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Differential contributions of hippocampus, amygdala and perirhinal cortex to recognition of novel objects, contextual stimuli and stimulus relationships

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Abstract

This study examined contributions of the hippocampus, amygdala and perirhinal cortex to memory. Rats performed a cover task, and changes to stimulus identity or relationships were used to test incidental memory. Rats with hippocampal damage showed deficient responses to relationship changes, but demonstrated knowledge of the position and identity of the target object. They over-focused on the most predictive stimuli, and failed to acquire associations including surrounding cues. Rats with amygdala damage responded to changes involving distal stimuli, and showed deficient responses to novel objects and object relationships. These rats may be highly reliant on relational representations, resulting in a reduced salience for individual novel stimuli. Rats with perirhinal damaged responded to novel stimulus relationships and distal cues, but showed deficient responses to novel objects, suggesting that changes in identity had reduced salience. Implications for declarative and conjunctive hippocampal theories are discussed.

Keywords: Learning; Memory; Novelty; Medial temporal; Incidental; Relational

1. Introduction

Different neural structures may be involved in learning about different types of stimuli. The current study examines the effects of hippocampal, amygdala and perirhinal cortex lesions on recognition of changes in proximal objects, distal cues and the relationships among them. Evidence suggests that these structures are differentially involved in learning about stimulus relationships, distal stimulus identity and proximal object identity.

1.1. Hippocampus

Theories regarding the role of hippocampal function have implicated this structure in configural, conjunctive and declarative memory. While these theories have subtle differences regarding the nature of the representations that are maintained by the hippocampus, all theories have a common thread in postulating that the hippocampus is critical for learning about relationships among stimuli [24]. An essential feature of this type of learning is that associations among multiple elements are combined to form a unique long-term memory representation [9,11,37–39,44].

Memory for spatial locations often requires relational memory, specifically when the subject uses cues to navigate to a goal from several different start locations [22,30,42].

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However, some types of navigational tasks can be non-relational in nature, and remain intact after hippocampal lesions. For example, rats with fornix lesions show normal performance on the Morris water task if they are released from the same start location and required to swim to the same goal location each time. They are subsequently impaired relative to controls when starting from a novel location. Compared to controls, their behavior is abnormally dependent on the particular cues directly in front of them [12]. This likely occurs because, without a relational representation, animals can only blend the distal cues, as viewed from one vantage point, into a unified representation.

A relational representation is often composed of more than just spatial cues. For example, the simultaneous representation of discrete predictive cues and surrounding non-essential contextual information requires an intact hippocampus. Rats with hippocampal damage can learn a simple association between contextual cues and an aversive event, such as a shock. However, if a discrete stimulus is added that immediately precedes the aversive event, such as a tone, rats with hippocampal damage show fear responses to the tone, and not to the contextual cues [32,33]. Thus, rats with hippocampal damage over-focus on the stimulus most directly predictive of the event, and fail to acquire a relational representation including associations involving the surrounding cues.

A similar phenomenon occurs with latent inhibition. Latent inhibition occurs when previous exposure to a stimulus results in slower acquisition of conditioned responses to that stimulus when it is paired with a positive or negative outcome. Hippocampal lesion rats show normal latent inhibition for discrete stimuli paired with reward. For example, pre-exposure to stimulus X leads to slower response acquisition rates for stimulus X compared to stimulus Y. However, hippocampal lesions lead to impaired latent inhibition for the stimuli surrounding the rewarded object. For example, following pre-exposure to stimulus X in context A rats with hippocampal lesions do not show normal reductions in response acquisition rates when trained in context A compared to context B [15]. They also fail to show a normal disruption in responding to a rewarded stimulus when transferred to a different context [15]. Again, these results suggest that the rats with hippocampal damage focus only on the cues that are most predictive of outcome, and fail to form a representation including the less-predictive surrounding cues.

Taken together, the previous studies support the idea that rats with hippocampal damage lack a relational representation of the environment. Rather, they form a rigid association comprised of the stimulus/stimuli most immediately predictive of outcome. This representation likely excludes the relationships among the predictive stimulus/stimuli and the surrounding cues, the nature/identity of the surrounding cues and the relationship of the surrounding cues to each other. Thus, we anticipated that in a distraction paradigm rats with hippocampal damage would show impaired incidental learning about all cues surrounding those that immediately control their behavior. They were expected to be disrupted following changes to those essential cues, and not following changes in surrounding cues.

1.2. Amygdala

The amygdala is important for associating objects or spatial relationships with positive or aversive outcomes in a passive classical conditioning setting [17,20,21,33,43]. However, it is unnecessary for remembering information about objects or spatial relationships [1,16,20,28,35,47]. There is evidence that amygdala lesions may lead to subtle deficits in spatial navigation due to an impaired ability to form a meaningful association between a specific location and its predicted valence [23].

The amygdala also appears to mediate fear responses to novel stimuli or neophobia. Rats with amygdala lesions show attenuated neophobia for novel foods [5,10,36,43]. In a familiar open-field setting, amygdala damage leads to abnormal responding to a novel proximal object, but exploration of novel distal cues remains unaffected [25]. This pattern of results may occur because the hippocampus can mediate responses to novel contextual information in the absence of an intact amygdala. In fact, the hippocampus and amygdala have competitive interactions for control of behavior. McDonald and White [21] demonstrated that additional relational knowledge of the cues in the test room, acquired in a pre-exposure session, led to slower acquisition of a cue preference task in normal rats. Disruption of the hippocampal system eliminated competition between amygdala- and hippocampal-mediated strategies, and hence rate of task acquisition was enhanced in fornix lesion rats. Conversely, it is possible that animals with amygdala damage may focus more on context and stimulus relationships, rather than on individual proximal items.

We expected that rats with amygdala damage would show normal incidental learning about relationships among cues, but may show impaired responding to individual novel proximal objects. We expected them to show normal disruption by the presence of novel stimulus relationships and novel contextual stimuli, as these behaviors may be mediated by the hippocampus. However, abnormal responses were anticipated in response to individual novel objects.

1.3. Perirhinal cortex

The perirhinal cortex is important for perception and memory of object features and identity but not spatial arrangements [3–5,7,8,13,18,19,23,27,29,34,46]. However, perirhinal cortex lesions can lead to subtle deficits in memory for spatial locations. This may occur because perirhinal lesions impair processing of cue identity information, which normally makes a non-essential contribution to solving a task that requires the formation of relationships among these cues [6,18,23,27]. It appears that when object identity becomes more important for solving a spatial task the perirhinal cortex becomes more essential to performance (for review,