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Brixton Spatial Anticipation Test performance in patients with focal lesions.

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Abstract

Introduction: The Brixton Spatial Anticipation Test is a widely used neuropsychological test, regarded to be a measure of executive function. It is thought to be sensitive and impaired specifically in patients with frontal lobe lesions. We tested this assumption in patients with focal frontal or posterior lesions.

Method: In this retrospective study, we compared performance on the Brixton in a sample of patients with focal frontal (n = 24) or posterior (n = 18) lesions and healthy controls (n = 22). Both overall performance on the test (total number of errors) and specific errors types were analysed.

Results: We found no significant differences between frontal and posterior patients and healthy controls in overall Brixton performance. Moreover, patients with focal frontal lesions did not generate a significantly greater number of any type of error than posterior patients or healthy controls. Performance was also intact in patients with lesions involving left lateral (n = 11), right lateral (n = 10) or superior medial (n = 18) frontal subregions. Although the error analysis showed that posterior patients had a greater tendency to guess and make more errors when following specific rules than healthy controls, this was no longer significant once fluid intelligence was controlled for.

Conclusions: While it is likely that the Brixton draws on a range of cognitive abilities, caution should be taken when drawing conclusions about its neural substrates.

Keywords: Rule detection; Rule induction; Focal lesions; Frontal Lobes; Executive functioning; Neuropsychology.

Introduction

Detection of executive impairment is crucial for the clinical management of many common neurological disorders. Executive dysfunction is known to be a good predictor of length of stay in hospital, independent living, return to previous employment and social participation (Barker-Collo & Feigin, 2006; Galski, Bruno, Zorowitz, & Walker, 1993; Mole & Demeyere, 2018; Perna, Loughan, & Talka, 2012; van Zandvoort, Kessels, Nys, de Haan, & Kappelle, 2005). Accurately determining the neural substrates underpinning performance on tests of executive function is also a clinical necessity. For example, such information can be used to anticipate the likely cognitive outcomes of injury/surgical resection involving the frontal lobes.

Whilst a number of tests are assumed to measure frontal lobe function, whether a test accurately identifies patients with frontal lobe dysfunction can only be established based on comparisons between patients with highly circumscribed focal frontal or posterior lesions (Stuss et al., 1998). Studies that have made such comparisons have shown several tests to be specific to frontal lobe dysfunction, including the Stroop test (Stuss, Floden, Alexander, Levine, & Katz, 2001), tests of phonemic and design fluency (Robinson, Shallice, Bozzali, & Cipolotti, 2012; Stuss et al., 1998), the Hayling Sentence Completion Test (Robinson et al., 2015) and the Cognitive Estimation Test (Cipolotti et al., 2018). However, both frontal and posterior patients have been found to be impaired on other tests that are commonly held to be specific to frontal lesions, including tests of ideational fluency and the Trail Making Test, part B (Chan et al., 2015; Robinson et al., 2012).

The Brixton Spatial Anticipation Test (Burgess & Shallice, 1996) is regarded to be a measure of frontal executive function and is widely used in Europe in clinical practice (Lezak,

Howieson, Bigler, & Tranel, 2012) and research (Bagshaw, Gray, & Snowden, 2014; Bayliss & Roodenrys, 2000; Cammisuli & Sportiello, 2017; Darcy et al., 2012; Hornberger et al., 2010; Lough et al., 2006; Lounes, Khan, & Tchanturia, 2011; Mang, Ridout, & Dritschel, 2018; McGuinness, Barrett, McIlvenna, Passmore, & Shorter, 2015; Primativo et al., 2017; Reay, Hamilton, Kennedy, & Scholey, 2006; Staios et al., 2013). The test requires participants to predict the location of a coloured dot as it moves over successive pages according to nine underlying rule occurrences. The Brixton was designed to overcome the limitations of the Wisconsin Card Sorting Task (WCST; Berg, 1948). In contrast to the WSCT, the Brixton requires patients to attain nine rules and allows different error types to be easily distinguished. Performance on the test is measured in terms of the overall number of errors. In the original study by Burgess and Shallice (1996), specific types of error were also categorised according to whether they were perseverations (type 1 errors), applications of an incorrect rule (type 2 errors), bizarre responses or guesses (type 3 errors) or moves away from an attained rule (move errors).

The Brixton has been shown to be sensitive to brain dysfunction associated with a range of aetiologies, including Alzheimer's disease (Hornberger et al., 2010), amnestic multi-domain mild cognitive impairment (Cammisuli & Sportiello, 2017), amyotrophic lateral sclerosis (Staios et al., 2013), behavioural variant frontotemporal dementia (Hornberger et al., 2010; Lough et al., 2006; Primativo et al., 2017), Korsakoff's syndrome (van den Berg et al., 2009) and stroke (van den Berg et al., 2009; Vordenberg, Barrett, Doninger, Contardo, & Ozoude, 2014).

Recently, it has been stated that the Brixton is "…very sensitive and impaired specifically in patients with frontal lesions" (p. 329, Primativo et al., 2017). However, to the best of our knowledge, so far, there is little evidence to support this. The original study by Burgess and Shallice (1996) reported that patients with anterior lesions (n = 40) made a greater number of

errors than posterior patients (n = 24) and healthy controls (n = 20). Moreover, an error analysis revealed that patients with anterior lesions had a greater tendency to guess ('type 3' errors in the Burgess and Shallice (1996) classification) and were more likely to abandon a correct rule once it had been attained ('move' errors in the Burgess and Shallice (1996) classification) than patients with posterior lesions. Notably, the patients classified as having anterior lesions had lesions that extended beyond the frontal lobes and, as such, their lesions cannot be considered focal. Another study did not include a group of posterior patients but included a group of patients with subcortical lesions. Vordenberg and colleagues (2014) reported that frontal stroke patients (n = 17) made significantly fewer overall errors on the Brixton than subcortical stroke patients (n = 40). Unfortunately, no further detailed error analysis was undertaken. In this study the performance of frontal patients was not compared with that of patients with focal posterior cortical lesions or healthy controls. Instead it was compared with that of patients with lesions to anterior subcortical structures (basal ganglia and thalamus). Given that these structures contain a high density of executive fronto-subcortical pathways (Rieger, Gauggel, & Burmeister, 2003; Van der Werf et al., 2003), it is unclear whether the results of this study are informative of whether the Brixton is a sensitive and specific test of frontal executive function.

Two further studies have contrasted the performance of frontal patients and healthy controls on the test. Reverberi and colleagues (2005) investigated the performance of frontal patients of mixed aetiology on a revised version of the Brixton test, comprising slightly fewer trials (n = 43; original Brixton n = 54) and different underlying rules. Reverberi and colleagues (2005) reported that patients with focal frontal lesions made significantly more errors than healthy controls. However, contrary to the findings of Burgess and Shallice (1996), analysis of errors showed that the frontal patients in Reverberi et al.'s (2005) study were not significantly

more likely than healthy controls to guess or abandon a correct hypothesis once it had been obtained. Andres and Van der Linden (2001) found no difference between patients with frontal lesions of mixed aetiology (n = 13) and healthy controls (n = 13), in terms of overall number of errors or the number of specific types of errors. However, there are a number of reasons that one may question whether their sample was representative of patients with focal frontal lesions. First, frontal patients did not significantly differ to healthy controls on general measures of cognitive functioning (Block Design (Wechsler, 1989) and Corsi Block-Tapping task (Milner, 1971)) or on any test of executive functioning. For example, Andres and Van der Linden (2001) found no differences between the groups on the Tower of London (Shallice, 1982), for problems three moves deep (number of moves, initiation time, time taken from first move to solution of each problem) or five moves deep (number of moves and initiation time), or the Hayling Sentence Completion Test (number of errors score 1, number of errors score 3, number of correct responses). The only significant difference was that the frontal patients took longer between initiating their first move and finding the solution on Tower of London problems that were five moves deep and had a slower response times on section B of the Hayling Sentence Completion Test. This is somewhat unexpected, as other studies have shown that, compared to patients with posterior lesions and healthy controls, patients with frontal lesions typically make a significantly greater number of moves on tower tests (Owen, Downes, Sahakian, Polkey, & Robbins, 1990; Owen et al., 1995; Shallice, 1982) and number of errors on the Hayling Sentence Completion Test (Cipolotti et al., 2016; Robinson et al., 2015). Second, half of the frontal patients (7/13) included by Andres and Van der Linden (2001) suffered from a traumatic brain injury. It is generally accepted that such injuries are of limited use for localisation of function. Third, the average age of the frontal patients (Mean = 33.2, SD = 13.75) included in Andres and Van der

Linden's (2001) study was younger than that of the frontal patients in the original study by Burgess and Shallice (1996) (Mean = 45.1, *SD* = 14.1). This is an important factor, as age is known to exacerbate the effects of frontal lesions on executive functioning (Cipolotti, Healy, Chan, MacPherson, et al., 2015). Forth, Andres and Van der Linden (2001) included only a small number of frontal patients (*n* = 13). Of note, only six had left frontal lesions. This is an important limitation, given that Reverberi and colleagues (2005) found that a larger group of patients with left lateral prefrontal cortex lesions (*n* = 10) made significantly more Brixton errors than healthy controls. Lastly, Andres and Van der Linden (2001) did not include patients with posterior lesions in their study.

An issue of both clinical and theoretical importance is whether impairments on tests of executive functioning can be explained by reduced fluid intelligence. One influential hypothesis is that a large frontal-parietal network, named the multiple demand network, carries out general control processes to match the requirements of the task being undertaken, independently of the type of information being processed (e.g. Duncan, 2001; Miller and Cohen, 2001). Consistent with this is evidence from functional imaging which has shown the multiple demand network is associated with a wide range of cognitive operations. This putative network has been proposed to be the seat of fluid intelligence (e.g. Woolgar et al., 2010). In support of this, fluid intelligence has been found to be positively correlated with tests of executive function (Duncan, Burgess, & Emslie, 1995). However, contrary to the predictions made by this perspective, reduced fluid intelligence following focal frontal lobe lesions has been found to be insufficient to explain deficits on several tests of executive functioning, including the Stroop, phonemic fluency, design fluency, Proverbs and Hayling tests (Cipolotti et al., In Press; Cipolotti et al., 2016; Murphy et al., 2013; Robinson et al., 2012). Thus, within the frontal part of the frontal-parietal network at

least, there is evidence to suggest that executive functions and fluid intelligence are to some extent separable. What remains less clear, however, is the role of posterior areas in executive function and fluid intelligence. As discussed, some tests purported to measure executive functioning, such as the Trail Making Test, part B, have been found to be impaired also in patients with focal posterior lesions (Chan et al., 2015). However, whether such impairments reflect executive dysfunction or can be better explained by factors such as fluid intelligence, is yet to be investigated.

The aim of our retrospective study was to compare performance on the Brixton in a sample of patients with focal frontal or posterior lesions and healthy controls. Both overall performance on the test (total number or errors) and specific errors types were analysed for differences between groups. We also sought to investigate whether impairments in Brixton performance could be explained by reduced fluid intelligence.

Materials and method

Participants

Patients with brain lesions, who attended the Neuropsychology Department at the National Hospital for Neurology and Neurosurgery (Queen Square, London, UK), were retrospectively evaluated for eligibility. Patients were included if they had suffered a stroke or undergone tumour resection. Diagnosis for all patients was confirmed by neurological investigations including neuroimaging (MRI or CT). Neuropsychological investigations were sought for all patients. The following exclusion criteria were employed: i) no Brixton Spatial Anticipation Test data, ii) no focal unilateral brain lesion, iii) current or previous psychiatric disorder, iv) previous neurological disorders including cerebrovascular accidents or tumours, v) previous head trauma, vi) chemotherapy previous to neuropsychological investigations, vii) history of alcohol or drug abuse,

viii), gross visual (i.e., cortical blindness), perceptual (i.e., neglect; agnosia), motor (i.e., hemiplegia) or language (i.e. dysphasia) impairment, and ix) a score below the 5th percentile on a test of fluid intelligence (Wechsler Adult Intelligence Scale – third edition, Performance IQ (WAIS-III; Wechsler, 1997) or Raven's Progressive Matrices (Raven, Raven, & Court, 2003)), or perception (Visual Object and Space Perception battery (VOSP), Incomplete Letters or Silhouettes; Warrington & James, 1991).

Application of these exclusion criteria resulted in 42 patients with focal unilateral lesions and Brixton data. The aetiologies of the lesions were tumour (n = 26; 16 Frontal; 10 Posterior) and stroke (n = 16; 8 Frontal; 8 Posterior: see supplementary Table 1)[1]. All tumour patients were tested following resection. The grouping together of focal patients with different aetiologies for the purposes of examining cognitive variables is a common approach (see Cipolotti et al, In Press for further discussion) and, importantly, is one that we have previously shown is methodologically justifiable (Cipolotti, Healy, Chan, Bolsover, et al., 2015; S. E. MacPherson et al., Under revision).

The patients were compared to 22 healthy adult controls with no neurological or psychiatric history. Healthy controls were recruited to match the patient group as closely as possible for age, gender and years of education. The research was done in accordance with the Declaration of Helsinki and approved by the NRES Committee London – Queen Square.

Neuropsychological Investigation

We retrospectively reviewed the performance of the 42 patients with Brixton test data on a single neuropsychological assessment comprising well-known tests with published standardised

[1] There was no significant difference between frontal and posterior patients in terms of the proportion of lesions causes by stroke versus tumour resection, χ^2 (1) = .538, p = .531.

normative data. All tests were administered according to published standard procedures and were converted to standard scores or percentiles using the test manuals referenced below**.** The only exception was that raw scores were used for the Brixton, as scores are not corrected for demographic factors in the test manual. National Adult Reading Test (NART; Nelson & Willison, 1991) standard scores were used to estimate optimal premorbid functioning, standard scores derived from WAIS-III Performance IQ or Raven's Progressive Matrices were used to measure Fluid IQ, Graded Naming Test percentiles (GNT; McKenna & Warrington, 1980) were used to measure naming skills and Recognition Memory Test percentiles (RMT for Words and Faces, Warrington, 1984) were used to measure verbal and visual recognition memory. Executive functions were evaluated using Stroop test percentiles (Trenerry et al., 1989), Phonemic Fluency test percentiles (No. of words named starting with the letter S in 60 seconds; Spreen & Strauss, 1998) and Brixton raw scores. Healthy controls were administered the same neuropsychological assessment battery as patients. The only exception being that the RMT for Words and Faces were not administered.

Brixton Spatial Anticipation Test

Test Design

The Brixton was administered to patients and healthy controls following the standard procedure. The test consists of 56 A4 pages, each containing a presentation of 10 circles, labelled one to ten. One of the ten circles is always filled, while the other nine are empty. Pages differ only in terms of the position of the filled circle. On each page there is a relationship between the circle that is filled on the current page and the circle that was filled on the proceeding page. This relationship

is determined by one of a number of rules. The exception to this is when a rule change occurs, where the position of the filled circle no longer relates to the proceeding page.

Overall, there are 9 rule occurrences. There are four major rule concepts, that can occur starting from different numbers, these are: i) position progresses by one addition at a time (i.e. 1, 2, 3…), ii) position regresses by one subtraction at a time (i.e. 10, 9, 8…), iii) position alternates between two numbers (i.e. 5, 10, 5…) and iv) position stays the same (i.e. 9, 9, 9…). The order of 9 rule occurrences is: ascending, descending, alternating, ascending, descending, ascending, alternating, repetition, alternating. The number of consecutive pages to which the rule is applied varies between three to eight, so that rule changes cannot be anticipated (for further details see Burgess & Shallice, 1996, 1997).

Analysis of Overall Brixton Performance

On the Brixton, the maximum numbers of errors possible is 54. We analysed overall performance on the Brixton Test using the total number of errors (Raw Scores).

Error analysis 1: Burgess and Shallice's (1996) approach

The first error analysis adopted the same error classification system developed by Burgess and Shallice (1996). Four types of error were identified. *Type 1*, 'perseveration', errors included all errors attributable to perseveration, either of reproducing the current stimulus or the preceding response or the application of the rule that immediately preceded the currently correct one to either the current stimulus or the previous response. *Type 2*, 'rule break', errors were classified when errors could be attributed to the application of an incorrect rule. This could have been either a previously correct rule or a rule that was not previously correct but is nevertheless logical. For

example, guessing that the filled dot will be in position 6 after it had been in positions 1, 2, 3, 4 and 5. *Type 3*,'bizarre', errors were coded when participants' responses bore no resemblance to the current or previous stimuli or any identifiable rule. For example, guessing that the filled dot will be in position 8 after it had previously been in positions 1, 2, 3, 4 and 5. *Move errors,* were classified when participants correctly attained a rule (e.g. rule 1, ascending) but then went on to make an error before the rule changed. Attainment of a rule was defined as at least two successive correct responses since the beginning of a new rule.

Error analysis 2: Rule-Based Error Analysis

The second analysis was based on the test's 9 underlying rule occurrences. This was informed by Burgess and Shallice's (1996) report that pilot data on the Brixton showed that some rule occurrences were better than others at discriminating between a small group of frontal (n = 6) and posterior (n = 5) patients, although data were not reported and the patients' injuries were not described in further detail. More recently, on an eye-tracking task based on the Brixton, patients with behavioural variant frontotemporal dementia were found to be significantly less accurate than healthy controls but only on trials based on more complex rules (Primativo et al., 2017). Thus, we investigated whether performance on specific rule occurrences on the Brixton would discriminate between patients with frontal or posterior lesions. Errors were classified according to whether they were made on the following trials: rule occurrence 1, ascending (trials 2-6); rule occurrence 2, descending (trials 7-12), rule occurrence 3, alternating (trials 13-19), rule occurrence 4, ascending (trials 20-26), rule occurrence 5, descending (trials 27-29), rule occurrence 6, ascending (trials 30-34), rule occurrence 7, alternating (trials 35-41), rule occurrence 8, repetition (trials 42-48) and rule occurrence 9, alternating (trials 49-55).

Neuroimaging

Patients were classified based on MRI T2-weighted (n = 39) or CT (n = 1) scans. In two cases scans were performed in different Trusts and could not be accessed, so these patients were classified on the basis of radiological details given in their clinical reports. Importantly, when all analyses were re-run with these two cases excluded the pattern of results remained unchanged. Lesions were traced using MRIcro (Rorden & Brett, 2000) and normalised to a standard template using statistical parametric mapping-5 software (Wellcome Department of Imaging Neuroscience, London, England; www.fil.ion.ucl.ac.uk). Patients were classified as frontal or posterior using templates based on Brodmann area maps provided with MRIcroN (http://www.sph.sc.edu/comd/rorden/mricron). Frontal patients were identified as those with a lesion in any part of the brain anterior to the central sulcus and superior to the lateral fissure. Posterior lesions were classified as falling within the temporal, parietal and/or occipital lobes (see Robinson et al., 2010 for a similar method). The distribution of the frontal and posterior patients' lesions is displayed in Figure 1.

Two analyses were carried out: standard and fine-grained, which were informed by the studies of Burgess and Shallice (1996) and Reverberi and colleagues (2005), respectively. In the standard analysis, comparisons were made between patients with focal frontal (n = 24) or posterior (n = 18) lesions and healthy controls (n = 22). In the fine-grained analysis, comparisons were made between patients with lesions involving the left lateral (n = 11), or right lateral (n = 10), or superior medial (n = 18) regions, previously described by (Stuss et al., 2002), and healthy controls. Patients were included in each of these groups if there was any overlap between the normalised mask of their traced lesion and a template of the region of interest (e.g. left lateral frontal lobe). As lesions could affect more than one frontal subregion, groups were not mutually exclusive. As very few

patients had lesions affecting the inferior medial or polar frontal region, these regions were not included in the analysis.

Statistical Analysis

Skewness and kurtosis were assessed, by inspecting boxplots, and homogeneity of variances was assessed, using Levene's test. In all cases where Levene tests showed that the error variances between the groups differed significantly, data were transformed using square root or log transformation. If error variances remained unequal, non-parametric statistics were used (Kruskal–Wallis and Mann–Whitney U-tests -for similar method see Turner et al., 2007).

The standard and fine-grained analysis adopted methods of previous studies (e.g. Robinson et al., 2012, 2015). For the standard analysis, ANOVAs were conducted and significant results were followed by post-hoc tests (frontal versus posterior versus healthy controls). In the fine-grained analysis, because groups were not independent, direct comparisons were made between patient groups and healthy controls using independent t-tests (left lateral/right lateral/superior medial versus healthy controls). Bonferroni's correction was applied to both analyses and only significant results are reported (see Robinson et al., 2012 for similar method).

This method was used to compare groups in terms of demographic variables (age, years of education and chronicity (months between stroke/tumour resection and neuropsychological assessment)) and scores on neuropsychological tests (NART IQ, Fluid IQ (WAIS-III Performance IQ or Raven's Progressive Matrices), GNT percentiles, RMT Words percentiles, RMT Faces percentiles, Stroop Test percentiles, Phonemic Fluency percentiles). The only exception was that gender differences were investigated using Chi-square goodness-of-fit tests.

To examine the relationship between fluid intelligence and performance on neuropsychological tests of executive functioning and the Brixton test, additional analyses were conducted using ANCOVA with Fluid IQ entered as a covariate when significant differences in performance on these tests were found between groups. Fluid IQ scores were significantly positively correlated with Stroop test scores and Phonemic Fluency percentiles ($r = .272$, $p = .037$; $r = .311$, $p = .027$, respectively) and negatively correlated with overall number of errors on the Brixton ($r = .-.401$, $p = .001$).

Results

Demographics

In the standard analysis, Frontal, Posterior and Healthy Control groups were well-matched (i.e. $p > 0.05$) for age, gender, years of education, time between diagnosis and assessment and lesion volume (see Table 1).

In the fine-grained analysis there were no differences between the Left Lateral, Right Lateral or Superior Medial groups and the Healthy Control group in terms of age, gender and years of education.

< Insert Table 1 about here >

Neuropsychological investigation

In the standard analysis, posterior patients had significantly lower percentile scores than frontal patients on a measure of visual recognition memory (RMT Faces: $t(18) = 2.128$, $p = .047$, $d = 1.00$;

see Table 2). There were no significant differences between Frontal, Posterior and Healthy Control groups in terms of NART, Fluid IQ, GNT, or RMT Words scores (all $p > 0.05$).

On the executive tests, there was a significant difference between Frontal, Posterior and Healthy Control groups in Stroop percentile scores ($F(2,45) = 5.678$, $p = .006$, $\omega^2 = .12$). The Frontal group had significantly lower Stroop percentile scores than the Posterior ($p = 0.29$) and Healthy Control groups ($p = .011$). We also found a significant difference between Frontal, Posterior and Healthy Control groups in Fluency S percentile scores ($F(2, 39) = 5.083$, $p = .011$, $\omega^2 = .15$). The Frontal group had significantly lower Fluency S percentile scores than the Healthy Control group ($p = .010$). In contrast, there was no significant difference between the performance of Posterior patients and Healthy Controls on these two measures (see Table 2). These results were unchanged when Fluid IQ was entered as a covariate, with the exception that the difference between the Frontal and Healthy Control group for Stroop percentile scores was no longer significant.

In the fine-grained analysis, the Left Lateral (Mean = 19.78, $SD = 22.01$) and Superior Medial (Mean = 36.89, $SD = 35.71$) groups had significantly lower Stroop percentile scores than the Healthy Control group (Mean = 76.21, $SD = 14.00$, $t(21) = -4.67$, $p < 0.001$, $d = 1.99$; $t(25) = -2.80$, $p = 0.005$, $d = 1.04$, respectively). The Left Lateral (Mean = 24.05, $SD = 20.57$) and Superior Medial (Mean = 38.59, $SD = 35.54$) groups also had significantly lower Fluency S percentile scores than the Healthy Control group (Mean = 69.65, $SD = 10.00$, $t(18) = -5.51$, $p < 0.001$, $d = 2.27$; $t(24) = -2.59$, $p = 0.008$, d = 1.08, respectively). When Fluid IQ was entered as a covariate, these differences on executive tests remained significant for the Left Lateral but not the Superior Medial group.

< Insert Table 2 about here >

Brixton Test

In the standard analysis, there was no significant difference between Frontal, Posterior and Healthy Control groups in overall performance on the Brixton test (see Table 3).

In the fine-grained analysis there were no differences between the Left Lateral, Right Lateral or Superior Medial groups and the Healthy Control group on the Brixton test.

< Insert Table 3 about here >

Error Analysis

Burgess and Shallice (1996) error analysis

The standard analysis showed no significant differences between the Frontal, Posterior and Healthy Control groups in type 1, type 2 and move errors. There was a significant difference between the Frontal, Posterior and Healthy Control groups in type 3 'bizarre' errors ($F(2,61) = 3.929$; $p = .025$, $\omega^2 = .08$). The posterior patients made significantly more type 3 bizarre errors than the Healthy Control group ($p = .022$). However, when Fluid IQ was entered as a covariate, there were no significant differences between the Frontal, Posterior and Healthy Control groups in type 1, type 2, type 3 and move errors.

In the fine-grained analysis there were no differences between the Left Lateral, Right Lateral or Superior Medial groups and the Healthy Control group in type 1, type 2, type 3 and move errors.

Rule-Based error analysis

In the standard analysis, there was a significant difference between the Frontal, Posterior and Healthy Control groups in the number of errors made on rule occurrence 7 'alternating' and rule occurrence 8 'repetition' ($F(1,61) = 3.349$, $p = .042$, $\omega^2 = .07$; $F(1,61) = 3.892$, $p = .026$, $\omega^2 = .08$, respectively). Post-hoc tests revealed no significant differences in the number of errors made on rule occurrence 7 'alternating' but posterior patients made significantly more errors on rule occurrence 8 'repetition' than the Healthy Control group ($p = .023$). However, when Fluid IQ was entered as a covariate, there were no significant differences between the Frontal, Posterior and Healthy Control groups on rule occurrence 7 'alternating' and rule occurrence 8 'repetition' errors (see Table 4).

In the fine-grained analysis, there were no significant differences between the Left Lateral, Right Lateral or Superior Medial groups and the Healthy Control group for any type of rule-based error.

< Insert Table 4 about here >

Discussion

To the best of our knowledge, this is the first study that has compared performance on the Brixton test in a sample of patients with focal frontal or posterior lesions and healthy controls. We investigated whether there were differences between groups in the total number of errors on the Brixton test and the number of specific types of error. Errors were classified using the system developed by Burgess and Shallice (1996) and according to the test's nine underlying rule occurrences.

The main finding was that there were no significant differences between frontal and posterior patients and healthy controls in terms of the total number of errors on the Brixton test. This is consistent with previous findings that patients with frontal lesions of mixed aetiology did not significantly differ from healthy controls (Andres & Van der Linden, 2001). However, our findings contrast with the results of the original study by Burgess and Shallice (1996), which showed that patients with anterior lesions made a significantly greater number of errors than patients with posterior lesions and healthy controls. It is unlikely that this discrepancy can be explained by demographic variables, as our patient and healthy control groups were similar to Burgess and Shallice's (1996) participants in terms of age and premorbid intelligence. Nor is it likely that the frontal patients in our sample were atypical of the wider population of patients with frontal lesions, as our frontal patients were impaired on the Stroop test and Phonemic fluency, two tests of executive functioning known to be sensitive to frontal lesions (Cipolotti et al., 2016; Robinson et al., 2012; Stuss et al., 1998; Stuss et al., 2001). In the absence of a plausible alternative explanation, the differences between our results and those reported by Burgess and Shallice (1996) may be explained by the fact that those included in the Burgess and Shallice's (1996) anterior group had larger, more extensive lesions, as their criteria allowed for patients that had lesions that extended into non-frontal areas.

Our error analysis revealed that patients with focal frontal lesions did not generate a significantly greater number of any type of error on the Brixton test than posterior patients or healthy controls. Interestingly, we found that posterior patients generated a significantly higher number of bizarre and rule-based errors than healthy controls. These findings suggest that specific errors are not associated exclusively with focal frontal lesions. Although Burgess and Shallice (1996) reported that patients with lesions involving the frontal lobes had higher rates of bizarre

and move errors, other studies including patients with focal frontal lesions reported that frontal patients did not generate a significantly greater number of such errors than healthy controls (Andres & Van der Linden, 2001; Reverberi et al., 2005). Taken together, the current and previous findings suggest that specific types of Brixton errors are not sensitive exclusively to damage to the frontal lobes in patients with focal lesions. It is notable that, once variance associated with fluid intelligence was controlled for, the difference in the number of errors made between posterior patients and healthy controls was no longer significant. This suggests that it is fluid intelligence rather than the focal function of posterior brain regions is driving errors on the Brixton. The same could not be said for performance on other tests of executive functioning that are known to be sensitive to frontal lesions, where frontal patients, particularly those with left lateral frontal lesions, had significantly impaired performance even when fluid intelligence was controlled for.

Interestingly, even when frontal patients were grouped using more specific methods of anatomical classification (Stuss et al., 2002), no differences in Brixton performance were observed between left lateral, right lateral or superior medial frontal patients and healthy controls. Reverberi and colleagues (2005) found that, on their revised version of the Brixton test, patients with left lateral lesions made significantly more errors than healthy controls and this patient group was the only group for which flawed performance on the test was not secondary to another impairment. While it may be argued that the left lateral patients in the current study may have had milder executive deficits than those included in the study by Reverberi and colleagues (2005), this seems unlikely, given that our left lateral patients were significantly impaired on other tests of executive functioning that are known to be sensitive to frontal lesions. Instead, the differences between the current findings and those reported by Reverberi and colleagues (2005) may be explained by the fact that they used a modified version of the Brixton test, which may have been more difficult as

the underlying rules upon which it was based were repeated less. For example, whereas the rule 'ascending' occurs three times in the original test, it occurs only once on the modified Brixton.

It is important to acknowledge that it remains possible that we may have found different results in a larger sample of patients. However, our sample size was sufficient to allow us to detect significant impairments in our frontal patients on other tests of executive function known to be sensitive to frontal lesions. Our sample size is also of a similar size to that of other studies that have investigated the performance of patients with focal frontal lesions on the Brixton (e.g. Andres & Van der Linden, 2001; Vordenberg et al., 2014) and other tests of executive functioning (Aron, Fletcher, Bullmore, Sahakian, & Robbins, 2003; Campanella, Skrap, & Vallesi, 2016; Goel et al., 2007; S. E MacPherson et al., 2014; Urbanski et al., 2016).

In conclusion, while it is likely that the Brixton draws on a range of cognitive abilities, caution should be taken when drawing conclusions about its frontal substrate. The Brixton has enjoyed considerable popularity in both research and clinical practice and may continue to have utility as a test of general brain dysfunction. However, the current findings question the assumption that the Brixton is sensitive and impaired specifically in patients with frontal lesions.

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Tables

Table 1

Demographic data: Standard analysis.

	Frontal ***n*** **= 24**	**Posterior** ***n*** **= 18**	**Control** ***n*** **= 22**
Age (years) $\bar{x}$ (SD)	43.75 (12.48)	48.58 (19.50)	49.76 (16.52)
Gender M/F	12/12	14/4	10/12
Education (years) $\bar{x}$ (SD)	15.56 (3.85)	15.14 (3.39)	15.06 (1.86)
Chronicity (months) $\bar{x}$ (SD)	8.62 (23.30)	15.41 (35.61)	-
Lesion volume $\bar{x}$ (SD)	46.14 (36.29)	33.06 (35.93)	-

Legend:

$\bar{x}$ = Mean

SD = Standard Deviation

Table 2.

Neuropsychological data: Standard analysis.

	Frontal ***n* = 24**	**Posterior** ***n* = 18**	**Control** ***n* = 22**
NART IQ $\bar{x}$ (SD)	109.00 (8.21)	110.92 (9.78)	109.09 (10.64)
Fluid IQ $\bar{x}$ (SD)	100.17 (18.08)	95.50 (13.54)	103.56 (10.21)
GNT Percentiles $\bar{x}$ (SD)	52.15 (33.15)	69.50 (28.30)	64.42 (30.97)
RMT Words Percentiles $\bar{x}$ (SD)	65.65 (22.94)	71.09 (30.13)	-
RMT Faces Percentiles $\bar{x}$ (SD)	35.08 (22.94)	14.14 (16.40) [b]*	-
Stroop Percentiles $\bar{x}$ (SD)	45.00 (34.40) [a, b]*	73.14 (34.22)	76.21 (33.98)
Fluency S Percentiles $\bar{x}$ (SD)	36.03 (33.39) [a]*	53.77 (24.67)	69.65 (16.16)

Due to the clinical nature of the data, the number of patients that completed each of the tests varied.

Legend:

[a] = indicates significant difference between the Frontal and Healthy Control groups.

[b] = indicates significant difference between the Frontal and Posterior groups.

* = $p < .05$,

NART = National Adult Reading Test

GNT = Graded Naming Test.

RMT = Recognition Memory Test.

$\bar{x}$ = Mean

SD = Standard Deviation

Table 3.

Overall Brixton performance: Standard analysis.

	Frontal ***n*** **= 24**	**Posterior** ***n*** **=18**	**Control** ***n*** **= 22**
Brixton Raw Score $\bar{x}$ (SD)	14.92 (7.06)	18.72 (9.26)	13.73 (2.62)
Brixton Scaled Score $\bar{x}$ (SD)	6.33 (2.35)	5.28 (2.63)	6.41 (0.91)
Standard Error Analysis			
Type 1 Perseveration $\bar{x}$ (SD)	6.38 (4.03)	7.72 (8.12)	6.41 (2.26)
Type 2 Rule Break $\bar{x}$ (SD)	7.58 (4.66)	8.83 (4.51)	6.73 (2.29)
Type 3 Bizarre $\bar{x}$ (SD)	0.92 (0.88)	2.00 (2.72) [a]*	0.59 (1.10)
Move Errors	2.13 (1.26)	2.11 (1.49)	1.95 (1.09)

Scaled scores were calculated using the original normative data provided by Burgess and Shallice (1997).

Legend:

[a] = indicates significant difference between the Posterior and Healthy Control groups.

* = $p < .05$

$\bar{x}$ = Mean

SD = Standard Deviation

Table 4

Rule occurrence error analysis: Standard analysis.

	Frontal ***n*** **= 24**	**Posterior** ***n*** **=18**	**Control** ***n*** **= 22**
Rule occurrence 1 Ascending $\bar{x}$ (SD)	0.38 (0.88)	0.22 (0.65)	0.09 (0.29)
Rule occurrence 2 Descending $\bar{x}$ (SD)	1.63 (0.88)	1.67 (1.61)	1.32 (1.09)
Rule occurrence 3 Alternating $\bar{x}$ (SD)	2.13 (1.48)	2.44 (2.12)	1.64 (0.95)
Rule occurrence 4 Ascending $\bar{x}$ (SD)	1.42 (0.93)	1.44 (1.15)	1.73 (1.12)
Rule occurrence 5 Descending $\bar{x}$ (SD)	1.29 (0.86)	1.78 (0.73)	1.82 (0.80)
Rule occurrence 6 Ascending $\bar{x}$ (SD)	1.29 (0.95)	1.78 (1.11)	1.45 (0.80)
Rule occurrence 7 Alternating $\bar{x}$ (SD)	2.88 (2.11)	4.06 (2.01)	2.59 (1.44)
Rule occurrence 8 Repetition $\bar{x}$ (SD)	1.96 (1.57)	3.00 (2.40) [a]*	1.50 (1.01)
Rule occurrence 9 Alternating $\bar{x}$ (SD)	1.96 (1.55)	2.33 (1.61)	1.59 (1.14)

Legend:

[a] = indicates significant difference between the Posterior and Healthy Control groups.

* = $p < .05$

$\bar{x}$ = Mean

SD = Standard Deviation

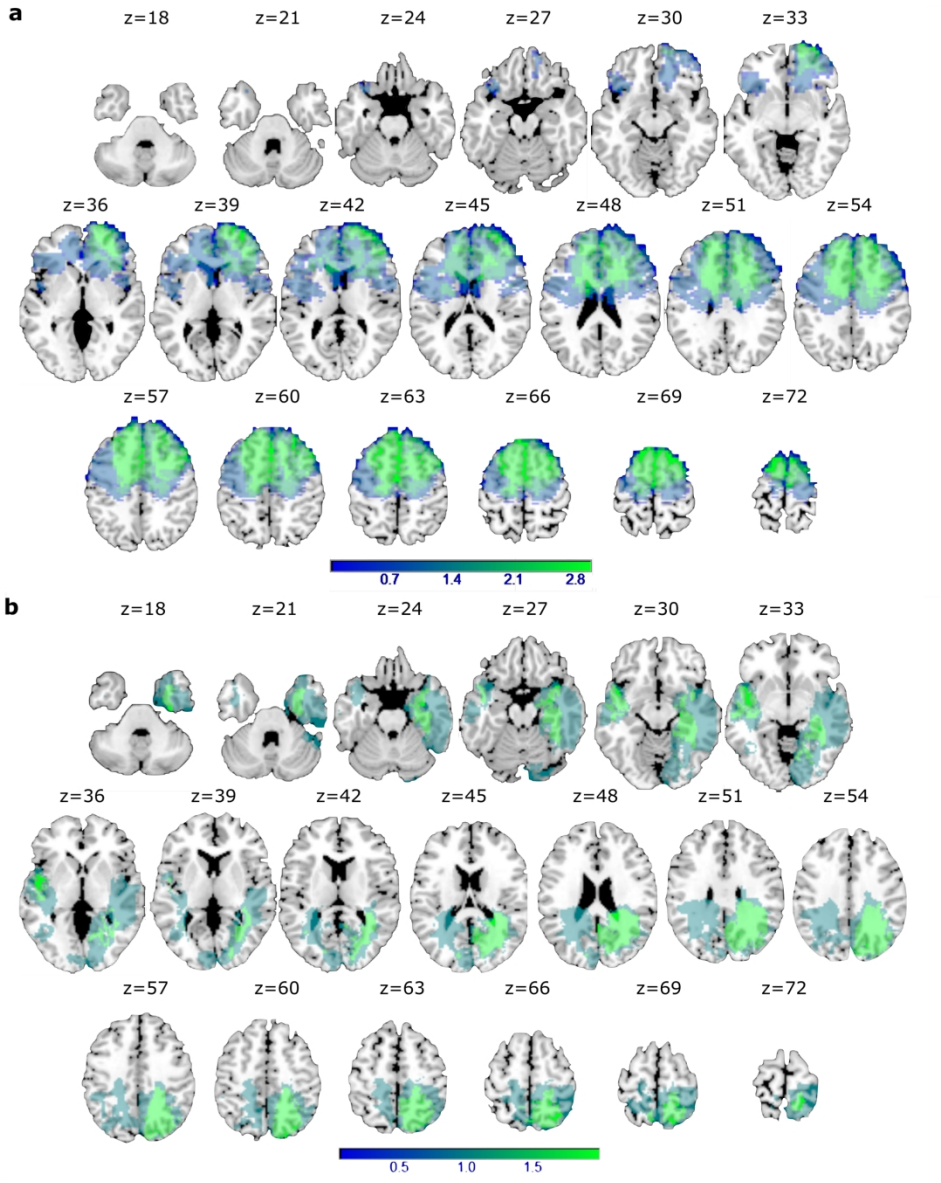

Figure 1. Lesion distribution volume map for (a) Frontal and (b) Posterior patients. Results are displayed on transversal slices (numbers indicate MNI coordinates) of the ch2better.nii.gz template in MRIcron (https://www.nitrc.org/projects/mricron). The colour code indicates in how many patients a given voxel was lesioned.

Supplementary Table 1.

Patient number	Imaging: MRI/CT	Aetiology	Time post-injury (months)
1	MRI	Left frontal glioblastoma	3.33
2	MRI	Left frontal grade II oligodendroglioma	15.7
3	MRI	Left frontal stroke	3.67
4		Left frontal stroke	107.1
5	MRI	Left frontal grade II oligodendroglioma	1.63
6	MRI	Left frontal metastasis	2.57
7	MRI	Left frontal grade II oligodendroglioma	1.40
8	MRI	Left frontal stroke	0.73
9	MRI	Left frontal grade II diffuse astrocytoma	1.20
10	MRI	Left frontal stroke	1.83
11	MRI	Left frontal grade II astrocytoma	108.43
12	MRI	Left frontal grade II oligodendroglioma	0.50
13	MRI	Right frontal grade II oligodendroastrocytoma	10.67
14	MRI	Right frontal grade II diffuse astrocytoma	0.90
15	MRI	Right frontal glioblastoma	1.07
16	MRI	Right frontal stroke	0.30
17	MRI	Right frontal stroke	0.40
18		Right frontal stroke	
19	MRI	Right frontal stroke	0.43
20	MRI	Right frontal meningioma	6.93
21	MRI	Right frontal grade II astrocytoma	2.83
22	MRI	Right frontal grade II oligodendroglioma	14.23
23	MRI	Right frontal grade II oligodendroglioma	26.00
24	MRI	Right frontal grade II oligodendroglioma	2.43
25	MRI	Left temporal stroke	0.07
26	CT	Left parietal stroke	2.17
27	MRI	Left occipital stroke	2.20
28	MRI	Left temporal grade II astrocytoma	2.07
29	MRI	Left temporal grade I ganglioglioma	2.80
30	MRI	Left parietal glioblastoma	0.13
31	MRI	Left temporal glioblastoma	0.03
32	MRI	Right occipital stroke	0.43
33	MRI	Right parietal stroke	0.43
34	MRI	Right temporal stroke	3.20
35	MRI	Right occipital stroke	2.83
36	MRI	Right temporal diffuse low-grade glioma (histologically unverified)	3.13
37	MRI	Right temporal stroke	2.70
38	MRI	Right occipital/parietal grade II oligodendroastrocytoma	32.00
39	MRI	Right parietal grade II astrocytoma	133.07
40	MRI	Right occipital/parietal grade II oligodendroglioma	83.67
41	MRI	Right temporal glioblastoma	6.43
42	MRI	Right parietal metastasis	0.07