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Learning temporal statistics for sensory predictions in mild cognitive impairment

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ABSTRACT

Training is known to improve performance in a variety of perceptual and cognitive skills. However, there is accumulating evidence that mere exposure (i.e. without supervised training) to regularities (i.e. patterns that co-occur in the environment) facilitates our ability to learn contingencies that allow us to interpret the current scene and make predictions about future events. Recent neuroimaging studies have implicated fronto-striatal and medial temporal lobe brain regions in the learning of spatial and temporal statistics. Here, we ask whether patients with mild cognitive impairment due to Alzheimer′s disease (MCI-AD) that are characterized by hippocampal dysfunction are able to learn temporal regularities and predict upcoming events. We tested the ability of MCI-AD patients and age-matched controls to predict the orientation of a test stimulus following exposure to sequences of leftwards or rightwards orientated gratings. Our results demonstrate that exposure to temporal sequences without feedback facilitates the ability to predict an upcoming stimulus in both MCI-AD patients and controls. However, our fMRI results demonstrate that MCI-AD patients recruit an alternate circuit to hippocampus to succeed in learning of predictive structures. In particular, we observed stronger learning-dependent activations for structured sequences in frontal, subcortical and cerebellar regions for patients compared to age-matched controls. Thus, our findings suggest a cortico-striatal–cerebellar network that may mediate the ability for predictive learning despite hippocampal dysfunction in MCI-AD.

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1. Introduction

Learning through supervised and extensive training is known to shape perceptual and cognitive skills in the adult human brain (Goldstone, 1998; Kourtzi, 2010). However, there is accumulating evidence that mere exposure (i.e. without feedback) to stimuli that co-occur in the environment facilitates our ability to learn contingencies and extract spatial and temporal regularities (for reviews see: Aslin and Newport (2012) and Perruchet and Pacton (2006)). In particular, observers report that structured combinations are more familiar than random contingencies after exposure to items (e.g. shapes, tones or syllables) that co-occur spatially or appear in a temporal sequence (Chun, 2000; Fiser and Aslin, 2002; Saffran et al., 1996, 1999; Turk-Browne et al., 2005). This statistical learning has been shown to facilitate object recognition (Brady and Chun, 2007; Brady and Oliva, 2008), language understanding (Misyak et al., 2010), social judgments (Kunda and Nisbett, 1986) and inductive reasoning (Kemp and Tenenbaum, 2009). This previous work suggests that observers acquire implicit knowledge of the regularities present in a scene, despite the fact that they may not be explicitly aware of its specific structure.

In our previous work (Baker et al., 2014), we have shown that exposure to temporal regularities in a scene facilitates observers to learn its global structure and use this knowledge to predict upcoming sensory events. Recent neuroimaging studies have implicated fronto-striatal and medial temporal lobe regions in the learning of temporal statistics. In particular, the striatum and the hippocampus have been implicated in learning of probabilistic associations (Poldrack et al., 2001; Shohamy and Wagner, 2008) and temporal sequences (Gheysen et al., 2011; Hsieh et al., 2014; Rauch et al., 1997; Rose et al., 2011; Schapiro et al., 2014, 2012; Schendan et al., 2003a).

Here, we ask whether patients with mild cognitive impairment due to Alzheimer's disease (MCI-AD) are able to exploit temporal regularities to predict upcoming events. MCI-AD patients are of particular interest as they show memory impairments (especially

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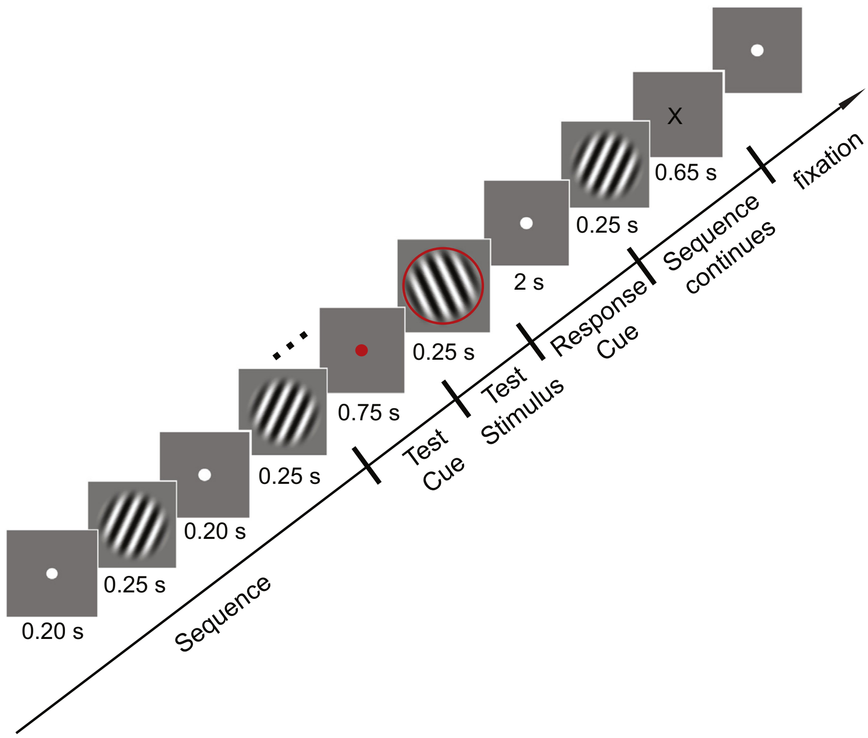

Fig. 1. Stimuli and trial design. A sequence of 8 gratings was presented twice. A stimulus cue followed by a test grating was presented at a random temporal position during the second repeat of the sequence. Following the response to the test stimulus, the remaining gratings of the sequence were presented. A black 'X' indicated the end of the trial.

in episodic memory tasks) (Hudon et al., 2006; Morris and Cummings, 2005; Petersen et al., 1999) and hippocampal dysfunction (Bakker et al., 2012; Celone et al., 2006; Dickerson et al., 2004, 2005b), but preserve their functional independence (Albert et al., 2011) and do not to meet the clinical criteria for dementia. Previous work suggests that MCI patients are not impaired in implicit temporal sequence learning, while explicit temporal sequence learning is shown to require longer training in amnestic MCI-AD compared to age-matched controls (Pirogovsky et al., 2013). However, the brain circuits that may support implicit learning of temporal structures in MCI-AD remain largely unknown. Here, using fMRI (functional magnetic resonance imaging) we test for alternate brain circuits that may support implicit learning of temporal regularities despite hippocampal dysfunction in MCI-AD. To this end, we use a predictive learning task (Baker et al., 2014), that allows us to test for brain circuits that support explicit predictions based on implicitly acquired knowledge.

In particular, we presented MCI-AD patients and age-matched controls with a sequence of leftwards and rightwards oriented gratings that was interrupted by a test stimulus (Fig. 1). Observers had to maintain attention throughout the temporal sequence as the temporal position of the test stimulus was randomly chosen across trials and were asked to indicate whether the orientation of the test stimulus matched the expected stimulus or not. This task provides an explicit recognition measure of implicitly acquired knowledge, avoiding reaction time measurements that may be confounded by differences in speed of processing or response time between patients and controls. Our behavioral results show that the ability to predict the orientation of the test stimulus following exposure to structured sequences improved in both MCI-AD patients and controls. Further, our fMRI results provide evidence for a cortico-striatal–cerebellar network that may facilitate learning of predictive structures despite hippocampal dysfunction in MCI-AD.

2. Materials and methods

2.1. Participants

Twenty-one volunteers (11 MCI patients, 10 age matched controls) participated in this study. The data from two patients and one control were excluded from further analysis due to excessive head movement; therefore data from nine patients (7 male and 2 female; mean age 69.8 years; range 53–86 years) and nine controls (6 male and 3 female; mean age 65.1 years; range 56–83 years) were considered for further analysis. There was no significant age difference between groups ($t(16)=1.02$, $p=0.321$). All participants were naïve to the aim of the study, had normal or corrected-to-normal vision and gave written informed consent. This study was approved by the University of Birmingham Ethics Committee and the NHS National Research Ethics Committe, West Midlands. Patients, diagnosed with MCI-AD by their consultant psychiatrist, were recruited from the Birmingham and Solihull Memory Assessment and Advisory Service. Age-matched controls were recruited through advertising at the local community or were relatives of the MCI patients that participated in the study ($n=3$).

The diagnosis of MCI due to Alzheimer's disease was made by an experienced consultant psychiatrist (PB) using the National Institute on Aging and Alzheimer's Association workgroup criteria (Albert et al., 2011) requiring: a deterioration in cognition reported by either the patient or a close informant; objective impairment in one or more cognitive domains (including memory, executive function, visuospatial skills, attention and language); preservation of independence in daily living activities; absence of dementia and an etiology consistent with Alzheimer's disease pathophysiological process. No patients with vascular-related disease were included in the study. Age-matched controls were screened using the Addenbrookes Cognitive Examination (ACE-III) (Dickerson et al., 2004). Scores for controls (mean=96.0; standard error

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