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Supplementary Materials for
Design of a neurally plausible fear learning model

This document contains supporting material for "Design of a neurally plausible fear learning model" by FB Krasne, MS Fanselow, and M Zelikowsky. The model is referred to as FRAT (for Fraidy Rat). The first main section of this paper provides a full mathematical presentation of the model. The second section presents a number of simulations that were not included in the main paper.

DETAILED DESCRIPTION OF FRAT

The Matlab program that implements the model is controlled by a graphical user interface that is shown in Fig. 1. The details of the interface are not described here, but it may be added to this website or published separately, along with the Matlab code, at a later time. Here it will be sufficient to note that the interface provides for convenient scheduling of experiments which allow presentation of either of two CSs (CS1 and CS2) in any of three contexts (A, B, and C) and the presentation of a shock US of controllable intensity. It also contains controls that activate a simulation of systems type consolidation, controls that allow for ablation or inactivation of FRAT's hippocampus, the lateral nucleus of the amygdala (LA), the lateral basal nucleus, (BL), the medial central nucleus (CEm), and the prefrontal cortex (PFC).

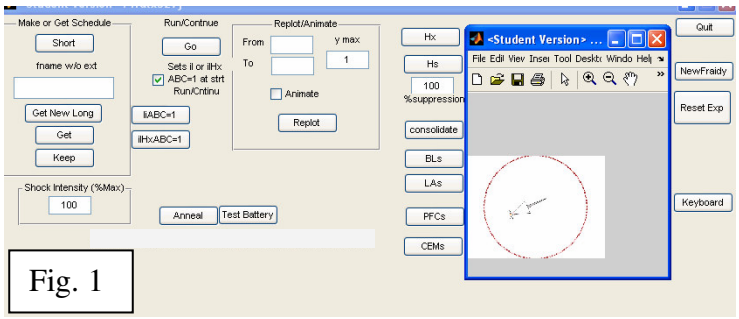
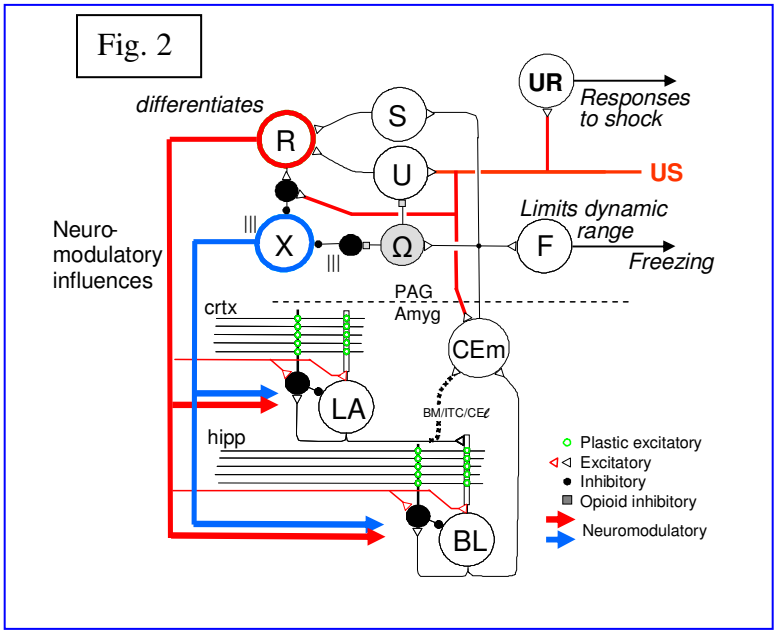


Fig. 1

Nomenclature and general.

LA and BL together are here referred to as BLA.

The overall circuit is shown in Fig. 2. The three amygdala sub-nuclei of the model are LA, BL, and CEm. The first two are composed of principal (projection) neurons **LAp** and **BLp** as well as inhibitory interneurons **LAi** and **BLi** (as in the main paper, neuron names are in bold type). All other nuclei have only projecting cells. **LAp** neurons innervate BL and both **LAp** and **BLp** innervate **CEm** neurons. The latter project to FRAT PAG where they innervate freezing neurons **F**, secondary reinforcing neurons **S**, and opioid inhibitoy neurons **Ω**. The PAG has two types of neuromodulatory neurons, reinforcing cells **R** and extinction cells **X**. Both project back to LA and BL. Each releases a different type of neuromodulator with different effects on plasticity of the LA and BL neurons. The **R** cells also provide ligand-gated (in addition to metabotropic, modulatory) input to the LA and BL cells. **R** cells inhibit **X** cells absolutely. The **R** cells are excited



by **U** neurons, which are recruited by USs, and by **S** neurons. The **X** cells are recruited via the **Ω** neurons by disinhibition. The **Ω** cells also inhibit the **U** neurons, which is part of the basis of blocking. Finally, in addition to exciting the **U** cells, USs provide excitatory input to **CEm** neurons, to the absolute inhibitors of **X**, and to **UR**, which cause active unconditioned responses to the shock that nullify freezing.

Plastic cortical and hippocampal input to LA and BL are described below.

Representation neurons innervating BLA

LA is innervated by representation cortex (thalamic inputs are not explicitly represented in FRAT) and BL by hippocampus. All representation neurons innervate principal cells (p) and inhibitory interneurons (i) in parallel. There are 4 broad categories of afferents to BLA:

(1) Pre-established (by developmental processes, not adult learning) cortical representation cells: **cxpCS1**, **cxpCS2**, **cxpA**, **cxpB**, **cxpC**. The number of cxp cells representing each CS is N_{Pcs}. The number of cxp cells representing each context is N_{Pcntxt}. this is to be thought of as the number of elemental contextual cues sampled at any given time. Strictly speaking, this would be some fraction of a larger set, and different such cues would be sampled from moment-to-moment. However, this feature was not built into the model, which treated the cxp cells as a fixed, constant population present whenever FRAT was in a given context. This simplification has little effect on the simulations of this paper, because in order to simulate the immediate shock deficit the number of cxp cells representing context was made extremely small. The model does not represent the individual elements of which contexts are composed nor provide a theory of how conjunctions of elements are established; it is simply assumed to happen as described below.

(2) Hippocampal neurons come to represent conjunctions of elementary cues by rules described below. There are 3 simple types and 6 compound types that can be established: **hcA**, **hcB**, **hcC**, **hcA1**, **hcA2**, **hcB1**, **hcB2**, **hcC1**, **hcC2**. There are N_{Hcntxt} of each simple type and N_{Hcnj} of each compound type. These cells are innervated by the appropriate cxp neurons.

(3) Cortical cells that are recruited by hippocampal pattern completion mechanisms ("Induced" cortical cells): **cxiA**, **cxiB**, **cxiC**. There are N_I of each of these types.

(4) Representation cortex cells can come to represent configurations of elemental cues either as the result of gradual consolidation in which the cortical cells replace corresponding hippocampal neurons or as the result of compensated incidental learning in which representations are formed rapidly in cortex in absence of hippocampus. One might expect that in the latter case a process of consolidation would still be necessary to integrate new and old representations; therefore, separate populations of neurons probably should have been used for cortical representations emerging from compensation and consolidation. However, since this would have had no computational implications for the kinds of simulations possible in the present version of FRAT, the same population of neurons was used for both types of cortical conjunctive representations. These are referred to as "transformed" cortical cells. These are of six kinds: **cxtA, cxtB, cxtC, cxtA1, cxtA2, cxtB1, cxtB2, cxtC1, cxtC2**. There are N_{Tcntxt} transformed context

simple cells of each type and NT_{cnj} of each compound type. These cells are innervated by relevant cxp neurons.

Activation of representation neurons and numbers of representation neurons active

The firing rates (*A* for "activation") of all representation neurons are numbers between 0 and 1. The number of neurons of a given type that are firing are a proportion (*r* for "ratio"-- a number between 0 and 1) of the total available population. Thus, the number of context A-representing hippocampal neurons firing would be given by $n_{hcA} = r_{hcA}\ N_{Hcntxt}$ and the firing rate would be denoted by A_{hcA}.

Summation, inhibition, and activation functions

As explained in the main paper the resting potential of FRAT neurons is taken as zero. Membrane potential (*V*) is specified as deviation from rest. Active synapses open postsynaptic ion channels (cause conductances) for particular ions. Excitatory input causes ion movements that depolarize the membrane potential toward an excitatory reversal potential *E* (taken as 100 mV above rest). Inhibitory input opens ion channels that have an equilibrium potential near the resting level and thus result in current flows that move the membrane toward the resting level (as with GABA-mediated chloride conductance in real neurons in cases where the neurons are not persistently depolarized by tonic excitatory input). Therefore, inhibitory input, rather than working by hyperpolarizing the cell, is effective mainly because it allows excitatory currents to pass out of the cell instead of depolarizing it, thus attenuating EPSPs (so called divisive inhibition).

When a FRAT neuron becomes depolarized beyond its firing threshold, its firing rate (also referred to as "activity" or "activation") increases linearly. Maximum activity, taken as unity, is reached at a depolarization level that varies according to neuron type. Individual spikes are not represented in FRAT, only firing rates. We define a "linear sigmoid" function (linsig)

$$\text{linsig}(x \mid Thrsh, Mxat) = \begin{cases} 0 & \text{if } x < Thrsh \\ 1 & \text{if } x >= Mxat \\ (x - Thrsh)/(Mxat - Thrsh) & \text{otherwise} \end{cases}$$

Using this function the activation of an LA or BL cell is given by

A=linsig($V \mid Thrsh, Mxat$)

Within the LA and BL of the amygdala, where fear conditioning actually occurs in FRAT, LA and BL principal (projecting) neurons are treated as having two electrical compartments, with excitatory inputs all converging on the more distal compartment and inhibition operating at the proximal compartment. It is assumed that conductances within the proximal compartment do not affect potentials or current flow in the distal compartment. LA and BL inhibitory interneurons have a single compartment and are innervated only by excitatory synapses. The conductances *G*, which enter into equations for computing depolarizations, are all expressed relative to the leakage conductance of the compartment.

Denoting the sum of all the conductances generated by excitatory input as G_e, the equilibrium potential for excitation as *E*, and the sum of inhibitory conductances by G_i, the depolarization produced by summed inputs is of the form

$$V = \left(\frac{G_e \cdot E}{1+G_e}\right)\left(\frac{1}{1+G_i}\right)$$

where V is the membrane potential at the proximal (or only) dendritic compartment.

At locations other than LA and BL simpler qualitatively plausible ad-hoc rules are used to compute the activation of a neuron from the activations of the neurons innervating it without considering intermediate conductances and membrane potentials. The equations used are equivalent to assuming that G_e remains sufficiently small that the activation of the output neuron is always a nearly linear function of its input activations.

The linsig function was also used for a variety of purposes other than calculating activation as a function of membrane potential.

Listing of Calculations done by the model/program

Variables in the program are updated at nominally 1 sec intervals of real time, which we refer to as "calculation intervals." There are also a number of procedures that can be invoked at will between one calculation interval and another.

During each nominally 1 sec long calculation interval the following things are done in order.

1. Calculate A and r for cxp cells.
2. Calculate A and r for hc cells
3. Calculate A and r for cxi cells
4. Calculate A and r for cxt cells.
5. Evaluate amygdala
6. Compute A_F and Freezing scores.
7. Compute A_R and A_X
8. Compute B_ps and $'Ca'_i$s (defined below)
9. Calculate changes in synaptic conductances (synaptic weights)
10. Re-evaluate amygdala with new weights
11. Update *LA-CEm* connectivity
12. Re-evaluate A_{CEm} and R_{inpt} with new weights.
13. Update hippocampal and cortical incidental learning factors (λ and μ)
14. Update eligibilities (see below and main paper)

Special calculations done as required between one calculation interval and another are:

Consolidate--Transfer of learning involving conjunctions from hippocampal-BL pathway to cortical-LA pathway.

Hx--Ablate hippocampus

Hs--Suppress hippocampus

PFCs--Suppress prefrontal cortex

BLs--Suppress BL

LAs--Suppress LA

CEMs--Suppress CEm

The regular calculation cycle

The values of *A* and *r* for all hc, cxi, and cxt cells, as well as eligibilities (defined below) start at zero until changed by the calculations listed below. Primed values below refer to the corresponding value for the previous interval.

Step 1: Calculate A and r for cxp cells

A and *r* of cxp cells are both unity if the CS or context represented is present and zero if not.

Step 2: Calculate A and r for hc cells

Hippocampal representations of contexts and context/CS conjunctions must be learned by incidental learning. The extent to which such learning has occurred is represented by a factor λ that is zero prior to any incidental learning and unity when such learning is maximal. The relevant change rule for λs is given following the amygdala change rules below (Step 13).

Taking context A as an example of a simple context, prior to consolidation

$$A_{hcA}=\lambda_A A_{cxpA} r_{cxpA} \quad \text{and} \quad r_{hcA}=\lambda_A A_{cxpA} r_{cxpA} .$$

In all the simulations of this work, all A_{cxp}s, and r_{cxp}s are zero if the stimulus is absent and unity if it is present. Therefore, if context A is present,

$$A_{hcA}=r_{hcA}=\lambda_A .$$

After consolidation is complete, λ_A becomes zero; cxt instead of hippocampal neurons now represent contexts.

Taking CS1 in context A as an example of a context/CS conjunction, prior to consolidation,

$$A_{hcA1}= \lambda_{A1} (A_{cxpA} r_{cxpA} \cdot A_{cxpCS1} r_{cxpCS1})^{1/2} \quad \text{and}$$
$$r_{hcA1}= \lambda_{A1} (A_{cxpA} r_{cxpA} \cdot A_{cxpCS1} r_{cxpCS1})^{1/2}$$

If context A and CS1 are both present,

$$A_{hcA1}=r_{hcA1}=\lambda_{A1} .$$

After consolidation is complete, λ_{A1} becomes zero; cxt instead of hippocampal neurons now represent configural stimuli.

Step 3: Calculate A and r for cxi cells

$$A_{cxiA}=\lambda_A A_{hcA} r_{hcA} \quad \text{and} \quad r_{cxiA}=\lambda_A A_{hcA} r_{hcA} .$$

So if context A is present,

$$A_{cxiA}=r_{cxiA}=\lambda^2_A$$

Step 4: Calculate A and r for cxt cells.

Cortical cxt cells are innervated by cxp cells via synapses that must become potentiated before they are effective. The extent of such potentiation is represented by a factor μ, analogous to the factor λ discussed above for the hippocampus, which ranges from zero to unity. The ability of cxp cells to recruit cxt cells can develop either as the result of stimulus exposure after hippocampal ablation (compensation) or as the result of consolidation of hippocampal incidental learning (the change rules for compensation and consolidation will be given below).

In either case, the expressions for *A* and *r* as a function of cxp input are similar to those given for hippocampal cells in Step 2 above:

Taking context A as an example of a simple context, prior to consolidation,

$$A_{cxtA} = \mu_A A_{cxpA} r_{cxpA} \quad \text{and} \quad r_{cxtA} = \mu_A A_{cxpA} r_{cxpA} .$$

Thus,

$$A_{cxtA} = r_{cxtA} = \mu_A$$

Taking CS1 in context A as an example of a context/CS conjunction,

$$A_{cxtA1} = \mu_{A1} \left(A_{cxpA}\, r_{cxpA} \cdot A_{cxpCS1}\, r_{cxpCS1}\right)^{1/2} \quad \text{and}$$

$$r_{cxtA1} = \mu_{A1} \left(A_{cxpA}\, r_{cxpA} \cdot A_{cxpCS1}\, r_{cxpCS1}\right)^{1/2} .$$

In the above two formulas *A* and *r* are geometric means of input activations. This was done for use when simulating partial lesions for various kinds for simulations not done in this paper. Here, where in all the simulations A_{cxp}s, and r_{cxp}s are either zero or unity, this detail is irrelevant. In these simulations, when context A and CS1 are both present

$$A_{cxtA1} = r_{cxtA1} = \mu_{A1} ,$$

and otherwise both *A* and *r* are zero.

Step 5: Evaluate amygdala

A. Evalutate LA and BL. The neuron types that innervate LA and BL are listed in the following two tables. Each is given an index (j for cortical neurons innervating LA and k for hippocampal neurons innervating BL)in the left column of the table; this index simplifies later expressions.

Table 1

index	Input cell type	Number of active neurons	Activation	Habituation factor
j		**$n_{cx}(j)$ (=value if stim present)**	**$A_{cx}(j)$ (=value if stim present)**	**$H_{cx}(j)$**
1	cxpA	$r_{cxpA}\, N_{Pcntxt}\ (= N_{Pcntxt})$	$A_{cxpA}\ (=1)$	H_{cntxt}
2	cxpB	$r_{cxpB}\, N_{Pcntxt}\ (= N_{Pcntxt})$	$A_{cxpB}\ (=1)$	H_{cntxt}
3	cxpC	$r_{cxpC}\, N_{Pcntxt}\ (= N_{Pcntxt})$	$A_{cxpC}\ (=1)$	H_{cntxt}
4	cxpCS1	$r_{cxpCS1}\, N_{Pcs}\ (= N_{Pcs})$	$A_{cxpCS1}\ (=1)$	H_{cs}
5	cxpCS2	$r_{cxpCS2}\, N_{Pcs}\ (= N_{Pcs})$	$A_{cxpCS2}\ (=1)$	H_{cs}
6	cxiA	$r_{cxiA}\, N_I\ (=\lambda^2_A N_I)$	$A_{cxiA}\ (=\lambda^2_A)$	H_{cntxt}
7	cxiB	$r_{cxiB}\, N_I\ (=\lambda^2_B N_I)$	$A_{cxiB}\ (=\lambda^2_B)$	H_{cntxt}
8	cxiC	$r_{cxiC}\, N_I\ (=\lambda^2_C N_I)$	$A_{cxiC}\ (=\lambda^2_C)$	H_{cntxt}
9	cxtA	$r_{cxtA}\, N_{Tcntxt}\ (=\mu_{cxtA} N_{Tcntxt})$	$A_{cxtA}\ (=\mu_{cxtA})$	H_{cntxt}
10	cxtB	$r_{cxtB}\, N_{Tcntxt}\ (=\mu_{cxtB} N_{Tcntxt})$	$A_{cxtB}\ (=\mu_{cxtB})$	H_{cntxt}
11	cxtC	$r_{cxtC}\, N_{Tcntxt}\ (=\mu_{cxtC} N_{Tcntxt})$	$A_{cxtC}\ (=\mu_{cxtC})$	H_{cntxt}
12	cxtA1	$r_{cxtA1}\, N_{Tcnj}\ (=\mu_{cxtA1} N_{Tcnj})$	$A_{cxtA1}\ (=\mu_{cxtA1})$	H_{cs}
13	cxtA2	$r_{cxtA2}\, N_{Tcnj}\ (=\mu_{cxtA2} N_{Tcnj})$	$A_{cxtA2}\ (=\mu_{cxtA2})$	H_{cs}
14	cxtB1	$r_{cxtB1}\, N_{Tcnj}\ (=\mu_{cxtB1} N_{Tcnj})$	$A_{cxtB1}\ (=\mu_{cxtB1})$	H_{cs}
15	cxtB2	$r_{cxtB2}\, N_{Tcnj}\ (=\mu_{cxtB2} N_{Tcnj})$	$A_{cxtB2}\ (=\mu_{cxtB2})$	H_{cs}
16	cxtC1	$r_{cxtC1}\, N_{Tcnj}\ (=\mu_{cxtC1} N_{Tcnj})$	$A_{cxtC1}\ (=\mu_{cxtC1})$	H_{cs}
17	cxtC2	$r_{cxtC2}\, N_{Tcnj}\ (=\mu_{cxtAC2} N_{Tcnj})$	$A_{cxtC2}\ (=\mu_{cxtC2})$	H_{cs}

Table 2

index	Input cell type	Number of active neurons	Activation	Habituation factor
k		**n_{hc}(k) (=value if stim present)**	**A_{hc}(k) (=value if stim present)**	**H_{hc}(k)**
1	hcA	$r_{hcA} N_{Hcntxt}$ $(=\lambda_A N_{Hcntxt})$	A_{hcpA} $(=\lambda_A)$	H_{cntxt}
2	hcA	$r_{hcB} N_{Hcntxt}$ $(=\lambda_B N_{Hcntxt})$	A_{hcpB} $(=\lambda_B)$	H_{cntxt}
3	hcA	$r_{hcC} N_{Hcntxt}$ $(=\lambda_C N_{Hcntxt})$	A_{hcpC} $(=\lambda_B)$	H_{cntxt}
4	hcA1	$r_{hcA1} N_{Hcnj}$ $(=\lambda_{A1} N_{Hcnj})$	A_{hcA1} $(=\lambda_{A1})$	H_{cs}
5	hcA2	$r_{hcA2} N_{Hcnj}$ $(=\lambda_{A2} N_{Hcnj})$	A_{hcA2} $(=\lambda_{A2})$	H_{cs}
6	hcB1	$r_{hcB1} N_{Hcnj}$ $(=\lambda_{B1} N_{Hcnj})$	A_{hcB1} $(=\lambda_{B1})$	H_{cs}
7	hcB2	$r_{hcB2} N_{Hcnj}$ $(=\lambda_{B2} N_{Hcnj})$	A_{hcB2} $(=\lambda_{B2})$	H_{cs}
8	hcC1	$r_{hcC1} N_{Hcnj}$ $(=\lambda_{C1} N_{Hcnj})$	A_{hcC1} $(=\lambda_{C1})$	H_{cs}
9	hcC2	$r_{hcC2} N_{Hcnj}$ $(=\lambda_{C2} N_{Hcnj})$	A_{hcC2} $(=\lambda_{C2})$	H_{cs}

In order to calculate the depolarization of an LA neuron from the values in Table 1, a coefficient is first calculated, and then this is used in calculating the voltage

$$coeff_{LA}(j) = n_{cx}(j) A_{cx}(j) H_{cx}(j)$$

The inhibitory interneuron response is calculated as

$$V_{LAi} = \frac{\sum_j coeff_{LA}(j)\, g_{eLAi}(j)}{1 + \sum_j coeff_{LA}(j)\, g_{eLAi}(j)}\, E$$

Activations are calculated from depolarizations using the linear sigmoid function defined above.

$$A_{LAi} = linsig(V_{LAi} \mid 0, V_{LAiMxat})$$

Depolarization of LA principal cell distal compartments are given by

$$V_{LApDst} = \left(\frac{\sum_j coeff_{LA}(j)\, g_{eLAp}(j)}{1 + \sum_j coeff_{LA}(j)\, g_{eLAp}(j)} \right) E$$

Distal and proximal compartments are assumed to be electrotonically sufficiently distant from each other so that there is no mutual shunting. Although this would imply electrotonic decrement of V from distal to proximal, this can be arbitrarily compensated by adjusting the threshold and saturation point (*Mxat*) of the principal cell activation function, and so for simplicity is ignored. Thus,

$$V_{LAp\,\mathrm{Prx}} = \left(\frac{V_{Dst}}{1 + A_{LAi}\, g_{iLA}} \right) E$$

and

$$A_{LAp} = linsig(V_{LAp} \mid 0, V_{LApPrxMxat}) \ ,$$

where here and elsewhere *Mxat* is the value of *V* at which the linear sigmoid activation function for *A* becomes unity.

The evaluation of BL proceeds in the same way as for LA above.

$$coeff_{BL}(k) = n_{hc}(k) A_{hc}(k) H_{hc}(k)$$

$$V_{BLi} = \frac{\sum_j coeff_{BL}(k)\, g_{eBLi}(k)}{1 + \sum_j coeff_{BL}(k)\, g_{eBLi}(k)}\, E$$

$$A_{BLi} = linsig(V_{BLi} \mid 0, V_{BLiMxat})$$

$$V_{BLpDst} = \left(\frac{A_{LAp}\, g_{LA-BL} + \sum_j coeff_{BL}(j)\, g_{eBLp}(j)}{1 + A_{LAp}\, g_{LA-BL} + \sum_j coeff_{BL}(j)\, g_{eBLp}(j)} \right) E$$

$$V_{BLpPrx} = \left(\frac{V_{BLpDst}}{1 + A_{BLi}\, g_{iBL}} \right) E$$

$$A_{BLp} = linsig(V_{BLp} \mid 0, V_{BLpPrxMxat})$$

B. Evaluate CEm. **CEm** is driven by **BLp** if BL is intact. In the absence of BL a single CS-US pairing is sufficient to cause potentiation of a pathway from **LAp** to **CEm**. Thus

$$A_{CEm} = \begin{cases} A_{BLp} & \text{if BL intact (i.e. BLs Switch = 0)} \\ g_{BL\text{-}CEm}\, A_{LAp} & \text{if BL inactivated (i.e. BLs Switch = 1) and LAp-CEm synapes have become potentiated; } g_{BL\text{-}CEm} <= 1 \end{cases}$$

Step 6: Compute A_F and Freezing scores.

$$A_F = \begin{cases} \text{linsig}(A_{CEm} \mid a, b) & \text{if } A_{US}=0 \\ 0 & \text{otherwise .} \end{cases}$$

Freezing is indexed by a variable Φ that ranges between 0 (maximal activity) and 1 (total stillness) and increases according to the following rules, which provide some inertia to changes in freezing scores:

First a "smeared" version of A_F, A_{F*} is computed. A_{F*} begins at zero. Subsequently, if A''_F is the value of A_F on the next interval, the change in A_{F*} is computed by

$$\Delta A_{F*} = \begin{cases} c(A''_F - A_{F*}) & \text{if } A''_F > A_{F*} \\ \text{d}((A''_F - A_{F*}) & \text{if } A''_F < A_{F*} \end{cases}$$

Then Φ is given by

$$\Phi = \begin{cases} A_{F*} & \text{if } A_{US}=0 \\ 0 & \text{otherwise} \end{cases}$$

Thus freezing is a temporally smeared version of A_F, A_{F*}, unless the automaton is being shocked, in which case freezing goes to zero to emulate an animal hopping about due to the shock.

Step 7: Compute A_R and A_X

The value of A_R during an interval is calculated as the increment in input to **R** on the current interval relative to that at the end of the previous interval (after the calculation of any weight changes and indicated by primed (') values below). Thus,

A_R =linsig(R_{input} - R'_{input} | 0,1) where
$R_{input} = A_U + \sigma A_S$
$A_U = A_{US}[1 - (1- \nu) (A'_\Omega)^\pi]$
A'_Ω= linsig (A'_{CEm} | Ω_{thrsh} , 1)
A_S= linsig (A_{CEm} | 0, S_{mx})

A_U is proportional to A_{US}, attenuated by any ongoing opiate-transmission-mediated inhibition of **U** (computed in the previous interval); this attenuation is part of the basis for blocking. It can be prevented by pharmacological opiate receptor blockage, the extent of which is represented by the ν (1~ to full blockage). The activity of **Ω** is proportional to the activity of **CEm** above a threshold Ω_{thrsh}.

The parameter σ controls the effectiveness of input from **S** to **R** and thus the effectiveness of secondary reinforcement, and S_{mx} determines the level of A_{CEm} activity at which **S** firing rate saturates, which limits the secondary reinforcement when contextual fear is already high.

Neuron **X**, which is recruited by **Ω** via disinhibition, fires at the same rate as **Ω** unless it inhibited (absolutely) by the activity of **R** or by the US.

$$A_X = \begin{cases} 0 & \text{if } A_R \text{ or } A_{US} > 0 \\ (1- \nu)A_\Omega & \text{otherwise} \end{cases}$$

Where A_Ω= linsig (A_{CEm} | Ω_{thrsh} , 1) and ν is as explained above.

Step 8: Compute B_ps and $'Ca'_i$s

Synaptic change in LA and BL is contingent both on neuromodulators released by **R** or **X** and by dendritic 'Ca' or voltage levels.

For principal cells, dendritic voltages affecting change are produced by a back-propagated, graded spike-like signal whose magnitude is determined by a combination of the depolarization of the proximal compartment and direct (not neuromodulatory) input from **R**:

B_{LAp} = 100 linsig(V_{LApPrx} + $\xi_{LA} A_R$ |0,100)
B_{BLp} = 100 linsig(V_{BLpPrx} + $\xi_{BL} A_R$ |0,100)
where ξ_{LA} and ξ_{BL} are multipliers that control the contribution to **B** of input from **R**.

For inhibitory interneurons 'Ca' levels are controlled by recurrent input from principal cells and input from **R**:
$'Ca'_{LAi}$ = 100 linsig(A_{LAp} $V_{LApMxat}$ + κ_{LA} A_R | 0, 100)
$'Ca'_{BLi}$ = 100 linsig(A_{BLp} $V_{BLpMxat}$ + κ_{BL} A_R | 0, 100)

Step 9: Calculate changes in synaptic conductances (synaptic weights)
If $A_R > 0$

$\Delta g_{LAp}(j) = e_{LA}(j) \cdot A_R \cdot R_{LAp}(B_{LAp})$ and $\Delta g_{BLp}(j) = e_{BL}(j) \cdot A_R \cdot R_{BLp}(B_{BLp})$
$\Delta g_{LAi}(j) = e_{LA}(j) \cdot A_R \cdot R_{LAi}('Ca'_{LAi})$ and $\Delta g_{BLi}(j) = e_{BL}(j) \cdot A_R \cdot R_{BLi}('Ca'_{BLi})$

and if $A_X>0$ and $A_R=0$ (latter condition only relevant if experimental procedure overrides absolute inhibition of **X** by **R**)

$\Delta g_{LAp}(j) = e_{LA}(j) \cdot A_X \cdot X_{LAp}(B_{LAp})$ and $\Delta g_{BLp}(j) = e_{BL}(j) \cdot A_X \cdot X_{BLp}(B_{BLp})$
$\Delta g_{LAi}(j) = e_{LA}(j) \cdot A_X \cdot X_{LAi}('Ca'_{LAi})$ and $\Delta g_{BLi}(j) = e_{BL}(j) \cdot A_X \cdot X_{BLi}('Ca'_{BLi})$

where the *B*s and *'Ca'*s are calculated as above, eligibilities $e_{LA}(j)$ and $e_{BL}(k)$ are as computed below, and *R*s and *X*s are as in Fig. 5C of the main paper and are calculated as follows (for the simulations of this paper $R(B)$ and $X('Ca')$ are the same in LA and BL):

$R_{LAp}(B) = \alpha_{LA}\ \mathrm{linsig}(B|\theta_{LApR}, E)$
$X_{LAi}('Ca') = \beta_{LA}\{1-\exp[-\gamma \mathrm{linsig}('Ca'|\theta_{LAiX}, E)]\}$
$R_{LAi}('Ca') = \eta_{LA}\ \mathrm{linsig}('Ca'|\theta_{LAiR}, E)$
$X_{LAp}(B) = \zeta_{LA}$ if B is between θ_{LApX} and δ_{LA}, and 0 otherwise

$R_{BLp}(B) = \alpha_{BL}\ \mathrm{linsig}(B|\theta_{BLpR}, E)$
$X_{BLi}('Ca') = \beta_{BL}\{1-\exp[-\gamma \mathrm{linsig}('Ca'|\theta_{BLiX}, E)]\}$
$R_{BLi}('Ca') = \eta_{BL}\ \mathrm{linsig}('Ca'|\theta_{BLiR}, E)$
$X_{BLp}(B) = \zeta_{BL}$ if B is between θ_{BLpX} and δ_{BL}, and 0 otherwise

Step 10: Re-evaluate amygdala with new weights.
Repeat the computations of 5A, above, with the now updated synaptic weights.

Step11: Update LA-CEm connectivity
According to Anglada-Figueroa and Quirk (Anglada-Figueroa and Quirk, 2005) post-training ablation of BL abolishes previously learned CRs to discrete cues but pre-training lesions allow normal learning and extinction of such responses. Although there is some recent data that raise questions about the generality of this finding (Amano et al., 2010), we decided to accept it for the purposes of constructing FRAT. In order to simulate these properties in FRAT we assume that the direct synapses between LA and CEm neurons are initially ineffective and remain so as long as BL is intact, due to some sort of inhibitory interaction. However, in the absence of BL (Switch *BLs*=1 (see below)), co-activity of LA principal neurons and US-driven activity of **CEm** neurons (Pare et al., 2004), cause potentiation of **LAp-CEm** synapses. Thus $g_{LA\text{-}CEm} = 0$ until it is simultaneously the case that switch $BLs = 1$, $A_{LAp}>0$, and $A_{US} > 0$, at which point its value switches irreversibly to $g_{LA\text{-}CEmON}$. However, if inactivation of BL is discontinued, transmission via this pathway is again inhibited, although the **LAp-CEm** synapse remains potentiated.

Step 12: Re-evaluate A_{CEm} and R_{inpt} ***with new weights.***

Calculate the current value of A_{CEm} by repeating the computations of 5B above with the current values of A_{LAp}, A_{BLp}, and $g_{LA\text{-}CEm}$.

Now using the current values of all the above variables, calculate A_Ω and R_{inpt} (as in step 7 above):

A_Ω= linsig (A_{CEm} | Ω_{thrsh} , 1)

A_U=A_{US}[1 - (1- ν)(A_Ω)$^\pi$]

A_S= linsig (A_{CEm} | 0, S_{mx})

R_{input} = A_U + ν A_S

The (primed) values needed for comparison in the next interval are:

R'_{input} = R_{input}

A'_Ω = A_Ω

Step13: Update hippocampal and cortical incidental learning factors (λ ***and*** μ***)***

The factor λ specifies the degree to which cxp cells can recruit hippocampal representations and μ the degree to which cxp cells can recruit cxt representations.

The rules for updating these factors as a function of exposure are slightly different for simple contexts and context/CS compounds. For simple contexts, taking context A as illustrative:

$\Delta\lambda_A$= k_λ(1- λ_A)^c_λ and $\Delta\mu_A$=k_μ(1- μ_A)^c_μ

where ^ denotes exponentiation. Without the exponent these would be the equations for negative exponential growth, but the exponents allows for somewhat different early and late rates of increase. This complexity was needed to allow adequate simulation of experimental data on the immediate shock deficit. Once λ or μ become greater than λ_{max} or μ_{max} , which are very close to unity, they are set to one.

The rules for compounds were based on the assumption that it should not be possible for the representation of a context/CS compound to be further developed than that of the context itself. Thus values were allowed to grow according to the same type of rule as above (though with parameters that gave faster learning than for pure contexts), but they were clipped at the current value of the factor for the pure context. Taking the context-A/CS1 compound as an example, the rules used were:

$\Delta\lambda_{A1}$= (λ_A - λ_{A1}) linsig[$k_{\lambda cnj}$(1 - λ_{A1})^$c_{\lambda cnj}$ |0, λ_A - λ_{A1}] and

$\Delta\mu_{A1}$= (μ_A - μ_{A1}) linsig[$k_{\mu cnj}$(1 - μ_{A1})^$c_{\mu cnj}$ |0, μ_A - μ_{A1}] .

When incidental learning causes an increase in the number of units representing a stimulus that has previously been associated with some outcome, the newly recruited units are not already conditioned. In order to avoid having to keep a separate tally of the synaptic efficacies of afferents of a given kind that have had different reinforcement histories, synaptic conductances per afferent were treated as *average conductances per afferent* over the population recruited by a given stimulus. Such average conductances decreased when afferents were recruited without further reinforcement. Taking as an example the per afferent conductance $g_{eLAp}(1)$ of context A representing neurons on LA principal cells: If λ_A were to increase to λ''_A as the result of implicit learning, the new average conductance per afferent would go to $g''_{eLAp}(1) = (\lambda_A/\lambda''_A)\ g_{eLAp}(1)$. Given that changes in synaptic weights are entirely additive in the model, this simplifying procedure gives exactly accurate results.

Step 14: Update eligibilities

Eligibility can range from zero to unity. Eligibility for the next interval is determined by the activity of each afferent at the end of the previous interval according to the rule,

$e(x)$ = linsig[$A(x)|\ \varepsilon,\ 1$], where ε is a small threshold activation.

Once incidental learning is complete, eligibilities are always either zero or unity. Note that eligibility levels are retained for one interval following the termination of a stimulus. This allows successful conditioning even if US onset occurs at the moment of CS offset.

Special events

Consolidation.

In FRAT consolidation amounts to shifting contextual and context/CS conjunctional representations from hippocampus to cortical cxt cells and adjusting the weights of cxt-LA principal cell and inhibitory interneuron synapses so that behavioral responses to all stimuli are similar to what they were before these changes. This is done by a four step process:

(1) Let $\lambda^*(i)$ be the current values of $\lambda(i)$
(2). For each type of hippocampal context and context/CS representation: Calculate A_{BLp} with the activation of the cxp representations that drive the representation set to unity, all inhibitory activity suppressed, $\mu(i)$=0, and $\lambda(i)$=$\lambda^*(i)$. Then find the value of g_{eLAp} that gives the same A_{BLp} when $\lambda(i)$=0 and $\mu(i)$=$\lambda^*(i)$.
(3) With V_{BLpDst} set by direct depolarization to a value that just barely makes A_{BLp}=1, (all excitatory input to *BLp* off), for each type of context and context/CS representation: Calculate A_{BLp} with the activation of the cxp representations that drive the it set to unity, all $\mu(i)$=0, and $\lambda(i)$=$\lambda^*(i)$. Then with $\lambda(i)$=0 determine what value of g_{eLAi} would produce the same A_{BLp}.
(4) Finally, set all $\lambda(i)$ to zero and $\mu(i)$=$\lambda^*(i)$.

Taking the representation for context A as illustrative, the formulas for the g_{eLAp}(A) and g_{eLAi} are as follows (much of this is as in Tables 1 and 2 of Step 5 above, but with representation names replacing index *j* and *k* values.

$g_{eLAp}(\text{cxtA}) = A_{BLp} / \{coeff_{LA}(\text{cxtA})\cdot[Z\,(1+g_{LA\text{-}BL}) - A_{BLp}(1+g_{LA\text{-}BL}\,Z)]\}$ where
$coeff_{BL}(\text{hc}_\text{A}) = n_{hcA}\ A_{hcA}\ H_{hcA}$
$n_{hcA} = \lambda^*_{hcA}\ N_{Hcntxt}$
$A_{hcA} = \lambda^*_{hcA}$
$H_{hcA}=H_{cntxt}$
$coeff_{LA}(\text{cxtA})$
$n_{cxtA} = \lambda^*_{cxtA} N_{Tcntxt}$
$A_{cxtA} = \lambda^*_{cxtA} N_{Tcntxt}$
$H_{cxtA}=H_{cntxt}$
$A_{BLp} = coeff_{BL}(\text{hc}_\text{A})\ g_{eBLp}(\text{hc}_\text{A})\ E / \{V_{BLpPrxMxat}\,[1 + coeff_{BL}(\text{hc}_\text{A})\ g_{eBLp}(\text{hc}_\text{A})]\}$
$Z = E/V_{LApPrxMxat}$

g_{eLAi}(cxtA) =(1-A_{BLp})(1+$g_{LA\text{-}BL}$) / {$coeff_{LA}$(cxtA)·[$Z_i A_{BLp}$ - (1- A_{BLp})(1+$g_{LA\text{-}BL}$)]}
$coeff_{BL}$ and $coeff_{LA}$ are as above
A_{BLi}= $coeff_{BL}$(hcA)·g_{eBLi} E/ {$V_{BLiMxat}$ [1+$coeff_{BL}$(hcA)]}
A_{BLp}= 1/(1+$g_{iBL}A_{BLi}$)
Z_i=g_{iLA} E / $V_{LAiMxat}$

The effect of LA or BL suppression during consolidation cannot really be predicted in the absence of a physiological model of the consolidation process. FRAT does not include such a model. Any such model would probably, as in the algorithm above, need to compute BL output in response to internally generated configural stimuli to be used as a target that cortical input would have to match after consolidation. And the matching process would presumably require intact function of both LA and BL. However, how the matching algorithm, whatever it was, would be affected by LA or BL suppression during the consolidation period would depend on the properties of the algorithm. We can be quite certain that normal consolidation would not occur with either LA or BL suppressed, but whether such manipulations would cause the development of no responses to configural cues after the consolidation period or spurious responses of some kind cannot be said.

In order to capture the flavor of all this to some degree, we have merely made the above algorithm inoperative if either BL or LA is suppressed during the consolidation period. Given this, if BL or LA is suppressed during consolidation, configural representations move from hc to cxt cells normally, but no LTP of cxt-to-LA cell synapses gets produced by the consolidation and so all responses to configural cues get lost.

Switches

For each of the following "switches", 0=off and 1=on. The following describes the consequences of the switch being on:

Hx -- Ablate hippocampus. All A_{hc} and r_{hc} = 0 and incrementing of μ enabled, as described in Step 13 above (referred to as in the main paper as "compensation.").

Hs -- Suppress hippocampus (e.g. muscimol). All A_{hc} and r_{hc} = 0; incrementing of μ not enabled.

PFCs -- Suppress PFC. Compensation does not occur. Consolidation does not occur. All A_{cxt}s =0 and r_{cxt}s=0 (see main paper Table 1, item W).

BLs -- Suppress BL. A_{BLp} and A_{BLi}=0 and plasticity of **LAp-CEm** synapses enabled as described in Step 11 above.

LAs -- Suppress LA. A_{LAp} and A_{LAi} =0. Only hippocampus-BL pathway can influence freezing.

CEMs-- Suppress CEm. A_{CEm}=0 and potentiation of **LAp-CEm** synapses cannot potentiate.

Parameters

Parameter	Value	Description and comment
α_{LA}	0.015	Reinforcement parameter for LA principal cells
α_{BL}	0.009	Reinforcement parameter for BL principal cells
β_{LA}	3e-6	Extinction parameter for LA interneurons
β_{BL}	7e-7	Extinction parameter for BL interneurons
η_{LA}	0.01	Reinforcement parameter for LA interneurons
η_{BL}	0.01	Reinforcement parameter for BL interneurons
ζ_{LA}	0	Extinction parameter for LA principal cells
ζ_{BL}	0	Extinction parameter for BL principal cells
N_{Pcs}	100	Number of cxp neurons representing each CS. 100 by definition
N_{Pcntxt}	1	Number of cxp contextual element -representing neurons that can be activated by each context.
N_I	0	Number of cxi neurons available to represent each context
N_{Tcntxt}	56	Number of cxt conjunction-representing neurons available to represent each pure context
N_{Tcnj}	250	Number of cxt neurons available to represent each context/CS conjunction.
N_{Hcntxt}	200	Number of hc neurons available to represent each pure context
N_{Hcnj}	250	Number of hc neurons available to represnt each context/CS conjunction
$V_{LAiMxat}$	30	Value of V at which activity of LA interneurons reach unity
$V_{BLiMxat}$	30	Value of V at which activity of BL interneurons reach unity
$V_{LApPrxMxat}$	80	Value of V at which activity of LA principal cells reach unity
$V_{BLpPrxMxat}$	66.67	Value of V at which activity of BL principal cells reach unity
$g_{BL\text{-}CDEm}$	1.0	Parameter specifying strength of fully potentiated **LAp** - **CEm** connection.
a	0.3	Activity of **CEm** that causes maximal **F** activity
b	0.66	Activity of **CEm** at which **F** begins to respond
c	0.9	Rate of rise of freezing
d	0.3	Rate of decay of freezing
σ	0.2	Parameter specifying effectiveness of secondary relative to that of primary reinforcement
S_{mx}	0.4	Activation of A_{CEm} at which A_S saturates at unity
π	1.25	Exponent controlling attenutation of A_U by Ω
Ω_{thrsh}	0.2	Threshold value of A_{CEm} at which Ω becomes activated
ξ_{LA}	100	Parameter specifying relative impact of A_R on back-propagated activity in LA principal cells
ξ_{BL}	100	Parameter specifying relative impact of A_R on back-propagated activity in BL principal cells
κ_{LA}	100	Parameter specifying relative impact of A_R on 'Ca' level of LA interneurons
κ_{BL}	100	Parameter specifying relative impact of A_R on 'Ca' level of BL interneuurons
θ_{LApR}	40	Threshold value of B at which R_{LAp} begins to increase
θ_{LAiR}	40	Threshold value of *'Ca'* at which R_{LAi} begins to increase
θ_{LAiX}	0	Threshold value of *'Ca'* at which X_{LAi} begins to increase
θ_{LApX}	20	Threshold value of B at which X_{LAp} increases
θ_{BLpR}	40	Threshold value of B at which R_{BLp} begins to increase
θ_{BLiR}	40	Threshold value of *'Ca'* at which R_{BLi} begins to increase
θ_{BLiX}	0	Threshold value of *'Ca'* at which X_{BLi} begins to increase
θ_{BLpX}	20	Threshold value of B at which X_{BLp} increases
δ_{LA}	50	Level of B at which X_{LAp} returns to zero (see Fig. 5C of main paper)
δ_{BL}	50	Level of B at which X_{BLp} returns to zero (see Fig. 5C of main paper)
γ	13	Rate of rise of X_i (see Fig. 5C of main paper)
k_λ	0.6	Rate of hippocampal incidental learning
k_μ	0.2	Rate of cortical incidental learning
c_λ	2.5	Exponent for hippocampal incidental learning
c_μ	2.5	Exponent for cortical incidental learning
$k_{\lambda\ cnj}$	0.1	Rate of hippocampal incidental learning for cntxt/CS conjunctions
$k_{\mu\ cnj}$	0.1	Rate of cortical incidental learning for cntxt/CS conjunctions
$c_{\lambda\ cnj}$	1.0	Exponent for hippocampal incidental learning for cntxt/CS conjunctions
$c_{\mu\ cnj}$	1.0	Exponent for cortical incidental learning for cntxt/CS conjunctions
λ_{max}	.9875	λ above which λ set to unity
μ_{max}	.98	μ above which μ set to unity
ε	0.05	Threshold activation for eligibility function.

SIMULATIONS

A variety of simulations for which there was not space in the main paper are shown here. Unless otherwise specified, CS duration was 30 sec, US duration 5 sec, and inter-trial interval 60 sec. Prior to the start of each experiment FRAT was given sufficient exposure to each context to cause full hippocampal contextual representations to form if the hippocampus was functional and full cxt representaions if hippocampus was ablated at the start of the experiment. Letters are item labels from Tables 1 and 4 of the main paper. Only items that were not illustrated in the main paper are discussed here.

Simulations for Table 1 of main paper

Table 1G. ***Extinction of CS fear and context fear should be stimulus-specific.*** Note that the second-extinguished CS (CS2) extinguished slightly faster in C than did CS1. That is because there is in fact some inhibition of BL principal cells by context C due to prior extinction of CS1 in C.

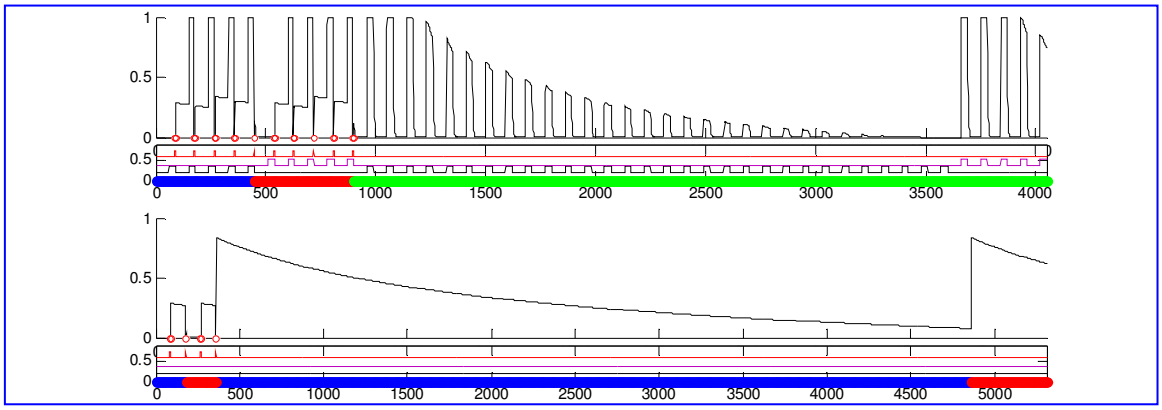


Table 1H. ***Renewal should have "gating-like" properties:*** Both CS1 and CS2 are extinguished, each in a different context. If the contexts in which they occur is then reversed, renewal occurs.

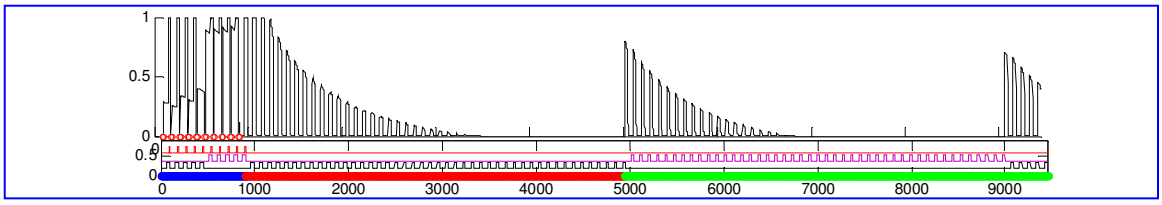


Table 1K. ***LA is required for learning of cued fear (tested in non-training context).*** When given CS training with standard conditions in one context and then CS fear is tested in a in a different context (so as to avoid background context fear), control FRAT shows trong CS fear, whereas LAs (i.e.LA suppressed) FRAT shows none. However similarly trained LAs FRAT shows good context fear in the training context.

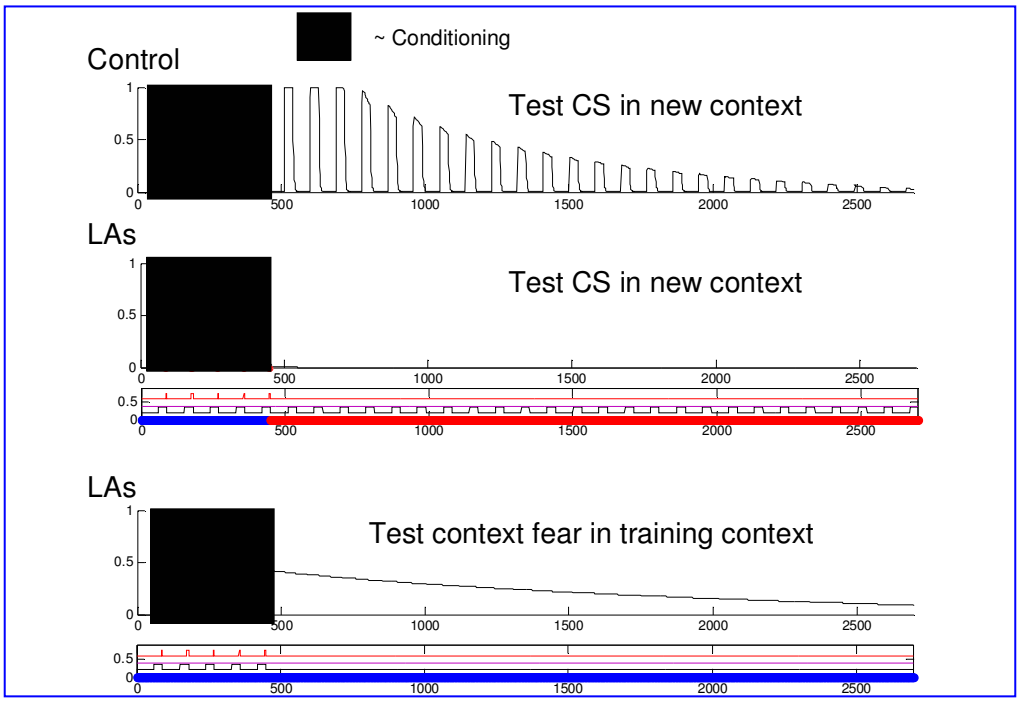


Table 1L. ***CEm is required for expression of both cue and context fear.***

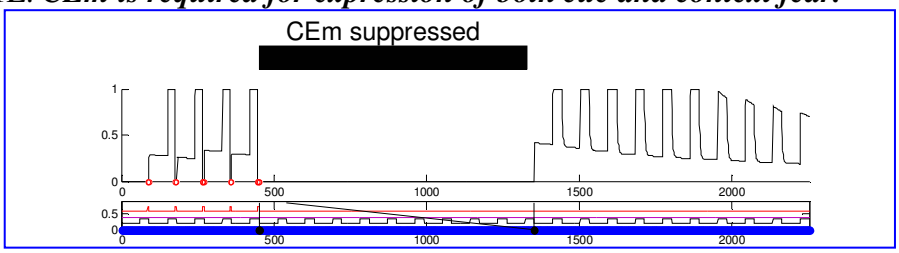


Table 1M. ***BL is required for expression of established CS fear, but CS fear can be established after pre-training BL inactivation.***

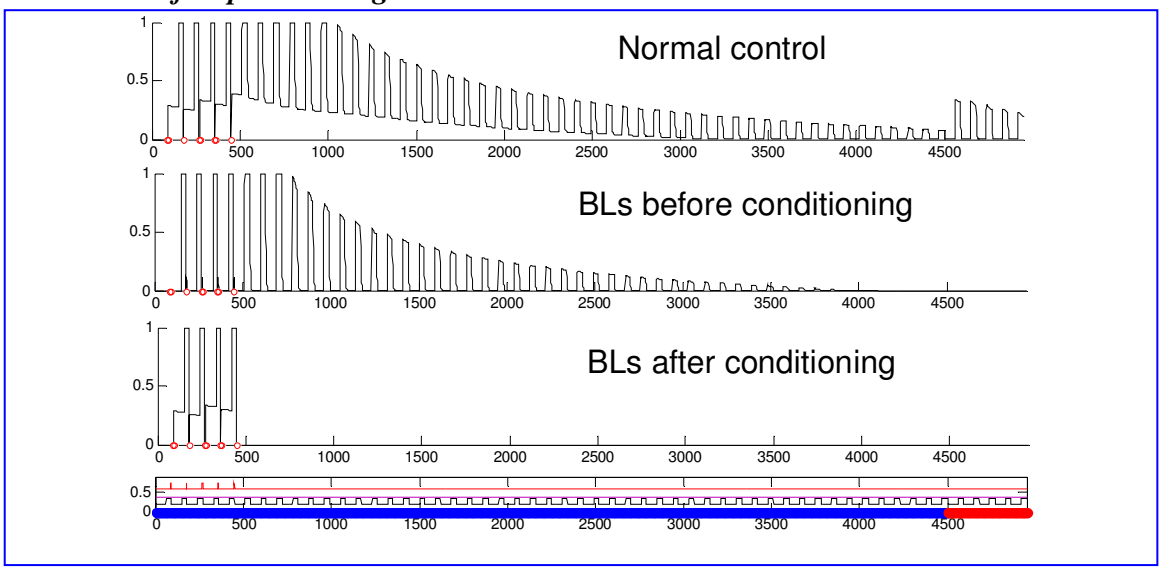


Table 1N. ***Pre-training lesions of BL prevent learning of context fear but not of cued fear.*** Also note that extinction occurs despite the inactivation of BL, because cue conditioning in absence of BL causes a path to form from **LAp** cells to **CEm** cells, and therefore the **X** neurons that are needed for extinction, can be recruited even though BL is inoperative.

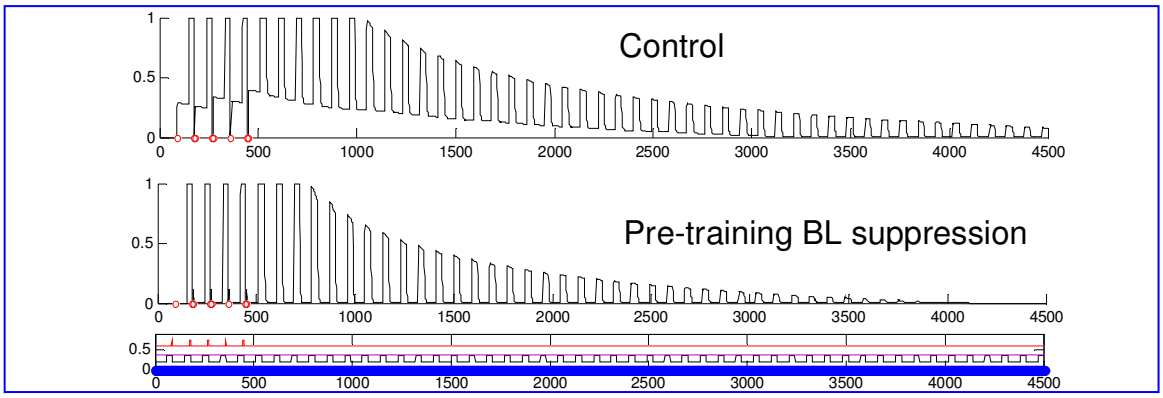


Table 1S. ***Retrograde amnesia for context fear does not occur if conditioning was to a long-familiar context:*** In both cases below there were 5 conditioning trials while FRAT was intact. Both CS fear and context fear were learned. Also in both cases, hippocampus was suppressed after the end of conditioning and test trials then given. In case 1, FRAT had had no experience with the training context prior to conditioning. In that case suppression of hippocampus caused retrograde amnesia of context fear. In case 2, prior to conditioning FRAT was give extensive experience with the context to be used for training, and consolidation was allowed to occur before the fear conditioning was done. In that case suppression of the hippocampus caused no retrograde amnesia for context fear.

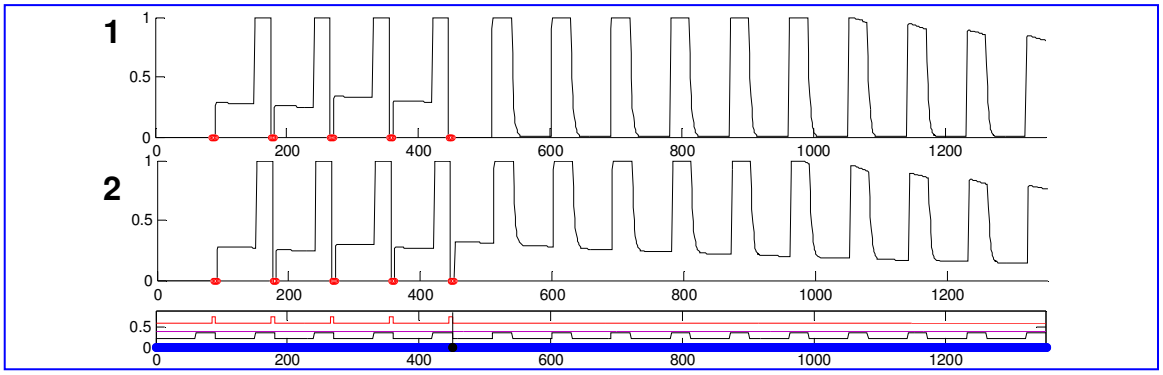


Table 1T. ***After pre-training hippocampal ablation, extinction should be context-specific, as evaluated by ABA, ABC, and AAB renewal.*** After hippocampal ablation FRAT was familiarized with all three contexts before running each of the experiments below. Note that only 3 conditioning trials were given and that US strength was 90% of maximal value usually used. This was done to enhance the difference between the three types of renewal. Because there was so much contextual fear in the ABA test, context fear was extinguished prior to the renewal test in the second frame. As in intact FRAT, renewal was in the order ABA, ABC, AAB.

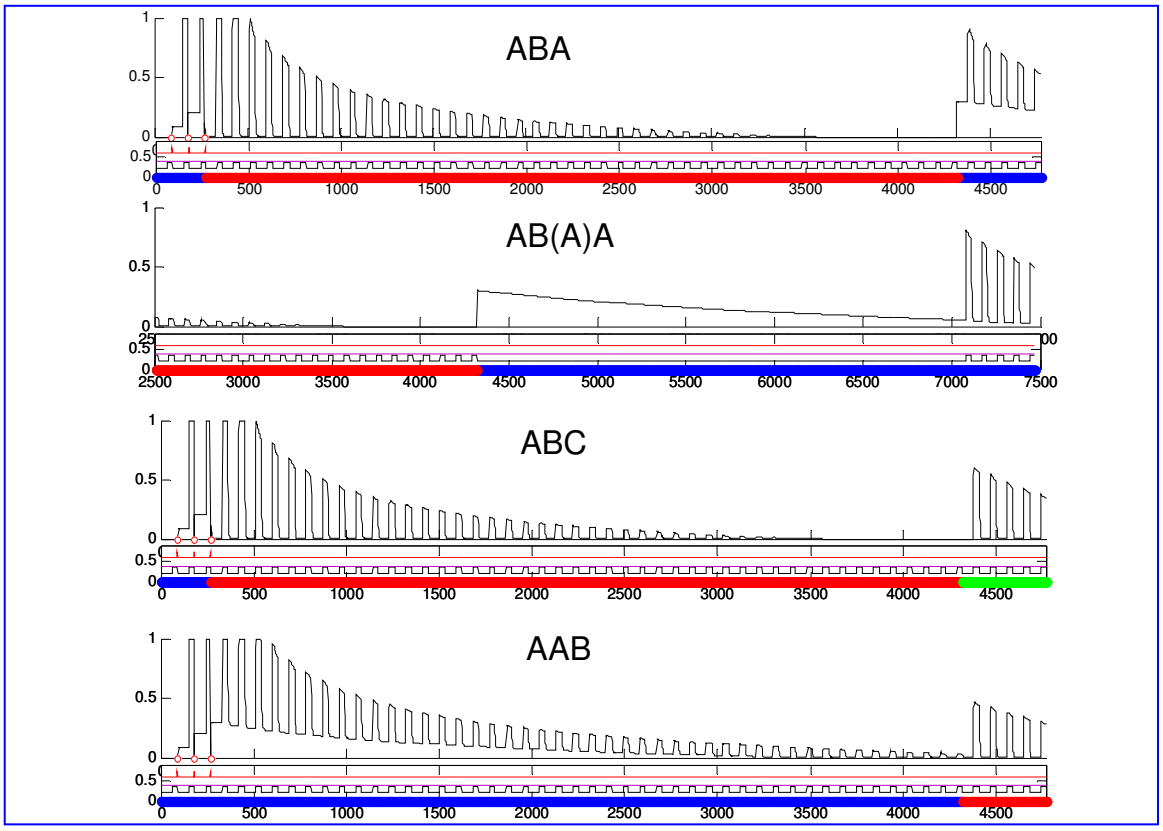


Table 1V. ***After hippocampal ablation, acquisition of context conditioning is PFC-dependent.*** Note that extinction is slow in the Hx + PFCs group because since PFCs prevents compensation, there is no contextual input to BL inhibitory interneurons.

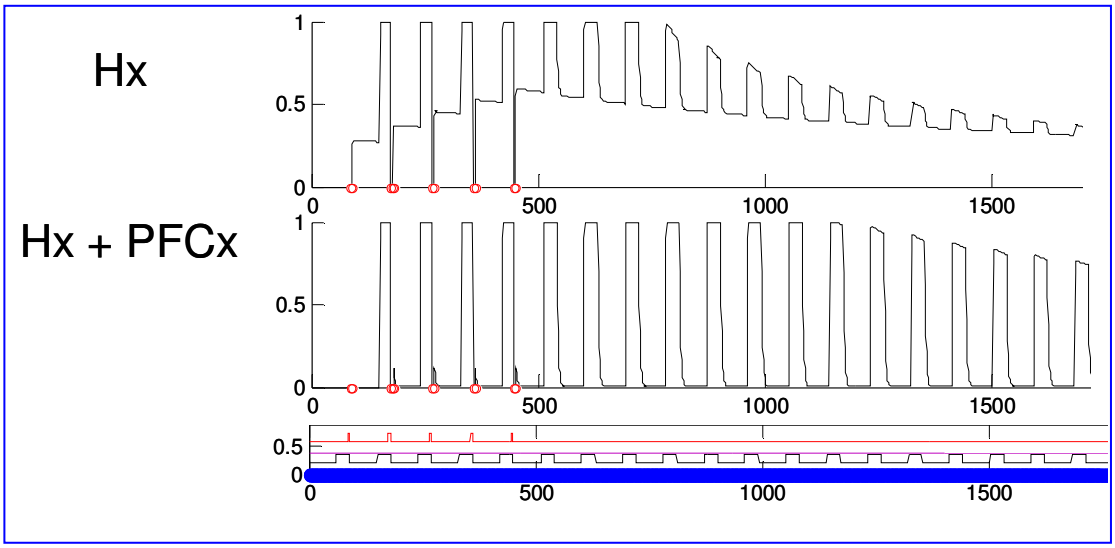
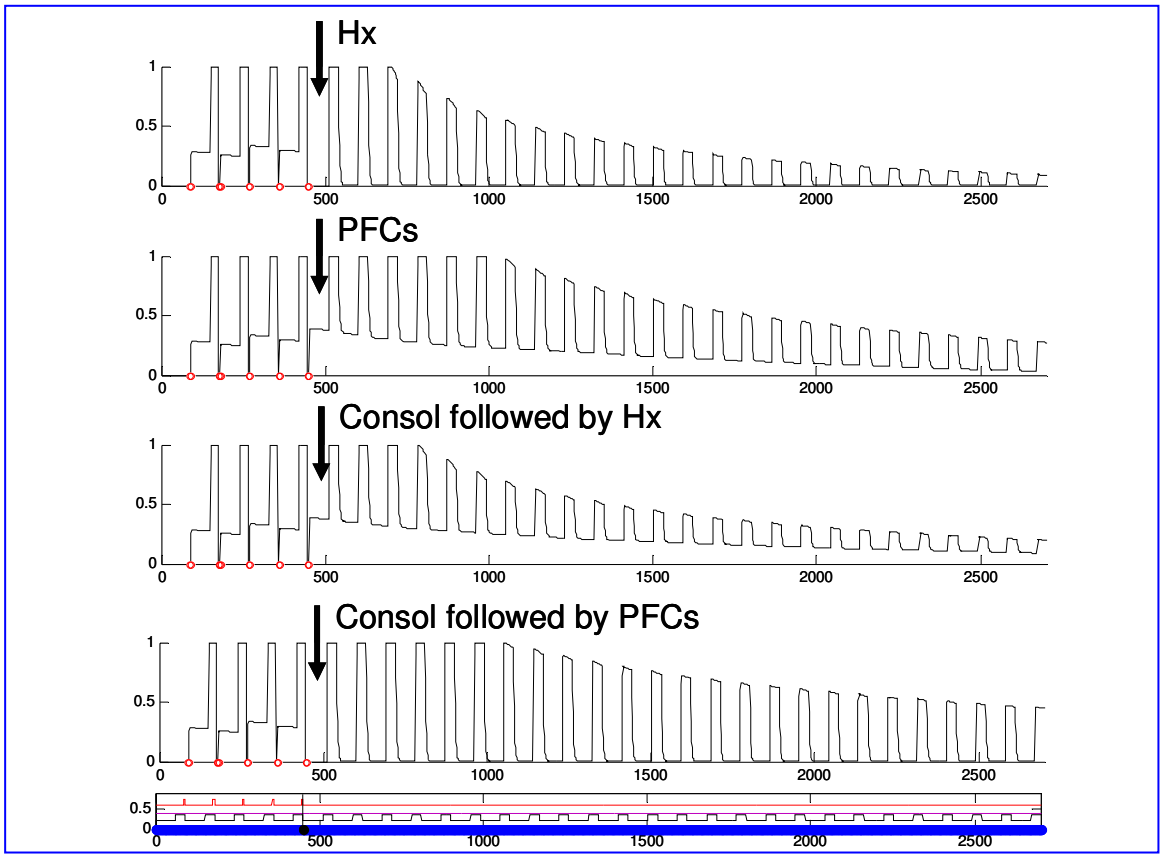


Table 1W. ***Expression of remote context fear is PFC-dependent.*** Experiments shown in order: (1) Hx prior to consolidation causes a loss of context fear (retrograde amensia). (2) PFCs alone causes no loss of context fear. (3) Hx after consolidation causes no loss of context fear (no retrograde amnesia). (4). PFCs after consolidation causes a loss of context fear; thus, expression of remote fear requires PFCs.



Simulations for Table 4 of main paper

Table 4B. ***Context-specificity of conditioning is unmasked by renewal after extinction in a novel context.*** Note that when at the end of the experiments CS1 is tested in its training context, responses are stronger and extinguish much less than when CS1 is tested in a context where CS2 was conditioned.

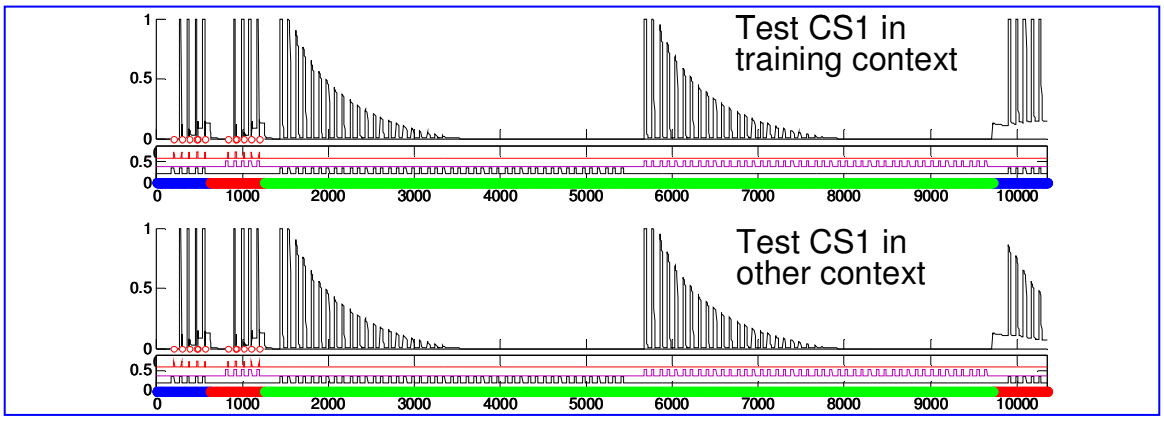


Table 4C. ***Extinction is enhanced if responses during extinction are strong.*** In the following simulations CS1 was conditioned using only a few conditioning trials with a weak US and then given 5 extinction trials with CS2, which either had been strongly conditioned or not conditioned. Finally, CS1 was tested alone. More extinction of CS1 occurred when it was accompanied during extinction by the strongly conditioned CS2. Co-occurrence of well-conditioned CS2 promotes the extinction of CS1 because it increases the amount of **CEm** activity, and thereby the amount of **X** activity during extinction.

Note that removal of CS2 at test causes the removal of any excitation that had been conditioned to it as well as any inhibition conditioned to it during extinction. Therefore, in the top case where mainly inhibition is removed, there is some renewal at test, wereas in the bottom case where both excitation and inhibition are removed, there is a small drop when CS2 is removed.

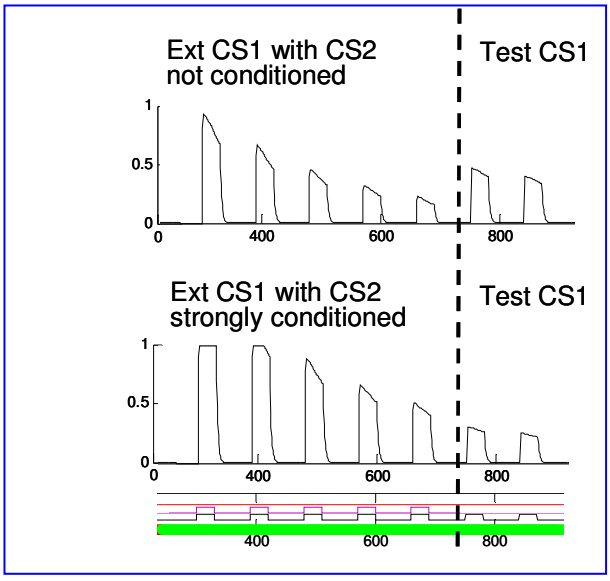


Table 4F. ***Extinction of (newly acquired) CS fear that is established with hippocampus suppressed (not ablated) does not show ABC or AAB renewal.*** Hippocampus suppressed starting at the dotted lines. ABC and AAB renewal do not occur.

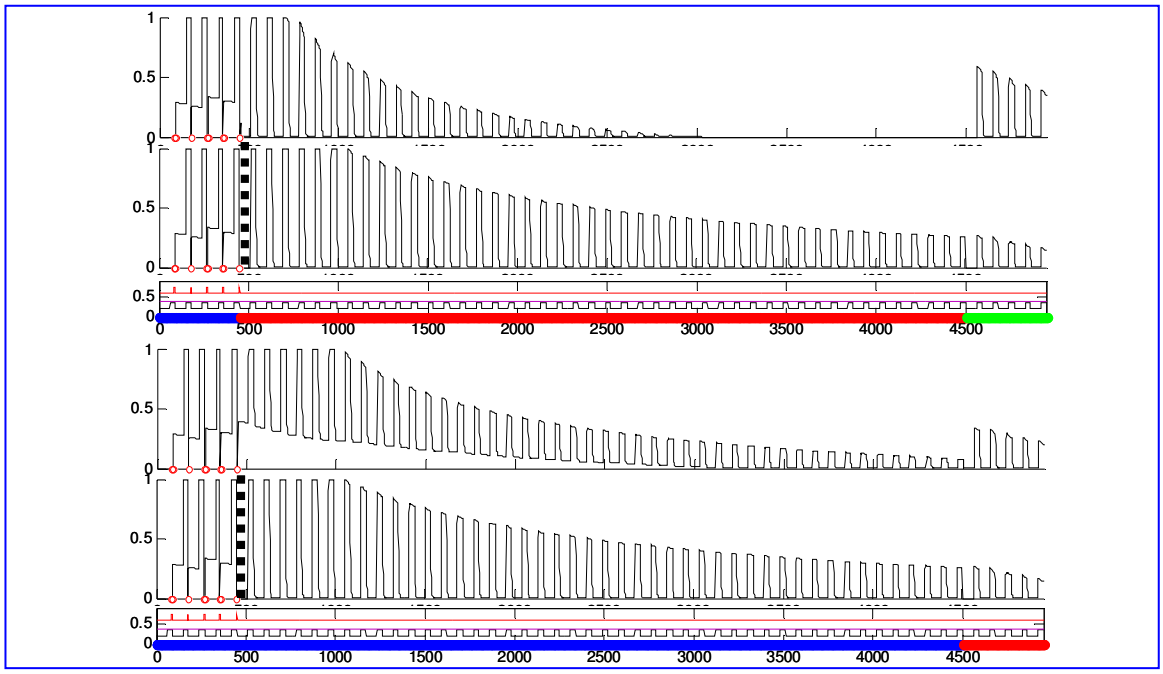
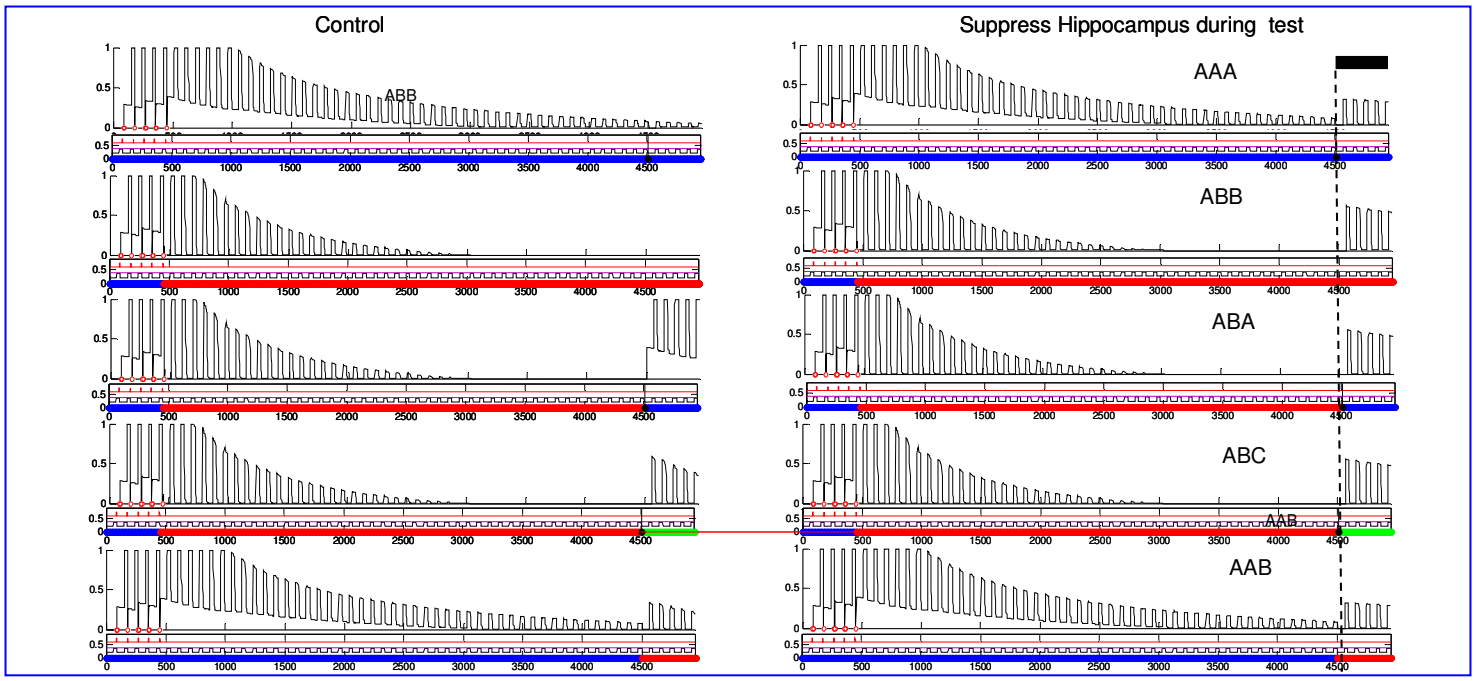


Table 4G. ***Suppression or ablation of hippocampus soon after extinction of newly acquired CS-fear causes partial recovery from extinction and abolishes all renewal due to context.*** The panels at the left of the figure below show conditioning, extinction,and test trials in various contexts in control FRAT. At the right are the same conditions but with suppression of hippocampus (Hs) during the five test trials at the end of each experiment. The effect of Hs is to cause a partial loss of extinction and bring responsiveness to a level that is independent of the context during the test but that does depend on whether extinction was carried out in the same context as conditioning or a different one. The amount of CS-specific inhibition that builds up during extinction is somewhat greater when extinction occurs in the context of training, because fear of the context and of the context/CS compound during extinction promote the development of inhibition.

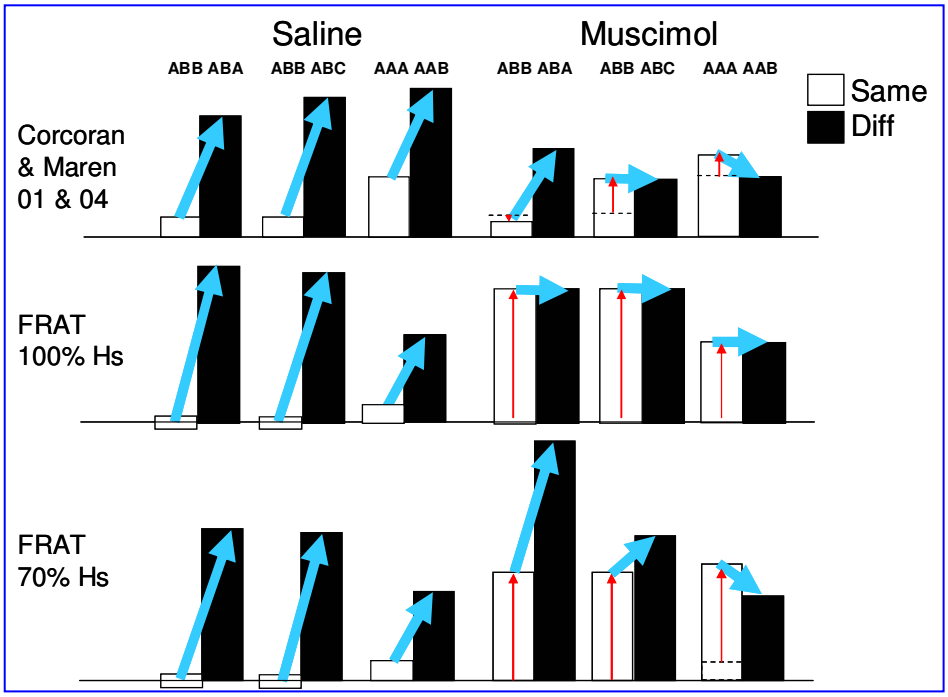
These data are compared to experimental data on the next page.



Corcoran and Maren (Corcoran and Maren, 2001; 2004) have done experiments, similar to those above, in which conditioning was done in context A, extinction in A or B, and then testing was carried out in one of the three contexts with or without muscimol being infused into the dorsal hippocampus during the test. Their data are shown in the top row below. The white bars show test freezing for tests in the context of extinction ("same") and the black bars show tests in a context different from that of extinction. Any baseline contextual freezing, which was presumably substantial during ABA renewal tests, was subtracted out but was not reported. The bold cyan arrows indicate the difference between the "same" and "different" tests and are the measure of renewal the authors used. In saline, ABA, ABC, AAB renewal all occur. Although ordinarily ABA renewal is stronger than ABC renewal, the procedure of subtracting contextual fear together with ceiling effects probably caused an under-estimation of extent of ABA renewal given the authors' methodology.

When the same experiments were done in the muscimol condition, no AAB or ABC renewal were seen, but ABA renewal was still substantial. There was also some tendency for muscimol to cause a little renewal of its own (red arrows), even when the rats remained in their original extinction context, though this trend is not said to be statistically significant. This trend was greatest in the 2001 experiment (Corcoran and Maren, 2001) in which muscimole appeared to increase responding in an ABB test, and it was seen somewhat in the AAA group of a 2004 experiment (Corcoran and Maren, 2004). It was not seen in the ABB group in the 04 data.

The second row shows FRAT simulation data graphed in the same manner as Corcoran and Maren's data. ABA, ABC, and AAB renewal were all abolished, and muscimole caused substantial renewal of its own. Note that extinction was more complete in the FRAT simulations than in the Cocoran/Maren experiments



Ordinarily ABA renewal is much more extensive than the other two forms. In FRAT this is the case because when a subject is returned to the conditioning context, cues that were present during conditioning and that have not been extinguished recur. However, in FRAT the representations of these cues all reach the amygdala via the hippocampus,

so the advantage of ABA renewal vanishes with hippocampus totally suppressed . However with sub-total hippocampal suppression, hippocampal cues promoting fear-responses do get reinstated to some degree when FRAT is returned to context A. We therefore did a set of simulations with suppression of hippocampus only 70% effective. Under those circumstances the renewal data from FRAT (bottom row) match that of Corcoran and Maren quite well.

Corcoran and Maren provide a long discussion which attempts to explain why suppression of the hippocampus during AAB and ABC renewal tests should prevent renewal, whereas suppression during an ABA test should not. At the end of this discussion they conclude "This pattern of effects could therefore be described such that when an ambiguous CS is tested in an ambiguous context, normal rats display a primacy effect, whereas rats with inactivated hippocampi display a recency effect." The explanation given above in terms of return during ABA renewal of non-extinguished cues that were present during conditioning seems to us more parsimonious than the Corcoran-Maren explanation. It certainly applies to FRAT and should be considered for real animals.

Table 4H. ***Well-conditioned CSs suppress post-shock freezing and this suppression is opiate-dependent.***

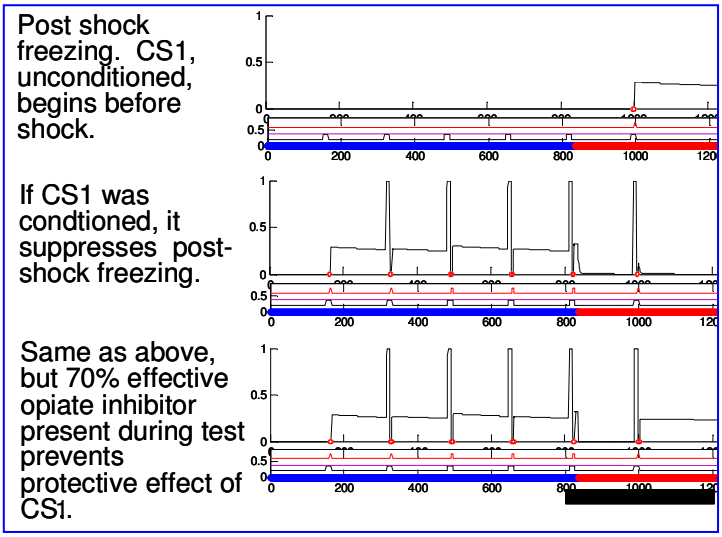


Table 4I. ***Fear acquired normally cannot be extinguished if BL is suppressed during extinction training.***

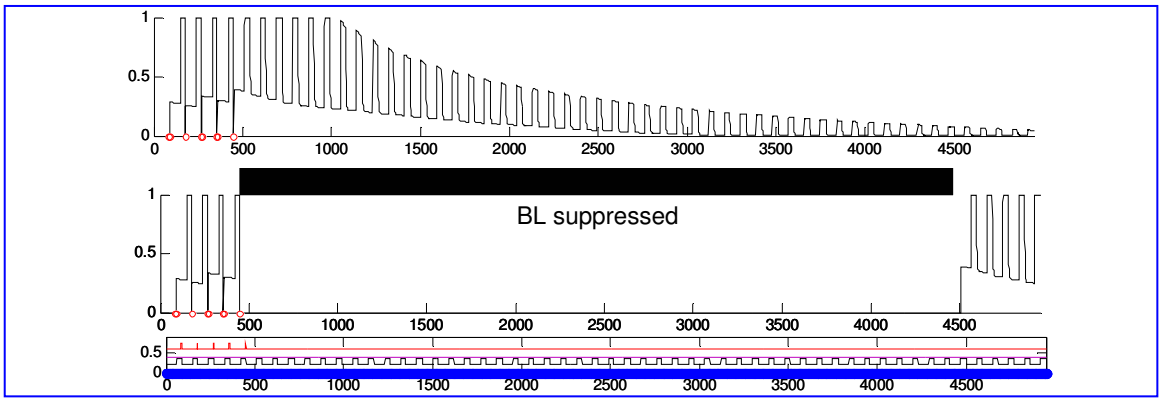


Table 4J. ***Extended post-training suppression of BLA prevents systems-type consolidation.*** Top and middle: Context fear is retained after post-training consolidation followed by hippocampal ablation or after consolidation alone. Bottom: If LA and BL are suppressed during the consolidation period (or in the case of FRAT the consolidation computation), context fear is lost even if Hx remains intact. This occurs because hippocampal contextual representations get replaced over time by cortical ones whether BLA is intact or not. However, without LA and BL operative, hippocampal-BL pathways established during conditioning cannot be replaced by cortical-LA pathways.

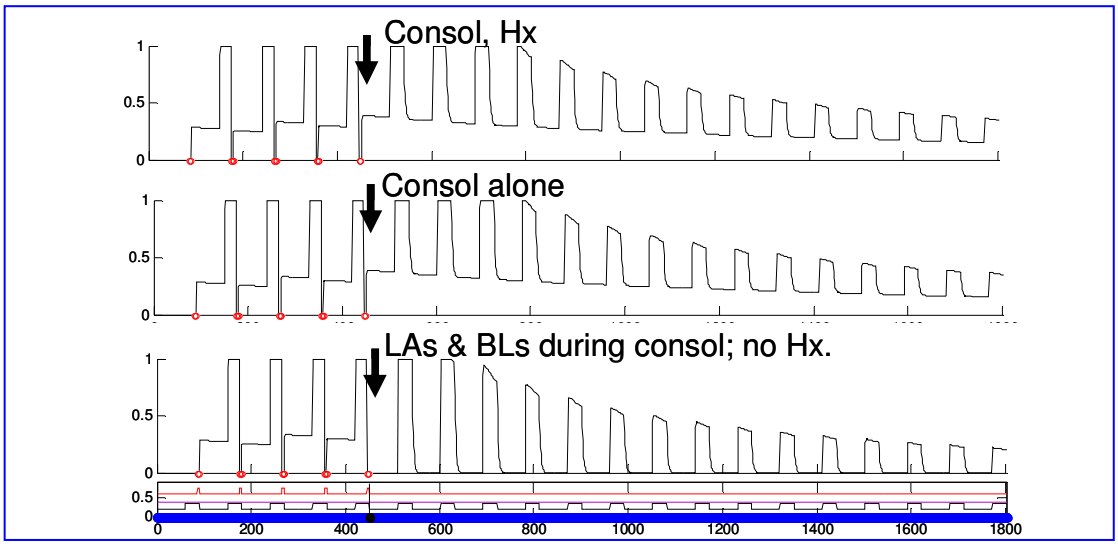


Table 4K. ***Pre- or post-training PFC lesions prevent systems-type consolidation.*** Top: Consolidation moves contextual representations from hippocampus to cortex and establishes potentiation of cortico-amygdala synapses that mediate fear responses similar to those produced by the former hippocampal-amygdala pathway. Thus contextual fear remains as it was and is no longer dependent on hippocampus. Middle: If PFC is inactivated during the consolidation period (or in FRAT during the consolidation calculations) no consolidation occurs, and the hippocampus pathway is not replaced by a cortical one (configural representations and thus remain hippocampal). So context fear remains normal. Bottom: If hippocampus is removed or suppressed after a PFC-suppressed consolidation period, context fear is lost.

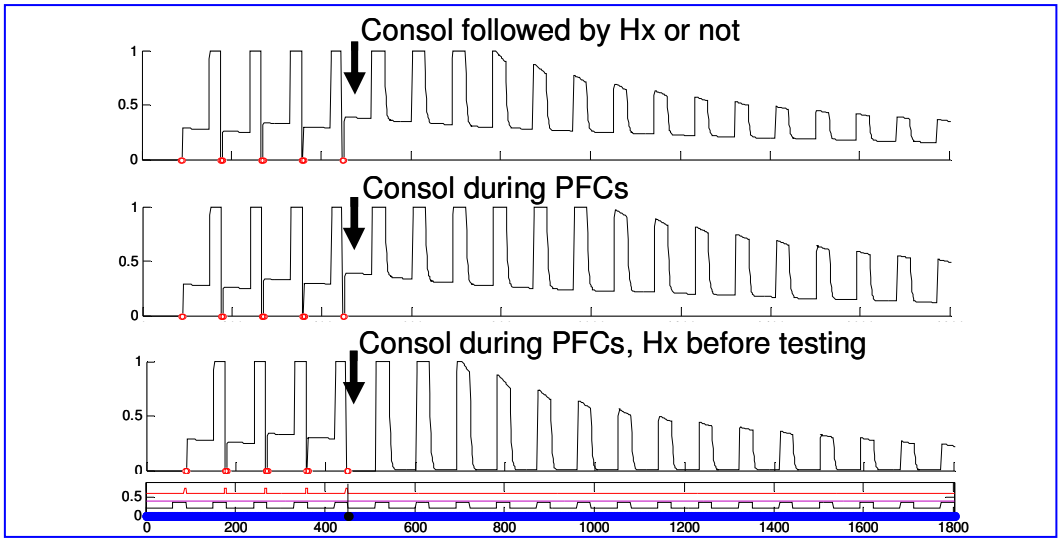


Table 4L. ***Extinction shows systems-type consolidation. After such consolidation, context shifts cause renewal even if hippocampus suppressed.*** Top: If hippocampus is removed or suppressed following post-extinction consolidation, extinction is retained. This should be contrasted with hippocampal removal or inactivation soon after extinction (see simulation above for item G of Table 4). Bottom: Consolidated extinction shows renewal despite Hs during test (in this case Hs without a context shift has no effect on expression of extinction--not shown).

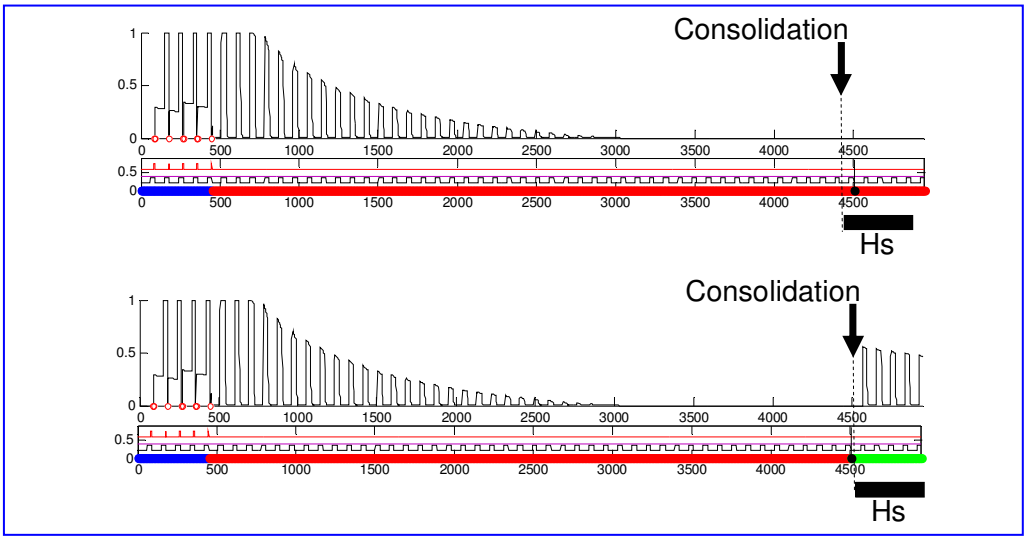


Table 4M. ***If hippocampus is suppressed (not ablated) after completion of systems-type consolidation, CS extinction is normal in the conditioning context but slow and context-independent in novel contexts.***

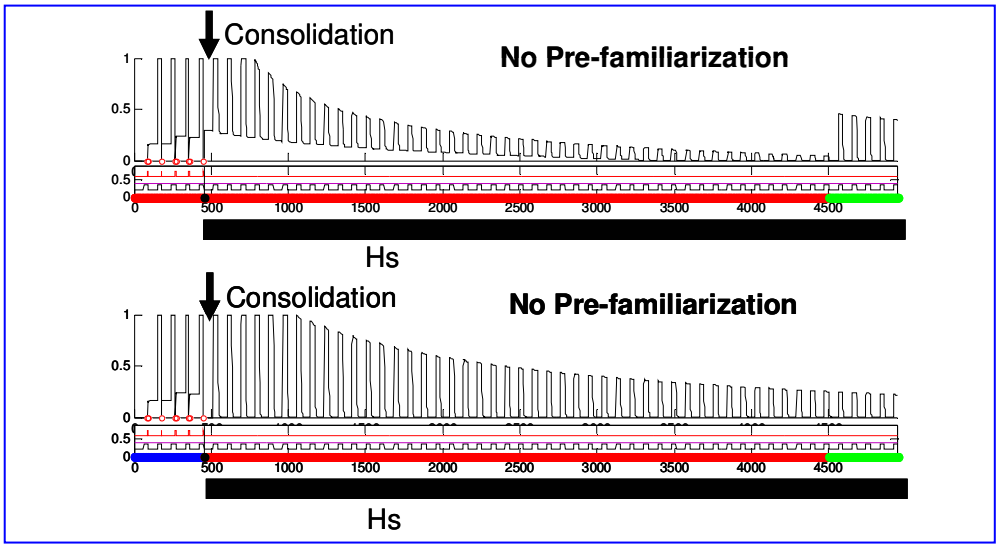


Table 4N. ***After ablation of LA, cue conditioning remains possible, but it is conditioning-context-specific.***

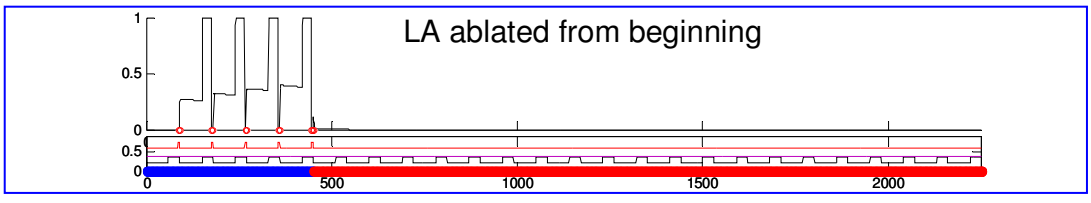


Table 4O. ***When cues predict shock onset, LA ablation increases context conditioning, but not as much as does removal of predictive cues.*** LA suppression partially enhances context conditioning when there are predictive cues because less blocking of context conditioning by cue conditioning occurs. However, some such blocking still occurs because conditioning still occurs to context/CS compounds via the hippocampal-BL pathway.

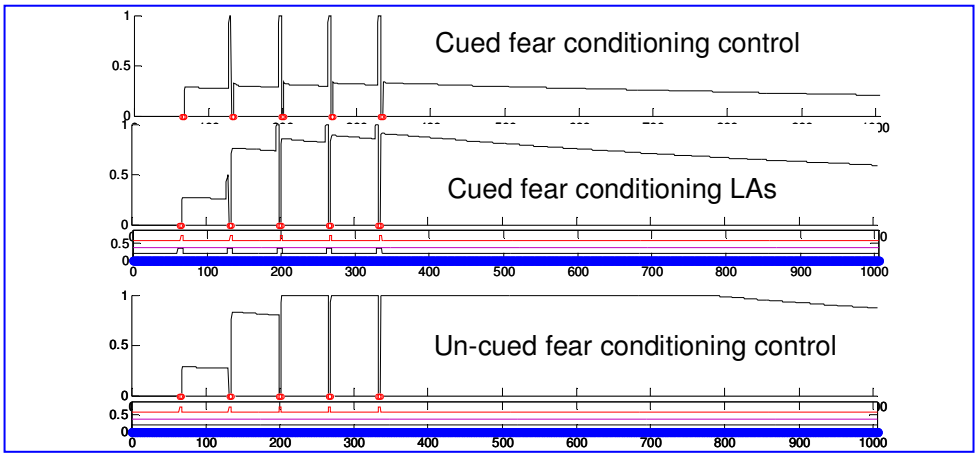


Table 4P. ***Inhibition of GABA within PAG promotes development of extinction.*** This occurs because **CEm** recruits **X** via GABA-mediated disinhibition. Thus, GABA agonists depress **X** activity and prevent extinction, whereas GABA blockers prevent inhibition of **X** and allow it to fire spontaneously, which promotes rapid extinction.

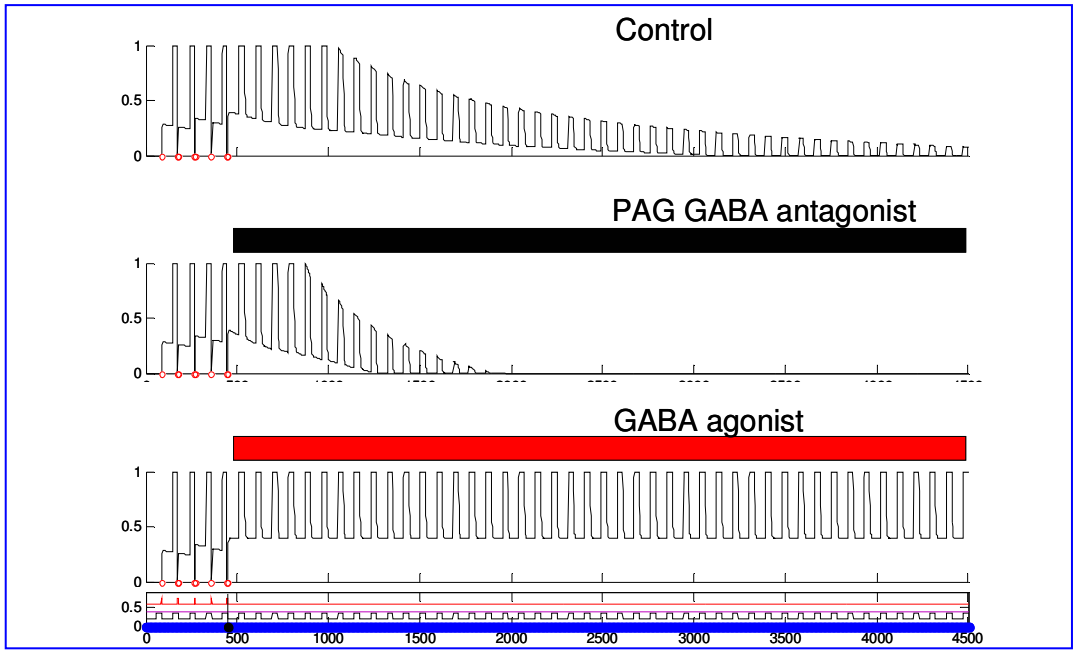


Table 4Q. ***BL lesions do not prevent context fear if hippocampus has been ablated.*** This is because compensation processes allow the cortical-LA pathway to take over the function of the hippocampal-BL pathway if hippocampus is ablated.

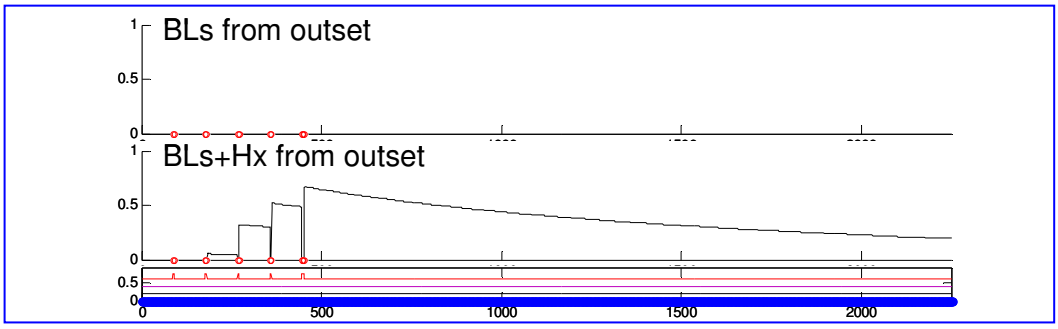


Table 4R. ***Joint pre-exposure to CS and conditioning context will enhance strength of one-trial CS conditioning.*** A single weak US-CS pairing was carried out with only context pre-exposure or with context plus CS pre-exposure. In the latter case, hippocampal context/CS representations formed during the pre-exposure, and conditioning to them occurred once the US was paired with the CS.

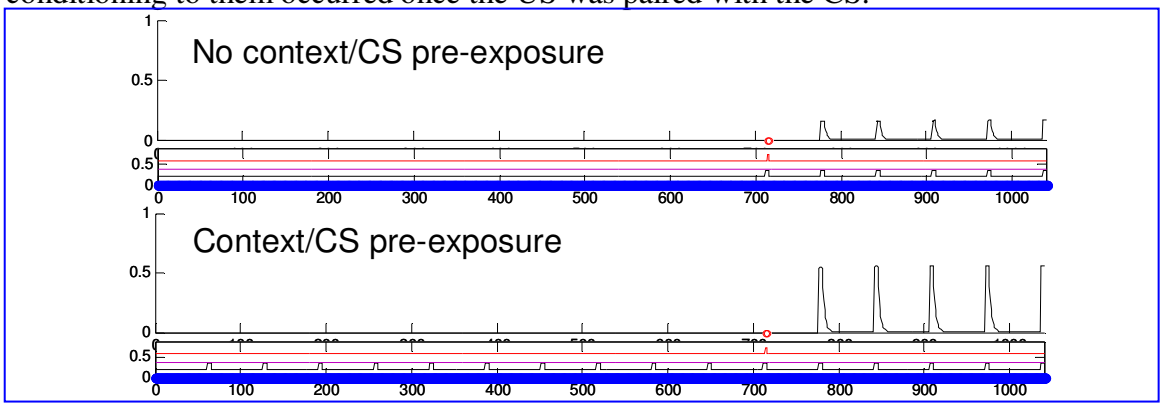
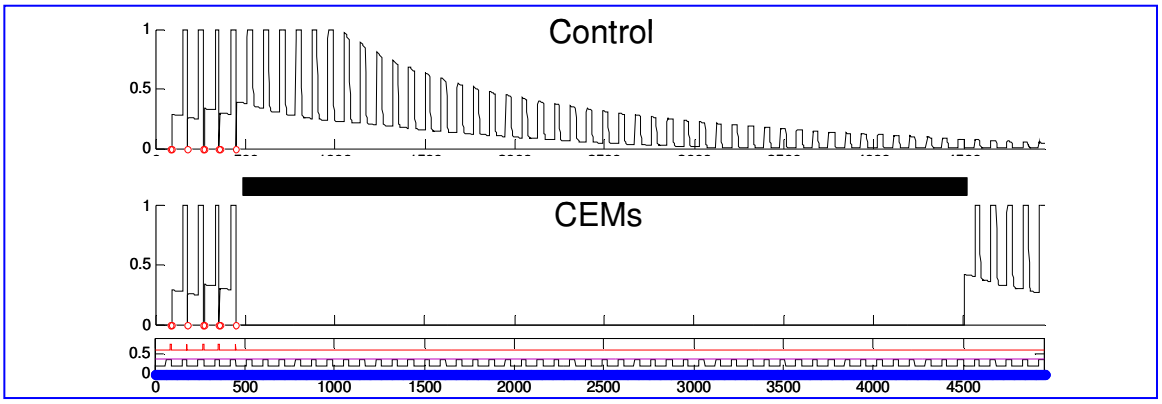


Table 4S. ***Inactivation of CEm during un-reinforced responding prevents extinction.*** In both cases the CS was repeatedly presented without reinforcement once conditioning was completed. However, if CEm was suppressed, **X** could not be recruited and so no extinction occurred, as seen by the test trials at the end of the experiment in the bottom frame.



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