were specifically prescribed a neuroactive HAART regimen due to pre-identified cognitive problems.

Overall, research continues to point to neuropsychological impairment in HIV, despite HAART. Indeed, 8-34% of individuals with HIV continue to show cognitive decline despite undetectable viral load (Cysique, Maruff, & Brew, 2006; Hammer et al., 1997). Bias has been introduced in the wider research by reporting several cross-sectional analyses from participants enrolled in longitudinal studies. Therefore, the same sample are reported several different times leading to over-representation in the research (e.g. Ferrando et al. 1998). Most studies also do not control for length of time individuals have been taking HAART thought to influence the magnitude of relationship with neuropsychological functioning (Lovejoy & Suhr, 2009).

Patterns of cognitive deficit

Recent studies (Dawes et al., 2008) have identified the prototypical profiles of cognitive difficulties in HIV, predominantly:

- Poor attention and working memory
- Slower speed of information processing
- Impaired executive functions and motor skills
- Relatively intact language, visuo-spatial perception and long term memory.

This pattern of difficulties is indicative of a subcortical dementing process of the frontal-striatal system (Heaton et al., 1995). Executive function deficits seem to be a central feature to most HIV-associated neurocognitive impairment patterns, especially important as executive functions are strongly associated with impairment in everyday activities (Heaton et al., 2004). While these are typical features, there seems to be considerable heterogeneity in this presentation.

Implications of Cognitive Deficits

Even minor cognitive deficits may have significant implications for employment (Albert et al., 1995; Heaton et al., 1994), financial

management, social support (Honn & Bornstein, 2002), adhering to medication regimes and mortality (Ellis et al., 1997; Mayeux et al., 1993). Many of these activities are cognitively demanding and require forward planning, strategising and ability to make decisions (Lovejoy & Suhr, 2009). Individuals with asymptomatic HIV and cognitive impairments are twice as likely to be unemployed (Heaton et al., 1995), or have difficulties at work (Grant et al., 1999), than those with asymptomatic HIV without neuropsychological impairment. Van Gorp, Baelwald, Ferrando, McElhiney and Rabkin (1999) found that people with HIV who were unemployed were more likely to exhibit deficits in memory, set-shifting and flexibility. Poor health, including cognitive impairments, may also cause social network size to diminish (Kaplan, Patterson, Kerner & Grant, 1997), which is consistently acknowledged as an important quality of life factor (Emlet, 2006).

Hinkin et al. (2002) examined the interactive effects of neuropsychological impairment and medication adherence in 137 people with HIV (aged 25 to 69 years, 18% women, 69% African American). Participants were assessed on a variety of neuropsychological measures including the Trail Making Test (TMT), Controlled Oral Word Association Test (COWAT) (Benton & Hamsher, 1976), Stroop (Stroop, 1935) (for a description of these measures see Appendix J) and medication adherence was monitored using electronic bottle caps (monitoring frequency and quantity of medication taken). The study found significantly lower medication adherence in individuals with cognitive impairments, particularly executive function impairment. The large culturally heterogeneous sample and stringent recording of medication adherence confer good external validity of the results (the validity of generalising the results to the wider population). However, longitudinal exploration might assist in determining causality, whether medication adherence affects cognitive abilities or cognitive abilities affect medication adherence. The link between medication adherence and executive functions (e.g. Wagner, 2002) has been supported by recent reviews of the literature (Lovejoy & Suhr, 2009).

Mediating Factors in Cognitive Impairment

Regardless of disease stage, not all infected individuals show cognitive difficulties (Basso & Bornstein, 2000). Wilkins et al. (1990) found the number of confounding factors had an additive effect on cognitive impairment. Neuropsychological performance is influenced by a number of medical, demographic and cognitive, behavioural and emotional factors which may act directly on cognition or affect general level of arousal and fatigue (Grant, 2008). Most research has used stringent exclusion criteria to control for these factors, leading to samples not being representative of the population (DeRonchi et al., 2002). This section considers the most important of these factors in more depth. For details of how these factors were accounted for in the current study see extended methodology.

Medical factors:

CD_4 Count

Although CD_4 count is a strong predictor for AIDS-defining illnesses, the research on the association between CD_4 count and neuropsychological impairment is less clear (Marcotte et al., 2003). In a ten-year longitudinal study Childs et al. (1999) found CD_4 counts of less than 200 cells per mm^3 was associated with a moderate risk for HAD. More recent longitudinal studies (Marcotte et al., 2003; Bhaskaran et al., 2008) also found an inverse relationship between neuropsychological impairment and CD_4 count. However, these studies only included a small number of participants with neuropsychological impairment and other authors have found CD_4 count could not predict neuropsychological impairment or had a weak relationship at best (Bornstein et al., 1993; Miller et al., 1990; Stern et al., 2001).

Plasma Viral Load

Childs et al. (1999) found high plasma viral load levels resulted in a greater risk of dementia. However, similar studies (e.g. Ellis et al., 1997) found no significant relationship between plasma viral load and neuropsychological impairment. More recently Reger, Martin, Cole and Strauss (2005) in 140 individuals with HIV, also failed to find a relationship between plasma viral load and risk of neuropsychological impairment. However, this study sample

was highly educated (mean 13.4 years of education) which may influence interpretation of the results, as higher levels of education could mean better 'meta-cognitive' coping skills and strategies. Although most authors agree cognitive impairment is more common in HIV positive individuals who are immune-suppressed, the evidence for those who have HIV without significant immune-suppression is inconclusive (Pereda et al., 2000). Since HAART, the utility of plasma viral load levels to predict cognitive impairment has reduced (Sevigny et al., 2004).

Time Since Diagnosis

Increased survival in people with HIV lengthens the exposure of viral agents to the brain and neurotoxic consequences (Robertson et al., 2007). Several authors have reported longer duration of seroconversion increases risk of cognitive difficulties (Bornstein, Nasrallah, Para, Whitacre & Fass, 1994). Bhaskaran et al. (2008) empirically validated this in a large multi-national observational cohort finding both older age and length of infection increased the risk of cognitive problems in HIV. However, this is confounded by the increased risk of neurological problems as individuals get older (Bhaskaran et al., 2008).

Co-morbidities

Out of the numerous co-morbidities often found in HIV, Hepatitis C (HCV) is often cited as the most difficult to manage. As many as 1/3 of all people with HIV also have HCV (Anderson, Guest & Rimland, 2004) and HCV may accelerate the course of the HIV, introducing further neuropsychological complications (Livry et al., 2003). However, Parsons et al. (2006) found individuals co-infected with HIV and HCV improved more (from baseline cognitive impairment) after starting HAART medications than individuals with HIV alone. Although this study used alternate test versions to improve test-re-test reliability there was a 35% drop-out rate and some discrepancies between group characteristics, which reduces internal validity of results.

Demographic Factors:

Age

Risk of cognitive impairment increases with age in the non-clinical population, for example, the prevalence increases from 1.5% in people aged 65-69 to nearly 25% in adults aged over 85 years (National Institute for Health and Clinical Excellence [NICE], 2006), whereas prevalence of dementia in adults younger than 65 is thought to be around 150 people per 250,000 of the population (Harvey, 1998). Risk of cognitive impairment in HIV also appears to increase with age (Janssen, Nwanyanwu, Selik, & Stehr-Green, 1992). Valcour et al. (2004) found individuals with HIV aged over 50 years had a prevalence of dementia at 25% compared to 13% of individuals aged 20-39. Older age especially affects novel tasks that require faster speed of processing (Grant, 2008). Research in this area is relatively sparse due to the recent introduction of HAART as the preferred treatment and the resulting increased life expectancy in people with HIV.

Ethnicity

Rivera Mindt et al. (2008) found HIV-positive Hispanic American participants performed worse on a neuropsychological battery (similar to Butters et al., 1990) compared to European Americans with HIV. A significant association was found between literacy and global neuropsychological functioning, but literacy did not predict executive function abilities. This may be because executive functions are more 'culturally mediated' than other cognitive abilities (Rivera Mindt et al., 2008). Rivera Mindt and colleagues (2008) used a large well described sample but did not include a HIV-negative control group which might have improved the validity of the results and helped to build a causative model of how these factors affect one another. Further empirical work is also needed to clarify the role of family history, environmental influences (such as education or literacy), and the neuropsychological tests and measures used (i.e. cultural validity) in mediating this difference in performance. Low socio-economic status can have multiple effects such as reduced access to healthcare services, which could influence treatment and thus directly impact on cognitive impairment (Shapiro, 1999), although research has not conclusively proven the

association between socioeconomic status and neuropsychological functioning (Rivera Mindt et al., 2008).

Gender

Most research with people with HIV has under-represented women, with only 31% of studies included women with approximate representational equality (Maki & Martin-Thormeyer, 2009), despite the rapidly increasing number of women being diagnosed as HIV positive (Durvasula, Miller, Myers & Wyatt, 2001). Women may be more likely to experience cognitive impairment in HIV than men (McArthur et al., 1997). A recent study (Failde-Garrdio, Alvarez & Simon-Lopez, 2008) found women showed slightly higher rates of neuropsychological impairment than men, though differences were not statistically significant. The matched HIV-negative control groups confer good internal validity for the results. However, there is little information on recruitment so it is not possible to determine any if the sample was subject to selection bias.

There may be many reasons for cognitive differences between men and women including sex hormones (Hafner et al., 1994; Kimura, 1992) and brain structure (Hamilton, 1986), with some researchers finding increased numbers of sex hormone receptors on the prefrontal cortex of females (Bixo, Backstrom, Winblad & Andersson, 1995). Females who are HIV-positive are also more likely to have a variety of other risk factors such as a history of drug abuse (Failde-Garrido et al., 2008), lower socio-economic status (Ickovics & Rodin, 1992) or lower education level (Stern, Silva, Chaisson & Evans, 1996). There is also some evidence to suggest females have less access to HAART compared to males (Lopez, Wess, Sanchez, Dew & Becker, 1999).

Cognitive, Behavioural and Emotional Factors:
Intravenous Drug Use
Much research has pointed to drug use having an effect on neuropsychological impairment, irrespective of HIV infection (e.g. Vasquez-Justo, Alvarez & Ferraces Otero, 2003; Carlin & O'Malley, 1996).

Approximately one third of people with HIV use illicit drugs (Waldrop-Valverde, Ownby & Kumar, 2005) and individuals with HIV who abuse drugs have higher rates of impairment than those who do not (Egan, Crawford, Brettle & Goodwin, 1990). Intravenous drug use in particular increases the risk of cognitive impairment in people with HIV with additive or interactive effects (Pereda et al., 2000), by further compromising the immune system or increasing susceptibility to depression (Waldrop-Valverde et al., 2005). On the other hand, research in this field is seriously limited by recruitment methods, for example, recruiting homeless participants directly from the streets. However, people may become homeless because they have cognitive impairment and are less able to manage their finances (Spence, Stevens & Parks, 2004). This recruitment method also does not account for intravenous drug users who are HIV-positive but retain their accommodation. There are also limitations in the accurate recording of drug use and subsequent ability to determine true relationships. Moreover, like women, injecting drug users are less likely to be prescribed HAART (Himelhoch et al., 2007).

Problem Alcohol Use

Prevalence rates of problem drinking in people with HIV range from 29% to 60% (Meyerhoff, 2001) compared with approximately 15% of people reporting hazardous drinking in the non-HIV population (Webb, Ashton, Kelly & Kamali, 1996). The frontal circuits of the brain seem to be affected both by alcoholism and HIV (Sullivan et al., 2003; Winsauer et al., 2002). Schulte, Mueller-Oehring, Rosenbloom, Pfefferbaum and Sullivan (2005) compared four groups of participants (HIV-negative controls, patients with alcoholism, patients with HIV, patients with HIV & alcoholism) on a computerised version of the Stroop test. They found participants in the HIV & alcoholism group had slower reaction times than controls, indicating compromised executive function. However, as the first research study of its kind, further research needs to develop these findings.

Psychiatric Disorders

Bing et al. (2001) found nearly half of people with HIV could be diagnosed with a psychiatric disorder, especially depression. This is twice as high as rates of depression in the healthy community (Chandra, Desai, & Ranjan, 2005). This may be due to the psychological impact of receiving a positive HIV diagnosis (Chandra et al., 2005), direct effects of HIV on the brain (Gibbie et al., 2006), side effects of medications (Rourke, Halman & Bassel, 1999), or exacerbation of pre-morbid conditions (Ellen, Judd, Mijch & Cockram, 1999). These prevalence estimates may be an under-estimate, as healthcare professionals see depression as a normal response to receiving a HIV diagnosis and therefore may not be diagnosed or reported (Chandra et al., 2005).

Large quantities of research point towards cognitive impairment in psychosis and mania (e.g. Kravariti, Morris, Rabe-Hesketh, Murray & Frangou, 2007). Although causality is a key issue in interpreting results as individuals with 'serious mental illness' are at high risk of HIV infection (Cournos & McKinnon, 1997) and those with HIV are more susceptible to psychiatric difficulties (Chandra et al., 2005). There is also some evidence that anxiety may affect performance with participants feeling threatened by instant feedback causing distraction and interfering with optimum performance (Satz et al., 1993).

Depression

Vasquez-Justo et al. (2003) found HIV-positive individuals experiencing depression performed significantly worse on neuropsychological tests than those in HIV alone or non-clinical control groups with a particularly detrimental effect on memory and executive functions (Ottowitz, Dougherty & Savage, 2002). Although it is useful to bear in mind, that depression is likely to be under-diagnosed in people with HIV. Likewise Gibbie et al. (2006) in a two-year cohort of 80 participants with HIV found depressed participants showed more neuropsychological impairment than those who were not depressed, independent of medical factors. However, this does not imply causality – depression may influence cognitive performance, cognitive

performance may influence depression or the relationships could be mediated through other factors. The minimal exclusion criteria of Gibbie et al. (2006) study (aged over 18 and English-speaking) allow for good statistical power and comprehensive statistical analyses infer good internal validity. However, the sample included very few women and all participants were in good physical health so results may not be widely generalisable. Additionally, the authors do not report on the test-retest reliability of the measures used (the Cambridge Neuropsychological Test Automated Battery (CANTAB) (Sahakian & Owen, 1992) and the HIV-Dementia Scale (HDS) (Power, Selnes, Grim & McArthur, 1995). Moreover, affective disturbances may increase complaints of cognitive problems irrespective or whether these cognitive problems are found in neuropsychological performance (Mapou et al., 1993).

As the mechanism for how depression affects cognitive functioning is unclear, it is also uncertain whether the effects of depression are long lasting (e.g. Reischies & Neu, 2000) or are reversed on remission of depression (e.g. Neu, Kiesslinger, Schlattmann & Reischies, 2001). Biringer et al. (2005) found after 26 months in a sample of 30 HIV-positive individuals who had experienced a major depressive episode, those who had improved in terms of their depressive symptomology also improved on measures of neuropsychological performance. However, there were high drop-out rates, who may have been the people who remained cognitively impaired. Despite these limitations these results were replicated by Westheide and colleagues (2007) using more sensitive measures (the Iowa Gambling Task). HAART may also have a role in reducing the prevalence of major depressive disorder from 31% to 14% of people with HIV (Gibbie et al., 2006). However, it is not possible to determine whether this is due to brain changes, a psychological response to cognitive deterioration, or indeed a placebo effect. Furthermore, rather than focusing on severity or dimensional models research in this area is limited by the dichotomisation of both depression and cognitive impairment, which loses the rich information in the raw data.

Level of Education and Pre-morbid IQ

People who have had more education tend to perform better on neuropsychological tests due to 'cognitive reserve'. The cognitive reserve hypothesis suggests individuals who have more cognitive resources, from longer time spent in education for example, will have a higher threshold before the effects of cognitive deterioration are shown (Satz et al., 1993). In essence cognitive resources act as a buffer against neurological insults (Pereda et al., 2000). Individuals with higher cognitive reserve have also had increased opportunities to learn facts and strategies implicit in many neuropsychological tests (Grant, 2008). Supporting this hypothesis, prevalence of HAD in people with HIV was higher in those who had less than six years of education (DeRonchi et al., 2002), despite the limited measures used and more than half of the sample were younger than 28 years old. Overall lower premorbid IQ does seem to lead to both risk of neuropsychological impairment and more rapid decline (LeCarret et al., 2005).

Executive Function

Executive functions are the skills required to organise domestic, community and professionals activities, social interactions and adaptation to a constantly changing environment (Chevingard et al., 2008). Executive function skills are used to create models of self-directed action through 'formation, planning and carrying out of goal-directed plans and effective performance' (Jurado & Rosselli, 2007, p214). These skills are also associated with insight and play a central organisational role, integrating and monitoring other cognitive and emotional functions (Hart, Whyte, Kim & Vaccaro, 2005). Executive function problems are therefore most evident in interpersonal interactions in the social world (Channon & Crawford, 1999). Impairment in these skills can be termed the 'dysexecutive syndrome' (DES) and, like HAND, are inextricably linked to frontal subcortical circuits (Verdejo-Garcia & Perez-Garcia, 2007).

Executive function poses a particular problem for clinical identification because of the association with lack of insight. This tends to mean self-report needs to be supplemented by neuropsychological testing. There are two main aims of neuropsychological testing – one is to determine level of impairment and the other to determine whether the difficulties will interfere with everyday life (Silverberg & Millis, 2009). Neuropsychological testing is based on the assumption that damaged brain processes give rise to poor test performance which represent poor processing outside of the testing environment (Chaytor, Schmitter-Edgecombe & Burr, 2006).

Models of executive function

Unitary Models

Several models of executive functions have been developed (e.g. Stuss & Benson, 1986; Duncan, 1995) to try and encapsulate the executive functions within a single unifying theory. The predominant model conceptualises executive function and skills as part of a unitary supervisory system (Norman & Shallice, 1980). This model suggests that a contentional scheduling system manages over-learned and routine behaviours whereas a supervisory attention system (SAS) regulates responses to novel and complex tasks, and the SAS is where the executive functions are required. However, there has been much speculation over the active role of the SAS in routine action (Schwartz, 1995) as there may not be clear categorical demarcation between novel and routine tasks (Chan, 2001).

Other unitary models have been proposed including:

- Attentional control (Stuss & Benson,1986)
- Goal-directed behaviour (Duncan et al., 2000)
- Working memory (Goldman-Rakic, 1992)
- Somatic marker hypothesis (Damasio, 1995)

For a review of these models refer to Chan (2008).

Fractionated Models

Stuss and Alexander (2007) have been instrumental in claiming there is no undifferentiated 'frontal lobe syndrome' or 'supervisory attention system' but three related systems: energisation (initiating and sustaining responses), task setting (setting a stimulus-response relationship and suppressing salient responses) and monitoring (checking the task over time). Nevertheless, other research models have categorised these systems differently, into different organisations and arrangements (e.g. Godefroy, 2003). For example, Fisk and Sharp (2004) also suggest three systems but term them: updating (monitoring and manipulation of information), inhibition (inhibit automatic or impulsive response when necessary) and shifting (flexible adaptations). Other authors have considered specific models of what the 'fractions' may look like, such as Levine et al. (1998) who identified that one of these fractions may be 'strategy application disorder' – 'a pattern of problems which manifest themselves most in real-life complex situations which require organisation and structuring of goal-related behaviour' (Burgess, 2000, p.279). Bechara, Damasio, Damasio and Lee (1999) have split executive functions into mechanistic and 'cold', such as multi-tasking and cognitive flexibility, and 'hot' tasks compared to those that involve emotional reasoning, such as decision-making and social behaviour. However, few of these system arrangements include the concept of decision-making (Bechara et al., 2001) or account for lack of insight or lethargy commonly associated with impaired executive function.

Taken together this makes for a complex, contradictory and hotly debated field of research. There is much debate about the definition of executive functions as the concept encompasses a wide range of skills, with different authors placing different emphasis on different skills (Jurado & Rosselli, 2007). Moreover, this vast range of theories are not detailed models but frameworks which are less able to predict and explain specific fractionations of executive functions (Burgess, 2000). This has strong implications for interpreting the research, where articles which claim to be researching 'executive functions' tend to be exploring one fraction of this system. Based on the empirical evidence so far it seems that 'executive functions' is a

useful macroconstruct label to describe abilities that allow us to 'engage in independent and purposive behaviour' (Jurado & Rosselli, 2007 p. 231).

Neurobiology of Executive Functions

It is useful to briefly consider the neurobiology of executive functions to make the links with the neurobiology of HIV. Executive functions are inextricably linked to the prefrontal cortex (PFC). In evolutionary terms this is the 'latest addition' to the brain and developmentally the slowest brain function to develop, showing much more individual variation (Fan, McCandliss, Sommer, Raz & Posner, 2002). Particular areas of the PFC have been identified as having a specific role in fractionated executive function (Table 5). However, these skills are not exclusively associated with frontal lobe functioning and research is often focused on individuals with discrete lesions after brain injury rather than neuro-degenerative changes as seen in people with HIV.

Table 5.
Executive function skills associated with areas of the prefrontal cortex

Lesion Site	Associated Skills
Orbito-frontal *Projects to Caudate Nucleus*	• impulsivity • distractibility • disinhibition • social behaviour
Dorso-lateral *Head of Caudate Nucleus*	• working memory/attention • set shifting and perseveration • planning and organisation • disinhibition • problem solving • abstract thinking and reasoning • ability to integrate information • self-monitoring
Ventro-medial *Anterior Cingulate projects to Nucleus Accumbens*	• motivation and apathy • initiation • attention • self-awareness • social behaviour • humour

Note. Adapted from information in Malloy, Bihrle, Duffy & Cimino, 1993; Alvarez & Emory, 2006; Bamdad, Ryan & Warden, 2003; D'Esposito, Postle & Rypma, 2000; Stuss & Levine, 2002; Ross & Stewart, 1981)

Executive Function and HIV

As outlined in previous sections, executive functions are affected early in the course of infection and tend to be the most severely impaired cognitive domain in people with HIV (Basso & Bornstein, 2000). Research has identified that people with HIV have impairments in inhibition (Hinkin, Castellon, Hardy, Granholm & Siegle, 1999; Llorente et al., 1998), working memory (Martin et al., 2001) planning and sequencing (Sahakian et al., 1995). Bearing in mind the variability in the frameworks used to describe executive functions and that most research with people with HIV has included broad global measures of cognitive assessment, this section focuses on the studies so far that have directly considered executive function in HIV.

In the pre-HAART era a case-control study (Sahakian et al., 1995) recruited 40 people with HIV, 19 participants were medication free, and 21 were on mono-therapy. Over two sessions participants were assessed on the CANTAB and the COWAT (Benton & Hamsher, 1976). The analysis showed a specific pattern of deficits, where participants with HIV solved significantly fewer problems correctly on more complex tasks, with no evident memory impairment, compared to 18 matched controls. These results point to inefficiency in executive functions, specifically planning, attention and flexibility. The COWAT, a frequently used test of executive function, failed to pick up these subtle deficits. These results may reflect that the CANTAB is more complex than the COWAT, however, Alzheimer's patients have shown a dissociable pattern, performing well on tests of executive function, and poorly on the COWAT. Sahakian et al. (1995) increased the validity of their results by using a matched seronegative control group, recruited after having taken a HIV-antibody test. However, by including only homosexual men, the external validity of results is severely limited and analysis of drug and alcohol use to consider alternative interpretations of the results would have been useful. One further crucial limitation is that this research was conducted prior to the wide-spread use of HAART.

The finding of executive function difficulties in people with HIV has been replicated in other pre-HAART research using the Stroop (Hinkin, et al., 1999; Martin, Robertson, Edelstein, Jagust & Sorensen, 1992). Hinkin, et al. (1999) used a traditional and a computerised version of the Stroop task to assess 51 individuals with HIV and 21 HIV-negative controls. They found that individuals with HIV had slower reactions times than seronegative controls. Castellon, Hinkin and Myers (2000) also used the Stroop and self-report measures (NeuroPsychiatric Inventory [NPI] (Cummings et al., 1994) to assess irritability and apathy in 86 participants with HIV (28 asymptomatic, 37 symptomatic, 2 AIDS; 71% were taking HAART) and 21 seronegative controls. After excluding individuals with previous neurological incidents, substance use disorder or a psychiatric history, the authors found apathy or irritability in people with HIV were associated with poor automatic thinking. However, participants had higher average IQ (110.7) than the non-clinical population (100) which may compromise generalisabilty of the results.

Most recently Hardy, Hinkin, Levine, Castellon and Lam (2006) explored one of the executive function skills, decision-making, in 67 individuals with HIV (58% AIDS; all receiving HAART) and 19 HIV-negative controls using the Iowa Gambling task (IGT) (Bechara, Damasio, Damasio & Anderson, 1994). Paralleling previous studies, Hardy et al. (2006) found individuals with HIV showed more impulsivity and were, more likely to choose immediate rewards over gradually accumulated smaller rewards compared to HIV negative controls. The study's strengths and originality lie in its use of a sensitive and newly developed measure (IGT), broader inclusion criteria to include drug dependence, and 34% female participants, which increase external validity. However, the HIV-negative control group had spent significantly longer in education (13.9 compared to 12.7 years) than the HIV-positive group, and the HIV-positive group were significantly more depressed, which might account for the differences over and above HIV infection.

This research is predominantly cross-sectional, with restricted evaluation of progression of executive function difficulties (Bornstein et al., 1993). In an eight-year longitudinal study with 114 participants (55 HIV-positive and 59 HIV-negative), Baldewicz et al. (2004) found deficits in motor and processing speed but no differences over time in executive function (as measured by the TMT and Stroop). This methodology increases the statistical power as each individual acts as their own control. However, although they controlled for depression and IQ, generalisability is limited by only including young homosexual men, especially as younger people show greater practice effects which lead to a regression towards the mean (Heaton et al., 2001).

Summary

Despite the evidence that executive function difficulties are a dominant part of the cognitive profile in HIV and the wealth of conceptual models, few studies have considered the underlying components of executive function or important functional outcomes (Woods et al., 2009). Sample sizes are small so the results cannot reliably inform public policy (Van Gorp, Lamb & Schmitt, 1993). The recommended large assessment batteries, assessing various cognitive domains, (Butters et al., 1990) increase the possibility of detecting a difference when no such difference exists (Type I error). It may also be that traditional tests are insensitive because of ceiling effects and reliance on psychomotor abilities to measure executive function (Basso & Bornstein, 2000). Moreover, there have been variable definitions of impairment, which more-or-less arbitrarily range between 1 and 2 SD's below the mean or on some occasions clinical judgement (e.g. Saykin et al., 1998). Some studies have used matched control groups, which provide internally valid results; although due to subset differences individual levels of change may be difficult to determine (Heaton et al., 2001). There are also queries as to group matching methodology which is rarely reported (e.g. Wacholder, Silverman, McLaughlin & Mandel, 1992).

Traditional measurement of executive functions

Due to the wide ranging consequences of deficits in executive function, correct identification is critical to provision of appropriate support (Manchester, Priestley & Jackson, 2004). However, the ongoing debate surrounding the construct of executive functions necessarily entails difficulties around assessment (Jurado & Rosselli, 2007). This section outlines how executive functions have been traditionally measured in nearly all HIV research. Traditional measures of executive functions include (for brief descriptions see Appendix J):

- Wisconsin Card Sort Test (WCST) (Heaton, Chelune, Talley, Kay & Curtis, 1993)
- Trail Making Test (TMT)
- Stroop Test
- Verbal Fluency/Controlled Oral Word Association Test (COWAT)
- Cognitive Estimates Test (CET) (Shallice & Evans, 1978)
- Tower of London (Shallice, 1982)

These traditional tests have been developed from construct-driven psychology rather than a function-driven perspective (Burgess et al., 2006). This has led several authors to question the use of traditional tests in assessing executive function. Further, the development in understanding executive functions theoretically as fractionated sub-systems suggests that no single measure can capture the whole range of executive functions. Instead, each individual measure provides information on one aspect of the concept (Boone, Ponton, Gorsuch, Gonzales & Miller, 1998).

Alvarez and Emory (2006) employed a comprehensive search strategy (inclusion criteria: adult brain injury, not solely focal frontal damage, a healthy control group, brain imaging data, appropriate analysis) to identify 27 studies to review the validity of three traditional measures (WCST, COWAT, Stroop). They found that although these tests are regularly used in research and clinical work, they were insensitive or, in the case of the WCST, sensitive but not specific, to frontal lobe damage. Indeed, the

validity of the commonly used Stroop, was based on one study, and had only been considered in five further studies (Alvarez & Emory, 2006). Furthermore, none of the measures examined the whole of the executive construct. Although it was a small study, Gouveia, Brucki, Malheiros and Bueno (2007) also found the WCST was remarkably insensitive in 35 adults with focal frontal lesions and comment that its place as a measure of executive function should be reviewed.

Although traditional tests may demonstrate statistical significance in discriminating between clinical and non-clinical groups there is little information about the size of the difference, and high specificity may mask poor sensitivity (Manchester et al., 2004). For example the discriminant validity of the Stroop test is reported as 61.2% but this is derived from 95.7% specificity and only 30.8% sensitivity (69.2% of the clinical group were misidentified) (Wildgruber, Kischka, Fassbender & Ettlin, 2000). Several further studies have reported that individuals with frontal brain damage perform within the normal range on other traditional tests such as the TMT or COWAT (e.g. Ahola, Vilki & Servo, 1996). However, much validity research uses individuals with brain injury which does not necessarily entail executive function problems so it may be more useful to establish validity in groups with pre-identified dysexecutive qualities.

Salthouse, Nesselroade and Berish (2006) found within-person variability could account for 50% of the change in test scores over time so a single assessment may not be sufficient to draw adequate conclusions on cognitive tests (Salthouse, 2007). Rather than conceptualising cognitive abilities at a single discrete level, they are arranged over a distribution with many potential levels of performance per individual (Salthouse, 2007). However, tests of executive function rely on problem solving novel situations and cross-sectional research methods without considering these within-person fluctuations (Heaton et al., 2001). Additionally, traditional tests are 'impure', triggering several executive process and non-executive processes (Burgess, Alderman, Evans, Emslie & Wilson, 1998). The recently devised Delis-Kaplan Executive Function System (D–KEFS) (Delis, Kaplan & Kramer,

2001) brings together modified versions of well-known measures (e.g. TMT, Stroop, COWAT); consequently this battery is vulnerable to some of the same limitations as these traditional tests.

Traditional testing environments may not be representative of real-life: a quiet distraction-free space where the examiner takes the lead and initiates rules, goals and prompts where the examiner 'acts as the participant's frontal lobes' (Manchester et al., 2004). The structured nature of traditional tests entails that participants do not have to select a task from competing possibilities (Stuss & Alexander, 2000) or may attempt to use strategies because they are aware they are being observed (Bennett, Ong & Ponsford, 2005). The use of overall scores might mask this increased effort and lead neuropsychologists to conclude the individual has no executive function difficulties in everyday life when this is not the case (Bennett et al., 2005). Alternatively, office tests may provide an over-estimate of everyday difficulties because participants find it hard to imagine the situation in reality and the concepts are too abstract (Channon & Crawford, 2008). Therefore, traditional tests should be interpreted with caution due to the rich contextual cues for expected behaviour provided by the testing environment (Manchester et al., 2004).

Ecological validity

There is increasing support for the idea that cognitive tests should not be looking to provide categorical diagnoses but outline the 'behavioural consequences of brain damage' (Ready, Steirman & Paulsen, 2001, p.314). Ecological validity describes the ability of a test to represent and predict real-world behaviour (Burgess et al., 2006). Ecological validity can be broken down into verisimilitude (the ability of tests to resemble real-life demands) and veridicality (the ability of tests to relate to measures of everyday function) (Chaytor & Schmitter-Edgecombe, 2003). Unlike other forms of validity, there has been no formal level set to define the strength of the relationship needed between test performance and everyday behaviour to claim good ecological validity (Chaytor & Schmitter-Edgecombe, 2003). By virtue of the concept, measures with good ecological

validity are more discriminative than traditional tests and have good predictive validity for behaviour outside of the 'lab' (Verdejo-Garcia & Perez-Garcia, 2007). For tests to be predictive of behaviour in the real world requires assessment of the individual within their day-to-day environment. Individuals may express no real world problems if their usual environment places little demand on executive functions or minor impairment may produce large disabilities in a highly demanding environment (Chaytor, Schmitter-Edgecombe & Burr, 2006). For people with HIV it is possible to hypothesise their environment would be high demand, especially when considering the complex nature of HAART medication adherence.

Inferences made from traditional tests have poor ecological validity, with weak-moderate relationships (correlations ranging from .2 to .5) with everyday behaviour (Burgess et al., 2006). Overall support has been found for superiority of tests that are based on verisimilitude where capturing the essence of everyday skills (Chaytor & Schmitter-Edgecombe, 2003). However, as verisimilitude is based on face validity which cannot be confirmed empirically (Chaytor & Schmitter-Edgecombe, 2003). Furthermore, there is also no gold standard way to measure veridicality or quantify performance outside of the testing environment as all assessments contain some degree of error (Chaytor et al., 2006).

A test with good ecological validity does not aim to assess what the client can do in an ideal environment (i.e. impairment) but what the client does (i.e. activity/participation) (Odhuba, van den Broek & Johns, 2005) including compensatory strategies, which are discouraged during assessment with traditional tests (Chaytor et al., 2006). This can be conceptualised using the WHO International Classification of Functioning (ICF) (2002) which translates HIV infection not only into changes in brain function and structure but how that affects the individual in their environment to create a more meaningful picture of the experience (Table 6 Description of levels of functioning). This moves away from a purely medical model (illness as a feature of the individual) to synthesise information from the social model (disability as socially created). This is especially important

because, as discussed, executive function difficulties lead to key quality of life issues (Semkovska, Bedard, Godbout, Limoge & Stip, 2004).

Table 6.
WHO-ICF Category Functioning Descriptions

Health condition	Impairment	Activity Limitation	Participation Restriction
	Problem with body function, structure, deviation or loss	Difficulties an individual has executing an activity	Problems experienced in involvement in life situations

Note. WHO-ICF=World Health Organisation-International Classification of Functioning

Chaytor et al. (2006) found the WCST, TMT, Stroop and COWAT varied in their degrees of ecological validity in different populations. Some research has compared these measures to functional outcomes: Pontius and Yudowitz (1980) found lower performance on the TMT was predictive of more criminal behaviour and Lysaker, Bell and Beam-Goulet (1995) found slower performance on the WCST was associated with reduced ability to understand work assignments or socialise with colleagues. However, these generic outcomes might not accurately reflect the unique complexity of people's lives (Kibby, Schmitter-Edgecombe & Long, 1998).

In light of the limitations of traditional tests, recent research has seen a surge in development of assessment measures of executive functions. These tests focus on participants completing multiple tasks over a period of time without external feedback, deciding for themselves how to proceed (Knight, Alderman & Burgess, 2002). These novel measures include (for a brief description of these measures see Appendix J):

- Multiple Errands Test (MET) (Shallice & Burgess, 1991)
- Six Elements Test (SET) (Shallice & Burgess, 1991)
- Virtual Reality Tests (O'Niel-Pirozzi & Goldstein, 2005)
- Hayling & Brixton (Burgess & Shallice, 1997)
- Iowa Gambling Task
- Behavioural Assessment of the Dysexecutive Syndrome (BADS)

Modest relationships have been found between tests with good ecological validity and traditional tests. Tranel, Hathaway-Nepple and Anderson, (2007) compared participants with focal damage to the ventromedial prefrontal cortex to participants with prefrontal damage, non-prefrontal damage and controls. They found that although the SET and MET were moderately associated with the WCST and TMT, traditional tests did not show any differences in performance of clinical sample compared to the controls, whereas the tests with good ecological validity did discriminate between clinical and non-clinical groups and were superior to traditional tests at outlining the behavioural sequelae of brain damage (Tranel et al., 2007). However, there were only small numbers of participants in each group (n=8/9) and participants were only included if they had stable focal lesions so the results may not be applicable for neurocognitive disturbances of HIV. Despite this, the superiority of tests with good ecological validity has been supported by previous research (Dimitrov, Grafman & Hollnagel, 1996; Evans, Chua, McKenna & Wilson, 1997; Norris & Tate, 2000).

Although comparing tests to each other provides useful information it is not possible to determine which tests reflect the 'true' score. To provide an alternative it is useful to compare cognitive tests to self- and proxy-report on measures such as the Dysexecutive Questionnaire (DEX). Burgess et al. (1998) compared 11 measures of executive function in a heterogeneous population (n=92) to proxy-report on the DEX. Like previous studies, they found most traditional measures (e.g. COWAT and CET) were insensitive to neurological disorders as measured by the DEX. A strength of the study lies in consideration of executive functions as a fractionated system and relation of measures to the underlying constructs. Nearly all measures were related to the sub-system inhibition, although this construct overlapped significantly with 'general intelligence'. Intentionality and goal-related behaviour was only related to the Six Elements Test (SET), with no overlap with IQ. Executive memory (confabulation, perseveration) was related to scores on the WCST. However, they also suggested there were two other factors: motivation and personality changes, which were not accounted for by

neuropsychological tests. Although this was a large multi-centre study, the population was very heterogeneous and the assessment was administered over a number of sessions which may not take into account within-subject differences (Salthouse, 2007). Research in this area uses different populations and types of neuropsychological tests which make findings hard to compare (Poole, Ober, Shenard & Vinogradov, 1999). Moreover, even significant correlations were only of moderate size, meaning that a large proportion of everyday skills are not unaccounted for (Chaytor et al., 2006). Ecological validity might not be categorically achieved but tests have better-or-worse ecological validity under defined circumstances (Chaytor & Schmitter-Edgecombe, 2003).

Therefore, when research in executive functions in HIV are re-appraised it is possible to see the Hardy et al. (2006) is the only study to have used a measure of executive function with good ecological validity to consider the difficulties people with HIV have in everyday life. However, the IGT only considers a single factor of executive function. A battery approach to assessment of executive functions with good ecological validity would be more appropriate. The Behavioural Assessment of the Dysexecutive Syndrome (BADS) (Wilson et al., 1996) assesses several aspects of the executive functions and can examine most aspects of executive functions using one battery (Kamei et al., 2008) but is not too time-consuming.

Behavioural Assessment of the Dysexecutive Syndrome (BADS)

The BADS has not been used in clinical research with people with HIV previously so this section briefly considers the potential contributions that using this measure could make to the research in executive functions in people with HIV. The BADS authors have developed normative data from a large stratified sample of non-neurologically impaired individuals (n=216). The authors report there were approximate equal numbers of men and women and adopted a rigorous recruitment strategy to avoid volunteer bias (Wilson et al., 1996). The age of the sample ranged from 16 to 87 years, with equivalent numbers of participants in below average, average and

above average IQ scores. The sample was recruited from participants who had previously been involved in collecting population norms, staff from healthcare centres and an organisation providing work experience for people who have been unemployed. Profile scores are converted to standard scores (mean 100, SD 15) which can classify BADS performance in the same way as full-scale IQ on the Wechsler Adult Intelligence Scale-Revised (Wechsler, 1981). The authors also report data for 78 brain injured individuals and 31 individuals diagnosed with schizophrenia. This large normative data study allows a baseline for individuals to be compared against. However, there is very limited data on describing the normative sample on gender or ethnicity.

Although the BADS is an office based test, it moves away from the traditional tests and has been designed to reduce load on working memory. Much research has shown that the scores on the BADS battery are dissociable from scores on tests of memory or language (e.g. Evans et al., 1997). The BADS has been used in several populations including people with problem alcohol use (Moriyama et al., 2002), substance dependence (Verdejo-Garcia & Perez-Garcia, 2007), schizophrenia (Jovanovski, Zakzanis, Young & Campbell, 2007; Katz, Tadmor, Felzen, Hartman-Maier, 2007) and Parkinson's Disease (Kamei et al., 2008). For example, Verdejo-Garcia and Perez-Garcia (2007) examined executive function deficits using the BADS, WCST and a questionnaire (Frontal Systems Behavioural Scale, similar to the DEX, Grace & Malloy 2001) in a heterogeneous group of 37 substance-dependent individuals and 37 controls (matched for age, education and pre-morbid IQ. The results of a MANOVA showed 'normal' performance on the WCST in the clinical group, whereas 5 out of the 6 subtests of the BADS were classified as 'impaired'. The benefit of having a matched control group gives the study strength but the cross-sectional nature does not control for within-person variability. Additionally there were only five women in the clinical group and two in the control group so the lack of representation in the sample reduces the external validity of the results. Moreover, the exclusion criteria (psychiatric disorder, HIV, neurological alteration) may also limit the generalisability of the results.

However, diagnoses such as schizophrenia and alcoholism are controversial and not sufficient to make predictions about behaviour (Bentall, 2003).

Reliability

Inter-rater reliability of the BADS is high, reported as .99 so clinicians can be confident in the scoring strategies suggested in the manual (Kamei et al., 2008). However, internal consistency data is not reported for the BADS and over six to twelve months most subtests fail to reach the critical level (.80) for good test-retest reliability (Jelicic, Henquet, Derix & Jolles, 2001). On the other hand, executive function assessments rely on presentation of novel tasks so test-retest reliability is often low (Jelicic et al., 2001).

Validity

Compared to other tests and self- or proxy-report

Even though the BADS is office-based, many authors report good face validity (Wood & Liossi, 2006). The BADS manual (Wilson et al., 1996) reports good discriminant validity between clinical (brain injury) and non-clinical groups. However, there is considerable overlap between the groups with 65% of the clinical group not classified as impaired. However, both of these results may reflect the heterogeneous sample and the level of disability experienced as opposed to poor sensitivity.

The manual reports a significant correlation between functional measures (DEX) and the BADS which suggests good ecological validity of the BADS (veridicality) in 78 individuals with a brain injury (Wilson, Evans, Emslie, Alderman & Burgess, 1998). The BADS profile score was the best predictor of proxy-report on the DEX with correlations coefficients on subtests of the BADS with the DEX-other ranging from -.31 to -.46 (poorer performance on the BADS subtests was associated with higher scores on the DEX). Stokes and Bajo (2003) found an association between two of the BADS subtests and the DEX, however, this effect disappeared once IQ had been partialled out of the regression. Wood and Liossi (2006) compared the same two subtests from the BADS to the DEX-other in 165 participants (mean age

33.86, range 17-64). Unlike Stokes and Bajo, they found the BADS was not correlated with the DEX and there were significant effects of IQ. However, as they only used selected subtests the results cannot be generalised to the entire BADS battery. Evans et al. (1997) found there were significant relationships to the DEX-clinician in people with acquired brain injury (n=35) but not in people diagnoses of schizophrenia (n=31), despite impairment on the BADS compared to controls (n=26). However, this study includes limited demographics sample information and considerable variability between the sample groups means it is hard to identify the internal causality of this study. Furthermore, the clinical significance of this association is questionable and has not always been replicated (Norris & Tate, 2000).

Norris and Tate (2000) examined construct and concurrent validity of the BADS in 73 participants from three samples (19 brain injury, 17 Multiple Sclerosis, 37 matched controls) using the WCST, TMT, Rey Figure, COWAT, a role functioning questionnaire and the DEX. They found the BADS had adequate concurrent validity with other tests of executive function, although this was small (correlations ranging from .23 to .34). This is to be expected as the BADS was developed in response to criticisms of these tests. However, only one subtest of the BADS correlated with the DEX-other, and this was not in the expected direction. Norris and Tate (2000) found specificity of the BADS was good (83.8%) although the BADS had a tendency for failing to detect effects when such effects really exist (Type II error) with only 63.9% of the clinical group were correctly classified. This may be because the overall score obscures subtest information and disguises sensitivity (Bennett, Ong & Ponsford, 2005). Alternatively this may be due to aspects of the executive function construct which are not represented in the BADS. As with all tests, the BADS is a compromise between the probabilities of committing Type I and Type II errors. The BADS accounted for 16.2% of the variance in role functioning. These statistics were still better than the traditional tests. However, the clinical groups were not screened for dysexecutive problems, which might have improved sensitivity of the results.

Bennett et al. (2005) assessed 64 brain injury participants (47 male, 17 female, 17 to 73 years old). Few exclusion criteria were used to maximise sample size and thus the statistical power of the study. Participants were assessed on the DEX, BADS, WCST, TMT, COWAT and several other, less commonly used measures of executive function. The authors concluded the BADS contained some useful subtests, in particular the Action Program and the SET. They conclude the BADS is more sensitive to executive dysfunction than traditional measures. However, this study would have benefitted from the inclusion of a control group. Moreover, although the study maximises its external validity by having flexible exclusion criteria, the internal validity is limited due to the multitude of confounding variables.

Despite the BADS being commonly used cross-culturally (e.g. Kamei et al., 2008), there is little information on the culturally validity of the BADS. Few ethnic minorities are part of normative samples and tests of executive function may be limited in considering the social context of the difficulties (Proctor & Zhang, 2008). Proctor and Zhang (2008) found in a large sample of college students from ethnic groups (African American, Latin American and European American), the BADS showed statistically significant differences between groups. However, effect sizes were small-moderate and no differences were found between groups on 5/6 subtests, but participants from an African American background had a larger range of profile scores.

Compared to other functional outcomes

Little research has compared the BADS to other functional outcomes such as employment status. Katz et al. (2007) found the predictive validity of the BADS for employment was good in people with schizophrenia. They reported a stronger relationship with the BADS and social communication than with more basic activities of daily living (ADLs), such as washing and dressing, emphasising the involvement of executive functions in complex tasks. Moriyama et al. (2002) found the BADS had greater discriminative power than the TMT in predicting occupational status in 22 males with

chronic alcoholism. However, unlike previous studies, this study found that the most useful subtest were Temporal Judgement and Zoo Map. The Zoo Map may be one of the most robust subtests, measuring a broadly similar process to the MET (Knight et al., 2002). Despite the small sample size, the strength of Moriyama and colleagues (2002) study is the longitudinal prospective methodology (18-month follow-up). However, employment outcomes were classified dichotomously and may have been better described on a continuum.

Justification for the use of the BADS

The BADS has been shown to have the best ecological validity of 'office-based' tests, over other batteries such as the D-KEFS (Norris & Tate, 2000). As well as ecological validity, the BADS employs a battery rather than a single executive measure, like the IGT, and includes only minimal load on working memory functions. Although the MET is one of the most naturalistic assessment methods involving real-world observation of participants necessitating good ecological validity, it is time-consuming and reliant on several other cognitive functions, such as memory (Sohlberg & Mateer, 2001). Moreover, some authors have questioned whether the MET still provides too much structure to relate to everyday life (Chevingard et al., 2008). The BADS might offer a useful practical alternative to the MET. Furthermore there is significant evidence for the validity and reliability of the BADS in clinical populations. The BADS also has evidence of superior predictive ability over traditional assessments in everyday functioning. This also begins to update the research in HIV, moving away from Butters et al. (1990) global measurement battery. This also is consistent with the future research directions suggested by a recent literature review (Woods et al., 2009).

Summary

Previous research has reported the specific, often subtle, deficits in executive functions dependent on the fronto-striatal circuits early in HIV infection, even since the widespread use of HAART medication. However,

most research has used measures not capable of predicting real world behaviour or considering more than one of the executive function fractions. Previous reviews have recommended the usefulness of a battery approach, especially one with good ecological validity, such as the BADS, to further develop research with people with HIV (Woods et al., 2009). Overall, the BADS is a useful measure that has been used in many populations with good validity, with an overall trend, albeit not conclusive, towards good ecological validity.

Research Question and Aims of Study

As a result of consideration of the above literature the research aims were derived. The research sample average BADS performance was compared to the normative data as suggested by the manual. This is in keeping with previous research which has suggested that ideally neuropsychological assessment needs to be a performance-based battery and interpreted using demographically appropriate normative data (Woods et al., 2009). This reflects the experience of neuropsychologists in the real world. It was hypothesised people with HIV would perform below what would be expected on the BADS relative to age-matched normative scores. The scores were kept on a continuum scale rather than dichotomised into impaired or not, which might hide variability (Lovejoy & Suhr, 2009). This avoids the confounds of unnecessary cut-offs for classification (Carey et al., 2004). The inclusion of the DEX encompasses a functional assessment as there are no widely agreed clinical measures of everyday functioning for executive functioning (Morgan & Heaton, 2009). This functional assessment improves the ecological relevance of neuropsychological assessment with HIV (Woods et al., 2009) and considers a functional rather than impairment perspective as suggested by the WHO-ICF. The inclusion of mediating variables should identify and assist in developing which of these factors may affect performance and thereby aims to understand the nature and place the experience of executive function problems in people with HIV within a context (Barker, Pistrang & Elliott, 2002).

Extended Methodology

This chapter expands on, and justifies the methodology used in this study. In particular, it discusses the epistemological framework guiding the study, expanded elements of the study procedure, details on the reliability and validity of the assessment measures used and ethical considerations.

Epistemological Position

Most quantitative research is conducted under the framework of positivism. Positivism states that there is an objective reality from which laws, rules and knowledge about human behaviour can be derived through observation and measurement (Guba, 1990). The philosophical position of positivism is closely related to reductionism and materialism, whereby all mental processes are ultimately reducible to their component parts, in a direct cause-and-effect mechanism relating to underlying biology and physical mechanisms. One of the fundamental tenets of positivism is that by understanding the world well enough, it might be possible to predict, control and manipulate it. By virtue of this, knowledge is considered as static and external to individuals.

However, there has been a strong critique against positivism within applied sciences and psychology, as not representing the true complexity in human action and behaviour. The positivist epistemological view seems to be apolitical and does not consider human behaviour within its context, history or meaning. Positivism also premises the potential of true objectivity in measurement and assessment, and the active role of the observer in deriving knowledge is not considered.

In response to the wide-spread malaise with positivism as a guiding framework for social sciences research, a social constructionist framework developed, closely aligned to post-modernism (Barker, Pistrang & Elliott, 2002). This puts forward a position which refutes the assumption that there is any objective reality at all; instead each individual idiographically constructs their reality through interactions with the social world leading to

increased focus on language constructions (Willig, 2001). However, many social science researchers have preferred a mid-ground perspective in critical realism. Within critical realism there is an independent reality, and thereby truth-conditional statements have a meaning, however, it is not possible to ever truly objectively measure and access this reality (Cook & Campbell, 1979). There are multiple interpretations and each individual interprets and constructs an individualised world view. Critical realism also acknowledges the active role of the observer as biased and imperfect. Therefore, all measurement is inherently fallible and importance is placed on multiple measurement, observations and triangulation which will all contain inherent errors, although even this approach will not obtain the laws and 'truth' as in positivism. Similarly, cognitive measures can only choose a small set of items that are good examples or salient features of the larger construct, but no measure can possibly capture all the iterations of the construct (Westerman, 2006). This thereby requires researchers to have a detailed knowledge of the limitations and assumptions of the measurement approaches used (Mingers, 2004).

Many researchers directly link epistemology with research methods and approaches. Subsequently, quantitative research is linked to positivism and qualitative research is linked to post-positivism, social constructionism and critical realism (Gergen, 2001). This tends to suggest that quantitative and qualitative research contrast with one another (Westerman, 2006). However, epistemological frameworks are not committed to single forms of research and several commentators have theoretically articulated how quantitative research can be considered from multiple epistemological frameworks (e.g. Mingers, 2004). Numbers and statistical analyses can contribute to critical realist understandings and exploring patterns of behaviour (Stiles, 2006). Statistical analyses can be regarded as quasi-experimental, imposing closure on an open system for the purposes of exploring the patterns. Statistical findings are not conclusive but point towards developments for further research (Mingers, 2004).

It is also important to acknowledge the role of hermeneutics and interpretivism in quantitative research. Hermeneutics (Merleau-Ponty, 1962; Wittgenstein, 1958; Heidegger, 1962) purports that knowledge emerges from interpretation, and these meanings assigned to concepts play a significant, yet often unacknowledged role, in quantitative research. For example, measures and language assessing concepts such as 'irritability' are heavily value-laden and based on a deep understanding of human behaviour (Westerman, 2006). These terms are meaningless unless they are employed with understanding and background knowledge. Likewise, meaning attributed to certain measurement strategies plays a central role in the development of research, for example, deciding research topics, approaches and/or measurement tools used; these are all interpretive processes embedded in the researchers' understanding and attribution of meaning (Westerman, 2006). There are even interpretations in deciding which statistical tests to perform, and determining the inferences of the results. From this perspective, quantitative research is clearly interpretive (Westerman, 2006).

Hermeneutics also acknowledges an observer can never be objective because they are always involved in meaningful activities in the world which influence their interpretations (Fischer & Bidell, 1998). Moreover, this focus on meaning suggests that research should always refer to context, what people are doing and meaningful activities they engage in on an everyday basis (Westerman, 2006). This is how it is possible to appreciate the significance of a subset of examples, because of the meaning that is attributed to them (Nagel, 1974).

Having discussed the advantages and disadvantages of various epistemological frameworks, a critical realist approach is the most relevant for the current research question. This approach acknowledges that, despite measurement, it is not possible to access the executive function construct exhaustively. This research study also placed emphasis on the context of the individual and how changes in the brain may influence behaviour in everyday life through ecological validity of measurement. In combining a

critical realist epistemology with quantitative research, this study aimed to develop the research body whilst recognising the limitations of all methods, including measures and statistics. This study also used triangulation, on this premise. In line with this framework, it is important to acknowledge the researcher's own interpretations will have influenced the interpretation of this research, from initial development through to write-up. For excerpts from personal reflective notes on the potential way the researcher's pre-reflective understanding influenced the design and interpretation of this study see Appendix K.

Methodology

Design:

This study did not include variables manipulated by the researcher but observes differences between existing groups. However, the literature has used various terminologies to describe this type of study design. These include 'passive-observational', 'group difference comparison' 'post-facto' 'experimenter-selected independent variable' and 'retrospective experimentation' (Cook & Campbell, 1979; Sprinthall, 2003; Solso & Johnson, 1998; Robson, 2002). Group difference comparison design was selected to describe the current study as this was deemed to provide the clearest brief explanation of the study.

Participants:

Sample Size

Traditionally, sample size calculations are conducted to determine the sample size for a research study based on the power, critical probability level and minimum effect size. Effect size is preferably calculated by past research; however, this pilot study is exploratory because no previous research has used an executive function battery approach with good ecological validity in this population. For example, although Sahakian et al. (1995) used a battery approach, the battery was not specific to executive functions and was conducted in the pre-HAART era so effect sizes are not easily transferable to inform the current study. Other studies which have

considered executive function using the Butters et al. (1990) battery have only included one/two measures assessing executive functions. Hardy et al. (2006), although they used a measure with good ecological validity, only assessed one aspect of the executive functions so is not applicable to a battery approach. The empirical research into people with HIV and their executive functions does not therefore specifically identify effect sizes which could have been appropriately used in a statistical power analysis. As this study was an explorative pilot study and without an appropriate effect size from previous research, a formal power calculation was not conducted.

Therefore, sample size was decided by considering previous pilot studies which had employed similar methodologies, but researching different questions (Jovanovski et al., 2007; Moriyama et al., 2002). These research studies have used samples sizes of between 20 and 30 participants. This was further discussed with professionals working with people with HIV and considered within the context of the practical constraints of DClinPsy research. From an inferential statistics point of view the larger sample size the better, however, recruitment of large samples is cost and time-intensive. Researchers need to prevent inappropriate spending of resources, and as such a pilot study into this area at this stage of theory development is an appropriate methodology (Falagas & Bliziotis, 2007).

Inclusion criteria:

- o Diagnosis of HIV-1 infection

  This was confirmed through contact with healthcare professionals who work with the participant (either through referral or contact to confirm diagnosis directly). The healthcare professional confirmed this through evidence of ELISA antibody tests.

    o Age range 18-60 years old

> This included participants who were not experiencing major cognitive changes associated with developmental stages and were able to give full consent to participate in the research. This also ensured that normative data on the tests being used was available for all the participants.

Exclusion criteria:

Each criterion was developed to balance the inevitable trade-off between internal and external validity as well as pragmatic demands, through discussion and operationalisation with experts working in the field. These criteria try to preserve scientific rigour, so performance on the BADS can be more confidently attributed to the executive function of HIV participants, rather than confounding factors such as substance misuse, whilst ensuring the generalisability of results to the wider population of people living with HIV.

    o Time since diagnosis less than three months, defined as:

> The first few months after a positive HIV diagnosis are likely to be distressing (Melrose et al., 2008). The individuals may be subject to a variety of medical tests and trialling medication regimes introducing variability in neuropsychological performance (Lovejoy & Suhr, 2009). Therefore, to protect the individual's emotional state and to ensure validity, individuals who were diagnosed less than three months prior to recruitment were excluded (based on discussion with clinicians).

    o Medically unstable, through discussion with clinicians defined as:

> ▪ Hospitalisation (>one night stay) for illness or infection over the last two weeks
>
> ▪ Changes in HIV medication regime in last two weeks

Fluctuating medical status, suggested by recent illness, can influence performance on neuropsychological tests by increasing levels of fatigue and decreasing concentration (Henderson, Safa, Easterbrook & Hotopf, 2005). It also takes a number of weeks for psychological adjustment to complex medication regimes such as Highly Active Anti-Retroviral Therapy (HAART) (Lovejoy & Suhr, 2009). These factors may lead to neuropsychological performance which does not provide a true reflection of abilities or a discrepancy between self-report and test performance (Lovejoy & Suhr, 2009).

o Major psychiatric disorder, defined as:

  ▪ Current episode of psychosis, mania or severe depression

Psychosis, mania and severe depression can result in moderate executive dysfunction (Chandra et al., 2005; Ottowitz et al., 2002). However, most evidence points to this recovering once the episode has remitted (Westheide et al., 2007). Other psychiatric disorders have limited or no evidence pointing to executive dysfunction so were not included in the criterion.

o Significant substance misuse, defined as:

  ▪ Self-reported intravenous drug use in the last week

Research has shown that substance misuse, in particular intravenous drug use is associated with executive dysfunction (Chandra et al., 2005). However, these effects are not thought to be long lasting so this criteria controls for the effects of current severe substance dependence but pragmatically tries to ensure representation of the population.

- Severe neurological deficits, defined as:
  - Self-report of any of the following:
    - Head injury/cerebral incident requiring hospital admission greater than 24 hours
    - Degenerative neurological diseases, for example, Multiple Sclerosis
    - Brain tumours

    Neurological deficits are known to have ongoing influences on executive functions (Marder et al., 1992) so excluding participants with neurological co-morbidities should improve internal validity.

- People who cannot complete the assessment
  - Visual impairment – unable to read a sentence on a card written in font size 28 with corrected vision
  - Hearing impairment – unable to hear the researcher in a quiet room with a hearing aid
  - Unable to understand and consent to the research process – based on the principles set out in the Mental Capacity Act (2005)

  As assessment of participants' executive function is the main aim of the study it is not possible to include people who cannot physically complete the assessment.

- Language ability
  - Score of less than 15 on the Sheffield Screening Test for Acquired Language (SST) (Syder, Body, Parker & Boddy, 1993)

The BADS involves understanding complex instructions. Therefore it is not possible to include people who cannot understand or communicate in English. The study screened for this using the SST to control for language impairment associated neuropsychological problems and language comprehension for those for who English is not their first language. Individuals were excluded if they scored below the cut-off of 15 as suggested by Blake, McKinney, Treece, Lee and Lincoln (2002).

Information

Table 7 summarises what information was collected and the purpose of collecting the information for this study. For a justification of variable information that was collected see extended background. Table 7 also includes data coding (if appropriate), level of measurement and data source. The sources listed are:

- o Referral – initial information given to the researcher

- o Medical Notes – information collected from the medical notes

- o Clinical Interview – information collected during the assessment session through discussion between the researcher and participant and selection of multiple choice options

Measures which have employed standard scores were treated as interval level data (Coolican, 2004). For further explanation of level of measurement see extended results section.

Table 7.
Details of information collected through the research study

Information	Purpose	Coding	Level of data	Source
HIV Medical Factors				
HIV Diagnosis	Inclusion criteria	-	-	Referral
Medical History	Exclusion Criteria	o Current major psychiatric disorder o Significant substance misuse o Severe neurological deficits o Hospitalisation in the last two weeks	-	Clinical Interview
Time since diagnosis	Exclusion Criteria Analysis	o Months	Ratio	Medical Notes

Medication Regime	Exclusion Criteria	o Length
		  ▪ Months
		o Type
		  ▪ Mono-therapy
		  ▪ Duo-therapy
		  ▪ Triple-therapy (HAART)
		  ▪ Quad-therapy
		  ▪ None
			Ratio
			
			Ratio
				Medical Notes

CD_4 count	Analysis	o Most recent test result (cells per cubic millimetre mm^3)	Ratio	Medical Notes
Plasma Viral Load	Analysis	o Most recent test results (copies per millilitre cc/mL)	Ratio	Medical Notes

		o Asymptomatic		
Current CDC Stage	Analysis	o Symptomatic	Ordinal	Medical Notes
		o AIDS		

Demographic Factors

Sexual Orientation	Description of Sample	o Homosexual o Heterosexual o Bisexual o Not sexually active	-	Clinical Interview

Employment	Description of Sample	o Employed
		  ▪ Part/Full time
		  ▪ Paid/Voluntary
		  ▪ Occupation
		o Unemployed
		  ▪ Disability related to HIV
		  ▪ Disability other than HIV
			-	Clinical Interview

Living Arrangements	Description of Sample	o Alone o With spouse/partner o With others	-	Clinical Interview
Ethnicity	Analysis	o Ethnic groups as specified on the census	Nominal	Clinical Interview

Cognitive, Emotional & Behavioural Factors

Language Ability	Exclusion Criteria	o Cut off <15 (Blake et al., 2002)	-	Sheffield Screening Test for Acquired Language Disorders (SST)
Drug and Alcohol Intake	Analysis	o None o Weekly frequency of use of: ▪ Alcohol (units)	Ratio	Clinical Interview

		▪ Cannabis (joints)			
		▪ Amphetamine (grams)			
		▪ Opiate (grams)			
		▪ Other			
Education	Analysis	○ Years of education ▪ <5 years ▪ 5-11 years ▪ 12-13 years ▪ 14-16 years ▪ 17+ years	Ratio	Clinical Interview	
Pre-morbid IQ	Analysis	○ Standard score	Interval	Wechsler Test of Adult Reading (WTAR)	
Mood	Analysis	○ Anxiety score ○ Depression score	Ordinal	Hospital Anxiety and Depression Score (HADS)	
Measures of Executive Function					
Self-report of executive function	Analysis	○ Self-report score	Ordinal	Dysexecutive Questionnaire (DEX)	
Proxy-report of executive function	Analysis	○ Proxy-report score	Ordinal	Dysexecutive Questionnaire (DEX)	
Executive Function	Analysis	○ Age-related standard score	Interval	Behavioural Assessment of the Dysexecutive Syndrome (BADS)	

Measures

This section expands on the descriptions, reliability and validity of the measured used in the current study. Examples of alternative measures are briefly discussed before a justification for why the measure used was chosen.

Sheffield Screening Test for Acquired Language Disorders (SST)
(Syder, Body, Parker & Boddy, 1993)

The SST consists of 20 verbal items (nine comprehension items and, eleven expression items). The comprehension items ask participants to point to objects in the room, follow simple and complex commands, identify the odd one out of a group of words and answer questions about a short paragraph. The expression items ask participants to generate a list of words, describe a sequence, express synonyms, describe the meaning of some common words and explain the purpose of some common activities.

Reliability and Validity

There is no reliability or validity data for this measure in people who are HIV-positive. However, it has been shown to be accurate, with 89% sensitivity and 100% specificity in one study comparing the SST to speech and language therapists' assessments in people with brain injury (Al-Khawaja, Wade & Collin, 1998). This study also found a strong association ($r = .91$) between the SST and the Short Orientation, Memory and Concentration test (SOMC) (Katzman et al., 1983) which the authors suggest that if comprehension and/or expression is impaired, it is unlikely that the patient will be able to complete the more complex neuropsychological tests. The SST is recommended as a screening measure for language difficulties in stroke (Blake et al., 2002) and multiple sclerosis (das Nair, 2007). The SST is also thought to be useful as it is independent of visual or verbal memory problems (Blake et al., 2002).

Alternative Measures Examples

There are several alternatives to using the SST: other screening measures or more comprehensive language batteries (a group of subtests measuring the same construct). For example:

- Frenchay Aphasia Screening Test (FAST) (Enderby, Wood, Wade & Langton Hewer, 1987)

This is also a brief screening measure of acquired language disorders with good reliability and validity (Salter, Jutai, Foley, Hellings & Teasell, 2006). However, this requires the use of stimulus cards and results may reflect visual rather than communication problems (Al-Khawaja et al., 1998). Furthermore, the FAST also assesses writing and reading ability, which are not required for participation in this study. The FAST may inadvertently assess executive functions, for example, verbal fluency – number of animals named in a minute making it less appropriate for this study. Al-Khawaja et al. (1998) examined the relationship between the FAST with the SST in adults with brain injury and found equivalent sensitivity but that the SST had higher specificity.

- Western Aphasia Battery (Kertesz, 1982)

This provides more comprehensive communication assessment. However, this takes up to one hour to administer and also relies on visual skills (McCabe, Sheard & Code, 2008). However, this depth of information is not required for participation in the present study.

Justification for the use of the SST

Although the SST has not been used with people with HIV, it does require comprehension of complex instructions required for completing the BADS, and has been used in previous neurological populations with good reliability and validity.

Hospital Anxiety and Depression Scale (HADS)
(Snaith & Zigmond, 1994)

The HADS is a quick and easy self-report measure which provides separate scales for depression and anxiety (seven items on anxiety; seven items on depression). The anxiety items encompass feelings of tension, anticipation, cognitions, ease, restlessness and panic. The depression items cover enjoyment, ability to laugh, cheerfulness, lethargy and interest in appearance and the environment (Dunbar, Ford, Hunt, & Der, 2000). The HADS does not include items related to physical functioning (Lewis & Wessely, 1990) and is more normally distributed than alternative self-report measures (Herrmann, 1997).

Reliability and Validity

A specific measure for understanding affective disorders in people with physical illnesses is needed as physical illnesses often represent a significant life event and particularly where cognitive processes are involved, impairments in these may mimic or mask affective difficulties (Dawkins, Cloherty, Gracey & Evans, 2006).

Internal consistency co-efficients range from .80 to .93 (e.g. Moorey et al., 1991) and test-retest reliability was above the acceptable level of .80 over a two week period (Herrmann, 1997). High levels of sensitivity and specificity are reported (Bjelland, Dahl, Haug & Neckelmann, 2002), for example, Whelan-Goodison, Ponsford and Schonberger (2009), showed the depression subscale had sensitivity of 62% and specificity of 92%, and the anxiety subscale had sensitivity of 75% and specificity of 69%. However, the HADS represents a dimensional rather than categorical measure. Therefore positive predictive power would be expected to be relatively small (Herrmann, 1997) and using clinical cut-off might not be useful (Golden, Conroy & O'Dwyer, 2007). There are some questions as to whether scores on the HADS are affected by cultural differences in emotional expression (Al-Adawi et al., 2007), although the HADS is widely used internationally and cross-culturally (Herrman, 1997).

In terms of construct validity, although some research has queried this two factor structure (Johnston, Pollard & Hennessey, 2000), the anxiety and depression subscales do seem to measure meaningfully different constructs, not just general distress (Herrmann, 1997). The HADS has reasonable correlation with other measures, such as the Beck Inventories with correlation coefficients ranging from .49 to .83 (Bjelland et al., 2002).

Examples of Alternative Measures

There are several alternative ways of assessing anxiety and depression, including: other self-report inventories or standardised clinical interviews.

- Beck Depression/Anxiety Inventory (BDI/BAI) (Beck, Steer & Brown, 1996)

These are commonly used self-report measures with good reliability and validity (Beck et al., 1996). However, they include physical health items, for example, appetite, making it inappropriate for this study. Moreover, the BDI has been reported to have significant floor effect (Zigmond & Snaith, 1983).

- General Health Questionnaire (GHQ) (Goldberg & Williams, 1988)

This is a similar measure to the HADS. However, it does not differentiate between anxiety and depression (Lewis & Wessely, 1990).

- Structured Clinical Interview for DSM Disorders (SCID) (First, Spitzer, Gibbon & Williams, 2002)

Despite structured interviews gathering detailed information, they are lengthy and this volume of information is not required for this study.

Justification for the use of HADS

The HADS has good reliability and validity for screening for mood (Barczak et al., 1988). Moreover, it has been developed for people with physical health problems and in previous research has been used with people with HIV (Barczak et al., 1988), people with Hepatitis C (Golden, Conroy & O'Dwyer, 2007) and neurological populations (Dawkins et al., 2006).

Wechsler Test of Adult Reading (WTAR)

(Wechsler, 2001)

Word reading estimates of pre-morbid IQ are commonly used because, for most people, an IQ test score is not available before they experienced changes in cognition (Graves, Carswell & Snow, 1999). The WTAR involves reading aloud a series of 50 unusual words with scoring is based on whether the words are pronounced correctly. Word reading estimates of IQ assume that IQ is correlated to reading ability, constant over time and not affected by current cognitive functioning (Willshire, Kinsella & Prior, 1991). This is supported by empirical research showing reading ability accounts for 38% of variance in IQ scores (Johnstone et al., 1997). There are standard scores and UK normative data for the WTAR for adults aged 16-89 which provide a good basis for comparison to the BADS. However, reading tests assume exposure to English language (Graves et al., 1999) and the WTAR UK standardisation sample was not ethnically diverse so it is important to use years of education to assist interpretation (Crawford, 1992).

Reliability and Validity

In the normative sample the WTAR displayed high internal consistency and high test-retest reliability (Wechsler, 2001). The WTAR has been found to be more accurate predictor of pre-morbid IQ and cognitive reserve than demographic-based assessment alone (Basso & Bornstein, 2000). However, the normative sample was only assessed over two to twelve weeks and is predominantly based on US data.

In terms of validity, the WTAR has been shown to be associated with performance on full scale IQ batteries (Wechsler Adult Intelligence Scale-III [WAIS-III]; Wechsler, 1999), with correlation coefficients ranging from .63 to .80. The WTAR also has good convergent validity with other word reading pre-morbid IQ measures such as the National Adult Reading Test (NART) (Nelson & Willison, 1991) with correlations coefficients ranging from .73 to .90. Pre-morbid IQ as estimated by word reading is thought to be influenced by age, so the authors developed age-appropriate normative

data. Although accuracy in IQ prediction appears to reduce as severity of dementia increases (Schmand, Geerlings, Jonker & Lindeboom, 1998), word-reading measures may still be a useful predictor of IQ (Paque & Warrington, 1995). In clinical samples there was clear dissociation of performance on the WTAR and performance on other measures of cognitive function (Wechsler, 2001) which provides evidence the WTAR is not inadvertently measuring other cognitive domains such as memory. However, it is important to remember accuracy of pre-morbid IQ is inferred, not based on actual data (Wechsler, 2001).

Examples of Alternative Measures

There are several other approaches and measures to assessing pre-morbid IQ including: other measures of reading ability, word recognition measures and demographic measures. For example:

- National Adult Reading Test (NART) (Nelson & Willison, 1991)

This measure also involves reading a series of words. However, it is older and considered more dated (Mathias, Bowden, Bigler & Rosenfeld, 2007).

- Spot-the-Word test (Baddeley, Emslie & Nimmo-Smith, 1993)

This is a lexical-decision task where the participant is presented with a real word and a non-word and has to decide which word is the real one. However, standard scores are not available for this assessment.

- Years of Education

This is not affected by the disease process but taken alone does not seem to be an accurate predictor of IQ (Graves et al., 1999). Moreover, this is based on the idea that all individuals with the same level of education will have the same IQ (Johnstone et al., 1997). However, there are obvious discrepancies in the delivery of education in different institutions, nations and cultures (Ryan, Byrd, Rivera Mindt, Rausch & Margello, 2008)

Justification for WTAR

As previous research as pointed to the importance of pre-morbid IQ in determining performance in other cognitive domains it is important to

collect this information. The WTAR is a quick and easy test to administer and has good normative data, with many studies reporting good reliability and validity data. The provision of standard scores provides a useful comparison, as this is on the same scale as the BADS standard scores, which is not possible using the Spot-the-Word test. Years of education were also collected to triangulate the evidence (Ryan et al., 2008), and move away from educational achievement measurement which might not be ethnically inclusive.

Dysexecutive Questionnaire Self-rater (DEX-S) Other-rater (DEX-O)
(Wilson et al., 1996)

The DEX gives a picture of executive functions in everyday life whilst still being quick to complete and easily understandable (Chan, 2001). It has been developed specifically with the BADS so is likely to represent the same constructs and includes both self- and proxy-scales to provide different perspectives. Items cover emotional, personality, behavioural and cognitive changes (Wilson et al., 1998). There is no normative data available to classify participants into clinical/non-clinical range. However, this encourages movement away from categorisation and dichotomisation which masks individual differences towards dimensional measurement of everyday functioning.

Reliability and Validity

The DEX has been shown to have high internal consistency (Cronbach α = .93, above .70 suggested by Nunnally, 1978) (Shinagawa et al., 2007). Shinagawa and colleagues (2007) also found moderate construct validity of the DEX compared to the Frontal Assessment Battery (FAB) (Dubois, Slachevsky, Litvan & Pillon, 2000). Most validation studies have taken place in Japan, with a translated version of the DEX, so coefficients may be different for the English version. However, most authors have reported good validity across cultures (e.g. Chan, 2001). Care should be taken over the use of total scores as potentially obscuring difficulties on particular aspects of executive functions (Chaytor & Schmitter-Edgecombe, 2007) and falsely

suggest that the data is continuous (Chan & Bode, 2008). In spite of this, research is not conclusive on systems for clustering the DEX scores, with different authors suggesting different clustering of scores and different labels for these clusters. Therefore, DEX total score is still predominantly used (Shinagawa et al., 2007). There is also evidence of convergent validity between the DEX and other functional measures of executive functions but differences may suggest that these measures are accessing different components of the executive function construct (Chaytor & Schmitter-Edgecombe, 2003).

There has been contradictory evidence on the ability of self- and other-rater comparison to provide a measure of insight. In a non-clinical sample participants reported more problems on self-report than other-report, which might be expected as this was the non-clinical sample (Chan, 2001). Although there is some evidence that self- and other-ratings may be weighted on different factors (Chan & Bode, 2008) there is considerable evidence to suggest the usefulness of both the DEX-S and DEX-O (Evans et al., 1997).

Examples of Alternative Measures

There are several alternative approaches to gather information on the functional impact of executive function difficulties. For example:

- Frontal Systems Behaviour Scale (Grace & Malloy, 2001)

This is a behaviour-rating scale with good normative data, which, similar to the DEX, has self- and proxy-report. However, it was not developed with the BADS, and research as suggested that it is weighted strongly on personality factors of executive function, which are not measured by the BADS (Stout, Ready, Grace, Malloy & Paulsen, 2003). Therefore, this measure might not provide the most useful comparison with the BADS.

- Frontal Behaviour Inventory (Kertesz, Davidson & Fox, 1997)

This is an informant-based interview with caregivers which has good reliability and validity (Kertesz et al., 1997). However, this measure is lengthy and includes items on physical functioning (e.g. incontinence,

hyperorality) (Malloy & Grace, 2005) which may be affected by the HIV-infection or side effects of the medications. Furthermore, this only considers the caregiver perspective and not individual experience.

- Barthel Activities of Daily Living Index (Mahoney & Barthel, 1965)

This assesses self-care abilities such as washing and dressing. However, as executive functions are higher-order cognitive abilities, basic activities of daily living are less likely to be affected (Alderman, Dawson, Rutterford & Reynolds, 2001).

Justification for use of the DEX

It is important to explore the functional outcomes specifically related to executive functions. The DEX has been designed for use with neurological populations, and maps well on to the constructs of the BADS compared to other measures (Grace & Malloy, 2001). Although the DEX has not been used in people with HIV before, it is widely used measure which avoids traditional categorisation and dichotomisation, and combines both self- and other-report to triangulate information sources.

Behavioural Assessment of the Dysexecutive Syndrome (BADS)
(Wilson et al., 1996)

For a further description, information on reliability and validity and consideration of examples of alternative measures to the BADS see the extended background section.

Procedure

This section outlines additional information on how participants were recruited and what happened to them through the research process. Figure 5 outlines the process of the research for participants.

Recruitment: Identification and Approach

The researcher maintained relationships with clinical staff at local NHS and the chair of a local charitable service by attending meetings and discussing the project, purpose of the research and recruitment and determining practical details of how recruitment would work in that service, including arrangements for collecting medical information. The researcher maintained regular contact with these individuals throughout the course of the research to answer any questions and maintain the profile of the study.

Pre-assessment

Contact details of the lead researcher (name, mobile number and e-mail address) and supervisors (name) were on all advertising and documentation to facilitate the two streams of referral: professional and self-referral. On initial referral name, date of birth, time since diagnosis, contact details (telephone number and/or address), name and position of referrer (if appropriate) were required. If a staff member felt unsure about whether a potential participant could be included or that a potential participant may be a risk to themselves (self-harm or suicide) or others (violence or aggression) they were advised to contact the researcher. However, no participants were excluded in this way. As detailed in Figure 5, once the referral was received, the potential participant was contacted by the lead researcher, to arrange the assessment. At this point the participant was assigned an ID code, used instead of names, on all further information. If the potential participant self-referred to the study a key member of staff was contacted (with participant consent), to confirm positive HIV diagnosis and ensure there were no risks to the participant from taking part.

Assessment

The location of the assessment was not standardised but all locations were quiet, distraction-free and confidential. Participants were offered a short break during the assessment session, as can be seen in Figure 5, to control for fatigue.

Post-assessment

The DEX-O was sent to the designated proxy for each participant with a covering letter stating the purpose of the DEX-O, that the participant had consented and included a stamped addressed envelope, to return to the researcher. In a similar way the medical note proforma was sent to relevant healthcare professionals who knew the participant to collect clinical information, again including a stamped addressed envelope.

Participants were offered feedback on their test performance if they desired. Results were only described in terms of above average/below average/average range. The report contained a disclaimer about its purpose and how it could be used. If participants desired, this report was forwarded to pre-identified healthcare professionals for their information.

Contact details of the researcher were made available if participants or healthcare professionals who wanted more information or had further questions. Referral pathways for psychological support were pre-identified at the outset of the research to manage the psychological impact of these results if required. However, no participants required or requested this referral.

```
                                                              Time
                                                             (weeks)

┌────────────────────────────────────────────────────────────┐
│     Recruitment and Identification of potential participants │
└────────────────────────────────────────────────────────────┘

┌──────────────────────────┐  ┌──────────────────────────┐
│ Staff-Referral – name, age,│  │ Self-Referral – name, age,│
│ diagnosis, contact details │  │ diagnosis, contact details│
└──────────────────────────┘  └──────────────────────────┘

┌────────────────────────────────────────────────────────────┐
│ Participant was contacted by the lead researcher by phone/letter │   1
└────────────────────────────────────────────────────────────┘

┌────────────────────────────────────────────────────────────┐
│ 'Caseworker' contacted (where appropriate and with participant │
│ consent) to consider risks to/from the participant and confirm HIV │
│ diagnosis                                                     │
└────────────────────────────────────────────────────────────┘
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Assessment with lead researcher and participant (1 ½ hours)

– Sight, hearing and communication test (SST)
– Check against exclusion information

Exclusion point – if did not meet criteria

– Information sheet discussed and written consent taken
– Dysexecutive Questionnaire (DEX-S)
– Wechsler Test of Adult Reading (WTAR)
– Hospital Anxiety and Depression Scale (HADS)

Short Break

– Behavioural Assessment of the Dysexecutive Syndrome (BADS)   3

Designated 'other' contacted to explain purpose of DEX-O. This was posted to them with a stamped addressed envelope to return to the researcher.

Medical note proforma completed by a staff member working in the service and returned to the researcher.   5

(Optional) Written/face-to-face feedback of results to participant.

6

(Optional) Written report forwarded to caseworker/referrer as required with consent from the participant

Figure 5. Flowchart and timeline of the research

Ethical Issues

As 'the dignity, rights, safety and well-being of participants must be the primary consideration of any research' (Department of Health, 2005, p.6), this section considers the main ethical issues of this research.

1. Potential Distress

    a. Participants excluded from the study

In the information sheet individuals were informed that there may be situations where they were not able to be included in the study. When this arose the researcher dealt with this sensitively and collaboratively by giving the potential participant the reasons for exclusion, any further information and discussing onward referral where appropriate. However, this was not requested or required by any of the participants.

    b. Poor performance on tests

This was addressed by the researcher by discussing that everyone has their own strengths and weaknesses and exploring onward referral where appropriate. However, although discussed this was not requested or required by any of the participants. As part of the debrief after the assessment and any feedback sessions, participants were asked if they had found anything distressing or had any concerns in relation to the study (Barker et al., 2002).

    c. Differing opinions on the DEX

The completion of the questionnaires was prefaced with a discussion about how the forms must be completed independently and it was not possible to share answers. It was emphasised that there are no right or wrong answers and everyone sees things differently. If problems arose from this the researcher had planned to deal with this sensitively and referred to further services in exceptional circumstances. However, this was not requested or required by any of the participants.

2. Confidentiality

Participants were informed that all data was kept confidential by assigning participants a unique research code, used instead of name on all information. Information was marked confidential, dated and will be stored in a locked filing cabinet at the university for seven years (for reference purposes). It will subsequently be destroyed securely in accordance with the University Research Code of Conduct. Electronic information was stored on password-protected databases. Participants were made aware of who had access to their information and if they chose to withdraw from the study this information would be retained, but not used.

Although their case−worker was contacted by the researcher, it was made clear that no information was shared with the case−worker without permission of the participant unless there was significant risk to the participants or others (for example, self-harm or violence).

All this information was within the information sheet which the participant had the opportunity to question and agreed to by signing the consent form.

3. Informed Consent

The participant was informed of the potential risks and benefits of participating through the information sheet. The information sheet provided information on what was expected of participation and information that they needed to know in order to make a rational decision about whether to take part (Barker et al., 2002). Participants were also informed of the wholly voluntary nature of their participation and that they were free to withdraw at any time. The principles of the Mental Capacity Act (2005) were used to assess informed consent: ability to understand and retain information and ability to consider the possible consequences. The participant had opportunities to ask questions. They were also given the details of the Trust complaints procedure should they have a complaint about the research.

As well as approval from a Research Ethics Committee approval was also sought from relevant Research and Development departments and honorary contracts obtained (Appendices L-O).

Supplementary Analysis Plan

This is a quasi-experiment, as the independent variables are not being truly manipulated, for example, people arrive with gender assigned already. In addition to the primary analyses, the association between BADS subtests was calculated through Spearman's rank correlation coefficients (two-tailed) to determine the potential fractionated executive function skills affected in people with HIV.

Parametric or non-parametric tests were used based on whether appropriate assumptions were met. Parametric tests were preferred because they are more robust and power efficient (Coolican, 2004).

Challenges in Conducting the Research

Some of the challenges that were encountered when conducting the research study are discussed with the strategies that were developed to manage these.

1. Some potential participants were not contactable.

Strategies were built into the protocol, so if no answer was obtained by phone, a letter was sent asking participant to get in touch with the researcher. If the participant did not respond the referrer was contacted to inform them that it had not been possible to contact the participant and to determine whether the potential participant was still interested in the research. Seven participants were non-contactable.

2. Despite participants having the information sheet prior to the assessment they often had not read it.

The researcher ensured that participants had the information sheet in advance of the appointment. At the start of the assessment the information sheet was discussed in detail, encouraging questions. The researcher asked strategic questions which required an answer which would convey understanding of the research.

3. It was hard to structure constructive feedback when participants performed within the 'impaired' range.

The terms below average, average and above average were used to denote performance instead of the labels from the manuals. This helped understanding and avoided emotionally-laden labels such as 'impaired'. The researcher also discussed with the participant their expectations and feelings about the results.

4. There was no standardised assessment location and the researcher was often lone-working outside of office hours.

The researcher negotiated the use of clinic rooms and did home visits, where appropriate. The researcher 'buddied' up with another trainee for out of office hours appointments in accordance with the Trust Lone Worker Policy.

Extended Results

This section describes the additional statistical analyses conducted within the study. This explains how results are presented, tests of assumptions (including normality), comparison tests to determine if the sample is representative of the wider population and comparison of participants who were included and excluded. Additional correlational analyses and multiple regressions of predictor variables for the BADS are reported. Finally a missing data analysis is conducted.

Background

As well as significance, actual *p*-values were reported to move away from the dichotomous reject/non-reject of hypotheses to provide meaningful interpretation of the data (Wright, 2003). Wherever a result is reported as significant, this should be interpreted as *statistically* significant, where chance is unlikely to be the explanation of the result (Kirk, 1999).

Standardised effect sizes were reported where possible to supplement null hypothesis testing, to describe the magnitude of the effect and to provide a way of communicating the results to allow for comparison with future research (Baguley, 2009). Of the several different types of effect sizes (for example, Cohen's *d*, Pearson's *r*, Hedges *g*), Pearson's *r* were used in the present study (converted from *t*-test data using Rosnow and Rosenthal (2005) statistic). *r* is a more flexible statistic and has a more direct relationship with power as it is sensitive to base-rate differences, which is a feature of other inferential statistics, making *r* more ecologically valid (McGrath & Meyer, 2006). *r* is a widely used effect size and easily understood as it is constrained to lie between -1.00 and 1.00 (Field, 2009). Benchmark classifications have been proposed to interpret size of effects (.10 small, .30 moderate, .50 large, Cohen, 1988; 1992). However, McGrath and Meyer (2006) have suggested that these classifications are too conservative and a different system should be used (.10 small, .24 moderate, .37 large). However, it is important to remember *r* is not measured on a linear scale so an effect size of .6 is not double .3 (Field, 2009). For a full discussion on effect sizes see Baguley (2009) and McGrath and Meyer (2006).

Assumptions

Statistical analyses are traditionally divided into parametric and non-parametric tests. Parametric tests are more powerful and are relatively robust to violations however, certain assumptions are made about the data: the data is normally distributed, interval or ratio level of measurement, independence and homogeneity of variance (Field, 2009). If these assumptions are seriously violated non-parametric tests are used which, although not as powerful, make fewer assumptions about the nature of data. Therefore, the general strategy adopted for the analyses of this study was to use parametric tests on those cases that meet the assumptions because they are more powerful, and to use non-parametric where the assumptions of parametric tests had been seriously violated.

Normally distributed data

A normal distribution describes data that is symmetrically distributed with the majority of scores clustered around a central mean. As scores start to deviate from the centre, their frequency and probability of obtaining them decreases. Deviations from the normal distribution are described as skew (lack of symmetry: scores are clustered at one end of the distribution) or kurtosis (too much or too little frequency in the ends of the distribution). If it is possible to assume the data to be a normal distribution it is possible to make certain justified inferences from samples to populations. In the current study this means inferring characteristics about the HIV population in general from the sample of participants. The central limit theorem purports that with a sample size of approximately 30 it is likely to have important distributional properties that approach a normal distribution. The current study sample has less than 30 participants so the data has been checked to determine whether it meets the assumptions for parametric tests.

Although normality can be judged visually from scatterplots/histograms, this is very subjective. z-skew and z-kurtosis scores can be calculated by converting scores to a z-distribution (mean 0 and sd 1), where values above 1.96 represent a significant deviation from the normal distribution, $p<.05$.

Shapiro-Wilk tests, used in preference to Kolmogorov-Smirnov tests when n<50, to compare the scores to a normally distributed sample. If the test statistic is non-significant then the sample is not significantly different from a normal distribution. Results of Shapiro-Wilk, z-skew and z-kurtosis calculations for interval or ratio level data are presented in Table 8.

Table 8 shows monthly alcohol use is statistically significantly different to the normal distribution (W(20) = .56, p=.001) and is significantly positively skewed and positively kurtotic (leptokurtotic). This suggests the distribution is weighted towards minimal alcohol use and the distribution is significantly peaked around the mean. The WTAR score is also significantly non-normally distributed (W(20) = .88, p=.01) and negatively skewed, which means that there was an unsymmetrical leaning towards higher scores on the WTAR. Although the HADS-A was not statistically significantly on Shapiro-Wilk's (W(20) = .91, p=.06), it was positively skewed and kurtotic, which means there was a weighting towards minimal anxiety and an excessively peaked mean. The BADS subtests were also statistically significant on the Shapiro-Wilk's but only the Action Program was significantly negatively skewed, with weighting towards higher scores. However, the BADS Total Score, DEX-S, DEX-O, HADS-D, length of current medication regime, CD_4 count, time since diagnosis and age were all normally distributed.

Table 8.
Tests of normality in the continuous data

Characteristic	Shapiro-Wilk statistic	Significance *p*-value	z-skew	z-kurtosis
Age (Years)	.95	.43	0.13	0.22
Alcohol (Units)	.56	<.01**	4.93*	5.56*
Length of Diagnosis (Years)	.91	.10	1.68	0.39
CD_4 count (cells per mm^3)	.94	.26	-0.22	-1.18
Length of current medication regime (Months)	.91	.13	1.09	-0.70
WTAR	.88	.02*	-1.96*	-0.01
HADS				
Anxiety	.91	.06	2.18*	2.82**
Depression	.95	.30	0.18	0.41
DEX				
Self	.98	.96	0.62	0.16
Other	.97	.88	0.86	0.25
BADS				
Total Score	.91	.06	-1.65	0.03
Card Sort	.82	.002**	-1.56	-0.36
Action Program	.63	.001**	-3.02**	1.04
Key Search	.81	.001**	-0.79	-1.54
Temporal Judgement	.87	.01**	0.07	-0.59
Zoo Map	.85	.005**	0.20	-0.58
Modified Six Elements Test	.85	.005**	-0.83	-1.23

Note. * p<0.05, ** p<0.01 denotes measures/characteristics that are significantly different from the normal distribution. WTAR: Wechsler Test of Adult Reading; HADS: Hospital Anxiety and Depression Scale; DEX: Dysexecutive Questionnaire; BADS: Behavioural Assessment of the Dysexecutive Syndrome

Level of measurement of data

In order to use parametric tests data should be at interval level. The researchers theoretical background and prior beliefs can influence how the researcher categorises the variable as well as the more objective properties of the variable (e.g. that height or weight has a true zero) (Field, 2009). Where nominal data is arbitrarily categorical, ordinal data is ranked and interval data is when the distance between each point on the scale is the same. Ratio data is when the distance between each of the points on the scale is the same and the scale has a true zero.

The BADS Total standard score data is clearly not arbitrarily categorical but also does not have a 'true zero'. The standardised scores of the BADS Total score are not 'ranked' but can be considered to have an equal difference between scale points (e.g. Coolican, 2004) and so the BADS Total standard score can represent interval level data, and is considered as such throughout the analysis.

Independence

This means independence of participants, the performance of one participant did not influence the performance of others (Field, 2009). In the current study participants were unable to confer about responses within the testing session and participants were asked not to share details of the test with others. Therefore independence of scores has been assumed for the analysis.

Homogeneity of variance

This final assumption claims that variance, or spread of the scores, should be the same throughout the data' (Field, 2009, p.133). When comparing two groups, this means both groups should have equivalent variance in scores, assessed using Levene's test for equality of variances (Levene, 1960). In correlational design this means that variance at different levels of variables should be roughly equivalent (Field, 2009), assessed using graphs. Where appropriate these tests/graphs have been presented.

Summary and Implications

On this basis, for Aim One, considering the BADS Total score, parametric statistics were used. However, for Aim Two and Three, to be consistent throughout, non-parametric statistics were used because the majority of data is not interval level (e.g. DEX, HADS) or not normally distributed (e.g. WTAR, alcohol use). Although non-parametric statistics have less statistical power, this is preferable to transforming the data to a normal distribution, as transforming the data changes the construct measured from geometric to arithmetic (Field, 2009). As a result, analyses of transformed data have implications for interpretation (Grayson, 2004; Games, 1984) making it less meaningful with questionable validity for the untransformed data (Tabachnick & Fidell, 2001). For a full discussion about transformation see Tabachnick and Fidell (2001).

Research sample characteristics compared to other populations

To inform interpretation and clinical implications of the study it is important to:

1. Determine if the study sample are representative of the wider population of people with HIV the sample was drawn from. To explore this, the characteristics of study sample were compared to regional demographic details of people accessing HIV services as published by the HPA (2008). The data available was the proportion of individuals living with HIV in the region by age category, gender and ethnicity.

2. Determine if the demographic characteristics of the study sample are broadly equivalent to the demographic characteristics of the BADS normative sample (as described in Wilson et al., 1996; Wilson et al., 1998). If these groups are comparable this supports the comparison between the average sample and normative data on the BADS. Only limited data is available to describe the BADS normative sample: approximate gender proportion, mean age and mean IQ.

Percentages of the participants with certain characteristics are presented in Table 9. Table 9 also presents the percentage of people with those characteristics in the regional population who were eligible for inclusion into the study (HPA, 2009) and BADS normative sample (Wilson et al., 1996).

Table 9.
Demographic details of the study sample compared to regional data and BADS normative sample data

Characteristic	Study Sample	Regional Data (HPA, 2009)	BADS Normative Sample Data (Wilson et al., 1996)
Sample Size	20	2466	216
Gender			
Male (%)	65	53.9	
Female (%)	35	46.1	
Age (years)			
Mean (SD)	43.5 (8.3)		46.6 (19.8)
Range	28-59		16-87
Age group (years)			
18-30 (%)	5.0	13.2	
30-40 (%)	21.1	41.1	
40-50 (%)	52.6	33.4	
50-60 (%)	21.1	12.3	
Ethnicity			
White (%)	75.0	39.4	
Black African/ Caribbean (%)	25.0	51.6	
IQ			
Mean (SD)	96.5 (21.0)		102.7 (16.3)
Range	50-120		69-129

Note. BADS=Behavioural Assessment of the Dysexecutive Syndrome

1. Compared to regional data for people living with HIV

Comparison to regional data for people who were eligible for the study was conducted to determine if the sample was representative or whether the sample is biased towards certain groups. Chi-squared tests were used to determine the degree of association between two categorical variables based on comparing observed frequencies to what would be expected by chance (Field, 2009).

Age

As sample size was small, age was collapsed into two categories: 20-40 years and 40-60 years. Although this does not allow for any detailed analysis, this gave a broad idea of whether the sample characteristics are what would be expected compared to the regional population data. The results showed a significant difference in the age proportions of the sample and the regional population age proportions χ^2 (1) = 15.01, *p*=.01. This means the proportional representations of ages in participants in the study sample was different to that seen in the regional population data. The study sample had significantly higher proportions of people in the older age groups than the regional population.

Ethnicity

Ethnicity was collapsed to ensure that there was sufficient data in each cell; this was collapsed to White British and Black African/Black Caribbean. The results showed a significant difference between the proportions of people from different ethnic backgrounds in the sample and the regional population χ^2 (1) = 35.22, *p*=.01. This means the ethnic proportions of participants in the study sample was different to that reported in the regional population data for people living with HIV, with significantly fewer sample participants in the non-White British ethnic groups compared to the regional population.

Gender

There was no significant difference between the sample and the population in terms of gender proportions χ^2 (1) = 0.49, *p*>.05. This means that the gender ratios in the sample were equivalent to the regional population.

Overall, the sample were different from the eligible regional population on proportion of participants within age and ethnicity categories but were broadly equivalent on gender ratios. Therefore, findings related to age and ethnicity should be interpreted with care.

2. Compared to BADS normative data

The comparison between BADS average score of the sample and the BADS normative data average assumed these samples are comparable on demographic factors. As assumptions of normality, independence and interval data have been met an independent samples t-test was conducted to test this. It was not possible to conduct Levene's test for homogeneity of variance as the raw data was not available for the BADS normative sample.

Age

On average, participants in the BADS normative sample (M = 46.40 years, SD = 19.80) were older than the sample of participants in this research study (M = 43.47, SD = 8.26). However, this difference was not statistically significant $t(234)$ = 0.70, p=.48, with an effect size of r = .05.

IQ

On average, IQ of participants in the BADS normative sample (M = 102.70, SD = 16.30, as measured by the NART) was higher than the sample of participants in the research study (M = 96.50, SD = 20.98, as measured by the WTAR). However, this difference was not statistically significant $t(234)$ = 1.59, p=.11, r = .10.

Overall these results show the sample recruited in this research study was not significantly different on age or IQ to the sample that provided the BADS normative data. This should mean that comparing average BADS scores from this sample to the average normative scores is valid, as the groups are matched in these variables. However, several characteristics, such as ethnicity of the BADS normative sample, were not recorded and therefore, could not be checked. Although homogeneity of variance between groups could not be statistically checked, an independent t-test was still the

most appropriate statistic, and as a robust test the *t*-test results are more likely to be valid even if an assumption is violated (Field, 2009).

Comparison between included and non-responders/excluded participants

It is also important to determine whether the sample included in the study were different to the potential participants who were excluded or could not be contacted. There is very limited information available on the excluded/non-responders in line with confidentiality. The demographic characteristics and reasons for exclusion are outlined in Table 10. Those who were included in the study were compared to those who were not included on: the proportion of males/females, using a Fisher's exact test, and mean age using an independent samples *t*-test. For the sake of simplicity participants who were not included for whatever reason are termed 'excluded participants'.

Table 10.
Demographic characteristics of participants not-included compared to included participants

Characteristic	Number of Participants Excluded	Number of Participants Included
Gender		
Male	6	13
Female	4	7
Age (years)		
Mean (SD)	40.44 (7.80)	43.58 (8.18)
Range	27-51	28-59
Referral Source		
Self	14	8
Healthcare Professional	6	2
Reasons for non-inclusion		
Not contactable	7	
Insufficient language ability	2	
Severe depression	1	

Age

On average, included participants were older (*M* = 43.47 years, *SE* = 1.88) than excluded participants (*M* = 41.30 years, *SE* = 2.48). The samples were normally distributed and Levene's test for homogeneity of variance was not significant, showing the variance between those included and excluded can be considered equivalent $F(27) = 0.004$, $p=.95$. An independent samples *t*-test found the difference in ages between the groups was not statistically significant $t(27) = 0.72$, $p=.48$, $r=.13$.

Gender

For a 2x2 frequency table when expected frequencies are low (cell frequencies less than 5) the sampling distribution is too deviant from the chi square statistic. A Fisher's exact test, based on exact probabilities, is used instead. A Fisher's exact test showed no significant association between gender and whether participants had been excluded or not (one-sided) $p=.55$.

Referral Source

A Fisher's exact test showed no significant association between referral source and whether participants had been excluded or not (one-sided) $p=.44$.

Overall these results point to no significant difference between included and excluded participants on the variables measured. As both included and excluded groups were roughly equivalent on age, gender and referral source, it is unlikely that these variables systematically influenced the pattern of results as a consequence of exclusion. However, there were several variables which were not collected on the referral forms and so could not be analysed. Further there was no information collected on participants who did not complete a referral form because they did not meet the inclusion criteria.

Aim One

Average sample scores on the BADS Total score and BADS subtests are presented in Table 11.

Table 11.

Means and SDs of the BADS and the BADS subtests

BADS Score	Mean	SD	Range
Total Profile Score	85.30	23.67	33-113
Card Sort	2.95	1.05	1-4
Action Program	3.40	1.05	1-4
Key Search	2.60	1.43	0-4
Temporal Judgement	2.25	0.85	1-4
Zoo Map	1.80	1.32	0-4
Modified Six Elements Test	2.65	1.35	0-4

Note. BADS=Behavioural Assessment of the Dysexecutive Syndrome

As the assumptions for parametric tests were met an independent samples *t*-test was used to compare the average BADS Total standard score in the sample to the average BADS Total standard score from the normative data. The independent *t*-test is used to test whether average performance in participants from different groups are statistically significantly different from one another, based on the null hypothesis that performance in different populations is roughly equal. As with previous analyses it was not possible to test the assumption of homogeneity of variance because there is insufficient data from the manual.

Internal Consistency of the BADS

It is worth noting the internal consistency of the BADS in this sample and determining whether scores on individual subtests are consistent with the BADS total score. Reliability of the BADS was analysed using Cronbach's α which assesses whether a measure can consistently reflects the construct it claims to be measuring (Coolican, 2004). Cronbach's α approximately represents splitting the measure in half in every possible combination, correlating each split with each other and taking the average correlation as Cronbach's α statistic (Field, 2009). Values of .80 to 1.00 traditionally represent an acceptable level of Cronbach's α to confer reliability and means that participants' performance on subtests was similar (Coolican, 2004). Kline (1999) suggests that .70 is a more suitable cut-off point for ability tests and high internal consistency suggests a test is measuring a very narrow aspect of a construct. However, this interpretation of using Cronbach's alpha to measure unidimensionality is discouraged (Cortina, 1993).

The BADS had satisfactory internal consistency within this sample (standardised Cronbach's α = .72). Standardised alpha was used because items are standardised before being summed to provide the BADS total score.

BADS subtest analysis

It is useful to look for associations between subtests to determine whether subtests are measuring similar executive functions skills. Two-tailed non-parametric Spearman's rank correlation coefficients (ρ) were calculated between the BADS subtests to determine the degree of association between them. Spearman's correlation coefficients were used in preference to Kendall's τ because there were only few tied ranks.

Table 12 presents these results. The Card Sort test was statistically significantly positively correlated with the Zoo Map test (r_s = .45, *p*=.05, two-tailed). The Key Search test was correlated with the Zoo Map (r_s = .65, *p*=.002, two-tailed) and also the Temporal Judgement test (r_s = .52, *p*=.02,

two-tailed). However, there were no other statistically significant correlations between subtests. This suggests the following pattern of subtest results may relate to the underlying aspects of the fractionated executive function these tests represent. This is represented visually in Figure 6. This might point towards weighting on different executive functions skills, although at this point it is not possible to conclusively identify which skills as all subtests are multi-faceted in nature in line with ecological validity.

Table 12.
Subtest correlations with each other (two-tailed)

Correlation coefficient: r_s (*p*-value)

	Card Sort	Action Program	Key Search	Temporal Judgement	Zoo Map
Action Program	.35 (.13)				
Key Search	.41 (.08)	.32 (.16)			
Temporal Judgement	.31 (.18)	.36 (.13)	.52 (.02)*		
Zoo Map	.45 (.05)*	-.02 (.95)	.65 (.01)**	.33 (.16)	
Six Elements Test	.25 (.29)	.40 (.08)	.14 (.55)	.13 (.60)	-.07 (.77)

Note. * p<.05, ** p<.01

r_s = .41, p=.08

Card Sort   Zoo Map   Key Search   Temporal Judgement

r_s = .45
p=.05

r_s = .65
p=.01

r_s = .51
p=.02

Action Program   Modified Six

r_s = .40
p=.08

Key

◯ BADS Subtest

⎯ Statistically significant correlation

•••••• Correlation approaching statistical significance
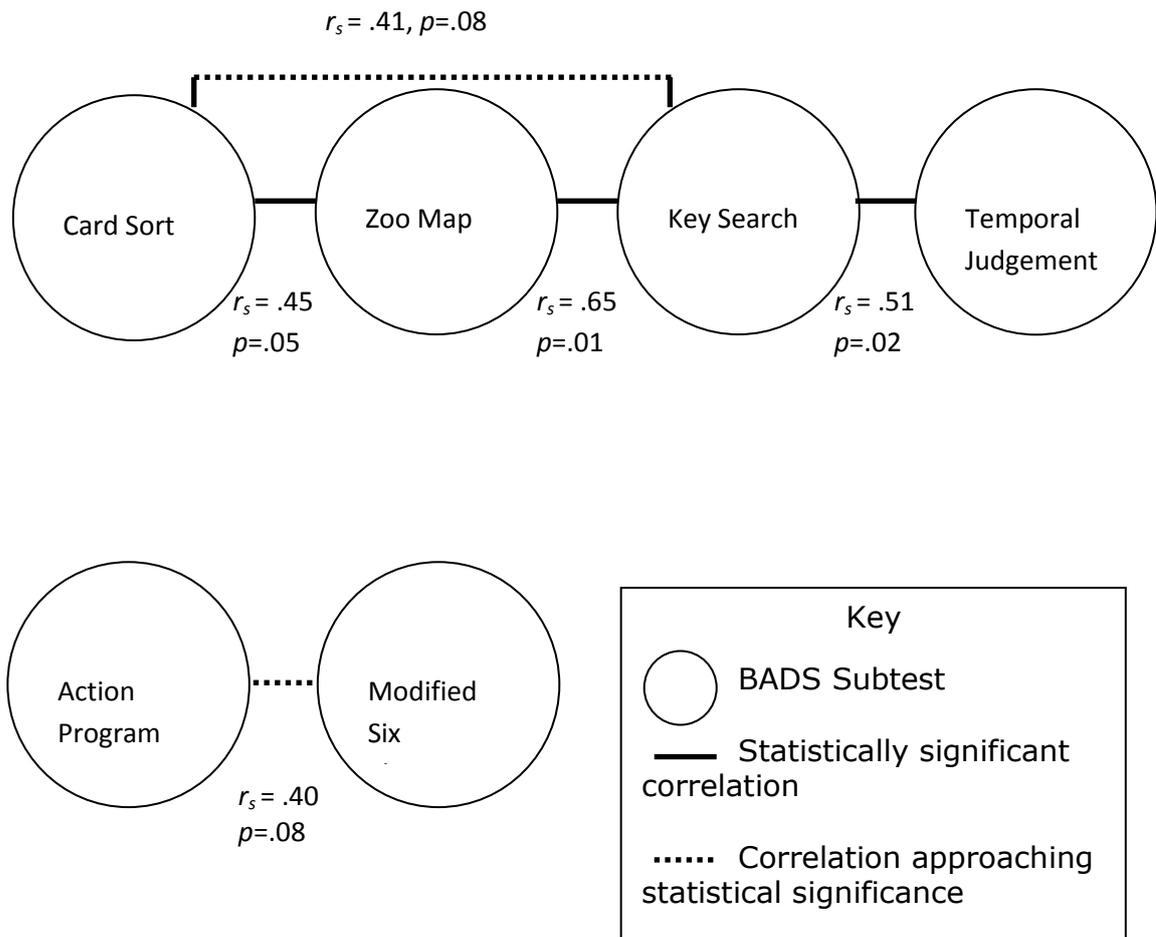
Figure 6. Visual depiction of the correlations between the BADS subtests

Aim Two

Non-parametric Spearman's ρ correlation coefficients were conducted to explore the association between the BADS, DEX-O and DEX-S. Non-parametric tests were used because although the DEX and BADS can be assumed to be normally distributed, the DEX is ordinal, rather than interval level data. One-tailed tests were carried out as previous research can hypothesise the predicted direction of the relationship between these variables. It is predicted that the BADS would be negatively correlated with the DEX-O and positively correlated with the DEX-S, based on suggestions about insight.

Internal consistencies of the DEX-S and DEX-O for both of these measures were high (Cronbach's α .91 and .83 respectively). This suggests that these measures have good reliability. A Mann-Whitney U, the non-parametric version of the independent t-test, showed that DEX-O scores from family/friends (Median 22.00) were statistically significantly lower than professionals (Median 33.00), U=12.50, z=-2.06, p=.04, r=-.50.

Comparison between BADS subtests, DEX-O and DEX-S

The DEX-S was not significantly correlated with any of the subtests: Card Sort (r_s = .16, p=.25, one-tailed), Key Search (r_s = .24, p=.16, one-tailed), Temporal Judgement (r_s = .08, p=.37, one-tailed), Zoo Map (r_s = -.05, p=.41, one-tailed) and SET (r_s = -.05, p=.41, one-tailed). Although the DEX-S approached significance with the Action Program (r_s = .36, p=.06, one tailed).

The DEX-O also not correlated with any of the subtests: Key Search (r_s=-.14, p=.30, one-tailed), Temporal Judgement (r_s = .01, p=.48, one-tailed), Zoo Map (r_s = -.08, p=.39, one-tailed) and SET (r_s = -.16, p=.27, one-tailed). Although this approached significance with the Card Sort (r_s = -.38, p=.07, one-tailed) and Action Program (r_s = -.38, p=.07, one-tailed).

DEX-O compared to DEX-S

A Wilcoxon signed-rank test showed participants rated themselves as having fewer problems with executive function in everyday life on the DEX-S (*Median*=22.50) than informants on the DEX-O (*M*=29.00), but this difference was not statistically significant, z = -1.80, p=.07, r=-.31, although this difference closely approaches significance. Previous research in non-clinical samples on the DEX-S and DEX-O (Chan, 2001) is descriptively compared to the study sample scores in Table 13. This demonstrates very little difference between participants in the sample and non-clinical sample on the DEX-S. Other-raters in the present study sample seem to report on average more problems than the raters in the non-clinical sample. However, as there is no formal normative data available for the DEX, it is not possible to statistically compare these scores.

Table 13.

Mean and SD of the DEX-O and DEX-S as compared to an example of a non-clinical sample

	Study sample	Non-clinical sample (Chan, 2001)
DEX-S		
Mean (SD)	22.80 (10. 07)	22.13 (8.86)
Range	4-46	4-49
DEX-O		
Mean (SD)	29.76 (13.31)	20.61 (10.52)
Range	9-60	0-48

Note. DEX-S=Dysexecutive Questionnaire-Self Report; DEX-O=Dysexecutive Questionnaire-Other Report

Aim Three

This associative hypothesis examined demographic and clinical factors that contribute to executive function impairment as measured by the BADS, DEX-S and DEX-O. Continuous variables were compared to the executive function measures using non-parametric Spearman's ρ correlations due to a number of the variables being non-normally distributed or ordinal level. One-tailed correlation coefficients were calculated because the direction of association can be predicted from previous research as outlined in Table 14. The dichotomous categorical variables were compared with the continuous variables of the executive function measures using point-biserial correlations. Point-biserial correlations (r_{pb}) consider dichotomous variables with two discrete categories (for example, gender, ethnicity, referral source), as opposed to biserial correlation coefficient where variables are on a continuous dichotomy (for example, passing or failing an exam).

Bonferroni Correction

It is worth a note on Bonferroni corrections which were not used in this study. The Bonferroni correction uses a more stringent criteria to judge whether a coefficient is statistically significant (critical *p*-value) by dividing the α level by the number of correlations conducted. In this analysis 12

variables were compared to the 9 executive function measures (BADS Total and subtest scores, DEX-S and DEX-O) amounting to 21 variables. Therefore, if a Bonferroni correction was to be used the significance level would be $.05/21=.002$. However, due to the development method of the Bonferroni correction, a significant result after applying the correction does not confirm that that specific variable is statistically significant, but that there is a statistically significant finding somewhere within the dataset (Perneger, 1998). Furthermore, Bonferroni corrections seem counter-intuitive as results are interpreted based on the number of other comparisons performed with little consistency on which comparisons warrant inclusion under the adjusted Bonferroni correction, for example, just those published or including those performed but not published, or how this relates to future research in similar areas (Perneger, 1998). Moreover, a Type II error is as much an error as a Type I, however, within positivistic frameworks a Type II is seen as more acceptable, stemming from the emphasis on statistical rather than practical significance (Nakagawa, 2004). However, the epistemological position and pilot nature of this study aimed to identify possible patterns and relationships to point to further research directions.

This section considers how the subtests of the BADS are related to the medical, demographic and cognitive, emotional and behavioural variables. It is worth noting that plasma viral load could not be included in the analysis as all but three participants had undetectable viral loads. Drug use, apart from alcohol use, could also not be included in the analysis as no drug use was recorded by the study. It is also important to acknowledge that a correlation does not imply causality. As one-tailed tests were conducted the predicted direction of associations are outlined based on previous research, outlined in the literature review in Table 14.

Table 14.

Expected direction of association between variables

Variable	Expected Direction of Association with EF
Medical factors	
Time since diagnosis	Longer time since diagnosis: poorer EF
HIV stage	Later HIV stage: poorer EF
CD_4 count	Lower CD_4 count: poorer EF
Medication regime	More medication: better EF
Months on medication regime	More months on medication: better EF
Demographic factors	
Gender	Female gender: poorer EF
Ethnicity	Non-white: poorer EF (or poorer performance)
Age	Older age: poorer EF
Referral source	Professional referral: poorer EF
Cognitive, emotional and behavioural factors	
Average monthly alcohol use	Higher monthly alcohol use: poorer EF
Years of education	More years education: better EF
WTAR	Higher IQ: better EF
HADS-A	More anxiety: poorer EF
HADS-D	More depression: poorer EF

Note. EF = executive function; WTAR = Wechsler Test of Adult Reading; HADS-A = Hospital Anxiety and Depression Scale-Anxiety; HADS-D = Hospital Anxiety and Depression Scale-Depression

Medical Factors

The subtest correlation coefficients associated with medical factors are presented in Table 15. The Action Program subtest of the BADS was positively correlated with length of diagnosis (r_s = .44, *p*=.04, one-tailed) so participants diagnosed for longer performed better on this subtest. Key Search was positively correlated with CDC stage (r_s = .55, *p*=.007, one-tailed) and negatively correlated with months on medication (r_s = -.50, *p*=.03, one-tailed). Therefore, participants in this sample who were in later stages of HIV-infection and who had been on medication regimes for longer performed worse on this specific subtest.

CD$_4$ count was positively correlated with months on medication (r_s = .72, p=.001, one-tailed) which suggests the medication was working through the mechanism indicated. Gender was associated with medication regime (r_{pb} = -.40, p=.04, one-tailed) such that female gender was associated with being on fewer medications.

Table 15.
Correlation coefficients of Medical Factors compared to BADS Subtests

	Correlation coefficients r_s / r_{pb} (*p*-value) one-tailed					
	Card Sort	Action Program	Key Search	Temporal Judgement	Zoo Map	Modified Six Elements
CD$_4$ count	.26 (.14)	.30 (.10)	-.18 (.24)	.14 (.29)	.15 (.26)	-.05 (.42)
Time since Diagnosis	-.21 (.20)	.44 (.04)[*]	.09 (.36)	.16 (.27)	-.02 (.47)	.14 (.30)
CDC stage	.35 (.07)	.22 (.18)	.45 (.03)[*]	.08 (.38)	.16 (.25)	-.10 (.35)
Medication regime	-.01 (.48)	.18 (.23)	.13 (.30)	-.10 (.34)	.01 (.50)	.30 (.10)
Length of Current Medication Regime	.35 (.10)	.12 (.34)	-.50 (.03)[*]	-.20 (.24)	-.02 .47)	-.13 (.32)

Note. [*]*p*<.05, CDC=Center for Disease Classification; BADS=Behavioural Assessment of the Dysexecutive Syndrome

Demographic Factors

On further consideration (Table 16) of the BADS subtests, gender was statistically significantly associated with the Key Search (r_{pb} = -.57, p=.004, one-tailed) where women perform less well than men on this subtest. Ethnicity was correlated with the Action Program task (r_{pb} = -.57, p=.004, one-tailed), Key Search (r_{pb} = -.63, p=.001, one-tailed) and Zoo Map (r_{pb} =-.443, p=.03, one-tailed) where White British participants tended to perform better on these tasks of the BADS than Black African/Caribbean participants. The Key Search test was positively correlated with age (r_s = .49, p=.02 one-tailed) so older participants performed better on this subtest. The Action Program subtest was positively correlated with referral

source (r_{pb}=.39, p=.05) so those who self-referred performed better on this subtest.

Table 16.

Correlation coefficients of Demographic Factors compared to BADS Subtests

	Correlation coefficients r_s / r_{pb} (p-value) one-tailed					
	Card Sort	Action Program	Key Search	Temporal Judgement	Zoo Map	Modified Six Elements
Age	-.06 (.40)	.26 (.13)	.49 (.02)*	.36 (.06)	.23 (.16)	.16 (.25)
Gender	-.37 (.05)*	-.19 (.22)	-.62 (.001)**	-.22 (.17)	-.37 (.05)*	-.25 (.14)
Ethnicity	-.31 (.09)	-.45 (.02)*	-.67 (.001)**	-.17 (.23)	-.45 (.02)*	.07 (.39)
Referral Source	.35 (.06)	.39 (.05)*	.11 (.32)	.20 (.20)	-.15 (.26)	.01 (.49)

Note. * p<.05, ** p<.01 BADS=Behavioural Assessment of the Dysexecutive Syndrome

Cognitive and Emotional Factors (Table 17)

The Card Sort was statistically significantly correlated with WTAR (r_s = .44, p=.03, one-tailed), suggesting that participants with higher pre-morbid IQ performed better on this subtest than those with lower pre-morbid IQ. However, the Action Program was statistically significantly negatively correlated with years of education (r_s = -.46, p=.02, one-tailed) which suggests the contrary relationship, participants with more education performed less well than participants with fewer years of education. The modified Six Elements Test was statistically significantly correlated with HADS Anxiety score (r_s = -.38, p=.05, one-tailed) so participants who were more anxious performed worse on this subtest.

A Wilcoxon signed-rank test, the non-parametric equivalent of the dependent *t*-test, was used to determine whether participants from the study performed equivocally on the BADS (standard score) and the WTAR (standard score) by ranking the data. The non-parametric option was chosen as the WTAR is non-normally distributed. Participants standard scores on IQ were found significantly higher (*Median* = 103.50) than their

standard scores on the BADS (*Median* = 88.00), *z* = -2.02, *p*=.04, with a moderate effect size, *r* = -.31.

WTAR was positively correlated with years of education (r_s = .50, *p*=.01, one-tailed), as would be expected those with longer in education had higher WTAR scores. CDC classification positively correlated with HADS Anxiety (r_s=.57, *p*=.005, one-tailed) so those who were at more advanced stages of HIV experienced more anxiety or those more anxious had increased disease progression.

Table 17.
Correlation coefficients of Cognitive, Emotional and Behavioural Factors compared to BADS Subtests

	Correlation coefficients r_s (*p*-value) one-tailed					
	Card Sort	Action Program	Key Search	Temporal Judgement	Zoo Map	Modified Six Elements
Monthly alcohol use	.05 (.42)	-.11 (.32)	.37 (.06)	-.23 (.16)	.28 (.12)	.24 (.15)
Years of Education	.17 (.23)	-0.46 (.02)[*]	.06 (.40)	-.16 (.24)	.31 (.10)	-.24 (.16)
WTAR	.44 (.03)[*]	-.20 (.20)	.13 (.29)	.08 (.38)	.29 (.11)	.26 (.13)
HADS-A	.12 (.31)	.08 (.38)	.15 (.27)	-.11 (.33)	-.14 (.28)	-.38 (.05)[*]
HADS-D	.01 (.48)	.02 (.47)	-.03 (.45)	-.17 (.23)	-.31 (.09)	0.22 (.18)

Note. [*] p<.05, BADS=Behavioural Assessment of the Dysexecutive Syndrome; HADS-A=Hospital Anxiety and Depression Scale-Anxiety Subscale; HADS-D=Hospital Anxiety and Depression Scale-Depression Subscale.

Further analysis of variables

Gender

Figure 7 displays the differences in gender on the individual BADS subtests. Women did not perform as well as men on any of the subtests. However, an independent *t*-test showed that there was no significant difference between males and females on pre-morbid IQ as measured by the WTAR, although homogeneity of variance cannot be assumed *t*(7.48) = 1.09, *p*=.31, *r*=.37.

Gender was also not significantly associated with years of education (r_{pb} = .15, p=.26, one-tailed) or alcohol use (r_{pb} = -.30, p=.10, one-tailed). The difference between men and women could also not be accounted for by differences in CD_4 counts (r_{pb} = .15, p=.27, one-tailed). However, gender was statistically significantly correlated with medication regime (r_{pb} = -.46, p=.03, one-tailed), with women less likely to be on more complex regimes.

Mean subtest score by Gender
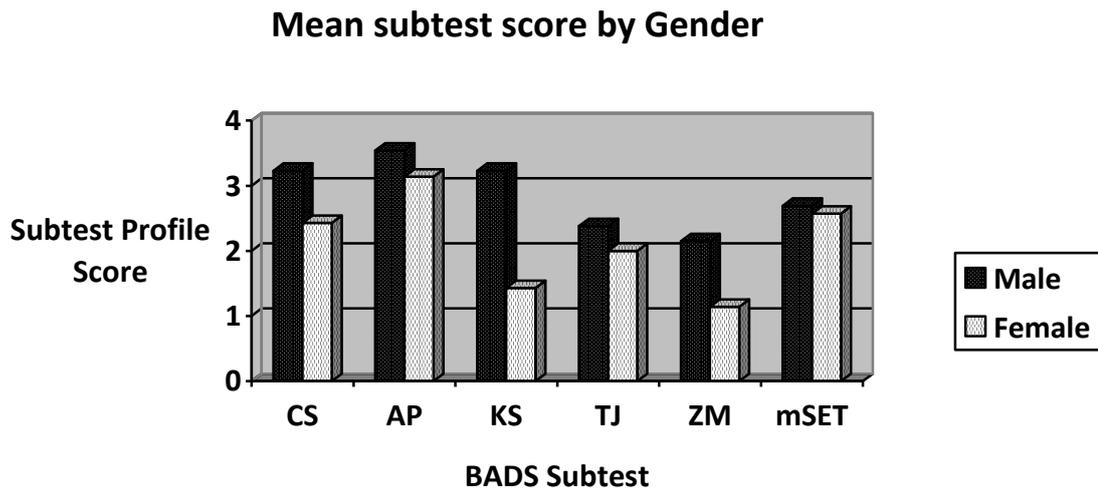
Note. CS=Card Sort; AP=Action Program; KS=Key Search; TJ=Temporal Judgement; ZM=Zoo Map; mSET=Modified Six Elements Test

Figure 7. Mean subtest score by gender

Ethnicity

On the WTAR there were no differences between the White British sample (M=96.67, SE=5.23) and the Black African/Caribbean sample (M=96.60, SE=11.44), $t(18)$=0.60, p=.95, r=.14, with the assumption of equal variance met (Levene's $F(18)$=0.78, p=.39). Ethnicity was also not significantly associated with years of education (r_{pb} = .03, p=.45, one-tailed), alcohol use (r_{pb} = -.23, p=.16, one-tailed), although association between ethnicity and medication regime approached significance (r_{pb} = -.35, p=.07, one-tailed), with Black African/Caribbean participants less likely to be on more complex regimes. In summary, this means Black African/Caribbean participants were not significantly different to White British participants on pre-morbid IQ, years of education and alcohol use. Therefore, these are unlikely to be the cause of the significant difference between these groups on the BADS. Although Black African/Caribbean

participants were less likely to be on complex medication regimes compared to White British participants.

Multiple Regression – BADS Total standard score

The data was further explored by a multiple linear regression to further explore these relationships. To maintain richness and depth of the data, the BADS was kept as a continuous rather than categorical variable, which necessitates the use of a multiple regression rather than a logistic regression. Previous research has suggested that one predictor variable can be entered into the regression for every 10 participants (Field, 2009). Therefore, as this study recruited 20 participants, entering two variables into the regression analysis is appropriate. Therefore gender and ethnicity were entered hierarchically into the regression to predict the BADS Total score.

The assumptions required to conduct a multiple regression are outlined in Table 18. Although the majority of the assumptions were met, including independence of errors and no perfect multi-collinearity. An analysis of the assumptions suggests that errors are not normally distributed and data from two participants may have undue influence on model. This is shown as the score for these participants was more than three times the average centred leverage value (0.35 compared to average of 0.10). However, this does not justify removing the case/s but it might mean regression models are less able to generalise to the wider population (Field, 2009).

Table 18.

Test of Multiple Regression Assumptions for Gender and Ethnicity as predictors of the BADS

Assumption		Test	Results
1. All predictor variables are quantitative or dichotomous with no zero variance			Both ethnicity and gender are dichotomous
2. Normally distributed errors	*i.*	Shapiro-Wilks test of Standardised Residuals	*W*=.85, *p*=.005 So distribution cannot be assumed to be normal
3. Homogeneity of variance			No funnel shape
	ii.	Visual analysis of scatterplot of residuals	No obvious curve shape
4. Linearity			Figure 8
5. Independence of errors	*iii.*	Durbin-Watson Statistic Significant if below 1 or above 3 (Field, 2009)	1.62, *ns*
6. No multi-collinearity	*iv.*	Correlation between gender and ethnicity Significant if *r* above .80 or .90 (Field, 2009)	*r* = .55 *p*=.007, *ns*
	v.	Variance Inflation Factor (VIF) Significant if above 10 or below 1 (Bowerman & O'Connell, 1990)	Average *VIF* = 1.42, *ns*
	vi.	Tolerance Significant if below 0.20 (Menard, 1995)	Tolerance 0.70, *ns*
7. No outliers	*vii.*	Cook's Distance Significant is greater than 1 (Cook & Weisberg, 1982)	One data point 1.59 (range 0.03 – 0.73)
	viii.	Mahalanobis distance for small samples with two predictors Significant if above 11 (Barnett & Lewis, 1978)	No Mahalanobis distance >11 (range 0.55 – 6.65)
	ix.	DFBeta should be within ±1 (Field, 2009)	Two data points have DFBeta outside of ±1

Note. DFBeta=difference between a parameter estimated using all cases and estimated when one case is excluded

BADS Standard Score
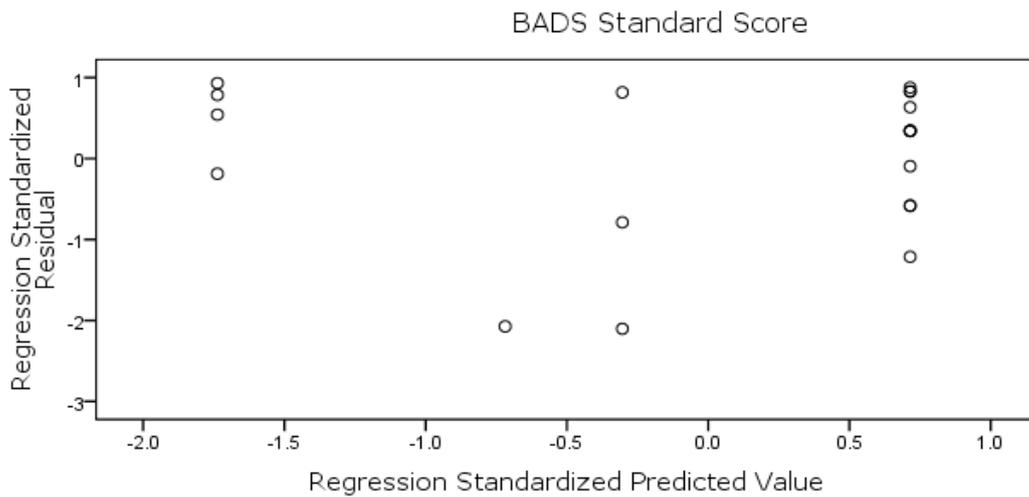
Figure 8. Scatterplot of Residuals

Results of the multiple regression are reported in Table 19. The regression model was statistically significant ($F2,17 = 3.950$, $p=.039$) and R^2 was 0.27, so the model accounted for 27% of the variance in BADS Total standard scores. Despite this model being significant neither predictor was individually statistically significant. This may be because the variables are associated with each other, although there was not perfect multicollinearity.

Table 19.

Results of Multiple Regression

	B	SE B	Beta	t
Step 1				
Ethnicity	-27.60	10.74	-0.52	-2.57* (p=.02)
Step 2				
Ethnicity	-19.35	12.66	-0.36	-1.53 (p=.15)
Gender	-13.75	11.50	-0.28	-1.20 (p=.25)

Note. R^2 = 0.27 for Step 1, R^2 change = 0.06 * p<.05

Missing Data Analysis

There were several data points that were missing for a variety of reasons:

- Unreturned or incomplete medical note proforma (7 data-points)
- Unreturned DEX-O (3 data-points)

This amounted to 10 data points, or 1% of the entire data set. The missing data is described in Table 20.

Table 20.

Characteristics of missing data

Characteristic	Number of missing values (%)	n included in analysis
Time since diagnosis	2 (10)	18
CDC Classification	1 (5)	19
Medication Regime	1 (5)	19
Length of Medication Regime	1 (5)	19
DEX-O	3 (15)	17

Note. CDC=Center for Disease Classification; DEX-O=Dysexecutive Questionnaire-Other Report

An independent *t*-test was conducted to determine if there was a significant difference between performance on the BADS for those who had some missing data (n=5) and those who did not (n=15). On average, participants with no missing data scored more highly on the BADS (*M* = 88.21, *SE* = 5.93) than those who did have missing data (*M* = 73.80, *SD* = 12.63). Equal variances can be assumed as Levene's test was not significant (*p*=.96). This difference between groups was not found to be statistically significant *t*(17) = 1.17, *p*=.26, *r*=.28. This shows that on the main measure there was no difference between those who had missing data and those who did not.

Extended Discussion

This section provides a supplementary interpretation of the study findings within the context of previous empirical research and theoretical background. A critical consideration of the strengths and limitations of this study and how this might inform future research is presented before discussing the clinical and everyday implications of these findings. Finally, reflections on the scientific, theoretical and ethical issues raised by this research are briefly discussed.

Aim One

- Explore executive function in people with HIV-infection using the BADS relative to published norms (Wilson et al., 1996).

The results show a proportion of people with HIV may have difficulties with executive functions, in that they are less able to create models of self-directed action (Jurado & Rosselli, 2007). This finding converges with the limited previous research which specifically assessed executive functions in people with HIV using the CANTAB (Sahakian et al., 1996), Stroop (Hinkin et al., 1999) and IGT (Hardy et al., 2006). This also corresponds to previous findings where impaired executive functions are a central feature in the prototypical cognitive profile in people with HIV, even from early in the course of infection (Dawes et al., 2008). The current study adds a unique contribution to the research literature in the post-HAART era by considering a neuropsychological battery with good ecological validity to measure executive functions. Furthermore, this is the first study since the introduction of HAART to provisionally break down an executive function battery into dissociable skills particularly affected in people with HIV, moving the research forward as suggested by recent reviews (Woods et al., 2009). This finding is also compatible with reports showing problems with executive functioning using the BADS in other populations including individuals with psychosis (Jovanovski et al., 2007) as well as other neurodegenerative diseases such as Parkinson's Disease (Kamei et al., 2008).

These findings support the clinical utility of the BADS as a measure of executive function above the global cognitive assessment advocated by Butters et al. (1990) or traditional tests such as the TMT or Stroop. This research thereby overcomes a significant limitation of previous research by assessing executive functions on a continuum rather than dichotomously determining whether individuals have/do not have global cognitive impairment.

Dissociable Executive Function Skills

The significant impairments shown by participants in the sample on the Zoo Map subtest may point to its utility and sensitivity for people with HIV and be useful in determining where to target interventions. This finding parallels research with men with chronic problem alcohol use (Moriyama et al., 2002) who also found the Zoo Map to be the most useful. On the other hand, the current finding diverges from research with adults with brain injury, where the Action Program and Modified Six Elements Test were reported as the most useful BADS subtests (Bennett et al., 2005). However, it is possible the Zoo Map is overly inclusive and results in false positive results (Type I errors) although this is unlikely as the BADS subtest is normally found to make Type II errors (Manchester et al., 2004).

It is useful to embed performance on measures of executive function within the theoretical models of executive functions. The pattern of performance on the BADS subtests in this sample does not support a unitary model of executive functions. In unitary models, such as the SAS (Norman & Shallice, 1980), executive functions are seen as underpinning and regulating response to novel and complex tasks. However, these results show that the least affected subtest was the novel task – the Action Program. Instead this study's findings support a fractionated model of executive function with different dissociable skills (e.g. Stuss & Alexander, 2007). This would further support the use of a battery approach to assess executive functions, rather than using traditional tests which only provide information on one single aspect of the executive function concept (Boone et al. 1998).

Considering the Stuss and Alexander (2007) proposed executive function sub-systems: energisation (initiating and sustaining responses), task setting (planning, choosing an appropriate plan and suppressing salient responses) and monitoring (checking the task over time) the results in this study suggest self-monitoring and task-setting were disproportionately affected in people with HIV in this sample, with relatively preserved energisation as evidence by their preserved performance on the Action Program. The pattern of subtest performance suggests involvement of orbito-frontal and dorso-lateral region brain areas (associated with monitoring and task-setting respectively) (Malloy et al., 1993; Bamdad et al., 2003); with the ventro-medial region (associated with energisation) (Stuss & Levine, 2002), largely spared. However, there are differing theoretical configurations of the executive functions systems (e.g. Fisk & Sharp, 2004) and there are significant overlaps between these executive function systems which can be seen both theoretically and in associated brain areas.

However, it may the BADS is actually not be sensitive the energisation subsystem, for example, initiation and apathy (Burgess et al., 1998). This may be, in part, due to the office-based testing environment required for administration of the BADS where the examiner taking the role of the initiator, providing rules, goals and prompts (Stuss & Alexander, 2000).

Aim Two

- To triangulate quantitative measurement of executive deficits on the BADS to self- and proxy-report questionnaires on day-to-day experience of executive functioning (DEX)

There was no statistically significant relationship between the BADS and the DEX-S which suggests limited insight as participants were no better than chance at predicting their executive function performance. This might be supplemented by the only subtest correlation which even approached significance with the DEX-S (Action Program) was in the positive direction – so people who had more executive function problems as suggested by the BADS reported fewer problems indicative of limited insight (Hart et al.,

2005). Although it is important to remember that this correlation only approached significance.

However, this lack of association between cognitive performance and self-report may be attributed to fluctuating medical status, leading to discrepant self-report and cognitive performance (Lovejoy & Suhr, 2009). However, the exclusion criteria for the study controlled for this variable, so limitations in participants' insight are a more probable explanation for this finding.

The close approach of significance in the inverse relationship between the BADS and DEX-O, where high scores on the DEX and low scores on the BADS represent more executive function difficulties, reflect similar appraisals of the participants' executive functions. Professionals' scores on the DEX-O were significantly higher than ratings from friends or family. This finding is in keeping with Fordyce and Roueche (1986) who found family and friends provided an under-estimate of participants' abilities compared to professionals. There may also be effects of differing interpretations by different raters on the DEX items as suggested by Chan and Bode (2008). Chan and Bode (2008) used a Rasch analysis in 92 patients to identify that patients and proxies disagreed on interpretation of items on the DEX, such as unconcern for social rules, distractibility, decision making, emotional regulation problems such as aggression and euphoria. It is not possible to make conclusions based on this as participants had only *either* professionals *or* family/friend to act as a proxy on the DEX. Participants who had more executive function problems may have either had fewer friends/family to complete the measure or felt uncomfortable asking friends/family.

The DEX-O was not significantly associated with any of the BADS subtests with correlations ranging from .01 to -.38. This is considerably lower than the correlations (-.31 to -.46) reported by Wilson et al. (1998). However, the negative correlations that approach significance between the DEX-O and Action Program and Card Sort in the current study suggests proxies more accurately report participants' responses to novel complex tasks, set-shifting and flexibility. Interestingly, these two subtests were the subtests on which participants performed best. These particular executive skills may

be more externally observable than others. This is supported by the finding that participants who had difficulties in the Action Program were more likely to have been referred by a professional rather than self-referral. This is despite participants themselves being less able to accurately report performance on this subtest. Perceptions of skills on novel tasks seem to be the point where self- and other- report conflict, where proxies report more accurately map onto BADS performance. Alternatively, the finding in relation to insight may represent proxies did not know the participants sufficiently well to accurately determine the impact of executive function ability in everyday life. However, this is unlikely as participants chose the proxy themselves.

The convergence of the DEX-O and BADS scores, compared to the DEX-S represents triangulation which suggests the DEX-O and BADS measures more closely represent how participants use their skills in social situations. Even if the individual is not experiencing the difficulties, the DEX-O demonstrates how their behaviour is being interpreted in social situations, which may well influence their social interactions. As assessment of executive functions presents a particular challenge for neuropsychologists, this finding supports the use of the BADS to assess executive functions, supplemented particularly by proxy report to triangulate the relative impact for individuals.

This study's findings significantly add to the evidence base by focusing on the functional outcomes of executive function for people with HIV, reflecting the predominance of day-to-day management issues (Melrose et al., 2008). This study begins to consider the behavioural consequences and activities of daily living associated with executive functions which are a defining feature of cognitive impairment in people with HIV. The findings of this study suggest the importance of assessing not just basic activities of daily living but behaviour associated with executive functions and abilities in social interactions, similar to Katz et al. (2007). By exploring these functional outcomes this study adds to the evidence base by using the WHO-ICF conceptualisation of an individual within their environment. This model, as

presented in Table 21, can be used to represent some of the difficulties an individual with HIV and executive function difficulties may have.

Table 21.

HIV understood within the WHO-ICF framework

Health condition	Impairment	Activity Limitation	Participation Restriction
	Problem with body function, structure, deviation or loss	Difficulties an individual has executing an activity	Problems experienced in involvement in life situations
HIV	Compromised immune system, reduced cognitive and executive function	Less capable of socially appropriate behaviour	People's reactions leading to fewer social relationships

Note. WHO-ICF=World Health Organisation-International Classification of Functioning

Aim Three

- To explore risk factors that might contribute to expression of executive deficits in people with HIV.

Medical factors:

CD_4 Count

The findings of this study that CD_4 count did not have an effect on BADS performance are in line with Reger et al. (2005) who found CD_4 count could not predict neuropsychological impairment. However, this does not reflect previous longitudinal studies, such as Childs et al. (1999), who found that a CD_4 count of less than 200 cells per mm^3 was a moderate risk for HAD. However, Childs et al. (1999) reported on research with participants prior to the introduction of HAART and was primarily concerned with the development of HAD rather than mild-moderate cognitive difficulties. The

current study adds to the evidence base as it offers specific information on the executive function cognitive domain. It seems that in the changing context of HIV treatment, the immuno-variables traditionally used to predict cognitive decline are less useful. This has implications for the use of traditional classification systems as well, which are strongly based on CD_4 level, as they may no longer be appropriate.

Plasma Viral Load

It was not possible to determine the relative impact of viral load to executive function in this sample as 85% of the sample had undetectable viral load levels. On the other hand, this strongly suggests that executive function difficulties can occur even in the context of maximum viral suppression; thus supporting other research which has found that cognitive impairment had no relationship with viral load (Ellis et al., 1997; Hammer et al., 1997; Reger et al., 2005;). For example, Cysique et al. (2006) found individuals with HIV continued to show cognitive decline despite undetectable viral load. However, the current sample had an even higher proportion of participants in the below average range (35-50%) compared to only 8-34% in Cysique et al. (2006).

Time since HIV-diagnosis

Time since HIV diagnosis was not related to BADS overall performance in this study. This does not correspond to previous research that participants living with the HIV infection for longer would have compounded neurological problems (Bhaskaran et al., 2008; Brew et al., 2009). However, there was a statistically significant positive association between the Action Program and duration of diagnosis. The direction of this relationship suggests participants who lived with the infection for longer performed better, possibly indicative of the development of specific compensation strategies to approach novel tasks. The Action Program subtest also approaches significance with the DEX-S, where participants who performed well on the Action Program, reported more problems on the DEX-S, and compensation may help explain this provisional relationship. Participants may consciously employ compensation strategies when they approach a novel task, however, the

subtest score does not measure this increased effort. On the other hand, compensation may not be a conscious process. Melrose et al. (2008) found people who had stable frontal lesions had increased activation in the parietal lobes on traditional executive function tests. However, it is important to bear in mind that time since diagnosis is not a conclusive measure as someone may have been living with the infection for an unspecified period of time before diagnosis.

Stage of Infection

The finding that the stage of HIV-infection was not associated with BADS performance does not sustain the vast majority of research findings (e.g. Grant et al., 1999), which found that cognitive impairment increased with disease progression. CDC stage was, however, statistically significantly positively associated with the Key Search task, which suggests, as above that there may be the development of some compensation strategies in the symptomatic/AIDS stages of infection. However, this may be related to the changing context of HIV treatment and utility of immuno-variables to predict cognitive decline as described above. It may be that CDC is no longer a useful or sensitive tool to describe the fluctuating and variable course of HIV with the modern treatment.

HAART

Medication regime was not associated with BADS overall performance. HAART may not improve the subtler cognitive functions in the same way it reduces the likelihood of HAD (Gibbie et al., 2006). There is some evidence to suggest there was a specific neurological detrimental effect as participants on HAART regimes for longer, performed statistically significantly worse on the Key Search subtest. This finding agrees with Starace et al. (2002), who also found individuals on HAART regimens to be more likely to have cognitive impairments than those not taking HAART. However, this finding may be due to prescribing procedures of HAART, with more medications prescribed pre-emptively because they were experiencing cognitive difficulties. There were also some potential benefits of medication on the Card Sort subtest, particularly mental flexibility, although

importantly this association only approached significance. This might suggest that similar to cognitive functions in general, HAART has non-uniform affect across the executive functions (Cysique, Maruff & Brew, 2004a). Subsequently, this research adds to the evidence base by confirming the necessity of using a battery approach with ecological validity, rather than individual traditional tests, to assess executive functions in HIV.

Demographic Factors:

Age

The lack of association between BADS performance and age does not replicate previous research which suggested older age had a negative effect on neuropsychological performance, especially on novel tasks that require faster speed of processing (Grant, 2008). Valcour et al. (2004) found individuals with HIV aged over 50 had a higher prevalence of cognitive problems than those with HIV younger than 50. However, the finding of the present study is in keeping with Sevigny et al. (2004) who also found no effect of age of neuropsychological performance. However, the lack of association with age in the current study might be expected as the majority of the sample included were under 50 years old (*SD*=8.26).

In fact, the Key Search subtest was significantly positively associated with age so older participants tended to perform better. As with medical characteristics, this suggests older participants developed compensation strategies and tasks such as the Key Search are amenable to compensation strategies. However, it may be generational differences affect approaches to planning tasks resulting in improved performance in older participants, not necessarily an improvement in participant executive function ability over time.

Gender

This study found a strong effect of gender on the BADS, where male participants achieved higher scores on each of the BADS subtests compared to female participants. Unlike Failde-Garrido et al. (2008), this gender difference in executive functions could not be accounted for by differences

in pre-morbid IQ, alcohol use or years of education. However, women were less likely to be taking HAART medication than men, which may have negatively influenced performance. It may have been medication was not indicated for the women in the sample, or that they chose not to take medication. However, there were no significant differences between men and women on CD_4 status as an immune variable, the mechanism of HAART, so the differences between men and women are not directly attributable to difference in medication.

Moreover, although gender was strongly correlated with the BADS total score, gender was only significantly associated with the Key Search subtest, although statistical significance was approached with the Action Program and Zoo Map tests. These subtests, particularly the Key Search and Action Program are the subtests which have potentially been associated with development of compensation strategies as age and disease progress. This could suggest that women are less able to develop these compensation strategies, leading to the discrepancy between male and female performance in this sample. However, this may instead be due to pre-existing structural or functional differences between male and female brains (Melrose et al., 2008).

However, neither self- nor other-report on the DEX was associated with gender. Women may be more likely to experience executive function difficulties and so are more likely to have limited insight into their difficulties and report them at levels similar to the men in the study or the non-clinical population (Hart et al., 2005). This is supported by the specific findings in the DEX, in relation to Aim Two. On the other hand, everyday problems may not be reported because executive function impairment do not cause significant problems in everyday life for the participants in this sample as their environments are low demand.

In a multiple regression analysis, gender only accounted for 6% of the variance in BADS score and was not a significant individual predictor. This might suggest that the differences in ethnicity were more significant, and differences in gender may in part be attributable to the 71% of the female

participants who were Black African/Caribbean. This study points to the value of considering cognitive domains individually to consider gender differences.

Ethnicity

The finding of cultural difference on the BADS supports the work of Proctor and Zhang (2007) who also found participants from non-White backgrounds performed worse on the BADS. In particular, Black African/Caribbean participants in the current study performed statistically significantly less well on the Action Program, Key Search and Zoo Map subtests. This is in line with Proctor and Zhang (2007) research, which reported that Latin and African American participants performed worse on the Zoo Map subtest. However, ethnicity only accounted for 27% of the variance in the BADS total score and when gender was included in the regression model, although the model was statistically significant, neither gender, nor ethnicity were significant individual predictors. This suggests that there is some combined effect, although these results cannot be generalised to the wider population due to a number of influential 'cases' violating the outlier assumption.

These differences in BADS performance based on ethnicity may be due to genetically different subtypes of HIV-1. The different genetic subtypes of HIV-1 have a subtle influence on medication resistance so it is conceivable that they influence development and patterns of cognitive difficulties. However, Proctor and Zhang (2007) found cultural differences on measures of executive function in the non-clinical sample, which indicates that genetic variations in the strains of HIV-1 is not sufficient to explain these differences.

There may still be different risk factors in people from BME backgrounds, similar to those between men and women (Rivera Mindt et al., 2008). For example, there may be differences in access to education (Kaufman, Cooper & McGee, 1997), acculturation (Lucas, 1998) or literacy (Manly, Touradji, Tang & Stern, 2003). Socio-economic status may also restrict access to services such as healthcare, and influence brain development (Brickman

Cabo & Manly, 2006). However, the current study did not find differences in executive function between ethnic groups could be accounted for by premorbid IQ, years of education or differences in language ability. However, there may have been other risk factors not accounted for by the current study, which mediate performance on the effects of ethnicity on the BADS. Alternatively this finding may be accounted for through inherent limitations of the BADS.

Cognitive, Behavioural and Emotional Factors:

Drug & Problem Alcohol Use

The lack of effect of alcohol use with the BADS performance does not agree with previous research finding the negative impact of problem alcohol use on cognitive and executive function (Schulte et al, 2005). However, the lack of any report of problems or hazardous drinking in the study sample is clearly lower than the 29-60% rates of problem drinking in people with HIV predicted from previous research (Meyerhoff, 2001). The average alcohol use of the sample was only two units/month; which does not equate to problem drinking. Therefore, alcohol use within the normal range in people with HIV does not seem to affect neuropsychological functioning. However, it is important to remember that this was based on self-report so alcohol use may have been under-reported due to social desirability. It was also not possible to consider the impact of co-morbid drug use on executive functions in HIV as only extremely low levels of drug use were recorded by participants, which might reflect social desirability or fears over legal consequences, despite reassurances over confidentiality.

Depression

The lack of association between depression and the BADS in this sample, bearing in mind that by virtue of the exclusion criteria, none of the participants were experiencing current severe depression, supports previous research which suggests that those in the non-clinical range for depression (i.e. diagnosable with a current major depression disorder) do not have increased executive function impairment (Gibbie et al., 2006). This was also

reflected in the lack of association between self- and other-report and levels of depression. This adds to the evidence base exploring non-clinical levels of low mood in people with HIV in a dimensional rather than categorical way. However, there is scope for further research to examine the relationship between more clinical levels of depression and HIV when considering executive function replicating the work of Westheide et al. (2007).

Anxiety

The lack of general association between anxiety and the BADS in this sample supports Hoffman and Al'Absi (2004) who suggested that anxiety does not have an effect on neuropsychological performance. However, other authors have suggested that the effects of anxiety are cumulative (Kizilbash, Vanderploeg & Curtiss, 2002). Moreover, like depression, on average participants did not score within the clinical range for anxiety and were not diagnosable with anxiety disorder. Anxiety at this level may not be expected to influence performance on the BADS.

Those participants with high levels of anxiety did perform statistically significantly less well on the modified Six Elements subtest as compared to those with lower levels of anxiety. As participants scores on average did not fall within the clinical range, this suggests that even low levels of anxiety may affect ability to multi-task, sequence and plan which supports previous research on the detrimental effects of anxiety (Kizilbash et al., 2002) but only to specific executive function processes. On the other hand, it is commonly acknowledged that the modified Six Elements Test is the least structured on the BADS (Manchester et al., 2004), allowing for the greatest comparison to everyday behaviour, so this association may be more generalisable to other executive function skills in the everyday world. However, as correlation cannot suggest causality, it may be that problems with multi-tasking in everyday life cause more anxiety. Although this is less likely to be the case as executive function difficulties are associated with impaired insight as described above.

Anxiety might also be a product of disease progression as high levels of anxiety were significantly associated with later CDC stages. However, it is not possible to determine whether disease progression contributes to increased anxiety, with increasing levels of uncertainty and hypervigilance, or whether high levels of stress hormones are implicated in additive effects of insult to the brain (Kopinsky et al., 2007).

Level of Education & Pre-morbid IQ

The finding that the BADS score was not associated with years of education or pre-morbid IQ does not agree with the findings of DeRonchi et al. (2002) or Basso and Bornstein (2000). These authors suggested cognitive impairment is mediated by pre-morbid ability and cognitive reserve in people with HIV. However, the current study directly and specifically considers executive functions rather than global cognitive functioning. Pre-morbid functioning may have less of a protective/buffering role in the development of executive function difficulties. Indeed, the significant difference between the standard score on the WTAR and BADS lends further support to the concept of executive function as distinct from generalised intelligence (Burgess et al., 1998).

There might be some differential effects of education and 'cognitive reserve' ability on more specific executive function skills: those with higher pre-morbid IQ performed statistically significantly better on the Card Sort subtask, however, those with fewer years of education performed better on the Action Program task, although this latter finding only approached significance. This might suggest that cognitive reserve has different benefits for different subtests. Anecdotally, the participants with more education seemed to 'over-think' their approach to novel tasks, perceiving the task as more complex than it was, anticipating some 'trick', whereas participants with fewer years of education approached the task in a more direct way. This ties in with the findings on compensation, and participants may be more consciously trying to apply a strategy to solve the task. Although it only closely approached significance the finding in relation to the Card Sort

was in the expected direction, suggesting that for tasks requiring mental flexibility, cognitive reserve did benefit for participants' performance.

Summary

As well as factors related to BADS overall performance, there are dissociable experiences of executive function skills by considering the BADS subtest analysis. This suggests that there is a dissociable fractionated executive function system, such as that suggested by Stuss and Alexander (2000) underlying the BADS, although at present this is hard to define. In people with HIV it might be the task-shifting and monitoring systems which are most affected as measured by the Zoo Map. In particular the Action Program subtest seems to provide valuable information on compensation and insight. Approaches and strategies to solve novel tasks are likely to be the most observable executive function characteristic. However, these compensation strategies seem to be limited to specific executive function skills and some participants may be less able to develop this compensation.

Overall, using the BADS as a battery measure has been shown to be useful. On the two dimensions of ecological validity: verisimilitude and veridicality, the BADS clearly shows greater verisimilitude than traditional measures in that it relates well to everyday activities on face validity. In terms of veridicality, this study has shown that the BADS approaches significant associations with the DEX-O. Although this association is not the extent found in previous research and does not quite reach statistical significance, this may confer a degree of veridicality to the BADS in this sample.

Strengths and Limitations

As the study sample is small these findings point to trends and patterns in the sample, rather than conclusions. The study sample also differed significantly from the regional population of people, in terms of proportional representation of age and ethnic groups. Therefore, generalisations of the findings to the wider population of people with HIV need to be considered with caution. However, the approximate representative proportion of gender is a strength of the study, as only 31% of studies with people with HIV include this approximate parity (Maki & Martin-Thornmeyer, 2009).

Furthermore, the broad inclusion and exclusion criteria attempt to recruit a sample more representative and less elitist of people living with HIV. However, the size of the sample limited the ability to analyse some of the variables. Several variables with discrete categories had to be collapsed together to allow for large enough sample sizes to be included in the analysis. This is not ideal and does not necessarily allow for fine-grained analysis of the results. Moreover, although effort was made to club items together logically and according to prior research and theory, there might have been alternative ways of combining this data which could have lead to different outcomes.

The recruitment methods attempted to be inclusive. However, there may be people with HIV who do not regularly access NHS or charitable services, and hence were not able to participate in the study. These may be participants who are able to work and effectively use their executive functions, which might bias the sample. However, it might equally be that the unsampled population experienced more problems with executive functions, and were unable to plan or organise sufficiently to attend appointments. Additionally, although the inclusivity of the sample can be seen as a strength, it also introduces heterogeneity into the sample, which means the internal validity of the study may be compromised.

As a small and hard-to-access population, people with HIV often participate in many research studies, possibly including neuropsychological research. This might influence expectations of the assessment procedure and outcomes. This was not controlled for through the exclusion criteria however, because no research has been conducted looking directly at executive functions in people with HIV using a measure with good ecological validity. No participants had previously completed the measures involved in this study so practice effects should not have influenced the results.

In referrals from professionals participants who reported more problems were more likely to be referred to the study, which might suggest that people participating in the study had pre-existing concerns about their cognitive status. However, this finding was not replicated by participants

who self-referred to the study, who made up the bulk of the participants. Further self-report of problems was actually negatively associated with BADS performance, although not statistically significant this points towards potential lack of insight in people with executive function difficulties. This would suggest the bias resulting from participants who took part due to pre-existing concerns may have only minimally affected the results.

A matched control group is often recommended in this methodology. Matching is a highly controversial issue as outlined by the contrast between the positive praise supporting its use by some authors (Pike, Hill & Smith, 1980) and strong refute by others (Howe & Choi, 1983). Matching does seem intuitively helpful to reduce the impact of confounding variables (Gefeller et al., 1998). However, there is significant controversy on matched control group selection, particularly the number of factors to match for (Wacholder et al., 1992) as over-matching (matching participants on many variables) can actually increase bias (Fletcher, 1997). All of the variables included in the correlational analysis could be considered as variables to match for, although this would be nearly impossible. The defining feature of a case-control is the recruitment of a sample with a particular characteristic compared to a sample without that characteristic. Previous research in people with HIV has used a variety of control groups, including people with HIV with no neuropsychological impairment, people who have been tested for HIV but had a negative result and people from other neurological populations, people from the non-clinical population. However, there is no obvious control group.

The inclusion of a traditional measure of executive function, such as the WCST, has often been used in previous studies to provide a supplementary analysis on which measure suggests more difficulties. This could have provided a more in-depth analysis and allowed more explorations of the utility of the BADS as a useful measure in people with HIV. However, a traditional measure was not included as there is already a significant evidence base to suggest the movement of neuropsychological assessment towards ecological validity (e.g. Jovanovski et al., 2007; Norris & Tate; 2000, Evans et al., 1997). Moreover, determining the ecological validity of

the BADS was not the aim of the present study, but the BADS was used for its validity in this area. This methodology is also consistent with maintaining the reflection of neuropsychologists working in the field, who often do not have time to complete several different measures of the same cognitive construct but opt for the most appropriate, based on the research evidence.

However, it is important to acknowledge and be aware of the limitations of the BADS and other measures used. As already mentioned above there are questions over the cultural validity and cultural equivalence of measures such as the BADS in non-White populations (Brickman et al., 2006). However, despite the growing research and commentary on this, there is currently no consensus as to how this should be approached, other than to consider the clients' ethnicity when interpreting their results and interpret with caution the results of people from different cultural backgrounds when measured on standardised measures like the BADS. This is further complicated by the significant lack of information provided about the normative sample provided in the BADS manual.

However, there may be inherent limitations of the BADS as 'eurocentric' as it was developed and normed in the UK, with European values and standards and with White participants who have been socialised with these values and standards (Helms, 1992). These standards and values may not apply to other cultural experiences. The BADS manual or related published articles do not comment on or provide any descriptive statistics for the ethnic diversity of their normative sample. Therefore, it is not possible to determine the cultural validity of the BADS and whether comparison with the normative data is appropriate for these participants. Normative data allows neuropsychologists to compare individual performance to a wider non-clinical sample to identify whether scores are comparable or not (Brickman et al., 2006). The BADS norms are useful as they were relatively recently created, included a large sample and stratified for age, education and sex (Brickman et al., 2006). The demographic similarities of the normative sample and the individual are crucial to increase validity of this inference. On this basis several authors have argued for race-specific norms

to increase the accuracy for individuals from non-White backgrounds (Lucas et al., 2005). However, race-specific normative data does not consider the cultural validity of these tests. Moreover, race-specific norms suggest that everyone from the same racial background has the same cultural experience which is not always the case (Brickman et al., 2006). Finally, given the number of different ethnic groups it is not possible to create specific normative data for each group and creates a conflict where there is dual heritage. Knowing someone's ethnic background does not measure level of acculturation or the level of socialisation they have had with the concepts behind the BADS (Helms, 1992).

This study only breaks ethnicity down into White British or Black African/Caribbean. There are other ethnic groups which were not accounted for in this research. Moreover, although not possible for the purposes of statistical analysis, the Black African/Caribbean group could be further sub-divided into regional and national differences.

Although the BADS has been shown to have good ecological validity, it is still an office-based test. Office-based tests have been criticised for creating an artificial environment. It is not often people have a quite distraction-free space with a non-judgemental examiner to explain the task and rules, to try and solve novel, complex and challenging problems with no long term consequences attached to them (Manchester et al., 2004). However, more observational measures such as the Multiple Errands Test are time-consuming and require high levels of physical ability and confidence from participants. Taking this into consideration the BADS seems like a viable alternative to the MET, being shorter and less physically demanding than the MET. Furthermore, the BADS does include a modified version of the Six Elements Test which is based on the same principles, so similar information should be gathered. Indeed the findings point towards some of the anxiety that administering the MET might cause.

The BADS, although allowing for some subtest analysis, requires further clarification of what each subtest is measuring and it is important to

acknowledge that the Total profile standard score might mask more specific difficulties as can be seen by the analyses in this study. The BADS also does not provide information on error analysis or strategies used to solve problems and their relative success. This information is invaluable as this could lead to the development of rehabilitation programs and strategies.

One of the strengths of this study is the maintenance of executive functions on a continuous rather than dichotomised (impaired/not impaired) scale. Furthermore, the present study includes a functional assessment of the everyday impact of executive function in the lives of people with HIV. This is in line with the WHO-ICF suggesting the importance of the person in a social and political context. This should be a regular feature of research in people with HIV and cognitive difficulties as the everyday impact is a major diagnostic feature. However, this study did not include a measure of individual environmental demands. This represents more than functional assessment, including an assessment of the demands an environment places on individuals. For example, for people on HAART, the complexity of the regime may place significant burden on individuals, and necessitate executive functions to plan and manage. In this context executive function difficulties are of large importance.

As there is no normative data available for the DEX it is difficult to determine whether participants' scores were what would be expected in the non-clinical population. On the other hand, this approach preserved the dimensional nature of the DEX, moving away from arbitrary categorisation of impaired/not impaired. In spite of this Likert scales, as used in the DEX still describe behaviour in narrow and absolute terms (Alderman, 2001).

There is also a question over the development of the circular validity of the BADS and DEX. Both measures have been used to validate each other: correlation with the BADS has validated the DEX as a functional measure of executive functions and correlation with the DEX has validated the BADS as a cognitive assessment tool with good ecological validity. Therefore, comparison between different subjective measure and the

BADS and different cognitive measures with the DEX is needed to confer greater validity and utility of thee measures.

Measures such as the WTAR, which focus solely on pronunciation, may not have given an accurate assessment of pre-morbid IQ, especially as with relatively high numbers of people for whom English was not a first language, it may have been appropriate to use an alternative measure such as the Spot-the-Word test. Although this is a factor to consider in future research statistically there was no difference between participants of different ethnic background on the WTAR in this study. Many researchers have suggested that when participants are being assessed in a language outside their first language, even if they are fluent, there will be a time lag in performance. As several of the BADS subtests include a measure of speed to determine the raw score, this may have had an effect on performance. However, it is unlikely that this is the sole factor associated with performance on the BADS as ethnicity was associated with performance on subtests that did not include timing in the raw score, for example, the Action Program subtest.

Other cognitive abilities, such as memory, may have had an effect on cognitive test performance. This might lead to the results being attributed to difficulties with executive function when in fact the difficulties were with memory. However, the BADS has been specifically designed to reduce load on memory and all written instructions for each subtest are placed in front of the participant throughout the subtest. Results may also be attributed to lack of sufficient effort, and secondary gains a participant may get through a poor neurocognitive performance, which could have been controlled for through the use of a brief test of 'effort' such as the Rey Fifteen Item Test (Rey-FIT). However, there were no obvious incentives for participants for a poor performance, as results did not inform medication prescription, legal cases or other variables often associated with insufficient effort in neuropsychological performance.

Other demographic variable information could have been collected such as family history of psychopathology, and socio-economic status which some

recent research has suggested may have an influence on neuropsychological ability (Brickman et al., 2006). More medical information could also have been collected such as specific antiretroviral medications used in each HAART combination. This could explore the neuroactivity of these medications in relation specifically to executive functions. However, in such a small sample this would unlikely have yielded enough similarities to conduct an analysis. Information on medication adherence was also not collected in this study. Poor medication adherence may account for the lack of effect of HAART on BADS performance. However, the vast majority of the sample had undetectable viral load levels, maximal viral suppression and length of the medication regime was associated with an improved CD_4 count which suggests that HAART improved CD_4 count over time, which is the mechanism through which HAART claims to work. So even if medication adherence was low the medical status is what would be expected for someone with good adherence to medication.

However, there would always be more information which could be collected and the researcher has to decide for themselves which appear to be the most important and valuable factors from previous research. In-line with the epistemological stance taken in this study, the variables chosen to be measured will inevitably be influenced by the researcher's interpretation.

Future Research Directions

As a pilot study there are several patterns that have been identified which would warrant further research. Future research should concentrate on trying to resolve these limitations of the current study and previous research. Recruitment should take place from a variety of sectors, possibly including culturally and gender sensitive charitable organisations. This should aim to recruit samples that are representatively diverse in terms of ethnicity and sexual orientation in an attempt to avoid selection bias and broaden the scope and applicability of the findings. A larger sample would allow for more analysis between diagnostic and severity groups as well as

testing the similarity of underlying constructs being measured. A longitudinal study would be useful ideally recruiting participants from a wider regional area, with a variety of severity presentations screening for executive function difficulties soon after initial positive HIV diagnosis and repeating this assessment over time. This might help to make sense of within-person fluctuations and individual variability over neuropsychological performance (Salthouse, 2007) and determine the long-term effects and implications of executive functions difficulties in people with HIV.

It might be useful to recruit a HIV-negative control sample. However, care needs to be taken over how a control group is recruited and the factors that participants are matched on. For example, previous research has suggested little statistical benefit in matching for more than four variables (Woodward, 1999; Ury, 1975). It would also be important to carry out a measure of exposure in both people with HIV and controls to improve validity of using a matched control group (Fletcher, 1997).

Future research should aim to move away from global cognitive assessments as suggested by Butters et al. (1990) and away from traditional measures capturing only one aspect of the executive functions. In place of this, measures with better ecological validity (verisimilitude and veridicality) could relate neuropsychological performance more directly to everyday experience of individuals. Using a measure with ecological validity has been shown to be superior to traditional laboratory measures as it allows for closer comparison to everyday experiences. However, future research should focus on the subtest analysis and the underlying executive function skills that these represent. This is especially important in the knowledge and findings of this research that overall scores may mask specific patterns of difficulties or strengths for individuals. Furthermore, moving away from overall scores may uncover the mask of increased effort (Bennett et al., 2005).

Increased focus on ecological validity would entail future research considering activities of daily living associated with executive function, moving away from categorical generic dichotomous functional outcomes,

such as employment status. The suggestion of compensation strategies in this study further points to the validity of using a measure with good ecological validity which aims to assess the participants within their context, what they do day-to-day rather than what they do in an ideal environment, as measured by traditional tests. Examining these behavioural consequences in future research should also include development of methods of assessment of environmental demands for individuals (Chaytor et al., 2006). Especially, as some participants may hold cognitive demanding occupations or have to adhere to cognitive demanding medication regimes, more subtle executive function deficits in early HIV-infection may have a large impact (Knippels et al., 2002).

The relationship between the BADS and DEX and the complex issue of insight when considering the everyday impact of people with HIV also merits further research attention. This might compare these quantitative measures to more qualitative interview approaches with both the individual and 'others'. Furthermore, exploration of the factor structure underlying the BADS would be useful, especially if this could be related to the fractionated aspects of executive functions, for example energisation, task setting and monitoring (e.g. Stuss & Alexander, 2000) and specific executive function skills such as impulsivity. Research in this direction may also clarify whether executive function measures truly tap into the entire executive function construct, especially as there have been pointers towards the lack of inclusion of apathy and inhibition (Bechara et al., 1999). Specifically in relation to the BADS there needs to be better description of the normative sample to determine the relevance of comparing individual performances against this baseline.

In a similar vein, it would be useful for future research to consider the strategies used by people to solve executive function tasks and consider adding to the BADS or indeed other executive function measures. It would be useful to design some appropriate way of recording these strategies and working out how they work for individuals. If research could find a way of meaningfully recording strategies that are used to successfully undertake activities that require executive functions then it might be possible to

identify rehabilitation strategies for people with HIV. This may lead to further research considering the benefit of these strategies compared to people who have not used them. This might also allow for consideration of the factors related to the employment of compensation strategies, for example, whether women are able to employ these strategies in the same way as men.

The neuroactive and differential effects of HAART need to be considered as a factor of newer research (Bhaskaran et al., 2008). It might also be useful for further research to include assessment of further variables. For example, more information on history of drug and alcohol use with more sophisticated recording procedures to avoid the social desirability factor. It would also be useful to include variables such as socio-economic status. Importantly, future research with people with HIV needs to consider tests of effort, possibly using the Rey FIT as a quick measure to determine how invested participants are in the assessment procedure. It might also be valuable to further consider the role of anxiety, cognitive reserve and insight in further research to determine the relative impact of this to self-reported problems, and the hypervigilance/lack of insight continuum, and executive functions.

It would also be useful to supplement quantitative research considering further the patterns of difficulties with qualitative research into the experiences of executive function difficulties in people with HIV and the people who live with/work with them. This might also offer some insight into how these factors impact on stigma of HIV and social isolation.

Clinical Implications

The implications of these results are wide ranging. Although there are some limitations which may restrict validity of the results, these results allow for the preliminary discussion of the clinical implications. The findings of this study confirm the need for neuropsychological provision for people with HIV. This also suggests a move away from reliance on tests which do not represent the skills required in everyday life and do not consider the individual within a wider community, social and political context. Table 22

shows examples of the potential of the ICF-WHO to be used to consider the levels of clinical implications.

Table 22.

HIV and potential intervention level considering the WHO-ICF

Health condition	Impairment	Activity Limitation	Participation Restriction
	Problem with body function, structure, deviation or loss	Difficulties an individual has executing an activity	Problems experienced in involvement in life situations
HIV	Compromised immune system, reduced cognitive and executive function	Less capable of 'socially appropriate' behaviour	People's reactions leading to fewer social relationships
Intervention Level	HAART	Rehabilitation/ Compensation strategies	Wider awareness of this issue

Note. WHO-ICF=World Health Organisation-International Classification of Functioning; HAART=Highly Active AntiRetroviral Therapy

Impairment Level

The mixture of positive and negative effects of HAART medication warrants further research. Prescribers should consider cognitive functioning when prescribing (Antony & Bell, 2008). It might be valuable for prescribing staff to develop clear information for people with HIV. This might inform people with HIV on the potential effects of HAART, more than just medical side-effects, but realistic and evidence-based consideration of the potential negative side-effects in relation to executive function. This might indicate that patients starting on a HAART regime should be offered the option of regular monitoring of executive functioning.

Activity Limitation

The potential evidence of some compensation strategies suggests that there might be some benefit of rehabilitation strategies. This might contribute towards the development of rehabilitation programs or information on rehabilitation which could be provided to patients after diagnosis. It might also point towards ways that others, including healthcare professionals, might provide help and useful approaches for the patient.

Participation Restriction

The implications of this study also highlight the limitations of the previous research often excluding women and people from non-White backgrounds. In fact the predominance of research samples containing solely white homosexual men severely limits the ability to use this evidence in day-to-day practice. New research needs to develop the applicability of the evidence base through more representational samples. This research goes some way to enabling executive functions in people with HIV to be understood in a more diverse group of people.

Executive functions in HIV also have clinical implications for participants' abilities to undertake substantial employment (Heaton et al., 1994), maintain social support structures (Honn & Bornstein, 2002) and medication adherence (Hinkin et al., 2002).

Further exploration of executive functions difficulties and the challenges impairment can cause to social relationships might be beneficial for both staff and families of people with HIV. As difficulties with executive function can make people seem eccentric, it is important that the findings of this study potentially provide a starting point for developing better information for families and patients themselves about executive functions. This may also assist staff in providing effective support strategies for people with HIV. This should on a wider level help to reduce the isolation of people with HIV and executive function difficulties and increase understanding.

This understanding of executive function difficulties might also work on a wider level to help social understanding and may help to reduce stigma.

Critical Reflection

This section briefly discusses the issues this piece of research has raised. This should be considered in addition to the epistemological position stated in the extended methodology section.

This reflection is a guided critical exploration of the central scientific, ethical and theoretical positions raised by this research and developing strategies for future action (Boud, Keogh & Walter, 1985). Reflection consists of three main stages: description of the events, reflective phase against relevant theories and finally the development of a learning component (Kim, 1999) to help make more sense of complex practice (Driscoll & Teh, 2001). As previous authors have suggested guiding structures improve learning outcomes from reflection (Platzer, Snelling & Blake, 1997) the Johns model (2000) for structured reflection has been flexibly used here. This model focuses on discrete events or generalised reflection, such as an individual research study rather than process reflection. Although this model was developed within nursing practice and has been criticised in its use in ongoing situations (Rolfe, Freshwater & Jasper, 2001), it is widely used and has strengths in its acknowledgement of the epistemological base of reflection (Platzer et al., 1997). However, there is no acknowledged validated mechanism for reflection (Platzer et al., 1997) and the evidence underlying the value of reflection is limited (Lockyear, Gondocz & Thivierge, 2004) with no empirically derived models (Lowe, Rappolt, Jaglal & Macdonald, 2007).

Reflection does not occur in isolation but within systems and therefore this reflection is based on discussion in formal and informal supervision (Ixer 1999). In addition, because this is reflection-on-action rather than reflection–in-action, this is based on my, probably biased, recollections of events (Jones et al., 1995). Furthermore, the critical reflective component is often seen as being opposed to evidence-based practice due to its basis in

the everyday world of the practitioner (Rolfe et al., 2001). In particular, critical reflection in research can 'make visible the vision and stance of the researcher, which might otherwise be hidden' (Jasper, 2005, p.249), particularly important given the epistemological framework of the study. Although this reflection does not focus on the narrative of the research journal it is written in the first person to allow for more creative and critical reflection to emerge.

Johns (2000) Model for Structured Reflection (Appendix P)

I have not focused on the descriptive elements of the reflection as these are covered elsewhere, including an example of the background factors to the experience (Appendix K – Example of reflective notes), or are not appropriate to be covered here, a description of the experience itself as a research narrative. Instead this reflection will focus on the issues that seem significant. Particularly this focuses on psychological research within a medical domain, commenting on expectations, epistemological frameworks and ecological validity.

Aesthetics (Knowledge from Subjective Sources)

The main aim of the research as I saw it was to attempt to bring meaningful neuropsychology into the everyday world of people living and working with HIV. Ecological validity is an approach which I tried to apply to the study as a whole not just the specific measures used, for example, by using pragmatic and real-world approaches to interpretation and scoring. From reading the neuropsychological research it seems the people behind HIV have sometimes been lost. It seems questionable how meaningful it is to dichotomise people into impairment/not impaired based on arbitrary cut-off points, with no back-up in the form of functional outcomes or self-report as to how cognitive difficulties might affect people in their day-to-day life. This may be because of the medical nature of HIV, and the focus until recently on preserving life as a very real and valid priority. However, although medication has progressed, it seems that research into the neuropsychology of people with HIV has become stuck in this phase. This is understandable

within the historical context, where cognitive impairment was seen as a sign of impending mortality.

I hope that the consequences of this research have started to facilitate a shift away from a solely medical model, and also positivistic research, perspective with people with HIV and executive function difficulties. If so the consequences may contribute an increasing acknowledgement of multiple narratives and available perspectives. Ideally this research attempts to empirically bridge a gap between quantitative research and alternative epistemological frameworks, which might have consequences for future research in this area.

Personal

I may have responded this way to the prior research, because although a scientist, as a psychologist my focus is on people, making sense of behaviour and the narrative that people tell about their lives, rather than HIV-infection per se. This focuses on the meaning people make of cognitive difficulties and how that meaning impacts, and is impacted by the social world within which we live.

Ethics

I attempted to minimise the limitations of recruitment strategies in previous research by being inclusive, in particular including women, people who describe their sexual orientation as heterosexual and people from non-White ethnic backgrounds. This has wider implications for the research body and the requirement to make samples more representative of the changing demographic of people with HIV.

I can also reflect on the complexity of giving neuropsychological feedback out of context for the individual. The value of considering the meaning of executive function impairment based on level of environmental demand and the potential effects of anxiety has been demonstrated in the study. This should look to influence the wider research and move towards considering the individual interpretation and importance of high level cognitive

functioning. Bearing in mind that individuals who have HIV will also be aware of the history of cognitive difficulties in HIV and the fear this may therefore inspire.

Empirics

This research approach was informed by awareness of different epistemological stances and a desire to empirically put into practice theoretical issues discussed by authors such as Westerman (2006). This provided a basis for understanding neuropsychology in HIV using ecological validity as a guiding concept. Despite its common use in neuropsychology there are significant controversies over using normative data and whether a 'normal curve' even exists (Johnson, 1999). Further the research has highlighted a personal need to explore alternatives to hypothesis-testing research in Bayesian theory (Johnson, 1999).

Reflexivity

These reflections therefore relate to future research studies both for myself and the wider scientific discourse:

- I would use a critical realist perspective again in quantitative research as I feel it has enabled a more reflective and honest approach, moving away from the assumption that quantitative research can be objective. This is a personal development and increased change in my approach to research from my previous experiences.
- A wider development and increasing personal awareness of the limitations of using the 'normal curve' assumption within psychology and neuropsychology.
- A greater use of ecological validity as a guiding principle in neuropsychology and HIV, focusing on the meaning attributed to cognitive functions by individuals and the functional outcomes for them.
- Although it is not possible to escape the history of cognitive impairment in HIV infection, it might be possible to see a new and different way forward that moves away from a purely medical model to incorporate the socially created aspects of disability taking the lead from the WHO-ICF.

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The corresponding author will receive a free pdf. This pdf can also be mounted on the authors' web pages. Offprints must be ordered when page proofs are returned. The offprint order form with the price list will be sent with your PDF.

Appendix B Referral Form (1 page)

Appendices

Assessment of executive functions in HIV infection using the Behavioural
Assessment of the Dysexecutive Syndrome: A pilot study

Name of Researcher: █████████ Supervisors: █████████████████

REFERRAL FORM

We are recruiting people with HIV aged 18 to 60 who meet the following criteria:
- Diagnosed at least 3 months ago
- No current intravenous drug use
- No history of psychosis or current severe depression
- English speaking
- Not blind or deaf
- No previous diagnosis of brain damage, dementia or other neurological disease

Please complete the following sections for anyone who you think **might** be
suitable and return the form for:

████████████████████████

**INSTITUTE OF WORK, HEALTH AND ORGANISATIONS, UNIVERSITY OF NOTTINGHAM,
INTERNATIONAL HOUSE, B FLOOR, JUBILEE CAMPUS,
WOLLATON ROAD,
NOTTINGHAM, NG8 1BB**

Name of Potential Participant: _____MALE /
FEMALE

Date of Birth: DD/MM/YYYY

Diagnosis more than 3 months ago: YES/NO

Telephone Number:_____

Address:_____

_____

Preferred contact time: Daytime/Evening/Weekend

Name of Referrer: Date: DD/MM/YYYY
Position of Referrer: Tel:

**If you think there is any risk in completing the research for the potential participant or have any other issues you think
the psychologist should know about please contact the researcher on the above details before referral**

===

CONSENT TO PASS ON THIS INFORMATION TO RESEARCHER NAMED ABOVE:

I consent to have the above mentioned details sent to ██████████ in order that they
can determine my eligibility for the study and provide me with further information about the
research

_____   _____ _____
(Potential Participant's Name)   (Signature)   (Date)

Study Title:

Assessment of executive functions in HIV infection using the Behavioural Assessment of the Dysexecutive Syndrome: A pilot study

We would like to invite you to take part in a research study. Before you decide to participate you need to understand why the research is being done and what it would involve for you. Please take time to read the following information carefully. You should:

- Talk to others about the study if you wish.
- Ask us if there is anything that is not clear or if you would like more information.
- Take time to decide whether or not you wish to take part.

Part one of this information sheet will outline the purpose and process of the study. Part two will detail the research procedures.

PART ONE

What is the purpose of the study?

HIV infection can sometimes influence how the brain works. This can affect skills such as problem solving, planning and decision making. This group of skills are called "executive functions" and are important in day to day life, to enable us to adapt to everyday situations and inhibit inappropriate social behaviour. Problems with these skills are often referred to as the 'dysexecutive syndrome' and can be measured on tests such as the Behavioural Assessment of the Dysexecutive Syndrome (BADS). The results of this study should give us an idea of the specific effects of HIV infection on executive functions (problems solving etc.) on everyday life. This will hopefully allow us to identify any problems early in the course of the HIV infection and provide recommendations and rehabilitation. The write up of this study will also contribute to completion of Doctorate in Clinical Psychology and may lead into further and larger research.

Why have I been invited?

You have been chosen because you are living with the day to day impact of HIV and are aged between 18 and 60 years. You may have seen some advertising and referred yourself or you may have been referred by one of the healthcare professionals working with you. We hope to recruit 20 participants to be assessed in the same way from NHS services for people with HIV in ▮▮▮▮▮▮

Do I have to take part?

It is up to you to decide. We will describe the study and go through this information sheet, which we will then give to you. We will then ask you to sign a consent form to show you have agreed to take part. You are free to withdraw at any time, without giving a reason. This would not affect the standard of care you receive in any way.

Appendix C

**What will happen to me if I take part?**

Once your details have been forwarded to us we will contact you within one week to confirm your details, answer any questions and arrange the assessment. With your consent, we will contact a healthcare professional who you have contact with (for example, your social worker, nurse, consultant, health advisor) – we will not pass on any information about you, this is just to inform them of your participation in this study and check you are ready to participate in this research.

The assessment will be one to two weeks after we contact you. Depending on what is best for you, you will meet with the researcher at the clinic/centre where you are normally seen, or your home. The appointment will be with you and the lead researcher and will last approximately an hour and a half. First we will collect some demographic information (this is general information which might describe you, such age, gender and ethnicity). We will then confirm that you understand what will be required of you. You will then be asked to fill in some brief questionnaires. These will look at how things are for you day to day (Dysexecutive Questionnaire – 20 multiple choice questions), a baseline measure of general ability (Wechsler Test of Adult Reading – reading some common and uncommon words) and a questionnaire on mood (Hospital Anxiety and Depression Scale – 14 multiple choice questions). At this point we will have a short break. The following part will involve a series of 6 short pencil and paper tasks. This will involve some drawing, answering questions and practical tasks that require 'executive' skills like planning and decision making. We will ask you for the name of a member of staff who works with you (for example, nurse, medical consultant, social worker, health advisor) or alternatively someone who knows you well. We will send them a questionnaire to complete about how they see any difficulties you might have. With your permission we will also find out your HIV stage, CD4 count, plasma viral load and what, if any, type of medications you are taking. This will help us understand your results.

After two weeks you will be sent written feedback. You can choose to meet with the researcher to discuss the results if you would like. Dependent on your consent, the people who work with you may also have a copy of your written report.

This is a **cross-sectional descriptive** study, which means that we are measuring what is happening already rather than trying to change anything. Therefore, this assessment should not interfere with your current treatment in any negative way. There is no arrangement for long-term follow-up. However, referrals to appropriate services can be made if we feel it might be useful for you.

There is the possibility that you may not be able to complete the research or that this is not the right time for you to complete this research. If this is the case, the researcher will discuss the reasons for this with you and we can refer you on to other services if you think this would be useful.

Appendix C

Flowchart

Recruitment

Staff-Referral	Self-Referral

You will be contacted by the lead researcher by phone/letter

Information sheet sent out to you

1

'Caseworker' contacted (with your consent) to consider risks for you from participation in the study

Assessment with lead researcher and you (about 1 ½ hours)

- Sight, hearing and communication test
- Demographic information

May stop here if you could not complete the assessment

- Information sheet and question discussed and take consent
- Dysexecutive Questionnaire (DEX)
- Wechsler Test of Adult Reading (WTAR)
- Hospital Anxiety and Depression Scale (HADS)

Break

- BADS

3

Designated 'other' will be contacted by phone to explain purpose of DEX. This will then be posted out to them with a stamped addressed envelope to return to the researchers.

Some clinical information from your notes will be collected by a member of staff working in the service or the lead researcher.

5

Written feedback of your test results – with option for face-to-face feedback if you would prefer

(Optional) Written report forwarded to caseworker/referrer as required with your consent.

6

Appendix C

Expenses and Payment?

We offer a £10 voucher for Boots for participation in the study.

What will I have to do?

If you agree to participate you will be asked to take part in one session (described above). As well as participation in the study you will be asked to give consent for:

- A member of healthcare staff to be informed of your participation
- Your medical notes to be reviewed by the lead researcher
- A person who knows you well to complete a questionnaire

You will not have to change any medication or treatment that you are currently receiving or any day-to-day activities.

What are the possible disadvantages and risks of taking part?

There are no particular risks for you in taking part. However, some people may find the results of the testing upsetting. However, we can help to refer you to support services in these circumstances if needed.

What are the possible benefits of taking part?

The results of the study might help you and others around you understand why you might find some things more difficult than other people. If the results do not show any problems this may help to put your mind at rest or provide a baseline for possible future assessments in other services. However, although we cannot promise the study will help you directly, the information we get from this study might help improve the treatment of other people with HIV.

What happens when the research study stops?

Your care and treatment continue as usual.

What if there is a problem?

Any complaints about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. Detailed information on this is given in Part 2.

Will my taking part in the study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2.

If the information in Part 1 has interested you and you are considering participation, please read the additional information in Part 2 before making any decision.

Appendix C

PART TWO

What will happen if I don't want to carry on with the study?

You are free to withdraw at any time in the study process without ongoing care being affected in any way. Although you do not have to give a reason for withdrawing, there will be the opportunity to express your reasons if you wish. If you withdraw from the study your information will be removed from the study and all information will be kept confidential (see **'Will my taking part in this study be kept confidential?'** below for details). However, information cannot be destroyed and has to be stored confidentially in accordance with the university policy

What if there is a problem?

It is unlikely that any harm will come to you by taking part in this study. However, if you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your question. If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Contact details for the Nottinghamshire Healthcare NHS Trust Complaints are:

Patient Advice and Liaison Service Telephone Number –

Or:

Service Liaison Manager
Nottinghamshire Healthcare NHS Trust Duncan Macmillan House

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against   Healthcare NHS Trust, but you may have to pay your legal costs.

Will my taking part in this study be kept confidential?

All data collected through your participation in the study will be kept completely confidential. If you join the study, some parts of your medical records might be looked at by the researcher to find out your CD4 count, plasma viral load and HIV medication details. Any information about you which leaves the hospital/surgery will have your name and address removed so that you cannot be recognised. You will be assigned a unique research code which will be used instead of your name on all information so you will not be identifiable. Data will be stored securely under responsibility of the custodian at the University of   esearcher's supervisor, Dr.   Paper information will be marked confidential and stored in a locked filing cabinet and electronic information will be stored on a password-protected database. People who have access to your information are: the lead researcher, research supervisor. They may also be looked at by authorised people (sponsors, regulatory authorities and R&D audit) to check that the study is being carried

Appendix C

out correctly. All who have access to your information have a duty of confidentiality to you as a research participant and we will do our best to meet this duty. Your information will not be retained for future studies although due to the University of ██████ policy, it has to be kept for reference purposes. The information will be dated and stored securely for 7 years and subsequently destroyed securely. You have the right to check the accuracy of data held about you and correct any errors.

The only time we would break your confidentiality is if we felt that you or someone else were at risk, and if this was the case we are obligated by law to disclose this to people in authority, on a need to know basis, but we would try and discuss this with you first.

Involvement of Other Healthcare Professionals?

If you have referred yourself to this study, with your consent, we would like to contact a member of healthcare staff who you have contact with (for example, your social worker, nurse, consultant, health advisor) to inform them of your involvement. This is to ensure that there are no risks to you in taking part at this time and that you can receive the best care if the study finds any problems. At the end of your time on the research study, dependent on your consent, the written report can be forwarded to relevant healthcare professionals. This report will include results of your participation in the study and any recommendations we think might help. We are happy to share or discuss any of this information beforehand.

What will happen to the results of the research study?

The overall results of the study are intended to be published in a scientific journal and possibly presented at conferences. At the end of the study you will be asked if you would like a summary of results to be sent out to you when these are available. You will not be identified in any report/publication.

Who is organising and funding the research?

This research is forming part of a Doctorate in Clinical Psychology qualification at the University of ██████

Who has reviewed this study?

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee to protect your safety, rights, wellbeing and dignity. This study has been reviewed and given favourable opinion by Leicestershire, Northamptonshire & Rutland Research Ethics Committee.

Appendix C

Further information and contact details

You might want further information for example about:

- General or specific information about the process

- Advice on whether to participate

- Who you should go to if you are unhappy with the study

In the first instance the researcher should be able to answer your questions. Further information sources are available on request from the researcher.

If you have any concerns during the study please contact:

Trainee Clinical Psychologist

Alternatively messages can be left with:
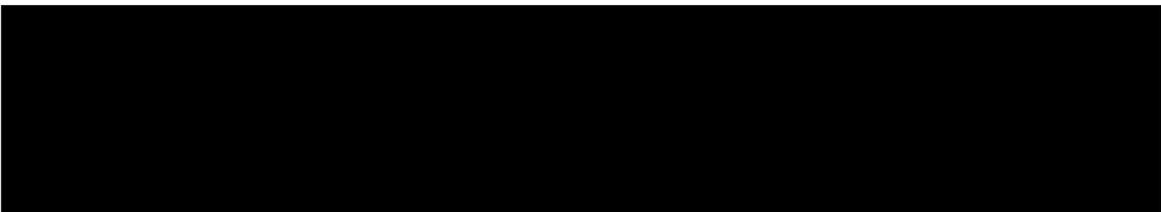
Volunteers Needed

For a study looking at problem-solving skills in people who are living with HIV.

We are looking for adults, aged between 18 to 60 years old, who have been living with the effects of HIV for more than 3 months, to participate in an assessment to explore problem-solving and decision making skills.

The results of this will help us learn how to identify people with HIV who have difficulties with problem solving. This will mean that we can design treatment programmes and services to offer appropriate support for these people. Feedback will also be available on your own performance on the tests.

You will receive a £10 Boots voucher for your participation.

If you would like more information or you want to express an interest in taking part then please discuss this with staff and/or contact:

I-WHO, University of Nottingham, International House, B

Telephone   e-mail:

Appendix E Consent Form

CONSENT FORM

Title of Project: Assessment of executive functions in HIV-1infection using the Behavioural Assessment of the Dysexecutive Syndrome: A pilot study

Name of Researcher: ███████████████
Supervisors: ███████████████████

<u>Please initial box</u>

1. I confirm that I have read and understand the information sheet (version 2 19/11/08) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.

3. I confirm that I have seen the medical note proforma and give permission for relevant sections of my medical notes to be accessed and recorded by the researcher.

4. I give permission for _____ to fill in a questionnaire to provide additional information in the assessment.

5. I understand that a healthcare professional who I have contact with will be informed of my participation.

6. I agree that my case-worker or the person who referred me may be informed of the results.

7. I agree to take part in the above study.

_____ _____ _____
Name of Patient   Date   Signature

_____ _____ _____
Name of Person   Date   Signature
taking consent

When completed: 1 for patient;
                1 for researcher site file;
                1 (original) kept in medical notes.

19/11/08   Version 2

Appendix F Assessment Proforma (4 Pages)

ID:

Date:

Sight test:	**YES/NO**
Hearing:	**YES/NO**
Sheffield Screening Test administered:	**YES/NO**

Hospitalisation (>1 night stay) for illness/infection in last 2 weeks: YES/NO

Medication change in the last 2 weeks:	**YES/NO**

Any of the following:

- Head Injury/Stroke   **YES/NO**
  Further Information:

- Degenerative neurological condition   **YES/NO**
  Further Information:

- Brain Tumour   **YES/NO**

- Schizophrenia   **YES/NO**

- Current Severe Depression   **YES/NO**

- Current injecting Drug Use   **YES/NO**

Consent Taken: **YES/NO**

Appendix F

Ethnicity: White

        A   British
        B   Irish
        C   Any other White background

Mixed

        D   White and Black Caribbean
        E   White and Black African
        F   White and Asian
        G   Any other mixed background

Asian or Asian British

        H   Indian
        J   Pakistani
        K   Bangladeshi
        L   Any other Asian background

Black or Black British

        M   Caribbean
        N   African
        P   Any other Black background

Other Ethnic Groups

        R   Chinese
        S   Any other ethnic group

        Z   Not stated

Sexual Practice: Homosexual

          Heterosexual

          Bisexual

          Abstinent

Appendix F

Education: 5-11 years

                    12-13 years

                    14-16 years

                    17+ years

Employment: Employed

                    Part/Full time

                    Paid/Voluntary

                        Occupation:

                    Unemployed:

                        Disability related to HIV

                        Disability other than HIV (specified)

Living Arrangements: Alone

                    With Spouse/Partner

                    With other/s – specified

Drug and Alcohol Intake per Week:

Type of Substance	Frequency (daily)	Frequency (monthly)
Alcohol		
Cannabis		
Amphetamine		
Opioid		
Other		

Appendix F

DEX Self Rated: **YES/NO**

DEX Other Rated: **YES/NO**

WTAR Administered: **YES/NO**

HADS Administered: **YES/NO**

BADS Administered: **YES/NO**

Designated Significant Other:

Relationship:

Contact Details (if known):

Feedback: **Face-to-face/Written/None**
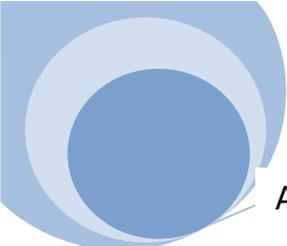
Medical Note Review

Title of Project: Assessment of executive functions in HIV-1infection using the Behavioural Assessment of the Dysexecutive Syndrome: A pilot study

Name of Researcher: ██████████████

Supervisors: ██████████████████████

ID Code:

Approximate Date of Diagnosis: DD/MM/YYYY

Current CDC Classification: Asymptomatic/Symptomatic/AIDS

(Circle one)

CD$_4$ Count: Most Recent:_____

Plasma Viral Load: Most Recent:_____

Medication Regime: Mono-therapy

(Circle one)   Duo-therapy

                           Triple-therapy (HAART)

                           Quad-therapy +

                           None

Date of last medication change: DD/MM/YYYY

Name of staff completing form:

Position:

NHS

National Research Ethics Service

Leicestershire, Northamptonshire & Rutland Research Ethics Committee 1

1 Standard Court
Park Row
Nottingham
NG1 6GN

Telephone: 0115 8839428
Facsimile: 0115 9123300

18 November 2008
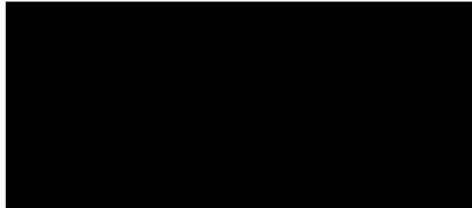
████████████████████████
████████████████████████
████████████████████████

Dear ████████████

Full title of study:	**Assessment of executive functions in HIV infection using the Behavioural Assessment of the Dysexecutive Syndrome: A pilot study**
REC reference number:	**08/H0406/195**

The Research Ethics Committee reviewed the above application at the meeting held on 07 November 2008. Thank you for attending to discuss the study.

Documents reviewed

The documents reviewed at the meeting were:

Document	Version	Date
Protocol	1	10 September 2008
Investigator CV		18 September 2008
Application	AB/133022/1	22 September 2008
Participant Consent Form	1	10 September 2008
Participant Information Sheet	1	07 March 2008
Investigator CV		
Letter of exclusion to participants who cannot be included	1	10 September 2008
Letter of invitation to participant	1	10 September 2008
Assessment Proforma		
Referral Form	1	10 September 2008
Medical Note Review	1	10 September 2008
Advertisement	1	10 September 2008

This Research Ethics Committee is an advisory committee to East Midlands Strategic Health Authority.
The National Research Ethics Service (NRES) represents the NRES Directorate within the
National Patient Safety Agency and Research Ethics Committees in England.

Appendix H

Provisional opinion

In discussion, the Committee noted the following ethical issues.

- The Committee asked why you will contact the patients' key workers after they have contacted her to volunteer for the study. You explained that she had two reasons; one was her personal safety in case people are not suitable for a one to one meeting and also in case the patient may have personal reasons why their case worker does not think it is a good time for them to take part.
- The Committee asked whether all data on drop outs would be destroyed. They thought that if a patient drops out because they are unable to complete the tests, rather than not wanting to take part, then their data may be valuable. You explained that it would depend on the reasons, if someone does not complete the measure she might not have enough data to analyse but if they complete part of it she would try to include the data.
- The Committee asked for more information on the questionnaires and measures as copies had not been submitted. You explained that the BADs are timed with six tasks so there is a limit on how long the session will take. The tests include a card rule test, a temporal perception test. A water and cork test and test where participants will have six small tasks to complete in ten minutes.
- The Committee asked how IQ will be measured. You explained that the Wechsler test is a test of pre-morbid IQ based on pronunciation of fifty words of increasing difficulty. The principle is that some words are not pronounced phonetically and have to be learned and the number that a participant knows will reflect their IQ.
- The Committee were concerned that if a patient's key worker did not think they should take part then their comments should not be fed back to the patient. You confirmed that no specific comments would be fed back, just the letter submitted.

The Committee would be content to give a favourable ethical opinion of the research, subject to receiving a complete response to the request for further information set out below.

The Committee delegated authority to confirm its final opinion on the application to the Chair.

Further information or clarification required

1. The Committee request a copy of any feedback back from the review carried out by the academic course research team.
2. The Committee request the following changes / amendments to the participant information sheet:
   a. The Committee found the flow chart used in the protocol much clearer than the one in the information sheet and requested that it should be used instead.
   b. Further explanation of the questionnaires and pencil and paper tasks should be included to allow the participant to make an informed choice.
   c. The term 'demographic data' should be explained in lay language.
   d. The sections 'What if there is a problem?' 'Harm' and 'NHS based research' should be condensed under the heading 'What if there is a problem?' and contact details for Trust complaints should be given.
   e. Statement one of the consent form should be updated to refer to the new version number and date of the information sheet.

Appendix H

When submitting your response to the Committee, please send revised documentation where appropriate underlining or otherwise highlighting the changes you have made and giving revised version numbers and dates. It would help to speed up review of your response if you would email your response as well as sending a hard copy.

The Committee will confirm the final ethical opinion within a maximum of 60 days from the date of initial receipt of the application, excluding the time taken by you to respond fully to the above points. A response should be submitted by no later than 18 March 2009.

Ethical review of research sites

The Committee agreed that all sites in this study should be exempt from site-specific assessment (SSA). There is no need to submit the Site-Specific Information Form to any Research Ethics Committee. However, all researchers and local research collaborators who intend to participate in this study at NHS sites should seek approval from the R&D office for the relevant care organisation.

Membership of the Committee

The members of the Committee who were present at the meeting are listed on the attached sheet.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

08/H0406/195	Please quote this number on all correspondence

Yours sincerely
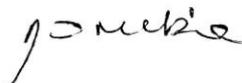
[signature]

Dr Carl Edwards / Miss Jeannie McKie
Chair / Committee Coordinator

Email: jeannie.mckie@nottspct.nhs.uk

Enclosures: *List of names and professions of members who were present at the meeting and those who submitted written comments.*

Copy to: ██████████████████████ *NHS Trust*
                  R&D Department for NHS care organisation at lead site █████

NHS

National Research Ethics Service

Leicestershire, Northamptonshire & Rutland Research Ethics Committee 1

1 Standard Court
Park Row
Nottingham
NG1 6GN

Telephone: 0115 8839428
Facsimile: 0115 9123300

26 November 2008
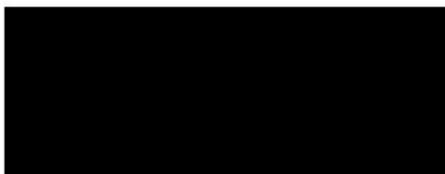
Dear ███████

Full title of study:	**Assessment of executive functions in HIV infection using the Behavioural Assessment of the Dysexecutive Syndrome: A pilot study**
REC reference number:	**08/H0406/195**

Thank you for your letter of 19 November 2008, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

The Committee has designated this study as exempt from site-specific assessment (SSA). The favourable opinion for the study applies to all sites involved in the research. There is no requirement for other Local Research Ethics Committees to be informed or SSA to be carried out at each site.

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission at NHS sites ("R&D approval") should be obtained from the relevant care organisation(s) in accordance with NHS research governance arrangements. Guidance on applying for NHS permission is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

This Research Ethics Committee is an advisory committee to East Midlands Strategic Health Authority.
The National Research Ethics Service (NRES) represents the NRES Directorate within the National Patient Safety Agency and Research Ethics Committees in England.

Appendix I

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	Version	Date
Protocol	1	10 September 2008
Investigator CV		18 September 2008
Application	AB/133022/1	22 September 2008
Investigator CV		
Letter of exclusion to participants who cannot be included	1	10 September 2008
Letter of invitation to participant	1	10 September 2008
Assessment Proforma		
Referral Form	1	10 September 2008
Medical Note Review	1	10 September 2008
Advertisement	1	10 September 2008
Response to Request for Further Information		19 November 2008
Participant Consent Form	2	19 November 2008
Participant Information Sheet	2	19 November 2008
Peer Review		16 October 2008

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Now that you have completed the application process please visit the National Research Ethics Website > After Review

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

We would also like to inform you that we consult regularly with stakeholders to improve our service. If you would like to join our Reference Group please email referencegroup@nres.npsa.nhs.uk.

Appendix I

08/H0406/195	Please quote this number on all correspondence

With the Committee's best wishes for the success of this project

Yours sincerely

[signature]

Dr Carl Edwards Miss Jeannie McKie
Chair / Committee Coordinator

Email: jeannie.mckie@nottspct.nhs.uk

Enclosures: "After ethical review – guidance for researchers" *[SL-AR1 for CTIMPs, SL- AR2 for other studies]*

Copy to: ████████████████████ *NHS Trust*
                    R&D office for NHS care organisation at lead site ████████

Appendix J Table of Brief Description of Most Commonly Used
Neuropsychological Tests of Executive Function (2 pages)

Measure (Abbreviation)	Author	Brief Description	Executive Function Skills Assessed
Traditional Tests			
Controlled Oral Word Association (COWAT/Verbal fluency/FAS)	Benton & Hamsher (1976)	People are asked to name as many words as they can within one minute. This is repeated for three letter: F, A, S and sometime for categories	• Generation of ideas • Set-shifting
Cognitive Estimates Test (CET)	Shallice & Evans (1978)	People are asked to estimate answers in response to questions relating to: quantity, size, weight, height, time	• Devising an appropriate cognitive plan
Tower of London	Shallice (1982)	People are asked to move four different sized disks stacked over three pegs to create a certain arrangement. However, only one disk can be moved at once and a larger disk can never be placed on top of a smaller one	• Problem-solving • Inhibition
Trail Making Test (TMT)	Reitan (1958)	People have to make a 'trail' first between a series of numbers and secondly alternating between numbers and letters	• Visuo-motor tracking • Set-shifting
Stroop Test	Stroop (1935)	People are presented with colour-words, for example 'blue', although typed in a consistent or different colour described by the word. People are instructed to say either the word or the colour the word is printed in	• Inhibition • Speed of processing

Wisconsin Card Sort (WCST)	Heaton, Chelune, Talley, Kay & Curtiss (1993)	People are presented with a series of cards and have to identify the rule governing them. This rule changes from time to time without informing the person; they have to identify that rule changes	• Abstract reasoning • Set-shifting

Neuropsychological batteries based on traditional tests

Cambridge Neuropsychological Test Automated Battery (CANTAB)	Sahakian & Owen (1992)	Computerised battery of 22 tests includes go/no-go, Cambridge Gambling task, Intra-extra dimensional set shift	• Decision-making • Complex attention • Planning • Verbal and visual memory
Delis-Kaplan executive Function System (D-KEFS)	Delis, Kaplan & Kramer (2001)	This battery has adapted and included versions of all of the above individual tests as well as new versions	• All as above

Measure with good ecological validity

Hayling & Brixton Tests	Burgess & Shallice (1997)	Used to assess people who might find the BADS easy. Assess sentence completion and spatial anticipation	• Logical reasoning • Inhibition • Speed of processing • Set-shifting
Iowa Gambling Task (IGT)	Bechara et al. (2001)	People are asked to select cards from four decks. Each card selection either results in winning or losing money and people have to amass as much money as possible	• Decision-making
Multiple Errands Test (MET)	Shallice & Burgess (1991)	People are observed carrying out a set of tasks within the naturalistic environment of a shopping centre	• Strategy application • All executive function skills
Virtual Planning Test (VIP)	O'Niel-Pirozzi, & Goldstein (2005)	People have to plan and sequence activities through a board game	• Planning • Sequencing

Appendix K Excerpts from Reflective Notes

Previous clinical experience with the BADS (25/01/08)

"I have had previous positive experiences, particularly in terms of client engagement, using isolated subtests of the BADS prior to conducting the research. This may make me more likely to point towards the benefits of the BADS. However, I have no used the battery as a whole before so this new experience may be an opportunity for me to revise my beliefs about it as a measure."

My understanding and values of relating to everyday functioning (23/03/09)

"As I have started the assessment it has brought to mind my own views on what 'good' everyday functioning might be. Although I am open to idiographic preferences and values for everyday I am also becoming aware that I place a value on employment which I am now beginning to question. This importance on employment may be due to the underlying cultural assumption that people are happiest when they are occupied and unless there is a physical reason preventing them people should work. This might make me place additional importance on functional outcomes such as employment, rather than other,

NHS
Trust **NHS**

Please reply to:

Telephone:
Fax:
E-mail:

27 January 2009

Dear

**ID: 08GM006   Assessment of executive functions in HIV infection using the
Behavioural Assessment of the Dysexecutive Syndrome: A Pilot Study**

The R&D Department has considered the following documents:

. NHS REC Application form, version 5.6
. Protocol, version 1dated 10/09/08
. Patient Information Sheet, version 2 dated 19/11/08
. Patient Consent Form, version 2 dated 19/11/08
. Invitation letter version 1 dated 10/09/08
. Referral Form version 1 dated 10/09/08
. Medical Note Review form version 1 dated 10/09/09
. Patient Exclusion letter version 1 dated 10/09/08
. Assessment Proforma
. Advertisement version 1 dated 10/09/08

Your study now has R&D approval, on the understanding and provision that you will follow the
conditions set out below.

Conditions of Approval

That you:

1. Accept the responsibility of Chief/Principal Investigator as defined in the current
    Research Governance Framework.
2. Request written approval from the R&D department for any change to the
    approved protocol/study documents you wish to implement
3. Ensure all study personnel, not employed by the
    hold honorary Contracts with this Trust, before they have access to
    any facilities, patients, staff, their data, tissue or organs.
4. Report any Serious Adverse Event involving the Trust to the R&D department,
    using the Trust 'policy for research safety reporting in human subjects'. Policy
    available from the R&D Department.
5. Complete the R&D Research Governance interim and final reports as requested.
6. Comply with the regulatory requirements and legislation relating to: Data
    Protection, Trust Caldicott Guidelines, Health and Safety and the use of Human
    Tissue for research purposes.
7. Comply with the current Research Governance Framework, available at
    www.doh.gov.uk or via the R&D office or Research Governance Web-site.
8. Agree to conduct this research project in accordance with ICH Good Clinical
    Practice and/or the MRC Guidelines for Good Clinical Practice (as appropriate)

Appendix L

relevant ethics committee.

Please note that the R&D department has a database containing study related information, and personal information about individual investigators e.g. name, address, contact details etc. This information will be managed according to the principles established in the Data Protection Act.

Yours sincerely

Director of R&D

cc ▮▮▮▮ Research Ethics Committee

Appendix M Trust A Honorary Contract (2 Pages)

NHS

NHS Trust

Department of Human Resources

Please ask for:

Ref:

8 December 2008

Dear ████████

LETTER OF AUTHORITY FOR: ████████████████
HONORARY CONTRACT AS HONORARY PSYCHOLOGIST

I am writing to confirm that with effect from **30 November 2008 to 30 October 2011** you will be authorised to work as a **Honorary Psychologist** at ████████████████████████

This letter is not a contract of employment and you will not be considered as an employee of the Trust.

The formal conditions of this contract are as follows:-

1.   There is no contract of employment between ██████████████████████ ████████████ and yourself, and you will receive no payment from the Trust.

2.   During your service commitment at ████████████████████████ you will work under the direct supervision of, and be responsible to ████████████████████ ██████████████████

3.   Your hours of work will be as agreed with your Manager.

4.   You are required to comply with the Health & Safety Policy of the Trust. This policy and any further requirements under the Health and Safety at Work Act 1974, may be drawn to your attention.

5.   During the attachment you will be regarded as a voluntary worker, for insurance purposes. As far as local liability and accidents are concerned there is no need for you to take out any extra special insurance.

6.   The Trust will not normally accept any responsibility in respect of theft, loss or damage to personal property. You are recommended to investigate the possibility of insuring yourself as far as you think proper against all such risks and to take advantage of any local facilities there may be for the safe keeping of property.

7.   You are required to maintain the confidentiality of all information with which you may come into contact in the course of your work.

Appendix M

8   The work you will be involved in will be of a confidential nature and any information with which you come into contact may not be disclosed without the prior approval of ███████████ ██

9   Copies of the Trust's Disciplinary Procedure can be found on the intranet ███████████████████████████████████████ This procedure covers the performance and conduct of all employees of the Trust and those working on honorary contracts.

10   The Trust reserves the right to terminate this arrangement at any time.

RESEARCH GOVERNANCE AND INTELLECTUAL PROPERTY

The Trust manages all research in accordance with the requirements of the Department of Health's "Research Governance Framework" (RGF). Employees with the Trust must comply with all reporting requirements, systems and duties of action put in place by the Trust to deliver research governance.

From 1 May 2004 all clinical trials using medicinal products for human use have a legal obligation to comply fully with the requirements of the EU directive on good clinical practice (2001/20/EC).

You are required to comply with the Data Protection Act 1998 and other local policies and procedures regarding the handling of information.

For further information on Research Governance requirements, employees should refer to the R&D website or the Research & Development Department. Further information on the RGF and EU Directive (2001/20/EC can be found on the Department of Health website.

If you have an invention, idea or innovation, you have an obligation to inform the Trust via the R&D Manager, or the East Midlands NHS Innovation Hub, and must not, under any circumstances, sell, assign, licence, give or otherwise trade Intellectual Property without the Trust's agreement

If you have any queries on the conditions of this contract, please do not hesitate to contact me.

I would like to take this opportunity to welcome you to ████████████████████ NHS Trust and I hope you enjoy working here.

Yours sincerely

████████████████████████

Directorate HR Manager / Medical Personnel Manager

I agree to abide by the conditions stated in my honorary contract whilst working at Nottingham University Hospitals NHS Trust, Nottingham.

Signed : ████████████...............................   Date : 19/01/09 ....

Name : ████████████...

Please find attached two copies of this contract, please sign both copies, retain one and return the other copy to :

Department of Human Resources

████████████████████████████

Page 2 of 2

NHS

NHS Foundation Trust

Ref: R&D141

Research and Development Committee

5 December 2008
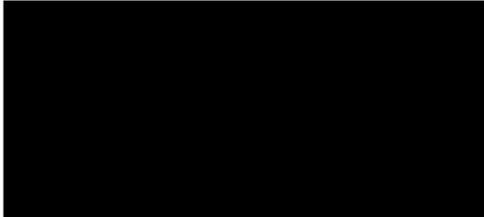
Dear

Full Title of Study: Assessment of executive functions in HIV infection using the BADS: a pilot study.

REC Ref: 08/H0406/195

The Research and Development Committee has approved the above research project.

<u>Conditions of Approval</u>

That you have read and agree to abide by the Research Governance Framework for Health and Social Care, and comply with all reporting requirements, systems and duties of action put in place to deliver Research Governance, including:

o   All projects are liable to be monitored internally by the Research Governance Monitor.

o   That a system for recording and reviewing all adverse events in research is in place. This is in addition to the reporting of serious or unexpected adverse events and adverse drug reactions (which may affect the conduct and continuation of the study) to the approving research ethics committee. All research-related incidents will be reported on the Trust's incident system.

o   Honorary contracts for all non ▇▇▇▇▇▇▇▇▇▇ NHS Trust employees, involved in the project are obtained from Human Resources.

o   All research staff taking consent are adequately trained to do so

o   All research, which is discontinued temporarily or permanently, should be reported to R&D Department.

o   All changes to the project protocol including amendments, changes in study personnel and change in duration/timescale of the project should be referred to R&D as well as the appropriate ethics committee.

o   That R&D are notified when project findings are published or disseminated in any way.

o   To complete yearly/final reports as requested.

1

INVESTOR IN PEOPLE

Chairman Tracy Doucét
Chief Executive Jeffrey Worrall

Page 1 of 2

Appendix N

NHS Foundation Trust

Copies of the Research Governance Framework for Health and Social Care and the EU directive can be found on the Department of Health's website:
http://www.dh.gov.uk/en/PolicyAndGuidance/ResearchAndDevelopment/A-Z/ResearchGovernance/index.htm

Acceptance of conditions of approval

Commencement of the research project is taken as acceptance of the conditions of Research and Development approval.

Any queries regarding the Research Governance Framework for Health and Social Care should be directed to Michael Hewitt.

Yours sincerely,
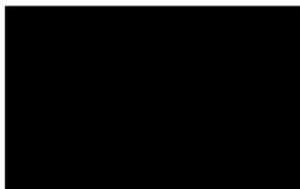
Chair
Research and Development Committee

c.c.
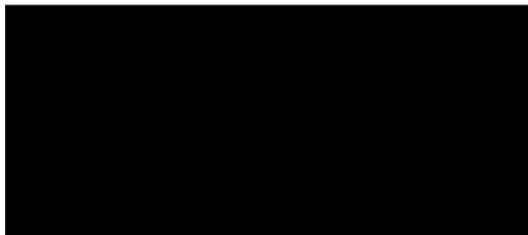
2

Chairman Tracy Doucét
Chief Executive Jeffrey Worrall

Page 2 of 2

HONORARY CONTRACT OF EMPLOYMENT

1   **NAME**   ███████████████

2   **ADDRESS**   ███████████████████████████████
     ███████████████████████████████████████

3   **POST TITLE**   Researcher

4   **CONDITIONS OF SERVICE**

This appointment is that of Researcher commencing 30th November 2008 until 30th October 2011, during the tenure of your appointment as Researcher.

The appointment will be subject to the terms and conditions of service of the NHS, as amended from time to time, and the appointment is offered in accordance with an agreement reached between the ███████████████ ███████████████

5   **BASE**

For the purposes of this Honorary Contract your base will be ██████████ Hospital and you may in exceptional circumstances by agreement between the Trust and yourself be required to work in any reasonable location necessitated by the duties of the post.

6   **DATE OF COMMENCEMENT**

Your date of commencement with ███████████████ NHS Foundation Trust is 30th November 2008.

7   **INCREMENTAL DATE AND ANNUAL LEAVE**

Your incremental date is as set out in your Contract of Employment with Nottinghamshire Healthcare NHS Trust.

Annual leave is proportionate to completed months of service in the current leave year, which runs from your incremental date. Your annual leave entitlement is as set out in your Contract of Employment with ████████ ██████████ NHS Trust.

8   **DUTIES AND RESPONSIBILITIES**

The duties of your appointment will be those normally undertaken by a Researcher and will be such as may be agreed between ███████████ ██████████ NHS Foundation Trust and yourself from time to time.

9   **MINIMUM PERIOD OF NOTICE ON EITHER SIDE**

The period of notice required from either side to terminate this Contract is four weeks, in writing but, this is not taken to prevent either party waiving the right

to notice, or from accepting payment in lieu of notice. Nor does it affect the right of either party to terminate the contract without notice by reason of the conduct of the other party.

10 PROCEDURES AND RULES

A number of procedures affecting your employment have been agreed through the Trust' machinery for consulting with staff interests. These may be amended from time to time. You will be notified of any changes to procedures or rules and these will form part of your Contract of Employment.

You are advised to acquaint yourself with these procedures, up to date copies of which are held by Divisional General Mangers, Staff Representatives and the Divisional Human Resources Teams and may be inspected on request.

Separate nationally negotiated arrangements shall apply to Nursing and Midwifery Staff in cases involving professional conduct or professional competence until such time as the Trust may negotiate separate agreements outside of these nationally negotiated conditions. These agreements will be subject to consultation with the Local Negotiating committee and the Joint Staffs Consultative Committee.

Your attention is drawn to the fact that all information about patients is always to be classified as confidential unless otherwise provided for in the Trust's Policy on Confidentiality. Breaches of confidence will result in disciplinary action, which may involve dismissal. You should be aware that under the Data Protection Act, regardless of any action taken by the Trust, a breach of confidence could result in a fine and a prosecution.

The Trust's Disputes and Grievances Procedure requires you to raise grievances with your immediate Senior Officer in the first instance. In your case you should raise the grievance with your Divisional General Manager. Should you remain dissatisfied you may pursue the issue through the levels of management described within the procedure.

11 SICKNESS/ACCIDENTS ON DUTY

If you are unable to attend for work because of illness you must notify your immediate line manger of his/her nominated deputy by telephone no later than 10.00am on the first day of sickness.

12 TRADE UNION/STAFF ORGANISATION

It is Trust policy to support the system of collective bargaining and the Trust therefore encourages membership of a recognised organisation. Through such bodies you can help decide opinion on your pay and conditions of service.

Such organisations also represent their members before committees on all kinds of individual problems.

All Trust staff is, therefore, urged to join an appropriate trade union, professional association or staff organisation and participate in its activities.

13 REGISTRATION AND INSURANCE

(a) You are required to be registered with the The British Psychological Society throughout the duration of your employment and to provide evidence thereof on request.

(b) You are normally covered by the NHS Hospital and Community Health Services indemnity against claims of medical negligence. However, in certain circumstances (especially in services of which you receive a separate fee), you may not be covered by the indemnity. The Health Departments therefore advise that you maintain membership of your medical defence organisation. See also Note 3.

14   HEALTH AND SAFETY

The Trust attaches great importance to the health and safety of its employees and recognises its duties under the Health and Safety at Work Act 1974.

Employees are required to carry out their work in manner which is safe, both to themselves and others and to co-operate by bringing to the notice of the supervisory staff any activity, or situation, which would adversely affect any person who may be within the health premises or working situation. A copy of the Trust's Health and Safety Policy is attached.

It is essential that you should know the fire precaution arrangements in health premises and you should read and thoroughly understand the fire notices, which are posted within the Trust's buildings. It is a condition of service that staff will attend fire lectures and fire drills as and when arranged.

15   PERSONAL PROPERTY

Your attention is drawn to the fact that the Trust can accept no responsibility for articles lost or damaged on duty whether by fire, burglary, theft or otherwise with the exception of money, jewellery or other small valuables which have been handed over to an authorised officer for safe custody and for which a receipt has been given. The employee is accordingly advised to insure, so far as he or she thinks proper, against such loss or damage.

16   MEDICAL EXAMINATION AND FITNESS FOR WORK

Your appointment is subject to satisfactory medical examination. The Trust may at any time require you by reason of your being considered unable to perform your duties as a consequence of illness or injury to offer yourself for a medical examination and other tests by a medical practitioner nominated by the Trust. Any expenses incurred in connection with such an examination will be met by the Trust.

17   STANDARDS OF BUSINESS CONDUCT

The acceptance of gifts and hospitality is regulated under the terms defined in Circular HM(62)21 and HSG(93)5. Please refer to the Trust's Standing Orders and Standing Financial Instructions; copies of which are available from your Divisional General Manager, your Divisional Management Accountant or the Finance Directorate.

18   IDENTITY CARDS/CAR PARK PASSES

Employees holding identity cards and car park passes must return them to the Divisional Human Resource Manager prior to terminating their employment.

19   RETIREMENT

It is a condition of this appointment that the provisions of the Trust's retirement policy apply. These provide that retirement will normally be at age 65 for both men and women. Extensions of service beyond the normal retirement age will only be given when the conditions specified in the policy are satisfied.

20   THIS APPOINTMENT IS ALSO SUBJECT TO THE FOLLOWING MUTUALLY AGREED CONDITIONS:

MEDICAL CLEARANCE

████████████████████ NHS Foundation Trust manages all research in accordance with the requirements of the Research Governance Framework. As a contract holder of ███████████████ NHS Foundation Trust you must comply with all reporting requirements, systems and duties of action put in place by the Trust to deliver research governance.

NAME OF OFFICER COMPLETING CONTRACT: ████████████

SIGNATURE OF OFFICER AUTHORISED TO SIGN CONTRACTS OF EMPLOYMENT

SIGNATURE...... ████████████████████

NAME ████████████████████

DESIGNATION   **ASSISTANT DIRECTOR OF HUMAN RESOURCES**

FORM OF ACCEPTANCE BY EMPLOYEE

I hereby accept the appointment on the terms and subject to the Conditions set on pages of this contract. I also recognise that this contract may be revoked by the Trust if the offer of appointment to which it relates was based on false information knowingly given by me either on the application form or at interview or on the medical questionnaire.

SIGNATURE. ████████ ..... DATE. 24/10/08 ....

NAME OF EMPLOYEE. ████████████ .....

(USE BLOCK LETTERS)

Appendix P John's Model of Reflective Practice (2000)

1.   Looking in
Find a space to focus on self
Pay attention to your thoughts & emotions
Write down those thoughts & emotions that seem significant in realising desirable work

2.   Looking out
Write a description of the situation surrounding your thoughts & feelings
Describe the 'here and now' experience
What essential factors contributed to this experience?
What are the significant background factors to this experience?

3.   What issues seem significant?

Aesthetics
What was I trying to achieve?
Why did I respond the way I did?
What were the consequences of my action for myself/the patient/family/the people I work with?
How did the others feel about it?
How did I know how others felt that way?

Personal
Why did I feel the way I did within this situation?

Ethics
Did I act for the best?
What factors (either embodied within me/within the environment) were influencing me?

Empirics
What knowledge did or could have informed me?

4.   Reflexivity
Does this situation relate to other experiences?
How could I have handled this situation differently?
What would be the consequences of alternative actions for the patient/others/myself?
How do I feel about this experience now?
Has this experience changed my way of knowing? (empirics, aesthetics, ethics or personal)