RAPID COMMUNICATION

A Tale of Two Paradigms or Metatheoretical Approaches to Cognitive Neuropsychology: Did Schmolck, Stefanacci, and Squire (2000) Show That Hippocampal Lesions Only Impair Memory, whereas Adjacent (Extrahippocampal) Lesions Impair Detection and Explanation of Sentence Ambiguity?

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This note discusses two fundamentally different paradigms or metatheoretical approaches that currently guide cognitive neuropsychology: the Theoretical- vs. Anatomical-paradigms. To illustrate these paradigms, we compare a Theoretical-paradigm paper (MacKay & James, 2001) with an Anatomical-paradigm paper (Schmolck, Stefanacci, & Squire, 2000): These papers report virtually identical experiments on relations between language, memory, and hippocampal systems, using the same task (the detection and explanation of ambiguities in sentences that participants know are ambiguous), virtually identical ambiguous sentences, and at least one identical participant (the amnesic HM). However, MacKay and James made strikingly different claims from Schmolck et al., and we show that the Schmolck et al. claims comport not with their data but with an unstated theory to which they are implicitly committed within the Anatomical-paradigm. © 2001 Academic Press

Cognitive neuropsychology is currently following two fundamentally different paradigms or metatheoretical approaches: the Theoretical- vs. Anatomical-paradigms. To illustrate these paradigms, we contrast two recent studies that examine relations between language, memory, and hippocampal systems: MacKay and James (2001) versus Schmolck, Stefanacci, and Squire (2000). What makes this contrast especially interesting is that both studies use the same task (the detection and explanation of ambiguities in sentences that participants know are ambiguous) and virtually identical

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materials presented visually to participants, some of whom were similar or identical (memory-normal controls and the amnesic HM). However, the two studies make strikingly different claims, and we argue that the Schmolck et al. claims follow not from their data but from an unstated theory to which they are implicitly committed within the Anatomical-paradigm. First some historical antecedents to place the conflict in context.

MACKAY–JAMES AND SCHMOLCK ET AL. IN CONTEXT: FOUR BACKGROUND PAPERS

Background Paper I (Milner, Corkin, & Teuber, 1968) described HM's "hippocampal amnesic syndrome," a concept that subsequent literature has referenced dozens of times and claimed (without data) that HM's language comprehension is "undisturbed," thereby preparing the ground for Background Paper II: Lackner (1974). In Lackner's ambiguity detection task, HM heard short spoken sentences that he knew were either ambiguous or unambiguous. After each sentence HM indicated whether one or two interpretations were possible, and, if two, HM described the two meanings. No problems with HM's meaning descriptions were reported, and Lackner concluded that HM's language comprehension is "essentially normal" because HM responded "two meanings" for 34% of the ambiguous sentences.

Background Paper III (MacKay, Stewart, & Burke, 1998) noted three weaknesses in Lackner's (1974) "normal comprehension" conclusion. One was that it contradicted his own data: HM's 34% correct fell well below 50%, the performance level that HM could have achieved by ignoring the sentences, tossing an unbiased coin on each trial, and responding "two meanings" for "heads" and "one meaning" for "tails." A second weakness in Lackner's conclusion concerned failure to run memory-normal controls: When MacKay, Stewart, et al. (1998) presented Lackner's ambiguous sentences to memory-normal controls matched with HM on intelligence (IQ), age, education, and work history, the controls detected both meanings significantly more often than HM. A third weakness concerned absence of theory in Lackner (1974): MacKay, Stewart, et al. had developed a new and detailed theory of relations between language, memory, and hippocampal systems that not only accurately predicted HM's basic ambiguity-comprehension deficit, but 10 additional deficits in how HM (in 1967–1973) comprehended experimenter requests, syntactically simple sentences (presented visually), and his own spoken output, relative to memory-normal controls and a patient with bilateral frontal lobe damage that equaled HM's medial temporal lobe (MTL) damage in extent.

Background Paper IV (MacKay, Burke, & Stewart, 1998) examined HM's language production abilities in 1970 and 1973 to test the new theory. In one double-blind study, judges rated HM's descriptions in the ambiguity detection/description task as less grammatical, less comprehensible, and less coherent than controls'. In a second experiment, HM described pictures and answered brief questions about current experience and universal childhood events, and naive judges again rated HM's responses as less grammatical, less comprehensible, and less coherent than those of controls, results which again pointed to production deficits and supported predictions of the new theory of relations between language, memory, and hippocampal systems.

THE CONTRASTING CONCLUSIONS OF MACKAY AND JAMES (2001) AND SCHMOLCK ET AL. (2000)

Procedures of MacKay and James (2001) and Schmolck et al. (2000) resembled those of Lackner (1974) except that presentation was visual: Participants read short

sentences aloud, decided whether each contained one or more than one meaning, and described the one or two meanings that they detected. In MacKay and James, HM detected ambiguities in the sentences significantly less often than six memory-normal controls carefully matched with HM on educational level, previous employment, age, overall IQ, and verbal IQ (see also MacKay, Stewart, et al., 1998, Experiment 1), and unlike controls, HM often changed his responses from "two meanings" to "one meaning" and vice versa, sometimes several times, as if basing his responses on subtle, evoked cues from the experimenter rather than comprehension per se. HM also made more uncorrected reading errors than controls, and HM's reading errors usually rendered the sentences ungrammatical, a further indication of sentence comprehension deficits. However, HM's comprehension and reading deficits were highly selective in nature, e.g., involving rare or novel phrases but not familiar phrases such as "for lunch." MacKay and James concluded that the ability to form new connections via binding mechanisms within hippocampal systems is not independent of the ability to detect ambiguity in sentences. They also concluded that HM's selective deficits form part of a general, theoretically coherent syndrome that generalizes to other patients and to many other aspects of HM's behavior, including visual cognition, episodic recall, meaning description, spontaneous speech, and the ability to read isolated words and pseudo-words (see also James & MacKay, 2001; MacKay & James, submitted).

Schmolck et al. (2000) presented their (virtually identical) sentences to 7 amnesics (with various amounts, causes, and loci of brain damage) and 11 controls with higher WAIS-R vocabulary scores than the patients. Ambiguity detection/explanation results indicated that 4 of the amnesics performed like controls, whereas 3 performed reliably worse than controls. The amnesics who performed worse than controls differed from the other amnesics in six respects: they were much more amnesic on WAIS-III memory subtests, they scored much lower on the Boston Naming test, they had less education and lower IQ, and they had very large, encephalitis-induced lesions (the other amnesics were nonencephalitic and had relatively small lesions, primarily to either the hippocampal formation or diencephalon). To illustrate the extent of the encephalitic damage, consider EP (not the most damaged encephalitic patient). EP had extensive bilateral damage to medial and lateral temporal lobes and adjacent structures, including the fusiform gyrus, and was dysfunctional on frontal lobe tests (a fact reported in Buffalo, Reber, & Squire, 1998, but not in Schmolck et al.).

From these data, Schmolck et al. made two general claims: that extrahippocampal structures adjacent to but outside the hippocampus underlie deficits in this task and that detecting and explaining ambiguities is unrelated to hippocampal function. The next section adopts a question–answer format to critique these claims, together with corollary claims in Schmolck et al. regarding HM.

CRITIQUES OF THE SCHMOLCK ET AL. CLAIMS

The Extrahippocampal Claim: Did Schmolck et al. Localize Deficits in Ambiguity Detection to Structures Adjacent to MTL (as Claimed)?

The patient group that is logically required to test this "extrahippocampal" claim must have no hippocampal damage and *only* damage to structures adjacent to MTL. The Schmolck et al. patients fail both logical prerequisites: None had damage confined to extrahippocampal structures, and all had hippocampal damage. Moreover, Schmolck et al. fail to report and/or ignore brain damage (reported elsewhere) that is well beyond extrahippocampal structures but logically could explain their results. Finally, the extrahippocampal claim of Schmolck et al. may be untestable with living

patients under current technology: As Squire and Zola (1998, p. 210) note, current technology cannot "reliably identify patients who have damage limited to the hippocampus and no damage to adjacent structures such as entorhinal cortex."

Logical problems aside, the Schmolck et al. study also suffers from methodological flaws: The allegedly pure-hippocampal group had superior IQ (107 vs. 97) and greater education (means 16 vs. 13 years) than patients with combined hippocampal and extrahippocampal lesions and more education than the controls (means 16 vs. 13.5 years), confounds that favored the Schmolck et al. claims. The patient and control groups were also unmatched for factors such as verbal IQ that Schmolck et al. found to be highly correlated with ambiguity detection.

The Hippocampal Claim: Did Schmolck et al. Demonstrate (as Claimed) That Hippocampal Functions Include Memory, but Not Detecting and Explaining Ambiguities?

Four logical prerequisites are required to sustain this claim: One is evidence that damage outside the hippocampus does not impair hippocampal functioning. Schmolck et al. provide no such evidence. A second prerequisite is hippocampal patients with no extrahippocampal damage, but the three patients that Schmolck et al. classified as "pure-hippocampal" do not unambiguously meet this criterion. The only evidence for pure-hippocampal damage in one patient was anoxia due to cardiac arrest for some unspecified period of time. However, confirmation of this lesion site is necessary since diffuse hippocampal, extrahippocampal, and cortical damage often accompanies anoxia. Two other patients were classified pure-hippocampal because their hippocampus was "reduced in size," without specifying *relative to what*, i.e., relative to control brains? relative to before their amnesia? relative to other brain areas? These patients should only count as pure-hippocampal if extrahippocampal areas were undiminished but the hippocampus was diminished relative to just before the amnesia-causing trauma or relative to more than five control brains *of similar age* (see the cell count data of Loftus, Knight, & Amaral, 2000). Under neither criterion did Schmolck et al. demonstrate pure-hippocampal status for these patients.

Prerequisite three for supporting the hippocampal claim is memory deficits but because Schmolck et al. never compared the memory performance of pure-hippocampals vs. matched controls, memory deficits were never established for these patients. Prerequisite four is evidence that pure-hippocampal patients perform no differently than a homogeneous control group matched on all pertinent dimensions. Here the relevant evidence in Schmolck et al. is inadequate in three respects. First, the relevant control group ($N = 5$, some unspecified number of whom belonged to a University of California retirement community) was neither homogeneous nor closely matched with the pure-hippocampals ($N = 3$): The controls exhibited great variability and a lower mean vocabulary score than the pure-hippocampals (54.2 versus 58), a direction of difference that favors the hippocampal claim. Second, the pure-hippocampals performed worse than the five controls (75.1% versus 84% correct), although this difference was not reliable at $p = .01$. Third, Schmolck et al. lacked adequate statistical power to reject the null hypothesis (that these groups did not differ at any acceptable or marginally acceptable p value, including $p = .10$).

Schmolck et al. also presented other analyses to support their hippocampal claim, but these analyses are incorrect: For example, Schmolck et al. published correlations involving so few participants as to be meaningless, they incorrectly applied t tests to small- and unequal-sized groups, and they incorrectly averaged together patients who received fundamentally different experimental treatments. Schmolck et al. also performed incorrect t test comparisons involving a single control group with unspeci-

fied background factors and patient groups with differing background factors and nonhomogeneous areas and types of brain damage.

Claims Associated with HM

Do HM's language-related deficits reflect a general deficit in semantic processing (as claimed)? This claim is unsustainable for four reasons: When his ambiguity detection was tested, HM had above-average verbal IQ (see MacKay, Stewart, et al., 1998); HM's brain damage does not fit the pattern for semantic dementia (see Hodges, Patterson, Oxbury, & Funnel, 1992); Controls in MacKay and James (2001) with verbal and performance IQs matched closely with HM's outperformed HM in detection/explanation of ambiguity; Finally, HM has selective rather than general sentence-meaning deficits: HM has deficits for novel or unfamiliar phrases but not clichés or familiar phrases.

Is HM basically similar to the Schmolck et al. patients with large, encephalitis-induced lesions (as claimed)? This claim is incorrect on behavioral and anatomical grounds. Behaviorally, Schmolck et al. incorrectly compared HM's performance on an auditory task with encephalitic performance on a visual task. However, compared on the same visual task, HM's ambiguity detection in MacKay and James (2001) was over 30% better than that of encephalitic patients in Schmolck et al. (72% vs. 41.6% correct) despite HM's greater age (71 vs. about 61).[1] Anatomically, HM's lesion was nonencephalitic and much less extensive than lesions in the encephalitics. For example, HM's neocortical damage resulted from insertion above the eyes of fine metal tubes that sucked out HM's MTL and was confined to the tips of the temporal lobes (see Corkin, Amaral, González, Johnson, & Hyman, 1997). However, EP (not the most damaged encephalitic patient) has neocortical lesions apparently extending from the fusiform gyrus and lateral temporal lobes to the frontal cortex. With such extensive damage in these areas, the headline title of Schmolck et al. would not have been news to Wernicke (1874); nor would the fact that EP has anomia (noted in Hamann, Cahill, & Squire, 1997, but not Schmolck et al.).

Did HM's extremely severe memory deficits arise solely from his damaged hippocampus (as claimed)? This claim is remarkable since Schmolck et al. note that memory deficits tend to be most severe and long lasting with damage resembling HM's, i.e., involving the hippocampus *and* adjacent structures.

Do HM's ambiguity deficits arise solely from his extrahippocampal damage (as claimed)? If correct, this claim is new and important since neocortical areas historically associated with comprehension deficits are undamaged in HM, unlike the Schmolck et al. encephalitics. However, the evidence provided does not support this claim.

In related claims, Schmolck et al. suggested that childhood epilepsy caused the ambiguity detection deficits of HM and 33 patients in Zaidel, Zaidel, Oxbury, and Oxbury (1995), who had unilateral left- vs. right-sided surgical lesions to the amygdala and hippocampus. Besides being unsupported, these claims suffer from theoretical and empirical problems. An empirical problem is that patient PH in Schmolck et al. had normal ambiguity detection, but apparently had epileptic attacks that were more severe than HM's. A theoretical problem is that attributing the language deficits of HM and the Zaidel et al. patients to epilepsy requires an account of how HM's

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[1] The fact that encephalitic performance (41.6%) fell below coin-toss levels (50%) may be due to response bias rather than deliberate falsification of responses (see Table 3 in Schmolck et al.). However, response bias cannot explain HM's above-coin-toss-levels of performance (72%) on this visual task (see MacKay & James, 2001).

epilepsy caused selective deficits involving novel but not familiar phrases and how childhood epilepsy caused developmental deficits in precisely those Zaidel et al. patients who (as adults) had unilateral left removals but not unilateral right removals (see Zaidel et al.; and MacKay, Stewart et al., 1998).

GENERAL COMMENTS ON THE CONFLICTING CONCLUSIONS: THE THEORETICAL- VS. ANATOMICAL-PARADIGMS

MacKay and James (2001) represents a clear example of the Theoretical-paradigm, where the basic goal is to develop a detailed theory with explanatory mechanisms that accurately predict specific patterns of spared and impaired function in one or more patients who can be said to exhibit a syndrome with causal relations to those mechanisms. Note that anatomical structures per se are not central to the Theoretical-paradigm: Theories can posit a particular theoretical construct or causal mechanism without committing to a specific brain locus for that causal mechanism (see MacKay & James). For example, the theoretical mechanisms known as binding nodes in Node Structure Theory (NST; see MacKay & James) that facilitate the formation of new theoretically defined connections *may* be located in bilateral hippocampal structures and/or connected entorhinal, perirhinal, and parahippocampal areas given current information (see e.g., Milner, 1975; O'Keefe & Nadel, 1978; Zola, 2000). However, this is a complex, challenging, and currently unsolved *empirical* question since hippocampal system damage can in principle diminish the efficacy of binding nodes located *outside* hippocampal systems and vice versa (see MacKay, 1990). Moreover, the issue of what precise brain areas house different types of NST binding nodes falls outside NST and the Theoretical-paradigm since there are no *theoretical* reasons why any given brain structure must house this particular theoretical construct.

In contrast, Schmolck et al. (2000) is a clear example of the Anatomical-paradigm, where the basic goal is to examine patients with lesions restricted to particular anatomical structures (e.g., the hippocampus) and to describe deficits common to this category of patients (e.g., a "pure-memory deficit") in the hopes of establishing what that particular structure does. Because establishing and describing deficits represent the goals of the Anatomical-paradigm (rather than developing and modifying theories, the Theoretical-paradigm goal), it is perhaps not surprising that Schmolck et al. make no explicit mention of theory or metatheory. Interestingly, however, several unsupported but fundamentally theoretical claims do crop up in Schmolck et al., and one (on "the ability to form new memories") directly contradicts NST. Moreover, an *unstated* theory clearly underlies this paper, namely, that the hippocampus is a pure-memory structure.[2] This unstated and unreferenced theory is developed in Alvarez and Squire (1994) and is unsustainable for at least three reasons under the Theoretical-paradigm. First, amnesia increases in severity when both hippocampal and extrahippocampal structures are damaged (see e.g., Zola, 2000). Second, no one (despite many attempts) has succeeded in establishing dividing lines, either empirically or theoretically, between where language comprehension ends and where memory storage of verbal materials begins or between where memory retrieval of verbal materials ends and where language production begins (see Bock, 1996; MacKay & Abrams, 1996; MacKay, Burke, et al., 1998; MacKay, Stewart, et al., 1998). Third, no *theoretical* reasons have ever been advanced for why episodic/

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[2] Like Schmolck et al., Lackner (1974) also made no explicit mention of theory, although an unstated theory with a long history in psychology underlies his work. As MacKay, Burke, et al. (1998) discuss in further detail, Lackner's unstated theory also lacks firm empirical support.

declarative memory is the one and only function of the hippocampus (see also Chun & Phelps, 1999).

Theoretical problems aside, many unsupported claims in Schmolck et al. follow from their unreferenced theory. The three main ones have already been discussed. Another concerns inaccuracies in how Schmolck et al. describe the Zaidel et al. (1995) data which strongly support NST (see MacKay, Stewart, et al., 1998), but contradict their unreferenced theory. For example, Schmolck et al. give inaccurate means from Zaidel et al. and claim that both of Zaidel et al.'s patient groups explained fewer second meanings than "a normative sample." However, Zaidel et al. did not run a control sample, and their patients with right-side lesions (who did not differ significantly from norms) discovered reliably more ambiguities than their patients with left-side lesions (a theoretically vital fact noted in MacKay, Stewart, et al., but not Schmolck et al.).

In a final unsupported claim, Schmolck et al. label HM as "less than ideal" for addressing relations between memory, language, and hippocampal function. Despite HM's extrahippocampal damage (well known since Scoville & Milner, 1957, and reestablished by Corkin et al., 1997), scores of references over 4 decades have portrayed HM as a "hippocampal amnesic" and an ideal patient for studies of memory. However, following recent demonstrations that HM had language comprehension deficits in 1967, in 1970–1973, and in 1997–1999 (MacKay & James, 2001; MacKay, Burke, et al., 1998; MacKay, Stewart, et al., 1998), HM has suddenly become less than ideal, thereby preserving the unstated and unreferenced theory of Schmolck et al.

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