CONTROLLED AND AUTOMATIC MEMORY RETRIEVAL IN ALZHEIMER'S DISEASE

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Aim

It is widely accepted that there are multiple forms of memory, which depend on distinct cerebral networks. One important distinction is between controlled (conscious and effortful) and automatic (relatively unconscious and effortless) memory processes. In early Alzheimer's disease, the most frequently affected form of memory is episodic memory, which refers to memory for events that have been personally experienced in a particular spatiotemporal context. Episodic memory is also thought to be influenced by both controlled and automatic memory processes. More specifically, personally experienced events can be retrieved via two forms of memory: recollection, a controlled memory function which designates the recall of the specific details from the initial experience of the events, including details about the spatiotemporal context, and familiarity, a relatively automatic memory function which refers to knowing that one has experienced something in the past without recalling details about the encoding episode. Although familiarity is an explicit form of memory (that can be verbalised), one important underlying mechanism is common to implicit memory: enhanced processing fluency due to prior exposure to the information, which also intervenes in priming. Depending on the task instructions, enhanced fluency is attributed to different sources and leads to different feelings. For instance, in a preference judgment task, a prior exposure to the stimulus (prime) will lead us to prefer this stimulus, without any awareness of the actual link between the prime and the preference judgment. In a memory task, increased fluency due to the prior exposure to the stimulus will lead us to feel that this stimulus has been encountered before (feeling of familiarity). Our work had the objective to assess how Alzheimer's disease affects controlled and automatic memory processes.

Materials and methods

One method to assess the separate contribution of controlled and automatic memory processes to performance within one memory task is the Process Dissociation Procedure. The distinction is made possible by a comparison of two conditions (inclusion and exclusion) in which controlled and automatic memory processes operate in different ways. Typically, in the inclusion condition, both controlled and automatic processes lead to the retrieval of a studied item. In the exclusion condition, automatic and controlled processes work in opposition, with the former leading to an erroneous answer, and the latter helping to avoid it.

We have used this method in two studies in order to compare the impact of very early Alzheimer's disease on controlled and automatic memory processes. The first study also examined the neural bases of controlled memory processes by means of correlation between controlled memory performance and cerebral metabolism (as measured by FDG-PET). In the second study, the neural substrates of controlled memory processing in Alzheimer's disease were assessed by functional magnetic resonance imaging (fMRI).

In a third study, following findings of preserved automatic processes in Alzheimer's disease in the first two studies, we examined whether recognition memory performance can be improved in mild Alzheimer's disease when the use of familiarity is facilitated by the salience of processing fluency due to an earlier encounter with the information. Alzheimer's disease patients and healthy controls performed a verbal recognition memory task where the salience of fluency was manipulated by means of letter overlap. Studied and unstudied words were constituted of either two separate sets of letters (no-overlap condition, high fluency salience) or the same set of letters (overlap condition, low fluency salience).

Results

In the first study, we observed that controlled memory retrieval was specifically affected in Alzheimer's disease, already when patients are in the predementia stage (Mild Cognitive Impairment). In patients with Mild Cognitive Impairment who subsequently converted to Alzheimer's disease, the

decrease in recollection preferentially correlated with lower metabolic activity in the posterior cingulate and dorsomedial prefrontal cortices. These two cerebral areas are core regions within a default network, which is notably involved in recollection, but also in internal mentation in general (thinking about one's past and future, self-reflection). The memory difficulties manifested by patients with Alzheimer's disease may stem from alteration of the default network.
Consistently, in the second study, we have provided evidence for a role of cerebral disconnection within a controlled memory network in the impaired capacity of patients with Alzheimer's disease to recollect the details from the encoding context of an episode. Indeed, successful recollection activated the posterior cingulate cortex in both healthy older adults and AD patients. Crucially, we observed that functional connectivity during recollection was impaired in AD patients. Indeed, in healthy older adults, the posterior cingulate cortex was connected to the hippocampus, the inferior parietal and the dorsolateral prefrontal cortex during recollection, but not in AD patients, suggesting that the residual recollection function in these patients is impoverished by the lack of some recollection-related aspects such as autonoetic quality, episodic details and monitoring.
In contrast to impaired controlled memory processes, automatic memory processes were preserved in early Alzheimer's disease in both studies.
In the third study, examining whether recognition memory performance can be improved in mild Alzheimer's disease when the use of automatic memory processes is facilitated by the salience of processing fluency due to an earlier encounter with the information, the results showed that, although performance was globally poorer in AD patients than in the controls, both groups performed significantly better in the no-overlap condition than in the overlap condition. This suggests that AD patients benefited as much as the controls from the salience of fluency.

Conclusions.
Our work has put forward the existence of a specific impairment of controlled memory processes in Alzheimer's disease, already when patients are in a prodromal phase of the disease and present with Mild Cognitive Impairment. This deficit was related to the alteration of the default network, and more specifically to disconnection between the posterior cingulate cortex on the one hand and the hippocampus, the inferior parietal and the dorsolateral prefrontal cortex on the other hand. Taking advantage of the relative preservation of automatic processes, it is possible to improve Alzheimer patients' memory performance. Nevertheless, fluency-based memory may sometimes lead to false recognitions. It is therefore important to identify circumstances where fluency-based memory alone can efficiently discriminate between old and new information.