Neuropsychologia 51 (2013) 385–391

Contents lists available at SciVerse ScienceDirect

Neuropsychologia

journal homepage: www.elsevier.com/locate/neuropsychologia

Metacognitive and online error awareness deficits after prefrontal cortex lesions

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ARTICLE INFO

Article history:
Received 30 May 2012
Received in revised form
5 October 2012
Accepted 14 November 2012
Available online 27 November 2012

Keywords:
Deficit awareness
Insight
Error monitoring
Error awareness
Brain lesions

ABSTRACT

Awareness of deficits after brain injury represents a significant clinical and theoretical challenge, but relatively little is known about the neuroanatomical correlates of specific types of deficit awareness. We examined the awareness correlates of left versus right prefrontal cortex lesions in comparison to left and right posterior lesions including two types of awareness measures—metacognitive and online error monitoring. Frontal lobe frontal lesion patients exhibited impaired metacognitive awareness and also showed deficits in monitoring errors as they occurred. In addition, frontal lobe lesion patients also showed reduced autonomic response to aware errors. Online and metacognitive awareness were not, however, significantly correlated, suggesting that distinct neuroanatomical systems may underpin these two types of awareness deficit. We hypothesize that while metacognitive awareness depends on both left and right frontal regions, accurate moment-to-moment processing of errors depends more on the right than on the left prefrontal cortex.

1. Introduction

Impaired awareness of deficit resulting from neural injury represent a substantial clinical problem, with numerous studies documenting the negative impact of insight on family members and caregivers (e.g., Prigatano, Borgaro, Baker, & Wethe, 2005), but also on rehabilitation effectiveness, vocational outcome (e.g., Prigatano, 2005) and treatment compliance (Worrall, Chen, Dimberg, & Katz, 2005). Over the past 20 years, such impaired deficit awareness has increasingly been recognised as a multifaceted neuropsychological problem, as distinct from a unitary psychiatric condition (Schacter & Prigatano, 1991), and theoretical models have since been proposed which distinguish between different types of deficit awareness. The most common classification differentiates between 'metacognitive' or 'intellectual' awareness, as separate from 'online' awareness (e.g., Crosson et al., 1989; Toglia & Kirk, 2000). These models view metacognitive awareness as an overall knowledge of one's disorder, while online awareness includes both the ability to recognize errors as they occur (online emergent awareness) and the ability to anticipate problems before they occur (online anticipatory awareness) (Toglia & Kirk, 2000). Whether these aspects of awareness interact in a hierarchical manner is currently under debate (e.g., Abreu et al., 2001; Abu-Akel & Shamay-Tsoory, 2011), with some findings suggesting that the two online components of self-awareness may be closely related to each other, but not necessarily to metacognitive awareness (O'Keeffe, Dockree, Moloney, Carton, & Robertson, 2007a). This is important, since most studies typically assess deficit-awareness using questionnaire discrepancies between patients' self-report and that of a significant other (Fleming, Strong, & Ashton, 1996), and thus arguably only measure metacognitive awareness, while neglecting other, more subtle aspects of awareness.

While the study of impaired deficit awareness among patients with traumatic brain injury (TBI) and degenerative disease such as Alzheimer's disease and fronto-temporal dementia has flourished over recent years, it must be acknowledged that these patients suffer from widespread neural damage, and hence even moderately precise brain–behaviour relationships are difficult to establish. What these patient groups have in common, however, is their vulnerability to frontal systems dysfunction, and indeed, many neuroanatomical models have emphasized the role of fronto-striatal circuits for higher cognitive functions including conscious self-awareness (e.g., Stuss, 1991; Stuss, Picton, & Alexander, 2001).

Theoretical models distinguishing between online awareness of errors and metacognitive knowledge may also be useful for the study of impaired awareness in specific neurological syndromes such as anosognosia following stroke. Within this population, it has been suggested that anosognosia may be the result of a failure of motor monitoring (e.g., Jenkinson, Edelstyn, Drakeford, & Ellis, 2009), which fits well with the notion of impaired error awareness potentially leading to difficulties in metacognitive understanding that one has an illness. Neuroanatomically, a number of

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http://dx.doi.org/10.1016/j.neuropsychologia.2012.11.019

studies have suggested that there may be asymmetry in deficit awareness among anosognosia patients, with right hemisphere, and in particular right frontal impairment, beings associated with greater deficit awareness. For example anosognosia for hemiparesis has been found to be particularly associated with right fronto-parietal dysfunction (see Pia, Neppi-Modona, Ricci, & Berti, 2004; Orfei et al., 2007 for reviews). Similarly, Vocat, Staub, Stroppini, and Vuilleumier (2010) report that networks involving right premotor, cingulate gyrus, temporoparietal junction and medial temporal lobe areas were implicated in chronic anosognosia for hemiplegia. In Alzheimer's disease, a number of studies have used single photon emission computed tomography (SPECT) to show that hypoperfusion of right dorsolateral prefrontal cortex us associated with patients' deficit awareness deficits (e.g., Starkstein et al., 1995).

No study has hitherto examined metacognitive and online awareness deficits in a focal lesion population. Thus, following from our previous research on these separate deficit awareness subtypes in traumatic brain injury (O'Keeffe et al., 2007a) and dementias known to involve atrophy of the frontal lobes (O'Keeffe et al., 2007b), in this study we test the hypothesis that frontal lobe lesions will be associated with one or both of these types of awareness deficit. Previous work from our lab has shown that impaired deficit awareness may be mediated by poor processing of errors associated with lowered autonomic response to errors as shown by skin conductance responses (SCR) (O'Keeffe, Dockree, & Robertson, 2004) and so we had an additional interest in testing a second hypothesis, that these responses will also be diminished in right frontal lesions patients. As the frontal lobe model of awareness was of particular relevance here, we focussed on recruitment of those patients with predominantly unilateral brain lesions in the frontal lobe or outside the frontal lobe, without further neuroanatomical specificity for non-frontal regions.

2. Method

2.1. Participants

Patients for this study were recruited on a voluntary basis through the Department of Psychology in Beaumont Hospital, Dublin, using the following inclusion criteria: Patients must be between the ages of 18 and 70 years, and have received a diagnosis of a focal brain lesion in any of the four cortical regions specified—right or left frontal, right or left non-frontal cortex, with the additional requirement that lesions did not include the motor cortex. Patients were also excluded from the study if any of the following applied: a history of alcohol/substance abuse, diagnosis of a major psychological/psychiatric disorder, any additional neurological disorder, current disorientation, aphasic difficulties, visuospatial impairment or neglect. This led to a sample of 12 left frontal (LF) and 7 right frontal (RF), as well as 14 left non-frontal (LNF) and 12 right non-frontal (RNF) focal lesion patients (total=45). Patient groups did not differ significantly for time since lesion (TSL) [$F(3,41)=2.03$; $p>0.05$]. Table 1 displays the clinical details for each patient, including diagnosis, time since lesion (TSL) and the type of clinical brain scan available. MRI scans were available for 29 patients, while CT images were provided for 16 patients. Representative slices of patients' MRI or CT scans are shown in Fig. 1a–d. Since all scans were clinical in nature and thus varied considerably in orientation and other parameters, lesions are shown on an individual basis, rather than on reconstructed lesion maps.

A sample of 15 healthy volunteer participants served as a control group. Exclusion criteria were the same as for patients, with the additional requirement that control participants must never have suffered a head injury leading to a loss of consciousness or memory.

Ethical approval for the study was obtained from the research ethics committees of Beaumont Hospital and Trinity College Dublin. Informed consent was obtained from all participants according to the Declaration of Helsinki. All participants received reimbursement for travel expenses.

2.2. Materials and procedure

All participants completed a testing session of approximately 2.5 h, which included the following neuropsychological measures:

2.2.1. Screening measures

Revised National Adult Reading Test for premorbid IQ estimate (NART-R; Nelson, 1982).

Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) for symptoms of anxiety and depression.

2.2.2. Neuropsychological measures

2.2.2.1. Memory

2.2.2.1.1. Working memory. Digit span and Spatial span subtests from the Wechsler Memory Scale (WMS) III (Wechsler, Wycherly, Benjamin, Crawford, & Mockler, 1998).

2.2.2.1.2. Verbal memory. Logical memory (immediate and delayed) subtest from the WMS III.

2.2.2.1.3. Visual memory. Faces (immediate and delayed) subtest from the WMS III.

All test scores were converted into scaled scores, which have a mean of 10 and a standard deviation of 3.

2.2.2.2. Attention

2.2.2.2.1. Visuomotor attention. Trail making test (TMT; Partington & Leiter, 1949)—total number of errors made in part B.

2.2.2.2.2. Sustained attention. Participants were required to perform three blocks of the fixed-sequence version of the sustained attention to response task (SART; Manly et al., 2003; Robertson, Manly, Andrade, Baddeley, & Yiend, 1997). Participants were instructed to press the left mouse button for all numbers presented in fixed ascending sequence, and withhold responses for the number '3'. The error score is the percentage of commission errors across all blocks (commission errors/ number of no-go targets $\times$ 100).

2.2.2.3. Executive functioning

2.2.2.3.1. Verbal fluency. For letters F, A and S, the total number of items generated during 60 s served as the score.

2.2.2.3.2. Semantic fluency. The total number of animals named within 60 s (Spreen & Strauss, 1998).

2.2.3. Awareness measures

2.2.3.1. Metacognitive awareness. Three questionnaires were administered to investigate metacognitive awareness:

Frontal Systems Behavior Scale (*FrSBe-Other*) (Grace & Malloy, 2002), which rates the frequency of symptoms associated with frontal systems damage. Higher scores indicate more symptomatology.
Cognitive Failures Questionnaire (*CFQ-Other*) (Broadbent, Cooper, FitzGerald, & Parkes, 1982), which rates the frequency of everyday cognitive failures and absentmindedness. Higher scores indicate more symptomatology.
Patient Competency Rating Scale (*PCRS-Other*) (Prigatano & Fordyce, 1986), which rates participants' competencies on activities of daily living, interpersonal, cognitive and emotional competencies. Higher scores indicate higher competencies on the PCRS.

We measured metacognitive awareness by calculating discrepancies between self- and other ratings on the CFQ, FrSBe and PCRS ('Self' minus 'Other' for CFQ and FrSBe; 'Other' minus 'Self' for PCRS[1]), so that negative discrepancy scores indicate an under-estimation of difficulties. A compound *z*-score served as the metacognitive awareness score.

2.2.3.2. Online emergent awareness

2.2.3.2.1. Error awareness on SART. Participants were required to verbally indicate awareness of commission errors on the SART as they occurred ('Hit!'). All digits were presented for 300 ms and 800 ms inter-stimulus interval, in a fixed and repeating sequences from 1 to 9.

2.2.3.2.2. Skin conductance response (SCR) during SART. SCR was measured during SART performance, using a Biopac Systems Inc. MP30 unit, electrodes and software (www.biopac.com). Two Ag/AgCl electrodes, mounted in individual housings and shielded to minimize noise interference, were filled with SIGMA® gel and attached to the distal phalanges of the index and middle fingers of participants'

[1] Since the PCRS measures *competency* rather than rather than *symptoms*, higher scores reflect higher competency. Therefore, when computing discrepancies, we calculated ''other'' scores minus ''self'' scores, so that negative discrepancy scores on the PCRS would indicate unawareness, consistent with the other questionnaires used in this study.