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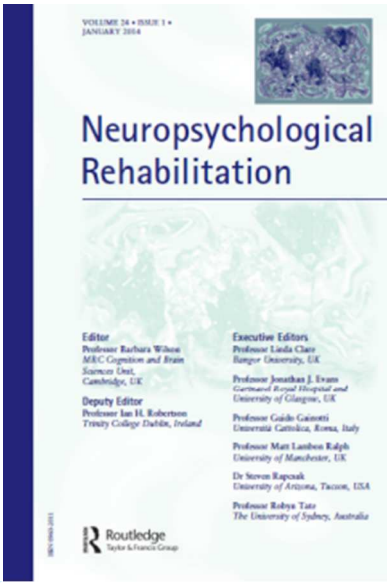

Using Virtual Reality to investigate multitasking ability in individuals with frontal lobe lesions

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Title: Using Virtual Reality to investigate multitasking ability in individuals with frontal lobe lesions

Authors. Tanya Denmark[1], Jessica Fish[1, 2], Ashok Jansari[3], Jignesh Tailor[4] Keyoumars Ashkan[1,4*] and Robin Morris[1,5*]

Affiliations.
[1]Institute of Psychiatry, Psychology and Neuroscience, Kings College London, London, United Kingdom

[2]The Oliver Zangwill Centre for Neuropsychological Rehabilitation, Cambridgeshire Community Services NHS Trust, Ely, UK.

[3]Department of Psychology, Goldsmiths University of London, United Kingdom

[4] Department of Neurosurgery, Kings College Hospital, London, United Kingdom

[5] Department of Clinical Neuropsychology, Kings College Hospital, London, United Kingdom

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*** Joint senior authors**

Corresponding author:
Correspondence should be addressed to Professor Robin Morris, PO BOX 78, Institute of Psychiatry, Psychology and Neuroscience, De Crespigny Park, London, SE5 8AF, E-mail: Robin.Morris@kcl.ac.uk.

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ABSTRACT

Individuals with lesions in the prefrontal cortex often show impairments with the organisation of their behaviour in everyday life. These difficulties can be hard to detect using structured formal tests. The objective of this study was to use Virtual Reality (VR) to explore the multitasking performance of individuals with focal frontal lobe lesions, specifically using the Jansari assessment of Executive Functions (JEF© Jansari et al., 2014). Nineteen individuals with frontal lobe lesions were compared with 19 matched controls on the test and a group of commonly used clinical measures of neuropsychological functioning, as well as questionnaire measures of everyday activity, anxiety and depression. There was a significant difference between groups on the overall JEF© score and on five of the eight individual constructs, namely the planning, creative thinking, adaptive thinking, event-based Prospective Memory (PM) and time-based PM constructs. There were no differences between groups on the non-VR EF individual measures apart from on one EF control measure, Trail Making A. These results demonstrate the potential clinical utility of the JEF© and highlight the value of ecologically valid VR measures in detecting impairments in EF in individuals with frontal lobe lesions.

Keywords: Executive function; Prefrontal cortex; Virtual Reality; Ecologically valid; Neuropsychology.

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INTRODUCTION

The term executive functioning (EF) refers to a set of cognitive abilities such as planning, initiation, goal management, prospective memory and self-monitoring, which can be flexibly used when individuals are faced with the multiple goals, sub-tasks and changing priorities commonly encountered in everyday life (Shallice, Burgess & Robertson, 1996). Many researchers have shown that the prefrontal cortex (PFC) significantly contributes to executive processes (e.g. Baddeley, 1986; Stuss and Benson, 1986; Elliott, 2003) and individuals with cognitive and behavioural impairment following damage to the PFC frequently present with a dysexecutive syndrome (Funahashi, 2001). Allied to EF impairment are difficulties with prospective memory (PM), remembering to perform an intended action in the future, with either time or event based retrieval, or retrieval associated with a specific activity (Einstein & McDaniel, 1990). PM is a common element of many executive tasks (Ellis, 1996; Ellis & Freeman, 2008) and is also supported by the PFC (Shallice and Burgess, 1991; Okuda, 1998; Neulinger, Oram, Tinson, O'Gorman & Shum, 2016).

There are numerous neuropsychological procedures for measuring EF, including well-used measures such as the Wisconsin Card Sorting Test (WCST; e.g. Heaton, 1981; Nyhus & Barcelo, 2009) and the Stroop Test (e.g. Delis, Kaplan & Kramer, 2001) among many more. While such procedures are frequently used they often fail to detect EF impairment, particularly in individuals with PFC damage (Shallice, 1982; Anderson, Bigler & Blatter, 1995). The lack of sensitivity presents a problem for neuropsychological assessment and formulation and is likely to be due to the tests eliciting cognitive activity that is too constrained to reflect the type of EF difficulties associated with everyday activities (Eslinger & Damasio, 1985; Shallice & Burgess, 1991; Burgess et al., 1998; 2006). This so-called 'frontal paradox' (Shallice & Burgess, 1991) has led to efforts being made to develop new assessment measures that have greater 'ecologically validity'. A specific example of this is the Multiple Errands Test (MET) developed by Shallice and Burgess (1991) in a landmark study; they designed a shopping task, which requires individuals to undertake a series of errands, for example, buy specified items in a pedestrian precinct. More complex tasks were also included, such as obtaining the necessary items to send a postcard and certain fact-finding errands and specific rules to follow. Shallice and Burgess (1991) demonstrated that three individuals with frontal lobe injuries had impaired

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performance on the MET, despite relatively normal performance on other EF tests. Such findings have been replicated in other studies, showing the tendency of individuals with PFC damage to have specific difficulties when applying efficient strategies in multitasking situations, but measured using simulation neuropsychological procedures (Goldstein, Bernard, Fenwick, Burgess, & McNeil, 1993; Crepeau, Belleville, & Duchesne, 1996; Bisiacchi, Sgaramella, & Farinello, 1998; Manly, Hawkins, Evans, Woldt & Robertson, 2002; Hsu, Zanto, Anguera, Lin & Gazzaley, 2015). Additionally, there are standardised EF procedures designed to mimic everyday EF activity, such as the Behavioural Assessment of the Dysexecutive Syndrome (BADS) test battery (Wilson, Alderman, Burgess, Emslie & Evans, 1996).

The 'ecological' approaches have tended to use either real world activity, which is time consuming, or 'paper and pencil' methodology to measure EF. With the advent of more powerful and flexible computing technology, however, there is now a potential role for Virtual Reality (VR) software use (Penn, Rose & Johnson, 2008). VR offers a way of creating more realistic 'real world' activities within the clinic or laboratory in which task demands can be made replicable and performance can be automatically recorded (Zhang et al., 2003; Parsons, 2015). The potential use within neuropsychological assessment and rehabilitation has been recognised (Schultheis & Rizzo, 2001; Rizzo et al., 2004a), including simulating situations and tasks that people experience in their daily lives, such as shopping (Lo Priore et al., 2003) and driving (Liu et al., 1999), within safe, controlled and standardised formats (Morris, 2005).

Nevertheless, there have been few examples of VR procedures developed to test EF. An early example is the VR 'Bungalow Task' (Morris, Kotsitsa, Bramham, Brooks & Rose, 2002) which has been shown to be sensitive to planning impairments in individuals with damage to PFC (see also Sweeney, Kersel, Morris, Manly & Evans, 2010). Participants are required to take on the role of a 'removal person,' moving around the rooms of a building to find specified furniture to be removed. Furniture had to be chosen appropriately for the rooms of the house and collected in a particular order, according to its category. Time-based and event-based tests of PM were embedded in the task. A frontal lobe lesion (FLL) group visited fewer rooms and showed less efficient strategies, increased rule breaks and impairments in PM compared to controls. There is also promising evidence that VR assessments can accurately identify EF impairments in individuals with acquired brain injury (ABI), rather than FLL specifically (Sweeney et al., 2010).

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Another VR task for measuring EF is the Jansari assessment of Executive Functions (JEF©). In this task, participants take on the role of an office worker whose primary objective is to organise and prepare for a meeting and the various subtasks successfully mimic everyday multitasking requirements. The JEF© can be considered a test of multitasking as it measures a person's ability to co-ordinate a set of distinct tasks sequentially; however it does not require continuous simultaneous task co-ordination, as would be required within dual task paradigms (Fischer & Plessow, 2015). This procedure has the advantage that it has been validated with different populations and it appears to be sensitive at detecting the impact of chemicals on EF (Montgomery, Hatton, Fisk, Ogden & Jansari, 2010; Montgomery, Ashmore & Jansari, 2011; Montgomery, Seddon, Fisk, Murphy & Jansari, 2012; Jansari et al., 2013; Soar, Chapman, Lavan, Jansari & Turner, 2016). In terms of concurrent validation, Renison, Ponsford, Testa and Jansari (2008) compared individuals with ABI and control participants on their performance on the task with other measures of EF, including the Modified Six Elements Test and the Zoo Map Test from the BADS, finding comparable sensitivity. Jansari et al., (2014) also compared the performance of 17 individuals with ABI with that of 30 healthy controls across eight JEF© EF constructs, namely: planning, prioritisation, selection, creative thinking, adaptive thinking, action-based PM, event-based PM, and time-based PM. The task differentiated between individuals with ABI and controls on each construct as well as on overall performance. In this study, JEF© was better able to detect more complex aspects of executive dysfunction than the other EF measures used (Jansari et al., 2014). The task may further have merit in being used to test rehabilitation strategies or pharmacological interventions that are used with individuals with ABI (Yesavage et al., 2007; Hosenbocus & Chahal., 2013).

In the Jansari et al., (2014) study, the ABI participants had widespread and heterogeneous lesions, including brain damage ranging from right fronto-parietal to frontal, temporal, anterior, and occipital areas, also consisting of a range of aetiologies including head injuries. Whilst such participants reflect the range of patients likely to be encountered in a neurorehabilitation setting, there are advantages in validating a task in groups of individuals who have more circumscribed brain lesions likely to affect EF. Studying the effects of focal brain lesions is a way of testing 'proof of principle' relating to specific tasks when considering the anatomical and functional relationships of particular brain areas. Additionally measured deficits can be shown to

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be more specific to the intended function, rather than a consequence of general under-function. Additionally, neurosurgical mapping techniques with focal lesion patients can demonstrate which neurocognitive systems are involved in task performance (e.g. Manes et al., 2002; Hornak et al., 2004; Pullen, Morris, Kerr, Bullock & Selway, 2006; Bramham et al., 2009; Lovstad et al., 2012).

In the present study, individuals with specific unilateral and bilateral surgical excisions for tumours in the frontal lobes were tested on JEF©, and their performance was compared with that of healthy controls. The primary objective of the current study was to determine whether a VR test of multitasking would detect the difficulties in EF that are frequently reported by and/or observed in individuals with circumscribed FLL in everyday life. Comparisons were made with non-VR EF measures and questionnaires frequently used in clinical practice. In line with Morris et al., (2002) we expected to find that the FLL group were impaired relative to controls on particular constructs of the JEF©, such as planning and PM.

METHODS

Participants

Nineteen individuals with focal frontal lobe (FLL) lesions were recruited from the joint neuro-oncology clinic at King's College Hospital, London. Only individuals with lesions exclusive to the PFC were selected. The exclusion criteria included the following: the presence of additional neurological conditions, autism spectrum disorder or attention deficit hyperactivity disorder, psychiatric conditions, a history of dependency on drugs or alcohol, language impairment, hearing or visual difficulties. The test procedures all involved verbal instructions in English, and as a consequence, potential participants who were not fluent in English were also excluded. During the first testing session, participants were screened on measures of current intellectual functioning and only those who had had IQ scores >70 were included. They were tested at least six months post-surgery (M: 38.52, SD: 36.09, range: 6-106) to reduce acute post-operative effects on cognitive functioning. All lived independently in the community.

Nineteen healthy controls were recruited, group matched with the FLL group for age, years of education, estimated pre-morbid IQ (using the Test of Premorbid Functioning, TOPF, Wechsler, 2011) and gender (FLL: 10F, 9M, controls: 10F, 9M, see Table 1).

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There was a statistically significant difference between groups on Full-Scale IQ measured using the abbreviated two-subtest version (Vocabulary and Matrix Reasoning) of the Wechsler Abbreviated Scale of Intelligence (WASI-II; Wechsler, 2011).

Participants gave written informed consent and the study was approved by a local research governance committee and the London Bridge National Research Ethics Service Committee.

(Table 1 about here)

The method used by Rowe, Bullock, Polkey & Morris (2001) was adopted to classify lesion areas (see Table 2). These were verified by the neurosurgeon by inspection of Magnetic Resonance Imaging (MRI) or Computerised Tomography (CT) scans and neuroradiological reports defining brain involvement in terms of Brodmann areas (Brodmann, 1909). Seven individuals had right frontal lobe lesions, nine had left frontal lobe lesions and three had bilateral lesions. Brodmann encroachment was amalgamated into three main PFC regions, (see Table 2), defined anatomically as dorsolateral (Brodmann areas 44, 45 and 46), medial (Brodmann areas 8, 9, 24, 25 and 32) and orbitofrontal regions (Brodmann areas 10, 11, 12 and 47).

(Table 2 about here)

Measures

A battery of standardised tests was administered to all participants to accurately characterise the sample and enable comparisons between JEF© and existing measures. In addition to intellectual functioning, these measured, memory and EF. The Logical Memory and Visual Reproduction subtests of the Wechsler Memory Scale- Fourth UK Edition (WMS-IV; Wechsler, 2009) were given as measures of auditory memory and visual memory respectively, with immediate recall and delayed recall and recognition memory tested. Measures of working memory consisted of the Digit Span subtest of the Wechsler Memory Scale-Third UK Edition (WMS-III; Wechsler, 1997) and the Spatial Span subtest of the Wechsler Memory Scale-Third UK Edition (WMS-III; Wechsler, 1997). The Sustained Attention to Response Task (SART; Robertson, Manly, Andrade, Baddeley, and Yiend, 1997) measured attention, administered using a

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laptop computer (see Table 6).

In addition, both groups were tested on a battery of frequently used EF tests, namely the Trail Making Test Part A and Part B (TMT; Army Individual Test Battery 1944; Reitan, 1992), the Hayling Sentence Completion Test and the Brixton Spatial Anticipation Test (Burgess and Shallice, 1997) and verbal fluency FAS measures from the Delis-Kaplan Executive Function System (DKEFS; Delis, Kaplan & Kramer, 2001).

Questionnaires

Two questionnaires that measure EF and are used widely in brain injury populations were administered to all participants. This includes the Frontal Systems Behaviour Scale (FrSBe, Grace & Malloy, 2001), a 46-item rating scale that provides a brief, reliable, and valid measure of three frontal systems behavioural syndromes: apathy, disinhibition, and executive dysfunction. The FrSBe quantifies behavioural changes over time by including both baseline (retrospective) and current assessments of behaviour, including apathy, disinhibition and executive function. Healthy controls were asked to only complete current ratings. In addition, the study used a revised and extended version of the Dysexecutive Questionnaire (DEX; Wilson, Alderman, Burgess, Emslie & Evans, 1997) developed by Simblett, Ring and Bateman (2016). Total scores were calculated for each of the four domains: Emotional-Behavioural Self-regulation (maximum score /36), Activation (maximum score /32), Metacognition (maximum score /32) and Executive Cognition (maximum score/ 40). Higher scores indicated greater difficulties.

Measures of apathy, anxiety and depression were also used, since such difficulties are common in people with tumours involving the frontal lobe. For apathy, the Apathy Evaluation Scale (AES) was used, an 18-item scale developed by Marin (1991) specifically for use in populations with brain-related pathology. The AES evaluates the overt behavioural, cognitive, and emotional aspects of goal-directed behaviour (Marin, 1991). Each AES form yielded a total score, with higher scores indicating the presence of a greater degree of apathy. Cut-off scores of 41 were used as stated in the AES guidelines. The Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) was used as a screening measure of anxiety and depression, with the two subscales each scoring in the ranges of 0-21: scores of 0-7 are considered normal, 8-10 borderline, and above 11 clinically significant.

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The Jansari assessment of Executive Functions (JEF©)

This task was presented in a desktop VR environment, on a laptop, with the systems unit using Microsoft Visual Basic and the 3D add-on software 3d State (http://www.3dstate.co.uk/wordpress/) as a platform for the specific software (see Figures 1-2 for visual representations). It was administered following the standard procedure outlined in the manual (Jansari, unpublished).

JEF© is set in an office environment and the participant is asked to imagine that they are starting their first day as an office worker. A scenario is presented whereby their manager has been called away so will not be able to oversee their work, but has left the participant a list of jobs that they need to do to prepare for a meeting. There are two rooms in the environment, an office and a meeting room. A corridor links these rooms and the participant can move freely between them. Realistic tasks that can be found in an average office environment are chosen for eight different cognitive constructs: planning, prioritisation, selection, creative thinking, adaptive thinking, time-based PM, event-based PM and action-based PM. The constructs were devised based on common areas of impairment in individuals with dysexecutive syndrome that are shown to be crucial in multitasking performance, such as planning and problem solving ability (Shallice & Burgess, 1991; Mateer, 1999; Burgess, Veitch, de Lacy Costello, & Shallice, 2000; Lezak, Howieson, & Loring, 2004). The three different types of PM were measured, given that these can be dissociated in patients with brain damage (Ellis, 1996; Ellis & Kvavilashvili, 2000; Burgess et al., 2000). (See Table 8 for further details of some constructs and their scoring). Tasks were designed to be ambiguous and have multiple solutions, to mimic real-life situations. The three main task categories related to a 'meeting', doing 'the post', and additional time-based tasks. A printed scenario sheet, the Manager's Tasks for Completion, and all relevant documents (post diary, list of the post to be sent, agenda topics, My Notes For Manager and plan of action) were provided to the participant, outside the virtual environment. They remained next to the computer throughout the assessment for participants. Participants were allowed to write on the material; for example, they could add to the notes for the manager or tick off the tasks on their plan of action, and use this as an aid to reduce the likelihood of errors being made due to failures of retrospective memory.

Before starting the task, the participant practised manoeuvring within the virtual environment using the arrow keys on a standard computer keypad. Objects

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were picked up by clicking the computer mouse. At the beginning, the task scenario was read to the participant from a script. After reading the Manager's Tasks for Completion, participants were required to construct a plan of action in their own time, before the VR component of the assessment formally commenced. The experimenter directed participants to the printed materials if they had task-specific questions. In addition, various PM tasks were built into the procedure. Specifically, individuals were handed a number of memoranda throughout the assessment, which required them to complete additional tasks at set points later in time. The responsibility for planning the overall task was given to participants with no clues as to solutions or courses of action. They were given 40 minutes to complete the list of tasks in time for the beginning of the meeting. If they exceeded this, they were allowed to continue and their total time taken was recorded, but not included in the overall score. The start time and the meeting time were both written down and participants had a digital clock in front of them so that they could monitor the time. The experimenter observed the assessment and filled out the score-sheet while participants were completing the task.

(Figures 1-2 about here)

DATA ANALYSIS

The analysis used t-tests, one-way analysis of variance (ANOVAs) and analysis of co-variance (ANCOVAs) statistics, conducted using SPSS (version 21; IBM Corp., 2012). Non-parametric analyses, such as the Mann Whitney test were used where the Shapiro-Wilk normality test demonstrated that the data was not normally distributed.

RESULTS

Background neuropsychological measures

For verbal memory (Logical Memory test), there were no significant differences between groups for immediate $t(36)= -0.53$, $p=0.59$ or delayed recall $t(36)= 0.15$, $p=0.88$. The FLL group had significantly worse immediate ($t(36) =2.7$, $p<.01$, $d=-.87$) and delayed ($t(36)=2.6$, $p<.02$, $d=-0.84$) visual recall on the Visual Reproduction test compared to controls, but no difference from the controls in visual recognition memory ($t(36)=1.3$, $p=0.18$). There were no differences on digit span $t(36)=0.87$, $p=0.38$, spatial span $t(36)=0.87$, $p=0.38$ and on the SART (errors of commission

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t(36)=0.95, p=0.34, omission t(36)=1.3, p=0.19 and mean reaction time t(36)=0.45, p=0.65) (See Table 6).

Non-VR EF measures

The non-VR EF measure results are shown in Table 3. The FLL group were significantly slower than the controls on the comparison Trail Making Test part A, but not on the Trail Making B, which measures mental flexibility. There were also no significant differences between groups on the Hayling and the Brixton. There was a marginally significant difference between groups in the total number of items generated on verbal fluency. Analyses were also conducted using an ANCOVA to covary for the significant difference in IQ between groups; there were no significant differences across any of the EF measures when the effect of FSIQ was covaried.

(Table 3 about here)

These findings suggest that with the exception of Trail Making Test part A, the standard measures of EF were unable to distinguish between the FLL and control groups.

Questionnaires

Questionnaires were completed by 16 individuals in the FLL group and 19 individuals in the control group through self-report. In addition, 10 informants of individuals in the FLL group completed questionnaires. Individuals with FLL reported significantly higher symptoms on the FrSBe as rated currently, compared to before their surgery t(13)=2.28, p<.041, d=-0.47 (after: M: 56.23, SD: 16.94, before: M: 48.7, SD: 11.17).

A comparison of the FLL and control groups revealed no significant differences between groups on the FrSBE t(27)=1.20, p=.24 or the four scales of the DEX: emotional behavioural self-regulation scale t(33)=1.48, p=0.14, activation scale t(33)=1.16, p=0.25, metacognition scale t(33)=1.72, p=0.95 and executive cognition scale t(33)=1.78, p=0.083. There were no between group differences on the AES t(32)=.44, p=0.66 or on HADS anxiety t(33)=1.68, p=0.10 and HADS depression scales t(33)=1.68, p=0.10.

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On the AES, one participant in the FLL group had scores above the cut-off on both self and informant ratings and another had scores above the cut-off, for the informant ratings. All the FLL group had scores within the normal range for anxiety and depression on the HADS (0-7), with the exception of one participant, who had a score of 11 falling in the moderate range for anxiety (11-14). This patient did not, however, show high test anxiety.

The Jansari assessment of Executive Functions

All tasks were scored on a three-point scale: 0 for failure, 1 for a partial or non-optimal completion and 2 for satisfactory completion (see Table 8 for further details). Construct scores were created by amalgamation of task scores with some constructs involving only one task and others including two; to allow comparisons, a percentage score was calculated for each construct. An overall percentage score was obtained by averaging the individual construct scores. In all, nine scores were derived for each participant, eight for the individual constructs and one for overall performance. A between subjects ANOVA demonstrated that the overall score of the FLL group was significantly lower than that of the control group, with the effect size of this difference being considered large according to Cohen's (1992) guidelines, $F(2, 37)=17.21$, $p<.001$, $\eta_p^2 =0.32$ (see Figure 3). Given the significant difference in FSIQ between groups, an ANCOVA was conducted to covary for the effect of FSIQ between groups. However, the difference remained significant $F(2, 37)=9.89$, $p<.003$, $\eta_p^2 =.22$ (group), $F(2, 37)=13.17$, $p<.001$, $\eta_p^2 =.27$ (FSIQ).

(Figure 3 about here)

Comparisons of the eight individual constructs were conducted using non-parametric analyses. There was a significant difference between groups on planning: $U(38) =254$, $p<.03$, creative thinking: $U(38) =252$, $p<.03$, adaptive thinking: $U(38) = 266.5$, $p<.01$, event-based PM: $U(38) =272.5$, $p<.006$, and time-based PM: $U(38) =276.5$, $p<.004$ (see Table 4 for effect sizes). There were no significant differences between groups for prioritisation, selection, or action-based PM.

Analysis of individual performance

To assess individual performance within the FLL group relative to the control group, percentiles were created for each construct using the control group data (see Table 4).

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(Table 4 about here)

Individuals in the FLL group with scores below the 5th or between the 6th and 10th percentile were then identified for each construct (see Table 5), and their frequencies examined. For the 5th percentile cut-off, the constructs upon which the greatest number of individuals within the FLL group showed impairment were adaptive thinking (n=6), followed by creative thinking (n=5), action-based PM (n=5), time-based PM (n=4) and prioritisation (n=4). It should be noted that some individuals in the control group also had impaired scores for two constructs: creative thinking (n=3) and action-based PM (n=5). Performance across the constructs was variable. None of the FLL individuals were impaired in all domains. Three out of nineteen individuals had impaired overall JEF scores. Five individuals each had impaired performance on none, one, and two constructs. This was followed by three constructs (n=1), or four constructs (n=3). When looking at the frequencies of FLL individuals with scores in the 6-10th percentile range, the average score had the greatest number (n=12), followed by adaptive thinking (n=6), prioritisation (n=6), creative thinking (n=5) and action-based PM (n=5). Six individuals in the FLL group had scores in this range on three constructs, this was followed by two constructs (n=3), five constructs (n=3), four constructs (n=1) and one construct (n=1).

(Table 5 about here)

Executive Function composite

The overall task score on the JEF© may be better able to identify group differences because it acts as a composite for many different individual task constructs including, for example, planning, prioritisation and prospective memory. The EF tasks used in this study measure fewer constructs than the JEF©, for example, the Hayling measures inhibition and response initiation, so the tasks may not be directly comparable to the overall JEF© score. In order to address this difference in measurement, an EF composite measure was created from the individual EF measures (Trails A percentile, Trails B percentile, Brixton scaled, Hayling scaled and FAS percentile) and this EF composite was compared with the overall score. To calculate the composite score, each individual EF measure was converted into a z-score using the mean and standard deviation of the healthy control group to ensure that all measures were on the same scale. An inter-item total correlation was carried out to ensure each z-score converted

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EF measure was a suitable variable to be included in the composite measure. An inter-item correlation cut-off of .03 was used to justify the inclusion of each measure and each item was above .05 (Streiner & Norman, 2008). Cronbach's alpha was .66 and this value did not change considerably when each measure was removed. Therefore, all five measures were included in the composite.

Independent t-tests demonstrated a significant difference between groups on the composite non-VR EF z-score measure $t(35)=2.05$, $p<.04$, $d=-0.66$ (FLL: M: -.46, SD: 1.30, control: M: .00, SD:1.00) as well as a significant difference in the overall JEF© z-score $t(36)=4.14$, $p<.001$, $d=-1.34$ (FLL: M: -1.56, SD: 1.30, control: M: .00, SD: 1.0). For the FLL group, a paired t-test showed that the overall JEF© z-score was significantly lower than the EF composite z-score $t(18)=3.48$, $p<.003$, $d=-0.92$ (FLL composite: M: -.46, SD: 1.30; FLL JEF© : M: -1.56, SD: 1.30) indicating that the JEF© is better at differentiating between groups compared to the EF composite.

Correlations between VR measures and standard test measures

The correlations between VR and standard test measures were explored for each main group. The only association was between the TMT B and the SART reaction time, in the control group, this being a trend, not surviving Bonferroni correction ($r=0.537$, $n=19$, $p=.026$.

Sensitivity and specificity analysis

The ROC curve graphically displays the trade-off between sensitivity and specificity and is useful in assigning the best cut-offs for clinical use (Florkowski, 2008). The area under the curve (AUC) determines the inherent ability of a test to discriminate between "healthy and diseased populations" (Hajian-Tilaki, 2013). In a Receiver Operating Characteristic (ROC) curve analysis applied to the overall JEF© score, the AUC was .83 and a cut-off value of 66.15 was determined. This resulted in 73.7% sensitivity and 89.5% specificity for the average score. This indicated that 73.7% of FLL individuals were correctly classified and 10.5% controls were incorrectly classified, which suggests good sensitivity and specificity (Harris & Taylor, 2014).

(Figure 4 about here)

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Lesion analyses

Supplementary analyses were conducted to investigate the effects of laterality and location of lesions within the frontal lobe group in terms of JEF© performance and the non-VR EF measures. The method used by Rowe et al., (2001) was adopted, where individuals who had an operation in a specific location were compared to the rest of the sample who did not have an operation in this region. For laterality analyses, unilateral left (n = 9) were compared with unilateral right hemisphere lesions (n = 7) (this excluded the three bilateral lesion individuals); for lesion location analyses dorsolateral, non-medial lesions (n = 4) were compared with non-dorsolateral, medial lesions (n = 15) and finally, orbitofrontal lesions (n=6) were compared with non-orbitofrontal lesions (n=13). No significant effects of laterality or lesion location were found on JEF© or non-VR EF measures.

DISCUSSION

A comparison between individuals with FLL and matched controls on an ecologically valid VR measure of EF, namely JEF©, demonstrated an overall group difference. The FLL group were impaired on five out of eight possible task constructs: planning, creative thinking, adaptive thinking, event-based PM and time-based PM, with no significant difference on prioritisation, selection, and action-based PM. In this group of people with circumscribed FLL lesions, the VR measure was shown to be sensitive to EF deficits whilst frequently used clinical tests of EF were not. Across all the standard EF tests, both groups differed on only one task: part A of the Trail Making Test. Since, part B of the test showed no difference, this deficit might be accounted for by processing speed reduction rather than set-shifting impairment.

In the study by Jansari (2014), the deficits were found in more constructs, which may reflect the more specific lesions and less generalised effect in our study. In the current study, the groups were matched on age, years of education, and pre-morbid IQ, whereas in the previous study, the groups were only matched on age and pre-morbid IQ. The ABI group tested by Jansari et al., (2014) used a mixed clinical sample, including participants with injuries of various aetiologies including stroke and traumatic brain injury, which are associated with larger lesions with more diffuse

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damage. They were thus more likely to have additional cognitive difficulties, which would exacerbate group differences in JEF© performance.

An analysis of individual performance in the FLL group using control group percentiles demonstrated that not all individuals were impaired on the same constructs. This finding of heterogeneity of performance was also found in Jansari et al.,'s (2014) study and reflects the fact that individual EF tasks in general tend to have low correlations with one another, including when measured using ecologically valid tasks (Burgess, Simons, Coates & Shannon, 2005).

There were no group differences on the questionnaires and no discrepancies between the FLL self and other report measures. This finding is consistent with other research. Gregg et al., (2014) compared frontal and non-frontal tumour groups on the FrSBe and found no differences between self and informant reports within their frontal group. In addition, Lengenfelder et al., (2015) found no significant differences between individuals with Traumatic Brain Injury (TBI) and family members' reports for any of the FrSBe subscales. The FLL group reported significantly higher post-injury difficulties as reflected in the overall scores of the FrSBe relative to pre-injury scores. This finding also replicates other research studies with similar populations (Gregg et al., 2014; Lengenfelder et al., 2015). The lack of significant difference between FLL and control groups on any of the questionnaire measures is notable, with little research directly comparing questionnaire responses from individuals with frontal lobe lesions and healthy controls. Grace, Stout and Malloy (1999) found significantly more 'frontal behaviour' in frontal lesion groups than controls. The lack of sensitivity in the current study might reflect the fact that we recruited subjects from an outpatient neuro-oncology department where patients attended for routine oncological follow up, rather than because they had cognitive or behavioural difficulties following their surgery. If the changes were subtle, they might be detected through a direct pre-versus post- injury comparison, but not when comparing with a normal group, where natural variations in functioning between individuals could mask behavioural change. Additionally, the lack of group difference might be partially explained by insight problems in the FLL group. In other studies, individuals with FLL may be recruited from inpatient and rehabilitation settings where these difficulties may be more prominent. Our findings may therefore indicate that the more subtle behaviour changes are not picked up in such patients by questioning, but can be measured using VR ecological valid procedures.

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The FLL and controls are distinguished on JEF© average performance and across five individual constructs. In contrast, the majority of EF measures did not distinguish between groups. These findings are congruent with a number of other studies in the field demonstrating a group difference on ecologically valid measures and comparable performance on non-VR well-used EF measures (Eslinger & Damasio, 1985; Shallice & Burgess, 1991; Burgess et al., 1998; 2006).

As there is a composite JEF© score sampling various executive domains, a composite measure was created for the individual non-VR EF tasks in order to provide a direct comparison with the VR measure. There was a significant difference in composite EF scores between FLL and control groups. A within-group analysis demonstrated the FLL group had poorer overall JEF© z-scores than EF composite z-scores. However, just as for previously used EF measures, whilst a group finding supports use of a composite score, heterogeneity between individuals on what particular measures show deficits suggest consideration of individual scores.

The current study is the first to use a clinical cut-off in order to explore the specificity and sensitivity of the JEF©. The focal lesion group was selected on the basis of the fact that they were a conservative test for sensitivity; they were unimpaired on other EF tasks with apparently more subtle deficits. The fact that the JEF© was able to distinguish between a group with such difficulties and controls suggests it has good sensitivity and specificity and indicates that other clinical groups may have larger deficits on the JEF©. More research should be carried out using the JEF© to differentiate between larger clinical samples and establish further clinical cut-offs for different conditions. Until further research is carried out exploring the validity and reliability of the JEF©, the cut-off should be used with caution, alongside other assessment measures and information about daily functioning. There is no gold standard measure currently available to establish construct validity; nevertheless, a short comparison between available psychometric tests such as the BADS (Wilson et al., 1996) and the JEF© would provide useful additional information. The JEF© could also be compared to other ecological tasks such as the Bungalow Task (Morris, Kotsitsa, Bramham, Brooks & Rose, 2002) or the Multitasking in the City Test (Jovanovski, Zakzanis, Ruttan, Campbell, Erb & Nussbaum, 2012) to further establish its validity. Reliability was not explored in the current study; however, Jansari (2008) has previously demonstrated that the JEF© has good inter-rater reliability, in which

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raters used the scoresheet to score the performance of individuals with ABI, the correlations ranged from r=0.956 to r=1.0.

The action-based PM was the most difficult task for those in the FLL group, and the second most-difficult task for those in the control group, with both groups achieving scores of 30-40%. There is little research on action-based PM. It is considered easier than time and event-based PM because it does not require the interruption of ongoing activity (Kvavilashvili & Ellis, 1996). Shum, Valentine and Cutmore (1999) showed that individuals with TBI and controls had better performance on action-based than time and event-based PM tasks. However, Brewer et al., (2011) found that action-based performance was more impaired than comparable event-based conditions in healthy volunteers. One potential contributor to the relatively weak performance on the JEF© action-based PM tasks is that this construct differs from the others, as it is a more complicated task, requiring two steps. The participant has to carry out an action and then write down that it had been completed rather than just reorganise the post. The result on action-based PM was not the focus of the current study, yet it raises interesting questions for further research.

Our results indicate JEF© is suitable for use with individuals with FLL, with all participants able to follow the basic procedures and navigate around the office scenario. The PFC group was challenged by the VR procedure and this may account for the task sensitivity. Marcotte and colleagues (2010) noted the difficulty in developing measures reflective of daily functioning in a manner that is "sufficiently challenging to provide a distribution of functioning across 'normal' individuals" (p24) such that ceiling and floor effects are avoided. JEF© was found to be appropriate for the range of control participants and patients used in the study and was not subject to such effects.

In the current study, supplementary analyses within the frontal lobe group indicated that there were no laterality and lesion location effects. The sample size and range of lesions mean it was not possible to make any firm conclusions on these matters. The majority of individuals recruited in the FLL group had parafalcine tumours, which resulted in medial lesions. Further exploration with a bigger and more varied sample of individuals with FLL needs to be conducted. Additionally, studies with larger sample sizes of individuals with FLL would also answer questions regarding how performance on the JEF© fits with theoretical accounts regarding fractionation of the EF system (Stuss and Alexander, 2007).

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Conclusions and implications

The study demonstrated that individuals with FLL did not differ significantly from matched controls in their self-reported difficulties with executive functioning, or on performance on non-VR EF measures. However, the FLL group were impaired relative to controls on their JEF© performance. The present study expands on previous research, providing support for the use of VR ecologically-valid measures that discriminate between individuals with FLL and controls. The findings suggest the task measures EF dysfunction more specifically related to frontal function. The task highlights specific cognitive constructs that individuals have difficulty with, for example, prospective memory, which can be directly targeted in interventions. There is still a need for more research to be carried out in this area to explore the test psychometric properties. In order to assess real life performance, using VR procedures such as the JEF© can be advantageous where more structured procedures or questionnaires may not be sufficiently sensitive to change. The JEF© and other VR approaches potentially provide an opportunity to observe an individual's performance across a range of activities, but in the clinic or laboratory. However, an important implication is that one should not presume that VR and non-VR measures of EF capture the same level of underlying process or neural substrate. Both measures may be useful and valuable and in combination they provide a more complete picture during clinical assessment.

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Tables

	FLL group n=19			Control group n=19			Statistics		
	M	SD	Range	M	SD	Range	t	p	d
Age (Years)	46.3	12.2	29.5-67.7	42.5	12.8	25.10-69.0	0.94	0.35	0.3
Years of education	15.7	3.4	10-22	16.8	3.3	11-24	-1.01	0.31	-0.32
TOPF (premorbid IQ)	101.2	10	86-123	107.3	9.9	88-121	-1.76	0.08	-0.61
FSIQ	98.36	12.17	76-123	106.73	9.62	81-123	-2.35	0.02*	-0.76

Table 1: Demographics and matching of the frontal lobe lesion and control group, * indicates a significant difference between groups

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	Gender	Left/ Right/ Bilateral	Orbito frontal	Medial	Dorsolateral	Tumour classification
1	M	R	X		X	Oligodendroglioma grade II
2	F	L		X		Oligodendroglioma grade II
3	M	R		X		Oligodendroglioma grade II
4	M	L	X	X		Glioblastoma grade IV
5	M	L		X		Meningioma grade II
6	M	L		X		Oligodendroglioma grade II
7	F	L		X		Meningioma grade II
8	F	R		X		Meningioma grade I
9	F	L	X		X	Primitive Neuroectodermal tumour grade IV
10	F	L	X		X	Glioblastoma grade IV
11	F	L		X		Meningioma grade I
12	F	L		X		Meningioma grade II
13	M	B		X		Meningioma grade II
14	F	R		X		Meningioma grade II
15	F	R			X	Gliola grade I
16	M	R	X	X		Oligodendroglioma grade II
17	M	R		X		Meningioma grade II
18	F	B	X	X		Meningioma grade I
19	M	B		X		Meningioma grade II

Table 2: Frontal lobe lesion group characteristics

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	FLL group			Control group			Statistics		
	M	SD	Range	M	SD	Range	t	p	d
TMT Part A time (secs)	32.63	16.07	15.20-70.26	23.89	7.26	11.51-36.88	2.14	0.03*	0.71
TMT Part B time (secs)	59.3	25.5	11.23-113.70	46.69	19.76	26.58-99.31	1.66	0.10	0.55
TMT Part A percentile	51.41	32.56	1-90	60	24.2	10-90	-0.9	0.37	-0.3
TMT Part B percentile	49.11	36.4	1-90	66.8	29	10-90	-1.19	0.24	-0.39
Hayling scaled score	5.76	0.9	4-7	6.21	1.22	4-9	-1.22	0.22	-0.4
Brixton scaled score	5.7	1.86	2-9	6.81	2	1-10	-1.6	0.11	-0.53
FAS total recall	39.76	11.9	18-67	47.7	11.7	22-64	-2.01	0.05*	-0.67
FAS percentile	46.4	27.82	10-90	57.36	26.84	10-90	-1.19	0.24	-0.39

Table 3: Executive Function measures by overall group comparison, * indicates a significant difference between groups

Percentile	PL	PR	ST	CT	AT	APM	EPM	TPM	Average JEF score
5	33.3	50	25	0	25	0	50	50	44.1
10	50	75	50	0	25	0	50	50	58.8
16.5	66.6	75	75	7.5	25	0	82.5	57.5	67.6
35	83.3	75	75	50	50	50	100	100	70.5
50	100	100	100	50	75	50	-	-	79.4
65	-	-	-	75	75	50	-	-	82.3
83.5	-	-	-	100	100	67.5	-	-	85.2
90	-	-	-	-	-	75	-	-	91.1

Table 4: Percentiles of the control group performance across the individual JEF© constructs. Construct abbreviations (PL, planning, PR, prioritisation, ST, selective-thinking, CT, creative-thinking, AT, adaptive-thinking, APM, action-based PM, EPM, event-based PM, TPM, time-based PM.

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N	PL	PR	ST	CT	AT	APM	TPM	EPM	Average JEF score	NCI 5th	NCI 6-10th
1	**	**	-	-	-	-	-	-	*	2	3
2	-	-	-	-	-	**	-	-	*	1	2
3	-	-	-	-	-	-	**	-	*	1	2
4	-	-	*	-	-	-	**	-	*	1	3
5	*	**	-	-	-	-	-	-	*	1	3
6	-	-	-	-	-	-	-	-	-	0	0
7	-	-	-	-	**	-	**	-	*	2	3
8	-	-	-	-	**	-	**	-	*	2	3
9	-	-	-	**	**	-	-	-	*	2	3
10	-	-	-	-	-	-	-	-	-	0	0
11	**	*	-	-	**	-	-	**	**	4	5
12	-	-	-	**	-	**	-	-	-	2	2
13	-	-	-	-	-	-	-	-	-	0	0
14	-	-	-	-	-	**	-	-	-	1	1
15	-	-	-	-	-	-	-	-	-	0	0
16	*	**	-	**	-	**	-	-	*	3	5
17	-	**	-	**	**	-	-	-	**	4	4
18	-	*	-	**	**	**	-	-	**	4	5
19	-	-	-	-	-	-	-	-	-	0	0
NPI 5th	2	4	0	5	6	5	4	1	3		
NPI 6-10th	4	6	1	5	6	5	4	1	12		

Table 5: Number of individuals with frontal lobe lesions who scored below the control group 5th and 6-10th percentile across the cognitive constructs. - = above 10th percentile, * <= 6-10th percentile cut-off, **5th percentile cut-off. N, participant number, NCI, the number of constructs impaired for each individual, NPI, the number of FLL individuals impaired on each construct).

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	FLL Group n=19			Control Group n=19			Statistics		
	M	SD	Range	M	SD	Range	t	p	d
Immediate verbal recall scaled score	9.94	3.09	1-14	10.42	2.24	6-13	-0.53	0.59	-0.17
Delayed verbal recall scaled score	10.41	3.39	1-14	10.26	2.49	4-14	0.15	0.88	0.04
Verbal recognition percentile	6.11	1.21	3-7	5.78	1.39	2-7	0.74	0.46	0.24
Immediate visual recall scaled score	9.57	2.87	4-15	11.84	2.11	8-15	-2.7	0.01*	-0.87
Delayed visual recall scaled score	9.64	2.84	4-17	12.26	3.01	7-18	-2.6	0.02*	-0.84
Visual recognition percentile	5.82	1.28	2-7	6.31	0.88	4-7	-1.3	0.18	-0.42
Digit span scaled score	11.7	3.49	7-19	12.62	2.41	9-18	-0.87	0.38	-0.28
Spatial span scaled score	9.68	2.7	5-15	10.41	2.2	5-14	-0.87	0.38	-0.28
SART number of errors of commission	12.27	5.71	1-23	10.17	7.2	1-24	0.95	0.34	0.30
SART number of errors of omission	15.72	5.8	7-27	18.7	7.43	7-38	-1.3	0.19	-0.42
SART mean reaction time (Msecs)	327.95	68.72	200.60-499.30	316.65	78.27	198.90-528	0.45	0.65	0.14

Table 6: Frontal lobe lesion and control group performance on background neuropsychological measures, * indicates a significant difference between the groups

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	FLL Group		Control Group		Statistics		
	Median	IQR	Median	IQR	U	p	d
DEX Self Emotional behavioural self-regulation	6	2.5	4	4	104.5	0.11	-0.53
DEX Self Activation	7	6	6	4	114	0.21	-0.40
DEX Self Metacognition	6.5	6.5	7	7	112	0.19	-0.43
DEX Self Executive Cognition	7	12.5	5	6	117	0.25	-0.36
DEX Other Emotional Behavioural Self-regulation	6	9	N/A	N/A	N/A	N/A	N/A
DEX Other Activation	3	13	N/A	N/A	N/A	N/A	N/A
DEX Other Metacognition	6	10	N/A	N/A	N/A	N/A	N/A
DEX Other Executive Cognition	6	10	N/A	N/A	N/A	N/A	N/A
FRSBE Self Overall after T-score	60	22	49	18	77.5	0.24	-0.34
FRSBE Self Apathy after T-score	51	22	48	10.5	85	0.42	-0.26
FRSBE Self Disinhibition after T-score	54	23	48	20	86	0.44	-0.25
FRSBE Self Executive Dysfunction after T-score	55	19	49.5	13	88	0.50	-0.22
FRSBE Other Overall after T-score	52	15	N/A	N/A	N/A	N/A	N/A
FRSBE Other Apathy after T-score	50	14	N/A	N/A	N/A	N/A	N/A
FRSBE Other Disinhibition after T-score	48	9	N/A	N/A	N/A	N/A	N/A
FRSBE Other Executive Dysfunction after T-score	50	6	N/A	N/A	N/A	N/A	N/A
AES Self	26	17	25	10	121	0.47	-0.24
AES Other	26	16	N/A	N/A	N/A	N/A	N/A
HADS Anxiety	4.5	5.5	4	5	107.5	0.14	0.49
HADS Depression	4	5	1	3	114	0.21	-0.42

Table 7: Questionnaire measures for the frontal lobe lesion versus control groups

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CONSTRUCT	TASK	REQUIREMENTS
Planning (6) Order items in a logical manner.	Write plan of action (4)	Plan includes all tasks (2) 25% of tasks are omitted (1) More than 25% of tasks omitted (0)
		Meeting, post, and time-based tasks placed together – 10% leeway (2) Only events regarding meeting placed together, other haphazard OR more than 10% leeway (1) No change/very little change from Managers' Tasks For Completion (0)
	Arrange furniture for meeting (2)	All members can see the whiteboard (2) 25% cannot see the whiteboard or 25% have their backs to the internal members of the meeting (1) Random arrangement (0)
Action-based PM (4) Remember to execute a task cued by a stimulus in the task.	Update the Post Diary (2)	The parcel is added immediately (2) The parcel is added at a later date, i.e. after checking the Plan of Action at the end of the task, OR written on My Notes For Manager (1) The Post Diary is not updated (0)
	Record if the equipment breaks (2)	It is recorded on My Notes For Manager when the OHP breaks (2) It is recorded on the Plan of Action when the OHP breaks, or only after referring to the Plan of Action (1) Nothing is written down (0)
Event-based PM (4) Remember to perform a task cued by an event.	Note the times of the fire alarms (2)	Both alarms are recorded on My Notes For Manager (2) Only 1 alarm is recorded, they are written on the Plan of Action or are written only after referring to the Plan of Action (1) None of the times are recorded (0)
	Turn on coffee machine when the first person arrives (2)	Turn on the coffee machine after the memo arrives without referring to the Plan of Action (2) Turn on the coffee machine after referring to the Plan of Action (1) The coffee machine is not turned on, or it is turned on before the memo arrives (0)
Time-based PM (4) Remember to perform an action at a certain time point.	Turn on projector 10 minutes before the meeting starts (2)	Turn on projector at exact time (2) Turn on projector but not at designated time (1) Never turn on the projector (0)
	Indicate whether the company postman has arrived (2)	Write down that the company postman has not arrived and be aware that the post must be sent another way (2) It is not recorded that the company postman has *not* arrived but the post is sent another way OR it *is* recorded that the postman did not arrive but the post is not sent in another way (1) Do not notice that the company postman has not arrived to take the post (0)

Table 8: Example of construct descriptions and scoring

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Figure 1: Screen capture of the Virtual Reality office and meeting room

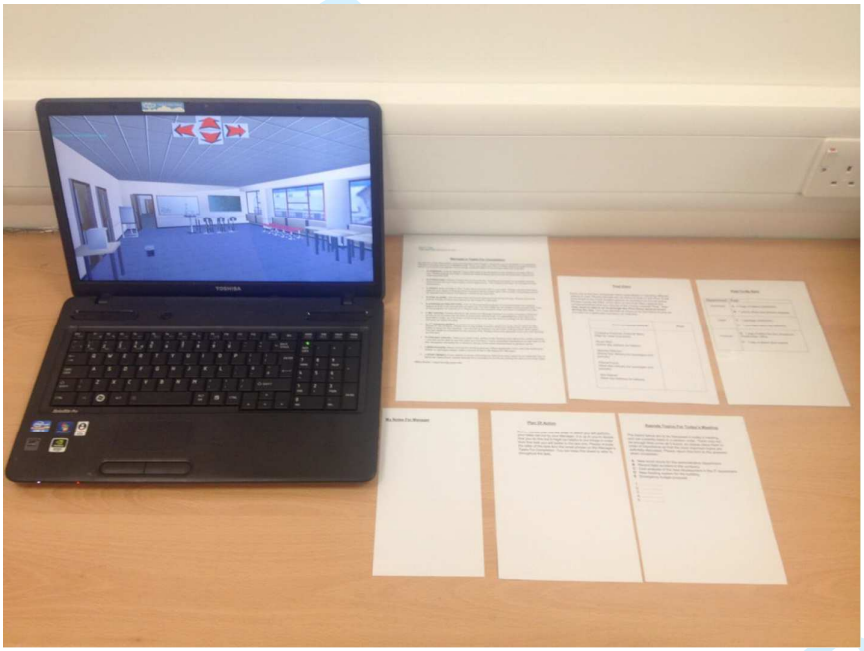

Figure 2: Setup of laptop and materials at the start of the assessment

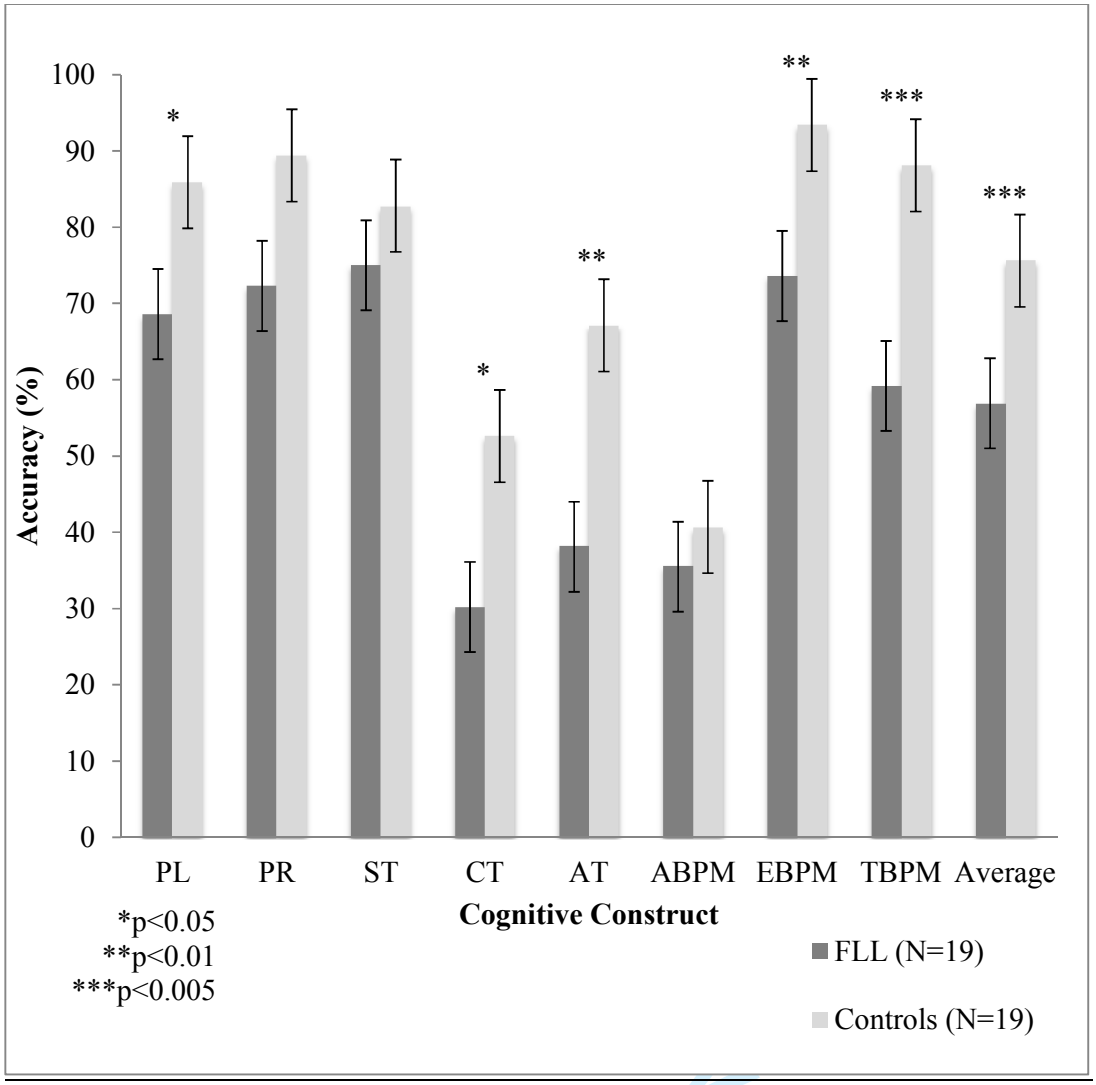

Figure 3: Performance on each construct on the JEF© for the frontal lobe lesion and control groups (error bars represent one standard error). Construct abbreviations (PL, planning, PR, prioritisation, ST, selective-thinking, CT, creative-thinking, AT, adaptive-thinking, APM, action-based PM, EPM, event-based PM, TPM, time-based PM.

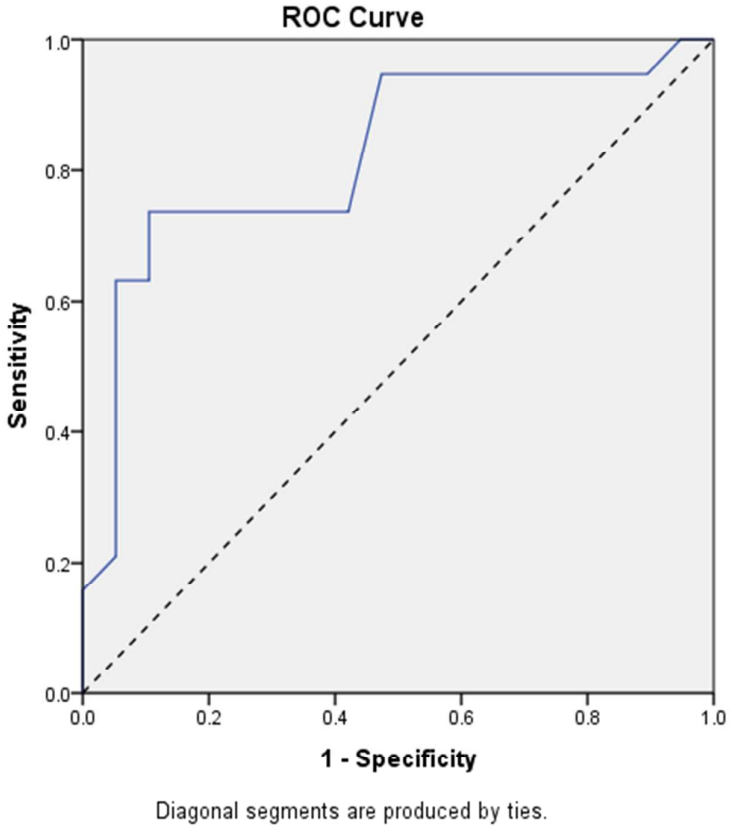

Figure 4: ROC curve for the average score on the JEF©. The area under the curve = 83% with a confidence interval of 0.68-0.92. Dashed line = diagonal reference line. Solid line = ROC curve

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