Title of the essay:
What have the impairments and abilities of people with amnesia taught us about long-term memory?

Exam candidate number: JRQP2

Word count:
1994

Abstract

Amnesics' impairments and abilities of long-term memory (LTM) demonstrate that the declarative theory, proposed by Squire and Zola (1998), is deficient but partially correct. While the hippocampus is necessary for normal episodic and semantic LTM, semantic LTM is less dependent on it. Reports of amnesics suggest that semantic LTM can be laboriously acquired independent of episodic memory and the hippocampus, possibly by the extrahippocampal medial temporal lobe or neocortex. Completely normal semantic LTM may depend on episodic memory subserved by the hippocampus, consistent with the declarative theory, but future studies must discriminate between competing theories.

Amnesics' impairments and abilities of long-term memory (LTM) provide testing grounds for LTM theories. Amnesia is characterized by damage to either or both of episodic LTM, the ability to remember events via mental time travel, and semantic LTM, general knowledge of facts and language (Tulving, 1972; Tulving & Markowitsch, 1998). This essay focuses on what amnesics have taught us about the declarative theory of LTM. Proposed by Squire and Zola (1998), the declarative theory holds that episodic LTM acquisition is a prerequisite to semantic LTM acquisition (Suzuki, 2003). Further, Squire and Zola (1998) proposed that damage to the hippocampus and the rest of the medial temporal lobe (MTL) causes equal impairments to both episodic and semantic LTM. First, this essay will evaluate amnesic patient data and find that hippocampus damage is sufficient to impair episodic LTM, consistent with the declarative theory. Then, the essay will analyze evidence that amnesics with completely destroyed episodic LTM retain slight semantic LTM acquisition, suggesting that semantic LTM can be acquired independently and is less dependent on the MTL. Next, the essay will investigate which brain regions subserve semantic LTM when episodic LTM is completely destroyed. Amnesic patient data demonstrate that weaker semantic memory acquisition with destroyed episodic memory can occur independent of the hippocampus and may be subserved by the extrahippocampal MTL or the neocortex. Lastly, the essay will demonstrate that semantic LTM acquisition is weaker following restricted hippocampus damage which teaches us that the hippocampus could facilitate semantic memory via episodic memory, as the declarative theory suggests. However, future studies are needed to determine if the hippocampus instead subserves the rapid encoding of associations between items in semantic LTM.

Hippocampal amnesics, with damage restricted to the hippocampus, have severely impaired episodic memory demonstrating that the hippocampus subserves episodic

LTM as the declarative theory suggests. Vargha-Khadem et. al (1997) reports on three developmental amnesics, people who developed amnesia in childhood, with severe hippocampus damage but normal brains otherwise. Evaluating the developmental amnesics' episodic memory, they found all three children had severe deficits in remembering autobiographical events and severe deficits in delayed recall of verbal information during episodic memory tests. Replicating these findings, Verfaellie et. al (2000) reports on patient PS who acquired damage restricted to the hippocampus as an adult but an otherwise normal brain. In a test consisting of five repetitions of fifteen nouns followed by recall after a twenty-minute delay, PS recalled zero words (Bean, 2011). Additionally, in a delayed recall of visual information and of a verbal story, patient PS was in the first percentile, further suggesting that their episodic memory was completely destroyed (Hori et. al, 2013). The developmental amnesics' and PS's impairments demonstrate that hippocampus damage is sufficient to impair episodic memory, teaching us that the hippocampus is essential for episodic LTM consistent with the declarative theory.

Amnesics with intact semantic memory acquisition despite completely destroyed episodic memory refute the declarative theory's claim that semantic memory is only acquired via episodic memory. Patient PS, reported by Verfaellie et. al (2000), had completely destroyed episodic memory. However, in a semantic memory test assessing knowledge of words which entered the language after the onset of amnesia, PS recalled some words although PS's performance was significantly worse than controls. Bayley et. al's (2008) report on patient G.P., who had severe damage to the entire MTL, replicates this finding. G.P. had scores of zero on an episodic memory test involving delayed recall of a short passage and paired-associate learning, an episodic memory test which involves remembering the word presented alongside another word (Karantzoulis et. al, 2011). Further, G.P. had significantly worse semantic LTM acquisition than controls as assessed by a

vocabulary test. However, G.P.'s intact knowledge of some words such as "website" which were introduced to the language after the onset of amnesia demonstrates that G.P. could acquire new semantic memories despite no episodic memory.

Further replicating this finding of intact semantic LTM despite destroyed episodic LTM, O'kane et. al (2004) reports on patient H.M. who had damage to the hippocampus and surrounding MTL. Patient H.M. has never demonstrated episodic memory acquisition following his amnesia, as demonstrated by scores of zero or extremely close to zero on delayed recall tests (Corkin, 1984). Since H.M.'s amnesia onset, he has never remarked about post-amnesia autobiographical events, confirming that his episodic memory acquisition is completely destroyed (O'kane et. al, 2004). When H.M. was presented with names of people who acquired fame after his amnesia onset, H.M. was able to provide unique identifying information for some people, demonstrating intact semantic LTM acquisition despite destroyed episodic memory (O'kane et. al, 2004). One weakness of this study is that O'kane et. al (2004) did not provide tests of H.M.'s current episodic memory and it is possible that H.M.'s brain reconfigured to support slight episodic memory acquisition.

G.P.'s, PS's and H.M.'s impaired episodic memory acquisition yet intact semantic memory acquisition suggests that semantic memory acquisition can occur in the absence of episodic memory. Additionally, semantic memory is less dependent on an intact MTL than episodic memory, contrary to the declarative theory of LTM. These amnesics' impairments and abilities demonstrate the plausibility of Tulving and Markowitsch's (1998) Serial Parallel Independent (SPI) model which claims that semantic memory is a prerequisite to episodic memory encoding. This essay will not completely evaluate the SPI model. However, the aforementioned evidence is consistent with the SPI model since episodic LTM is not a prerequisite for semantic LTM as the declarative theory holds.

Amnesic patient data suggest that intact weak semantic LTM acquisition, despite annihilated episodic memory, occurs independent of the hippocampus. Patient G.P. was able to weakly acquire new semantic LTM without intact episodic memory acquisition despite having only 4% of the normal hippocampus volume as measured by magnetic resonance imaging (Bayley et. al, 2008). Gold and Squire's (2005) study comparing magnetic resonance imaging and histological analyses of amnesic patients' brains found that a hippocampus volume of around 60% of the normal volume likely corresponds to the destruction of nearly all neurons in the hippocampus. Patient G.P. had only 4% of the normal hippocampus volume, thereby G.P.'s abilities suggest that weaker semantic LTM acquisition with destroyed episodic memory acquisition occurs independent of the hippocampus. Semantic and episodic LTM are not equally reliant on the same brain structures, refuting the declarative theory.

Amnesic patient data equivocally suggest that both the extrahippocampal MTL and neocortex could subserve the weaker semantic LTM acquisition observed in G.P. which occurs independent of the hippocampus and episodic memory (Bayley et. al., 2008). Patient H.M., who had damage to the MTL including and beyond the hippocampus, had very severe semantic memory damage as demonstrated by his inability to learn the meaning of a word even after over 100 training trials (Gabrieli et. al, 1988). However, Vargha-Khadem et. al's (1997) three developmental amnesics with restricted hippocampus damage performed well in school and developed normal vocabularies. Vargha-Khadem et. al (1997) and Eichenbaum (1997) thereby attributed H.M.'s more substantial semantic deficits to his damaged extrahippocampal structures within the MTL and argued that the extrahippocampal MTL supports semantic memory independent of episodic memory and the hippocampus. However, there may be confounding variables in this comparison since developmental amnesics developed damage early in life when their brains may

have been more resilient (Suzuki, 2003). Therefore, this comparison is only a weak suggestion for the extrahippocampal MTL subserving semantic memory independent of episodic memory and the hippocampus.

On the other hand, computational modeling studies propose that the neocortex supports slow semantic LTM acquisition but the hippocampus subserves quick semantic LTM acquisition (O'Reilly & Rudy, 2001). The best empirical evidence for this view comes from Bayley et. al's (2008) report of amnesic patient G.P. Patient G.P. had an almost completely destroyed MTL, an intact neocortex, totally destroyed episodic memory acquisition, and slightly intact semantic memory acquisition. Importantly, G.P. had a small amount of remaining parahippocampal cortex tissue in the MTL, with 29% of the normal parahippocampal cortex volume. Due to the tiny amount of MTL intact, Bayley et. al's (2008) report suggests that an area other than the MTL, possibly the neocortex, subserves weaker semantic LTM acquisition. However, this study can not rule out that the remaining extrahippocampal MTL subserved semantic LTM acquisition as the amount of parahippocampal cortex intact is substantially greater than G.P.'s remaining hippocampus tissue. The aforementioned data suggest that semantic memory acquisition with destroyed episodic memory can occur independent of the hippocampus, but future studies are required to tease apart which of the neocortex and extrahippocampal MTL subserve semantic LTM acquisition independent of the hippocampus.

Completely destroyed episodic LTM is not sufficient to totally destroy semantic LTM acquisition; however, damage to the hippocampus suffices to cause abnormally slow and weaker semantic LTM acquisition. Therefore, the hippocampus is necessary for normal semantic memory and there are two possible explanations for the hippocampus' role in semantic memory acquisition. Partially consistent with the declarative theory, one possible account holds that the hippocampus subserves

episodic memory and normal semantic memory requires episodic memory (Henke, 2010; Squire & Zola, 1998). The second account, which this essay will denote as the rapid association theory, holds that the hippocampus facilitates quick semantic memory encoding by enabling the rapid formation of associations between items in semantic memory (Duff et. al, 2020). Evidence that hippocampus damage impairs episodic memory, which requires rapid encoding of associations between components of an experience, implicates the hippocampus in facilitating rapid encoding of associations in episodic memory acquisition (Henke, 2010). Holding that normal semantic memory acquisition also requires quick encoding of associations between items in memory, Duff et. al (2020) argues for the hippocampus subserving this role in semantic LTM.

Patient PS, with damage restricted to the hippocampus, had significantly worse than normal recall of word definitions that entered the language after their amnesia, demonstrating that hippocampus damage is sufficient to weaken semantic LTM (Verfaellie et. al, 2000). Replicating this finding, one of Vargha-Khadem et. al's (1997) developmental amnesics, Jon, demonstrates a similar pattern of semantic deficits. Gardiner et. al (2008) administered an obscure fact learning test to Jon and a group of age-matched controls, consisting of the experimenter asking obscure questions and participants providing answers or getting told the answers if they do not know. Compared to controls, Jon required many more learning trials to retain the facts. PS's and Jon's tasks required them to associate definitions to words and facts to questions respectively. Thereby, under the rapid association theory, the amnesics' impaired performance can be ascribed to their lack of a hippocampus whose role is to enable the rapid encoding of associations in semantic LTM. On the other hand, the hippocampus damage may inhibit rapid semantic LTM acquisition which is normally facilitated by episodic memory internally rehearsed and decontextualized into semantic memory (Henke, 2010). The reports of PS and Jon teach us that both

accounts of the hippocampus' role in semantic LTM are possible and future studies are required to determine which account is correct. Thereby, the declarative theory may show to be partially correct in its assumption that completely normal semantic LTM requires normal episodic LTM.

This essay analyzed what the impairments and abilities of amnesics have taught us about LTM by focusing on how amnesic patient data demonstrate the strengths and weaknesses of the declarative theory of LTM. Consistent with the declarative theory, episodic memory is subserved by the hippocampus such that hippocampus damage alone causes severe episodic memory deficiencies. Inconsistent with the declarative theory, however, amnesics taught us that semantic memory can be obtained independent of episodic memory, demonstrating the plausibility of semantic memory being a prerequisite to episodic memory as the SPI model suggests. Amnesic patients' abilities show that weaker semantic memory acquisition can occur without episodic LTM and the hippocampus but future studies are needed to clarify whether the extrahippocampal MTL or neocortex subserves this role. Additionally, hippocampal amnesics taught us that the hippocampus does support normal semantic LTM which could be partially consistent with the declarative theory or alternatively explained by the rapid association theory.

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