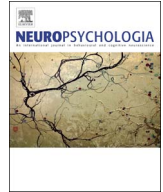




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## Cognitive estimation: Performance of patients with focal frontal and posterior lesions

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## ABSTRACT

The Cognitive Estimation Test (CET) is a widely used test to investigate estimation abilities requiring complex processes such as reasoning, the development and application of appropriate strategies, response plausibility checking as well as general knowledge and numeracy (e.g., Shallice and Evans, 1978; MacPherson et al., 2014). Thus far, it remains unknown whether the CET is both sensitive and specific to frontal lobe dysfunction. Neuroimaging techniques may not represent a useful methodology for answering this question since the complex processes involved are likely to be associated with a large network of brain regions, some of which are not functionally necessary to successfully carry out the CET. Instead, neuropsychological studies may represent a more promising investigation tool for identifying the brain areas necessary for CET performance. We recently developed two new versions of the CET (CET-A and CET-B; MacPherson et al., 2014). We investigated the overall performance and conducted an error analysis on CET-A in patients with focal, unilateral, frontal ( $n = 38$ ) or posterior ( $n = 22$ ) lesions and healthy controls ( $n = 39$ ). We found that frontal patients' performance was impaired compared to healthy controls on CET. We also found that frontal patients generated significantly poorer estimates than posterior patients on CET-A. This could not be explained by impairments in fluid intelligence. The error analyses suggested that for CET-A, *extreme* and *very extreme* responses are impaired following frontal lobe damage. However, only *very extreme* responses are significantly more impaired following frontal lobe than posterior damage and so represent a measure restricted to frontal "executive" impairment, in addition to overall CET performance.

## 1. Introduction

Cognitive estimation tasks require the ability to generate responses to questions for which exact answers are not readily available. These estimation tasks assess an important form of problem-solving which is often required in everyday activities (e.g., estimating your next shopping bill or the size of an item of clothing you should buy as a gift). Estimation relies on complex processes such as reasoning, the development and application of appropriate strategies, response plausibility checking as well as general knowledge and numeracy (e.g., Shallice and Evans, 1978; MacPherson et al., 2014). Patients, who experience brain

damage, often involving the frontal lobes, are reported to have impaired judgement and problem-solving abilities and generate estimates that are considered to be bizarre. For example, Shallice and Evans (1978) described a patient who, following a large right frontal lesion caused by an explosion, showed a severe impairment in producing adequate cognitive estimates. When he was asked, 'What is the height of the highest building in London?', he replied "18,000 to 20,000 feet" (approximately 5500-6000 m). Strikingly, the patient did not appear to realize that his answers were bizarre and instead continued to justify them, even when pressed about the appropriateness of the responses.

Shallice and Evans (1978) developed the Cognitive Estimation test

**Abbreviations:** CVA, cerebrovascular accident; GNT, Graded Naming Test; HC, healthy comparisons; IQ, Intelligence Quotient; LF, left frontal; NART, National Adult Reading Test; No. Number; PFC, prefrontal cortex; RAPM, Raven's Advanced Progressive Matrices

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(CET) to formally investigate estimation abilities in frontal patients. The original CET comprised of 15 questions and has long since been used to assess estimation abilities in both clinical and research settings. Several different versions of the CET have been developed (e.g., Brand et al., 2003; Bullard et al., 2004) and studies have reported normative data for these different CET versions (e.g., Axelrod and Millis, 1994; Della Sala et al., 2003; Scarpina et al., 2015, for a review of the different CET versions see Wagner et al., 2011). We have recently developed two new 9-item parallel versions of the CET (i.e., CET-A and CET-B) with the aim of providing more up-to-date items that can be administered in different countries, on more than one occasion (MacPherson et al., 2014).

The CET is widely considered to be a test of executive function and has been included as such in several handbooks of neuropsychology (e.g., Denes and Pizzamiglio, 1999; Strauss et al., 2006; Gurd et al., 2010). Executive functions refer to a variety of general purpose control mechanisms thought to modulate and organize more basic cognitive sub-processes to achieve goal-oriented behaviour (e.g., Stuss and Levine, 2002). In order to provide appropriate estimates, individuals need to identify and select the appropriate way of thinking or interpreting information, retrieve and manipulate particular details or estimates, monitor how appropriate their response is and finally repeat this procedure if a better estimate is required. However, there are also studies that do not support the notion that the CET assesses executive abilities, as performance on the CET and other executive measures such as verbal fluency, the Trail Making Test, the Wisconsin Card Sorting Test or the Frontal Assessment Battery do not significantly correlate (e.g., Spreen and Strauss, 1998; Appollonio et al., 2005; Spencer and Johnson-Greene, 2009; Barabassy et al., 2010; D'Aniello et al., 2015). Recently D'Aniello and colleagues (2015) suggested that the CET, "... may be considered a useful instrument for the assessment of crystallized intelligence and of cognitive reserve..." but it is not a "...specific measure of executive functions." (p. 3).

Executive functions are thought to be mediated primarily by the frontal lobes (e.g., Stuss and Levine, 2002). However, the precise nature of the frontal lobes' contribution to executive abilities remains poorly understood (e.g., Hornberger and Bertoux, 2015). Several theories suggest that component processes of executive functions rely on specific subregions within the prefrontal cortex (e.g., Stuss and Alexander, 2007; Shallice et al., 2008; Petrides, 2005). In contrast, some other theories suggest that a large fronto-parietal network, named the *multiple-demand network*, carries out general control processes that match the requirements of the task being undertaken, independently of the type of information being processed (e.g., Duncan, 2001; Miller and Cohen, 2001). This putative network has been proposed to be the seat of general fluid intelligence or Spearman's *g* (e.g., Spearman, 1904, 1927; Woolgar et al., 2010), which is known to positively correlate with performance on tests of executive function and is impaired following frontal lesions (Duncan et al., 1995).

These different theories have important implications for understanding frontal patients' impairments on executive tests, such as the CET. In an influential paper, Roca et al. (2010) argued that fluid intelligence is a substantial contributor to frontal-executive deficits. The authors reported that impairments in fluid intelligence can explain executive impairments on several well-known 'executive tests' such as the Wisconsin Card Sorting Task or letter fluency. In frontal patients, after partialling out the contribution of fluid intelligence, impairments remained only for a small number of 'frontal' tasks. This finding has raised questions regarding the diagnostic significance of executive tests. However, very few studies have investigated whether executive impairments in frontal patients can be explained by a loss in fluid intelligence. Recently, Cipolotti et al. (2016) have reported that impairments on the Hayling and Stroop tests in frontal patients cannot be fully explained by fluid intelligence. Therefore, it remains important to establish the extent to which a loss of fluid intelligence can account for CET impairments in frontal patients.

It also remains important to establish whether the CET is a test sensitive and specific to frontal lobe damage. It has been reported that CET performance is impaired in a variety of neurological conditions such as stroke (Shoqeirat et al., 1990), Alzheimer's disease (Della Sala et al., 2004), frontotemporal dementia and corticobasal syndrome (Bisbing et al., 2015), Korsakoff's syndrome (Brand et al., 2003), Huntington's disease (Brandt et al., 1988) and traumatic brain injury (Schretlen, 1992) and psychiatric conditions such as schizophrenia (e.g., Roth et al., 2012; Gansler et al., 2014). However, these studies do not allow us to determine whether the CET is a test specific to frontal lobe damage.

Surprisingly, only a handful of focal lesion studies have specifically investigated the frontal specialization of the CET. The evidence reported so far is inconsistent or sparse. Shallice and Evans (1978) first reported that patients with unilateral left or right anterior lesions produced significantly more bizarre answers than patients with posterior lesions on the CET. Similarly, Smith and Milner (1984) found that right unilateral frontal lobectomy patients ( $n = 12$ ) made significantly more errors than healthy controls (HC), and left and right temporal lobectomy patients on a price estimation task. However, no CET impairments were detected in the small left frontal group ( $n = 7$ ) who had smaller lesions than the right frontal group. In contrast, Taylor and O'Carroll (1995) did not find a significant difference between anterior and posterior patients performing the CET. Stanhope et al. (1998) reported a significant difference between the performance of frontal patients ( $n = 9$ ) with stereotactic subcaudate tractotomy for treatment of intractable affective disorders and HCs. However, they found no significant difference between frontal, diencephalic and temporal lesion patients.

Notably, from these studies it remains unclear whether the reported lesions were indeed confined to the frontal or the posterior lobes. For example, approximately 50% of the anterior patients reported by Shallice and Evans (1978) had large tumours extending beyond the frontal lobes (i.e., fronto-temporal or fronto-parietal lesions). Almost half of Taylor and O'Carroll (1995)'s anterior patients (7 out of 15) suffered a head injury whilst the posterior group included patients with head injury and focal cortical atrophy. The diencephalic and temporal patients reported by Stanhope et al. (1998) had alcoholic Korsakoff syndrome or herpes encephalitis or anoxia. More recently, MacPherson and colleagues (2014) reported that a group of patients with focal lesions confined to the frontal lobes based on clinical CT or MRI scans, performed more poorly than HCs on both versions of the CET. However, no data from patients with posterior lesions were included. Hence, it remains unknown if the two new CET versions are specific to frontal lobe lesions.

Despite rapid advancements in neuroimaging methodologies such as PET, fMRI, EEG and MEG for identifying the brain regions associated with specific cognitive processes, to our knowledge, no neuroimaging study has examined the neural correlates of the CET. This is perhaps not surprising. Complex processes such as those involved in cognitive estimation are likely to be associated with the activation of large brain networks. Critically, the activation of brain areas in a functional imaging study does not necessitate that these areas are functionally necessary to successfully carry out the task (e.g., Gilaie-Dotan et al., 2015). Hence, neuroimaging techniques may not represent a useful methodology for the investigation of cognitive estimation. Instead, neuropsychological studies may represent a more promising investigation tool for identifying the brain areas that are necessary for CET performance.

The aim of the current study was to investigate these theoretical and anatomical issues in relation to one of our two recently developed versions of the CET (CET A) in patients with focal, unilateral, frontal or posterior lesions and HCs. We grouped together focal non-traumatic frontal lesions due to tumour or stroke, as our previous work has shown that the grouping of patients with frontal lesions due to low- and high-grade glioma, meningioma or stroke ( $n = 100$ ) is a pragmatic and

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