# Supplement 1

## S1. Methods of computer simulation

We assume that the thalamic output can be described by a single variable, the bursting rate of relay cells (in particular in nucleus reuniens). We know that NMDAR antagonist stimulates burst output of relay cells (1). However, there are no recordings yet of single-unit activity from nucleus reuniens in the presence of NMDAR blocker. We assume that this activity is the same as that of nRT cells, from which recordings have been made in the slice preparation (2). We model nRT cells as not bursting if the resting potential is above a critical threshold voltage. Both dopamine and NMDAR antagonists produce hyperpolarization (these influences sum linearly); once a critical hyperpolarization is reached, bursting is proportional to the additional hyperpolarization. We assume that bursts in relay cells are driven by bursts from nRT (relay cells will fire at the cessation of inhibitory input). The excitation of the hippocampus is proportional to the excitation from the thalamus and the feedback inhibition from hippocampal interneurons. The VTA fires in proportion to the sum of hippocampal input and a term that represents the effect of stress. The overall simulation involves coupling these equations to reveal the dynamics of the system as a whole.

The hippocampal activity is described as a firing rate model (3).

*(1)* $$\tau_H \frac{d}{dt} H = -H + F(I) + baseline$$

in which H represents the activity of the hippocampal principal cells, *baseline* is the basal activity, $\tau_r$ is a relaxation time constant, and *F(I)* is

*(2)* $$F(1) = Excitation + Inhibition$$

The hippocampus receives excitatory inputs from the thalamus, which has activity *R*,

*(3)* $Excitation = k_1 R$

We assume R is the bursting of the relay cells, which is triggered by hyperpolarization of membrane potential (*V*) (which deinactivate T-type $Ca^{2+}$ channels; see 2.1 in the text). Bursting occurs when the membrane potential is hyperpolarized below a critical threshold level ($V_{th}$).

*(4)* $R = k_3(V_{th} - V)$ , *when* $V_{th} > V$

$= 0,$ *otherwise*

V is hyperpolarized by dopamine (*D*) that is released from VTA and NMDAR antagonist ($NMDAR_{antagonist}$).

*(5)* $$V = k_4\left(\frac{D}{K_V + D} + k_{NR}k_2\frac{NMDAR_{antagonist}}{K_A + NMDAR_{antagonist}}\right)$$

in which $K_V$ and $K_A$ are half-maximum concentrations of dopamine and NMDAR antagonist, respectively.

The hippocampal activity and the level of stress increase the amount of dopamine release.

*(6)* $D = k_5 H + k_s stress$

$k_1$, $k_2$, $k_3$, $k_4$, $k_5$, $k_s$, and $k_{NR}$ are unit conversion factors.

Inhibitory input to the hippocampus (*inhibition*) is provided from inhibitory interneurons in the hippocampus that are excited by the principle cells. Inhibition keeps the level of hippocampal activity to the control level ($C$=0.045).

*(7)* $$Inhibition = -I_{\max}\frac{G(H - C)}{K_I + G(H - C)}$$

in which $I_{max}$ is the maximum inhibition, $G$ is a gain, and $K_I$ is a half-maximum activity of the controlled hippocampal activity.

Parameters of the model are listed in Table S1. The numerical simulations were done with the fourth-order Runge-Kutta method using MATLAB (version 7.0, The MathWorks Inc.).

**Table S1.** Simulation parameters

| | |
|---|---|
| $\mathbf{k_1}$ | 14 |
| $\mathbf{k_2}$ | 1 |
| $\mathbf{k_3}$ | 1 |
| $\mathbf{k_4}$ | -2 |
| $\mathbf{k_5}$ | 10 |
| $\mathbf{k_S}$ | 0.1 |
| $\mathbf{k_{NR}}$ | 0.05 |
| $\mathbf{I_{max}}$ | 7 |
| **G** | 100 |
| $\boldsymbol{\tau_r}$ | 1 |
| $\mathbf{K_I}$ | 5 |
| $\mathbf{K_v}$ | 5 |
| $\mathbf{K_H}$ | 1 |
| $\mathbf{K_A}$ | 1 |
| **baseline** | 0.05 |
| $\mathbf{V_{th}}$ | -0.15 |
| **C** | 0.045 |
| **stress** | 0 (normal condition) |
| $\mathbf{NMDAR_{antagonist}}$ | 0 (normal condition) |

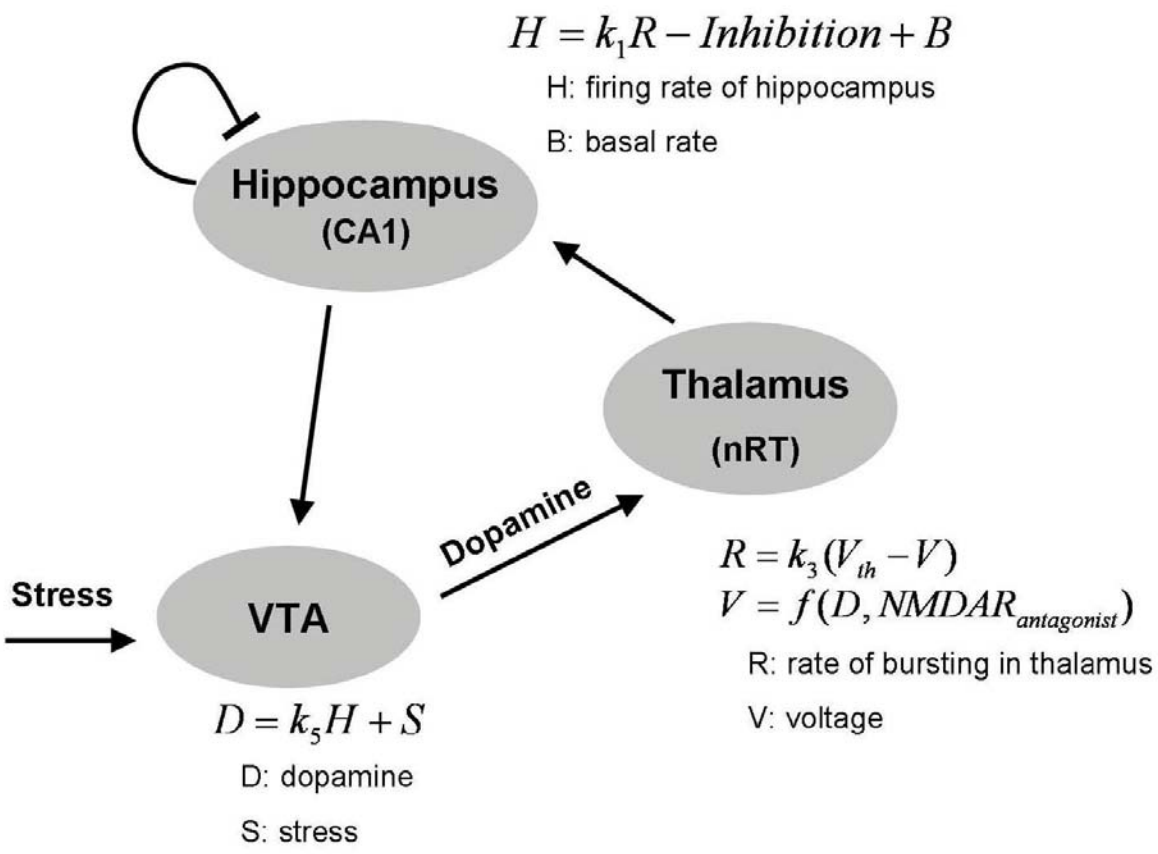


**Figure S1**. Diagram of loop interactions in the computational model. Equations describe the factors that control firing in the region.

## S2. Dopaminergic innervation of thalamus

It was originally thought that the dopaminergic innervation of the thalamus is negligible, but later anatomical work provided strong evidence for such innervation (reviewed in (4)). As judged by dopamine and DAT immunoreactivity, the most dopamine-reach thalamic nuclei in primates are the mediodorsal and midline nuclei. Also strongly innervated is the nRT (5-7). The presence of D2-type DA receptors in some nuclei was reported in primates (8). Tracing studies suggest that the mediodorsal nucleus gets dopamine from meso-cortical system (VTA and dorsal portion of substantia nigra) (9). Other work suggests that virtually all dopaminergic nuclei project to the primate thalamus (7).

Dopaminergic innervation is also present in rats. Thalamic D1- and D2-type ligand binding was reported in multiple studies (10-13). Also, D1 (14), D5 (15), and D4 (16) protein immunoreactivity in thalamus was demonstrated. The strongest dopaminergic markers are present in the reticular nucleus (5). VTA supplies dopamine to a number of nuclei in the rat thalamus (anterodorsal, mediodorsal, centromedial, reuniens; reviewed in (4)). Later studies confirmed that nucleus reuniens (17) and mediodorsal nucleus (18) get afferents from VTA. The reticular nucleus gets dopamine mostly from substantia nigra compacta (19), but axons from VTA were also reported (20).

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