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# From contextual fear to a dynamic view of memory systems

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**The brain does not learn and remember in a unitary fashion. Rather, different circuits specialize in certain classes of problems and encode different types of information. Damage to one of these systems typically results in amnesia only for the form of memory that is the specialty of the affected region. However, the question of how the brain allocates a specific category of memory to a particular circuit has received little attention. The currently dominant view (multiple memory systems theory) assumes that such abilities are hard wired. Using fear conditioning as a paradigmatic case, I propose an alternative model in which mnemonic processing is allocated to specific circuits through a dynamic process. Potential circuits compete to form memories, with the most efficient circuits emerging as winners. However, alternate circuits compensate when these 'primary' circuits are compromised.**

## What is the origin of memory systems?

Neuroscientists recognize that there is no single form of memory. Different aspects of a memory and different kinds of learning are handled by different brain regions. With such recognition, it is crucial to understand why certain problems are solved with one circuit and not another. Current approaches assume that this distribution of information processing reflects the hardwired organization of the brain. Here, I challenge that view and argue that the data suggest that this organization reflects a more dynamic process. Instead, circuits actively compete during learning, such that the most efficient path to solving a particular problem gains control of the necessary information processing and memory formation.

## The current view of neural systems for learning and memory

The dominant view of the neural systems responsible for learning and memory is multiple memory systems theory (MMST), which states that there are specific circuits that serve specific classes of learning and memory problems [1]. The view was initially stimulated by findings with Patient H.M. who lost 'declarative' memory but, equally important, retained 'nondeclarative' memory after removal of most of his medial temporal lobe [2]. MMST points to the hippocampus for spatial learning and episodic memory, the cerebellum for learning reflexive movements and the striatum for habit learning [3]. According to MMST, these regions each constitute a crucial junction that is essential for processing, storing and retrieving the information that is necessary for the category of memory that they serve.

Fear learning is typically taken as a perfect exemplar for MMST. Fear serves the crucial biological function of defense [4]. The consequences to reproductive fitness are greater for a single failure to defend than a single failure to mate or eat. This urgency of defense has resulted in the evolution of a near-perfect fear-learning circuit that has rapid and potent plasticity. Significant Pavlovian fear conditioning occurs with a single trial and is not forgotten over the adult lifespan [5,6].

## Discrete versus contextual fear cues

The most familiar examples of conditioning focus on discrete conditional stimuli (CS; e.g. Pavlov's bell), which are present briefly and immediately before the unconditional stimulus (US; typically an electric footshock for fear conditioning). However, there are also static contextual cues that are present continually throughout the entire conditioning experience. Discrete and contextual CSs share the ability for one-trial permanent conditioning [6,7]. However, contextual cues do not seem to play by the same rules as discrete CSs. A ubiquitous finding in the conditioning literature is that, whereas the best conditioning occurs with the CS starting before the US, the shorter the interval between CS onset and US onset the better the conditioning (Figure 1). Although the time constant differs for different types of conditioning (e.g. it is very short for eyeblink conditioning [8] and long for taste aversion conditioning [9]) the rule is the same. However, whereas this rule applies to fear conditioning with discrete CSs [10], it is violated by contextual conditioning [11].

I named this violation the immediate shock deficit (ISD), although it has been documented with other aversive USs, such as loud noise [12] and several CRs [11–14]. Simply put, the greater the time between placement in a novel context and the delivery of the US (CS–US interval; i.e. placement-to-shock interval), the greater the conditioning. Whereas simultaneous presentation of tone and shock produces robust one-trial conditioning [7], a delay of at least 20 sec between placement in a context and shock is needed for even minimally detectable conditioning [5]. I proposed that this deficit arises because contexts are made of many stimulus elements that 'would not be experienced until the animal engages in some exploration' and that 'the pattern of stimulation would change as the animal explores the chamber' [11]. Therefore, 'the subject must learn to treat the complex compound of stimuli that make up a context as a whole...or Gestalt...before such a

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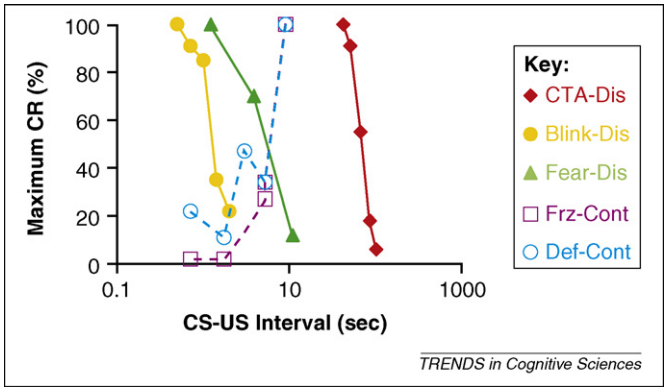


**Figure 1**. CS–US Interval: The maximum possible conditional response (CR) is plotted for three types of conditioning with discrete trials [conditioned taste aversion in rats (CTA-Dis) [9]; eyeblink conditioning in rabbits (Blink-Dis) [8] and fear conditioning in rats (Fear-Dis)] [10] using solid lines. Dashed lines present two measures of context fear: freezing (Frz-Cont) [11] and defecation (Def-Cont) [11]. Because of the range of CS–US intervals between eyeblink and taste aversion learning, the abscissa plots the square root of the number of seconds between CS and US onset on a log scale. The time range for discrete and contextual fear conditioning overlaps, whereas the direction of the functions is opposite.

stimulus can enter into association as a CS' [11]. None of these requirements is present for a discrete CS: one does not need to explore a brief, simple stimulus such as a tone, and all of its elements are immediately present at the time of reinforcer delivery.

The slope of the CS–US interval function provides a diagnostic for elemental versus configural learning (Figure 1). If that slope is negative, with conditioning degrading as CS-exposure increases, learning about the CS occurs in an elemental manner. However, if the slope is positive, where learning increases with CS exposure, learning about the CS occurs in a configural fashion. Figure 1 shows that the positive slope is unique to contexts. This function provides an experimental tool for probing the nature of learning about stimuli and I will show how it can be used later.

Furthermore, support for this view of the context as a configuration comes from the finding that giving the animal the opportunity to explore the environment enables it to form this unitary representation prior to conditioning, thus mitigating the ISD, [5]. Importantly, this pre-exposure must involve all of the context elements at once; separately exposing the elements does not attenuate the ISD [15]. The fact that context pre-exposure facilitates conditioning is also different from what happens with discrete CSs, where pre-exposure leads to a reduction in conditioning termed latent inhibition [16]. The context pre-exposure design is a variant of the placement-to-shock interval experiment in that the interval in the latter also increases experience with the CS prior to shock. In addition, both facilitate the formation of a configural representation of the context through experience.

If the polymodal features of the context must be linked together as a unified representation, a brain structure that processes polymodal stimuli is a probable place. Nowhere else does the brain compresses multi-sensory information as completely as the hippocampus [17]. Therefore, the hippocampus is predicted to be particularly important for conditioning to contextual as opposed to discrete stimuli, because contextual stimuli are a configuration of multisensory elements, whereas discrete stimuli are not. Lesion studies confirm this prediction [18–20].

If the hippocampus forms the contextual configure, there should be some neural signature that reflects this process. Hippocampal neurons prefer to respond in specific locations and it is thought that the relationship of firing patterns between these place neurons enables animals to distinguish one context from another [21]. To become stable, these hippocampal place fields require a period of exploration and estimates of the time needed for stability are similar to the time needed to overcome the ISD [22]. Furthermore, just as conditioning occurs with less time between placement and shock in a pre-exposed context, hippocampal place fields stabilize more rapidly when rats are replaced in a familiar environment [22]. Thus, there is at least a rough correspondence between the temporal pattern of hippocampal place neuron activity and contextual fear conditioning.

Whereas fear conditioning requires labeling a cue with emotional content, formation of a contextual representation by the hippocampus is independent of emotional valence. In the pre-exposure experiments, formation of the representation occurs in the absence of the US [5,23]. The amygdala is a structure that has long been linked to emotion and fear conditioning [24–28]. Hippocampal inputs to the basolateral amygdaloid complex [lateral and basal nuclei, amygdalae basolateralis anterior (BLA)] support synaptic plasticity and damage to these hippocampal-BLA projections attenuates context but not tone conditioning [26]. However, damage to neurons in the BLA attenuates both [26].

Figure 2 shows a well-accepted view of a circuit for contextual fear that is uniquely capable of executing the requisites of this form of learning [27,28]. A contextual representation is assembled in the hippocampus and this representation, similar to that of a simpler discrete CS, is associated with a negative affect at the BLA. This gives the CS the ability to activate the BLA on its own. BLA activation descends to generate the many overt responses that constitute a fear reaction via the central nucleus. Importantly, the ventral periaqueductal gray organizes a freezing response. I say, 'organize' because the initial component of freezing is to retreat to the nearest good location to freeze (e.g. the closest dark corner) and then arrest visible motor activity [29].

## Multiple memory systems theory

Contextual fear conditioning fits elegantly within multiple memory systems theory (MMST). There are several unique attributes to this learning process and specific neural circuits that carry out the necessary work. Damage to the circuit and pharmacological blockade of systems required for synaptic plasticity and its consolidation all cause a loss in conditioning [30].

MMST suggests that the circuits underlying a specific form of learning should be essential in carrying out that form of learning. According to MMST, damage to an essential circuit before or after training will have similar effects; that is, anterograde amnesia and retrograde amnesia should be proportional [31]. Early studies were consistent

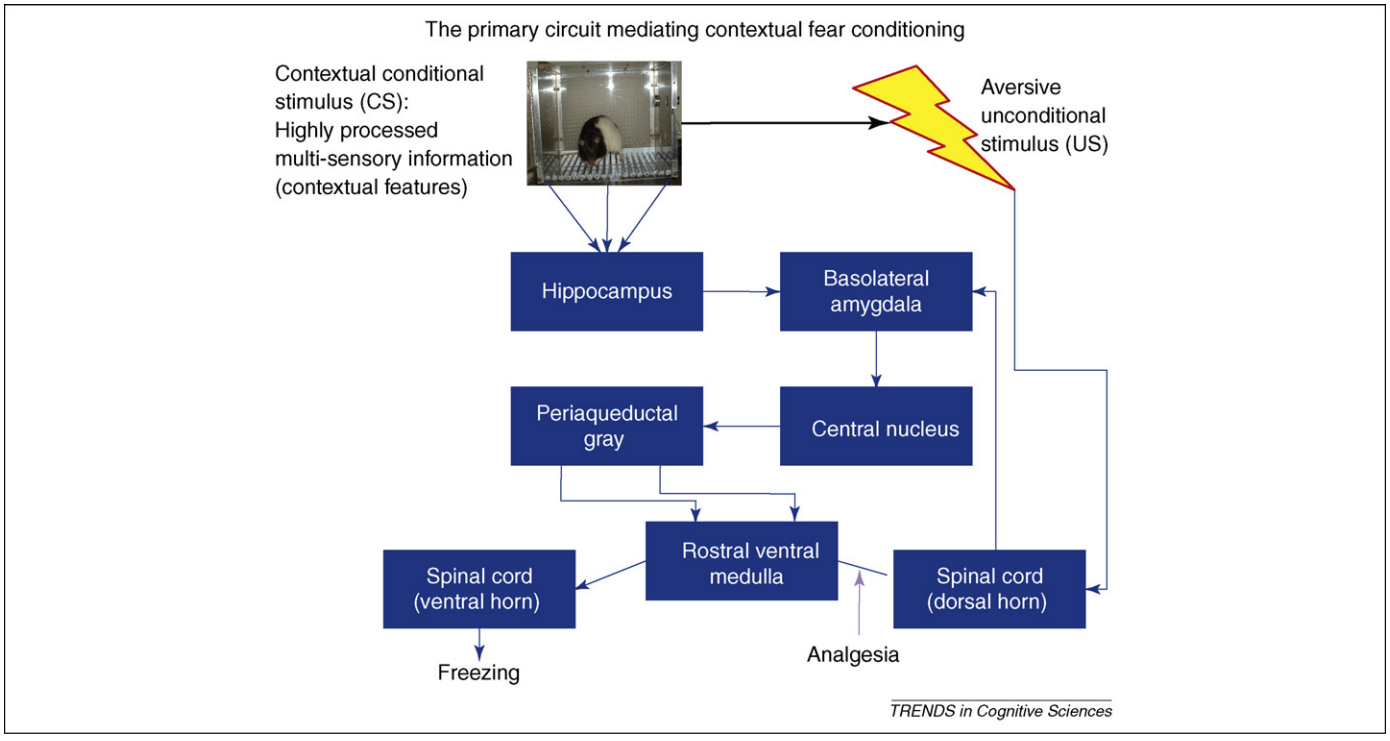


**Figure 2**. Integration of multimodal sensory information constituting the context at the hippocampus and its association with shock in the basolateral amygdala. Descending circuitry from the basolateral amygdala generates conditional responses, such as freezing and analgesia. The analgesic effects on ascending pain information from the dorsal horn constitute the error-correcting negative feedback arm of the circuit. Reviewed in Refs [27,28].

with just that. Both pre- and post-training hippocampal lesions produced what appeared to be complete deficits in contextual fear conditioning [18,20,32,33]. The one caveat, that hippocampal lesions made a month or more after training had little effect on context fear [18], had already been built into MMST. As in H.M., whose older presurgery memories were preserved, the hippocampus was expected to have an initially important role that gradually faded over time as memory consolidated into cortical networks [1,2,31,34]. The retrograde amnesia produced by post-training hippocampal lesions was temporally graded in contextual fear conditioning, similar to the medial temporal lobe amnesia in the patients that stimulated development of MMST.

## So what is wrong with this picture?

A problem with the above theory was found in an explicit test of whether anterograde and retrograde amnesia were proportional [35]. Despite identical training parameters, retrograde amnesia was profound but there was no indication of anterograde amnesia. Why were these results discrepant with earlier studies? In the first retrograde amnesia study, strong training parameters were used (15 trials) to be assured of strong conditioning to both tones and contexts to allow direct comparison. Initial anterograde amnesia studies used a more typical context conditioning preparation with just a few unsignaled shocks [32,33]. Philips and LeDoux [19], who also observed anterograde amnesia, specifically titrated their conditioning parameters to be the minimal amount that supported context conditioning. The fact that context conditioning was abolished in all these cases suggested an invariant dependence on the hippocampus. However, the conclusion was confounded by the use of weak training parameters in the pre-training lesion studies and strong training parameters in the retrograde amnesia study. Using a moderate set of parameters, Maren *et al.* [35] revealed that anterograde amnesia and retrograde amnesia were not proportional and these results in rats were also replicated in mice [36].

What should be made of this surprising result? It was already known that 'elemental' conditioning to discrete CSs occurred without the hippocampus. Perhaps, without the hippocampus, some element from the context conditioned just like an elemental discrete stimulus [35,37]. Because configural cues are more salient than the weak elements of the context, they normally overshadow elemental conditioning. Pavlovian overshadowing refers to a form of associative competition where a CS that supports conditioning when paired with a US on its own, fails to condition when it is reinforced in conjunction with a more salient stimulus [38]. The hippocampal configure normally overshadows any individual elements in the context. Without the configure to compete with, some element of the context acquires associative strength. Anterograde amnesia is not seen because pre-training lesions do not weaken the net magnitude of conditioning. Instead, they switch the nature of what is learned from configural to elemental. Given that animals with an intact hippocampus learn configurally, and the hippocampus is necessary to retrieve the configure, post-training lesions are strongly amnestic [35,36].

Recently, this hypothesis has been developed more fully [37], with the suggestion that the hippocampal system

learns through a conjunctive or configural process that operates through pattern completion, where sampling one aspect of the configure retrieves the entire configure. However, there is also a neocortical system that learns in a feature-based manner where learning changes the value of elements individually. According to Rudy, contextual fear is mediated by this neocortical/elemental system when the hippocampus is not available.

If pre-training lesions shift the nature of what is learned during contextual fear conditioning from configural to elemental it should be easy to find fundamental differences in how learning progresses. A one-trial context conditioning experiment by Wiltgen *et al.* [39] looked at this more closely. All the arguments suggesting that contextual learning is a configural or Gestalt process rest on the ISD and the inverse function between CS onset and US onset between context and discrete cue conditioning. Therefore, the placement-to-shock-interval function was used to diagnose between elemental and configural learning in rats with hippocampal ablations. If a pre-training lesion switches the nature of learning, it should switch the direction of the function and make context learning follow the principles of elemental conditioning. Placement-to-shock interval functions were generated in intact and lesioned rats [39] and two sets of parallel curves emerged, with the lesioned rats showing a rightward shift in the effects of increasing delay between context placement and shock. This was contrary to the prediction that hippocampal lesions turn rats into elemental information processors. The slope of the function was still positive, showing that lesioned animals just needed more time to explore to condition comparably.

The Pavlovian literature is clear that elemental conditioning will suffer when there is a delay between placement in the context and US delivery. Although the context is made of many cues, they fall into two classes from a temporal perspective. Some cues are statically present throughout the entire interval (e.g. background noise from a ventilation fan) others are phasic, present only when attended to (e.g. tactile cues from a whisker stroking a corner). Longer periods to explore should hurt conditioning to static cues by lengthening the CS–US interval. Phasic cues have multiple onsets and terminations before they have the opportunity to be paired with shock. The longer the time to explore the context, the more CS presentations occur prior to the conditioning event. These CS presentations should reduce conditioning through latent inhibition [16] and they should also reduce the element-shock contingency [40], both of which would be detrimental to elemental conditioning. Animals without a hippocampus cannot be learning elementally, given that they benefit from more time to explore, similar to intact animals. They must be using this time to learn configurally. Although lesioned animals are less efficient than are intact animals, the nature of the learning is similar. This inefficiency in configural learning is further illustrated by the finding that increasing the number of conditioning trials eliminates any anterograde amnesia [39].

The suggestion that contextual fear learning in the absence of the hippocampus is configural is a major point of departure from previous views [35–37,41,42]. Rudy [37] suggests that the crucial test between elemental (feature-based) and configural (conjunctive) learning is whether contextual pre-exposure can benefit animals trained with immediate shock. I agree on the importance of this test and relevant data [23] are presented in Figure 3. The crucial comparison is between lesioned animals with and without context pre-exposure. It is clear that lesioned rats with pre-exposure freeze more than their lesioned counterparts without pre-exposure. Therefore, similar to the positively sloped placement-to-shock interval function, the pre-exposure data support the conclusion that both the hippocampal system and the alternate system learn in a configural manner. Although lesioned rats benefit from context pre-exposure, they do so to a lesser degree than intact animals (Figure 3). One should remember that pre-exposure to discrete CSs produces a loss in conditioning, the classic latent inhibition effect [16]. Together, these data support the hypothesis that hippocampal-lesioned animals use a quantitatively (i.e. less efficient), not qualitatively (i.e. configural versus elemental) different process compared with intact animals.

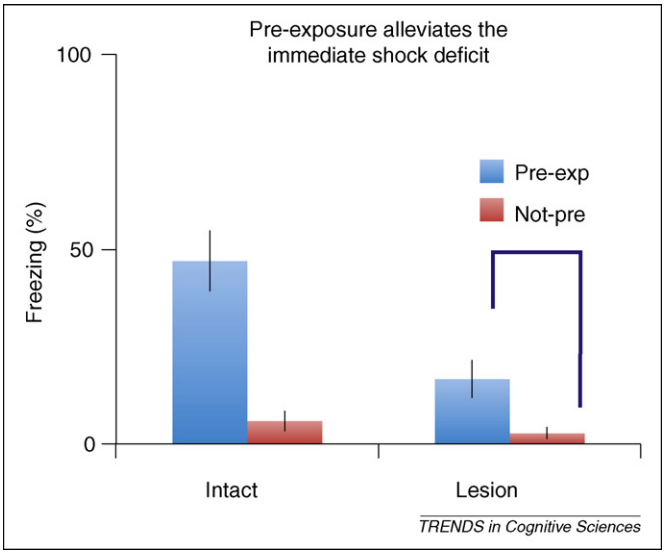


**Figure 3**. Context Pre-exposure and Hippocampal Lesions Rudy *et al.* [42] pre-exposed intact and hippocampus-lesioned rats to a context without shock on one day. The following day, the rats received a shock immediately upon placement in either the same chamber (Pre-exp) or a different chamber (Not-pre) as pre-exposure. The data illustrated measure freezing in the shocked chamber during a test given on the third day. The immediate shock deficit is illustrated by the lack of freezing in both No-pre groups. Pre-exposure increased freezing in the lesioned rats, albeit to a lesser extent than the unlesioned rats. The critical contrast showing lesioned rats profited from pre-exposure is indicated by the dark blue brackets. Modified from [42], with permission from the author.

## A pattern emerges

There are three key observations from these hippocampal lesion studies. First, configural learning occurs with or without a hippocampus. Second, with weak conditioning parameters, hippocampal lesions produce anterograde amnesia, but with less challenging parameters no anterograde amnesia is found. Finally, with post-training lesions, there is a profound retrograde amnesia even with generous training parameters. These observations can be easily explained by the hypotheses in Box 1.

These hypotheses lay to rest several troubling findings in the hippocampal literature. For example, Sutherland and Rudy [43] suggested that the hippocampus

**Box 1. Hypotheses accounting for hippocampal effects on context conditioning**

(i) Animals normally learn about contexts by using the hippocampus to form a configural representation of the context.
(ii) Animals without a hippocampus can use some alternative structure (or pathway) to form a similar contextual representation but they do so less efficiently (i.e. they need more time to explore the context or more training trials). This explains the parametric dependence of anterograde amnesia.
(iii) When the hippocampus learns, the alternative structure does not. Therefore, losing the hippocampus shortly after learning produces a parameter-independent retrograde amnesia.

is necessary for learning a discrimination when the solution requires the use of configural cues. They proposed negative patterning, where two stimuli are reinforced when presented separately but not reinforced when presented together, as the crucial test of the theory. To withhold responding to the compound, the learner must use the compound as a unique configural stimulus [44]. If the hippocampus is crucial for configural memory, then learners without a hippocampus should be unable to solve this problem. Although the prediction was initially confirmed [45], other experiments found that animals with lesions could learn the problem [46]. This was taken as an insurmountable problem for the theory. However, one of the experiments taken as a disconfirmation is particularly instructive. Richardson *et al.* [47] trained intact rats on a negative patterning task and found that post-training hippocampal lesions eliminated discriminative performance. However, with retraining, the animals acquired negative patterning. This is directly analogous to another experiment with contextual fear conditioning [39] in which rats were first trained to fear a context. Whereas complete lesions of the hippocampus eliminated this memory, retraining resulted in normal fear. In both experiments, rats with an active hippocampus appear to learn normally, but when the hippocampus is not available, other region(s) can compensate.

## Pharmacological manipulations of the hippocampus

Direct infusion of drugs into the hippocampus offers a way of temporarily manipulating the hippocampus around the time of learning but leaving it normal during testing. Of particular interest is a comparison of substances that inactivate the hippocampus and those that block synaptic plasticity while preserving synaptic transmission. Inactivating the hippocampus with a local anesthetic (lidocaine) or a drug mimicking the inhibitory transmitter GABA (muscimol) immediately before or after contextual fear learning cause, at most, a small deficit in context fear learning unless a demanding contextual fear conditioning task is used [23,48,49]. This is consistent with the pattern described above with permanent pre-training lesions in that, when the hippocampus is inactivated, other structures compensate but they have trouble when the task is particularly demanding.

A different picture emerges with infusion of an N-methyl-d-aspartic acid (NMDA) antagonist (2-amino-5-phosphono-valeric acid; APV) into the hippocampus prior to training. NMDA blockade during training is devastating to context fear learning even with robust training procedures [50]. Importantly, hippocampal place fields form and place cells fire under NMDA-receptor blockade. However, place cell activity induces long-term plasticity only when NMDA receptors are normally activated [51]. Under an NMDA antagonist, the hippocampus is processing context during training so the alternate is not engaged; however, given that the hippocampus forms no long-term memory, there is profound anterograde amnesia.

## Retrieval and the hippocampus

Surprisingly, inactivation of the hippocampus during testing causes no loss of fear in an animal given standard training [48,49,52]. This lack of effect on retrieval does not fit easily into any of the current views of context conditioning, including the current one. One key to this puzzle is the suggestion that the hippocampus is important to retrieval only when the situation consists of ambiguous information [53]. In standard contextual fear conditioning, the context is not ambiguous; the only previous experience with the context was when the animal received a shock. Hippocampal inactivation does prevent retrieval of contextual fear when animals learn with context pre-exposure and subsequent immediate shock [23]. In that design, animals receive a safe exposure to the context on one day and a shock in the context on another. In that sense, the context is ambiguous at the time of testing. The role of the hippocampus in resolving ambiguity during retrieval might be different from its role in learning about contexts. Although the hippocampus is not involved in cued fear when straightforward tone-shock training is used [18,19], it does have a role when cued fear is rendered ambiguous through extinction [53], minimal training [54], when the cue and reinforcer are separated in time [55] or when the tested cue is different from the trained cue [56].

## Beyond the hippocampus

The general pattern present in these three observations (Box 1) about hippocampus can be recognized for the role of the BLA role in contextual fear conditioning. The BLA is considered essential for fear conditioning and interfering with BLA function has pronounced effects on fear learning. However, following large BLA lesions, rats can acquire fear if given an extensive regimen of overtraining [57]. Importantly, animals overtrained with the BLA intact lose their fear if given post-training lesions [57]. In an extension of Maren's findings [57], muscimol was used to inactivate the BLA temporally [58] (Figure 4). Rats normally acquire fear rapidly with some learning after a single trial. When the BLA was inactivated, no one-trial learning was seen. However, the rats did begin to learn after approximately ten trials. Learning was slow in that it took 50 trials for the inactivated rats to catch up. During a subsequent memory test, all groups tested with the BLA intact showed similar levels of fear. Whereas pre-test inactivation of the BLA abolished memory recall in the rats trained with the BLA functional, animals that learned fear without the BLA were unaffected by BLA inactivation at the time of test. Therefore, fear can occur with or without the BLA, but learning is inefficient without the BLA. If learning occurred with the BLA, then this structure is needed to

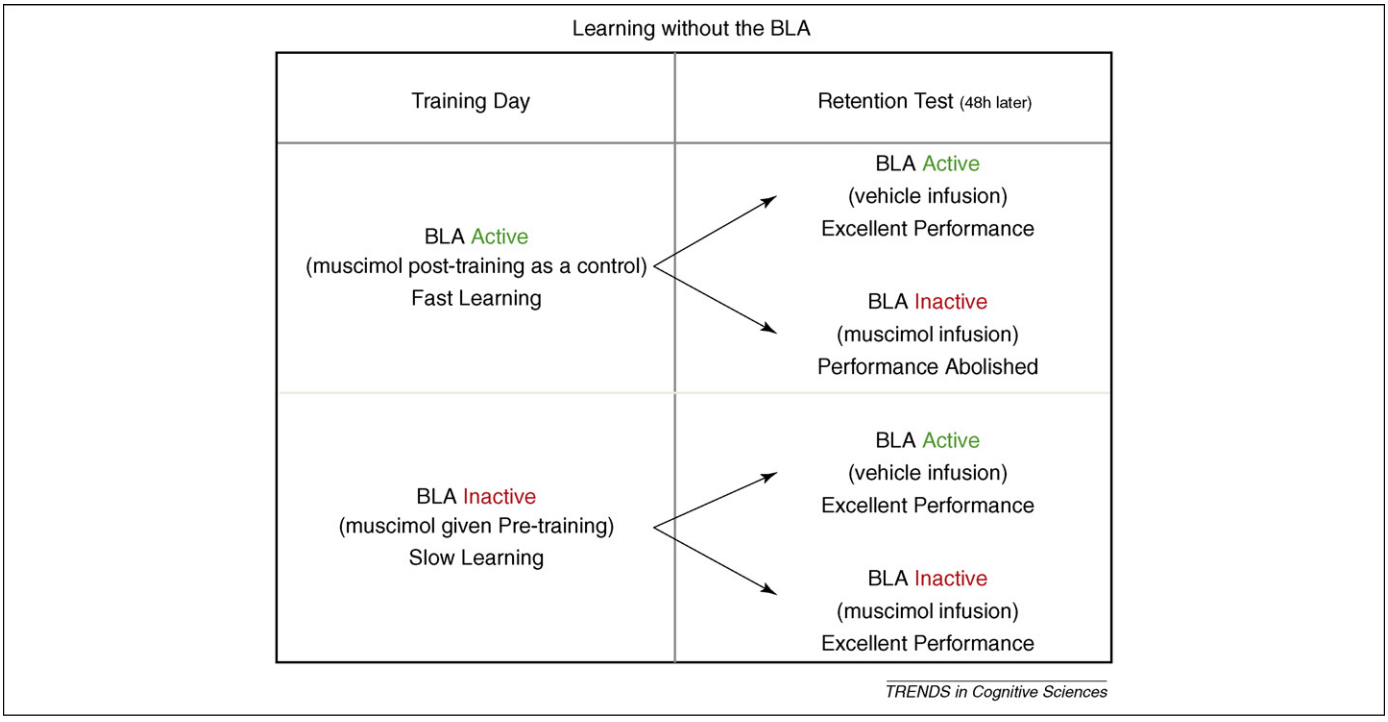


**Figure 4.** The design and summary of results of an overtraining experiment [58] showing that rats learn context fear, albeit slowly, when the BLA is shutdown by direct infusions of the GABA agonist muscimol. Despite overtraining, rats that learn with a functional BLA needed the BLA to express fear. However, rats that learned without the BLA did not need the BLA to express fear.

express fear regardless of the training regime (e.g. normal or overtraining). However, if learning occurred without the BLA, then the BLA is not needed to express fear.

The pattern is present not only for the BLA complex as a whole, but also for nuclei within the BLA. Using auditory conditioning, Anglada-Figueroa and Quirk found that pre-training lesions of just the basal nuclei had no effect on acquisition of fear [59]. However, if the same lesions were made after conditioning, tone fear was abolished. Normally, rats use the basal nuclei for auditory conditioning, but if they are not available, alternative routes support learning.

An additional example from auditory cortex also highlights the generality of this point. Auditory information arrives at the BLA from two routes: one pathway is a monosynaptic projection from medial geniculate to lateral amygdala and the other pathway to the lateral amygdala is via the auditory cortex [60]. Pre-training lesions to one of these pathways does not affect fear conditioning to a tone, but lesions of both pathways impair learning. These findings suggest that both pathways are equally capable of auditory fear conditioning but leave open the question of what normally happens during learning. Subsequently, Boatman and Kim [61] found that post-training lesions of the auditory cortex abolished tone fear memory. Although both pathways have the potential for learning, the cortical input normally mediates acquisition.

## A dynamic model

Together, the first four assumptions in Box 2 can account for this entire data set [58]. Normally, one learns by using the most efficient circuit for producing learning, so if that circuit is unavailable, learning is possible but requires a more forgiving training regimen. Deficits are therefore seen with pre-training lesions but only if the training regimen is demanding. Post-training lesions in the primary pathway are devastating because, when this pathway is strengthened, it prevents learning in the alternate pathway.

How does the primary pathway downregulate learning in the alternate pathway? Why is the alternate pathway not strengthened when the primary pathway learns? An appeal to basic pavlovian processes provides an answer. It has long-been recognized that potential CSs compete for the acquisition of associative strength [44] and such competition could be achieved by a circuit that detects differences between obtained and expected outcomes (error detection) and then uses this difference to reinforce

**Box 2. The dynamic origins of memory systems**

(i) There are primary and alternate pathways able to mediate fear behavior.
(ii) The alternate pathways are less efficient compared with the primary pathway.
(iii) The more-efficient primary pathway dominates the learning and simultaneously prevents significant learning in the alternate pathway(s).
(iv) The alternate pathways compensate when the dominant pathway is compromised.
(v) Plasticity in these circuits might be regulated by the same mechanisms responsible for competitive learning between stimuli and described by Pavlovian principles [65].
(vi) This model provides a set of rules for how the brain can select specific and efficient circuits for production of specific adaptive behaviors.

changes in the predictive value of the CS (error correction) [62,64] (Figure 1). If a US is unpredicted, it reinforces learning; if the US is predicted, it does not reinforce. Again an important example is overshadowing [38]. Mackintosh [63] described an experiment where a not particularly salient light conditioned well on its own but failed to condition when presented in compound with a more salient tone. The effect occurs because salient (more intense) stimuli condition more quickly and come to predict the US more rapidly [44]. Given that the more salient tone predicts the US before the less efficiently learned-about light acquires much associative strength, the light never has a chance to condition well. When the light is on its own, nothing else predicts the US, so learning proceeds, albeit inefficiently. This pattern for conditioning to stimuli is analogous to what the assumptions (i–iv) in Box 2 say about neural pathways.

Whereas traditional models of Pavlovian conditioning speak of increasing the associative strength of stimuli, in reality a circuit is strengthened. When light is conditioned alone, visual inputs to the amygdala undergo synaptic strengthening, but when the light is reinforced together with a tone, only the auditory input to the amygdala is strengthened. Thus, associative competition selectively strengthens a more efficient (dominant) circuit over a less efficient (secondary) circuit. This leads to postulate (v) of the model; associative competition rules explain how the brain selects specific circuits for learning and why these circuits are particularly effective at the type of learning they mediate. Given that learning is driven by error signals arising from the failure to predict significant events: for example, loss of a region that normally accomplishes the learning results in continued error signals, and this continued reinforcement eventually strengthens the next best alternative. There are also some limits to this compensation. When the amygdala is deprived of both thalamic and cortical auditory input, no tone conditioning occurrs [60]. In this case, one would expect that continued error signals would have driven context fear to an exceptionally high level, as it served as the only predictor of shock. Although Romanski and LeDoux [60] never measured context fear, context fear is greater under unsignaled than signaled shock conditions [65].

## Implications for MMST

Whereas MMST views the neural circuit that serves a particular class of learning as hard-wired and essential, the model described in Box 2 suggests a more dynamic process. The origin of a 'memory system' reflects an ontogenetic rather than phylogenetic process where, through experience and the rules of associative competition, the brain selects the most efficient circuits for solving a particular problem. A memory system is not 'essential' but rather the brain tends to use a particular circuit for a particular class of problem because this circuit is the best it has available to solve the problem. Although the evidence might be most developed for the case of contextual fear conditioning, postulate (iv) suggests that these principles are applicable to memory systems in general. The model in Box 2 is certainly consistent with both the generalities and specifics in food-reinforced negative patterning studies [47].

### Box 3. Predictions about alternate pathways

**What are the alternate pathways?**

Although the model postulates the existence of alternate neural pathways for solving particular problems, these regions and/or circuits are currently unknown. The model suggests an anatomical and a functional strategy for identifying potential candidates. Anatomically, an area that compensates for the role of the amygdala in contextual fear conditioning needs to get information about context from the hippocampus and project it to areas that generate fear behaviors such as freezing. The bed nuclei of the stria terminalis (BST) is a strong candidate [66–68]. The functional strategy asks what areas contribute to similar behaviors. Because of its role in mediating some types of anxiety responses, the BST is again a good candidate [69].

**Place cells**

The alternate region to the hippocampus in processing contexts as a configure should have place fields but these place fields should be slower to form; this time course should also match the longer placement-to-shock interval function of lesioned rats. To the extent that anything is known about place fields outside the hippocampus, the time for stabilization is longer [22].

**Preferential training**

It is possible that certain types of parameters will favor learning in the alternate system over the primary system. With such a set of parameters, post-training lesions to the primary system should have no effect, whereas post-training lesions to the alternate pathway should be devastating. Recently, Lehman *et al.* [70] confirmed the first part of this prediction; giving multiple reinforced context exposures spaced a day apart renders context conditioning immune to post-training hippocampal lesions.

## Future directions

To further develop this approach, future work will need to detail precisely the alternate pathways and determine where compensatory plasticity occurs. This search should be guided by neuroanatomy. Some predictions of the model with respect to alternate pathways are described in Box 3. Furthermore, the exact neural mechanisms responsible for down-regulation of plasticity in potential pathways need to be revealed. What is known about error-correction circuits should provide keys to that research. Hopefully, the dynamic approach detailed in Box 2 not only provides some insight into previously troubling experimental data, but will also result in new approaches to those individuals who, because of brain damage to the circuits normally responsible for memory formation, must learn to use alternative pathways.

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