CORTEX 49 (2013) 668–678

Available online at www.sciencedirect.com

SciVerse ScienceDirect

Journal homepage: www.elsevier.com/locate/cortex

Research report

Neuroanatomy of impaired self-awareness in Alzheimer's disease and mild cognitive impairment

Giovanna Zamboni [a,b,*], Erin Drazich [a], Ellen McCulloch [a], Nicola Filippini [b], Clare E. Mackay [b], Mark Jenkinson [b], Irene Tracey [b] and Gordon K. Wilcock [a]

[a] Oxford Project to Investigate Memory and Ageing (OPTIMA), Nuffield Department of Clinical Medicine, University of Oxford, UK
[b] Oxford Centre for Functional Magnetic Resonance Imaging of the Brain (FMRIB Centre), Nuffield Department of Clinical Neurosciences, University of Oxford, UK

ARTICLE INFO

Article history:
Received 15 November 2011
Reviewed 7 February 2012
Revised 7 March 2012
Accepted 20 April 2012
Action editor Robin Morris
Published online 8 May 2012

Keywords:
Anosognosia
Self-awareness
Self-appraisal
Alzheimer's disease
Mild cognitive impairment
Medial prefrontal cortex
Anterior temporal lobe

ABSTRACT

Introduction: Patients with Alzheimer's disease (AD) and mild cognitive impairment (MCI) may be unaware of their cognitive impairment. The neuroanatomical mechanisms underlying this symptom, termed *anosognosia* or *impaired self-awareness*, are still poorly understood. In the present study we aimed to explore the functional correlates of self-awareness in patients with MCI and AD.

Methods: Fifty-one participants (17 healthy elderly, 17 patients with MCI, and 17 patients with AD), each accompanied by a study partner, took part in a functional magnetic resonance imaging (fMRI) study, in which they were presented with questions regarding themselves (Self condition) or their study partner (Other condition). The study partner was asked to complete a paper questionnaire answering the same questions so the responses of participant and study partner could be compared and "discrepancy" scores calculated for each of the 2 conditions (Self and Other).

Results: Behavioural results showed that AD patients had significantly higher "Self discrepancy scores" than controls and MCI patients, whereas there were no significant differences between groups for "Other discrepancy scores". Imaging results showed a significant group-by-condition interaction in brain activation in medial prefrontal and anterior temporal regions, with AD patients showing significantly decreased activation in these regions only for the Self condition. There were no significant differences between Self and Other conditions in either control or MCI groups, suggesting that, in these groups, Self- and Other-appraisal share similar neuroanatomical substrates.

Conclusions: Decreased functional activation of medial prefrontal and anterior temporal cortices is associated with impaired self-awareness in AD patients. This dysfunction, which is specific for Self- but not for Other-appraisal, may be a contributing factor to anosognosia in AD.

* *Corresponding author*. FMRIB Centre, University of Oxford, John Radcliffe Hospital, Oxford, OX3 9DU, UK.
0010-9452/$ – see front matter © 2012 Elsevier Ltd. All rights reserved.
doi:10.1016/j.cortex.2012.04.011

1. Introduction

Patients with Alzheimer's disease (AD) and mild cognitive impairment (MCI) may be unaware of their cognitive or behavioural disturbances. The inability to recognize one's own neurological and psychiatric impairment (i.e., motor, sensory, cognitive or behavioural) is termed *anosognosia*. It usually indicates a condition in which patients have a preserved capacity to evaluate feedback given by others but nevertheless fail to recognize their medical condition. In the context of MCI and AD, *anosognosia* has also been referred to as *impaired self-awareness* to cover the entire range of disturbances in self-awareness, including less severe forms of anosognosia (Prigatano, 2009).

Several studies investigating the neuropsychological correlates of anosognosia in MCI and AD (for review see Kaszniak and Edmonds, 2010; Roberts et al., 2009; Ecklund-Johnson and Torres, 2005; Souchay, 2007), have shown that anosognosia cannot be explained by dementia severity (Hannesdottir and Morris, 2007; Reed et al., 1993), episodic memory deficit (Reed et al., 1993; Zamboni et al., 2010) or executive dysfunction (Vogel et al., 2005; Derouesne et al., 1999) alone, although considerable variability has been shown across studies, with some, but not all, demonstrating relationships with measurements of episodic memory (Hannesdottir and Morris, 2007) and executive functions (Lopez et al., 1994; Dalla Barba et al., 1995; Kashiwa et al., 2005). Nor can anosognosia be accounted for by patients' difficulties in grasping and understanding tasks or questionnaires or difficulties in judging and estimating people's features (Kaszniak and Edmonds, 2010). Instead, support has been provided for the hypothesis that anosognosia in MCI and AD may reflect, at least in part, a failure to update the enduring self-awareness system based on the set of beliefs of one's own capacities, attitudes, and traits in relation to those of others (Agnew and Morris, 1998; Kaszniak and Edmonds, 2010). In relation to this, a neuropsychological model which distinguishes between anosognosia *secondary* to memory or executive dysfunction, which may affect the immediate ability to judge cognitive performance, and *primary* anosognosia, which instead directly affects this longer-term and enduring self-awareness system, has been proposed (Hannesdottir and Morris, 2007; Morris and Hannesdottir, 2004).

Whereas the mechanisms of anosognosia in terms of neuropsychological correlates have been largely studied, their brain correlates have been little investigated. Indeed, the few studies performing anatomical investigations have mainly looked at correlations between measurements of anosognosia and variables representing brain function or morphology, without explicitly testing neuropsychological models of anosognosia. In addition, most of these studies have exclusively focused on specific region of interests in the brain (for a review see Zamboni and Wilcock, 2011). The only two studies that used task-related functional MRI to study mechanisms of anosognosia in MCI (Ries et al., 2007) or AD (Ruby et al., 2008), failed to find differences between patients and controls in the performance of the task used to measure self-awareness during scan or a functional-behavioural correspondence, thus limiting the interpretability of imaging results.

Here, we used task-related functional magnetic resonance imaging (fMRI) to directly explore the neural basis of self-awareness in MCI and AD. We adopted an approach that fosters an operational definition of self-awareness in relation/opposition to non-self or others (Lieberman, 2007; Northoff and Bermpohl, 2004), in line with several recent neuroimaging studies showing that the neural activity of certain cortical areas is specific for the evaluation and processing of self-related information relative to non-self-related stimuli. These studies have been mostly conducted on healthy adults (Johnson et al., 2002; D'Argembeau et al., 2005; Ochsner et al., 2004; Mitchell et al., 2006, 2002; Northoff and Bermpohl, 2004). Using experimental paradigms requiring appraisal of one's own characteristics (self-appraisal) in comparison with appraisal of other people's characteristics (other-appraisal), they have consistently shown the involvement of medial prefrontal cortex (MPFC) (Northoff et al., 2006; Amodio and Frith, 2006; Schmitz and Johnson, 2007), posterior cingulate/precuneus (Northoff et al., 2006), and lateral temporo-parietal regions (Decety and Sommerville, 2003) in self-referential processing. Self-awareness refers to the capacity to reflect upon and identify with one's own abilities, attitudes, and behaviour. Therefore experimental paradigms used to study self-awareness may provide important information in settings in which this capacity is lost, such as in the case of demented patients with anosognosia (Klein et al., 2003; Prigatano, 2009; Ries et al., 2007).

We used an fMRI paradigm adapted to the needs of patients with cognitive impairment similar to paradigms used in previous fMRI studies of self-awareness conducted on healthy adults (self- and other-appraisal), which included appraisal of cognitive, behavioural and physical traits so that we could study different aspects of self-awareness. In contrast to previous fMRI studies on anosognosia (Ries et al., 2007; Ruby et al., 2008), we included both participants with MCI and participants with AD so that we could compare these two different stages of cognitive impairment with normal ageing.

Importantly, we used several methodological improvements to obtain a reliable characterization of changes in functional MRI signal independently from differences in brain structure (i.e., brain atrophy) between groups.

We hypothesized that patients with MCI and AD would show a gradient of impaired self-appraisal, which would be reflected in altered neural response to self- relative to other-appraisal in patients with respect to healthy elderly. We anticipated the involvement of anterior regions of the MPFC, which are known to be involved in personal knowledge specifically related to self-representation in healthy adults (Amodio and Frith, 2006; Northoff et al., 2006) and have been recently shown dysfunctional in patients with autism and other psychiatric diseases characterized by altered self-awareness (Blair et al., 2010; Lombardo et al., 2010).

2. Methods

2.1. Subjects

Fifty-one elderly participants took part in the study. Seventeen had a diagnosis of probable AD, 17 had a diagnosis of MCI, and 17 were age- and education-matched healthy controls.