Review

# Elements of episodic-like memory in animal models

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## ABSTRACT

Representations of unique events from one's past constitute the content of episodic memories. A number of studies with non-human animals have revealed that animals remember specific episodes from their past (referred to as episodic-like memory). The development of animal models of memory holds enormous potential for gaining insight into the biological bases of human memory. Specifically, given the extensive knowledge of the rodent brain, the development of rodent models of episodic memory would open new opportunities to explore the neuroanatomical, neurochemical, neurophysiological, and molecular mechanisms of memory. Development of such animal models holds enormous potential for studying functional changes in episodic memory in animal models of Alzheimer's disease, amnesia, and other human memory pathologies. This article reviews several approaches that have been used to assess episodic-like memory in animals. The approaches reviewed include the discrimination of what, where, and when in a radial arm maze, dissociation of recollection and familiarity, object recognition, binding, unexpected questions, and anticipation of a reproductive state. The diversity of approaches may promote the development of converging lines of evidence on the difficult problem of assessing episodic-like memory in animals.

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## Contents

## 1. Introduction

Shettleworth (1998) emphasized the important role that convergent lines of evidence play in the assessment of psychological processes in animals. Any single approach is likely to be limited by a set of competing, alternative explanations. However, a careful selection of multiple approaches is desirable to overcome weaknesses that may exist if each approach were treated separately. The focus of the current review is the development of a rodent model of episodic-like memory and a comparative analysis with other species; the development of such a model holds enormous potential for gaining insight into the neurobiology of human memory and disorders of memory. Multiple approaches have been adopted,

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largely by different groups of researchers, to begin the development of animal models of episodic-like memory. Although the variety of approaches stems from a lack of agreement on what constitutes evidence for episodic-like memory in non-human animals, the diversity of approaches may promote the development of convergent lines of evidence, consistent with Shettleworth's approach.

### 1.1. Episodic memory in people

A critical feature of human memory consists of records of unique events from one's own personal, past experience. Students of human cognition distinguish between episodic and semantic memory. Episodic memory stores representations of one's own personal past, experience. By contrast, semantic memory stores facts about the world. Episodic memory may be defined in terms of its content and the subjective experiences that accompany it. The content of episodic memory is information about what, where, and when a specific event occurred. The subjective experiences that accompany episodic retrieval are described as a conscious recollection or experience of the event occurring (Tulving, 1983, 1985, 2001, 2005). Thus, investigations of human memory exploit behavioral and subjective sources of information. The later source comes from self-reports about the experiences that accompany memory in people. Although subjective experience is a rich source of information for generating hypotheses about human memory, the focus on subjective experiences represents an intractable barrier to the development of animal models of human cognition because phenomenology cannot be evaluated in non-verbal animals. Consequently, Clayton et al. (2003a) developed behavioral criteria for studying episodic memory that focus on Tulving (1972) classic definition of episodic memory: *what* occurred, *where* did it take place, and *when* did it transpire. This conceptualization is significant because it can be evaluated in non-human animals (henceforth animals). The focus is on the content of memory – knowledge of what, where, and when a unique event occurred. Clayton and Dickinson (1998) introduced the term *episodic-like memory* to emphasize that behavioral criteria do not assess subjective experiences.

### 1.2. Clayton and Dickinson's episodic-like memory in scrub jays

Clayton and Dickinson (1998) classic experiment has opened a new area of comparative research by providing the first evidence of what-where-when memory in non-humans. Food-storing scrub jays cached either peanuts followed by wax worms or, on other trials, worms followed by peanuts; they retrieved the caches after a short or long retention interval (RI). For some birds, the worms were decayed after the long retention interval, and for other birds they were replenished with fresh worms (peanuts did not decay and worms were always fresh after the short retention interval). The birds learned to prefer the worm rather than peanut cache sites when the worms were fresh, but reversed this preference when the worms were decayed. These data suggest that the jays are sensitive to what (food type), where (location in the tray), and when (time of caching and recovery). Since this initial demonstration, Clayton and Dickinson (1998, 1999a,b,c), Clayton et al. (2001, 2003b), de Kort et al. (2005) have demonstrated that scrub jays have a detailed representation of what, where, and when food was cached. For example, decreasing the expected value of the to-be-recovered food item (e.g., degrading or satiating that food type) or increasing the expected value (e.g., ripening it) have been used to demonstrate the discrimination of what, where, and when. Recently, another food storing bird, magpies, has been shown to have what-where-when memories for food caches (Zinkivskay et al., in press).

## 2. Episodic-like memory in rats

The development of animal models of memory holds enormous potential for gaining insight into the biological bases of human memory. Moreover, given the extensive knowledge of the rodent brain, the development of rodent models of episodic memory would open new opportunities to explore the neuroanatomical, neurochemical, neurophysiological, and molecular mechanisms of memory. Development of such animal models holds enormous potential for studying functional changes in episodic memory in animal models of Alzheimer's disease, amnesia, and other human memory pathologies.

Three approaches that bear on episodic-like memory in rats are reviewed. One approach was directly inspired by Clayton and Dickinson's research. Two other approaches focus on recollection and object recognition.

### 2.1. Discrimination of what, where, and when

We adopted Clayton's approach to ask if rats can discriminate what, where, and when. In our experiments (Babb and Crystal, 2005, 2006a,b), rats were required to enter four runways that contained food on a radial maze (in which eight runways radiate from a central chamber, with access to each controlled by a guillotine door). Three of the accessible runways contained standard rat-chow flavored reward pellets, but the fourth runway contained a highly valued reward of chocolate-flavored pellets; we refer to this initial experience as a *study phase* because the rat had an opportunity to encode the trial-unique location of chocolate, as well as other locations of food. Next, the rats waited during a retention interval, after which the trial continued in a *test phase* with all eight doors open. After a short retention interval, only the previously inaccessible runways contained chow pellets in the test phase. In the test phase after a long retention interval, the previously inaccessible runways contained chow pellets, but the arm on which they had found chocolate earlier now contained chocolate again. The observation that the rats learned to revisit the chocolate location more frequently after long than after short retention intervals suggests that they learned that chocolate-locations replenish after the long, but not after the short, delay. This finding is significant because it suggests that the rats remembered *what* food they encountered on the maze (chow or chocolate), *where* they encountered these foods (runways on the maze), and *when* they had encountered the chocolate (short or long retention intervals).

If rats remember unique events from the past, then they should have a detailed representation of the event. In support of this prediction, we documented that rats remember the specific flavor at each location. With multiple flavors, it is possible to devalue or degrade one flavor while leaving the other flavors unchanged. In such circumstances, the rats flexibly adjusted their subsequent visits to avoid locations that replenish devalued flavors while continuing to exploit other locations that replenish valuable flavors (Babb and Crystal, 2006b). This finding is significant because it suggests that rats have a detailed representation of earlier events and that they flexibly adjust their behavior given new information.

In one of our studies, the time of day at which study and test phases were conducted was carefully controlled (Babb and Crystal, 2006a). In particular, the short and long retention intervals were 1 and 25 h, respectively, and the time of testing was always constant. Specifically, each study phase occurred at a constant time of day (e.g., 12:00 h for a particular animal). Because the short and long retention intervals differed by 24 h, the test phase also occurred at a constant time of day (13:00 h in the example above). Note that the study and test phases occurred on the *same* day when the reten-

tion interval was short; by contrast, when the retention interval was long, the study and test phases occurred on *successive* days. Importantly, it is not possible to solve the discrimination based on time of day. The observation that the rats learned to discriminate what, where, and when in this experiment suggests that what-where-when discrimination is not based on time of day. In our report (Babb and Crystal, 2006a), we emphasized that the discrimination of what, where, and when could not be based on adopting different revisit strategies at different times of testing. However, it is worth noting that the same conclusion can be made about the time of study phases – the discrimination could not be based on the time of day at the study phase because it was a constant time of day throughout the experiment. By contrast, the rats could have timed short and long retention intervals. Alternatively, the rats could have discriminated alternate days (i.e., did the study occur today or yesterday). There is independent evidence that rats can time long intervals (e.g., Crystal, 2001, 2006; for a review see Cheng and Crystal, 2008) and that they can discriminate alternate days (Pizzo and Crystal, 2007).

Recently Naqshbandi et al. (2007) replicated our study using somewhat different methods. To control time of day at the test phase, all test phases occurred at a constant time of day. By contrast, study phases occurred at different times of day (i.e., a short or long time before the test phase). The rats learned to discriminate what, where, and when. Naqshbandi et al. argued that the rats could not solve this discrimination by using time of day at test as a cue to adopt different search strategies. By contrast, the rats could encode time of day at the study phase and respond in the test phase contingent on the remembered time of the study. Alternatively, the rats could have used time of day at the study phase as a cue to encode (or fail to encode) the distinctively baited location; this encoding failure hypothesis could then explain the observed rates of revisiting the distinctive location at the subsequent test phase.

Recently Roberts et al. (2008) pointed out that most studies of what-where-when confound time of day at study with how long ago the study phase occurred. Consequently, they designed an elegant series of experiments to unconfound these variables. They conducted a series of trials, some of which had study phases that started at a constant time of day (thereby having test phases at varying times of day); other trials had the test phases occur at a constant time of day (thereby having study phases start at varying times of day). For some animals (designated as the *when* group), the distinctive flavor replenished on the subset of trials with a consistent study phase time (thereby having inconsistent replenishment associated with each retention interval); for other animals (designated as the *how-long-ago* group), the distinctive flavor replenished on the subset of trials with a consistent retention interval (thereby having inconsistent replenishment associated with the study phase time). The how-long-ago group learned the discrimination, but the when group did not. Roberts et al. concluded that (1) rats are not sensitive to the time of day when they encounter a distinctive food item in the study phase and (2) rats are able to use the elapsed time or how long ago they found food to predict the replenishment of the distinctive flavor. Moreover, they argue that the rats may remember only how much time has passed since an event occurred without remembering when food was encountered (Roberts et al., 2008).

It is generally the case that the failure to learn should be interpreted with some caution. One strength of the design employed by Roberts et al. (2008) is that the failure to learn in the *when* group is accompanied by documented successful learning in the *how-long-ago* group, using the same procedures and parameters. Nonetheless, an alternative explanation of these data is the hypothesis that when both *when* and *how-long-ago* information are available, the rats appear to rely on how-long-ago (or learn about it more rapidly). This latter hypothesis does not preclude the possibility that time of study may be encoded, which may require different experimental techniques to reveal.

Although the anatomical basis of what-where-when memory has not been explored in this paradigm, the hippocampus is a promising target (Eacott and Easton, 2007) given its role in integrating temporal relations (Amin et al., 2006). For example, immediate-early gene expression (*c-fos* and *zif268*) in the hippocampus responds to a novel temporal configuration of familiar distal visual–spatial cues. These findings suggest that the hippocampus is involved in processing the temporal rearrangement of visual stimuli (Amin et al., 2006).

### 2.2. Recollection and familiarity

Other researchers have taken a different approach toward examining episodic-like memory. Eichenbaum and co-workers have capitalized on the observation that recognition memory in people may be based on two independent mechanisms, episodic recollection of a specific event and a sense of familiarity of a previously experienced stimulus. Signal detection theory has been used to distinguish recollection and familiarity because these two processes have different profiles. Receiver operating characteristic (ROC) curves (which plot the probability of a hit as a function of the probability of a false alarm) have been used to characterize performance of human subjects on lists of single items. The ROC curve has a curvilinear (i.e., bowed) shape, but it is also asymmetrical (meaning that the $y$-intercept is above zero). The asymmetry has been interpreted as evidence for a threshold for recollection, and the curvilinear component has been interpreted as reflecting the strength of familiarity (Yonelinas, 2001; Yonelinas and Parks, 2007).

Fortin et al. (2004) trained rats to dig for a piece of food in a cup of sand using a food-rewarded old–new odor recognition task. In each trial, each rat was presented with a sequence of ten cups, each with a unique odor. After a 30-min delay, each rat was presented with a sequence of an additional 20 cups, half with new odors and half with the previously presented odors. Additional food could be obtained by digging in the new-odor cups and by refraining from digging in the old-odor cup (i.e., approach a different cup at the back of the cage). A hit was defined as a correct identification of an old item and a false alarm was defined as a misidentification of a new item. To trace out ROC curves, the pay-off ratio (i.e., reward magnitude) for correct new and old responses was manipulated across sessions, and the height of the test cup was varied. ROC curves from the rats showed both asymmetrical and curvilinear components, suggesting that performance was based on both recollective and familiarity processes. Next, some of the rats received selective lesions to the hippocampus, and others received a sham control operation. ROC curves of control rats continued to show both asymmetrical and curvilinear components. By contrast, ROC curves of animals with hippocampal lesions were fully symmetrical and curvilinear; the absence of the asymmetry suggests that destruction of the hippocampus eliminated recollection, leaving performance based solely on familiarity. The contribution of the recollective component was algebraically removed from the ROC of control rats, which produced a ROC curve that superimposed on that of rats with hippocampal lesions. These data are consistent with the hypothesis that the hippocampus mediates recollection (Fortin et al., 2004).

The loss of asymmetry (an index of recollection) combined with the retained curvilinearity (an index of familiarity) following selective damage to the hippocampus provides compelling evidence that recollection and familiarity may have distinct neural substrates. Additional support for this hypothesis comes from a recent study by Sauvage et al. (2008), in which they showed that damage to the

hippocampus causes a shift toward reliance on familiarity while eliminating reliance on recollection. In this study, odors were mixed in different digging substrate (e.g., wood chips, beads, sand) in a cup. Odors were paired with substrate using ten unique combinations each day. After a 30-min delay, a series of 20 odor–substrate combinations were presented. Half of the pairs in this series were exact combinations that were presented earlier (old) in the trial, and half were rearranged pairings (new) of the same odors and substrates that were presented earlier (i.e., the elements had been presented earlier, but not presented jointly). As in earlier studies, food was obtained using a nonmatching rule (food appeared in new items but was available in a different cup when old items were presented), and bias was induced by varying pay-off (i.e., reward size in the different cup) and varying the size of the test cup. Recollection was indexed by the *y*-intercept of the ROC curve, and familiarity was indexed by the degree of curvilinearity. Sham-operated control rats relied mainly on recollection to solve the task (positive *y*-intercept and absence of curvilinearity), with a familiarity score of zero, suggesting that there was no contribution from familiarity. Hippocampal damage reduced reliance on recollection and increased reliance on familiarity. Thus, hippocampal damage had *opposite* effects on recollection and familiarity (i.e., a deficit in recollection and an enhancement of familiarity). Moreover, rats with damage to the hippocampus obtained approximately the same level of overall accuracy as control rats by shifting from reliance on recollection to reliance on familiarity. This study documents that recollection and familiarity are qualitatively dissociable by hippocampal lesion and suggests that the hippocampus supports recollection and not familiarity (Sauvage et al., 2008).

The serial odor task has also been used to assess memory for what, where, and when (Ergorul and Eichenbaum, 2004). Rats encountered a sequence of four individually presented odors in sand-filled cups, each baited with food and presented along the periphery of a square platform. In *standard tests*, two items from a recently presented list were simultaneously presented in their original locations, and rats were rewarded for choosing the *earlier* item (the later item in the pair was not baited); this test preserved location (i.e., the items were presented in test using the same locations that these odors occupied during the earlier, sequential presentation). Finding the reward in the standard test required *temporal* information to select the earlier item from the daily odor and spatial-location items. In the standard tests, the rats first approached the correct cup at a rate higher than expected by chance, suggesting that the rats used spatial location (independent evidence suggests that the rats could not detect the odors from the distance used to score first approaches). In addition, the initial visits (defined as digging in a sand-filled cup) to the correct cup occurred at a significantly higher rate than the observed first-approach rate; this increment in accuracy suggests that rats confirmed their initially spatially guided choice by smelling the odor at the cup (and thereby rejecting some potential errors when the incorrect odor was detected at the incorrect location).

In *odor probes*, spatial cues were eliminated by placing the two odor items in the middle of the platform, and the rats were rewarded for choosing the earlier odor. In *spatial probes*, odor cues were eliminated, but the cups were presented in their original locations along the periphery; the rats were rewarded for choosing the earlier location in spatial probes. Removal of the spatial cue in odor probes did not impair performance, but removal of the odor cue in spatial probes reduced performance to the level expected by chance. The profound impairment when odor cues were eliminated is surprising given that the rats' first approach (which was not based on odor) was above chance. These data suggest that the rats expected to re-confirm their first approach based on odor, and the absence of odor at that point produced a random selection of

locations. It should be noted that probes were *rewarded*; thus, it is possible that some of the data reflect *new* learning about appropriate behavior in these tests in addition to reflecting knowledge learned in earlier training using standard tests.

Next, some rats received selective lesions of the hippocampus. Rats with lesion of the hippocampus, unlike sham controls, showed impaired (i.e., chance) performance in digging choices on standard tests. First approaches were reliably *below* chance on standard probes in the hippocampus-lesion group, suggesting that spatial information was retained but was used inappropriately (e.g., a habit to return to the most recently rewarded location). By contrast, damage to the hippocampus did not impair performance on odor probes. These data suggest that odor cues were used to solve the *odor probe* but could *not* be used to solve the *standard test*. The authors noted that the odor cues were in close proximity in odor probes but not in standard tests; thus, a comparison of relative strength of memory traces for the odors may have supported performance on odor probes but not on standard tests. By contrast, in the standard test (i.e., when the odors were not in close proximity), rats with lesions to the hippocampus appear to be unable to make judgments about memory for the order of events, despite the retained ability to compare order when the cues are not spatially separated. Moreover, damage to the hippocampus was selective to the *integration* of what-where-when information given that the rats retained the ability to make odor judgments, to use spatial information, and to make judgments about order in some test conditions.

### 2.3. Object recognition

Recollection of a recent event has also been investigated by using a habituation paradigm with trial-unique objects. When rats are presented with two objects, one familiar and one novel, rats spontaneously prefer the novel object (Mumby et al., 1995). Eacott et al. (2005) exploited this preference to develop a clever method to document recollection in rats. Their basic insight was to make available a contextual cue but to displace the novel and familiar objects out of sight so that the rat was required to make a choice without being able to see the objects. They used an E-shaped maze with the rat starting in the middle arm; objects could be placed along the backbone of the E so that they were within view from the choice point, or the objects could be displaced to the ends of the other two arms so that they were out of sight when the initial left/right choice was made. Eacott and co-workers argued that familiarity with the objects could not mediate this latter choice because the objects were not visible at the time of choice. Thus, the study was designed to encourage the use of contextual cues to prompt recollection of the objects' locations.

In the Eacott et al. (2005) study, rats were given experience encountering daily-unique objects in particular locations and in a particular context (i.e., what, where, and *which*—which stimulus context). In one context (e.g., smooth black maze), two objects were in stable locations across two presentations within a day. In another context, (e.g., wire mesh maze), the locations of the objects were reversed across the two presentations. A copy of one of the objects was placed in a holding cage to permit the rat to explore (i.e., habituate to) that object. Without training or reinforcement, rats approached the relatively novel object. Initially, the rats were permitted to choose between the two objects when these objects were within view from the choice point in the maze. In a subsequent experimental stage, the rats were required to choose one of two runways at a point from which the objects were not yet within view; in a final control condition, the objects were removed to control for extraneous stimuli (e.g., odors) associated with the objects. The rats selected the relatively novel object (i.e., the object not explored in the holding cage) at above chance levels in each

of the conditions described above. Eacott et al. argued that when the objects are within view at the choice point, the observed preference for the nonhabituated object can be based on familiarity alone. However, when the objects were not visible to the rat upon emerging from the start box, the rat had to recollect the prior experience in that context in order to choose the location of the relatively novel object; this choice response could not be based on familiarity with the objects because the objects were not in view at the time of the choice response. This argument is similar to that of Brown (1992), Brown and Bing (1997), Brown and Moore (1997) and Brown et al. (1993) about spatial navigation with respect to a map-like representation. Rats that received a lesion to the fornix (the major output from the hippocampus) had impaired recollection (i.e., performance was reduced to the rate expected by chance; Eacott and Easton, 2007). However, these same rats on the same trials showed normal preferential exploration of the same nonhabituated object. These data suggest that the lesion impaired recognition but spared familiarity-based processes (Eacott and Easton, 2007).

Another approach with object recognition focused on an integrated representation of what, where, and when (Kart-Teke et al., 2006; see also Dere et al., 2005a,b). Kart-Teke and co-workers presented objects in an open field, using a sequence of two sample presentations followed by a test. In the first sample presentation, four identical objects (i.e., each identical object will be referred to as item A) were placed in four of nine available quadrants. In the second sample presentation, a new set of four identical objects (i.e., four B's) were presented; two B's were presented in locations previously occupied by two A's, and the other two B's were in previously unoccupied locations. In the test, two copies of A and two copies of B were presented, each in a familiar location (i.e., a location that was occupied in at least one previous sample phase). One of the A's was presented in a location previously occupied by an A in the first sample (old familiar stationary object A), and one of the B's was presented in a location previously occupied by a B in the second sample (recent familiar stationary object B). The other identical copies of the objects were placed in a location not previously occupied by that type of object in the previous sample (i.e., old familiar displaced object A appeared in a location not previously occupied by an A, but in a location occupied by a B; the recent familiar displaced object B appeared in a location not previously occupied by a B, but in a location occupied by an A). Note that the test permits an assessment of preference for object type (i.e., A vs. B), location (i.e., stationary vs. displaced), and temporal order (i.e., old vs. recent), which corresponds to what, where, and when. The rats spent more time exploring the stationary old familiar object compared to the stationary recent familiar object, suggesting that the rats recognized the objects and their order of presentation. The rats also spent more time exploring the displaced recent familiar object relative to the stationary recent familiar object. By contrast, the rats spent less time exploring the displaced old familiar object compared to the stationary old familiar object. These data suggest that the rats were sensitive to the location of the objects (i.e., displaced or stationary). The rats preferred the displaced recent familiar object compared to stationary recent familiar object; they preferred the stationary old familiar relative to the displaced old familiar. The authors argue that this interaction between recency and spatial displacement suggests that they integrated what, where, and when. Performance on this task appears to be quite fragile given the observation that a single i.p. saline injection eliminated discrimination of recency and spatial displacement of objects (Kart-Teke et al., 2006). However, this apparent stress-induced disruption can be partially reversed by injection of D-cycloserine (DCS), a partial agonist of N-methyl-D-aspartate (NMDA) receptors (Kart-Teke et al., 2006) and by injection of SR140333, a selective non-peptide neurokinin-1 (NK-1) receptor (Kart-Teke et al., 2007).

## 3. Other approaches

### 3.1. Binding

A critical element of episodic-like memory is that the retrieved memory is about an integrated event; consequently, the representation of what-where-when should be integrated (Clayton et al., 2003a). Skov-Rackette et al. (2006) developed novel tests designed to determine if what-where-when memories are integrated or independent. Skov-Rackette et al. trained pigeons in a matching to sample task using one of two colored shapes, one of eight locations on a touch screen, and one of two retention intervals (2 vs. 6 s). In particular, the sample was a red disk or a green triangle that was presented in one of eight locations around the periphery of the touch screen; the sample stimulus was presented 2 or 6 s before the test. Three types of test phases could occur after presentation of the sample and retention interval. To test 'what', the red disk and green triangle appeared in the center of the screen, and reinforcement was presented contingent on pecking the stimulus that matched the sample presented earlier. To test 'where', two grey squares appeared in two peripheral locations, one of which matched the location of the sample presented earlier. To test 'when', a yellow star and blue paw shape appeared in the center of the screen, and a peck to one of the shapes was correct after the 2-s retention interval, while the other stimulus was designated as correct after the 6-s retention interval. Initially, the birds were trained on each factor on separate sessions. Next, the tasks were presented in each session, using progressively smaller trial blocks of each test type. In the final phase of training, the test types were randomly mixed across trials. After completing this training regime, the birds accurately reported identity of the sample, its location, and the length of the retention interval.

To assess whether identity, location, and time were encoded independently or bound together in memory, Skov-Rackette et al. (2006) presented two different tests in succession on occasional non-rewarded probes. If any of the features were stored in independent memories, the probability of responding correctly on the second test should be independent of the probability of responding correctly on the first test of the same trial. By contrast, if what, where, and when elements are bound in a single representation of the preceding event, then it should be possible to document dependence between the first and second tests of accuracy. Performance on the second test was unrelated to performance on the first test, suggesting that although the birds remembered all aspects of the sample presentation, they accomplished this based on independent memories for the features present in the sample. Skov-Rackette et al. noted that the second test occurred rarely and that the presentation of a test previously signaled the end of the trial (which is a cue to forget the most recent sample; Roper and Zentall, 1993). Consequently, an alternative approach would be to train the animals with multiple tests from the outset and evaluate independence in this case.

In another test of binding, Skov-Rackette et al. (2006) trained pigeons with two features, sample-stimulus identity and location. The samples were one of two differently colored shapes presented in one of eight locations along the periphery of the touch screen. After a brief retention interval, one of several tests occurred. On standard tests, both sample stimuli were presented at the center of the screen (i.e., a test for sample stimulus identity). On other standard tests, two identical test stimuli (that differed from the sample) were presented at the location previously occupied by the sample stimulus and at a different location (i.e., a test for sample stimulus location). Skov-Rackette et al. designed three novel tests that assessed binding of features. In the first test, both sample stimuli (i.e., the recently presented sample and the other stimulus that

was sometimes presented as a sample) were presented adjacent to the location of the most recently presented sample. In the second test, two copies of the sample stimulus were presented, one at the location previously occupied by the sample and the other at a different location. If both identity and location of the sample were bound in a single memory, then the untested feature presented in the latter two tests might facilitate memory retrieval of the tested feature. In the third test, four alternatives were presented that combined all aspects the preceding two tests (i.e., both types of sample stimuli were presented at locations adjacent to the recently presented sample and near another location). If memories of location and identity were bound, then performance would be expected to be higher when the untested feature was presented on some of the tests. However, although the birds appeared to encode the multiple features of the sample, there was no evidence for the predicted improvement. These data are consistent with the hypothesis that the memories of location and identity were stored independently.

The methods developed by Skov-Rackette et al. (2006) suggest that although multiple features of an event (e.g., what, where, and when) may be encoded from the presentation of a single event, it is possible to do so without remembering a single, multi-dimensional event. Consequently, this study highlights the importance of testing for an integrated representation of a single event.

In a recent study of integrated memories, Iordanova et al. (in press) documented integrated what-where-when memories in rats. An auditory stimulus (what: X or Y) was presented in location (where: context A or B) and temporal (when: morning or afternoon) contexts. In particular, X occurred in context A and Y in context B in the morning; in the afternoon, these arrangements were reversed (X in B and Y in A). Next, X (but not Y) was paired with footshock at midday. In a subsequent test of contextual fear to A and B in the morning and afternoon, rats showed more fear in A than in B in the morning and the reverse (more fear in B than in A) in the afternoon. Thus, this study documents an integration of what (X or Y), where (A or B) and when (morning or afternoon).

### 3.2. Unexpected question

Another element of episodic memory is that it can be used to report information when the test of memory is unexpected. One problem with many of the paradigms used to evaluate episodic-like memory is that extensive training is required (Singer and Zentall, 2007; Zentall, 2005, 2006; Zentall et al., 2001). Zentall and co-workers argued that it is not possible to preclude semantic-like knowledge in the discrimination of what-where-when because the contingencies of food availability are explicitly trained; the explicit training might foster the development of semantic knowledge about experimental contingencies. They proposed that the capacity for episodic-like memory can be assessed in animals by using an unexpected question about a recent event. According to this view, documenting episodic-like memory requires a demonstration that the animal can report a recent event when there was no expectation that such a report would be required (i.e., an unexpected question).

Zentall et al. (2001) trained pigeons in a symbolic matching task to respond to the nonverbal question "Did you just peck or did you just refrain from pecking?" In this part of the experiment, the birds were trained on a symbolic matching task in which a line orientation (i.e., vertical vs. horizontal line) sample was followed by the requirement to peck or withhold pecking, followed by the selection of one of two colors (i.e., red and green). Therefore, the presentation of one line orientation signaled that a particular behavior (i.e., pecking or its absence) is required, which was then followed by the requirement to select one color to obtain reward. Next, the pigeons were provided with conditions that would elicit pecking or the absence of pecking, but without the requirement (and hence without the expectation) that a report will be given about the pecking behavior. In this part of the experiment, one color (e.g., yellow) was paired with food (which elicited pecking) and another color (e.g., blue) was presented but not paired with food (which elicited the absence of pecking). In the test, the sample stimuli that elicit pecking or the absence of pecking (i.e., yellow or blue) but that do not elicit the expectation of a question about pecking were presented. Next, the red and green comparison stimuli were presented, thereby unexpectedly providing the birds with the opportunity to report about their recent behavior (pecking vs. not pecking). When the pigeons were first asked the unexpected question, they reported accurately whether they had been pecking or not. In a further test, the birds were presented with a novel event that would elicit pecking (i.e., a new stimulus that occasioned generalized pecking) or a novel event that would elicit the absence of pecking (i.e., presentation of no stimulus on the test). Next, the birds were unexpectedly asked whether they had recently pecked (i.e., by presentation of the red and green comparison stimuli), they again accurately reported whether they had pecked or not.

Singer and Zentall (2007) pointed out that the presence vs. absence of pecking may give rise to residual proprioceptive cues that may be present when the unexpected question occurs. Consequently, the discrimination of motor aftereffects is an alternative explanation when the unexpected question is responding vs. refraining from responding. To circumvent this potential problem, Singer and Zentall trained pigeons to report on the location of a previous response, which should produce equivalent residual motor aftereffects (i.e., answering the nonverbal question "Where did you just peck?"). As a further precaution, after a left or right initial response, the birds were required to peck at the center, thereby reducing the likelihood that the position of the beak could serve as a cue at the time of test. In this part of the experiment, a white side key was followed by a center triangle and then by a red and green choice presented on the left or right side keys. One color was correct after illumination on the right, and the other color was correct after illumination on the left; thus the birds were trained to report which side they had pecked earlier (i.e., before pecking the center triangle) when a triangle is presented. Next, the pigeons were trained on a symbolic-matching task in which blue or yellow was presented in the center and a left or right choice was required when vertical and horizontal lines appeared on the side keys. At this stage of the trial, a peck on the left or right side was an incidental aspect of the task. In the test, the trial started with the symbolic-matching task (i.e., yellow or blue followed by a choice of vertical or horizontal side keys) but continued (for the first time) with the presentation of a center triangle and a choice of red or green (i.e., an opportunity to report which side had incidentally been pecked at an earlier stage in the test). When the pigeons were first asked the unexpected question, they reported accurately whether they had pecked on the left or right side. These data suggest that pigeons can retrieve information about a past event, although the location of their choice of line orientation had never before been requested.

It should be noted that episodic memory is generally regarded as a kind of long-term memory. Therefore, it is noteworthy that the experiments on unexpected questions have thus far used relatively short delays between encoding and test (nominally 0 s in Zentall et al., 2001 and less than 2 s in Singer and Zentall, 2007).

## 4. Comparative analysis

The investigation of episodic-like memory has been comparative from its outset, particularly with the classic demonstration by Clayton and Dickinson's scrub jays. Indeed, recently Zinkivskay et

al. (in press) have extended the comparative analysis by examining what-where-when memories in magpies, another corvid, but one that is only distantly related to scrub jays. Both scrub jays and magpies have similar hippocampus to brain and body size ratios, and both hoard many food types opportunistically, including ones that decay over time. Both discriminate what, where, and when events occurred.

In the sections that follow, two other ecologically inspired studies of what-where-when are reviewed. Male meadow voles remember the what-where-when of exposure to females, in particular, the reproductive state, location and amount of time since exposure to female voles (Ferkin et al., 2008). Honeybees remember visual patterns by using spatial and temporal information (Pahl et al., 2007; Zhang et al., 2006).

### 4.1. Meadow voles

Ferkin et al. (2008) tested the hypothesis that male meadow voles (a microtine rodent) use what-where-when memories to keep track of the changing state of receptivity of potential mates. Female voles occupy widely dispersed territories that are fixed spatially, whereas males live in large ranges that overlap with several females. The reproductive state and sexual receptivity of females varies during the breeding season. Heightened sexual receptivity occurs during postpartum estrus (PPE), relative to other states (pregnant, lactating, both pregnant and lactating, neither pregnant nor lactating). Importantly, PPE females are more likely to mate with a male vole relative to other reproductive states, and females enter PPE asynchronously. Moreover, male voles mate with multiple females (thereby increasing their fitness). Therefore, based on the above reproductive ecology, Ferkin and co-workers hypothesized that male voles would remember the reproductive state (what), location (where), and how long she will be in a reproductive state (when) based on a single visit to a female.

Male voles explored a T-shaped set of enclosures (Ferkin et al., 2008). One chamber contained a female vole that would become PPE in 24 h (i.e., she was on day 20 of pregnancy, 24 h prepartum). As a control condition, the other chamber contained a sexually mature female that was not pregnant and not lactating. After 24 h, the male was returned to the apparatus and permitted to choose between the two chambers (both chambers were empty and clean). By this time, the pregnant female would have entered PPE and would be in a heightened state of sexual receptivity. The males first chose and spent more time in the chamber that had housed the pregnant female than the control chamber; this preference was not expressed if the choice was made 0.5 h after exposure (i.e., at a time when the female would not yet be in PPE). In another study, the initial exposure involved a currently PPE female and a control female. When tested 24-h later (i.e., when the female would now be lactating and not sexually receptive), the male voles did not show a preference (in initial choice or time spent investigating) for the PPE chamber. However, if the test was 0.5 h after exposure to a PPE female, the male voles preferred the chamber that recently contained the PPE female (i.e., at a time when she would still be in PPE).

Male voles remember the reproductive state of female voles that they recently encountered, in addition to where they were located. After a delay (when the female is out of sight), the males go to the location that would be expected to have a receptive female based on the time course over which reproductive states change. This suggests that the male voles not only remember where they encountered the female and her previous reproductive state, but that the male also anticipates the reproductive state at the time of test. This finding is particularly interesting in light of the mental time travel hypothesis – the hypothesis that animals with the

capacity for episodic-like memory (i.e., recollect previous events) also would have the capacity to anticipate future events (Raby and Clayton, 2009; Suddendorf and Corballis, 2007). The voles anticipate the reproductive state of females based on their earlier encounter. This ability suggests that the male voles remember what-where-when about the recently encountered female voles. Moreover, because the choice is expressed after a single encounter with the females, their choices are presumably based on constructing a representation of the future state of the females as proposed by the mental time travel hypothesis. The connection of this work to the mental time travel hypothesis is particularly interesting given that some human patients with injuries to frontal lobes lack both episodic memories and the ability to plan for the future (Atance and O'Neill, 2001; Klein et al., 2002; Raby and Clayton, 2009). Moreover, some animals have both retrospective episodic-like memories and prospective cognition (Correia et al., 2007; Raby et al., 2007; Raby and Clayton, 2009).

### 4.2. Honeybees

There is emerging evidence that honeybees plan their activities in time and space (Pahl et al., 2007; Zhang et al., 2006). Bees were trained to choose one of two locations in a Y-maze, with one rewarded and one non-rewarded side. The sides had different colors and patterns at different times of day. For example, in the morning the choice was between a yellow vertical pattern (which was rewarded) and a yellow horizontal pattern (non-rewarded). At another site in the afternoon, the choice was between blue horizontal (rewarded) and blue vertical (non-rewarded) patterns. The bees readily learned these contingencies, and then a number of transfer tests were conducted. In each transfer test, a cue type was removed (e.g., color, pattern, location) and some tests occurred at midday (i.e., "removal" of the temporal cue). The bees were able to find the correct pattern shape without the color cue (i.e., at the correct maze location and time of day, the bees preferred the corresponding pattern despite the absence of a corresponding color cue). When a novel maze at a novel location was used, the bees relied on time of day to select the correct pattern and color. These results suggest that bees would be able to forage from different kinds of flowers at different times of day and at different locations based on their profitability. Moreover, when visiting a new location they would be able to select the most profitable flower for a particular time of day. The temporal information is likely from a circadian system because circadian time of day appears to be the temporal variable that most readily modulates memory retrieval of color information (Prabhu and Cheng, 2008a,b). Thus, Pahl et al. (2007) named this type of performance circadian timed episodic-like memory (i.e., discrimination of circadian time, color, shape and location). The use of circadian time makes ecological sense given the nectar and pollen feeding opportunities likely follow a circadian pattern. By contrast, an opportunistic generalist feeder (e.g., rats) would be expected to be tuned to how long ago food was discovered, rather than the time of day, and there is evidence that foraging decisions in such opportunistic contexts are based on elapsing intervals (Devenport and Devenport, 1994; Devenport et al., 1997).

### 5. Conclusions

The diverse approaches that have been used to assess episodic-like memory in animals may promote the development of converging lines of evidence on the difficult problem of assessing memory for a specific event. Although each approach may have limitations, the use of multiple, independent approaches may be used to test the hypothesis that rats and other animals have episodic-like memory. One advantage of a multi-method approach includes

the ability to obtain a comprehensive description of the elements of episodic-like memory in rats. In particular, it is possible that rats possess some aspects of episodic-like memory, but that in some significant ways this aspect of memory differs from that observed in people or other animals. Thus, the use of multiple criteria and assessment methods may document a more complete picture of an animal's representational systems than could be obtained if a single, critical method were selected.

Advances in our understanding of cognition occur by evaluating behavior in animal studies of comparative cognitive, in addition to the valuable contributions of studying cognition in people. The primary advantages of investigating cognitive processes in non-human animals include: (1) the ability to focus exclusively on operationally defined criteria that rely on objective behavioral measures (thereby eliminating the focus on subjective experiences that may accompany cognitive processes in people) and (2) the ability to use animals in investigations of the neurobiological underpinnings of cognitive processes. Combining these two factors holds enormous potential for translational research that may foster the development of therapeutic approaches to human diseases with profound cognitive impairments, such as Alzheimer's disease, amnesia, and other human memory pathologies.

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