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Category learning in Alzheimer's disease and normal cognitive aging depends on initial experience of feature variability

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ABSTRACT

Semantic category learning is dependent upon several factors, including the nature of the learning task, as well as individual differences in the quality and heterogeneity of exemplars that an individual encounters during learning. We trained healthy older adults (n=39) and individuals with a diagnosis of Alzheimer's disease or Mild Cognitive Impairment (n=44) to recognize instances of a fictitious animal, a "crutter". Each stimulus item contained 10 visual features (e.g., color, tail shape) which took one of two values for each feature (e.g., yellow/red, curly/straight tails). Participants were presented with a series of items (learning phase) and were either told the items belonged to a semantic category (explicit condition) or were told to think about the appearance of the items (implicit condition). Half of participants saw learning items with higher similarity to an unseen prototype (high typicality learning set), and thus lower between-item variability in their constituent features; the other half learned from items with lower typicality (low typicality learning set) and higher between-item feature variability. After the learning phase, participants were presented with test items one at a time that varied in the number of typical features from 0 (antitype) to 10 (prototype). We examined between-subjects factors of learning set (lower or higher typicality), instruction type (explicit or implicit), and group (patients vs. elderly control). Learning in controls was aided by higher learning set typicality: while controls in both learning set groups demonstrated significant learning, those exposed to a high-typicality learning set appeared to develop a prototype that helped guide their category membership judgments. Overall, patients demonstrated more difficulty with category learning than elderly controls. Patients exposed to the higher-typicality learning set were sensitive to the typical features of the category and discriminated between the most and least typical test items, although less reliably than controls. In contrast, patients exposed to the low-typicality learning set showed no evidence of learning. Analysis of structural imaging data indicated a positive association between left hippocampal grey matter density in elderly controls but a negative association in the patient group, suggesting differential reliance on hippocampal-mediated learning. Contrary to hypotheses, learning did not differ between explicit and implicit conditions for either group. Results demonstrate that category learning is improved when learning materials are highly similar to the prototype.

1. Introduction

Category knowledge is fundamental to the way that humans perceive, think about, and interact with the world. Furthermore, the ability to learn new and ad hoc categories throughout the lifespan is one indicator of healthy cognitive aging. In age-related diseases such as Mild Cognitive Impairment (MCI) and mild Alzheimer's disease (AD), patients exhibit declarative memory difficulty despite minimal deficits in other cognitive domains (Dubois et al., 2007; Mickes et al., 2007). Patients with age-related disease nevertheless retain a limited capacity for novel category learning (Bozoki et al., 2006; Koenig et al., 2008). These findings hint at the potential to leverage patients' residual category knowledge and learning capacity in novel coping strategies or cognitive interventions. Clarifying the mechanisms behind older adults' successful category learning is critical to developing efficient learning protocols, both in neurodegenerative disease and cognitively normal aging.

Several task- and stimulus-centered factors may influence the speed, robustness, and transferability of category learning (Koenig et al., 2007; Maddox et al., 2010; Zeithamova et al., 2008). Such factors may include the quality of the exemplars that an individual encounters when initially learning a category. In real-world situations, for exam-

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ple, individuals' experiences with a given class of items (for example, animals or fruits) may vary according to their background—in particular, some participants may encounter greater variability among the features of category members than others. We hypothesized that the similarity of learning items to an unseen prototype (and thus, to other learning items) would affect learners' ability to extract the central tendency of a novel category. Although several studies have reported successful category learning in AD (Bozoki et al., 2006; Heindel et al., 2013) and MCI (Nosofsky et al., 2012), the effect of experiential factors, such as feature variability, on patients' learning has received little attention.

Furthermore, evidence from functional magnetic resonance imaging (fMRI; Reber et al., 2003; Smith and Grossman, 2008; Zeithamova et al., 2008), computational modeling (Ashby et al., 2011; Kéri et al., 2002; Nomura and Reber, 2008, 2012), and patient-based studies (Heindel et al., 2013) suggests that successful category learning may be supported by multiple neurocognitive mechanisms (Poldrack and Foerde, 2008; but see Nosofsky et al. (2012)). Explicit mechanisms include rule-based learning, which taxes working memory and executive function (Grossman et al., 2013; Nomura et al., 2007), as well as similarity-based learning, which involves episodic memory for previously studied exemplars (Koenig et al., 2005, 2007). Explicit learning is rapid and transferable to novel contexts (Reber et al., 1996), but it may also be sub-optimal for learning categories defined by complex or non-verbal features (Ell and Ashby, 2006). Patients with AD and MCI exhibit marked atrophy in the hippocampus, which may prevent them from using declarative learning approaches (Gifford et al., 2015; Libon et al., 1998). Implicit mechanisms include perceptual learning of stimulus features, where modality-specific cortical representations may be modified (Folstein et al., 2012, 2013; Xu et al., 2013), as well as procedural learning of stimulus-response associations through striatally-mediated dopaminergic signaling (Ashby and Maddox, 2011; de Vries et al., 2010; Shohamy et al., 2008). Implicit learning may be relatively spared in MCI and AD (Knowlton and Squire, 1993). Individuals with AD and MCI exhibit relatively intact learning on tasks that are thought to involve procedural learning, such as perceptual-motor sequence learning (Gobel et al., 2013) and probabilistic classification (Eldridge et al., 2002). This procedural learning may be related to relatively preserved striatal anatomy in AD. Perceptual representations in temporo-occipital cortex (TOC) are also spared relative to the hippocampus and MTL (Frisoni et al., 2007) and are thought to support visual semantic representations (Grossman et al., 2013; Peelle et al., 2014), suggesting modification of TOC representations as a possible mechanism for preserved learning of perceptual feature knowledge in AD (Kéri et al., 2001).

In the current study, we used a prototype extraction task (Smith and Grossman, 2008) to investigate category learning differences between older adults with normal cognition and those with a clinical diagnosis of AD or MCI. Participants were trained to identify members of a novel visual category, the "crutter" (Koenig et al., 2005), while rejecting non-crutters. Learning conditions varied in learning items' similarity to an unseen category prototype (higher or lower) and the nature of instructions given to participants (promoting either explicit or implicit learning). The target category was probabilistically defined by the combination of 10 discrete visual features, and learning was modeled as a process of assigning subjective decision weights to features based on their perceived association with the target category. Overt categorization decisions were assumed to represent a mathematical integration of decision weights (i.e., by averaging) to produce an overall estimate of a test item's likelihood of belonging to the target category. We note that such a feature-integration framework underlies several computational models of category learning, including those which capture individual differences in learning mechanisms (e.g., Ashby et al., 2011; Love et al., 2004).

We predicted that cognitively normal controls and patients with AD or MCI would demonstrate significant category learning. Controls were expected to demonstrate superior learning, endorsing more typical items and rejecting less typical items at higher rates than patients. Learning was expected to be more efficient for controls and patients alike when they learned from items that were highly similar to the category prototype, with little between-item variability, allowing them to more easily discover the prototype. In contrast, we predicted that individuals who encountered learning items with lower typicality (and thus greater between-item feature variability) were likely to learn less efficiently, even when learning items were derived from the same prototype as the set of higher-typicality exemplars. We further predicted that controls would learn under both explicit and implicit instruction conditions, and that learning set typicality effects would be reduced among controls who used an explicit learning approach, as their intact declarative memory would help them to overcome feature variability and learn the category prototype. In contrast, we predicted that patients would exhibit impaired learning in the explicit condition but relatively preserved implicit learning.

2. Methods

2.1. Participants

A total of 93 older adults with normal cognition ("controls") or a clinical diagnosis of Alzheimer's disease (AD) spectrum disorder participated after giving informed consent according to the guidelines outlined by the Institutional Review Board of the University of Pennsylvania. Exclusion criteria included any history of psychiatric illness, including major depression, or other neurological conditions such as stroke or hydrocephalus. Patients were recruited through the University of Pennsylvania Cognitive Neurology Clinic and were diagnosed in clinical consensus meetings with either MCI or AD. AD patients met McKhann et al. (2011) criteria for probable AD, while MCI patients met the core clinical criteria of Albert et al. (2011). Data from 10 participants (2 control, 3 MCI, 5 AD) were excluded due to non-compliance with instructions on the behavioral task: 9 of these participants endorsed all test items at a rate of 95% or more, indicating a likely misunderstanding of task instructions, while 1 AD participant had a high non-response rate coupled with very long response times. These exclusions left a total of 39 controls and 44 patients. The patient group comprised 37 individuals with AD and 7 individuals with MCI; patients with MCI were distributed evenly across experimental conditions. Post-hoc analyses of behavioral effects indicated no reliable difference in category learning performance between patients with AD and MCI, and no reliable association between patients' learning and measures of global cognition (Section 3.1). Neuroimaging analyses involved the subset of participants (control=14; AD=13; MCI=2) that had anatomical image data collected within 6 months of the behavioral experiment. Post-hoc analyses confirmed that participants in the neuroimaging sample displayed the same pattern of behavioral effects as in the full behavioral dataset (Section 3.5).

Table 1 provides means and standard deviations of several participant characteristics by experimental condition. Mean MMSE score in the patient group (mean=20.3, s.d.=4.9) was significantly lower than in the control group (mean=28.8, s.d.=0.8) [$t(69)=-9.1$, $p < 0.001^{***}$], reflecting patients' global cognitive impairment. Controls were screened to verify their negative neurological history (e.g., MMSE > 27 or self-report) and negative psychiatric history (e.g., no depression or substance abuse). Patients were administered the MMSE at a mean interval of 115.5 (123.6) days from the experimental session; MMSE data were available for 29 of 39 controls, at a mean interval of 42.5 (108.5) days. MMSE did not differ by learning set or instruction type [both $F(1,63) < 1.3$, $p > 0.2$], and in direct contrasts patients' MMSE scores did not differ by learning set [$t(40)=-1.2$, $p < 0.23$] or instruction type [$t(40)=0.8$, $p < 0.44$]. Education level did not differ between groups, learning sets, or instruction types [$F(1,75) < 0.8$, $p > 0.3$ for all main effects and interactions]. No effects of age were found [all $F(1,75)$