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Anterior prefrontal involvement in episodic retrieval reflects contextual interference

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Different patterns of prefrontal activation are commonly found in studies of episodic and source memory (typically anterior and lateral) compared to those found in studies of autobiographical memory (typically ventromedial). We investigated a proposal that the former pattern reflects contextual interference when retrieving events that occurred in similar contexts. We used virtual reality to simulate contextually varied life-like events, in which subjects received distinct objects from a number of people in a number of locations. We compared fMRI data from two experiments in which the number of events per context varied. The first experiment (Burgess, N., Maguire, E.A., Spiers, H.J., and O'Keefe, J. 2001. A temporoparietal and prefrontal network for retrieving the spatial context of lifelike events. Neuroimage 14, 439–453) involved 16 objects received from one of two people in one of two locations. The second experiment involved 20 objects, each received from a different person in a different location. The first experiment showed extensive bilateral activation of anterior and lateral prefrontal cortex, as well as a medial temporal and parietal network characteristic of both autobiographical and episodic memory. In the second study, the prefrontal activations were largely absent, while the medial parietal and temporal activations remained, and a ventromedial prefrontal area was additionally activated. Direct comparisons revealed large areas of significantly reduced activation in BA10, with lesser reductions in lateral prefrontal regions. We suggest that involvement of these prefrontal regains in episodic and source memory reflects the use of paradigms involving many events and few sources rather than any fundamental processing requirement of contextual retrieval in the absence of interference.

Keywords: Anterior prefrontal cortex; Episodic retrieval; Contextual interference; Context-dependent memory; Source memory; Autobiographical memory

Introduction

Episodic memory (Tulving, 1983), the recollection of events we have experienced in the past, has been considered in terms of two different types of information that might be retrieved (Burgess et al., 2001; Johnson et al., 1993)—the content of the event and the external context in which it occurs. Content refers to the change in the world that forms the event, while context is taken to mean the ongoing external circumstances relating to the event, such as the location, the time, the prevailing weather, and so on. Episodic recollection is often operationally defined by the ability to remember contextual information, while the content of an event can be recognised or "known" in the absence of any contextual information (Gardiner and Java, 1991; Yonelinas and Levy, 2002). There is a growing consensus that the medial temporal lobes (and the hippocampus in particular) provide the neural basis for episodic memory (Aggleton and Brown, 1999; Cohen and Eichenbaum, 1993; Kinsbourne and Wood, 1975; O'Keefe and Nadel, 1978; Scoville and Milner, 1957; Squire and Zola-Morgan, 1991), i.e. context-dependent memory for personally experienced events (Tulving, 1972, 1983). Evidence from neuroimaging (Cabeza et al., 2004; Maguire and Frith, 2003; Maguire et al., 2000, 2001; Piefke et al., 2003) suggests that autobiographical memory involves a temporal and parietal network consistent with this picture. In addition, it also involves a region of ventromedial prefrontal cortex which has been implicated in processing personal information (Gusnard et al., 2001; Johnson et al., 2002; Kelley et al., 2002).

Researchers interested in prefrontal contributions to memory have focused on a theoretical categorisation of memory, related to context-dependent memory, known as 'source memory'. Source here refers to a combination of characteristics that together define the conditions under which a memory was acquired. This includes context and also the media and modalities by which the content was received (Johnson et al., 1993). Despite the close relationship between source memory and context-dependent episodic memory, source memory performance correlates with performance on 'frontal' tasks (Glisky et al., 1995; Schacter et al., 1984) and with frontal electrophysiological activity (Johnson et al., 1997) and is

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usually characterised as impaired by prefrontal damage (Schacter et al., 1984; Shimamura et al., 1990; Janowsky et al., 1989) rather than by medial temporal damage. Consistent with this difference, functional neuroimaging studies of source memory for laboratory-type stimuli reveal a different pattern of prefrontal activation than the autobiographical memory studies, see Gilboa (2004) for a review. Typically, anterior, dorsolateral, and ventrolateral prefrontal cortices are implicated in source memory studies (Henson et al., 1999; Rugg et al., 1999). While these prefrontal areas are unlikely to provide the storage sites for context-dependent memory, they clearly have an important role to play in the strategic organisation of retrieval (Christoff and Gabrieli, 2000; Dobbins et al., 2002; Henson et al., 1999; Rugg et al., 1999; Stuss and Benson, 1984), see Simons and Spiers (2003) for a review. Indeed, disconnection of the frontal and temporal lobes has been proposed as a cause of organic amnesia (Levine et al., 1998; Markowitsch, 1995; Warrington and Weiskrantz, 1982).

This paper concerns the nature of the prefrontal role in context-dependent memory. We focus on the intriguing differences between the patterns of prefrontal activation found in source memory compared to episodic recollection of autobiographical stimuli, despite the apparent operational similarity of testing these two processes. One potential explanation for these differing patterns (Burgess et al., 2001) is that prefrontal cortex is involved in selecting the correct event in the face of interference from several other events sharing a similar context. Source memory paradigms typically use a limited number of sources (such as 2 locations, 2 voices, or 2 lists presented at 2 different times), which is also typical of many laboratory tests of episodic or context-dependent memory. Real world episodic memories (or autobiography), on the other hand, tend to have richer and more distinct contexts, and thus the recall of episodic source or context involves the recall of a more unique set of information for each event.

Consistent with this interpretation, prefrontal cortex has been associated with interference (Henson et al., 2002; Incisa della Rocchetta and Milner, 1993; Smith et al., 1995) and competition (Sohn et al., 2003) in memory tasks. A previous experiment (Burgess et al., 2001) used controlled pseudorealistic events presented within a virtual environment (VE) to ensure a rich contextual element to the memoranda. During learning, subjects received a series of objects from one of two people in one of two locations. Between each event, the subject followed a marked route to the next location. Subjects were tested for their memory of the place and person associated with each object, as well as context-independent object recognition, in a forced choice recognition paradigm. Testing took place during fMRI scanning. In each test, subjects were presented with a pair of objects in a location containing a person and cued to indicate which object was associated with either (a) the person (context-dependent memory) or (b) the place (also context), or (c) which object was familiar (content/object familiarity), or (d) which was wider (perceptual control). Crucially, all 16 events involved reusing the same 2 characters and 2 locations due to limitations in the technology available at the time. Extensive activations were found in dorsolateral, ventrolateral, and anterior prefrontal cortex in context-dependent memory compared to object recognition, resembling those found in source memory studies. This finding suggests that contextual richness is not the causal difference between prefrontal involvement in source memory and autobiographical paradigms. By contrast, the repeated use of the same contexts leaves open the possibility that interference is the determining factor in lateral and anterior prefrontal involvement.

Here, we present an experiment using a similar paradigm to Burgess et al. (2001), in which subjects' memory is again tested for the context or content of events, but in which each event occurs in a unique context (i.e. involving a different person and place). We hypothesised that the pattern of prefrontal recruitment would be more like that found in autobiographical memory studies, while the recruitment of posterior areas would be largely unchanged from the previous study of Burgess et al. (2001). In addition, we included a condition in which the target object is re-presented with both contextual cues (place and person). This might be thought to aid more complete re-experiencing of the event or 'ecphory' compared to the individual contextual cues alone, possibly associated with episodic memory (Tulving, 1983). The number and duration of questions required to test memory for the contexts of the simulated events ruled out experimental designs in which interference was manipulated within a single session (see Materials and methods).

Materials and methods

The methodology of the present study was similar to that used by Burgess et al. (2001), including using the same MRI scanner and scanning parameters, see below. By increasing the number of locations and characters so that each event had a unique context, we reduced the amount of contextual interference. The previous study featured 16 events in only 2 locations involving 2 characters. By increasing the number of events to 20, we hoped to maintain a similar level of difficulty. The virtual town consisted of several buildings connected by roads and staircases (see Fig. 1a). The 20 locations in the town chosen to be the loci for events were selected to provide views that were as different from each other as possible.

The participants were 13 healthy right-handed male volunteers with ages ranging from 18 to 45 years (mean 26.9 years, SD 6.3 years). All gave informed written consent in the study which was approved by The National Hospital for Neurology and Neurosurgery and The Institute of Neurology Joint research ethics committee. Prior to scanning, participants practiced procedural aspects of the task, experiencing and answering questions on 3 trial events. For the main experiment (conducted in the MRI scanner), each participant started the experiment at the same location in the VE, from where a path was indicated by green markers. The participant followed the markers, controlling their movements using four keys (forward and back, and left and right turns), to the location of the first encounter, where 1 of 20 characters was waiting. When the participant approached within 5 virtual metres of the character, it stepped to one side (randomly chosen) and presented a large image of a common object on the other side (see Fig. 1b for an example). The subject was instructed to study the scene and remember the object, which person gave it to them, and in which place. After a self-paced study delay, they moved forward into the object, which caused it and its (now out of view) "owner" to disappear and the markers to the next location to appear. This process was repeated for a total of 20 events, after which the testing phase of the experiment and fMRI scanning took place.

Testing involved presentations of images taken from standard viewpoints of the event locations in the VE to standardise the stimuli used in the scanning phase of the experiment. The test images were composed from viewpoints typically seen by the subjects and consisted of 1 of the 20 characters in 1 of the 20 locations together with two of the presented objects (see Fig. 1c for an example). These pictures were used to ask 5 types of