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Research report

Relating pessimistic memory predictions to Alzheimer's disease brain structure

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ABSTRACT

Patients with Alzheimer's disease (AD) show impairment of episodic memory and related metacognitive processes. The present study examined subjective metacognitive judgments preceding objective memory retrieval and investigated the neural correlates of pessimistic predictions for successfully retrieved memories in AD patients.

AD patients and healthy older (HO) participants provided predictive judgments on their recognition performance before retrieval of famous (semantic) and recently learned (episodic) names. Correlations between gray matter volume (GMV) in T1 images and behavioral scores were examined with multivariate (partial least square – PLS) and univariate (general linear model – GLM) analyses in AD patients.

AD patients showed a significant proportion of successful name recognition preceded by pessimistic prediction in episodic memory. PLS revealed that the behavioral pattern in AD patients was related with a mainly right lateralized pattern of GMV decrease including medial temporal lobe and posterior cingulate cortex (PCC), but also right ventrolateral prefrontal cortex (VLPFC). GLM further confirmed that pessimistic prediction negatively correlated with GMV in VLPFC.

Thus, impaired monitoring processes (possibly influenced by inaccurate beliefs) allowing inferences about one's own memory performance are primarily related to decrease GMV in VLPFC in AD patients.

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1. Introduction

Patients with Alzheimer's disease (AD) are characterized by severe (although variable) memory impairments. One striking feature highlighted by previous fine examination of memory retrieval of recent memories in AD patients is the dissociation between automatic and controlled processes with the former being relatively preserved (based on familiarity or fluency for the memory trace) while controlled and conscious access to recently encountered information in memory (i.e., episodic memory retrieval) is particularly impaired (Dalla Barba, 1997; Genon et al., 2013, 2014). One relevant aspect that can be examined to better understand the neurocognitive mechanisms of episodic memory retrieval in AD is the insight or subjective judgment that the patients have on their current memory functioning when they are in the context of retrieving information from memory. The extent to which AD patients have conscious access to the memory trace and are able to use this access to monitor their memory functioning during a memory task can be assessed by the patients' overt metacognitive judgments on their memory performance (Souchay & Moulin, 2009). Traditionally, metamemory theoretical framework (Nelson & Narens, 1990) distinguishes metacognitive judgments that are performed during retrieval attempt, with feeling-of-knowing (FOK), from metacognitive judgments that are performed directly after target retrieval, expressed as judgments of confidence (JOC). The few studies that have examined post-retrieval metacognitive judgments (JOC) in AD patients suggested that such metacognitive processes can be relatively preserved (Gallo, Cramer, Wong, & Bennett, 2012; Moulin, James, Perfect, & Jones, 2003), although it might depend on task-demands and the stage of dementia (Dodson et al., 2011). In contrast, predictive metacognitive judgments (FOK) have been found to be altered in AD-like pathology with AD patients and patients with mild cognitive impairment (MCI) tending to overestimate their abilities (Perrotin, Belleville, & Isingrini, 2007; Souchay, Isingrini, & Gil, 2002). Such alteration seems to be specific to judgments related to newly formed episodic memories [word pairs (Souchay et al., 2002)] as studies examining these judgments for general knowledge (semantic memory) suggest that they may be relatively preserved (Backman & Lipinska, 1993; Lipinska & Backman, 1996). Thus, AD patients' abilities to consciously access and monitor the memory content related to recently encountered information are impaired in such a way that predictive judgments on their retrieval performance for these memories are inaccurate.

At the brain level, task-based functional magnetic resonance imaging (fMRI) studies in healthy young participants showed that predictive judgments on episodic memory retrieval performance engage the medial temporal lobe and posterior medial structures, as well as prefrontal regions supporting monitoring processes (e.g., Maril, Simons, Mitchell, Schwartz, & Schacter, 2003). In line with those findings, patients with frontal damage showed impaired abilities to predict their episodic memory performance in a FOK paradigm (Pannu & Kaszniak, 2005; Souchay, Isingrini, & Gil, 2006). Therefore, we assume that cerebral perturbations in prefrontal regions may be related to impaired metacognitive processes supporting subjective judgments on the memory content for newly presented information in AD patients. This hypothesis, and more precisely the neural correlates of inaccurate predictive subjective judgments on available memory content reflecting metacognitive dysfunction, can be examined by relating interindividual variations of fine cognitive performance in a prediction-recognition task to cerebral gray matter variations (Kanai & Rees, 2011).

Importantly, a prediction-recognition task should be distinguished from the traditional paradigm used to examine metacognitive judgments at memory retrieval stage, that is, the FOK paradigm. In this latter, the participants are first asked to overtly recall the target associated to a cue and only when they fail, they are asked to indicate their subjective FOK of the target that they are currently not able to recall. Comparing the FOK (FOKyes *vs* FOKno) of the participant to his/her actual performance (success-failure) in such paradigm allows measuring the global accuracy of online metacognitive processes in clinical populations (such as AD patients) when compared to healthy controls. However, a fine examination of different combinations of judgment and subsequent memory success/failure may be required to tackle AD patients' specific impairment and then examine the neural correlates of such alteration. Furthermore, the identification of the neural correlates of metacognitive abilities within a memory task in AD patients is further complicated by the close relationship between memory and metamemory (Nelson & Narens, 1990). Specifically targeting metacognitive alterations within an associative memory task in AD patients requires performance well above chance level in those patients. In this end, encoding should be deep and successful. That is, efficient encoding should promote persistence of the target memory trace in the subsequent prediction-recognition stage.

In the present study, we designed a new task targeting daily life difficulties of AD such as naming people from their faces and we examined the subjective prediction judgment that preceded correct name recognition. An encoding procedure based on immediate recall and relational encoding of the face and the name ensured deep and efficient encoding of the item. Furthermore, in order to ensure that the revealed prediction-recognition patterns were specific to newly formed memories (i.e., episodic memories), we included a similar task based on famous people (i.e., semantic task) carefully designed to match the episodic task. In the prediction phase, we provided a range of four options to the participants for them to indicate their subjective feeling (Schnyer, Nicholls, & Verfaellie, 2005). This behavioral paradigm allowed examining subjective feeling of failure despite objective memory trace persistence. The corresponding structural correlates at the brain level were then investigated by capitalizing on two statistical approaches and conservative thresholds. Finally, in order to explore whether the revealed behavior–brain relationship pattern was specific to AD patients, we performed similar cognitive-morphologic correlation in a healthy older sample from an independent fMRI study (HOfmri).

2. Methods and materials

2.1. Participants

Seventeen HO adults and 23 patients diagnosed with clinical mild probable AD (McKhann et al., 1984) participated in this

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