

WHAT DO ANIMAL MODELS OF MEMORY MODEL?

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The model proposed by Eichenbaum, Otto, and Cohen (EO&C), by virtue of its directness, represents definite progress in the quest for understanding of the role that various medial temporal lobe structures play in various laboratory learning tasks used with animal subjects, especially rats. Its major shortcoming lies in the claim that it applies not only to animals but also to humans. We find that claim ill founded.

A large variety of animal models have been described in the literature. There are animal models of toxicity, brain atrophy, leprosy, drug use, dementia, schizophrenia, delirium, and so on and on. What one does not find are animal models of things such as artistic creativity, mathematical reasoning, or language. Why not?

We can think of at least two plausible reasons. One, these expressions of the human brain are thought to be so unique that trying to learn something about them - for instance their neuroanatomical correlates - by experimenting with rodents, or even nonhuman primates, is difficult if not impossible. Two, the same reason that there are no human models of olfactory discrimination learning in rats, or climbing skills in monkeys: the models do the job too poorly to throw much light on the real thing.

Now, it is, or at least should be, beyond dispute that human memory is both similar to and different from the memory of rats and monkeys. It seems reasonable to assume that the similarities and differences in memory of these species are comparable to similarities and differences between their modes of locomotion, or their physical appearance.

Given that the similarities do exist, it is reasonable to hope that animal models of memory may illuminate those aspects of human memory that do not distinguish the species. Given that differences exist, it is also reasonable to assume that animal models are less useful, and may even turn out to be outright misleading, for the understanding of those features of human memory that are unique to humans.

The question then becomes exactly what aspects of human memory is the EO&C model supposed to model? The answer given by EO&C is 'declarative memory,' which they claim is characterized by the hippocampal-dependent relational representations. Declarative memory is said to be "exemplified by our recall of everyday facts and events. Such memories can be brought to conscious recollection, are typically subject to verbal reflection or other explicit forms of recall, and can be used flexibly in a variety of situations outside that of the learning experience" (p. xxx, emphasis added). This sounds acceptable for humans, although we find it more reasonable to assume that conscious recollection and explicit recall characterize episodic memory but not semantic memory (Tulving, 1993). But the main problem is, how can one ascribe declarative memory, as described by EO&C, to animals? No one knows any method that would allow one to identify 'conscious recollection' in nonverbal animals. No one knows, yet, how to get the animals to 'reflect' on their past experiences. Although the distinction between explicit and implicit forms of retrieval is now firmly established in human memory (Roediger & McDermott, 1993; Schacter, Chiu & Ochsner, 1993), it has not, yet, been introduced into work with animals, presumably because no

one knows how to operationalize the distinction in an animal experiment. Finally, in human memory the concept of 'recall' is clear and sharp, primarily by virtue of its thoroughly studied contrast to another form of expression of propositional knowledge, namely recognition. But the same distinction in the study of animal memory is fuzzy at best, and some claim it is meaningless. These simple facts suggest that the concept of 'human and animal declarative memory', central to EO&C's theory, is a Procrustean bed. Facts concerning human and animal memory can be fitted into it, but at a cost of considerable suffering.

There are other reasons why we think that higher forms of human memory, such as declarative, cannot be meaningfully modelled by animals. Our critique focuses on the anatomical basis on which research on rats (and to a lesser degree also that on monkeys) relies and on which EO&C base their hypothesis. We question the comparability of the hippocampal formation of rats, "monkeys"², and man. We base our reservations primarily on morphologic (cytoarchitectonic), hodologic, and phylogenetic criteria, assuming that structural inequalities imply behavioral inequalities.

EO&C state that "with regard to the hippocampal formation, each of the subdivisions of this area are well defined and largely comparable in the monkey and rat". They refer to the paper of Rosene and Van Hoesen (1987 [not 1988 as cited by EO&C]) in support of their statement. This is puzzling, because Rosene and Van Hoesen (1987) point to "striking differences between hippocampal formation cytoarchitecture of the rat and the monkey or man as well as clear differences between monkey and man" (p. 353). Rosene and Van Hoesen (1987) further point out that an underlying theme of their chapter is that the hippocampal formation of both monkey and man is not simply an enlarged version of the hippocampal formation of the rat, but rather "a structure that has undergone a progressive development in primate phylogeny that is reflected in many levels of its morphological organization (cytoarchitectonics, histochemistry, connectivity) and suggests a functional progression as well" (p. 360).

Similar points have been made by other outstanding comparative neuroanatomists of our day (Crosby & Schnitzlein 1975; Stephan 1975). Stephan (1975) devoted a whole section of his magnum opus to "specialities of the human hippocampus", and especially emphasized the differential appearance of the fornical system. He pointed out that the fornix projections to the mammillary bodies increase in importance as one moves higher in the phylogenetic hierarchy, and that the septal projections in man differ distinctly from those of other mammals. Furthermore, in humans (and possibly in other higher primates) the fornix contains isocortical fibers, that is fibers of a non-hippocampal origin. Stephan declared that only a minority of the fimbrial fornix fibers originate from Ammon's horn, and that the majority originates from the parahippocampal cortex. This being the case, the neuroanatomical foundation of EO&C's two-stage model (temporary storage and parahippocampal region vs. relational processing and hippocampal formation [summary and p. xxx] becomes shaky, at least for non-primate species.

Two other prominent changes (Stephan, 1975) within the hippocampal formation are especially relevant to the EO&C model: (1) the proportional relations between the entorhinal cortex and field CA1, and (2) the grossly disproportional enlargement of this field in human beings. Field CA1 receives the main alveolar afferents from the progressive entorhinal cortex. Stephan found that both structures enlarge to almost the same high degree in man compared to other primates.

Thus, even a cursory glance at the comparative neuroanatomy of the medial temporal lobe region reveals that, on the grounds of elementary cytoarchitectonics of CA-subfields alone, the structures discussed by EO&C lack the comparability needed for the justification of conclusions about the similarity of function drawn by the authors. Facts concerning the hodological and biochemical diversification compound the difficulty.

The anatomical disparities of the hippocampal regions of rat, monkey and man reflect ecological and behavioral adaptations and may lead to emphasizing roles in spatial memory processing (Angeli, Murray & Mishkin, 1993; Jarrard 1993; Murray, Gaffan & Mishkin, 1993; Nadel 1991; Wilson & McNaughton 1993), in attention and expectation (Salzmann 1992), or in (verbal) memory processing (Zola-Morgan, Squire & Amaral, 1986).

In humans, the processes of encoding and retrieval of episodic memory may furthermore be shared between the hemispheres, with the encoding being primarily guided by left prefrontal regions and retrieval by right ones (Tulving et al., 1994). Both the degree and complexity of functional hemispheric asymmetry and the phylogenetic expansion of the prefrontal area make it unlikely that comparable sharing mechanisms exist in the brains of nonhuman species. The results of Tulving et al. (1994) provide further grounds for believing that human and nonhuman memory processes differ qualitatively rather than quantitatively. Trying to understand the highly evolved unique processes of human memory through animal models makes no more sense than trying to understand mathematical reasoning or artistic creativity using the same methods.

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NOTES

¹ E.T.'s research is supported by an endowment by Anne and Max Tanenbaum in support of research in cognitive neuroscience, and by the Natural Sciences and Engineering Research Council of Canada. H.J.M.'s stay at the Rotman's Research Institute was supported by a grant from the German Research Council (DFG; Ma 795/16-1).

² Although it may be reasonable to speak about "the rat," the general reference to "monkey" is unjustified. Huge differences--in brain development, natural habitat, social behavior, life time, and so on--exist among the hundreds of species ranging from tiny rat-like looking creatures to nearly human-size species (Stephan, Baron & Frahm, 1988).