

defined. We selected the sites in frontal areas (Fs) for the CNV. As the P300 component was largely distributed, we pooled the electrodes per areas (AFs, Fs, Cs, Ps, and Ts). As we noted lateralized effects in the distribution of these components, we focused on lateralized sites.

Results

Behavioural data. ANOVA on correct detection with Condition (1-back, 2-back, and 3-back) as a within-subject factor and Group (MCI, Elderly Controls, Young) as between-subject factor showed a Group effect ($p = .027$). Post-hoc analysis indicated that MCI and older subjects tended to perform worse than young subjects ($p = .07$ and $p = .06$, respectively), but did not differ from each other. The Condition effect ($p = .001$) indicated that performance decreased with increasing load for all subject groups. The Group by condition interaction was not significant.

Electrophysiological data. On the P300 amplitude, the ANOVA with Condition (1-back, 2-back, and 3-back), Areas (AFs, Fs, Cs, Ps, and Ts), Hemispheres (2) as repeated factors, and with Groups (MCI, Control old, and Young) as the between-subject factor showed a Condition by Group interaction ($p = .021$). The post-hoc analysis indicated that the young subjects showed greater activity (i.e., larger P300 amplitude) than old subjects and MCI patients in the 2-back condition ($p = .01$ and $p = .007$, respectively) and in the 3-back condition ($p = .009$ and $p = .0001$, respectively). Furthermore, in the 3-back condition, elderly control subjects showed significantly larger P300 amplitude than MCI patients ($p = .02$). There was also a Region by Group interaction ($p = .007$). Young subjects showed greater P300 amplitude than old and MCI subjects in central area ($p = .04$ and $p = .004$, respectively), in parietal area ($p = .02$ and $p = .0007$, respectively), and in the temporal area ($p = .03$ and $p = .001$, respectively).

On the CNV area, ANOVA showed a Group effect ($p = .017$). Post-hoc analysis indicated that the CNV was larger for MCI subjects than old subjects ($p = .05$) and for young than old subjects ($p = .031$). The Condition effect was also significant ($p = .05$).

Discussion

The performance of normal aged persons is affected more greatly than the young by increasing the memory load in a working memory task and this is associated with a change in the neural correlates related to the task. In particular, the P300 in the posterior areas was reduced in both normal elderly persons and MCI persons relative to young adults. Although behavioural performance in working memory was comparable between MCI patients and elderly normal subjects, MCI patients presented a greater CNV than old subjects. MCI patients showed also lower P300 amplitude in the most demanding condition compared to older subjects. It could be suggested that MCI subjects could compensate in order to reach equivalent performance to normal elderly subjects. Furthermore, the neural correlates of the working memory seem to vary between old control subjects and MCI patients. These preliminary data must be confirmed with larger number of subjects.

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8. The hippocampal complex facilitates semantic memory retrieval: Positron emission tomography (PET) studies

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Declarative memory involves at least three distinct processes: encoding, storage, and retrieval. Lesion studies indicate that, although the hippocampus complex (HC) is essential for the encoding process of declarative memory, the retrieval of semantic memory can be achieved by directly accessing the storage sites for semantic memory within the neocortex. We provide evidence, however, from two PET studies in normal elderly subjects indicating that the HC is active in semantic memory retrieval and increases the efficiency of this process. In Experiment 1 CBF increases in the right hippocampal gyrus correlated with faster picture naming and, in Experiment 2, CBF increases in the left hippocampus correlated with faster word meaning judgments. We suggest that the HC contributes to more efficient semantic memory retrieval in the elderly.

Report

Withdrawn

9. Qualities of autobiographical memory modulate hippocampal activation during retrieval:

Preliminary findings of an fMRI study

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Autobiographical memory (AM) retrieval appears to specifically activate the hippocampus. It is likely that qualities of AMs that contribute to re-experiencing, such as detail, emotionality, and personal significance, modulate hippocampal activation. We conducted an event-related fMRI study, in which participants retrieved 40 AMs, and rated each for either level of detail, emotion or personal significance. Two control tasks (sentence completion and size discrimination) were also included. Retrieval of AMs activated a previously

reported, predominantly left-lateralized memory network. Retrieval of AMs rated high in detail, emotionality or personal significance resulted in greater hippocampal activation than AMs low in these qualities. Other brain regions showed differential engagement depending on the quality rated, suggesting the activation of different networks of which the hippocampus is a key structure.

Report

It is well established that the medial temporal lobe is important in the retrieval of episodic memory. Recent neuroimaging studies have reported the activation of a predominantly left-lateralized memory network during memory retrieval (Maguire, Vharga-Khadem & Mishkin, 2001). This network includes medial temporal structures, such as the hippocampus and parahippocampal gyrus, in addition to the medial prefrontal cortex, temporal pole, thalamus, posterior cingulate, retrosplenial cortex, and the temporoparietal junction. Consistent with lesion evidence, it appears that medial temporal structures play a critical role in this memory network, particularly in the retrieval of certain types of episodic memory, namely autobiographical memory (AM). For example, Maguire et al. (2001) report that retrieval of autobiographical events activated the left hippocampus. Ryan et al. (2001) found that both recent and remote AMs activated the hippocampus bilaterally.

It is still not clear, however, why the hippocampus is preferentially activated by the retrieval of AMs. While this could be related to the personal nature and temporal specificity of AMs, there is evidence to suggest that hippocampal activation is modulated by the retrieval of certain AMs requiring integration of rich detail and a re-experiencing of the event. Maguire and colleagues (2001) investigated the neural correlates of AM retrieval in a patient who, because of hippocampal damage, distinguished between AMs which he remembered and those which he only knew about. The retrieval of remembered AMs resulted in greater activation of the hippocampus bilaterally than known events, suggesting that hippocampal activation is related to the re-experiencing of AMs. Thus, qualities that contribute to re-experiencing, such as detail, emotionality, and personal significance, may be particularly relevant. As yet, however, the modulating effect of these qualities on the hippocampal activation evident during AM retrieval has not been investigated directly.

Accordingly, we conducted an event-related fMRI study to investigate whether level of detail, emotionality, and personal significance modulates hippocampal activation during AM retrieval. We predicted that first, we would see activation of a left-lateralized memory network during AM retrieval, and secondly, that AMs high in detail, emotionality and personal significance would result in a greater level of hippocampal activation relative to memories low in these qualities.

Methods

Twelve healthy adults (6 male, 6 female, age range, 20–40 years) with no history of neurological or psychiatric impairment, participated in this study. At least 48 h prior to scanning, each participant completed a 2-h pre-scan interview, in which they produced 40 AMs. A list of cues (e.g., “an accident”) was provided to facilitate retrieval, but event memories did not have to be limited to these cues. Participants provided a very brief “title” for each AM, to be later used as a cue during scanning. Each AM was also rated on a five-point scale for the level of detail, emotionality (i.e., the level of emotion the memory currently evokes for the participant), and personal significance (i.e., how life-changing or self-defining the event is).

Immediately prior to scanning, the AM titles produced in the pre-scan interview were repeated to the participant. This was done to avoid any confusion during scanning that could potentially arise from using

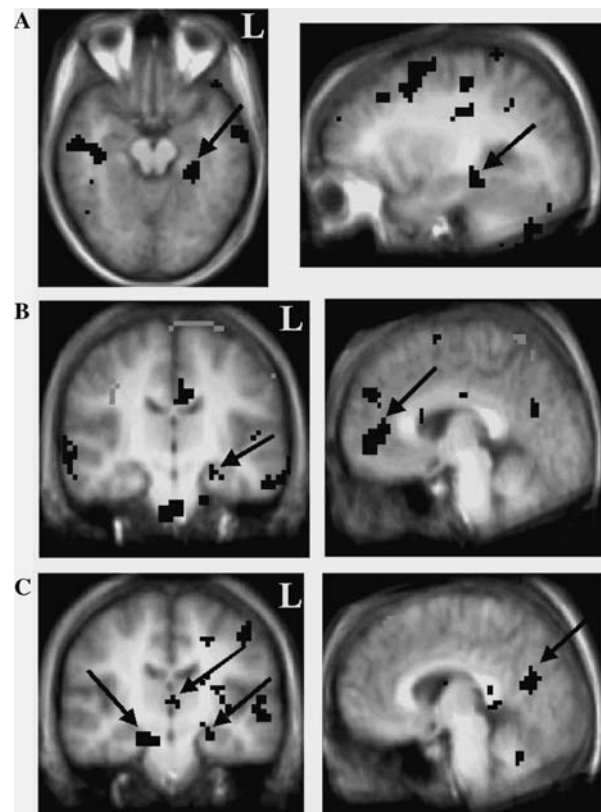


Fig. 1. Activations showing modulation by AM qualities: (A) detail; (B) emotionality; and, (C) personal significance. In each case, increased activity was seen for retrieval of AMs high in these qualities. Arrows indicate activations of interest, including hippocampus (A–C), anterior cingulate (B), and thalamus and precuneus (C).

very brief memory titles. Participants were also presented with the five-point rating scales they would be using in the scanner.

Participants completed two functional scans in a single session. During each scan, 20 of the AMs given in the pre-scan interview were presented. Each AM title was presented visually for 6 s, and participants had been instructed to retrieve the relevant memory. They were then presented with a five-point rating scale (either level of detail, emotionality or personal significance) for 4 s. During this time, they rated the memory by lifting the corresponding finger of the right hand (thumb = 1, etc.), which was recorded by a researcher present in the scanning room. The rating scale remained the same over the duration of a scan, but differed between the two scans. This was followed by a rest period of 6 s; participants had been instructed to focus on resting.

Two control tasks were randomly interspersed between the AM tasks. Ten sentence completion tasks were included in each scan (Ryan et al., 2001), which consisted of a sentence missing the last word (e.g., “The dog ate a _____”). Participants were instructed to silently complete each sentence with a word. The inclusion of this task was to provide a control that involved the retrieval of information from semantic rather than AM. To provide a similar control for visuospatial information, 10 size discrimination tasks were included in each scan. Participants were required to judge the larger of two items. Thus, the names of two objects were presented (e.g., “CD or coin”) along with the word “Biggest” to remind participants of the judgement required. Each control task was presented for 4 s. This was followed by the 4-s presentation of a five-point rating scale for difficulty of task completion, included as a control for the rating made in the memory task. Participants then rested for 8 s.

Functional data were acquired on a 1.5 T Signal MR System (GE Medical Systems, Milwaukee, WI), using single-shot spiral acquisition

(TE = 40 ms, TR = 2000 ms, FOV = 220 mm). Slices were 5 mm thick, with a 1 mm gap, covering the entire brain. These were acquired in a coronal-oblique orientation, with each slice being perpendicular to the long axis of the hippocampus. Preliminary event-related, fixed-effects analyses were conducted using AFNI software. Four comparisons were made: (1) AMs versus the two control tasks; (2) high detail versus low detail AMs; (3) high emotion versus low emotion AMs; and (4) high personal significance versus low personal significance AMs. The last three contrasts included only those AMs given the highest and lowest in-scanner ratings by a subject on the relevant dimension.

Results

The comparison of AM retrieval with the two control tasks, sentence completion and size discrimination, revealed the activation of a predominantly left-lateralized memory network. This network included the medial prefrontal cortex, hippocampus, parahippocampal gyrus, thalamus, posterior cingulate, retrosplenial cortex, and precuneus. The comparisons of AMs high and low in different qualities revealed a modulation of hippocampal activation. The retrieval of AMs rated high in detail resulted in greater activation of the left posterior hippocampus and parahippocampal gyrus. Retrieval of AMs high in emotion was associated with increased activation of the left hippocampus and the anterior cingulate. Finally, the retrieval of AMs high in personal significance resulted in greater activation of the hippocampus bilaterally, the left thalamus, and the precuneus.

Discussion

We replicated the finding of the activation of a predominantly left-lateralized memory network during the retrieval of AMs documented in previous studies (Maguire et al., 2001). The major preliminary finding of this study, however, is that the activation of the hippocampus during AM retrieval appears to be modulated by the level of particular qualities contributing to the re-experiencing of AMs. Thus, we confirmed our hypothesis that the retrieval of AMs high in detail, emotionality, and personal significance activates the hippocampus to a greater extent than AMs low in these qualities. This is consistent with the idea that the hippocampus integrates the various aspects of an AM during retrieval. Thus, if a particular AM requires the integration of a greater level of detail, emotion, and personal significant qualities upon retrieval, the level of hippocampal involvement may be increased accordingly.

It is notable that the nature of hippocampal activations differs in terms of extent of lateralization and the location of activation along the axis of the hippocampus, depending on the quality rated. Specifically, retrieval of greater detail was associated with left posterior hippocampal activation, compared with the more anterior activations associated with retrieving AMs high in emotion (left hippocampus) and personal significance (bilateral hippocampus). This suggests that different regions of the hippocampus may have specific roles in the integration and retrieval of different aspects of autobiographical memories.

An unexpected, but interesting finding is that other brain regions showed differential engagement depending on the particular quality rated. This suggests that, depending on the qualities of an AM, retrieval may require the activation of different networks, of which the hippocampus is always a key structure. When retrieving AMs high in detail, the left parahippocampal gyrus is also activated, consistent with evidence that this region plays a role in retrieving the contextual details of AMs (Burgess, Maguire, Spiers, & O'Keefe, 2001). The retrieval of AMs rated high in emotion also activated the anterior cingulate, a region of known importance in emotional processing (Whalen et al., 1998). The retrieval of AMs high in personal significance also activated the left thalamus and notably, the precuneus. This suggests that this region, known to be active during episodic memory retrieval (Cabeza,

Dolcos, Prince, Rice, Weissman, & Nyberg, 2003), may play a role in the retrieval of information regarding personal significance. Further analyses using functional and effective connectivity will enable confirmation and clarification of these different AM retrieval networks.

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10. The effects of prenatal and current marijuana exposure on response inhibition: A functional magnetic resonance imaging study

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fMRI was used to investigate the effects of prenatal exposure to marijuana and current use of marijuana on response inhibition of 18–22-year-olds as they performed a Go/No Go task. Subjects were recruited from The Ottawa Prenatal Prospective Study, which provides a unique body of information, including drug exposure (prenatal–current), and cognitive/behavioural performance from infancy to adulthood. During response inhibition, current marijuana use was most significantly related to increased right dorsolateral-prefrontal-cortex (DLPFC) and the activity for quitters resembled that of users rather than non-users. Prenatal marijuana exposure was most significantly related to increased activity in left DLPFC, and attenuated right DLPFC activity. In summary, both types of marijuana exposure affect neurophysiological aspects of response inhibition in young adulthood.

Report

Introduction

The Ottawa Prenatal Prospective Study (OPPS) is an ongoing longitudinal study that provides a unique body of information collected over 20 years that includes prenatal drug history, detailed cognitive/behavioural performance from infancy to young adulthood, current and past drug usage, and other lifestyle variables. One of the