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Prototype learning and dissociable categorization systems in Alzheimer's disease

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ABSTRACT

Recent neuroimaging studies suggest that prototype learning may be mediated by at least two dissociable memory systems depending on the mode of acquisition, with A/Not-A prototype learning dependent upon a perceptual representation system located within posterior visual cortex and A/B prototype learning dependent upon a declarative memory system associated with medial temporal and frontal regions. The degree to which patients with Alzheimer's disease (AD) can acquire new categorical information may therefore critically depend upon the mode of acquisition. The present study examined A/Not-A and A/B prototype learning in AD patients using procedures that allowed direct comparison of learning across tasks. Despite impaired explicit recall of category features in all tasks, patients showed differential patterns of category acquisition across tasks. First, AD patients demonstrated impaired prototype induction along with intact exemplar classification under incidental A/Not-A conditions, suggesting that the loss of functional connectivity within visual cortical areas disrupted the integration processes supporting prototype induction within the perceptual representation system. Second, AD patients demonstrated intact prototype induction but impaired exemplar classification during A/B learning under observational conditions, suggesting that this form of prototype learning is dependent on a declarative memory system that is disrupted in AD. Third, the surprisingly intact classification of both prototypes and exemplars during A/B learning under trial-and-error feedback conditions suggests that AD patients shifted control from their deficient declarative memory system to a feedback-dependent procedural memory system when training conditions allowed. Taken together, these findings serve to not only increase our understanding of category learning in AD, but to also provide new insights into the ways in which different memory systems interact to support the acquisition of categorical knowledge.

1. Introduction

Considerable evidence has emerged from studies utilizing a variety of approaches within cognitive neuroscience that category learning is not a unitary process supported by a single memory system, but rather a multiply-determined process that can be supported by different memory systems depending on the nature of the underlying category structure and the conditions under which the categorical information is acquired (for reviews, see Ashby & O'Brien, 2005; Kéri, 2003; Poldrack & Foerde, 2008; Smith & Grossman, 2008). For example, categories defined by salient and verbalizable rules (i.e., rule-based category structures) may be learned explicitly through a declarative memory system mediated by prefrontal cortex and medial temporal lobe structures (Smith, Patalano, & Jonides, 1998; Filoteo, Maddox, Salmon, & Song, 2005). In contrast, categories defined by largely non-verbalizable rules that require the integration of information from two or more stimulus dimensions (i.e., information-integration category structures) may be learned implicitly through a striatum-dependent procedural memory system that gradually associates category responses with regions in stimulus space (Ashby & Waldron, 1999; Nomura et al., 2007; Seger & Cincotta, 2002). Rule-based categories can be learned equally well under both observational and feedback training conditions. In observational training conditions, the category membership of the exemplar (i.e., the category label) is presented along with the exemplar prior to the subject's response. In feedback training conditions, the correct category label is provided only after the exemplar is presented and the subject has made a categorical response. Unlike rule-based categories, categories that require information integration are learned much more effectively under feedback than observational training conditions (Ashby, Maddox, & Bohil, 2002). The selective advantage of trial-and-error feedback

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training for information-integration category learning is consistent with the critical role of procedural memory in this type of learning since feedback-associated dopamine release is thought to mediate the learning of associations between exemplars and categorization responses within the striatum (Ashby & Casale, 2003; Ashby, Alfonso-Reese, Turken, & Waldron, 1998; Reynolds & Wickens, 2002).

A form of category learning that has not been studied as extensively from a cognitive neuroscience perspective as rule-based or information-integration category learning is prototype learning. In prototype learning, the underlying category structure is defined by a central prototype that is distorted to various degrees to form category exemplars. Neuroimaging studies suggest that prototype learning can be mediated by at least two dissociable memory systems depending on the mode of acquisition of the categorical information (Zeithamova, Maddox, & Schnyer, 2008). One mode of acquisition, A/Not-A prototype learning, appears to engage a perceptual representation system (e.g., Schacter, 1990) mediated by posterior visual cortex (Aizenstein et al., 2000; Reber, Stark, & Squire, 1998b; Zeithamova et al., 2008). In A/Not-A prototype learning, exemplars from a single category (i.e., Category A) are presented to the subject during a training phase, often incidentally without reference to a subsequent test phase. During the test phase, subjects are presented with a series of additional exemplars (some from Category A and others either from a different category or random stimuli) and asked to decide whether each exemplar does or does not belong to Category A. Because only exemplars from one category are shown during training, the perceptual representation system can be used to abstract out the central tendency or prototype of this category, and subjects can then base their category membership decision on the similarity (or familiarity) of each exemplar to the Category A prototype (Casale & Ashby, 2008).

In contrast to A/Not-A prototype learning, A/B prototype learning appears to engage the declarative memory system rather than the perceptual representation system (Seger et al. 2000; Zeithamova et al., 2008). In A/B prototype learning, exemplars from both Category A and Category B are presented to the subject during the training phase along with information regarding the category membership of each exemplar (typically through trial-by-trial feedback). During the test phase, subjects are asked to decide whether each of a series of additional exemplars belongs to either Category A or Category B. Because exemplars from both categories are presented during training, subjects cannot rely solely on the abstraction of a central tendency or single prototype through the perceptual representation system, but must instead rely on declarative memory processes to flexibly acquire representations underlying two distinct categories.

Neuropsychological studies in brain-damaged populations support the distinction observed with neuroimaging between dissociable memory systems that mediate prototype learning. It should be noted, however, that these studies have focused almost exclusively on A/Not-A prototype learning. In a seminal study using a dot-pattern categorization task, Knowlton and Squire (1993) found that amnesic patients with medial temporal lobe damage had normal prototype learning under incidental A/Not-A conditions despite impaired explicit memory for the training exemplars. Furthermore, the amnesic patients endorsed the previously unseen prototype pattern more strongly than either the low or high distortion exemplars, thus indicating that the prototype had been effectively abstracted. A similar pattern of results was observed in a subsequent study with amnesic patients using more realistic cartoon animal stimuli defined by a set of discrete features (Reed, Squire, Patalano, Smith, & Jonides, 1999). In subsequent studies, A/Not-A prototype learning was found to be intact in patients with Parkinson's disease (Reber & Squire, 1999) and schizophrenia (Kéri, Kelemen, Benedek, & Janka, 2001). Taken together, these studies support the view that A/Not-A prototype learning does not critically depend on declarative memory processes mediated by medial temporal lobe structures (disrupted in amnesia) or procedural learning processes mediated by the striatum (disrupted in Parkinson's disease). However, because A/Not-A prototype learning remains intact in all of these patient groups, these studies do not provide additional insight regarding the neural substrates that support this form of prototype learning.

To our knowledge, the only patient population that has been found to exhibit impaired A/Not-A prototype learning is Alzheimer's disease (AD). In an intriguing early study utilizing a dot-pattern classification task, Kéri et al. (1999) found that AD patients were selectively and markedly impaired at classifying the previously unseen prototype pattern following exemplar training despite demonstrating intact categorization of new low and high distortion category exemplars. The categorization performance of normal control subjects, in contrast, was strongest for the prototype pattern even though this pattern was never seen during training. Thus, control subjects acquired category information in a prototype-based manner, while AD patients appeared to learn in an exemplar-based manner that did not result in the induction of the category prototype. Kéri and colleagues hypothesized that the impaired prototype categorization in AD patients may be due to a selective disruption of lateral connections within visual cortex. Computational models have shown that impairment of intrinsic connectivity within early visual cortical areas could disrupt the critical integrative processes required for prototype induction, but still allow for the acquisition of exemplar information (Kéri et al., 1999, 2002). Such a deficit in intrinsic connectivity could occur in AD patients. Neuropathological studies have shown that AD produces systematic disruption of corticocortical projections connecting functionally related cortical regions (Delacoste & White, 1993; Hof & Morrison, 1999). In addition, psychophysical studies have shown that AD patients have a selective deficit in binding visual perceptual information processed in different visual cortical regions into coherent representations (Festa et al., 2005). These findings provide support for the possibility that disruption of the perceptual representation system underlies deficits in A/Not-A prototype learning in patients with AD.

Despite this striking early finding, subsequent studies examining A/Not-A prototype learning in AD patients have not consistently found a clear prototype categorization deficit (Kéri, Kálmán, Kelemen, Benedek, & Janka, 2001; Zaki, Nosofsky, Jessup, & Unverzagt, 2003). Notably, a follow-up study by Kéri et al. (2001) with a larger group of AD patients found relatively intact category learning with no selective deficit for prototypes. It is possible, however, that this failure to replicate was due to a change in procedure: subjects in this study (and the study by Zaki et al., 2003) were only exposed to high distortion exemplars during training, while subjects in the initial study were exposed to both low and high distortion exemplars. Because strength of prototype learning decreases with increasing distortion of the exemplars presented during the training phase (e.g., Casale & Ashby, 2008), the use of only high distortion exemplars in the follow-up study may have reduced the sensitivity of the task for detecting a difference in prototype induction between AD patients and controls. Consistent with a loss of sensitivity, control subjects correctly classified the previously unseen prototype over 85% of the time in the initial study, but only about 72% of the time (as estimated from the figure) in the follow-up study.

Two studies that examined incidental A/Not-A prototype learning in AD patients using more realistic novel animal stimuli found at least some evidence that this form of category learning is impaired (Bozoki, Grossman, & Smith, 2006; Koenig et al., 2008). Although the AD patients in both studies demonstrated significant levels of category acquisition, the performance of AD patients was