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Functional abnormalities of the visual processing system in subjects with mild cognitive impairment: An fMRI study

Arun Lawrence Warren Bokde[a,b,*], Patricia Lopez-Bayo[a], Christine Born[c], Wentian Dong[a], Thomas Meindl[c], Gerda Leinsinger[c], Stefan Johannes Teipel[a], Frank Faltraco[a], Maximilian Reiser[c], Hans-Jürgen Möller[a], Harald Hampel[a,b]

[a]*Dementia and Neuroimaging Research Section, Alzheimer Memorial Center and Geriatric Psychiatry Branch, Department of Psychiatry, Ludwig-Maximilian University, Munich, Germany*
[b]*Discipline of Psychiatry, School of Medicine, Trinity College, The Adelaide and Meath Hospital incorporating The National Children's Hospital (AMiNCH), Dublin, Ireland*
[c]*Institute for Clinical Radiology, Ludwig-Maximilian University, Munich, Germany*

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Abstract

Subjects with mild cognitive impairment (MCI) have a higher risk of developing Alzheimer's disease compared with healthy controls (HC). Sensory impairment can contribute to the severity of cognitive impairment. We measured the activation changes in the visual system between MCI and HC subjects. There were 16 MCI subjects with either amnestic MCI or multiple-domain+ amnestic MCI and an HC group of 19 subjects. There were two tasks: (a) a face matching and (b) a location matching task. Brain activation was measured using functional magnetic resonance imaging. There were no differences in task performance. The HC group selectively activated the ventral and dorsal pathways during the face and location matching tasks, respectively, while the MCI group did not. The MCI group had greater activation than the HC group in the left frontal lobe during the location matching task. There were no areas of increased activation in the HC group compared with the MCI group. The MCI group, as a compensatory mechanism, activated both visual pathways and increased activation in the left frontal lobe during the location matching task compared with the healthy controls. To our knowledge, this is the first study that has examined visual processing in MCI.

Keywords: Functional magnetic resonance imaging; Object matching; Location matching; Visual system; Face matching; Alzheimer's disease

1. Introduction

Progression of cognitive decline to dementia is a major concern in individuals as they age. There seems to be a transition period between a range of normal cognitive function and dementia, and this "transitional" period has been defined using various clinical syndromal terms such as mild cognitive impairment (MCI), incipient or preclinical dementia, and prodromal dementia. The various concepts reflect an attempt to operationalize in part the range within cognitive dysfunction that can be present in subjects that do not yet fulfill the definition of dementia. Even though amnesic MCI is more sensitive and specific for

* Corresponding author. Discipline of Psychiatry, Trinity College, Trinity Centre for Health Sciences, The Adelaide and Meath Hospital, incorporating The National Children's Hospital (AMiNCH), Tallaght, Dublin 24, Ireland. Tel.: +353 1 896 4104; fax: +353 1 896 1313.
E-mail address: Arun.Bokde@tcd.ie (A.L.W. Bokde).

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discriminating between preclinical Alzheimer's disease (AD) and healthy controls (HC) than MCI in general (Petersen et al., 2001a,b), some studies that have examined subjects suffering from multiple-domain MCI including an amnestic domain have found a higher conversion rate to AD than in groups of only amnesic MCI subjects (Bozoki et al., 2001; Palmer et al., 2003). It has been found that the sensitivity and specificity for differentiating between preclinical AD and HC were similar in measures of episodic memory (Tierney et al., 1996; Small et al., 1997; Elias et al., 2000; Backman et al., 2001), perceptual speed (Fabrigoule et al., 1998; Fox et al., 1998; Albert et al., 2001), and visuo-spatial skill (Howieson et al., 1997; Albert et al., 2001). Thus, multiple systems of the brain may be altered in the preclinical (predementia) phases of AD.

As accurate visual function facilitates memory, attention and executive functions, perceptual dysfunction contributes to the severity of cognitive impairment (Cronin-Golomb et al., 1995; Rizzo et al., 2000). Some studies seem to indicate that the ventral visual pathway is more affected (Mendola et al., 1995; Rizzo et al., 2000) while others support greater dysfunction along the dorsal visual pathway (Gilmore et al., 2004). Various imaging studies have suggested that AD patients were more impaired in tasks that activated the dorsal visual pathway than in tasks that activate the ventral visual pathway (Mentis et al., 1996, 1998). Mentis et al. (1996) showed that area MT/V5 in the visual cortex was activated in HC when they attended to motion, but AD patients did not show activation in this area. Area MT/V5 receives input only from magnocellular neurons, the main neuronal population in the dorsal visual pathway. The perceptual effects were not limited to the visual system, as similar effects have been found within the auditory domain. Uhlmann et al. (1989, 1991) found that a significantly greater number of AD patients compared with HC had a hearing loss greater than 30 dB and there was a dose–response relationship between hearing loss and greater adjusted relative ratios of having dementia.

Given the evidence that visual function is impaired in AD, we asked the question whether a group of MCI subjects would exhibit deficits in the visual system. To investigate the effects of visual function along both visual pathways, we developed two visual processing paradigms that preferentially activated either the ventral or dorsal pathway of the visual system. The hypothesis was that MCI subjects would exhibit greater dysfunction for tasks that recruit the dorsal pathway compared with the ventral pathway. We expected that the compensatory processes would include increased activation in the frontal lobes and in the ventral pathway. To our knowledge, this is the first imaging study to investigate visual processing in both pathways in a group of MCI subjects.

2. Methods

2.1. Subjects

There were 16 MCI and 19 HC subjects included in the study (demographic and neuropsychological profiles in Table 1). The MCI patients were recruited from a specialized university-based memory clinic. The clinical assessment included detailed medical history, neurological and neuropsychological examinations, and laboratory tests (routine hematology and biochemistry screen, thyroid function tests). Major systemic, psychiatric, or neurological illnesses were carefully investigated and excluded in all subjects by clinical and neurological examinations, blood testing (complete blood count, sedimentation rate, electrolytes, glucose, blood urea nitrogen, creatinine, liver-associated enzymes, cholesterol, high-density lipoprotein, triglycerides, antinuclear antibodies, rheumatoid factor, HIV, serum B12, folate, thyroid function tests, and urine analysis), and psychiatric examination. Subjects were excluded if they had cortical infarction, excessive subcortical vascular disease, space-occupying lesions, any type of dementia, depression, or other psychiatric or neurological disease. The diagnostic criteria (Petersen et al., 1999, 2001a) were (a) single memory impairment for the age and education of the subject, (b) corroboration of memory impairment by a close family member, (c) relatively preserved cognition for age, (d) no impairment in activities of daily living, and (e) no dementia. Clinical judgment was used to determine whether there was impairment in activities of daily living. The patients were systematically evaluated for the presence of affective symptoms, particularly depression; none of the MCI subjects had depression. The threshold for determining a cognitive impairment was 1.5 standard deviation (S.D.) below the age norms (Welsh et al., 1994; Berres et al., 2000) in the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) neuropsychological test battery (Morris et al., 1989). The diagnosis of the MCI subjects was established through consensus among the responsible psychiatric consultants (SJT, FF and HH). In particular, none of the MCI subjects could be classified as AD using standard clinical criteria (McKhann et al., 1984). The MCI subjects did not have the essential features of AD such as (a) memory impairment, (b) aphasia and/or apraxia, agnosia or impairment in executive function. In