Neuropsychologia 79 (2015) 42–52

Contents lists available at ScienceDirect

Neuropsychologia

journal homepage: www.elsevier.com/locate/neuropsychologia

Remote semantic memory is impoverished in hippocampal amnesia ☆

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ARTICLE INFO

Article history:
Received 4 August 2015
Received in revised form
9 October 2015
Accepted 10 October 2015
Available online 22 October 2015

Keywords:
Semantic memory
Semantic richness
Hippocampus
Consolidation
Remote memory

ABSTRACT

The necessity of the hippocampus for acquiring new semantic concepts is a topic of considerable debate. However, it is generally accepted that any role the hippocampus plays in semantic memory is time limited and that previously acquired information becomes independent of the hippocampus over time. This view, along with intact naming and word-definition matching performance in amnesia, has led to the notion that remote semantic memory is intact in patients with hippocampal amnesia. Motivated by perspectives of word learning as a protracted process where additional features and senses of a word are added over time, and by recent discoveries about the time course of hippocampal contributions to online relational processing, reconsolidation, and the flexible integration of information, we revisit the notion that remote semantic memory is intact in amnesia. Using measures of semantic richness and vocabulary depth from psycholinguistics and first and second language-learning studies, we examined how much information is associated with previously acquired, highly familiar words in a group of patients with bilateral hippocampal damage and amnesia. Relative to healthy demographically matched comparison participants and a group of brain-damaged comparison participants, the patients with hippocampal amnesia performed significantly worse on both productive and receptive measures of vocabulary depth and semantic richness. These findings suggest that remote semantic memory is impoverished in patients with hippocampal amnesia and that the hippocampus may play a role in the maintenance and updating of semantic memory beyond its initial acquisition.

1. Introduction

Semantic memory refers to knowledge of vocabulary, facts and concepts about the world, and general information about oneself (Tulving, 1972). The role of the hippocampus in its support of semantic memory has been a topic of considerable debate. According to one view, the hippocampus is necessary for the acquisition of new semantic knowledge, providing the relational binding of the arbitrarily related phonological, conceptual, and orthographic components of word knowledge and the arbitrarily related pieces of content that make up a semantic fact about the world or ourselves (e.g., Cohen and Eichenbaum, 1993; Eichenbaum and Cohen, 2001; Gabrieli et al., 1988; Manns et al., 2003; Postle and Corkin, 1998; Warren and Duff, 2014). A second view holds that the hippocampus may not be necessary for the acquisition of semantic information and that other medial and/or lateral temporal lobe structures can accomplish, at least some aspects of this type of learning, on some occasions, in the absence of normal hippocampal functioning (e.g., Vargha-Khadem et al., 1997; O'Kane et al., 2004; Sharon et al., 2011; Tulving et al., 1991).

While these two views differ regarding the role and nature of the hippocampus in *acquiring* new semantic memory, there has been more general consensus that remote semantic memory, acquired long in advance of any pathology, and outside the window of any retrograde amnesia or temporal gradient effects, is intact following hippocampal and more widespread MTL damage (e.g., Winocur and Moscovitch, 2011). With respect to vocabulary, patients with hippocampal amnesia perform within normal limits on neuropsychological measures of vocabulary knowledge and naming, and do not have aphasia or semantic dementia (Kensinger et al., 2001). In experimental tasks examining remote word knowledge (e.g., when asked to name items, or match a label with a short phrase, definition, or sentence explaining its meaning) patients with hippocampal pathology do not differ significantly from healthy comparison participants (Gabrieli et al., 1988; Verfaellie et al., 2000; Manns et al., 2003). The notion that remote semantic memory is intact in amnesia has fit well with the view that over time, semantic information becomes independent of the hippocampus through neocortical consolidation (e.g. McClelland

☆Supported by: Grant sponsor: NIDCD; Grant number: R01 DC011755 to MCD.
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http://dx.doi.org/10.1016/j.neuropsychologia.2015.10.017
0028-3932/

et al., 1995; O'Reilly and Rudy, 2000) and that the storage, processing, and use of semantic information are also hippocampally independent, depending more on anterior and lateral temporal lobes (Tranel et al., 1997; Binder et al., 2009; Schmolck et al., 2002; Smith and Squire, 2009).

Beyond the acquisition phase, the hippocampus and its associated processes may also support the retrieval and use of previously acquired semantic memory. Neuroimaging studies point to hippocampal involvement during retrieval of semantic memory in healthy individuals (e.g., Burianova and Grady, 2007; Burianova, McIntosh, and Grady, 2010; Ryan, et al., 2008; Ryan, et al., 2010; Whitney et al., 2009; Sheldon and Moscovitch, 2012) and studies in amnesia have reported deficits in the flexible and rich *use* of semantic information during communication (Race et al., 2013; Verfaellie et al., 2014). Some authors have also linked deficits in semantic memory retrieval to impaired episodic memory (Sheldon et al., 2013; Greenberg et al., 2009). Despite these links in the literature between hippocampus and semantic memory beyond the acquisition phase the broader consensus has remained that remote semantic memory in amnesia is intact.

In the current study, we revisit the notion that remote semantic memory is intact in amnesia and independent of the hippocampus by examining the depth of vocabulary knowledge in patients with hippocampal amnesia. In addition to the work mentioned above, the specific motivation for this study comes from consideration of perspectives on word knowledge and learning from the psycholinguistic and second language acquisition literatures, and recent discoveries about the time course of hippocampal contributions to on-line processing and reconsolidation. Bringing together these perspectives and findings, we predict deficits in remote semantic memory in amnesia. Two primary observations lead to this prediction.

The first observation relates to depth of word knowledge, the amount of information associated with a word or concept. Studies of semantic knowledge in hippocampal amnesia have examined associative knowledge of famous people including tests requiring participants to pick out famous names from foils or match famous faces with their names (e.g., Westmacott and Moscovitch, 2002; Reed and Squire, 1998). This work supports the view that the hippocampus plays a time-limited role in supporting semantic memory, with amnesic patients performing similarly to healthy comparison participants. Most studies of semantic memory in amnesia, however, have focused on surface-level pairings of vocabulary or lexical information. Across studies, participants might be shown a picture of a lemon and asked to name it, asked to identify whether L-E-M-O-N or L-E-N-A-K are real words, or asked to match the label 'lemon' to a short definition (e.g. *a yellow citrus fruit*). The fact that patients with hippocampal amnesia do not differ from healthy comparison participants on these types of tasks has been taken as evidence that their remote semantic memory is intact.

In other literatures, what it means to know a word extends beyond surface-level pairings to include how much information is associated with a word or concept, how words are used, and how they co-occur with other words in language use (Read, 1993, 1998). Returning to the example of 'lemon', under the umbrella term of semantic richness (defined as the amount of semantic information associated with a word or concept; Pexman et al., 2002), measures of depth of knowledge include the number of features of a word or concept (e.g., tastes sour, native to Asia, grows on small evergreen trees, eaten in pies, used in tea) (Pexman et al., 2002; Yap et al., 2011), the number of different senses a word can take (e.g., the fruit, the tree, the color, the scent, a defective automobile) (Taler et al., 2013), and the number of word associates or collocates of the concept (e.g., lime, juice, zest, marmalade, rind, wedge, sole, sour) (Laszlo and Federmeier, 2011). While vocabulary breadth (the number of words one knows) and surface-level pairing information may not differ significantly between patients with amnesia and healthy comparison participants, less is known about vocabulary depth of remotely acquired words in amnesia.

The second observation relates to the time course over which a word is learned. In studies of word learning with patients with hippocampal amnesia, participants either fail or succeed in reaching criterion of a surface-level pairing within several trials or sessions seldom stretching more than a day or two (e.g., Gabrieli et al., 1988; Duff et al., 2006). Yet, various literatures on word learning suggests that the learning process is more protracted, spanning days, weeks, and even years (Carey, 2010; McMurray et al., 2012). Over time, and with extensive experience with a word or concept, people associate more and more information with each concept (McGregor et al., 2002). That is, the number of features and senses associated with a word grows over time as the learner acquires more information about the varied ways the word or concept can be used across a multitude of situations.

If word learning is a protracted process, one that is possibly never fully complete, then the hippocampus may support "remote" knowledge by strengthening and creating new connections among and between words and adding new features or senses to existing representations. From the perspective that the hippocampus does support word learning, and the updating of relational representations more broadly (e.g., Eichenbaum and Cohen, 2001), the hippocampus could be involved in adding new features, senses, and other information about a word or concept over time with preexisting information. This perspective would fit with recent work showing that the hippocampus contributes to the updating and maintenance of relational information in the moment (Hannula et al., 2006; Warren et al., 2011) and to the updating and strengthening of previously acquired information through reconsolidation (McKenzie and Eichenbaum, 2011; Lee, 2008).

Using measures of semantic richness, we revisit the notion that remote semantic memory is intact in amnesia and independent of the hippocampus by examining vocabulary depth of remotely acquired words in patients with hippocampal amnesia. We predict that patients with bilateral hippocampal damage will display impoverished semantic memory, performing worse on a receptive measure of vocabulary depth and richness and will produce fewer features and senses for target words than a group of demographically matched healthy comparison participants and a group of brain damaged comparison participants. Such a finding would go beyond previous reports that the hippocampus supports the processes associated with retrieving and using semantic memory to also suggest that hippocampus may play a protracted and sustained role in the life-long development and maintenance of semantic knowledge by establishing new relations within and across items in the semantic memory system.

2. Methods

2.1. Participants

Participants were five (one female) patients with bilateral hippocampal damage and severe declarative memory impairment (HC group), five (four female) brain damaged comparison participants with damage outside the medial temporal lobe and no declarative memory impairment (BDC group), and 24 healthy comparison participants free of neurological and psychiatric disease (NC group), matched to the HC and BDC participants on sex, age, and level of education. The patients were recruited from the Patient Registry of the University of Iowa's Division of Behavioral Neurology and Cognitive Neuroscience and were characterized