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Simultaneous object perception deficits are related to reduced visual processing speed in amnestic mild cognitive impairment

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ABSTRACT

Simultanagnosia, an impairment in simultaneous object perception, has been attributed to deficits in visual attention and, specifically, to processing speed. Increasing visual attention deficits manifest over the course of Alzheimer's disease (AD), where the first changes are present already in its symptomatic predementia phase: amnestic mild cognitive impairment (aMCI). In this study, we examined whether patients with aMCI due to AD show simultaneous object perception deficits and whether and how these deficits relate to visual attention. Sixteen AD patients with aMCI and 16 age-, gender-, and education-matched healthy controls were assessed with a simultaneous perception task, with shapes presented in an adjacent, embedded, or overlapping manner, under free viewing without temporal constraints. We used a parametric assessment of visual attention based on the Theory of Visual Attention. Results show that patients make significantly more errors than controls when identifying overlapping shapes, which correlate with reduced processing speed. Our findings suggest simultaneous object perception deficits in very early AD, and a visual processing speed reduction underlying these deficits.

1. Introduction

Deficient memory is considered the hallmark of Alzheimer's disease (AD), already manifesting in mild dementia and amnestic mild cognitive impairment (aMCI) as a symptomatic predementia phase of AD (Albert et al., 2011; Morris et al., 2001; Petersen, 2004). However, growing evidence suggests the presence of visual attentional impairments early in the course of AD (Alescio-Lautier et al., 2007; Bonney et al., 2006; Bublak et al., 2011; Finke et al., 2013; Perry and Hodges, 1999; Perry et al., 2000; Rapp and Reischies, 2005; Redel et al., 2012; Rizzo et al., 2000). Significant relationships of such impairments to hypometabolism and functional connectivity changes in frontoparietal attention systems have been documented (Neufang et al., 2011, 2014; Sorg et al., 2007, 2012). Of note, frontoparietal hypometabolism and atrophy overlapping with β-amyloid accumulation at the aMCI stage have been revealed even to precede similar changes in memory-relevant temporal structures (Drzezga et al., 2011; Engler et al., 2006; Kemppainen et al., 2007; Mattsson et al., 2014; Mintun et al., 2006; Sorg et al., 2012). Among the affected attention functions, for example, visual processing speed shows a staged decline (Bublak et al., 2011), implying that individual cases suffer from more or less severe slowing. Critically, for diverse patient groups, it has been suggested that reduced visual processing speed can lead to impairments in the ability to perceive several objects at the same time, that is, to perceive symptoms of simultanagnosia (Chechlacz et al., 2012; Duncan et al., 2003; Finke et al., 2007). Thus, in the present study, we asked whether patients with aMCI show deficits in simultaneous object perception and, if so, whether these deficits are associated with a reduction of processing speed.

Patients with simultanagnosia are not able to integrate the objects within a visual scene to achieve a meaningful interpretation, although recognition of single objects is usually preserved (Bálint, 1909; Coslett and Saffran, 1991; Holmes, 1918; Wolpert, 1924). In patients with full-blown simultanagnosia, perception

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appears to stick to a single object at a time in the scene, resulting in the acquisition of visual information in a piecemeal fashion (Rizzo and Vecera, 2002). Particular severe problems occur if 2 or more objects are presented in an overlapping manner (e.g., Bálint and Harvey, 1995; Luria, 1959). For example, Luria reported that patients with simultanagnosia were not able to identify 2 overlapping triangles of different colors that formed the "star of David"; rather, they reported only one of them (Luria, 1959). Interestingly, the neural damage in cases with simultanagnosia due to acquired lesions typically involves extensive bilateral frontoparietal areas (Chechlacz et al., 2012; Ptak, 2012), including the same regions (e.g., Corbetta, 1998) that are affected in predementia phases of AD (Perry and Hodges, 1999). Thus, some degree of simultanagnosia can be expected to be present in aMCI patients, too.

A crucial step towards a systematic analysis of processing speed and visual short-term memory (VSTM) as putative causes of simultaneous object perception deficits was taken by applying parametric measurement of attention based on the "Theory of Visual Attention" (TVA; Bundesen, 1990) to patients with simultanagnosia. TVA is a unified computational account for visual single-stimulus recognition and attentional selection from multielement displays (Bundesen, 1990), essentially implementing a mathematical formalization of the biased competition model (Desimone and Duncan, 1995). Within TVA, both visual recognition and attentional selection consist in making perceptual categorizations (Bundesen, 1998). There are 2 fundamental capacity parameters that can be independently estimated based on the TVA formalization: visual processing speed *C* and VSTM storage capacity *K*. Parameter *C* is a quantitative estimate of the number of objects that can be processed in parallel per second; parameter *K*, in turn, is the estimate of the maximum number of objects that can be maintained simultaneously in the VSTM store. Both *C* and *K* parameters can be derived from an individual's performance in a whole-report task, where observers' ability to perceive and report multiple letter stimuli is assessed as a function of the effective array exposure duration (Bundesen, 1990) (for application in clinical samples, see Bublak et al., 2011; Finke et al., 2005; McAvinue et al., 2015). Using TVA assessment, Duncan et al. (2003) found severely reduced visual processing speed, even with single-item presentation, in 2 patients with both dorsal and ventral simultanagnosia, while VSTM storage capacity appeared to be preserved (Duncan et al., 2003). Furthermore, Finke et al. (2007) conducted a first group analysis based on TVA: an assessment of patients with Huntington's disease, who typically suffer from increasingly severe visual processing speed deficits (Finke et al., 2006). Finke et al. (2007) found that patients with more pronounced slowing displayed greater impairments in simultaneous object perception. They concluded that a slowing of the rate of visual information uptake gives rise to impaired perception of multiple overlapping stimuli in Huntington's disease (Finke et al., 2007). These results were also replicated in a recent study in patients with posterior cortical dementia (Neitzel et al., 2016). Of note, a staged decline of visual processing speed was also found in the amnestic form of Alzheimer's disease (Bublak et al., 2011). Thus, given the relevance of deficient visual processing speed in diverse patient groups, in the present study we, too, focused on the role of this specific attentional (dys)function with regard to potential deficits in simultaneous object perception in aMCI patients.

In particular, we aimed to ascertain whether there are deficits in simultaneous object perception in aMCI due to AD, and, if so, whether these deficits are associated with a reduction of visual processing speed. To this end, we compared aMCI patients and healthy control (HC) participants on several simultanagnosia tests and a TVA-based whole-report paradigm.

2. Materials and methods

2.1. Participants

Sixteen patients with a diagnosis of aMCI due to AD (9 females; mean age 70.9 ± 7.8 years; 11.6 mean years of education) and 16 age-, gender-, and education-matched HCs (9 females; 69.9 ± 7.4 years old, 11.6 mean years of education) participated in our study. Patients were diagnosed at, and recruited from, the Memory Clinic of the Department of Psychiatry, Technische Universität München, Germany, and controls were recruited from the general community through flyers and word-of-mouth recommendation. All participants gave written informed consent to take part in this study according to the Declaration of Helsinki II, and the study had local ethical committee approval.

Participants underwent a standardized diagnostic process that included medical, psychiatric, and neurological examinations. Patients had additionally brain-imaging diagnostics including structural magnetic resonance imaging and fluorodeoxyglucose positron emission tomography. All participants had undergone an informant-derived Clinical Dementia Rating (Morris, 1993), with patients having values of 0.5 and controls of 0, and neuropsychological assessment using the neuropsychological battery of the Consortium to Establish a Registry for Alzheimer's Disease (CERAD; German version; Berres et al., 2000), including the Mini–Mental State Examination (MMSE; Folstein et al., 1975) and the clock-drawing test (Shulman et al., 1993). Based on this assessment, aMCI patients fulfilled cognitive impairment criteria according to Petersen (Petersen et al., 1999, 2001), along with largely preserved activities of daily living (Bayer ADL scale; Hindmarch et al., 1998), and no dementia according to the International Classification of Diseases, Tenth Revision criteria (WHO, 2010). Furthermore, all aMCI patients of this study met the criteria for MCI due to AD (Albert et al., 2011). Beyond patients' MCI, they had biological signs of AD in terms of bilateral temporoparietal hypometabolism as shown in fluorodeoxyglucose positron emission tomography (Albert et al., 2011). Criteria for exclusion from the study were history of other neurological diseases and imaging evidence of marked brain lesions that affected cognition (e.g., stroke lesions). Three of the 16 patients were under antidepressant medication ($n = 1$ with selective serotonin reuptake inhibitors, $n = 1$ with tricyclic, and $n = 1$ with noradrenergic and specific serotonergic antidepressants). Concerning genotyping, 11 patients had either 1 ($n = 9$) or 2 ($n = 2$) alleles of the APOE $\varepsilon 4$ allele.

HCs were free of any current, or history of, psychiatric or neurological condition. Patients and controls did not differ in age, gender, or education (see Table 1). As expected from the diagnosis, aMCI patients had significantly lower MMSE scores, that is, a lower global cognitive state, than controls [$t(30) = -4.025$, $p < 0.001$] (Table 1 for all demographic details). All aMCI patients were able to follow verbal instructions and to concentrate sufficiently during the tasks. All participants had normal or corrected-to-normal vision and were not color-blind.

2.2. Procedure

After their routine clinical assessment, aMCI patients and controls underwent testing of simultanagnosia and visual attention, specific for the present study. This testing was conducted in 2–3 one-hour sessions. Well-established clinical test batteries known to be sensitive to simultanagnosia symptoms were administered to most of our study participants ($n = 13$ aMCI and $n = 10$ HC). Moreover, the simultaneous perception task (SPT), a time-unlimited experimental task that allows for different levels of