Research report

Cognitive and neuroimaging evidence of impaired interaction between self and memory in Alzheimer's disease

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ABSTRACT

In human cognition, self and memory processes strongly interact, as evidenced by the memory advantage for self-referential materials [*Self-Reference Effect* (SRE) and *Self-Reference Recollection Effect* (SRRE)]. The current study examined this interaction at the behavioural level and its neural correlates in patients with Alzheimer's disease (AD). Healthy older controls (HC) and AD patients performed trait-adjectives judgements either for self-relevance or for other-relevance (encoding phase). In a first experiment, the encoding and subsequent yes—no recognition phases were administrated in a Magnetic Resonance Imaging (MRI) scanner. Brain activation as measured by functional MRI (fMRI) was examined during self-relevance judgements and anatomical images were used to search for correlation between the memory advantage for self-related items and grey matter density (GMD). In a second experiment, participants described the retrieval experience that had driven their recognition decisions (familiarity *vs* recollective experience). The behavioural results revealed that the SRE and SRRE were impaired in AD patients compared to HC participants. Furthermore, verbal reports revealed that the retrieval of self-related information was preferentially associated with the retrieval of contextual details, such as source memory in the HC participants, but less so in the AD patients. Our imaging findings revealed that both groups activated the medial prefrontal cortex (MPFC) at encoding during self-relevance judgements. However, the variable and limited memory advantage for self-related information was associated with GMD in the lateral prefrontal cortex in the AD patients, a region supporting high-order processes linking self and memory. These findings suggest that even if AD patients engage MPFC during self-referential judgements, the retrieval of self-related memories is qualitatively and quantitatively impaired in relation with altered high-order processes in the lateral PFC.

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1. Introduction

The concept of self has received much attention during the last decade. Current theoretical views suggest that despite a phenomenal appearance of unity, the self is actually made of several components. According to Klein and Gangi (2010), the self is formed by different, functionally isolable components including, notably, episodic memories of one's life events and semantic summary representations of one's personality traits. The multiplicity of functionally isolable cognitive components implies that the self might be supported by several brain regions each specialised in one aspect and that some aspects of the self may be preserved while others are impaired in neurocognitive pathologies (Klein and Gangi, 2010; Martinelli et al., 2013b). In this view, Damasio (1999; see also Northoff et al., 2006) distinguished three main systems: the "proto self" that refers to a "bodily-self", the "core-self" which supports the discrimination of self-related stimuli from self-unrelated stimuli, and the "autobiographical self" which reflects the linkage of self-referential stimuli to the memory domain. The "core-self" is supramodal and receives afferent connections from all sensory modalities. It allows for an active and explicit distinction between self and non-self-related intero- and exteroceptive stimuli. In contrast, the "autobiographical self" is related to high-order cognitive processes. Actually, the authors proposed that the core self filters, selects, and provides those stimuli that are relevant for a particular person's self. Only self-related stimuli are then elaborated further by higher-order processing (i.e., in the autobiographical self). The interaction between the self and memory has also been conceptualised in the Self-Memory System (SMS; Conway and Pleydell-Pearce, 2000; Conway, 2005). The SMS contains two main components: *the working self* and *the autobiographical knowledge base*. The working self refers to control processes based on currently active goals. This executive component manages the encoding and controlled retrieval of information in and from the autobiographical knowledge base.

Strong evidence for the interaction between self and long-term memory can be found in studies using laboratory self-referential materials. Indeed, in these studies, retrieval performance is better for information that has been encoded in reference to the self than for information that has been processed semantically or in reference to other people. This well-known cognitive phenomenon, named the Self-Reference Effect (SRE; Rogers et al., 1977), is a strong characteristic of human cognition since it has been observed in various populations including healthy older people (Gutchess et al., 2007), with various materials and various paradigms at encoding and recognition and with different designs (for a review see Symons and Johnson, 1997).

This interaction between self and long-term memory seems to be mediated by complex cognitive mechanisms. Self-reference at encoding may promote elaborate and organized processing, leading to a memory representation having item-specific and relational information (Symons and Johnson, 1997; Klein, 2012). At retrieval, such deeply encoded information would promote recollection [i.e., controlled and conscious episodic retrieval of information together with the context and elaborations from encoding (Tulving, 2002)] rather than

familiarity [i.e., a relatively automatic process of global assessment of memory strength or stimulus fluency (for reviews, see Yonelinas, 2002; Yonelinas et al., 2010)]. In support of this hypothesis, several authors have shown that the retrieval of information associated to the self is more likely to be associated with a recollection-based retrieval as reflected by recollective experience [as assessed by the Remember/Know procedure (Tulving, 1985; Gardiner, 1988)] and source memory (Conway and Dewhurst, 1995; Conway et al., 2001; Carroll et al., 2001; Van den Bos et al., 2010). This phenomenon, termed the Self-Reference Recollection Effect (SRRE; Conway et al., 2001), suggests that recollection-based processes support episodic retrieval of information that has been previously associated to the self.

Alzheimer's disease (AD) is characterized by impaired recollection-based processes, such as controlled retrieval (Knight, 1998; Smith and Knight, 2002; Adam et al., 2005; Genon et al., 2013a) and experience of remembering (Dalla Barba, 1997; Rauchs et al., 2007). In the same line, the quality of the recollective experience for autobiographical memories is impaired in AD patients (Irish et al., 2011a, 2011b; Piolino et al., 2003). In particular, AD patients are impaired across a range of behavioural characteristics inherent to recollective experience, such as self-referential imagery, vividness and retrieval of contextual details (Irish et al., 2011a, 2011b). In summary, these findings suggest that most aspects of recollection-based retrieval, i.e., episodic retrieval, are impaired in AD patients.

In this context, if the retrieval of self-referential information is primarily supported by recollection-related processes (i.e., episodic retrieval), one may assume that it is impaired in AD. More precisely, the impairment of the recollective experience in AD may lead to poor retrieval of self-referential information at the quantitative and qualitative levels, so that patients do not benefit from encoding information in reference to themselves. In other words, one may expect the SRRE and SRE, i.e., interaction between self and memory, to be altered in AD patients. To our knowledge, three studies have investigated the SRE and the SRRE in AD patients. The results of these studies suggest that SRE and SRRE, at the group level, may be relatively preserved when driven by emotional material in AD patients (Lalanne et al., 2010; Kalenzaga et al., 2013; Kalenzaga and Clarys, 2013). Thus, self-reference may, in some cases, promote relational encoding and therefore recollection-based processes at retrieval, in particular, retrieval of contextual details (Carroll et al., 2001) in AD patients. However, to our knowledge, the quality of retrieval experience has never been rigorously examined in AD patients for information encoded in reference to the self.

In healthy young populations, judgements about the self are known to engage cortical midline structures such as the medial prefrontal cortex (MPC; D'Argembeau et al., 2005, 2007; for a review see Northoff et al., 2006). According to Northoff et al. (2006), the ventral part of the MPFC discriminates self-related stimuli from self-unrelated stimuli, hence supporting the core self. As stated above, this self-referential processing filters, selects, and provides those stimuli which are relevant for a particular person's self. Some studies investigated the neural correlates of this self-referential processing (i.e., the core self) in MCI and AD patients and suggested that, in many