available at www.sciencedirect.com

ScienceDirect

www.elsevier.com/locate/brainres

BRAIN RESEARCH

Research Report

A neurocomputational model of classical conditioning phenomena: A putative role for the hippocampal region in associative learning

Ahmed A. Moustafa[a,*], *Catherine E. Myers*[b], *Mark A. Gluck*[a]

[a]*Memory Disorders Project and Center for Molecular and Behavioral Neuroscience, Rutgers University-Newark, 197 University Avenue, Room 209, Newark, NJ 07102, USA*

[b]*Memory Disorders Project and Department of Psychology, Rutgers University-Newark, 101 Warren Street, Newark, NJ 07102, USA*

ARTICLE INFO

Article history:
Accepted 9 April 2009
Available online 18 April 2009

Keywords:
Pavlovian conditioning
Model
Hippocampal region
Hebbian learning

ABSTRACT

Some existing models of hippocampal function simulate performance in classical conditioning tasks using the error backpropagation algorithm to guide learning (Gluck, M.A., and Myers, C.E., (1993). Hippocampal mediation of stimulus representation: a computational theory. Hippocampus, 3(4), 491–516.). This algorithm is not biologically plausible because it requires information to be passed backward through layers of nodes and assumes that the environment provides information to the brain about what correct outputs should be. Here, we show that the same information-processing function proposed for the hippocampal region in the Gluck and Myers (1993) model can also be implemented in a network without using the backpropagation algorithm. Instead, our newer instantiation of the theory uses only (a) Hebbian learning methods which match more closely with synaptic and associative learning mechanisms ascribed to the hippocampal region and (b) a more plausible representation of input stimuli. We demonstrate here that this new more biologically plausible model is able to simulate various behavioral effects, including latent inhibition, acquired equivalence, sensory preconditioning, negative patterning, and context shift effects. In addition, the newer model is able to address some new phenomena including the effect of the number of training trials on blocking and overshadowing.

1. Introduction

We propose here a computational model that simulates performance in classical conditioning following a similar architecture to that of the Gluck and Myers (1993) model. The newer model, however, uses Hebbian learning which is more plausible than the error backpropagation algorithm used earlier. The new model simulates all the tasks originally simulated by the Gluck and Myers model while also accounting for several subtle additional classical conditioning phenomena. The brain areas simulated in the new model represent the simplest system needed to capture the role of hippocampal region in different classical conditioning phenomena.

The Hebbian learning algorithm is a simple model of associative learning, which is a process that has been ascribed to the hippocampal region function (Bunsey and Eichenbaum, 1995; Henke et al., 1997). It is also a simple model for synaptic

* *Corresponding author*. Fax: +1 973 353 1272
E-mail address: ahmedhalimo@gmail.com (A.A. Moustafa).

0006-8993/$ – see front matter. Published by Elsevier B.V.
doi:10.1016/j.brainres.2009.04.020

change through Long Term Potentiation (LTP) in the hippocampus (Bilkey, 1996; Bliss and Lomo, 1973). Using the Hebbian learning algorithm in the current model also helps account for new behavioral effects not simulated by the Gluck and Myers (1993) model. For example, recent studies showed that blocking and overshadowing depend on the number of training trials of compound cues (i.e., two conditioned stimuli presented together) employed in these paradigms, such that blocking and overshadowing fade with extended training (Pineno, 2006; Stout et al., 2003). The use of Hebbian learning, and not error backpropagation, in the model is key for accounting for these effects, as we describe below. Also, the hippocampal module in the current model responds to the presentation of all cues, including conditioned stimuli (CSs) and unconditioned stimuli (USs). This is in agreement with existing neurophysiological studies reporting that hippocampal neurons respond to the US presentation (McEchron and Disterhoft, 1997, 1999).

Associative learning processes are integral aspects of the performance and learning of classical conditioning tasks. Associative learning involves either learning to associate a neutral stimulus with a biologically salient stimulus (e.g., food or shock) as in classical conditioning paradigms (Ito, Everitt, and Robbins, 2005; Ito et al., 2006; Selden et al., 1991; Solomon et al., 1983) or learning to associate two neutral stimuli as in the paired associate paradigms, which are used with both humans and animals (Eichenbaum, 2003; Henke et al., 1997; Zeineh et al., 2003).

In classical conditioning, a neutral stimulus comes to elicit a conditioned response (CR) after being consistently paired with a US. An unconditioned stimulus is a biologically salient stimulus, such as food or eye air puff, which is capable of eliciting an instinctual response—known as the CR. Various manipulations to the standard classical conditioning task serve to explain the factors under which associative learning occurs. These factors include a potential role for background contextual information, number of training trials, and the salience or novelty of stimuli employed in conditioning paradigms. By context, we mean spatial or olfactory features of the testing box and/or other external cues that might have been used by subjects during learning. A good example of such a manipulation is the blocking paradigm in which prior training that one stimulus A predicts reinforcement hinders ("blocks") subsequent learning about a second stimulus B that is presented together with A (Kamin, 1969). The blocking paradigm demonstrates that predictiveness of a cue—and not its co-occurrence with the US—is what drives learning to associate that cue with the US. Another example is the latent inhibition paradigm which is a phenomenon in which prior exposure to a cue slows subsequent acquisition of a CR to that cue when it is subsequently paired with a US (Lubow, 1973).

The hippocampus and the overlaying cortices are found to play an important role in Pavlovian conditioning and associative learning tasks (Allen et al., 2002a; Berger et al., 1976; Phillips and LeDoux, 1992; Rudy et al., 2002; Shohamy et al., 2000). Lesion studies found that, although simple conditioning is generally spared following hippocampal lesion, the hippocampal region is key for many more complex classical conditioning paradigms including latent inhibition, acquired equivalence, and sensory preconditioning (Coutureau et al., 2002; Gluck and Myers, 1993; Nicholson and Freeman, 2000; Port and Patterson, 1984; Puga et al., 2007; Solomon and Moore, 1975).

Sensory preconditioning describes the phenomenon that if an animal is first given unreinforced trials with stimuli A and B presented together as a compound cue (AB–), then training the animal that A (alone) predicts the US will lead some of this association to be transferred to B (Thompson, 1972). Acquired equivalence, on the other hand, describes the findings that contexts (say X and Y) in which similar events take place acquire equivalent status, such that if X is subsequently paired with a US, Y will elicit a stronger CR than in a control condition in which no common events take place in other contexts (say Z; see Table 1 for explanation).

Similarly, in humans, it has been shown that the hippocampal region is important for incremental learning of the paired associate task (Eichenbaum, 2003; Henke et al., 1997; Zeineh et al., 2003). In addition, associative learning deficits have been reported in patients with mild cognitive impairment (Collie et al., 2002) who possibly have hippocampal damage (Apostolova et al., 2006; de Leon et al., 1989). Both the classical conditioning and the paired associate paradigms (McClelland et al., 1995; Scoville and Milner, 1957) are similar in that both usually require many trials to establish learning and both involve learning to associate different stimuli. The findings that the hippocampal region contributes to performance in both the classical conditioning and paired associate tasks suggest that (a) the hippocampal region is key for incremental learning and that (b) the biological salience of stimuli may not matter much for the hippocampus processes.

Table 1 – Tasks simulated in the model.

Simulation	Phase 1	Phase 2	Phase 3
A+	AX+		
A–	AX–		
Sensory preconditioning	ABX–	AX+	BX–
Latent inhibition	AX–	AX+	
Context shift	AX+	AY+	
Context sensitivity of latent inhibition	AX–	AY+	
Learned irrelevance	AX–; USX–	AX+	
Acquired equivalence	AX–; AY–, Z–	X+	Z–; Y –
Easy–hard transfer learning	A1X+; B1X–	A2X+; B2X–	
Blocking	AX+	ABX+	BX–
Compound preconditioning	ABX–	AX+; BX–	
Overshadowing	ABX+	AX+, BX+	
Negative patterning	AX+, BX+, ABX–		

In all simulation experiments, contexts are referred to as X, Y, and Z; cues as A and B. "AX–" means A is presented in context X. ';' separates different trials in the same phase. In the easy–hard learning task, A1 and B1 have very different representations in the input layer, whereas A2 and B2 have similar representations. In the overshadowing task, A is more salient than B. This is simulated as A activates more input units in the layer. In each of these phases, the corresponding context is presented to the network by itself before cue presentation mimicking the presence of animal inside a box (see Experimental procedures).

In addition to the hippocampal region, several studies also showed that the cerebellum is key for learning classical conditioning tasks, particularly the eye blink conditioning paradigm (Chapman et al., 1990). Chapman et al. (1990) found that deactivating the interpositus nucleus of the cerebellum in rabbits using lidocaine interferes with learning the eye blink conditioning task. Similarly, Hu et al.(2009) recently found that deactivating the cerebellum in guinea pigs using muscimol interfered with learning the same task but did not interfere with eliciting conditioned responses. Initiating conditioned responses was shown to be mediated by cerebellar projection to the red nucleus of the brain stem (Chapman et al., 1990). In one interesting study, Woodruff-Pak et al. (1993) found that inactivating different segments of the cerebellum *after* learning the eye blink conditioning task does not interfere with performing the task, suggesting that the cerebellum is key for learning processes. Furthermore, patients with essential tremor—who were shown to have loss of cerebellar Purkinje cells—show impairment at learning classical conditioning tasks (Shill, De La Vega et al., 2009). Based on these studies, we suggest that the cerebellum is key for learning to elicit conditioned responses (for more discussion, see Gluck et al., 2001).

We now discuss different models of classical conditioning performance. Like our model, the Rescorla and Wagner (1972) model also simulates performance in different classical conditioning phenomena. This model posits that the predictiveness of a cue and not just their co-occurrence with a US is what derives learning to associate this cue with a US. In other words, the Rescorla–Wagner model assumes that the difference between the (predictive) value of that cue and US value is what derives associative learning. Although the Rescorla–Wagner model accounts for some classical conditioned phenomena, such as blocking and overshadowing, it does not account for others including latent inhibition, sensory preconditioning, compound preconditioning, negative patterning, and acquired equivalence (Coutureau et al., 2002; Farkas et al., 2008; Hall et al., 1993; Myers et al., 2003a; Spiker, 1956; Ward-Robinson and Hall, 1999). Moreover, the Rescorla–Wagner model accounts for classical conditioning phenomena that can be simulated using a one-layer feedforward network that learns based on the delta learning rule (Gluck and Bower, 1988; Gluck and Myers, 2001). Gluck and Myers (1993) proposed a connectionist model showing that augmenting this network with an autoencoder is sufficient to simulate many of the classical conditioning tasks not accounted for by the Rescorla–Wagner model. In the Gluck and Myers (1993) model, the autoencoder forms either a compressed or differentiated representation of input stimuli. By compression, we mean stimuli that tend to co-occur will have similar (compressed) representations. Differentiation is the opposite of compression, and it means forming spare (differentiated) representations of stimuli that do not co-occur. Another main idea of the Gluck and Myers model is that compression and differentiation of input stimuli is one function of the hippocampal region. The current study builds on these earlier models, incorporates a similar architecture, addresses their limitations (e.g., using error backpropagation algorithm), and also addresses a potential role for the number of training trials on behavioral effects, as reported in experimental studies of blocking and overshadowing (see the Experimental procedures section for more details on model and tasks simulated).

2. Results

First, we will present data regarding how the intact model performs the different classical conditioning tasks described in Table 1. Then, we will describe the effects of lesioning the hippocampal module on classical conditioning performance.

2.1. *Intact model*

The simplest conditioning task to learn is to show a conditioned response to a cue that is associated with the US presentation but not to context alone. This is the case in the model as shown in Fig. 1a. The model shows an increase in response to cue A, while it shows a decrease in response to the context since it is not consistently associated with the US presentation, though the context and the US occasionally overlap. Similarly, the CR decreases to the cue and context presentations when neither is associated with the US presentation (Fig. 1b).

In the subsequent simulation studies, the conditioned response to contexts is always the same as in the A+ and A– simulations (Fig. 1). Furthermore, data in early phases in subsequent simulation studies are very similar to the A+ and A– simulation results. Accordingly, we will not present these results again.

The model also simulates performance in the blocking paradigm. Training the model on A+ trials and then on AB+ trials blocks B from being associated with the US. This is because the CR to B at the beginning of phase 3 in this paradigm is lower than the CR to B in a control condition that does not include A+ training (see Fig. 2a). Furthermore, we found that extended training of AB+ trials abolished the blocking effect: here, B elicits a CR comparable to that of the control condition (see Fig. 2b). The findings that the number of training trials of the compound cue (AB) plays a role in whether we obtain the blocking effect have been reported experimentally (see Azorlosa and Cicala, 1988; and for similar effects see Pineno, 2006), and to our knowledge, were not previously simulated in a neural network or abstract model.

Similarly, the model accounts for the overshadowing effect. Training the model on AB+ trials where A is more salient than B leads to A eliciting a stronger CR than B—this is known as the overshadowing effect (Fig. 3a). Like the blocking paradigm, extensive training of the compound cue (AB+) abolishes the overshadowing effect (Fig. 3b), in agreement with experimental studies (see Stout et al., 2003).

In addition, the model shows that shifting background contexts during learning temporarily slows down the model's performance (Fig. 4a). This is known as the context shift effect. Supporting this finding, using fMRI, Hayes et al. (2007) found that changing background contexts slows down learning a recognition task, and that hippocampal region activation is key for correct task performance. Further, we also found that the context shift effect depends on the number of training trials in phase 1, such that extended training abolishes the

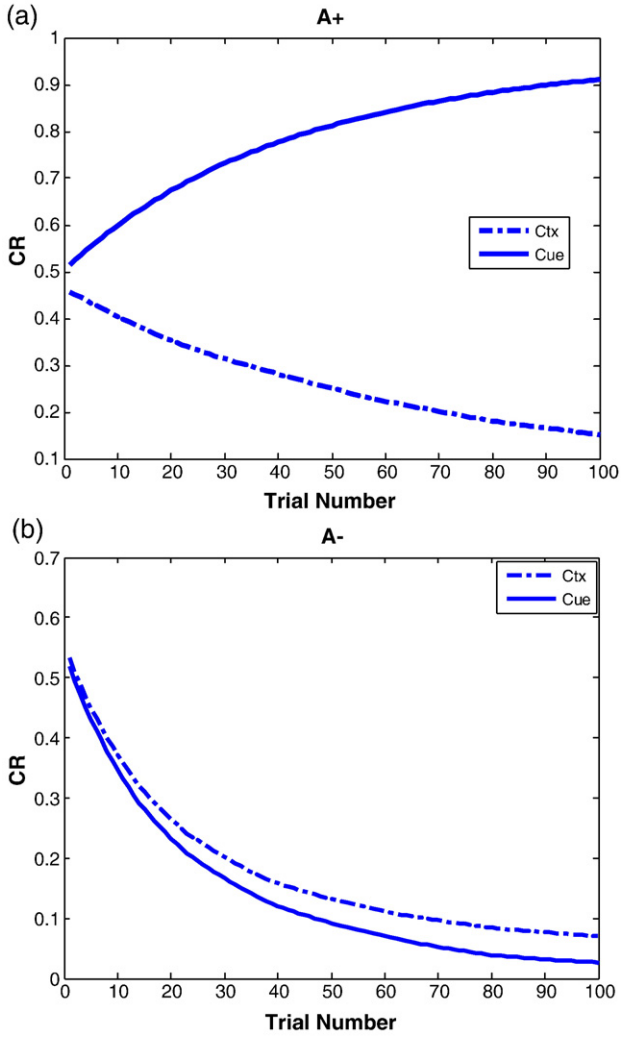

Fig. 1 – Simulation of the A+ and A– tasks. (a) A+ simulation: the model shows an increase in response to cue A, while it shows a decrease in response to the context since it is not always associated with the US presentation. A trial involves the presentation of context (alone) and then the presentation of context, A, and US (see Experimental procedures). (b) A– simulation: the model shows a decrease in response to both the context and cue A since neither is associated with the US presentation. A trial here involves the presentation of context alone and then the presentation of context and cue A. Abbreviation: ctx, context; CR, conditioned response (same abbreviation is used in all simulation studies mentioned below).

context shift effect (Fig. 4b) (see Hall and Honey, 1990). The interpretation of the context shift effect is that the model compresses the representations of the cue and context and shows a CR to their combined representation. A decrease in CR after shifting contexts is because the cue alone and not the context elicits the response. However, with extensive training, the model differentiates the representations of the cue and contexts and learns that it is only the cue that is consistently associated with the US and thus elicits a CR. Accordingly, a context shift after extensive training of A+ learning in phase 1 does not slow down learning.

Also, the model accounts for the sensory preconditioning effect. Training the model first on AB– trials and then on A+ trials leads to B eliciting a stronger CR than in a control condition that does not include AB– training (Fig. 5a). According to the model, this occurs because the hippocampal module compresses the representations of stimuli A and B during training in phase 1. Accordingly, training the model that A predicts the US leads some of this association to be transferred to B. This is not the case in a control condition in which the model is not trained on AB– trials (Fig. 5a). This is in agreement with experimental findings (Nicholson and Freeman, 2000). As conceptually similar to the sensory

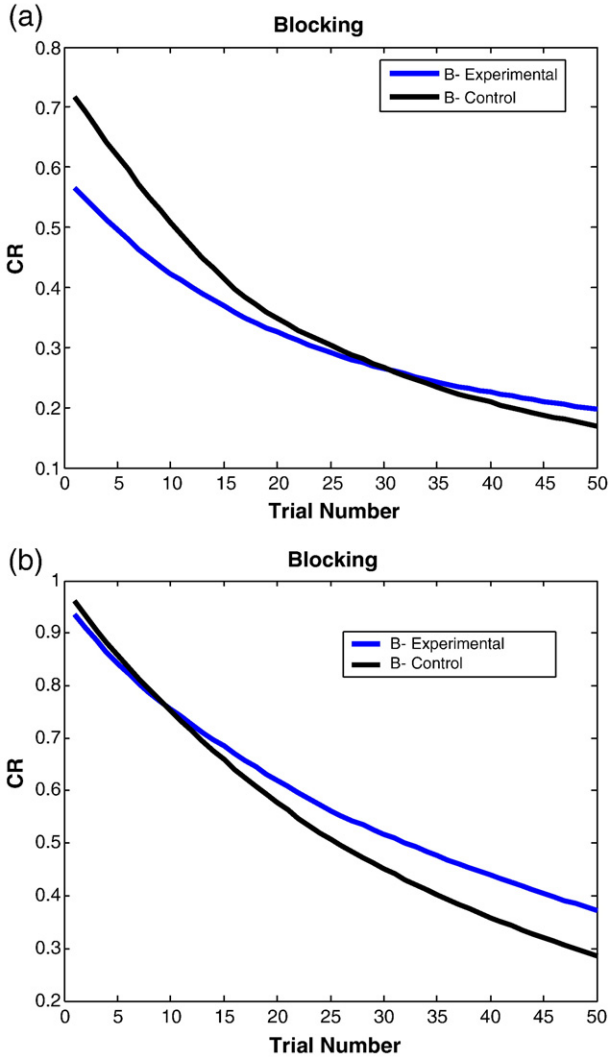

Fig. 2 – Performance in phase 3 of the blocking paradigm. (a) Standard blocking performance. A+ training followed by compound (AB+) training leads to B eliciting a weaker response than that of a control condition that does not include A+ training—hence the blocking effect. (b) Extended training in phase 2 of the compound (AB+) cue abolishes the blocking effect. Experimental and Control in the legend refer to experimental and control conditions.

preconditioning task, the model also accounts the compound preconditioning effect. Here, compound (AB–) training in phase 1 slows down learning to subsequently differentiate A– and B+ learning. Like the sensory preconditioning task, this is because the hippocampal module compresses the representations of stimuli A and B during training in phase 1. Learning to differentiate A+ and B– is faster in a control condition that does not include AB– training (Fig. 5b). Simulation results are qualitatively consistent with experimental findings of Lubow et al. (1976).

Along the same lines, the model also accounts for the latent inhibition effect: pretraining the model on A– trials, that is pre-exposure to cue A alone, slows down learning to subsequently associate A with the US (Fig. 6a). This is because the model compresses cue A with the background context during learning in phase 1, and this slows down learning to respond differently to the cue and context in phase 2. This is not the case in a control condition in which the model is not pretrained with A– trials. These simulation results are consistent with experimental findings (Shohamy et al., 2000). Interestingly, shifting background contexts at the beginning

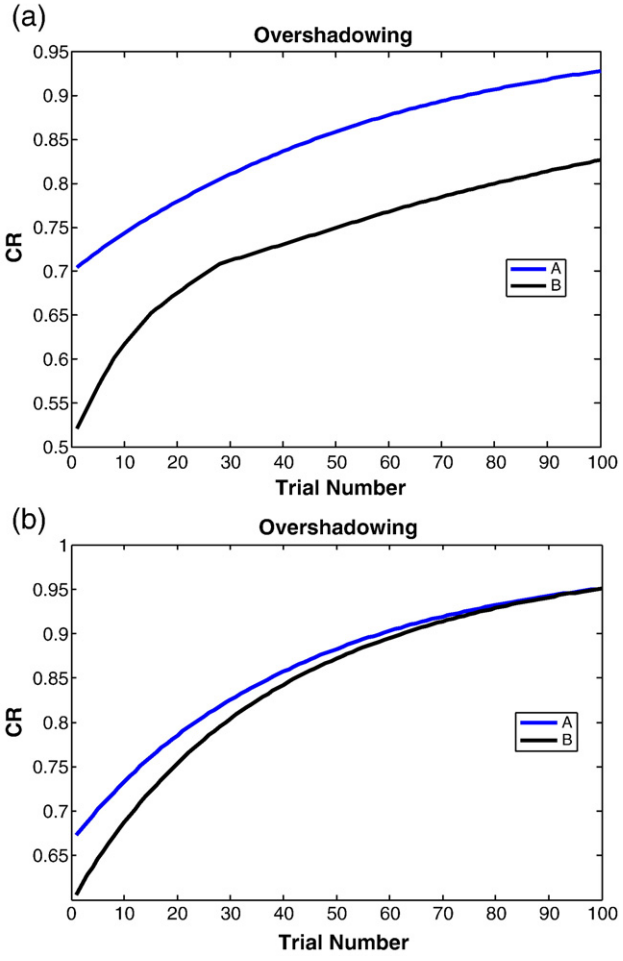

Fig. 3 – Performance in phase 2 of the overshadowing paradigm. (a) Standard task. A is more salient than B; here A elicits a stronger CR than that of B. (b) Extended training of phase 1 abolishes the overshadowing effect, as reported in experimental studies (Stout et al., 2003).

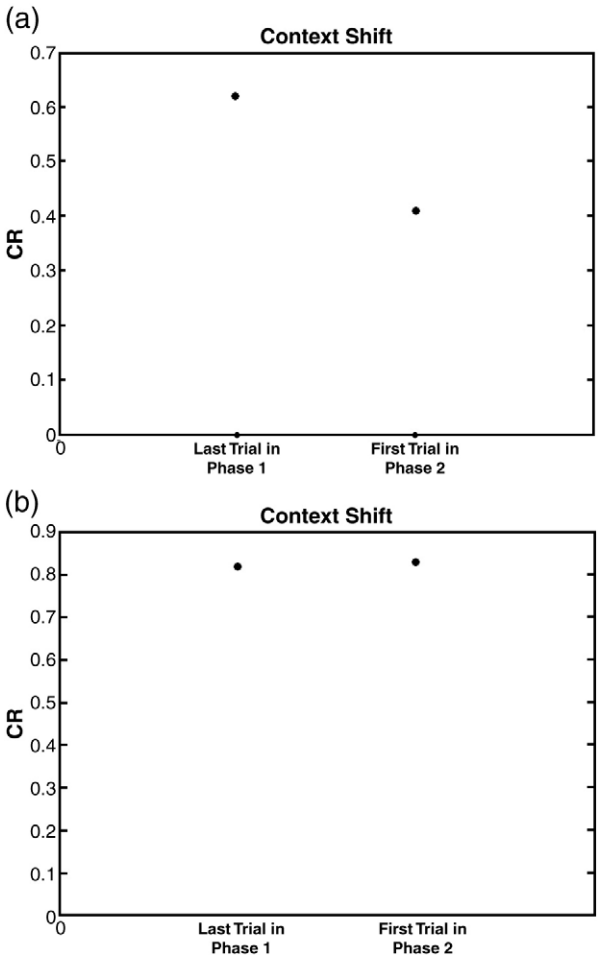

Fig. 4 – (a) Context shift slows down learning (i.e., context shift effect). (b) However, extended training in phase 1 abolishes the context shift effect.

learning in phase 2 (see Table 1) abolishes the latent inhibition effect (Fig. 6b), which is also qualitatively consistent with recent experimental results (Yap and Richardson, 2005). These findings support the theory that combining both the cue and context during training in phase 1 is possibly the mechanism underlying the latent inhibition effect (see below for further discussion on that).

Similarly the model accounts for the learned irrelevance effect (Fig. 6c). Simulation results show that prior exposure to A and US, uncorrelated with each other, slows subsequent acquisition of the CS–US association. Further, we found that extended training in phase 1 of the latent inhibition or learned irrelevance task exacerbates the observed effect. This is in agreement with the simulation results of the Turnock and Becker (2007) modeling study (described below). The same simulation results hold true with the simulations of the sensory preconditioning or compound preconditioning tasks (figures not shown).

The model also simulates performance in the acquired equivalence task. The model learns that two contexts become equivalent when similar events take place in them: In phase 1, the model learns that contexts X and Y are equivalent because cue A occurs in both and also learns that both contexts are

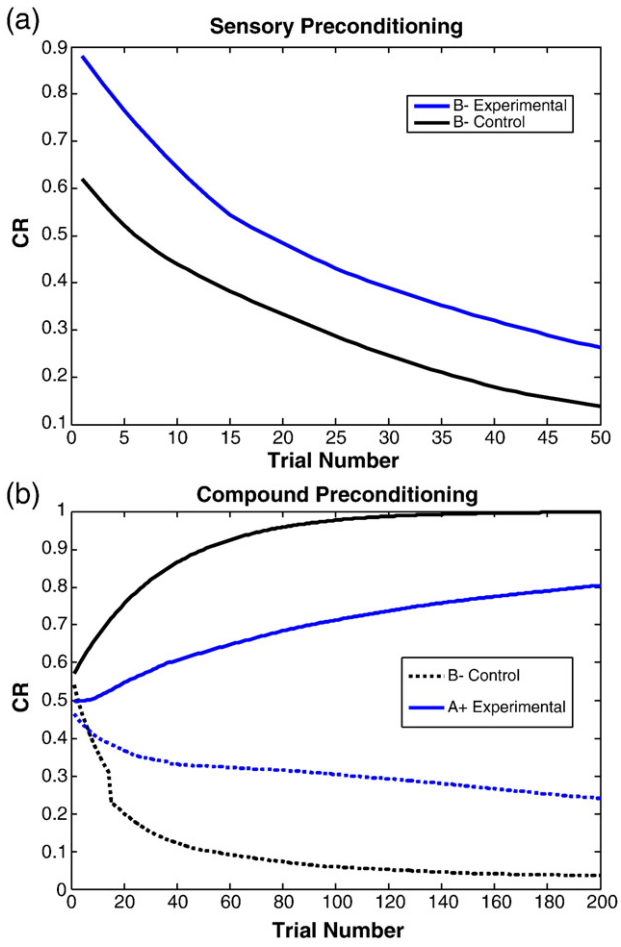

Fig. 5 – (a) Performance in phase 3 of the sensory preconditioning paradigm. Training the model first on AB– trials and then on A+ trials leads to B eliciting a stronger CR than in a control condition that does not include AB– training. (b) Performance in phase 2 in the compound preconditioning task: Compound (AB–) training in phase 1 slows down learning to respond differently to cues A and B in phase 2. As mentioned above, Experimental and Control in the legend refer to experimental and control conditions.

different from context Z since A does not occur in Z. Note that performing the acquired equivalence task requires both the compression of the representations of contexts X and Y and the differentiation of Z from both X and Y. Given that context X is associated with the US (because of learning in phase 2) and that context X is equivalent to context Y (because of learning in phase 1), the model learns that context Y predicts the US. Accordingly, in the third phase, the model's response to Y is stronger than its response to context Z (Fig. 7a). These simulation results are generally in agreement with experimental findings (Coutureau et al., 2002).

The model also simulates performance in the easy–hard transfer learning paradigm (Terrace, 1963). Here, training the

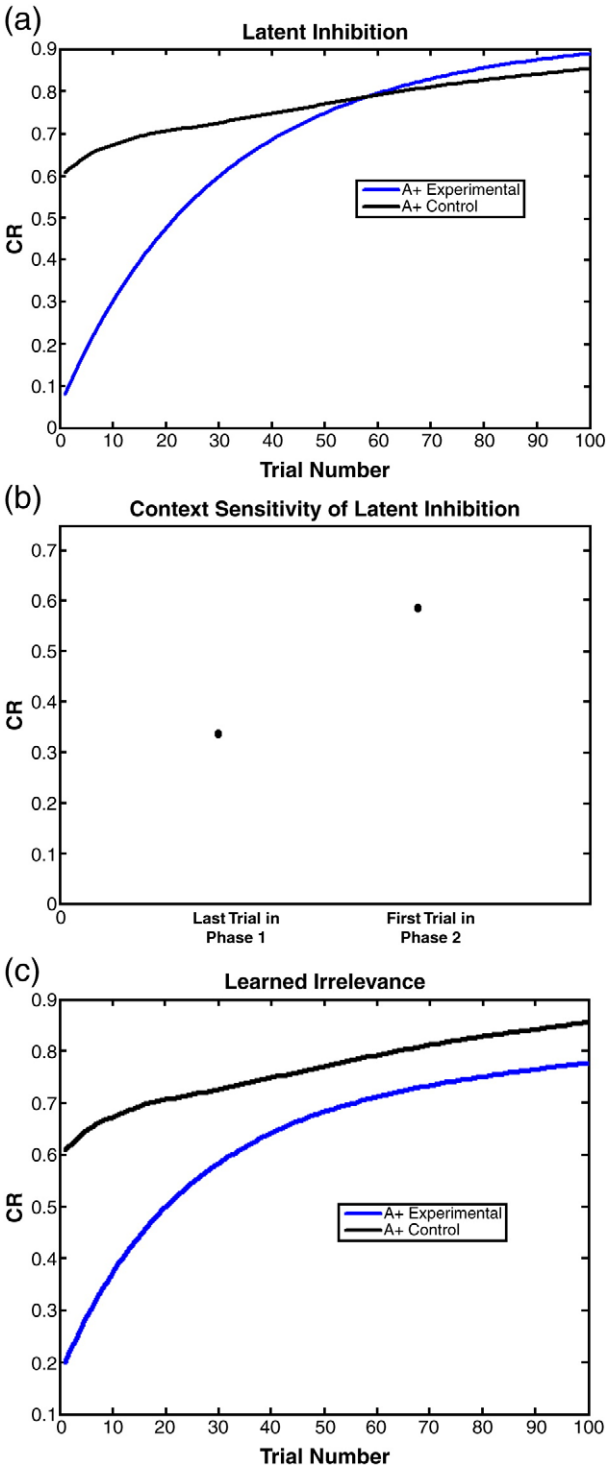

Fig. 6 – Latent inhibition and learned irrelevance. (a) Performance in phase 2 of the latent inhibition paradigm. Pretraining with cue A (alone) slows down learning to subsequently associate A with the US. (b) Context sensitivity of latent inhibition. Context shift between the preexposure (A–) and acquisition (A+) phases of the latent inhibition paradigm interferes with the latent inhibition effect. This is contrasted with the latent inhibition effect in which A– learning in phase 1 slows down learning in phase 2. (c) Performance in phase 2 of the Learned Irrelevance task. As similar to the latent inhibition effect, prior exposure to A and US, uncorrelated with each other, slows subsequent acquisition of the CS–US association.

model on easy discrimination (i.e., discriminating between two stimuli that have very different representations) facilitates learning a hard discrimination (i.e., discriminating

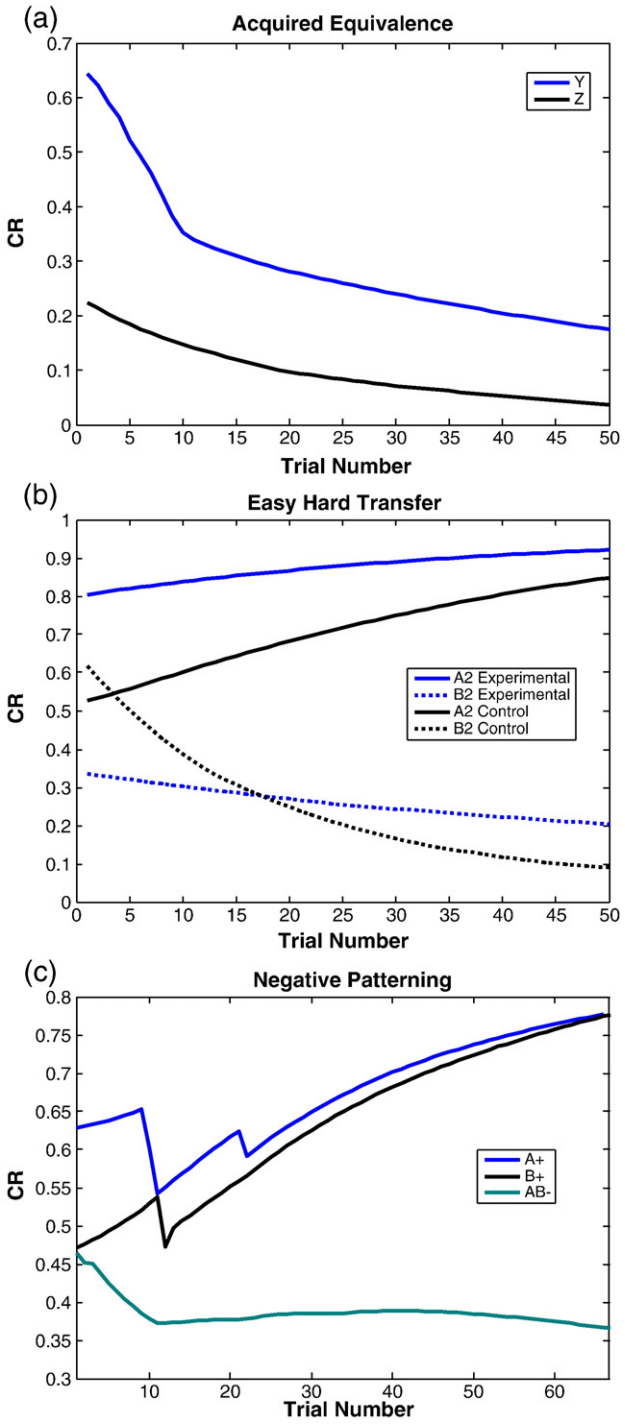

Fig. 7 – (a) Performance in phase 3 of the acquired equivalence task. The response to context Y is stronger than the response to context Z (see text for explanation). (b) Performance in phase 2 of the easy–hard transfer learning task. Training the model on easy discrimination facilitates learning a hard discrimination. This is not the case in a control condition in which the model is not trained on easy discrimination. (c) Negative patterning. The model learns to show a stronger response to cues A and B than to the compound cue (AB).

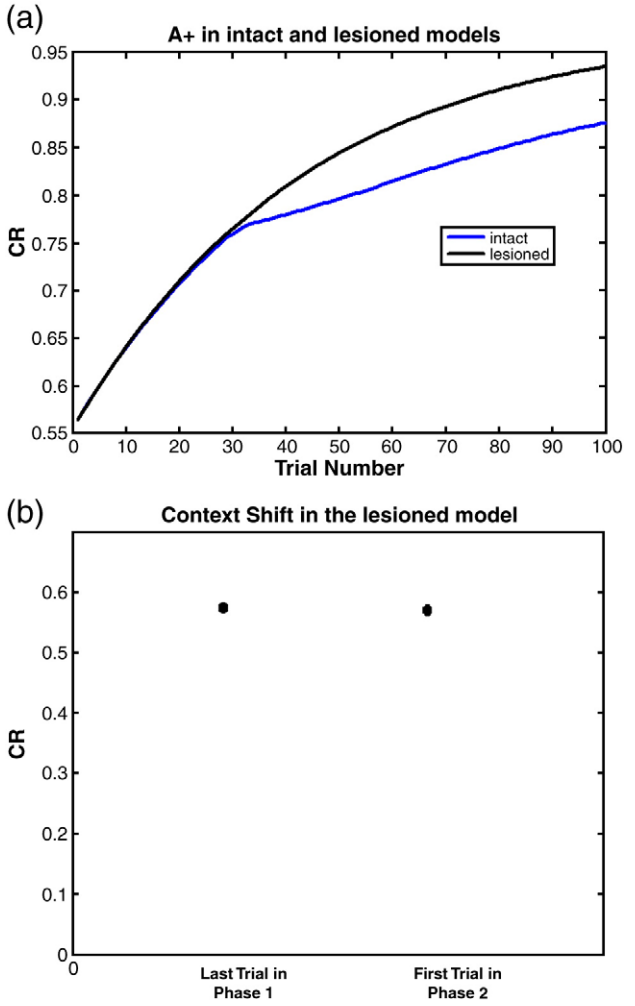

Fig. 8 – A+ and context shift performance in the hippocampal-lesioned model. (a) Lesioning the hippocampal module does not impair A+ learning but actually speeds up learning. (b) Unlike the intact model, the lesioned model did not show the context shift effect.

between two stimuli that have similar representation) (Fig. 7b). Finally, the model simulates performance in the negative patterning paradigm (Fig. 7c). The model learns to show a stronger response to cues A and B than to the compound cue (AB). This is because the model learns to form a representation of the compound cue (AB) that is different from the representations of A and B.

In short, the model here provides a unified account for performance in many different classical conditioning paradigms, including sensory preconditioning, compound preconditioning, acquired equivalence, easy–hard transfer, negative patterning, learned irrelevance, and latent inhibition.

2.2. *Lesion studies*

Here we test the behavioral effects of lesioning the hippocampal module on classical conditioning performance. Lesioning the hippocampal module is done by disabling learning in this module (see Fig. 11). The hippocampal-

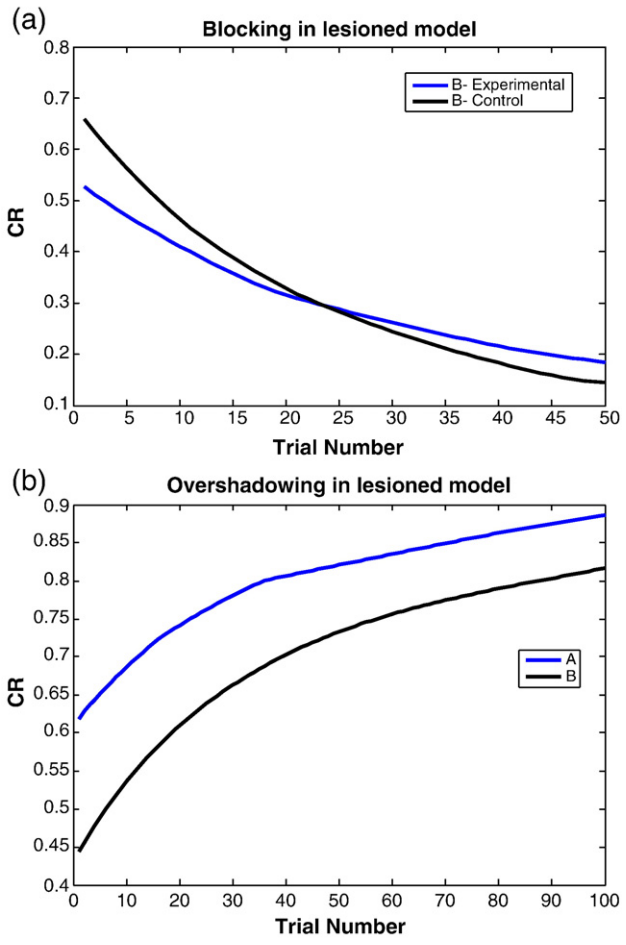

Fig. 9 – (a) Performance in phase 3 of the blocking paradigm in the hippocampal-lesioned model. Lesioning the hippocampal module does not have an effect on performance in the blocking paradigm; like the intact model, the lesioned model shows the blocking effect. (b) Performance in phase 2 of the overshadowing paradigm in the hippocampal-lesioned model. Lesioning the hippocampal module does not abolish the overshadowing effect, also in agreement with existing experiment studies (Garrud et al., 1984; Good and Macphail, 1994; Holland and Fox, 2003).

lesioned model does not form a representational code of input stimuli which could in turn lead to changes to classical conditioning performance.

For example, lesioning the hippocampal did not impair A+ performance. These simulated lesions actually speed up learning in our model (Fig. 8a), which is in agreement with many experimental studies (Eichenbaum et al., 1988; Gluck and Myers, 1993; Ito et al., 2005; Ito et al., 2006; Port et al., 1985; Schmaltz and Theios, 1972). The reason the intact model is slower than the lesioned model to learn A+ is because the intact model takes many trials to learn to dissociate the representations of the context and cue in the hippocampal module. In other words, the intact model learns (a) to differentiate the representations of context from cue in the hippocampal module and then (b) associate the representations of the cue and context in the MTC layer with the US presentation (and response). The lesioned model, however, only learns the latter mechanism—and thus it is faster. As for context shift, the lesioned model did not show the context shift effect even after a few learning trials (Fig. 8b) since it did

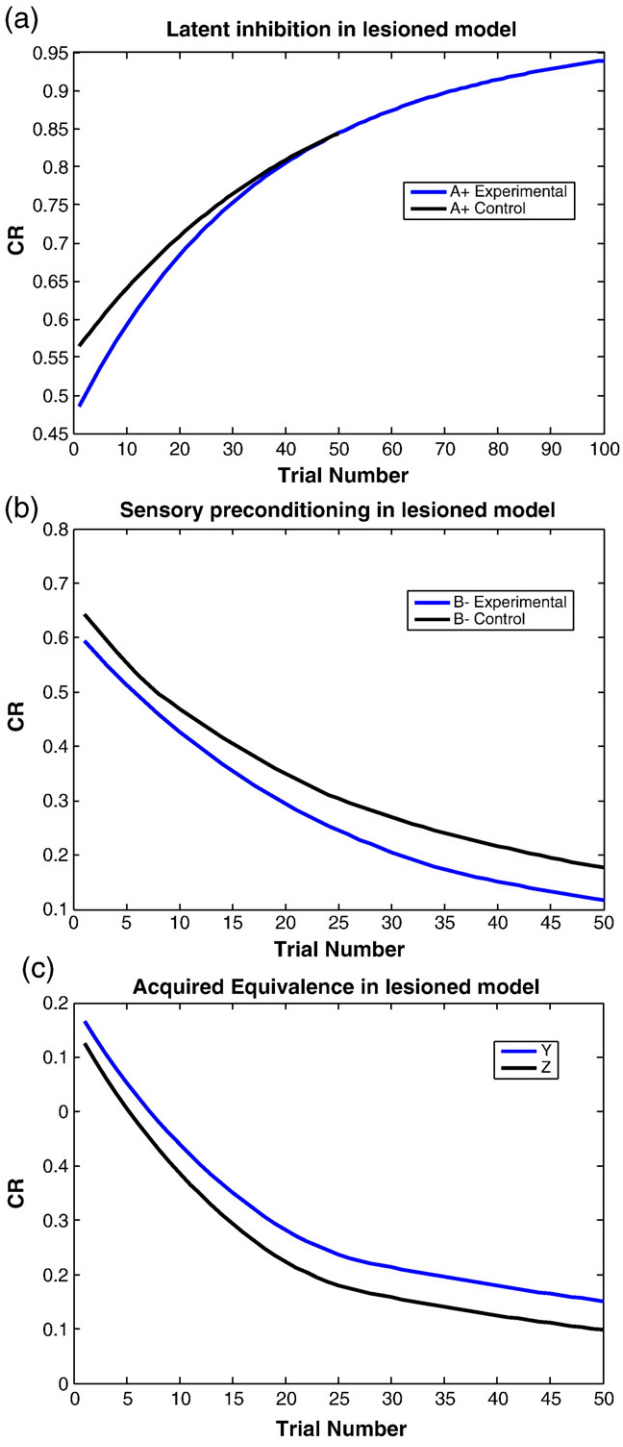

Fig. 10 – Performance in the latent inhibition, sensory preconditioning and acquired equivalence tasks in the hippocampal-lesioned model. In all of these tasks, the lesioned model did not show much difference between the control and experimental conditions, meaning that the lesioned model does not successfully simulate performance in these tasks.

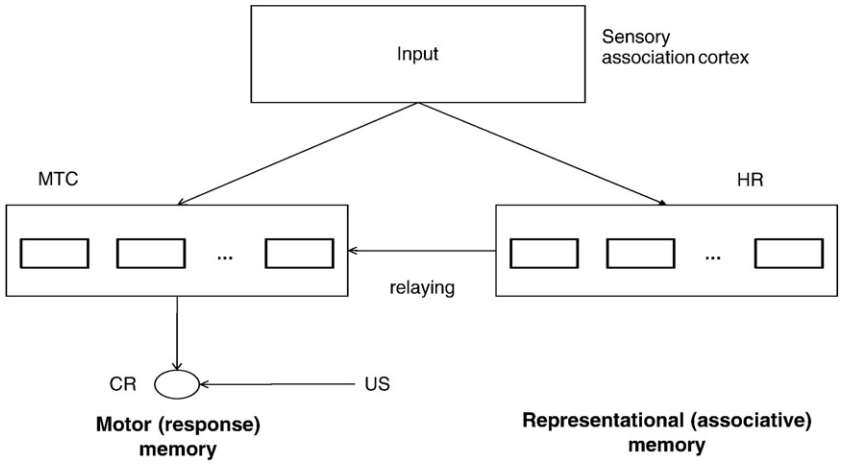

Fig. 11 – Model architecture. The model has four modules: cortical input, hippocampal region, MTC, and response unit. The sensory association layer represents input information. The hippocampal module is the key for associative memory (see text). The conditioned response (motor) learning module learns to make responses based on information relayed from the hippocampal layer. Each box inside the hippocampal module and MTC modules represents a patch of nodes. Hippocampal layer sends information to the MTC layer through a topographical mapping. The MTC layer is fully connected to the response unit. Activation of the response unit represents probability of conditioned response. The response unit possibly corresponds to a cerebellar mechanism (M. A. Gluck et al., 2001). Abbreviations: HR, hippocampal region; MTC, medial temporal cortex; CR, probability of a conditioned response (throughout the text will be used interchangeable with conditioned response or just response for simplification); US, unconditioned stimulus.

not learn to compress the representations of the cue and context.

Lesioning the hippocampal module also did not affect performance in the blocking paradigm (Fig. 9a), which is generally in agreement with existing experimental studies (Allen et al., 2002b; Garrud et al., 1984; Good and Macphail, 1994; Holland and Fox, 2003). Further, lesioning the hippocampus did not affect performance in the overshadowing task (Fig. 9b). Unlike the intact model, the hippocampal-lesioned model did not show much difference between the control and experimental conditions in the latent inhibition, sensory preconditioning, and acquired equivalence paradigms (Figs. 10a, b, and c), which means that the lesioned model does not successfully simulate performance in these tasks. These simulations results are generally in agreement with existing lesioning studies (Coutureau et al., 2002; Myers et al., 2003b; Nicholson and Freeman, 2000; Shohamy et al., 2000).

3. Discussion

Our revised model extends the Gluck and Myers (1993) model of classical conditioning by proposing an alternative more biological instantiation of the earlier model's theory of cortico–hippocampal interactions in classical conditioning. Like the earlier model, the new version captures the key findings in intact and hippocampal-lesioned animals for various classical conditioning phenomena including the latent inhibition, learned irrelevance, sensory preconditioning, acquired equivalence, easy–hard transfer learning, context shift effects, blocking, overshadowing, compound preconditioning, and negative patterning. Unlike the Gluck and Myers model, the current model shows that the use of Hebbian learning as well as plausible representation of inputs to the hippocampus can account for these classical conditioning effects. The findings that the hippocampal region is key for some classical conditioning tasks such as latent inhibition, acquired equivalence, and sensory preconditioning, but not others such as blocking, overshadowing, or simple conditioning, poses a theoretical problem since it is not clear what kind of computational processes the hippocampal region employs so that it can specifically account for these classical conditioning tasks. Our theory proposes that the hippocampal region is key for forming a representational code of input stimuli, which depends on their co-occurrence (Gluck et al., 2003; Gluck and Myers, 1993). This feature of our model explains why and how damage to the hippocampal region does not impair performance in the A+, overshadowing, or the blocking tasks (Allen et al., 2002b; Garrud et al., 1984; Good and Macphail, 1994; Holland and Fox, 2003) but impairs performance in latent inhibition, sensory preconditioning, and acquired equivalence tasks.

Specifically, the simulated hippocampal region in our model is key for compressing stimulus inputs that repeatedly co-occur. This mechanism explains the latent inhibition effect as described above (see Results section). One alternative theory of the latent inhibition effect is that presenting cue A by itself in phase 1 habituates subjects and makes them less prone to subsequently learn that A is associated with the US (Meeter et al., 2005). This theory is similar to the attentional theory of classical conditioning (Mackintosh, 1975) which assumes that the hippocampal region is key for attentional processes (Schmajuk and DiCarlo, 1992). This theory, however, does not account for the context sensitivity of latent inhibition effect, as found experimentally (Yap and Richardson, 2005). In addition, our theory also explains performance in the

sensory preconditioning and acquired equivalence tasks, all within a unified framework. Gluck and Myers (1993) simulated latent inhibition in a similar fashion. The Turnock and Becker (2007) model also simulated the latent inhibition effect yet it is not clear what role the hippocampus plays during the performance of latent inhibition tasks in this model (see below for a description of this model).

In addition, two features allow our model to form sparse representations of input stimuli. First, input stimuli that do not co-occur will have differentiated representation since it is not very likely that different input stimuli will be mapped to the same representations in the hippocampal module. Having a large number of hippocampal nodes in the model also further increase the likelihood that different input stimuli will be mapped to different nodes in the simulated hippocampal region. Differentiation of input stimuli is the default mode of the hippocampal module in our model. In other words, different input stimuli are very likely to be mapped to different representation in the hippocampal module unless these stimuli co-occur and will thus be compressed. This mechanism allows the model to account for performance in the acquired equivalence task, since the representations of control context Z will be mapped to different hippocampal nodes from nodes representing contexts X and Y (see Table 1 for task description). Second, simulating the hippocampal region's responses to the US presentation in our model helps increase the sparse representations of input stimuli. In other words, cues associated with the US presentation are more likely to have different representations from cues that are not associated with the US presentation. This mechanism allows the model to account for performance in the easy–hard transfer and negative patterning tasks. For example, in the negative patterning task, the model learns to form different representations of cues A and B from those of the compound cue (AB). Simulating the hippocampal region's responses to the US presentation in our model is also in agreement with neurophysiological studies (McEchron and Disterhoft, 1997, 1999). Gluck and Myers (1993) did not simulate performance in the negative patterning paradigm.

We also found that representational processes in the hippocampal module depend on the number of training trials employed in simulation studies. For example, the context shift effect is obtained if the number of training trials before changing the background context is low. Extended training of A+ in phase 1 makes the model learn that the cue alone predicts the US presentation and that context is irrelevant. Similarly, we found that extended training of the compound cue (AB+) abolished the blocking effect. This is because with extended training the representations of both A and B are compressed in the hippocampal module, and thus the model responds in a similar fashion to both A and B. This might explain why the blocking effect cannot be successfully established in some experimental studies; extended training could be one reason for not obtaining the blocking effect (Azorlosa and Cicala, 1988). The same rationale applies to the overshadowing effect which is also abolished with extensive training, as reported experimentally (Stout et al., 2003).

The findings that lesioning the hippocampal region does not affect performance in the overshadowing or blocking paradigms is generally in agreement with many existing experimental studies (Allen, Padilla et al., 2002b; Garrud et al., 1984; Good and Macphail, 1994; Holland and Fox, 2003), though some older studies found that lesioning the hippocampal region impairs blocking (Solomon, 1977). The findings that the number of training trials of compound cues plays a role in whether we obtain the overshadowing or blocking effects were shown experimentally (Azorlosa and Cicala, 1988; Good and Macphail, 1994; Pineno, 2006; Stout et al., 2003) but to our knowledge was not previously simulated in any model. The Rescorla–Wagner model does not account for these behavioral effects. The use of Hebbian learning in our model is key for accounting for these effects. This is because unlike the error backpropagation algorithm, the Hebbian learning algorithm allows weights to be continuously strengthened with further training. Thus, extended training of compound cues (AB) increases the associative links between the representations of cues A and B making it unlikely to obtain the blocking or overshadowing effects.

We have argued here that a computational model incorporating interactions among different memory systems can simulate various classical conditioning tasks including latent inhibition, learned irrelevance, sensory preconditioning, compound preconditioning, and acquired equivalence. Performance in these tasks cannot be accounted for by a response learning system alone, such as the Rescorla–Wagner model.

3.1. *Lesioning the hippocampus*

Electrophysiological studies showed that the hippocampus is involved in classical conditioning (Berger et al., 1976; McEchron and Disterhoft, 1997, 1999). However, some researchers argued that the hippocampal region is not key for classical conditioning because lesioning the hippocampus does not have a major impact on Pavlovian conditioning performance (Dusek and Eichenbaum, 1997; Phillips and LeDoux, 1992; Selden et al., 1991; Solomon et al., 1983). In agreement with such claims, we found that lesioning the hippocampal region does not impair simple classical conditioning learning as reported experimentally; in fact, these lesions actually speed up learning in our model, which is in agreement with experimental findings (Eichenbaum et al., 1988; Ito et al., 2005; Ito et al., 2006). In other words, the findings that hippocampal neurons respond to conditioned and unconditioned stimuli are in agreement with our model. We argue that responses of hippocampal neurons to conditioned and unconditioned stimuli are key for representational processes and not conditioned response learning. We, however, argue that the cerebellum is key for conditioned response learning, as suggested by several lesion studies (Chapman et al., 1990; Hu et al., 2009).

Finally, manipulations of the standard classical conditioning task, such as in the latent inhibition and sensory preconditioning tasks, were found to depend on the integrity of the hippocampal region (Nicholson and Freeman, 2000; Shohamy et al., 2000). In agreement with experimental studies, the model also shows that lesioning the hippocampal module impairs latent inhibition, sensory preconditioning, and acquired equivalence but not the standard blocking or simple conditioning tasks, which is in qualitatively consistent

with much of the existing lesion studies of the hippocampal region. Furthermore, our simulation results are generally in agreement with the findings that hippocampal region is key for contextual processes as reported in both animals (Bucci et al., 2000; Eacott and Gaffan, 2005) and humans (Hayes et al., 2007).

3.2. *Acquired equivalence*

It is important to note here that there are two different variations of the acquired equivalence task used in the literature. First, in the acquired equivalence task used by Coutureau et al. (2002), different contexts become equivalent (i.e., acquire similar representations) because similar events occur in them (e.g., cue A appears in both contexts; see Table 1). This is conceptually different from another acquired equivalence task (Bonardi et al., 1993) in which cues become equivalent because they are associated with the same response (or same cue). We simulated the former acquired equivalence task motivated by data regarding the role of the hippocampal region in its performance. We do not know of any lesion study that tests if the hippocampal region subserves performance in the latter version of the acquired equivalence task, though one neuropsychological study suggests that the hippocampal region is key for its performance in humans (Myers et al., 2003a).

The acquired equivalence paradigm (see Table 1) can alternatively be simulated in a computational model that has different nodes representing different cues and contexts and only learns to strengthen connections between these nodes during learning. For example, in AX– trials, such model can learn to strengthen a connection between the representations of X and A. The same holds true for AY– and X+ trials. Through successive activations of different units, the presentation of Y will elicit a stronger response than the response associated with context Z. This is because weights connecting Z to A, X, or the US, were not strengthened during learning. In our model, compression of contexts X and Y and the differentiation of both of them from Z is the mechanism by which the model performs the acquired equivalence task. We do not have much experimental data by which we can assess which model is more psychologically or biologically plausible. However, the neural mechanism underlying the performance of the acquired equivalence task in our model also explains performance in other classical conditioning tasks, such as latent inhibition and context shift, which cannot be simulated using the other hypothetical network model. Thus, our model provides a unified account for performance in different classical conditioning phenomena.

One difference between the acquired equivalence and sensory preconditioning paradigms is that two cues become equivalent (i.e., acquire similar representations) in the sensory preconditioning task because they are presented together as a compound cue while in the acquired equivalence task two cues or contexts become equivalent because each is separately associated with the same cue or response. Another difference between these two paradigms is that performing the acquired equivalence task may require differentiation processes (i.e., forming different representations of contexts X and Y from those of Z) while this does not seem to be the case in the sensory preconditioning paradigm. It is important to note here that Gluck and Myers (1993) did not simulate performance in the acquired equivalence paradigm though that model can readily simulate this task.

3.3. *Comparison to other models*

Most models of the hippocampal region focus on simulating episodic and spatial learning tasks (Foster et al., 2000; Hasselmo et al., 2002; Hasselmo and Eichenbaum, 2005; Hasselmo and Wyble, 1997; McClelland et al., 1995; O'Reilly and Norman, 2002; Siekmeier et al., 2007). Some other modeling work, however, suggests that the hippocampal region including the parahippocampal region is important for buffering information across short delays (Hasselmo et al., 2000). Even though our models do not incorporate such a mechanism, they do not necessarily disagree with Hasselmo's (2000)model. The Hasselmo model simulated performance in delayed sample to matching tasks, which requires subjects to maintain a cue during a delay and respond when that cue matches one of many cues presented during the delay. It might be the case that the hippocampal region implements both functions: buffering information across short delays (i.e., short-term memory) and associative memory. Short-term memory buffering was not necessary for the simulations of the Pavlovian conditioning paradigms presented here, although it probably plays a key role in classical conditioning where there is a long interval between cue onset and US onset as in the trace conditioning paradigm (see section below on Model limitations).

3.3.1. *Hippocampal models of Pavlovian conditioning*

Unlike episodic memory, fewer models in the literature have addressed the role of the hippocampal region in Pavlovian conditioning. One notable exception is a neurocomputational model proposed by Turnock and Becker (2007) which simulated performance in contextual conditioning tasks. This model assumes that the hippocampal region subserves rapid encoding of contextual information and is key for gating prefrontal cortex information into the basal ganglia. Accordingly, the model shows that the hippocampus (via interaction with the ventral striatum and prefrontal cortex) is key for flexible behavioral control especially when context is shifted (Hall and Channell, 1986; Yap and Richardson, 2005). The Turnock and Becker model simulates interactions between the hippocampus and ventral striatum that are beyond the scope of the current hippocampal model. Turner and Becker did not, however, simulate some classical conditioning paradigms that are known to be subserved by the hippocampal region, such as sensory preconditioning and acquired equivalence.

Further, unlike Turner and Becker's model, our hippocampal model does not treat (background) contexts any differently from other cues. It is not plausible to assume beforehand that contextual information, but not other neutral or conditioned cues, has a special or privileged input to the hippocampus. The findings that the hippocampal module treats contextual information differently from other cues, as reported in many experimental studies (O'Reilly and Norman, 2002; Phillips and LeDoux, 1992; Rudy and O'Reilly, 1999), was not assumed

beforehand but came out from the dynamics and learning processes in our model.

Gluck, Myers, and other colleagues (Gluck et al., 2003; Gluck and Myers, 1993; Meeter et al., 2005; Myers et al., 1996) provided a series of connectionist models that attempt to explain how the hippocampal region contributes to performance in different classical conditioning paradigms. Specifically these models argue that the hippocampal region is key for differentiation and compression of the representations of stimuli (see Introduction for description of these processes). This is a plausible theory because it accounts for many associative learning paradigms whose performance was found to rely on the integrity of the hippocampal region. Some of the models' predictions have also been recently confirmed in recent fMRI studies in healthy subjects, including findings that the hippocampal region subserves stimulus differentiation (Kumaran and Maguire, 2006) and is also key for associative learning tasks (Poldrack et al., 2001). Subsequent models attempt to address the differential functions of hippocampus subregions, including the septum (Myers et al., 1998; Myers et al., 1996) and entorhinal cortex (Myers et al., 1995), in associative learning. Unlike these earlier models, our model assumes that the hippocampal region responds to all input stimuli: cues (CSs and US) and contexts.

Further, Myers et al. (1995) proposed a computational model which suggests that the entorhinal cortex is important for stimulus compression. Though this model accounts for the latent inhibition and context shift effects, it did not simulate tasks that are presumably supposed to require differentiation processes, such as negative patterning, acquired equivalence (Coutureau et al., 2002), and easy–hard transfer (Terrace, 1963). Myers et al. argue that differentiation processes are subserved by the hippocampus proper (including dentate gyrus) (for more discussion on this, see Gluck et al., 2003).

3.4. *Model limitations*

Although the model accounts for various classical conditioning phenomena, it has some limitations. First, the model simulates the hippocampal region only as one module and only simulates a subset of processes ascribed to the hippocampal region. Our model is not intended to provide a unified theory of the hippocampal function; it only attempts to provide a theory of the role of the hippocampal region in associative learning and classical conditioning. The model does not provide an account for how the hippocampal region is key for recognition (Hasselmo et al., 2000) or episodic memory (Hayes et al., 2007; Moscovitch et al., 2006). The model also does not simulate performance in delayed matching tasks, which are known to depend on the integrity of the entorhinal cortex (McGaughy et al., 2005; Young et al., 1997). This is because our model is a trial-level model and simulating delayed matching tasks requires the simulations of intra-trial temporal information. Moreover, the model does not simulate performance in trace conditioning tasks where there is a long interval between cue offset and US onset. Experimental studies show that performance in trace conditioning tasks depends on the integrity of the hippocampal region (Ryou et al., 2001; Solomon et al., 1986).

Furthermore, one limitation of the model is that it only provides a qualitative fit to existing behavioral data, even though simulation and experimental results are generally in the same direction. This is because the model has a few free parameters and attempts to account for various experimental data. In order to provide a quantitative fit to various behavioral results, a neural model will require having many free parameters and possibly more complex architecture. So we believe that the simplicity of the model is the reason for why it only provides a qualitative fit to experimental data.

Furthermore, the model does not address the roles of some brain areas in classical conditioning. It is known that different brain areas, including the basal ganglia, play a role in classical conditioning tasks, such as sensory preconditioning (Suri, 2001;Young et al., 1998) and blocking (Gallo and Candido, 1995). Current work at our lab attempts to simulate intra-trial information and thus address the role of the hippocampal region in trace conditioning as well as other cognitive tasks. We will also seek in future work to further address the role of the hippocampal region in interacting with other brain regions. It is possibly the case that simulating the contributions of other relevant brain structures to classical conditioning will allow our future extension of the model to provide quantitative fits to behavioral data.

Furthermore, our model simulates the role of the hippocampus in acquisition of classical conditioning tasks. With regard to long-term retention processes, it is not clear in the literature what the exact contributions of the hippocampus and medial temporal cortex are, even though some physiological studies point to a key role of the hippocampus in learning but not necessarily performance or long-term retention (McEchron and Disterhoft, 1999). Our model, in its current form, assumes that the hippocampal region is needed to transfer learned representational codes of the input stimuli to other brain structures. However, one possible extension of the model could be the inclusion of a cortical learning mechanism that acquires information about learned representational codes that does not require hippocampal processes in late stages of learning, as has been proposed in other models of the basal ganglia function (Ashby et al., 2005; Frank, 2005; Moustafa and Maida, 2007).

To sum up, our model provides a unified mechanistic account for (a) many classical conditioning tasks, such as latent inhibition, sensory preconditioning, and compound conditioning; (b) how the number of training trials of compound cues might interfere with classical conditioning effects, including blocking and overshadowing; and (c) how lesioning the hippocampal module impairs, enhances, or has no effect on the performance of classical conditioning tasks.

4. Experimental procedures

Here, we describe the model architecture, learning algorithms, and behavioral tasks we simulate.

The model has four modules: cortical input, hippocampal region, medial temporal cortex (MTC), and response unit (Fig. 11). The hippocampal and MTC modules employ different memory processes, and learning is different in each segment. In the hippocampal module, learning is Hebbian (Bilkey, 1996).

The MTC module, on the other hand, is key for (conditioned) response learning (Gluck et al., 2001). Both the MTC and hippocampal layers have many patches (i.e., a separate group of neurons). Within each patch of the hippocampal layer, a winner-take-all (WTA) network computes the most active neuron, and silences the remaining neurons in the patch, a process representing lateral inhibition through interneuron interactions with principal cells (de Curtis and Pare, 2004).

4.1. Simulation details

The model simulates performance in different classical conditioning tasks (see Table 1). In all simulation studies presented here, A and B are used to refer to cues while X, Y, and Z are used to refer to background contexts (e.g., different features of the testing box and/or other external cues that might have been used by the subjects during learning). We also study the effects of lesioning the hippocampal region on classical conditioning performance. Lesioning the hippocampal module is done by disabling learning in this module.

The model was implemented using Matlab. The model has four segments: sensory association cortex (input layer), hippocampal region, MTC, and output node. The input layer is fully connected to both hippocampal module and MTC. The MTC is fully connected to the output node.

Each trial has 4 time steps; the first two time steps always included the presentation of context alone mimicking the presence of animal inside a box (i.e., context) before the cue presentation. Depending on the simulation experiments, the latter two time steps might include the presentation of cues as well as contexts (see Table 1 for more details).

The input pattern consists of a 48-bit stimulus vector. This can specify the values of up to 2 conditioned stimuli, 3 contextual cues, and one unconditioned stimulus. Each stimulus is represented using an 8-bit vector.

Activation levels of all units in the model are computed as follows:

$$A_j(t) = f\left(\sum_{i=1}^{n} u_{ji}(t)x_i(t)\right)$$

where u_{ji} is the weight connecting unit i to unit j, n is the number of units in the input; the input units take binary (0,1) values (for similar simulation details see Barto, 1995; Schultz et al., 1997; Suri and Schultz, 1999); t is time step, f is the logistic sigmoid function:

$$f(x) = \frac{1}{1+e^{-x}}$$

Weights are updated at every time step. Weight update is different in the different modules (see below).

4.2. Hippocampal module (associative learning system)

The hippocampal module is a 2-layer network in which the sensory association cortex (input) layer is fully connected to the hippocampal layer. Learning in this network is Hebbian. The weight update rule here is as follows:

$$w_{ji}(t+1) = w_{ji}(t) + \alpha_h x_i(t) y_j(t)$$

where α_h is the learning rate for the hippocampal module (0.002 in the simulations presented here); x_i represents activation level of cortical input unit i; y_j represents the activation level of the unit j in the hippocampal layer. The hippocampal layer consists of many patches of neurons (10 patches and each patch has 20 nodes), each forms a separate representational code of the input. Winner-take-all networks are used to simulate lateral inhibitory connections among neurons in each patch. A hippocampal representation is projected to the MTC layer. There is one-to-one connection from hippocampal layer to MTC, with non-adaptive, fixed weights.

4.3. MTC module (response learning system)

The MTC module is a 2-layer network. The cortical input layer is fully connected to the MTC layer which in turn is fully connected to the response unit. Weights from the input layer to the MTC layer are non-adaptive, making hippocampal input to the MTC layer more effective in driving its activity. Weights from MTC layer to the response unit are updated according to the delta rule as follows:

$$w_i(t+1) = w_i(t) + \alpha_c(\gamma(t) - R(t))m_i(t)$$

where α_c is the learning rate for the MTC module (0.02 in the simulations presented here); γ represents the presence/salience of the US (it takes the value 1 if the US is present and 0 if not present); m_i is the activity of MTC unit i; $R(t)$ is the activation of the response unit. All weights in the model were initialized to random values in the range [0, 0.4].

We simulated lesion by disabling weight update in the hippocampal module. Activation of the MTC module's output node is interpreted as the probability of producing a conditioned response, which in turn represents the likelihood that the model will produce a conditioned response. This can be directly compared to observed conditioned responses in experimental studies.

REFERENCES

Allen, M.T., Chelius, L., Masand, V., Gluck, M.A., Myers, C.E., Schnirman, G., 2002a. A comparison of latent inhibition and learned irrelevance pre-exposure effects in rabbit and human eyeblink conditioning. Integr. Physiol. Behav. Sci. 37 (3), 188–214.

Allen, M.T., Padilla, Y., Myers, C.E., Gluck, M.A., 2002b. Selective hippocampal lesions disrupt a novel cue effect but fail to eliminate blocking in rabbit eyeblink conditioning. Cogn. Affect. Behav. Neurosci. 2 (4), 318–328.

Apostolova, L.G., Dinov, I.D., Dutton, R.A., Hayashi, K.M., Toga, A.W., Cummings, J.L., 2006. 3D comparison of hippocampal atrophy in amnestic mild cognitive impairment and Alzheimer's disease. Brain 129 (Pt 11), 2867–2873.

Ashby, F.G., Ell, S.W., Valentin, V.V., Casale, M.B., 2005. FROST: a distributed neurocomputational model of working memory maintenance. J. Cogn. Neurosci. 17 (11), 1728–1743.

Azorlosa, J.L., Cicala, G.A., 1988. Increased conditioning in rats to a blocked CS after the first compound trial. Bull. Psychon. Soc. 26, 254–257.

Barto, A.G., 1995. Adaptive critics and the basal ganglia. In: Houk, J.C., Davis, J.L., Beiser, D.G. (Eds.), Models of Information

Processing in the Basal Ganglia (pp. xii, 382 p.). MIT Press, Cambridge, Mass.
Berger, T.W., Alger, B., Thompson, R.F., 1976. Neuronal substrate of classical conditioning in the hippocampus. Science 192 (4238), 483–485.
Bilkey, D.K., 1996. Long-term potentiation in the in vitro perirhinal cortex displays associative properties. Brain Res. 733 (2), 297–300.
Bliss, T.V., Lomo, T., 1973. Long-lasting potentiation of synaptic transmission in the dentate area of the anaesthetized rabbit following stimulation of the perforant path. J. Physiol. 232 (2), 331–356.
Bonardi, C., Rey, V., Richmond, M., Hall, G., 1993. Acquired equivalence of cues in pigeon autoshaping: effects of training with common consequences and common antecedents. Anim. Learn. Behav. 21, 369–376.
Bucci, D.J., Phillips, R.G., Burwell, R.D., 2000. Contributions of postrhinal and perirhinal cortex to contextual information processing. Behav. Neurosci. 114 (5), 882–894.
Bunsey, M., Eichenbaum, H., 1995. Selective damage to the hippocampal region blocks long-term retention of a natural and nonspatial stimulus–stimulus association. Hippocampus 5 (6), 546–556.
Chapman, P.F., Steinmetz, J.E., Sears, L.L., Thompson, R.F., 1990. Effects of lidocaine injection in the interpositus nucleus and red nucleus on conditioned behavioral and neuronal responses. Brain Res. 537 (1–2), 149–156.
Collie, A., Myers, C., Schnirman, G., Wood, S., Maruff, P., 2002. Selectively impaired associative learning in older people with cognitive decline. J. Cogn. Neurosci. 14 (3), 484–492.
Coutureau, E., Killcross, A.S., Good, M., Marshall, V.J., Ward-Robinson, J., Honey, R.C., 2002. Acquired equivalence and distinctiveness of cues: II. Neural manipulations and their implications. J. Exp. Psychol., Anim. Behav. Processes 28 (4), 388–396.
de Curtis, M., Pare, D., 2004. The rhinal cortices: a wall of inhibition between the neocortex and the hippocampus. Prog. Neurobiol. 74 (2), 101–110.
de Leon, M.J., George, A.E., Stylopoulos, L.A., Smith, G., Miller, D.C., 1989. Early marker for Alzheimer's disease: the atrophic hippocampus. Lancet 2 (8664), 672–673.
Dusek, J.A., Eichenbaum, H., 1997. The hippocampus and memory for orderly stimulus relations. Proc. Natl. Acad. Sci. U. S. A. 94 (13), 7109–7114.
Eacott, M.J., Gaffan, E.A., 2005. The roles of perirhinal cortex, postrhinal cortex, and the fornix in memory for objects, contexts, and events in the rat. Q. J. Exp. Psychol., B. 58 (3–4), 202–217.
Eichenbaum, H., 2003. How does the hippocampus contribute to memory? Trends Cogn. Sci. 7 (10), 427–429.
Eichenbaum, H., Fagan, A., Mathews, P., Cohen, N.J., 1988. Hippocampal system dysfunction and odor discrimination learning in rats: impairment or facilitation depending on representational demands. Behav. Neurosci. 102 (3), 331–339.
Farkas, M., Polgar, P., Kelemen, O., Rethelyi, J., Bitter, I., Myers, C.E., et al., 2008. Associative learning in deficit and nondeficit schizophrenia. Neuroreport 19 (1), 55–58.
Foster, D.J., Morris, R.G., Dayan, P., 2000. A model of hippocampally dependent navigation, using the temporal difference learning rule. Hippocampus 10 (1), 1–16.
Frank, M.J., 2005. Dynamic dopamine modulation in the basal ganglia: a neurocomputational account of cognitive deficits in medicated and nonmedicated Parkinsonism. J. Cogn. Neurosci. 17 (1), 51–72.
Gallo, M., Candido, A., 1995. Dorsal hippocampal lesions impair blocking but not latent inhibition of taste aversion learning in rats. Behav. Neurosci. 109 (3), 413–425.
Garrud, P., Rawlins, J.N., Mackintosh, N.J., Goodall, G., Cotton, M.M., Feldon, J., 1984. Successful overshadowing and blocking in hippocampectomized rats. Behav. Brain Res. 12 (1), 39–53.
Gluck, M.A., Bower, G.H., 1988. From conditioning to category learning: an adaptive network model. J. Exp. Psychol. Gen. 117 (3), 227–247.
Gluck, M.A., Myers, C.E., 1993. Hippocampal mediation of stimulus representation: a computational theory. Hippocampus 3 (4), 491–516.
Gluck, M.A., Myers, C., 2001. Gateway to Memory: An Introduction to Neural Network Modeling of the Hippocampus and Learning. MIT Press, Cambridge, Mass.
Gluck, M.A., Allen, M.T., Myers, C.E., Thompson, R.F., 2001. Cerebellar substrates for error correction in motor conditioning. Neurobiol. Learn. Mem. 76 (3), 314–341.
Gluck, M.A., Meeter, M., Myers, C.E., 2003. Computational models of the hippocampal region: linking incremental learning and episodic memory. Trends Cogn. Sci. 7 (6), 269–276.
Good, M., Macphail, E.M., 1994. Hippocampal lesions in pigeons (*Columba livia*) disrupt reinforced preexposure but not overshadowing or blocking. Q. J. Exp. Psychol. B. 47 (3), 263–291.
Hall, G., Channell, S., 1986. Context specificity of latent inhibition in taste aversion learning. Q. J. Exp. Psychol., B. 38 (2), 121–139.
Hall, G., Honey, R.C., 1990. Context-specific conditioning in the conditioned-emotional-response procedure. J. Exp. Psychol., Anim. Behav. Processes 16 (3), 271–278.
Hall, G., Ray, E., Bonardi, C., 1993. Acquired equivalence between cues trained with a common antecedent. J. Exp. Psychol., Anim. Behav. Processes 19 (4), 391–399.
Hasselmo, M.E., Eichenbaum, H., 2005. Hippocampal mechanisms for the context-dependent retrieval of episodes. Neural. Netw. 18 (9), 1172–1190.
Hasselmo, M.E., Wyble, B.P., 1997. Free recall and recognition in a network model of the hippocampus: simulating effects of scopolamine on human memory function. Behav. Brain Res. 89 (1–2), 1–34.
Hasselmo, M.E., Fransen, E., Dickson, C., Alonso, A.A., 2000. Computational modeling of entorhinal cortex. Ann. N.Y. Acad. Sci. 911, 418–446.
Hasselmo, M.E., Bodelon, C., Wyble, B.P., 2002. A proposed function for hippocampal theta rhythm: separate phases of encoding and retrieval enhance reversal of prior learning. Neural. Comput. 14 (4), 793–817.
Hayes, S.M., Nadel, L., Ryan, L., 2007. The effect of scene context on episodic object recognition: parahippocampal cortex mediates memory encoding and retrieval success. Hippocampus 17 (9), 873–889.
Henke, K., Buck, A., Weber, B., Wieser, H.G., 1997. Human hippocampus establishes associations in memory. Hippocampus 7 (3), 249–256.
Holland, P.C., Fox, G.D., 2003. Effects of hippocampal lesions in overshadowing and blocking procedures. Behav. Neurosci. 117 (3), 650–656.
Hu, B., Lin, X., Huang, L.S., Yang, L., Feng, H., Sui, J.F., 2009. Involvement of the ipsilateral and contralateral cerebellum in the acquisition of unilateral classical eyeblink conditioning in guinea pigs. Acta. Pharmacol. Sin. 30 (2), 141–152.
Ito, R., Everitt, B.J., Robbins, T.W., 2005. The hippocampus and appetitive Pavlovian conditioning: effects of excitotoxic hippocampal lesions on conditioned locomotor activity and autoshaping. Hippocampus 15 (6), 713–721.
Ito, R., Robbins, T.W., McNaughton, B.L., Everitt, B.J., 2006. Selective excitotoxic lesions of the hippocampus and basolateral amygdala have dissociable effects on appetitive cue and place conditioning based on path integration in a novel Y-maze procedure. Eur. J. Neurosci. 23 (11), 3071–3080.
Kamin, L.J., 1969. Predictability, surprise, attention, and conditioning. In: Campbell, B.A., Church, R.M. (Eds.),

Punishment and Aversive Behavior. Appleton-Century-Crofts, New York, pp. 279–296.
Kumaran, D., Maguire, E.A., 2006. The dynamics of hippocampal activation during encoding of overlapping sequences. Neuron 49 (4), 617–629.
Lubow, R.E., 1973. Latent inhibition. Psychol. Bull. 79 (6), 398–407.
Lubow, R.E., Rifkin, B., Alek, M., 1976. The context effect: the relationship between stimulus pre-exposure and environmental pre-exposure determines subsequent learning. J. Exp. Psychol. 2, 38–47.
Mackintosh, N.J., 1975. A theory of attention: variations in the associability of stimuli with reinforcement. Psychol. Rev. 82, 276–298.
McClelland, J.L., McNaughton, B.L., O Reilly, R.C., 1995. Why there are complementary learning systems in the hippocampus and neocortex: insights from the successes and failures of connectionist models of learning and memory. Psychol. Rev. 102 (3), 419–457.
McEchron, M.D., Disterhoft, J.F., 1997. Sequence of single neuron changes in CA1 hippocampus of rabbits during acquisition of trace eyeblink conditioned responses. J. Neurophysiol. 78 (2), 1030–1044.
McEchron, M.D., Disterhoft, J.F., 1999. Hippocampal encoding of non-spatial trace conditioning. Hippocampus 9 (4), 385–396.
McGaughy, J., Koene, R.A., Eichenbaum, H., Hasselmo, M.E., 2005. Cholinergic deafferentation of the entorhinal cortex in rats impairs encoding of novel but not familiar stimuli in a delayed nonmatch-to-sample task. J. Neurosci. 25 (44), 10273–10281.
Meeter, M., Myers, C.E., Gluck, M.A., 2005. Integrating incremental learning and episodic memory models of the hippocampal region. Psychol. Rev. 112 (3), 560–585.
Moscovitch, M., Nadel, L., Winocur, G., Gilboa, A., Rosenbaum, R.S., 2006. The cognitive neuroscience of remote episodic, semantic and spatial memory. Curr. Opin. Neurobiol. 16 (2), 179–190.
Moustafa, A.A., Maida, A.S., 2007. Using TD learning to simulate working memory performance in a model of the prefrontal cortex and basal ganglia. Cogn. Syst. Res. 8, 262–281.
Myers, C.E., Ermita, B., Hasselmo, M., Gluck, M.A., 1998. Further implications of a computational model of septohippocampal cholinergic modulation in eyeblink conditioning. Psychobiology 26 (1), 1–20.
Myers, C.E., Gluck, M.A., Granger, R., 1995. Dissociation of hippocampal and entorhinal function in associative learning: a computational approach. Psychobiology 23 (2), 116–138.
Myers, C.E., Ermita, B.R., Harris, K., Hasselmo, M., Solomon, P., Gluck, M.A., 1996. A computational model of cholinergic disruption of septohippocampal activity in classical eyeblink conditioning. Neurobiol. Learn. Mem. 66 (1), 51–66.
Myers, C.E., Shohamy, D., Gluck, M.A., Grossman, S., Kluger, A., Ferris, S., et al., 2003a. Dissociating hippocampal versus basal ganglia contributions to learning and transfer. J. Cogn. Neurosci. 15 (2), 185–193.
Myers, C.E., Shohamy, D., Gluck, M.A., Grossman, S., Onlaor, S., Kapur, N., 2003b. Dissociating medial temporal and basal ganglia memory systems with a latent learning task. Neuropsychologia 41 (14), 1919–1928.
Nicholson, D.A., Freeman Jr, J.H., 2000. Lesions of the perirhinal cortex impair sensory preconditioning in rats. Behav. Brain Res. 112 (1–2), 69–75.
O Reilly, R.C., Norman, K.A., 2002. Hippocampal and neocortical contributions to memory: advances in the complementary learning systems framework. Trends. Cogn. Sci. 6 (12), 505–510.
Phillips, R.G., LeDoux, J.E., 1992. Differential contribution of amygdala and hippocampus to cued and contextual fear conditioning. Behav. Neurosci. 106 (2), 274–285.
Pineno, O., (2006). When more is less: Extending training of the blocking association following compound training attenuates the blocking effect.
Poldrack, R.A., Clark, J., Pare-Blagoev, E.J., Shohamy, D., Creso Moyano, J., Myers, C., et al., 2001. Interactive memory systems in the human brain. Nature 414 (6863), 546–550.
Port, R.L., Patterson, M.M., 1984. Fimbrial lesions and sensory preconditioning. Behav. Neurosci. 98 (4), 584–589.
Port, R.L., Mikhail, A.A., Patterson, M.M., 1985. Differential effects of hippocampectomy on classically conditioned rabbit nictitating membrane response related to interstimulus interval. Behav. Neurosci. 99 (2), 200–208.
Puga, F., Barrett, D.W., Bastida, C.C., Gonzalez-Lima, F., 2007. Functional networks underlying latent inhibition learning in the mouse brain. NeuroImage 38 (1), 171–183.
Rescorla, R.A., Wagner, A.R., 1972. A theory of Pavlovian conditioning: variations in the effectiveness of reinforcement and non-reinforcement. In: Black, A.H., Prokasy, W.F. (Eds.), Classical Conditioning II: Current Research and Theory. Appleton-Century-Crofts, New York, pp. 64–99.
Rudy, J.W., O Reilly, R.C., 1999. Contextual fear conditioning, conjunctive representations, pattern completion, and the hippocampus. Behav. Neurosci. 113 (5), 867–880.
Rudy, J.W., Barrientos, R.M., O Reilly, R.C., 2002. Hippocampal formation supports conditioning to memory of a context. Behav. Neurosci. 116 (4), 530–538.
Ryou, J.W., Cho, S.Y., Kim, H.T., 2001. Lesions of the entorhinal cortex impair acquisition of hippocampal-dependent trace conditioning. Neurobiol. Learn. Mem. 75 (2), 121–127.
Schmajuk, N.A., DiCarlo, J.J., 1992. Stimulus configuration, classical conditioning, and hippocampal function. Psychol. Rev. 99 (2), 268–305.
Schmaltz, L.W., Theios, J., 1972. Acquisition and extinction of a classically conditioned response in hippocampectomized rabbits (*Oryctolagus cuniculus*). J. Comp. Physiol. Psychol. 79 (2), 328–333.
Schultz, W., Dayan, P., Montague, P.R., 1997. A neural substrate of prediction and reward. Science 275 (5306), 1593–1599.
Scoville, W.B., Milner, B., 1957. Loss of recent memory after bilateral hippocampal lesions. J. Neurol. Neurosurg. Psychiatry 20 (1), 11–21.
Selden, N.R., Everitt, B.J., Jarrard, L.E., Robbins, T.W., 1991. Complementary roles for the amygdala and hippocampus in aversive conditioning to explicit and contextual cues. Neuroscience 42 (2), 335–350.
Shill, H.A., De La Vega, F.J., Samanta, J., Stacy, M., 2009. Motor learning in essential tremor. Mov. Disord.
Shohamy, D., Allen, M.T., Gluck, M.A., 2000. Dissociating entorhinal and hippocampal involvement in latent inhibition. Behav. Neurosci. 114 (5), 867–874.
Siekmeier, P.J., Hasselmo, M.E., Howard, M.W., Coyle, J., 2007. Modeling of context-dependent retrieval in hippocampal region CA1: implications for cognitive function in schizophrenia. Schizophr. Res. 89 (1–3), 177–190.
Solomon, P.R., 1977. Role of the hippocampus in blocking and conditioned inhibition of the rabbit's nictitating membrane response. J. Comp. Physiol. Psychol. 91 (2), 407–417.
Solomon, P.R., Moore, J.W., 1975. Latent inhibition and stimulus generalization of the classically conditioned nictitating membrane response in rabbits (*Oryctolagus cuniculus*) following dorsal hippocampal ablation. J. Comp. Physiol. Psychol. 89 (10), 1192–1203.
Solomon, P.R., Solomon, S.D., Schaaf, E.V., Perry, H.E., 1983. Altered activity in the hippocampus is more detrimental to classical conditioning than removing the structure. Science 220 (4594), 329–331.
Solomon, P.R., Vander Schaaf, E.R., Thompson, R.F., Weisz, D.J., 1986. Hippocampus and trace conditioning of the rabbit's classically conditioned nictitating membrane response. Behav. Neurosci. 100 (5), 729–744.

Spiker, C.C., 1956. Experiments with children on the hypotheses of acquired distinctiveness and equivalence of cues. Child. Dev. 27 (2), 253–263.
Stout, S., Arcediano, F., Escobar, M., Miller, R.R., 2003. Over-shadowing as a function of trial number: dynamics of first- and second-order comparator effects. Learn. Behav. 31 (1), 85–97.
Suri, R.E., 2001. Anticipatory responses of dopamine neurons and cortical neurons reproduced by internal model. Exp. Brain Res. 140 (2), 234–240.
Suri, R.E., Schultz, W., 1999. A neural network model with dopamine-like reinforcement signal that learns a spatial delayed response task. Neuroscience 91 (3), 871–890.
Terrace, H.S., 1963. Discrimination learning with and without "errors". J. Exp. Anal. Behav. 6, 1–27.
Thompson, R., 1972. Sensory preconditioning. In: Thompson, R.F., Voss, J.F. (Eds.), Topics in Learning and Performance. Academic Press, New York, pp. 105–129.
Turnock, M., Becker, S., 2007. A neural network model of hippocampal–striatal–prefrontal interactions in contextual conditioning. Brain Res.
Ward-Robinson, J., Hall, G., 1999. The role of mediated conditioning in acquired equivalence. Q. J. Exp. Psychol., B. 52 (4), 335–350.
Woodruff-Pak, D.S., Lavond, D.G., Logan, C.G., Steinmetz, J.E., Thompson, R.F., 1993. Cerebellar cortical lesions and reacquisition in classical conditioning of the nictitating membrane response in rabbits. Brain Res. 608 (1), 67–77.
Yap, C.S., Richardson, R., 2005. Latent inhibition in the developing rat: an examination of context-specific effects. Dev. Psychobiol. 47 (1), 55–65.
Young, B.J., Otto, T., Fox, G.D., Eichenbaum, H., 1997. Memory representation within the parahippocampal region. J. Neurosci. 17 (13), 5183–5195.
Young, A.M., Ahier, R.G., Upton, R.L., Joseph, M.H., Gray, J.A., 1998. Increased extracellular dopamine in the nucleus accumbens of the rat during associative learning of neutral stimuli. Neuroscience 83 (4), 1175–1183.
Zeineh, M.M., Engel, S.A., Thompson, P.M., Bookheimer, S.Y., 2003. Dynamics of the hippocampus during encoding and retrieval of face–name pairs. Science 299 (5606), 577–580.