

What does the limbic memory circuit actually do?

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Abstract: We applaud Aggleton & Brown's affirmation of limbic diencephalic-hippocampal interaction as a key memory substrate. However, we do not agree with a thesis of diencephalic-hippocampal strict dedication to episodic memory. Instead, this circuitry supports the production of context-specific patterns of activation that subserve retrieval for a broad class of memory phenomena, including goal-directed instrumental behavior of animals and episodic memory of humans.

Support marshaled by Aggleton & Brown (A&B) for the essential involvement of hippocampal-diencephalic (H-D) interactions in recollection (but not recognition) has potential to confer on the limbic diencephalon its long-deserved (and widely ignored) status as a legitimate participant in the limbic memory circuit. Yet, we find problematic the main thesis: H-D dedication to episodic memory. We argue instead that the H-D interactions subserve a broader mnemonic function, cue-, and context-encoding in the service of retrieval. This function is used in multiple memory paradigms including basic instrumental learning of goal-directed behavior of animals and episodic memory.

Our studies of the neurophysiological bases of discriminative instrumental learning in rabbits (cited in the target article; Gabriel 1993) indicate an essential involvement of the limbic diencephalon, and a clear relevance of H-D interactions to this learning. The results are in accord with A&B's general thesis that the H-D axis is involved in memory-relevant processing. We appreciate their acknowledgment of our work (sect. 9, "Final comments"). Yet, A&B were ambivalent concerning the relevance of our data to their account, as indicated by their comment that "the basic avoidance task is unlikely to provide a direct measure of episodic memory and hence is of limited application." This arises from the authors' conviction that the hippocampus, clearly important in mediation of episodic memory, is not involved in basic instrumental learning. Admittedly, the hippocampus is not essential for acquisition of discriminative avoidance behavior. However, it modulates the behavior as well as the task-relevant neuronal activity of the anterior thalamus, as indicated below.

Extensive recordings of neuronal activity during behavioral acquisition demonstrate unique topographic distributions of brief latency, S+elicited neuronal activity across distinct nuclei of the anterior thalamus and the layers of posterior cingulate cortex. Certain thalamic nuclei and cortical layers were maximally activated by the S+ in the initial session of training, others in intermediate training stages, and still others as the rabbits attained asymptotic discriminative performance (Gabriel et al. 1991). The distributions of activation changed systematically, not only across time (training stage) but also with respect to the spatial context. The same physical cues elicited different patterns of activation, depending on whether the subjects were engaged in a moderately-learned discriminative avoidance task, or (in a separate training apparatus) a well-learned discriminative approach task (Freeman et al. 1996). Thus, the distribution patterns coded both the spatial and temporal context. These context-specific patterns, elicited at brief latency (80 msec) by the cue (S+) that calls forth the learned response, are arguably the brain's earliest sign (in the millisecond series) of context-specific retrieval.

Other evidence suggests that the context-specific patterns depend on the integrity of hippocampal efferent flow to the limbic diencephalon and cingulate cortex. Subicular, hippocampal, and entorhinal cortical lesions alter anterior thalamic and cingulate cortical task-related neuronal activity in ways that are likely to degrade the value of the patterns as a spatio-temporal context code (Freeman et al. 1997; Gabriel et al. 1987; Kang & Gabriel 1998). Moreover, the lesions impair contextual processing. Rabbits with

lesions failed to reduce avoidance responding when the familiar training context was altered (reviewed by Gabriel 1993; see also Freeman et al. 1997). This failure of context-specificity was not simply a "response inhibition" problem as the rabbits inhibited normally when S+ quality was altered instead of the context (Gabriel 1993, p. 515).

These and many other findings implicate the hippocampus and the anterior thalamus in mediation of context-specific retrieval of discriminative, instrumental, goal-directed behavior of rabbits. We propose further that these areas are involved in the retrieval of episodic memory, a point on which we and the authors are in agreement. However, our account does not place responsibility for the whole of episodic memory on the hippocampal-diencephalic circuitry. The circuitry does not, in our view, store items or contents of memory as A&B seem to suppose (sect. 7). Rather, associative synaptic modifications are stored, which allow familiar and significant stimuli to elicit context-specific patterns of activation. The patterns, in turn, retrieve context-appropriate contents of memory. The contents of memory, be they goal-directed behaviors or experiential recollections (episodic memories), are stored elsewhere in the brain (in different functional circuitries) and are recalled by virtue of their association with the limbic retrieval patterns. Thus, the more general issue concerns the appropriate mapping of components of a complex construct (e.g., episodic memory) onto the brain's distinct functional circuits.

Our view integrates many findings in addition to the foregoing. For example, the limbic diencephalon's mediation of discriminative avoidance behavior is *time-limited*. Retention of the behavior was severely impaired when anterior and MD thalamic lesions were made after training to criterion, but no impairment was found when the lesions were made after 10 days of post-criterial overtraining (Hart et al. 1997). Just as for episodic and declarative memory, discriminative avoidance learning undergoes gradual "consolidation," that is, a progressively acquired independence from limbic circuit processes. (Given the strong consensus that episodic memory is subject to consolidation, we were surprised that A&B did not explicitly address this issue.)

The fact that hippocampal lesions do not impair acquisition of discriminative behavior (whereas they do impair episodic memory) is not a compelling justification for regarding these forms of learning as products of entirely separate memory systems. Discriminative avoidance behavior is acquired normally by subjects with damaged hippocampi because original acquisition poses little challenge to the limbic retrieval circuit. Retrieval during acquisition does not require or use the exquisite thalamic spatio-temporal patterns endowed by hippocampal efferents for disambiguating inputs or for response selection. It occurs instead as a result of direct information flow from the limbic thalamus and cingulate cortex to areas involved in priming and execution of the locomotor response.

The absence of a hippocampus is noticed when there is potential for substantial mnemonic interference, such as when multiple, similar tasks are learned concurrently, when retrieval cues are similar to cues associated with already-stored items, or when subjects are required to use different configurations of contextual stimuli for selection among response alternatives. It is therefore not surprising that a hippocampal contribution to instrumental performance is detected when transfer-of-training tests are given, such as testing in a novel context, training with cue-reversal, or requiring subjects to base their behavior on complex spatial configurations. Substantial interference is commonplace, however, in studies of episodic memory, which typically involve complex stimuli and multiple response items.