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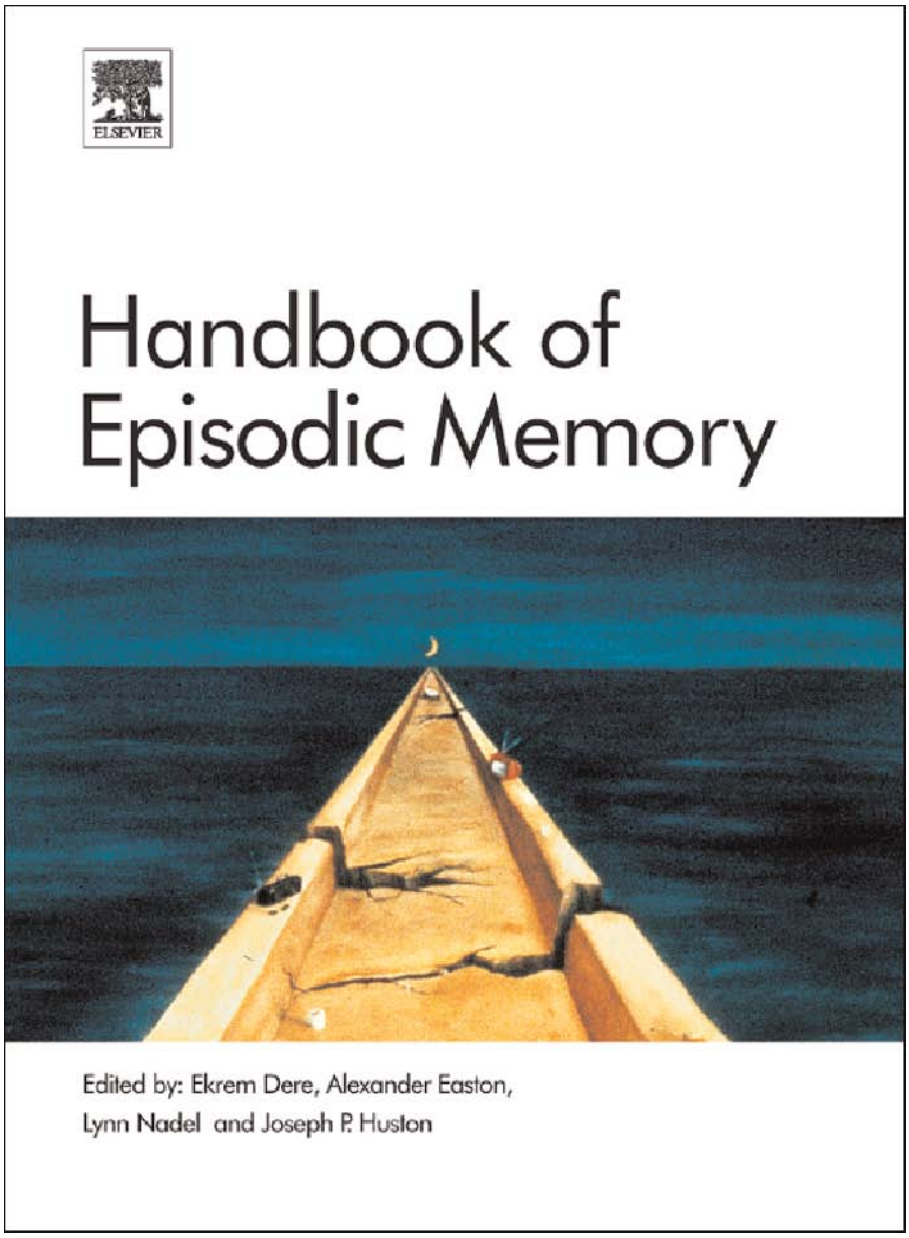

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From Michael R. Hunsaker and Raymond P. Kesner, The attributes of episodic memory processing.
In: J. P. Huston, editor: Handbook of Behavioral Neuroscience, Vol 18, Handbook of Episodic Memory,
Ekrem Dere, Alexander Easton, Lynn Nadel and Joseph P. Huston. The Netherlands: Elsevier, 2008,
pp. 57–79.
ISBN: 978-0-444-53174-2
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CHAPTER 1.5

The attributes of episodic memory processing

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Abstract: Despite decades of research on episodic memory in humans, a universally accepted model of episodic memory processes in animals has not been developed. Selectively isolating and probing the "what," "when," and "where" of a given behavioral episode has proven very difficult in nonhuman primates, rodents, and birds. In this chapter, a novel description of episodic memory processing in rodents is presented in which the processes underlying behavioral episodes are dissected into component domains called attributes. It is subsequently demonstrated that the concurrent presence or behavioral relevance of any or all attributes does not necessarily make a given memory process episodic in nature. It is demonstrated that a specific type of interaction between temporal, sensory/perceptual, and spatial attributes results in behavioral episodes that can be retrieved via hippocampus-dependent episodic retrieval processes. The role of the hippocampus in mediating these attributes will be discussed, followed by a discussion of contributions from the amygdala, caudate, and perirhinal cortex to episodic-like memory processes and how damage to these structures cause episodic-like memory deficits.

Keywords: sensory/perceptual; temporal; spatial; response; affect; episodic memory; rodents; attributes

I. Introduction

Since Tulving suggested that there may be a unique memory system underlying autobiographical (i.e., episodic or autonoetic) memory as separate from semantic (or noetic) memory (Tulving, 1972, 2001; Tulving and Markowitsch, 1998), there has been a quest to not only thoroughly characterize this dissociation in humans (Vargha-Khadem et al., 1997), but also develop models of episodic and semantic memory in rodents (Aggleton and Brown, 1999, 2007; Aggleton and Pearce, 2001), nonhuman primates (Gaffan, 1994), and birds (Clayton and Dickinson, 1998, 1999; Griffiths et al., 1999; Clayton et al., 2001). Convergent PET, fMRI, and neuropsychological data collected from patients with developmental amnesia due to perinatal hypoxia suggest that the hippocampus mediates episodic, but not semantic, memory processes (Nadel and Moscovitch, 1997; Vargha-Khadem et al., 1997; Mishkin et al., 1998). In nonhuman mammals, the hippocampus has similarly been proposed to subserve episodic memory processes (Morris, 2001, 2007; cf. Dere et al., 2006). The difficulty in studying episodic memory processes in animals and thoroughly characterizing it in humans is that an experience or memory can be classified as episodic only after it is recalled via a mechanism involving self-conscious awareness (i.e., mental time travel, autonoetic consciousness, or self-awareness; Tulving, 1972, 2001).

It has proven exceptionally difficult to develop animal models of episodic memory processing. At the heart of this issue are the difficulties in precisely defining the terms episodic and semantic for nonhumans without assuming that animals have a similar form of consciousness as is

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E. Dere, A. Easton, L. Nadel and J.P. Huston (Eds.)
Handbook of Episodic Memory, Vol. 18
ISBN 978-0-444-53174-2

DOI: 10.1016/S1569-7339(08)00205-1
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attributed to humans. Clayton and colleagues (Clayton and Dickinson, 1998, 1999; Griffiths et al., 1999; Clayton et al., 2001) have suggested that there are three fundamental elements that underlie episodic memory processes in animals: "what," "when," and "where." They also posit that all three of these elements must be simultaneously computed and bound into a single representation to perform a given task for it to specifically test episodic memory processes as opposed to nonepisodic and semantic memory processes. Others have suggested that it is not the presence of these three elements per se that determines the episodic nature of a memory process, but the manner in which they interact during a behavioral experience that actually defines an episode (Tulving, 1972, 2001). Additionally, it has been suggested that single-trial learning does not suffice as episodic unless the single trial specifically contains a behavioral episode that is recalled via an autonoetic retrieval process (Morris, 2001, 2007).

An alternative way to describe or characterize both episodic and semantic memory processes is to break each behavioral episode down into component parts – in this chapter called attributes (cf. Kesner, 1986, 1998, 2007). Identifying each of these attributes and characterizing the nature of their interactions with other attributes may lead to a more basic understanding of the neural substrates that underlie episodic memory processing. An added benefit of an attribute model of episodic memory processing is that such a model provides a theoretical framework that can be used to develop behavioral tasks to specifically evaluate the individual components, domains, or attributes of episodic memory processes.

II. Contemporary viewpoints on the neurobiological basis of episodic memory

There have been many proposed neurological substrates for episodic memory that will be covered in this volume and have been discussed elsewhere (Baddeley et al., 2001). Some have proposed that the medial temporal lobe (Squire and Zola, 1998), the hippocampus proper (Nadel and Moscovitch, 1997; Vargha-Khadem et al., 1997; Mishkin et al., 1998), or cortical–subcortical interactions (cf. Papez, 1937; Gaffan and Gaffan, 1991; Gaffan et al., 1991; Aggleton et al., 2000) mediate episodic memory processing. Although it is difficult to localize any memory process (episodic or nonepisodic) to discrete anatomical loci, these hypotheses have provided the theoretical rationale for research and the development of tests to more thoroughly characterize the precise nature of episodic memory processing (Aggleton and Pearce, 2001; Morris, 2001, 2007).

There are various models for episodic memory, but only two models will be briefly discussed here prior to describing a novel approach the study of episodic memory processing in rodents. It has been suggested that the hippocampus itself underlies episodic, but not semantic, memory processing (Vargha-Khadem et al., 1997; Mishkin et al., 1998) because perinatal damage to the hippocampus causes apparent episodic memory processing deficits without concomitant deficits for semantic memory processes. This is not to suggest that the hippocampus is the only important substrate, but in these models hippocampal integrity is critical for episodic memory, but not semantic memory, processing. An alternate hypothesis is that the hippocampus is a component of a network of interacting subcortical and cortical brain structures (Papez, 1937; Gaffan, 1994; Aggleton and Brown, 1999, 2007; Aggleton and Pearce, 2001). This interaction among subcortical and cortical areas may underlie episodic memory, so damage to any of a number of structures (including selective damage to the hippocampus, fornix, mammillary bodies, and the anterior thalamus) may be sufficient to cause similar episodic memory processing deficits without apparent deficits for semantic memory processing. These theories appear to be partially reconcilable since hippocampal damage results in similar deficits under both models; but nevertheless, vehement discussions have ensued and competing models have been postulated to create a universally accepted model of episodic and semantic memory processes (cf. Baddeley et al., 2001; present volume).

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II.A. Models focused on the hippocampus

In recent years, it has become vogue to place episodic memory processes in the hippocampus. This model derives from convergent PET and fMRI findings that demonstrate specific activations within the hippocampus during episodic encoding and retrieval (Nyberg et al., 1996; Schacter and Wagner, 1999). Experiments characterizing the pattern of memory deficits of developmental amnesic patients with damage limited to the hippocampus have revealed a putative severe episodic amnesia devoid of a severe semantic amnesia (Vargha-Khadem et al., 1997; Mishkin et al., 1998; but cf. Squire and Zola, 1998; Morris, 2001, 2007). This theory is so widely accepted and prevalent in the literature that even autistic spectrum disorders have been described as the result of deficits in episodic memory processing or autonoetic awareness without concomitant disruptions in semantic memory processing (Ben Shalom, 2003).

Despite its prevalence in the literature and appeal deriving from the plethora of recent research into hippocampal function (cf. Morris, 2007), there are some lingering issues with a hippocampus-centered model of episodic memory processing. The evidence provided by Vargha-Khadem and colleagues (1997) with developmental amnesic patients is compelling, but it is still uncertain how specific these deficits really are. As pointed out by Morris (2007), the reports provided by the authors did not include interviews with educators who may have noticed potential semantic memory problems, just the parents who were more likely to notice the day to day episodic memory deficits. Also troublesome to this model is the notion that semantic memory processing has not as yet been shown to be exclusively nonhippocampus dependent and thus the episodic–semantic memory processing dissociation becomes difficult to verify empirically.

Also, it is perhaps a bit naïve to assume that the hippocampus can bind behavioral episodes without the assistance of other neurological substrates beyond simply sending information to the hippocampus. For example, it is usually important to know the importance of an experience based upon previous affective (or emotional) experiences. The generation or retrieval of this previously learned internal context would require the cooperation and interaction of extrahippocampal regions to generalize from previous experiences (e.g., the amygdala, insular cortex, and orbitofrontal cortex would potentially interact with the medial temporal lobe and hippocampus). Also, it has proven difficult to identify and adequately characterize selective hippocampal atrophy without concomitant extrahippocampal damage in vivo (Squire et al., 2006), or even to identify selective hippocampal activation using current PET or fMRI imaging technologies (Kirwan et al., 2007). Also, this model neglects (or at least fails to fully account for) the extensive afferent and efferent cortical and subcortical connectivity of the hippocampus (cf. Amaral and Witter, 1989).

II.B. Subcortical–hippocampal interactions

An alternative to mapping episodic memory processing to a single anatomical substrate is to distribute the component processes underlying episodic memory formation and then demonstrate that episodic memory processing results from online interactions between these distributed anatomical loci, with no single substrate dominating the process per se. It has been demonstrated that lesions to the white matter tracts along the Papez circuit (i.e., fornix lesions; Papez, 1937), in primates, cause memory impairments that appear to be episodic in nature (Gaffan, 1994). This model has rapidly gained prevalence since fornix lesions are a fairly common experimental manipulation performed on primates, and numerous labs have perfected this manipulation (Gaffan, 1994). Fornix lesions have a long history in rats, as well (Olton et al., 1979). Humans with putative fornix damage have also been identified and the nature of their episodic and nonepisodic memory deficits has been characterized (Gaffan and Gaffan, 1991; Gaffan et al., 1991; Aggleton et al., 2000). Patients with Korsakoff's amnesia, some with selective mammillary body damage, show deficits in tasks that emphasize episodic memory processing. These deficits approximate the effects of both focused hippocampal damage and fornix damage, and appear to be episodic in nature (cf. Vann and Aggleton, 2004).

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Although this model suppose that the hippocampus is a component within a fairly extensive network of interacting brain structures interconnected via the fornix and makes only passing commentaries concerning semantic memory processing, there are various issues and points of debate concerning this model of episodic memory. It is assumed that the patients with Korsakoff's amnesia have mammillary body damage without concomitant hippocampal or medial temporal lobe atrophy. This is a difficult proposition since there have been reports of hippocampal damage in Korsakoff's pathology (cf. Vann and Aggleton, 2004). More promisingly, patients with damage to the fornix itself have been identified (usually resulting from third ventricle tumors; cf. Gaffan and Gaffan, 1991; Gaffan et al., 1991; Aggleton et al., 2000). The problem is that these patients all have extrafornical damage, in addition to their damage to the fornix itself. In animal models of Korsakoff's pathology, animals with mammillary body damage do not have trouble with single-trial or working memory tasks, just cumulative learning during tasks such as acquisition of a delay nonmatching to place task on an eight arm maze (Sziklas and Petrides, 1993, 1998; Vann and Aggleton, 2004). Vann and Aggleton (2004) have suggested that (at least for spatial learning) the mammillary bodies may assist in making the mental conversion between egocentric and allocentric reference frames (e.g., determining behaviorally relevant egocentric position in overall allocentric space; cf. Rolls and Treves, 1998; Redish, 1999). This is a necessary function for spatial memory processing, but may not be necessary for episodic memory processing if locale is not critical for recalling the specific behavioral experience.

II.C. The current proposal: an attribute model of episodic memory processing

Despite the large number of models of episodic and semantic memory processing prevalent in the literature (cf. Tulving, 1972, 2001; Squire, 1992; Cohen and Eichenbaum, 1993; Eichenbaum and Cohen, 2001), few provide a theoretical framework for selectively evaluating the component processes that underlie episodic learning and memory. The attribute model proposed by Kesner (1986, 1998, 2007) and modeled by Rolls (Rolls, 1996; Rolls and Treves, 1998; Rolls and Kesner, 2006) suggests that there are multiple memory systems that have access to all sensory modalities; thus each memory system receives both processed and unprocessed sensory/perceptual and temporal information. Within each of these memory systems, individual sensory/perceptual modalities can be broken down into component processes that interact and combine to form memories and episodes by interacting among and within anatomical loci.

This theory supposes that all memory systems have access to information and the nature of the processing determines whether a memory processes is episodic or nonepisodic. Hippocampus-dependent episodic memory processes integrate information about what an episode was, when it occurred, and where it occurred (cf. Dere et al., 2006). Hippocampus-dependent semantic memory processing can contain the same information, but it will be processed via a different mechanism. Additionally, there are possible episodic-like memory processes mediated by nonhippocampal substrates that differ from hippocampus-dependent episodic memory processing in that spatial information is not critical to recall (e.g., there is no "where"). This means that other brain systems may process incoming stimuli via an episodic-like mechanism but according to their own specific roles and the precise nature of the information that they receive. In this sense, the dynamic nature of the memory processing determines whether a memory process is episodic or nonepisodic in nature, not the specific types of information being processed or the neural substrate underlying the processing per se. We concur with Clayton's general thesis that what, when, and where are important for episodic memory processing and with Dere et al. (2006) that the hippocampus mediates the binding of these three into a single unit. However, we assert that episodic-like processes that do not contain these three elements can be treated as episodic due to the dynamic, online memory processes and that a variety of attributes could activate the hippocampus or other brain regions, depending on the precise nature of the

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information that need to be recalled. From a dynamic viewpoint, single-trial learning and memory tasks that require recalling the entire behavioral experience will be referred to as episodic in this chapter.

III. Attribute model of memory

The memory systems proposed by Kesner (1986, 1998, 2007) are event-based, knowledge-based, and rule-based memory systems (cf. Fig. 1) that have access to information comprised of sensory/perceptual, temporal, spatial, linguistic, affect, and response domains (or attributes – cf. Fig. 2). These attributes interact in a unique manner within and among each different memory system, and different overlapping and nonoverlapping subsets of neuroanatomical substrates contribute to each memory system. This is akin to parallel information processing within the framework of multiple memory systems. It must be emphasized that these proposed memory systems are not to be thought of as compartmental models such as the declarative/nondeclarative memory model proposed by Squire (1992), since no memory system is assumed to operate independently of the others. The attribute model is better described as a catalog of component processes that facilitates behavioral dissociations of memory systems and memory processes based on the attributes subserved by each anatomical region, as well as the sum total and the nature of interactions with other brain regions within and among these distinct memory systems (Kesner, 1986, 1998, 2007).

III.A. Event-based memory system

The event-based memory system provides a temporary, highly plastic, short-term representation of information concerning the immediate

<table>
<tr><th>Event-Based Memory System</th><th>Knowledge-Based Memory System</th><th>Rule-Based Memory System</th></tr>
<tr><td colspan="3">Processes</td></tr>
<tr><td>Selective filtering of interference (pattern separation) of temporary memory representations</td><td>Selective attention and selective filtering associated with permanent memory representations of familiar information</td><td rowspan="2">Selection of strategies and rules for maintaining or manipulating information for subsequent action</td></tr>
<tr><td>Short-term and intermediate-term memory for new information</td><td>Perceptual memory</td></tr>
<tr><td>Consolidation of elaborative rehearsal of new information</td><td>Long-term storage</td><td rowspan="2">Short-term memory for new or familiar information</td></tr>
<tr><td>Retrieval of familiar information based on flexibility, action, and pattern completion.</td><td>Retrieval of familiar information based on flexibility and action</td></tr>
</table>

Fig. 1. Information processing systems. Event-based, knowledge-, and rule-based memory systems and the mnemonic processes associated with each.

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	Event-Based Memory System	Knowledge-Based Memory System	Rule-Based Memory System
Attributes	Brain Region	Brain Region	Brain Region
place	Hippocampus (H,M,R)	Parietal Cortex (H,M,R)	Lateral prefrontal cortex (H,M) Infralimbic/Prelimbic Cortices (R)
time	Hippocampus (H,M,R)	Dorsal prefrontal (H,M) Anterior Cingulate (R)	Dorsal prefrontal (H, M) Anterior cingulate (R)
language	Hippocampus (H)	Posterior Parietal Cortex (H) Wernike's and Broca's areas (H)	Lateral prefrontal cortex (H)
response	Caudate (H,M,R)	Pre-motor cortex (H,M), Supplementary motor cortex (H,M) Precentral cortex (R) Cerebellum (H,M,R)	Pre-motor cortex (H,M), Supplementary motor cortex (H,M) Precentral cortex (R) Cerebellum (H,M,R)
affect	Amygdala (H,M,R)	Orbitofrontal Cortex (H,M,R)	Orbitofrontal Cortex (H,M,R) Infralimbic/Prelimbic cortices (R)
sensory-perceptual	Sensory Cortices (H,M,R)	Inferotemporal Cortex (H,M) TE2 cortex (R)	Lateral prefrontal cortex (H,M) Infralimbic/Prelimbic cortices (R)

Fig. 2. The attributes of memory. The different attributes that combine to form memories organized by information processing system with the anatomical substrate of each labeled for humans (H), monkeys (M), and rats (R) where applicable.

past, the present, and the immediate future. The event-based memory system rapidly encodes data and events that are personal (or egocentric) in nature and occur within specific external and internal contexts. In other words, the emphasis of the event-based memory system is on processing available information and comparisons with only very short-term representations of the immediate past and immediate future goals. During initial learning, emphasis is placed on the event-based memory system. Later, during continued or longer-term learning, the event-based memory system will be important in situations where trial-unique (or novel) information needs to be rapidly utilized. The event-based memory system is also critically involved in episodic memory processing because it is capable of rapidly binding short series of events into coherent behavioral episodes. This memory system mediates short-term retrospective memory processes. The organization of individual attributes within the event-based memory system is as short-term, plastic, transient, and cognitive representations that interact with each other. This memory system can be described as a short-term working memory system (cf. Olton et al., 1979).

III.B. Knowledge-based memory system

The knowledge-based memory system provides lasting, relatively inflexible, intermediate, and

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long-term representations of information previously encoded by the event-based memory system and direct sensory/perceptual input. The result of this processing can be thought of as general knowledge of a given task or world at large, similar to semantic memory processing. The knowledge-based memory system is capable of processing information in an egocentric frame of reference and can derive allocentric frames of reference from the egocentric representations (cf. Redish, 1999; Rolls and Kesner, 2006). The knowledge-based memory system is important after a task has been initially encoded, given that the situation is invariant and/or sufficiently familiar. The knowledge-based memory system mediates intermediate- and long-term retrospective memory. The individual attributes within the knowledge-based memory system take many forms, usually as sets of attribute-dependent, long-term, cognitive representations and their interactions. The knowledge-based memory system can be thought of as an intermediate-term and/or long-term reference memory system (cf. Olton et al., 1979).

III.C. Rule-based memory system

The rule-based memory system receives information from the event-based memory system, knowledge-based memory system, and direct sensory information and integrates the information by applying rules and strategies to guide subsequent actions. It not only computes and provides goal-related information to guide future behavioral decisions, but also allows for behavioral flexibility and generalization between contexts, rules, and strategies, depending upon task requirements and the animal's previous behavioral experiences. The rule-based memory system mediates both retrospective and prospective memory processes. The organization of individual attributes within the rule-based memory system is based on a high order set of rules and schema to guide behavioral decisions across contexts and during novel behavioral experiences. The rule-based memory system contributes to both working and reference memory processing by providing a representation of internal contexts to guide behavioral decisions and responses (cf. Olton et al., 1979).

III.D. The attributes that make up each memory system

III.D.1. Temporal

The temporal attribute within the attribute model of memory processing involves memory representations of the duration of a sensory/perceptual stimulus and the temporal sequence or order of noncontiguous stimuli. From a "time" perspective, the temporal attribute defines a memory representation as past, present, or future relative to any and all other representations available for comparison (Howard et al., 2005). The temporal attribute is involved not only for temporal ordering and sequencing, but also for providing directionality and continuity to stimuli that are either spatially or temporally discontinuous (e.g., separated by a trace interval; Kesner et al., 2005; Hunsaker et al., 2006; Rogers et al., 2006). It is also involved in the formation of associations between noncontiguous sensory/perceptual stimuli. It has also been demonstrated that the temporal attribute may contain information about time per se (e.g., interval duration), as demonstrated during delay-dependent differential conditioning in mice (cf. the "time left" paradigm; Cordes et al., 2007).

III.D.2. Sensory/perceptual

The sensory/perceptual attribute within the current framework involves memory representations of sensory/perceptual stimuli that are part of a specific experience. Each sensory/perceptual modality (olfactory, auditory, visual, vestibular, somatosensory, and gustatory) is represented by the sensory/perceptual attribute. Although these sensory/perceptual stimuli are often used to compute and generate maps of space to be used by the spatial attribute (cf. Cohen and Eichenbaum, 1993; Eichenbaum and Cohen, 2001; O'Reilly and Rudy, 2001; Rolls and Kesner, 2006), or used to generate sensory–response and action–outcome contingencies that are represented by the response attribute (Yin and Knowlton, 2006),

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the sensory/perceptual stimuli also are represented as independent entities (cf. Cohen and Eichenbaum, 1993; Eichenbaum and Cohen, 2001; Rolls and Kesner, 2006; Hunsaker et al., 2007).

III.D.3. Space

The spatial attribute within the framework of multiple memory systems under the attribute model of memory processing involves memory representations of egocentric and allocentric spatial locations and relationships between spatial locations and sensory/perceptual stimuli. These processes are exemplified by the ability to rapidly encode and retrieve spatial maps (e.g., cognitive maps; cf. Tolman, 1948; O'Keefe and Nadel, 1978; Redish, 1999) and to localize sensory/perceptual stimuli in both egocentric and allocentric reference frames (cf. Gallistel, 1990; Redish, 1999). The spatial attribute specifically refers to processed information that is the result of a combination of all the available sensory/perceptual cues into an egocentric and allocentric representation of the environment (O'Keefe and Nadel, 1978; Redish, 1999; Vann and Aggleton, 2004; Rolls and Kesner, 2006). These processes underlying the computation and generation of "space" have been modeled extensively as configural or conjunctive processes (O'Reilly and Rudy, 2001), as competitive pattern separation and pattern completion processes (Rolls, 1996; Rolls and Treves, 1998; Rolls and Kesner, 2006), or as relational processes (Cohen and Eichenbaum, 1993; Eichenbaum and Cohen, 2001). Memory representations of the spatial attribute are further subdivided into more specific features including allocentric spatial distance, egocentric spatial distance, allocentric direction, egocentric direction, allocentric location in space, and egocentric location in space (discussed in greater detail by Kesner (1986, 1998, 2007) and analyzed quantitatively by Redish (1999) and Rolls and Kesner (2006)).

III.D.4. Response

The response attribute refers to the cumulative habit, stimulus–response associations, and action–outcome contingencies available during an experience. A response attribute within this framework encapsulates memory representations of motor responses (often based on vestibular and proprioceptive sensory/perceptual stimuli) and memory representations for learned stimulus–response associations. Also, the response attribute subserves action–outcome learning (cf. Yin and Knowlton, 2006).

III.D.5. Affect

The affect attribute involves memory representations of reward value (both positive and negative), positive or negative emotional experiences, and associations between sensory/perceptual stimuli and rewards or punishers. The affect attribute increases or reduces the saliency of each individual piece of information present during a given experience by aggregating a reward value to the individual stimuli (cf. O'Reilly and Frank, 2006). This is accomplished online during a behavioral episode or offline after the behavioral episode has concluded and is being consolidated to provide behavioral and internal contextual saliency to memory representations based on previous and subsequent experience.

III.D.6. Language

The language attribute is, presumably, unique to humans, and contains the semantic and phonological processes underlying language production, comprehension, and information coding via semantic or phonological mechanisms. Within this framework, a language attribute involves memory representations of phonological, lexical, syntactical, and semantic (or verbal) information.

III.E. Neural substrates underlying processing of each attribute

Within each memory system, a different subset of anatomical structures mediates a particular attribute or subset of attributes. Understanding the nature of the interactions within and among these brain regions and memory systems can lead to a more complete understanding of how memories are processed.

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III.E.1. Event-based memory
The hippocampus and interconnected neural substrates mediates memory for spatial, temporal, and language attributes. The caudate and interconnected neural substrates mediate memory for the response attribute. The amygdala and interconnected neural substrates subserve memory for the affect attribute. Sensory cortices mediate the sensory-perceptual attribute. For example, the perirhinal cortex mediates olfactory and visual information and the piriform cortex mediates olfactory information.

III.E.2. Knowledge-based memory
The posterior parietal cortex and interconnected neural substrates supports memory for the spatial attribute. The dorsal and dorsolateral prefrontal cortex (in monkeys and humans), the parietal cortex (in monkeys and humans), and anterior cingulate (in rats) support memory for the temporal attribute. The premotor cortex, supplementary motor cortex, and cerebellum (in monkeys and humans) and precentral cortex and cerebellum (in rats) support memory for the response attribute. The orbitofrontal cortex and interconnected neural substrates mediates the affect attribute. The inferotemporal cortex (in monkeys and humans) and TE2 (in rats) subserves memory for the visual sensory/perceptual attribute.

III.E.3. Rule-based memory
The dorsolateral and ventrolateral prefrontal cortex and interconnected neural substrates (in monkeys and humans) and infralimbic cortex/prelimbic cortex and interconnected neural substrates (in rats) support spatial, sensory/perceptual (visual object), and language attributes. The premotor and supplementary motor (in monkeys and humans) and precentral cortex (in rats) support the response attribute. Dorsal, dorsolateral, and mid-dorsolateral prefrontal cortex and interconnected neural substrates (in monkeys and humans) and anterior cingulate (in rats) mediate the temporal attribute. Orbital prefrontal cortex and interconnected neural substrates (in monkeys and humans) and agranular insular cortex and interconnected neural substrates (in rats) support the affect attribute.

IV. Attributes of episodic memory processing

Based upon Clayton's assertion that episodic memory processing depends on a combination of three elements or factors: "what," "where," and "when" (Clayton et al., 2001; cf. Dere et al, 2006), we propose a conceptual framework to characterize the interactions between sensory/perceptual and temporal attributes in forming behavioral episodes that are learned and recalled via an episodic or autonoetic retrieval mechanism that depends on intact hippocampal function. To study hippocampus-dependent episodic memory processing, the animal is required to process the overall configurations and relationships between sensory/perceptual stimuli and compute a coherent spatial representation that is represented by the spatial attribute. In a similar manner, it is possible that the "what" of episodic memory processing as proposed by Clayton may be the behavioral episode itself that is contained within a spatial and temporal framework (i.e., the constellation of sensory/perceptual stimuli bound together in both space and time). If this is the case, it is possible that the formation of behavioral episodes may not be hippocampal dependent per se; just the spatial processing of the experience. In that case, the "what" contains combinations of information from the sensory/perceptual, temporal, and spatial attributes.

IV.A. Interactions between attributes

IV.A.1. When: temporal
In the literature, it is becoming increasingly popular to research temporal coding in the hippocampus (cf. Rolls and Kesner, 2006). For episodic memory processing, either the hippocampus or prefrontal cortex could provide temporal tags to bind or encapsulate episodes. This binding would separate one behavioral episode from an adjacent one to facilitate efficient recall (Tulving, 1972, 2001). Both Kesner and Eichenbaum have demonstrated numerous disruptions in the

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temporal processing of sensory/perceptual stimuli and spatial information after excitotoxic hippocampal, selective dorsal CA1, and selective ventral CA1 lesions (Fortin et al., 2002; Gilbert et al., 2002; Kesner et al., 2005; Hunsaker et al., 2006; Rogers et al., 2006). This is not to suggest that only the hippocampus processes temporal information, lesion studies in both the amygdala and striatum have shown temporal gradients in deficit patterns (cf. Kesner et al., 1993; Kesner and Williams, 1995).

Temporal processing provides continuity and a linearity or sequential order to the relationships and behavioral experiences that combine to make up any behavioral episode (Tulving, 1972, 2001). Clayton and colleagues (Clayton and Dickinson, 1998, 1999; Griffiths et al., 1999; Clayton et al., 2001) named this phenomenon, "when" and declared it necessary for an experience to be considered an episode and for the memory process to be considered episodic. Also, the contribution of temporal processing cannot be escaped since everything occurs in a temporal context: before, during, or after some stimuli (cf. Howard et al., 2005; Rolls and Kesner, 2006). Reducing the relevance of the temporal contribution to task demands experimentally controls for time per se, but that does not dampen the importance of temporal contiguity or discontinuity in binding and separating behavioral episodes. Interestingly, temporal processing has been modeled to account for an array of nonepisodic processes, but it has not been widely applied to episodic memory processing (cf. Tulving, 1972, 2001; Lisman, 1999).

IV.A.2. Where: spatial

Even before O'Keefe and Nadel published *The Hippocampus as a Cognitive Map* (1978), spatial processing was recognized as highly important. Scoville and Milner described the pattern of deficits displayed by patient HM (Scoville and Milner, 1957), which included deficits in spatial information processing. Later, O'Keefe and Dostrovsky (1971) described place cells in the hippocampus of freely moving rodents. Similar cells have been characterized in primates (cf. Rolls and Kesner, 2006) and humans (Ekstrom et al., 2003). Since then, the majority of research into hippocampal function has focused on spatial information processing (cf. Poucet, 1993; Redish, 1999; Rolls and Kesner, 2006; Morris, 2007).

Space, much like time, is impossible to escape. Everything that occurs does so in a spatial context. The contribution of contextual information can be minimized, but the spatial context is implicitly encoded and integrated into every behavioral episode (cf. O'Reilly and Rudy, 2001). The spatial attribute results from computations carried out upon collections of sensory/perceptual stimuli represented by the sensory/perceptual attribute. Although there has been much debate and disagreement as to the precise nature of this calculation (Cohen and Eichenbaum, 1993; Eichenbaum and Cohen, 2001; O'Reilly and Rudy, 2001; Rolls and Kesner, 2006), the importance of the spatial attribute cannot be overestimated. With respect to episodic memory processing, the spatial attribute provides contextual or spatial tags to facilitate efficient recall of both similar and dissimilar experiences. This corresponds to the "where" information postulated by Clayton and colleagues (Clayton and Dickinson, 1998, 1999; Griffiths et al., 1999; Clayton et al., 2001). Space can be controlled for in a given task by homogenizing both local and distal environmental sensory/perceptual stimuli, or by making these sensory/perceptual stimuli irrelevant to task demands, but there is a high likelihood that a memory of the overall configuration and geometry of the environment may be used to guide or facilitate later episodic recall (cf. Cheng, 1986; Gallistel, 1990; O'Reilly and Rudy, 2001).

IV.A.3. What: sensory/perceptual

The critical nature of the sensory/perceptual stimuli is harder to define, except that it contains the data used to generate spatial representations (cf. Cohen and Eichenbaum, 1993; Eichenbaum and Cohen, 2001; O'Reilly and Rudy, 2001; Rolls and Kesner, 2006), the data used to compute sensory–response associations and compute action–outcome contingencies represented by the response attribute (O'Reilly and Frank, 2006; Yin

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and Knowlton, 2006), and the information used for computing affect (O'Reilly and Frank, 2006). However appealing this cursory analysis may seem, it is incomplete. Sensory/perceptual stimuli, via computational processes, make up space; but the same sensory/perceptual stimuli used to compute space are then free to interact independently within that computed space (cf. Cohen and Eichenbaum, 1993; Kesner, 1986, 1998, 2007; Eichenbaum and Cohen, 2001; Rolls and Kesner, 2006; Hunsaker et al., 2007). Kesner and colleagues have extended this finding in their spatial exploration paradigms involving controlled manipulations of cues within an environment (cf. Poucet, 1989, 1993; Goodrich-Hunsaker et al., 2005; Lee et al., 2005; Hunsaker et al., 2007). One can even dissect out what the component sensory/perceptual features of space are and how changes to different subsets of the total environmental sensor/perceptual stimuli can lead to different behavioral phenotypes (cf. Cheng, 1986; Gallistel, 1990; Poucet, 1993; Hunsaker et al., 2007).

IV.B. Episodic and nonepisodic interactions between what, when, and where

IV.B.1. Nonepisodic interactions

Nonepisodic (or semantic memory processing when the hippocampus is involved) tasks place impetus on learning a complex behavioral response over numerous training trials or sessions to reach an asymptotic level of performance. Examples of such tasks are Olton's reference memory task on the 8- or 17-arm radial maze (Olton et al., 1979), Initial phases of learning on the Morris water maze as it is gradually learned over 8–12 trials (Morris et al., 1982), and paired-associate learning in rats (cf. Gilbert and Kesner, 2003a).

Biconditional discrimination tasks (paired-associate learning) do not contain discrete learning and remembering phases, so no episodes can be defined beside each specific trial itself being made up of an individual behavioral episode. The summed total of the outcome of these individual episodes determines learning, so these tasks cannot be thought of as episodic. For spatial paired-associate learning, the emphasis is on learning a rule that can be later applied over repeated trials to perform correctly and consistently in order to receive a reward (e.g., when a particular spatial location (a) and a Garfield toy (1) are presented together, the animal is rewarded (a1+). If a different spatial location (b) and a truck toy are presented together (2), the animal is also rewarded (b2+). If spatial location a and the toy truck are presented together, there is no reward (a2–), similarly for spatial location b and a Garfield toy (b1–)) This can be viewed as a conjunctive or configural encoding process during which each of the four combinations (a1+, b2+, a2–, b1–) are slowly and gradually represented as individual, orthogonal units that are used to correctly perform the task (cf. O'Reilly and Rudy, 2001). No recall of a specific episode is sufficient to learn this task. Since the task cannot be learned or recalled by remembering or recalling a single or small subset of discrete behavioral episodes, it fails the test of episodic recall as defined by Tulving (1972, 2001), but it may be a form of rodent semantic memory.

IV.B.2. Episodic interactions

A clever modification of a similar biconditional discrimination task for rats that is episodic in nature was developed by Morris and colleagues (Day et al., 2003), and modified by Kesner to test spatial information processing. This task involves (in Kesner's laboratory) 50 visual objects and 48 spatial locations on a cheese board, resulting in nearly 2,500 unique pairings to avoid repetition of any given object–place pairings during the course of the experiment. During the study phase, two rewarded object–location pairings are presented to the rat sequentially (e.g., object #1 in hole #right 12 followed by object #2 in hole #left 24 after a very brief interval). The animals are then presented with either one of two retrieval cues; either one of the spatial locations used in a pairing is presented (either location #right 12 or #left 24), or one of the sensory/perceptual stimuli used in a pairing (either object #1 or object #2) depending on the experimental group. The animal is required to displace the corresponding object or a neutral block in the corresponding spatial location during the test to receive a reward (this means that if

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location #right 12 were given as a retrieval cue, the animals would displace object #1 and not object #2 to receive a reward, and that if object #2 were given as a retrieval cue, the animal would displace a neutral block in location #left 24 and not #right 12 during the test to receive a reward – see Fig. 3). Correct performance of this task requires that the rat be able to discriminate the two behavioral episodes (each pairing in this case was a distinct event) based upon the retrieval cue provided.

Effective performance on this task requires relational processing of the sensory/perceptual

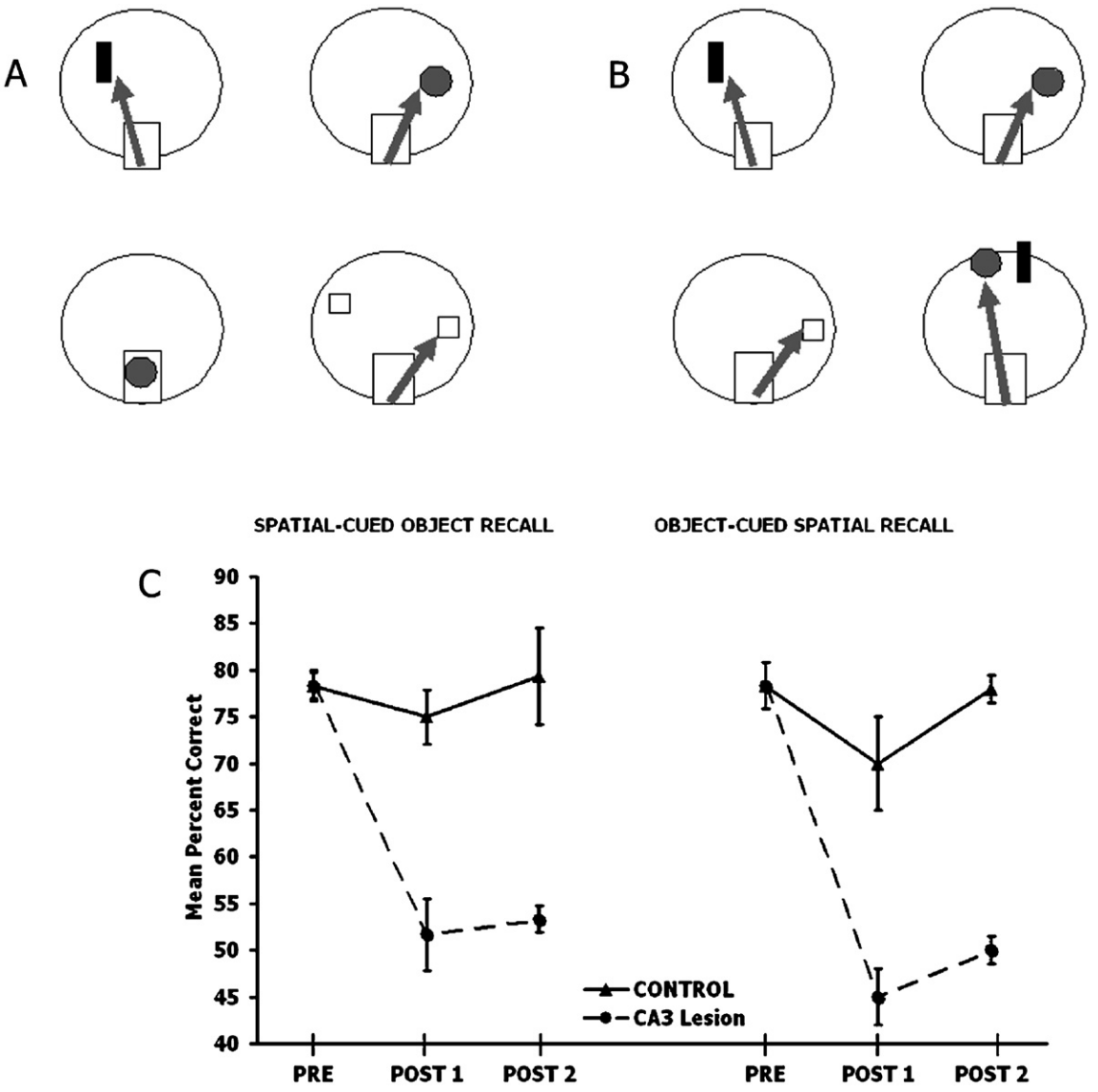

Fig. 3. Episodic paired-associate task. This is a visual/object and spatial location paired-associate task modified from Day et al. (2003) as used in Kesner's laboratory. (A) Object-cued spatial location recall paradigm. (B) Spatial location-cued visual object recall paradigm. (C) Preliminary data showing that control animals, but not animals with dorsal CA3 lesions, can efficiently perform both tasks equally well.

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stimuli present during the episode. Even though recalling a correct pairing is all that is necessary for correct performance, only a single element present during the episode is provided to cue recall of the rest of the episode. This supports assertions that animals rapidly learn relationships between sensory/perceptual stimuli and form overall spatial representations while maintaining the sensory/perceptual stimuli represented independently to guide effective and flexible recall (Cohen and Eichenbaum, 1993; Eichenbaum and Cohen, 2001; Rolls and Kesner, 2006). Animals are required to recall the specific episodes to match the retrieval cue with the corresponding portion of the episode to be rewarded, so no temporal ordering mechanism or logical reasoning could be used to solve the task via a nonepisodic mechanism (cf. Morris, 2007). The fact that the animals can be reciprocally cued with either element of the episode is also important – no single attribute is more important than any other during recall. This suggests that upon cued-recall, the animal recalls all of the sensory/perceptual stimuli present during the behavioral episode as well as the spatial relationships between those stimuli (and thus the episode itself), not just an abstract rule to guide behavior or a previously learned conjunctive representation.

IV.B.3. The nature of the interactions among attributes

The nature of the interactions between memory systems can be evaluated to dissect out the processes involved in both episodic and nonepisodic behavioral experiments. For illustration, two hippocampus-dependent tasks involving specific and easily identifiable sensory/perceptual stimuli (what), spatial information (where – computed from a combination of sensory/perceptual and temporal attributes), and temporal relationships between the stimuli (when) will be compared and contrasted. One task will require episodic memory processes and the other task can be solved via nonepisodic memory processes. The nature of the interactions between these three attributes corresponding to "what," "when," and "where" will be analyzed to differentiate between the two tasks.

The nonepisodic task requires that a pair of associations be acquired over multiple training trials. It is an object–trace–place paired-associate task involving sensory/perceptual stimuli (what), a temporal discontinuity (trace interval; when), and spatial information (where). This task is designed as follows: when a particular spatial location (a) and a Garfield toy (1) are paired across a 10 s trace interval, the animal is rewarded (a_1+). Also if a different spatial location (b) and a truck toy are matched (2), the animal is rewarded (b_2+). If spatial location (a) and the toy truck are paired, there is no reward (a_2−), similarly for spatial location (b) and (a) Garfield toy (b_1−). The trace interval separates the sensory/perceptual stimulus and the presentation of the spatial location (cf. Hunsaker et al., 2006). If the association presented during a trial were rewarded, the rat would receive a reward upon displacing a block in the correct spatial location, which is then represented by the affect attribute, signaling a correct choice. This should bind the sensory/perceptual stimulus and spatial location association across the temporal discontinuity (an association involving what, when, and where). Then, the animal is presented with a new sensory/perceptual stimulus and spatial location association. If rewarded, then the process continues as before; if not rewarded, the animal does not receive any reward, and the affect attribute signals an error. Learning this task within only the event-based memory system would be difficult because the event-based memory system is susceptible to trial-by-trial interference. Both temporally adjacent (e.g., subsequent) and spatially adjacent (e.g., occurring in the same or very similar spatial locations irrespective of temporal contiguity) episodes would interfere and degrade each other during acquisition. Learning these associations involves comparing accumulated behavioral episodes or events within the knowledge-based and rule-based memory systems to develop appropriate rules, goals, and schemas to perform the task efficiently. Also, these two latter systems generate and apply abstract rules and generalize temporal, spatial, and internal contexts. In other words, the knowledge-based and rule-based systems read the accumulated behavioral episodes, clarify the relevant contextual

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information, and apply this information to guide future actions. Once the knowledge-based and rule-based memory systems have processed the data and generated the schemas necessary to perform the task, the event-based memory system does not significantly contribute to performance of this task since the four discriminations or associations (a_1+, b_2+, a_2−, b_1−) have been efficiently encoded and only need to be discriminated from each other (O'Reilly and Rudy, 2001).

In contrast to the above biconditional discrimination, the task developed by Morris (Day et al., 2003) and modified by Kesner allows rats to perform a very similar sensory/perceptual stimulus and spatial location association in an episodic manner. During the study phase, the animal receives two rewarded object–place pairings (i.e., single sensory/perceptual stimulus in a spatial location defined by the sum total of sensory/perceptual stimuli in the environment) separated by a short temporal interval. Since there are two distinct behavioral episodes in close temporal proximity to each other, information pertaining to temporal relationships between stimuli (e.g., temporal contiguity) discriminates the two episodes and facilitates retrieval (Howard et al., 2005). During the test phase, the animal is provided with a retrieval cue. The animal has to learn that the sensory/perceptual stimulus provided as a retrieval cue is a signal to displace a neutral block in the corresponding spatial location previously paired with the cue (or to the sensory/perceptual stimulus cued by a spatial location). Since none of the 50 sensory/perceptual stimuli and 48 spatial locations are frequently paired (there are nearly 2,500 possible combinations), each pairing is trial (or behavioral episode) unique. Since the animal receives two distinct behavioral episodes followed by a retrieval cue to signal which of the two episodes needs to be recalled, the animal not only has to remember the relevant episode to receive reward, but also to discriminate between the relevant episode and the episodes presented either immediately before or after the relevant episode, as well as all previous episodes that occurred in the same or a similar spatial context (Cohen and Eichenbaum, 1993; Eichenbaum and Cohen, 2001; Howard et al., 2005; Rolls and Kesner, 2006).

The critical difference between the two tasks is not the cued-recall nature of the latter task per se, but that the associations to be remembered are trial-unique. This allows each behavioral episode to be coded as unique, but increases potential interference from previous or subsequent behavioral episodes. To overcome this interference and to guide efficient recall of the correct behavioral episode, this task is performed with the contribution of the knowledge-based and rule-based systems such as traditional biconditional discrimination tasks, but the trial-specific episodes make it necessary to depend on the event-based memory system to compare the retrieval cue to the stored episodes to efficiently recall the correct, and only the correct, behavioral episode to guide behavioral decisions and actions.

V. Tests of the attribute model of episodic memory processing

If one assumes that the hippocampus (as an example) supports processing of the spatial attribute within the framework of event-based memory, then a task that minimizes the contribution of the spatial attribute while emphasizing the contribution of other attributes (e.g., response or affect), will not likely depend upon intact hippocampal function. This is an example of the logic behind using the attribute memory model to dissociate processes underlying episodic memory processes in a given memory system from one another as well as from similar attributes processing information in other memory systems.

Episodic and episodic-like interactions between sensory/perceptual stimuli and temporal information will be described for each neural system. This will entail a description of the "what" and "where" contents that constitutes an episode. This will be followed by a description of how the other relevant types of information are computed in each brain region using combination of sensory/perceptual and temporal information (i.e., space, response, affect). This discussion will be followed by a description of similar information processed via nonepisodic memory processes in the same substrates. Fig. 4 shows the critical interactions among attributes that form episodic and episodic-like memories.

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V.A. Hippocampus dependent

V.A.1. Episodic

For hippocampus-dependent episodic memory processing, the critical interaction is between information represented by the temporal and spatial attributes. The temporal attribute is computed in the hippocampus as far as it pertains to spatial information, and has been shown to be critical for temporal ordering tasks (Chiba et al., 1994; Gilbert, Kesner and Barua, 2002; Hoge and Kesner, 2007) and for maintaining information over intermediate-length intervals (Lee and Kesner, 2003). The spatial attribute is computed from the sensory/perceptual information entering the hippocampus (cf. Cohen and Eichenbaum, 1993; O'Reilly and Rudy, 2001; Rolls and Kesner, 2006). Also, direct inputs from the medial entorhinal cortex that contain idiothetic sensory/perceptual information and inputs from the lateral entorhinal cortex that contain visual object and olfactory sensory/perceptual information have been dissociated in the hippocampus (Hunsaker et al., 2007). This means that the spatial attribute contains both "what" and the "where" components of an episode since it is made up of individual sensory/perceptual stimuli and the spatial and temporal relationships among them.

The generation of spatial representations in the hippocampus takes the following form. Sensory/perceptual stimuli (e.g., external cues) enter the hippocampus via the lateral entorhinal cortex. Sensory/perceptual stimuli concerning idiothetic information (e.g., self-motion cues required for path integration) enter the hippocampus via the medial entorhinal cortex. The dentate gyrus, due to its connectivity with the entorhinal cortex, orthogonalizes the incoming information into unique spatial representations (Rolls, 1996; Rolls and Treves, 1998; O'Reilly and Rudy, 2001; Rolls and Kesner, 2006). This information is then transmitted to CA3 via the mossy fiber projection. In CA3, the spatial representations from the DG are compared and associated with sensory/perceptual stimuli from the medial and lateral entorhinal cortex that project directly into CA3 via the direct perforant path. Due to this connectivity, associations can be made between the sensory/perceptual

EPISODIC MEMORY	
Interactions among attributes	Anatomical Substrate
Temporal (when) + Sensory/Perceptual (what) + Spatial (generated from sensory/perceptual) (what/where)	Hippocampus
Temporal (when) + Sensory/Perceptual (what) + Affect (generated from sensory/perceptual) (what)	Amygdala
Temporal (when) + Sensory/Perceptual (what) + Response (generated from sensory/perceptual) (what)	Caudate
Temporal (when) + Sensory/Perceptual (what) + Sensory/Perceptual (what)	Perirhinal Cortex

Fig. 4. Critical interactions among attributes for episodic memory. Many neurological substrates can mediate episodic memory processes. Notice that temporal and sensory/perceptual attributes are involved in all processes, even when the sensory/perceptual attribute is used in computing the other attributes.

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stimuli that make up space and space itself in CA3 (cf. Rolls and Kesner, 2006; Hunsaker et al., 2007). This mediates paired-associate learning when spatial locations are involved (Gilbert and Kesner, 2003a). These associations are then sent to CA1 via the Schaffer collateral projections to be compared and further associated with direct inputs from the medial and lateral entorhinal cortices, and then temporally processed and sequenced to assist in efficient consolidation and facilitate late recall (Rolls, 1996; Rolls and Treves, 1998; Rolls and Kesner, 2006; cf. Hunsaker et al., 2007).

The cued recall paired-associate tasks developed by Morris (Day et al., 2003) and extended by Kesner appear to require episodic memory processing since each trial contains two behavioral episodes whose elements must be dissociated in subsequent retrieval tests following the presentation of a retrieval cue. In both Kesner's and Morris' variants, the sensory/perceptual stimulus and spatial location information interact with the temporal and affect attributes. These attributes interact within the knowledge-, rule-, and event-based memory systems since each pair of behavioral episodes is trial-unique and the retrieval cue guides recall of a specific episode.

Temporal ordering tasks have been proposed to be episodic in nature since they involve recalling and discriminating similar and dissimilar episodes and to show a preference for one over the other via selective reexploration. During sensory/perceptual stimulus temporal ordering, the sensory/perceptual attribute interacts with the temporal attribute in the event-, knowledge-, and rule-based memory systems. For temporal order for spatial locations, the spatial attribute interacts with the temporal attribute within the event-, knowledge-, and rule-based memory systems. Since space is generated in the hippocampus by computations based on the relationships among sensory/perceptual, the "what" of spatial tasks is contained within the spatial component (or the "where").

Chiba et al. (2002) ran a continuous and differential reinforcement task involving spatial location memory in rats. Optimal performance on the differential reinforcement task required that a rat recognize and avoid locations previously visited within a session, and thus they need to learn the rule that an arm is reinforced only once per session. In this case, rats should demonstrate slower response times for the repeated items. In this sense, the spatial, temporal, and sensory/perceptual (contained within the spatial) attributes interact within the event-, knowledge-, and rule-based memory systems. They found that hippocampal lesions disrupted the learning of the differential reinforcement condition, which has been described as episodic.

Delay contextual and auditory trace fear conditioning has been shown to be hippocampal dependent (Phillips and LeDoux, 1992; Lee and Kesner, 2004). During contextual fear conditioning, the spatial, affect, temporal, and sensory/perceptual attributes interact in the event-, knowledge-, and rule-based memory systems. During auditory trace fear conditioning the temporal attribute is emphasized by separating the sensory/perceptual stimuli from the affect attribute in time, the spatial attribute remains omnipresent. These tasks are episodic since they are learned rapidly and recall of the entire episode is necessary to recall and display appropriate conditioned fear to the individual sensory/perceptual, temporal, and spatial elements when each is presented in isolation (Phillips and LeDoux, 1992; Lee and Kesner, 2004; Rogers et al., 2006).

V.A.2. Nonepisodic

The hippocampus has been long implicated in spatial paired-associate learning of all forms (Gilbert and Kesner, 2003a). In these tasks, a pair of associations is made over literally hundreds of individual trials or behavioral episodes. The sensory/perceptual, affect, and spatial attributes interact within the knowledge- and rule-based memory systems and cannot be tested for recall per se, just acquisition to an asymptotic level. Recall of any given trial or behavioral episode is insufficient to efficiently perform this task, so an episodic recall mechanism is not involved. Although this task is nonepisodic, it does depend on intact hippocampal function. This task could be a model for semantic memory processing as evident in rats as they are required to learn rules

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and associations devoid of any specific learning episode.

Perhaps adding a more quantifiable temporal component would make these associations episodic. A trace interval added between two sensory/perceptual stimuli to be associated during a paired-associate task forms a temporal discontinuity that must be crossed. In an object–trace–odor task (Kesner et al., 2005), the sensory/perceptual attribute interacts with the temporal and affect attributes. This, however, still requires hundreds of trials to learn and the relevant interactions are within and among the knowledge- and rule-based memory systems. The same applies to an object–trace–place task. When the sensory/perceptual stimulus and spatial location are separated during an object–trace–place task (Hunsaker et al., 2006), the sensory/perceptual, spatial, temporal, and affect attributes interact within the knowledge and rule-based memory systems over hundreds of trials of acquisition. Recall of any single trial or episode is insufficient to perform adequately on this task, so an episodic recall mechanism is not involved (Tulving, 1972, 2001).

V.B. Amygdala dependent

V.B.1. Episodic

During amygdala-dependent episodic memory processing, the temporal attribute and the affect attribute interact. It has been shown that amygdala lesions result in delay-dependent deficits in tasks measuring magnitude of reinforcement (i.e., performance declines as a function of increased delay length; cf. Kesner and Williams, 1995). This suggests the amygdala receives temporal information that can be used to generate or compute the affect attribute. The affect attribute is made up of sensory/perceptual stimuli and the internal context provided by the reward system (also a sensory/perceptual stimulus). The amygdala uses these cues to compute affect (O'Reilly and Frank, 2006). In this sense, much like space, affect is computed or generated from sensory/perceptual stimuli and encapsulates the "what" component of the episodic memory processing.

Delay contextual and auditory trace fear conditioning has been shown to be amygdala dependent (Phillips and LeDoux, 1992; Churchwell and Kesner, unpublished observations). During these tasks, the spatial, affect, and sensory/perceptual attributes interact in the event-, knowledge-, and knowledge-based memory systems. During auditory trace fear conditioning, separating the sensory/perceptual stimuli from the affect attribute in time emphasizes the temporal attribute. Any aversive conditioning task that is learned rapidly can be viewed this way since it will have similar properties.

Additionally, a task requiring an animal to learn a trial-unique object association appears episodic in nature (Kesner and Williams, 1995). During the study phase, an animal receives an object–reward pairing consisting of a low reward (25% sucrose) or a high reward (50% sucrose). During the test phase, the animal receives one of two objects paired with reward. Half of the animals had learned to knock over the object for a reward if the object was paired with the low reward previously and half if the object were paired with the high reward. Since the object–reward associations were trial-unique and the sensory/perceptual stimulus had to be displaced to discover the reward (the reward was not available except as a memory trace at the time the sensory/perceptual stimulus was presented), the animal had to remember and discriminate between object–reward behavioral episodes to perform this task. This means the sensory/perceptual and affect attributes interact with the temporal attribute within the event-, knowledge-, and rule-based memory systems. Intact amygdala function, but not the hippocampus, was required for efficient performance of this task.

V.B.2. Nonepisodic

It must be noted that the amygdala provides information concerning or pertaining to affect during a large number of tasks and interacts during episodic tasks in which a reward is provided for correct responses. An example of this has been demonstrated during conditioned cue preference or conditioned place preference tasks (McDonald and White, 1993). The provision of an internal

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context is important during rewarded learning and memory tasks. In this sense, what may appear to be an episodic memory deficit may be due to the absence of affect during learning or an inability to recall reward contingencies during retrieval. The attenuation of affect would cause every experience to be encoded with equivalent saliency, which would lead to uncontrolled interference during recall since none of the experiences would be more important than any other for the animal.

A simple biconditional discrimination task involving an odor and a reward is a nonepisodic task dependent upon the amygdala (Wood et al., 2004). These tasks are nonepisodic for the same reasons that similarly designed spatial paired-associate learning tasks are nonepisodic; recall of any given episode cannot guide performance, only forming a conjunctive representation of the association and discriminating that representation from others will guide correct performance on this task. During this task, the affect and sensory/perceptual attribute interact within the knowledge- and rule-based memory systems since the associations have been well-learned and recall of a single episode does not guide efficient recall.

V.C. Caudate dependent

V.C.1. Episodic

In caudate-dependent episodic memory processing, the temporal attribute interacts with the response attribute. It has been shown that the caudate mediates sequential learning when the sequence is made up of body movements (DeCoteau and Kesner, 2000). This sequence learning is mediated by the temporal attribute, which is present in the caudate during response learning. The response attribute is made up of a collection of sensory/perceptual stimuli in the environment, proprioceptive feedback, and the computation of sensory–response associations and action–outcome contingencies. In this sense, much like space and affect, response is computed from sensory/perceptual stimuli and encapsulates the "what" component of the episode. Also, temporal contiguity and sequential order of the movements are encoded by the caudate, suggesting the temporal attribute is present in the caudate during behavioral experience.

An egocentric memory task developed by Kesner et al. (1993) involves episodic memory processing. Animals were required to turn right or left into an adjacent door in a box with six doors, three on each side. After a 15 or 30 s delay, the animals were then moved to the other side of the apparatus and tested on recall of the behavioral episode. Animals with caudate lesions, but not hippocampus lesions, showed deficits for processing this response. In this task, the sensory/perceptual stimuli (i.e., proprioceptive and vestibular feedback) was computed on the caudate into response information (in this case, egocentric information), which was trial-unique and bound temporal contiguity. Interactions between these attributes were within the event-based, knowledge-based, and rule-based memory systems.

V.C.2. Nonepisodic

A nonepisodic caudate-dependent task is presented by McDonald and White (1993). The conditioned cue preference task was learned over a large number of trials and could not be learned or recalled via an episodic mechanism. In the conditioned cue preference task, the response attribute, temporal attribute, and the sensory/perceptual attribute interact within the knowledge- and rule-based memory systems.

Also, reversal learning on a plus maze is nonepisodic in nature since it involves inhibiting a previously learned rule and the adoption of a new rule over repeated trials (Palencia and Ragozzino, 2005). During reversal learning, the response attribute interacts with the sensory/perceptual attribute in the knowledge-based and rule-based memory systems. In fact, during reversal learning recall of past episodes involving the old rule would impede new learning and result in perseveration.

V.D. Perirhinal cortex

V.D.1. Episodic

In perirhinal-cortex-dependent episodic memory, the temporal attribute interacts with the

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sensory/perceptual attribute directly (e.g., the sensory/perceptual attribute per se interacts, not subsequent neural representation based on computations carried out on the sensory/perceptual stimuli). This involvement has been shown in temporal ordering tasks (Hannesson et al., 2004).

Temporal order tasks have been proposed to be episodic in nature since they involve remembering discrete events or behavioral episodes and to show a preference for either one behavioral episode or the other. In the context of the attribute model, for sensory/perceptual temporal ordering (i.e., visual objects or odors), the sensory/perceptual attribute interacts with the temporal attribute. The preference test simply requires the rat to differentiate between the two behavioral episodes and to display a preference for one over another via selective reexploration. This has been shown to be perirhinal-cortex dependent.

It is also possible to observe episodic memory in cases where there is an interaction between the sensory/perceptual attribute and the temporal attribute. Kesner et al. (2001) ran animals on a continuous discrimination task for visual object information that depends on an intact perirhinal cortex. The animals had to remember objects they had seen to discriminate them from those never encountered, as well as to determine if a repetition was rewarded or not. This task was not sensitive to hippocampal damage (Jackson-Smith et al., 1993), medial entorhinal cortex damage, or lateral entorhinal cortex damage (Kesner et al., 2001), suggesting that the perirhinal cortex was the critical substrate, and not a downstream target. During this task, the sensory/perceptual attribute and the temporal attribute interact within the event-, knowledge-, and rule-based memory systems.

V.D.2. Nonepisodic

A nonepisodic visual discrimination task was performed by Gilbert and Kesner (2003b) in which a configuration of visual objects was presented to the animal on the study phase. If during the test phase the objects were identical to the study phase, the animal was rewarded. If there were any differences, then the animal was not rewarded. Although they found a pattern separation effect (e.g., animals reacted differently depending upon whether 1, 2, 3, or all 4 objects were changed), the task was nonepisodic in nature. In this task, the sensory/perceptual and temporal attributes interact within the knowledge-based and rule-based memory systems.

Additional nonepisodic tasks that depend on intact perirhinal function are the tasks performed by Bertko et al. (2007). They rewarded rats for successfully discriminating between stimuli that had varying levels of perceptual similarity. In this case, animals had to differentiate between an object they had just seen and a distracter that was either very different or very similar to the one they had just experienced. They experimentally minimized the role of mnemonic process other than spontaneous recognition. They found that the perirhinal cortex, but not the postrhinal cortex, was important for disambiguating very similar objects. They report that although the perirhinal cortex is involved, it is not critical for the same task when the study and test objects were very perceptually dissimilar. Winters and Bussey (2005) have also demonstrated that the perirhinal cortex is involved in all stages of memory processing for sensory/perceptual information for visual stimuli, even when processed nonepisodically.

VI. Conclusions

The attribute model of memory processing is not new, but its extension to provide a method to evaluate episodic memory processes is novel. Breaking episodic memory processes down into attributes provides not only a descriptive tool, but also a novel theoretical viewpoint that focuses on dissociating the individual elements of any given behavioral episode to better understand how the memory is processed (cf. Kesner, 1986, 1998, 2007).

In this chapter, we have ventured to provide a novel, alternative perspective for viewing episodic memory. In short, we have described a methodology for breaking down episodes into their basic components and evaluating the nature of how each of these components interacts with other

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components to form episodes. This chapter was not intended to dissolve or attenuate the discussion about episodic memory research itself, but to provide a novel perspective on the issue from a finer scale of behavioral analysis.

We have shown that, although the hippocampus may be highly important for episodic memory, it is not the only neural substrate that can mediate dynamic memory processing that is referred in this chapter as episodic and episodic-like memory processing. The nature and demands of the task may determine which mechanism proves most effective for subsequent recall of a given behavioral episode. Any dysfunction within a distinct memory system that processes a given set of attributes, that combine to form a behavioral episode, may disrupt episodic memory processing similarly to hippocampal dysfunction.

We have suggested and provided evidence that extrahippocampal structures may mediate episodic-like memory processes, just not those emphasizing the spatiotemporal context of an episode. The critical determinant of episodic memory is the interaction between the sensory/perceptual attribute and the temporal attribute. For hippocampus-dependent episodic memory processing, the sensory/perceptual stimuli are used by the hippocampus to generate spatial representations that are used to bind episodes within distinct spatial contexts. Episodic memory is also hippocampus dependent when there is a requirement that sensory/perceptual stimuli be processed temporally into a discrete sequence or codes, such as temporal ordering tasks (cf. Dere et al., 2006). Alternatively, the hippocampus mediates a number of nonepisodic (or semantic) memory processes, most notably paired-associate learning and reference memory task performance.

In the caudate, the sensory/perceptual stimuli and temporal relationships among them are used to process and compute action–outcome and sensory–response contingencies that constitute the response attribute. In the amygdala, the sensory/perceptual stimuli are combined and evaluated with internal reward-value information (also sensory/perceptual stimuli) to generate the affect attribute. Within the perirhinal cortex, temporal ordering of sensory/perceptual stimuli is calculated and used to guide behaviors. Both the response and affect attribute interact with the temporal attribute and the sensory/perceptual attribute to form episodic-like memories, whenever the learning process depends on an episodic-like mechanism.

Acknowledgments

The research from the lab of RPK that appears in this chapter was supported by NSF Grant IBN-0135273 and NIH Grant R01MH065314.

References

Aggleton, J.P. and Brown, M.W. (1999) Episodic memory, amnesia, and the hippocampal-anterior thalamic axis. Behav. Brain Sci., 22: 425–489.

Aggleton, J.P. and Brown, M.W. (2007) Interleaving brain systems for episodic and recognition memory. Trends Cogn. Sci., 10: 455–463.

Aggleton, J.P., McMackin, D., Carpenter, K., Hornak, J., Kapur, N., Halpin, S., Wiles, C.M., Kamel, H., Brennan, P. and Gaffan, D. (2000) Differential effects of colloid cysts in the third ventricle that spare of compromise the fornix. Brain, 123: 800–815.

Aggleton, J.P. and Pearce, J.M. (2001) Neural Systems underlying episodic memory: insights from animal research. In: Baddeley, A. Aggleton, J.P. and Conway, M.A. (Eds.), Episodic Memory: New Directions in Research. Oxford University Press, Oxford, pp. 204–231.

Amaral, D.G. and Witter, M.P. (1989) The three-dimensional organization of the hippocampal formation: a review of anatomical data. Neuroscience, 31: 571–591.

Baddeley, A., Aggleton, J.P. and Conway, M.A. (2001) Episodic Memory: New Directions in Research. Oxford University Press, Oxford.

Ben Shalom, D. (2003) Memory in autism: review and synthesis. Cortex, 39: 1129–1138.

Bertko, S.J., Winters, B.D., Cowell, R.A., Sakisida, L.M. and Bussey, T.J. (2007) Perceptual functions of perirhinal cortex in rats: zero-delay and simultaneous oddity discriminations. J. Neurosci., 27: 2548–2559.

Cheng, K. (1986) A purely geometric module in the rat's spatial representation. Cognition, 23: 149–178.

Chiba, A.A., Kesner, R.P. and Jackson, P.A. (2002) Two forms of spatial memory: a double dissociation between the parietal cortex and the hippocampus in the rat. Behav. Neurosci., 116: 874–883.

Author's personal copy

Chiba, A.A., Kesner, R.P. and Reynolds, A.M. (1994) Memory for spatial location as a function of temporal lag in rats: role of hippocampus and medial prefrontal cortex. Behav. Neural Biol., 61: 123–131.

Clayton, N.S. and Dickinson, A. (1998) What, where, and when: episodic-like memory during cache recovery by scrub jays. Nature, 395: 274–284.

Clayton, N.S. and Dickinson, A. (1999) Scrub jays (*Aphelocoma coerulescens*) remember when as well as where and what food items they cached. J. Comp. Psychol., 113: 403–416.

Clayton, N.S., Griffiths, D.P., Emery, N.J. and Dickinson, A. (2001) Elements of episodic-like memory in animals. In: Baddeley, A. Aggleton, J.P. and Conway, M.A. (Eds.), Episodic Memory: New Directions in Research. Oxford University Press, Oxford, pp. 232–248.

Cohen, N.J. and Eichenbaum, H. (1993) Memory, Amnesia, and the Hippocampal System. MIT Press, Cambridge.

Cordes, S., King, A.P. and Gallistel, C.R. (2007) Time left in the mouse. Behav. Process, 74: 142–151.

Day, M., Langston, R. and Morris, R.G.M. (2003) Glutamate-receptor-mediated encoding and retrieval of paired-associate learning. Nature, 424: 205–209.

DeCoteau, W.E. and Kesner, R.P. (2000) A double dissociation between the rat hippocampus and medial caudoputamen in processing two forms of knowledge. Behav. Neurosci., 114: 1096–1108.

Dere, E., Kart-Teke, E., Huston, J.P. and De Souza Silva, M.A. (2006) The case for episodic memory in animals. Neurosci. Biobehav. Rev., 30: 1206–1224.

Eichenbaum, H. and Cohen, N.J. (2001) From Conditioning to Conscious Recollection: Memory Systems of the Brain. Oxford University Press, Oxford.

Fortin, N.J., Agster, K.L. and Eichenbaum, H.B. (2002) Critical role of the hippocampus in memory for sequences of events. Nat. Neurosci., 5: 468–562.

Gaffan, D. (1994) Scene-specific memory for objects: a model of episodic memory impairment in monkeys with fornix transection. J. Cogn. Neurosci., 6: 305–320.

Gaffan, D. and Gaffan, E.A. (1991) Amnesia in man following transection of the fornix. Brain, 114: 2611–2618.

Gaffan, E.A., Gaffan, D. and Hodges, J.R. (1991) Amnesia following damage to the left fornix and to other sites. Brain, 114: 1297–1313.

Gallistel, C.R. (1990) The Organization of Learning. MIT Press, Cambridge.

Gilbert, P.E. and Kesner, R.P. (2003a) Memory for objects and their locations: the role of the hippocampus in retention of object-place associations. Neurobiol. Learn. Mem., 81: 39–45.

Gilbert, P.E. and Kesner, R.P. (2003b) Recognition memory for complex visual discriminations is influenced by stimulus interference in rodents with perirhinal cortex damage. Learn Mem., 10: 525–530.

Gilbert, P.E., Kesner, R.P. and Barua, L.A. (2002) The role of the hippocampus in memory for the temporal order of a sequence of odors. Behav. Neurosci., 116: 286–290.

Goodrich-Hunsaker, N.J., Hunsaker, M.R. and Kesner, R.P. (2005) Dissociating the role of the parietal cortex and dorsal hippocampus for spatial information processing. Behav. Neurosci., 119: 1307–1375.

Griffiths, D., Dickinson, A. and Clayton, N. (1999) Episodic memory: what can animals remember about their past? Trends Cogn. Sci., 3: 74–80.

Ekstrom, A.D., Kahana, M.J., Caplan, J.B., Fields, T.A., Isham, E.A., Newman, E.L. and Fried, I. (2003) Cellular networks underlying human spatial navigation. Nature, 425: 184–188.

Hannesson, D.K., Howland, J.G. and Phillips, A.G. (2004) Interaction between perirhinal and medial prefrontal cortex is required for temporal order but not recognition memory for objects in rats. J. Neurosci., 24: 4596–4604.

Hoge, J.S. and Kesner, R.P. (2007) Role of CA3 and CA1 subregions of the dorsal hippocampus on temporal processing of objects. Neurobiol. Learn. Mem., 88: 225–231.

Howard, M.W., Fotedar, M.S., Datey, A.V. and Hasselmo, M.E. (2005) The temporal context model in spatial navigation and relational learning: toward a common explanation of medial temporal lobe function across domains. Psych. Rev., 112: 75–116.

Hunsaker, M.R., Mooy, G.G., Swift, J.S. and Kesner, R.P. (2007) Dissociations of the medial and lateral perforant path projections into dorsal DG, CA3, and CA1 for spatial and nonspatial (visual object) information processing. Behav. Neurosci., 121: 742–750.

Hunsaker, M.R., Thorup, J.A., Welch, T. and Kesner, R.P. (2006) The role of CA3 and CA1 in the acquisition of an object-trace-place paired associate task. Behav. Neurosci., 120: 1252–1256.

Jackson-Smith, P., Kesner, R.P. and Chiba, A.A. (1993) Continuous recognition of spatial and nonspatial stimuli in hippocampal-lesioned rats. Behav. Neural Biol., 59: 107–119.

Kesner, R.P. (1986) Biological views of memory. In: Martinez, J.L. Jr., and Kesner, R.P. (Eds.), Learning and Memory: A Biological View. 2nd edn. Academic Press, San Diego, pp. 499–547.

Kesner, R.P. (1998) Neurobiological views of memory. In: Martinez, J.L. Jr., and Kesner, R.P. (Eds.), Neurobiology of Learning and Memory. 1 edn. Academic Press, San Diego, pp. 361–416.

Kesner, R.P. (2007). Neurobiological views of memory. In: Kesner, R.P. and Martinez Jr., J.L. (Eds.), Neurobiology of Learning and Memory, 2 edn. Elsevier, Amsterdam, pp. 361–405.

Kesner, R.P., Bolland, B.L. and Dakis, M. (1993) Memory for spatial locations, motor responses, and

Author's personal copy

objects: triple dissociation among the hippocampus, caudate nucleus, and extrastriate visual cortex. Exp. Brain Res., 93: 462–470.
Kesner, R.P., Hunsaker, M.R. and Gilbert, P.E. (2005) The role of CA1 in the acquisition of an object-trace-odor paired associate task. Behav. Neurosci., 119: 1140–1143.
Kesner, R.P., Ravindranathan, A., Jackson, P., Giles, R. and Chiba, A.A. (2001) A neural circuit analysis of visual recognition memory: role of perirhinal, medial, and lateral entorhinal cortex. Learn. Mem., 8: 87–95.
Kesner, R.P. and Williams, J.M. (1995) Memory for magnitude of reinforcement: dissociation between the amygdala and hippocampus. Neurobiol. Learn. Mem., 64: 237–244.
Kirwan, C.B., Jones, C.K., Millar, M.I. and Stara, C.E. (2007) High-resolution fMRI investigation of the medial temporal lobe. Hum. Brain Map., 28: 625–633.
Lee, I., Hunsaker, M.R. and Kesner, R.P. (2005) The role of hippocampal subregions in detecting spatial novelty. Behav. Neurosci., 119: 145–153.
Lee, I. and Kesner, R.P. (2003) Differential roles of dorsal hippocampal subregions in spatial working memory with short versus intermediate delay. Behav. Neurosci., 117: 1044–1053.
Lee, I. and Kesner, R.P. (2004) Differential contribution of dorsal hippocampal subregions to memory acquisition and retrieval in contextual fear conditioning. Hippocampus, 14: 301–310.
Lisman, J.E. (1999) Relating hippocampal circuitry to function: recall of memory sequences by reciprocal dentate-CA3 interactions. Neuron, 22: 233–242.
McDonald, R.J. and White, N.M. (1993) A triple dissociation of systems: hippocampus, amygdala, and dorsal striatum. Behav. Neurosci., 107: 3–22.
Mishkin, M., Vargha-Khadem, F. and Gadian, D.G. (1998) Amnesia and the organization of the hippocampal system. Hippocampus, 8: 212–216.
Morris, R.G.M. (2001) Episodic-like memory in animals: psychological criteria, neural mechanisms and the value of episodic-like tasks to investigate animal models of neurodegenerative disease. In: Baddeley, A. Aggleton, J.P. and Conway, M.A. (Eds.), Episodic Memory: New Directions in Research. Oxford University Press, Oxford, pp. 181–203.
Morris, R.G.M. (2007) Theories of hippocampal function. In: Andersen, P. Morris, R.G.M. Amaral, D. Bliss, T. and O'Keefe, J. (Eds.), The Hippocampus Book. Oxford University Press, Oxford, pp. 581–713.
Morris, R.G.M., Garrud, P., Rawlins, J.N.P. and O'Keefe, J. (1982) Place navigation impaired in rats with hippocampal lesions. Nature, 297: 681–683.
Nadel, L. and Moscovitch, M. (1997) Memory consolidation, retrograde amnesia, and the hippocampal complex. Curr. Opin. Neurobiol., 7: 217–227.
Nyberg, L., McIntosh, A.R., Cabeza, R., Habib, R., Houle, S. and Tulving, E. (1996) General and specific brain regions involved in encoding and retrieval of events: what, where, and when. PNAS, 93: 11280–11285.
O'Keefe, J. and Dostrovsky, J. (1971) The hippocampus as a spatial map: preliminary evidence from unit activity in the freely moving rat. Brain Res., 34: 171–175.
O'Keefe, J. and Nadel, L. (1978) The Hippocampus as a Cognitive Map. Clarendon Press, Oxford.
Olton, D.S., Becker, J.T. and Handelmann, G.E. (1979) Hippocampus, space, and memory. Brain. Behav. Sci., 2: 313–365.
O'Reilly, R.C. and Frank, M.J. (2006) Making working memory work: a computational model of learning in the prefrontal cortex and basal ganglia. Neural Comput., 18: 283–328.
O'Reilly, R.C. and Rudy, J.W. (2001) Conjunctive representations in learning and memory: principles of cortical and hippocampal function. Psych. Rev., 108: 311–345.
Palencia, C.A. and Ragozzino, M.E. (2005) The contribution of NMDA receptors in the dorsomedial striatum to egocentric response learning. Behav. Neurosci., 119: 953–960.
Papez, J.W. (1937) A proposed mechanism of emotion. Arch. Neurol. Psychiatry, 38: 725–743.
Phillips, R.G. and LeDoux, J.E. (1992) Differential contribution of amygdala and hippocampus to cued and contextual fear conditioning. Behav. Neurosci., 106: 274–285.
Poucet, B. (1989) Object exploration, habituation, and response to a spatial change in rats. Behav. Neurosci., 103: 1009–1016.
Poucet, B. (1993) Spatial cognitive maps in animals: new hypothesis on their structure and neural mechanisms. Psych. Rev., 100: 163–182.
Redish, A.D. (1999) Beyond the Cognitive Map: From Place Cells to Episodic Memory. MIT Press, Cambridge.
Rogers, J.L., Hunsaker, M.R. and Kesner, R.P. (2006) Effects of ventral and dorsal CA1 subregional lesions on trace fear conditioning. Neurobiol. Learn Mem., 86: 72–81.
Rolls, E.T. (1996) A theory of hippocampal function in memory. Hippocampus, 6: 601–620.
Rolls, E.T. and Kesner, R.P. (2006) A computational theory of hippocampal function, and empirical tests of the theory. Prog. Neurobiol., 79: 1–48.
Rolls, E.T. and Treves, A. (1998) Neural Networks and Brain Function. Oxford University Press, Oxford.
Schacter, D.L. and Wagner, A.D. (1999) Medial temporal lobe activations in fMRI and PET studies of episodic encoding and retrieval. Hippocampus, 9: 7–24.
Scoville, W.B. and Milner, B. (1957) Loss of recent memory after bilateral hippocampal lesions. J. Neurol. Neurosurg. Psych., 20: 11–21.

Author's personal copy

Squire, L.R. (1992) Memory and the hippocampus: a synthesis from findings with rats, monkeys, and humans. Psych. Rev., 99: 135–231.

Squire, L.R., Shrager, Y. and Levy, D.A. (2006) Lack of evidence for a role of medial temporal lobe structures in visual perception. Learn Mem., 13: 106–107.

Squire, L.R. and Zola, S.M. (1998) Episodic memory, semantic memory, and amnesia. Hippocampus, 8: 205–211.

Sziklas, V. and Petrides, M. (1993) Memory impairments following lesions to the mammillary region of the rat. Eur. J. Neurosci., 5: 525–540.

Sziklas, V. and Petrides, M. (1998) Memory and the region of the mammillary bodies. Prog. Neurobiol., 54: 55–70.

Tolman, E.C. (1948) Cognitive maps in mice and men. Psych. Rev., 45: 1–41.

Tulving, E. (1972) Episodic and semantic memory. In: Tulving, E. and Donaldson, W. (Eds.), Organisation of Memory. Academic Press, New York, pp. 381–403.

Tulving, E. (2001) Episodic memory and common sense: how far apart? Philos. Trans. R. Soc. Lond. B, 356: 1505–1515.

Tulving, E. and Markowitsch, H.J. (1998) Episodic and declarative memory: role of the hippocampus. Hippocampus, 8: 198–204.

Vann, S.D. and Aggleton, J.P. (2004) The mammillary bodies: two memory systems in one? Nat. Rev. Neurosci., 5: 35–44.

Vargha-Khadem, F., Gadian, D.G., Watkins, K.E., Connelly, A., Van Paesschen, W. and Mishkin, M. (1997) Differential effects of early hippocampal pathology in episodic and semantic memory. Science, 277: 376–380.

Winters, B.D. and Bussey, T.J. (2005) Glutamate receptors in perirhinal cortex mediate encoding, retrieval, and consolidation of object recognition memory. J. Neurosci., 25: 4243–4251.

Wood, E.R., Agster, K.M. and Eichenbaum, H. (2004) One-trial odor-reward association: a form of event memory not dependent on hippocampal functions. Behav. Neurosci., 118: 526–539.

Yin, H.H. and Knowlton, B.J. (2006) The role of the basal ganglia in habit formation. Nat. Neurosci., 7: 464–476.