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Neural correlates of autobiographical memory in amnestic Mild Cognitive Impairment

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ABSTRACT

Episodic memory dysfunction, commonly assessed with word list recall, is the main characteristic of amnestic Mild Cognitive Impairment (aMCI). While brain pathology underlying this kind of memory impairment is well established in aMCI, little is known about the effect of neurodegeneration on autobiographical memory. The present study investigated neuronal correlates of autobiographical memory in aMCI patients ($n=12$) and healthy elderly controls ($n=13$) using functional magnetic resonance imaging (fMRI). Additionally, voxel-based morphometry (VBM) was employed to reveal brain pathology in aMCI patients. Neuropsychological assessment showed significant impairment in episodic memory tasks (immediate and delayed word list recall) in aMCI patients. Moreover, VBM revealed significantly reduced gray matter concentration, which was most pronounced in the temporal lobes of aMCI patients. Despite episodic memory impairment and atrophy in areas that are associated with encoding and recall of episodic memories, aMCI patients showed no alterations in brain activation associated with autobiographical memory retrieval. These findings could suggest that autobiographical memory is subserved by a different neuronal network than episodic memory and that the two memory systems are differently affected by aMCI.

1. Introduction

Amnestic Mild Cognitive Impairment (aMCI) is characterized by slight cognitive deficits, especially for episodic memory, in the context of otherwise normal daily functioning and has been suggested as a transitional stage between normal aging and early dementia (Petersen, 2004). People suffering from aMCI have a high risk to develop Alzheimer's disease with progression rates of approximately 12% per year (Petersen, 2004). The main characteristic of aMCI is a selective impairment of memory function beyond that expected for age, commonly confirmed by neuropsychological tests. The key criterion for the diagnosis of aMCI is a performance of 1.5 standard deviations below age norms in a mnemonic test (Petersen, 2004) that typically comprises learning and retrieval of word lists (e.g. California Verbal Learning Test, Delis et al., 1987 (Consortium to Establish a Registry for Alzheimer's Disease (CERAD) word list, Morris et al., 1988). Retrieval of previously learned material under laboratory conditions is commonly considered to involve episodic memory. Since this form of episodic memory typically concerns stimuli encoded in the laboratory, it sometimes has been termed "laboratory" episodic memory (see Cabeza and St Jacques, 2007; Burianova et al., 2010). Neuroimaging studies have shown that the medial temporal lobes (MTL) play an important role for encoding and retrieval of "laboratory" episodic memories. (Markowitsch, 1995; Fink et al., 1996; Burianova and Grady, 2007). Episodic memory impairment in aMCI as assessed with neuropsychological tests is most likely a result of a functional degradation of this brain area. This assumption is corroborated by neuroimaging studies with

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aMCI patients that have revealed gray matter loss in the medial temporal lobes (Pantel et al., 2003; Pantel and Schröder, 2006; Hämäläinen et al., 2007; Whitwell et al., 2008) and have shown a correlation between atrophy in this region and "laboratory" episodic memory (word list recall and recognition) dysfunction (Convit et al., 1997; Chételat et al., 2003; Leube et al., 2008). In addition, several functional neuroimaging studies have shown alterations in the neural network subserving "laboratory" episodic memory retrieval in aMCI patients (e.g. Johnson et al., 2006; Petrella et al., 2006; Kircher et al., 2007; Dickerson and Sperling, 2008).

Autobiographical memory refers to the recollection by subjects of their earlier lives. The contents of autobiographical memory consist of memories for personally experienced episodes, as well as knowledge about personal facts such as the name or date of birth (e.g. Wheeler et al., 1997). Episodic memory and autobiographical memory are both considered to entail a conscious recollection of events and the context in which they occurred (e.g. Tulving, 1984). Despite this commonality, there is an important distinguishing characteristic: the contents of the autobiographical memory system are generally meaningful to the person, they have a high self-relevance and they can encompass the entire lifespan (e.g. Nelson, 1993; Conway and Pleydell-Pearce, 2000; Conway, 2001). Episodic memories, in contrast, such as the retrieval of previously learned word lists, are typically not very high in self-relevance and are stored only for a limited time. A recent fMRI study of "laboratory" episodic and autobiographical retrieval reported an engagement of neural structures that are involved in self-referential processing (ventromedial prefrontal cortex and posterior cingulate cortex) during autobiographical, but not episodic memory retrieval (Burianova and Grady, 2007).

Whereas alterations in networks associated with episodic memory retrieval are well established in aMCI patients (e.g. Johnson et al., 2006; Petrella et al., 2006; Kircher et al., 2007; Dickerson and Sperling, 2008), little is known about the neuronal underpinnings of autobiographical memory retrieval in this patient group. So far, only one study has investigated autobiographical memory in aMCI patients with neuroimaging techniques (Poettrich et al., 2009) and has shown alterations in the neuronal network subserving autobiographical memory retrieval. Behavioral studies on autobiographical memory in aMCI patients have produced ambiguous results. Depending on the method of autobiographical memory assessment, studies have shown either an impairment of autobiographical event memory (Murphy et al., 2008; Gamboz et al., 2010, using an Autobiographical Interview) or intact recall of a personally experienced event (Budson et al., 2007, investigating memories for the September 11, terrorist attacks) in aMCI patients.

The self-defining features of autobiographical memory distinguish it from episodic memory; this is also reflected in the neuronal network associated with the retrieval of autobiographical episodes. Based on the assumption that autobiographical and episodic memory are distinct memory systems, both forms of memory could be differentially affected by brain pathology underlying aMCI. We have investigated the neuronal underpinnings of autobiographical memory in aMCI to shed light on the question whether or not the common findings of altered episodic memory networks in aMCI also pertain to the neuronal network of autobiographical memory. The self-defining characteristics of autobiographical memory might render it less susceptible to degradation , a possibility that should be reflected in a functioning neuronal network even in the presence of brain pathology.

2. Methods

2.1. Participants

Twelve patients with aMCI (7 women, range 59–77 years, mean age 68 years, mean years of education 13.4, see Table 1) were recruited during a 6-month period from our memory disorders clinic. The control group consisted of 13 healthy, elderly participants, matched for age, gender and education (7 women, range 58–72 years, mean age 65 years, mean years of education 13.8, see Table 1), who were recruited through the database of the clinic's research laboratory during the same period. All participants were right-handed and native German speakers. Informed consent was obtained for participation in the study, which was approved by the ethics committee of Johann Wolfgang Goethe University Frankfurt.

Table 1
Demographic characteristics and neuropsychological test scores.

	Normal controls ($n=13$)	aMCI patients ($n=12$)	Statistic	p-values
Demographics				
Sex Female:Male	7:6	7:5		
Age	64.6 (4.0)	68.2 (5.6)		0.25
Education (years)	13.8 (2.7)	13.4 (3.3)		0.64
Neuropsychological assessment				
CDR	0 (0)	0.5 (0)		
MMSE (scale range: 0–30)	29.3 (1.0)	27.0 (1.9)	$t(23)=3.9$	<0.01
Verbal memory				
CERAD list immediate free recall (max 30)	23.7 (2.5)	16.8 (3.9)	$t(23)=5.4$	<0.01
CERAD list delayed free recall (max 10)	8.2 (1.2)	4.5 (1.9)	$t(23)=5.7$	<0.01
Visual memory				
CERAD figure recall (max 11)	10.3 (1.8)	7.5 (3.5)	$t(23)=2.5$	<0.05
Language				
CERAD Verbal fluency	21.3 (4.1)	19.3 (4.1)	$t(23)=1.5$	0.16
Boston Naming Test (max 15)	14.8 (1.9)	14.4 (0.8)	$t(23)=0.9$	0.37
Constructional Praxis				
CERAD figures (max 11)	10.6 (1.12)	10.1 (1.11)	$t(23)=-0.9$	0.36

MMSE = Mini Mental State Examination (Folstein et al., 1975); CERAD = A Consortium to Establish a Registry for Alzheimer's Disease (Morris et al., 1988). The values in parentheses are standard deviations.

Diagnostic assessment of aMCI patients was performed involving by a cooperating multiprofessional team (neurologists, psychiatrists and psychologists). The test battery of the Consortium to Establish a Registry for Alzheimer's Disease (CERAD, Morris et al., 1988) was done by a trained neuropsychologist. Inclusion criteria for the patient group were a) a subjective memory complaint that was confirmed by a performance rating of less than 1.5 standard deviations (adjusted for age and education) below the mean in memory tests (immediate word and delayed word list recall, CERAD); b) normal functioning in everyday life, defined as a score below one on the Clinical Dementia Rating Scale (Morris, 1993); and c) no severe impairment in any cognitive domain other than memory, defined as performance within 1.5 standard deviations of normative data in a neuropsychological test battery (CERAD). Exclusion criteria comprised a history of head injury, neurological or psychiatric disorder and focal lesions in gray matter areas.

2.2. fMRI experiment

2.2.1. Study materials and procedure

Participants were interviewed with a semi-structured Autobiographical Memory Interview (Bielefelder Autobiographical Memory Inventory) several weeks prior to scanning. They were required to retrieve two autobiographical memories from each of four remote lifetime periods (early childhood/late childhood/adolescence/early adulthood) and eight memories of events that happened in the last 5 years (recent). The interviews were transcribed and used to construct verbal stimuli describing specific situations of the reported episodes. Two different stimulus sentences were constructed for each reported autobiographical episode. Thus, four sentences were generated for each of the remote time periods (early childhood/late childhood/adolescence/early adulthood), and 16 sentences were generated for the recent (last 5 years) time period.