Circuit property of the cortico-mesocortical system

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Abstract

It has been shown that dopamine (DA) modulates memory fields of dorsolateral prefrontal cortex (PFC) neurons. The DAergic neurons which project to the PFC are localized in the midbrain. We here developed a computational model network which includes the PFC circuit and the mesencephalic DA unit to analyze the circuit property of the cortico-mesocortical system. In our computer simulation, the cortico-mesocortical system can regulate the DA level in the PFC and the sustained activity of the PFC neurons during the delay period. In addition, we suggest that the stabilization of the DA level requires the cortical feedback.

Keywords: Cortico-mesocortical; Dopamine; Midbrain; Prefrontal cortex; Working memory

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1. Introduction

Recent studies have suggested that the dopaminergic (DAergic) modulation via D1 receptor activation in the prefrontal cortex (PFC) plays critical roles not only in the regulation of memory fields [1,12] but also fundamental cognitive operations [9,10]. Since the DAergic innervation of the frontal cortex comes from the midbrain [4,11], the investigation of the cortico-mesocortical system is useful to understand the mechanisms of the DAergic modulation of the cortical dynamics. Although interests in the DAergic modulation of the PFC have been growing, the circuit properties of the cortico-mesocortical system are still controversial. These circuit properties need to be examined in detail. In particular, the control of fundamental cognitive operations by DA has been proposed recently by Tanaka [10]. The question we ask here is how the DA release is controlled by the cortico-mesocortical system. To address this question, we constructed a network model of the system. The part of model that includes the DAergic effects in the PFC is based on our previous study [13].

2. Model

Prefrontal cortex

Our PFC model contains 1080 pyramidal neurons and 240 inhibitory interneurons. All of the neurons are described by a single compartment, leaky integrate-and-fire neuron model [3,5,8,9,10,13]. We here simulate the oculomotor delayed-response (ODR) task (fixation period: 0-200 ms; cue period: 200-300 ms; delay period: 200-3000 ms). The DAergic modulation on each conductance is based on the experimental studies [2,6,7] and our previous research [9,10,13]. In the cases of g_{AMPA}, g_{NMDA}, and $g_{K(Ca)}$, the DAergic modulation is expressed by: $g_{replace} = r_{conductance} g_{max,original}$. Here $r_{conductance}$ is the DA concentration-dependent coefficient which obeys the following equation: $r_{conductance} = AZ_{DA}^4 + BZ_{DA}^3 + CZ_{DA}^2 + DZ_{DA} + E$ (Fig. 1A). The effect on the persistent sodium current is characterized by the leftward shift of the voltage-current curve (Fig. 1B). The DAergic effects on the PFC neurons are due to the D1 receptor activation level.

Mesencephalic DA unit

Our model describes the interaction between the PFC and the midbrain by including the direct projection from the PFC to the mesencephalic DA unit (Fig. 1C). The model mesencephalic DA unit is initially driven by the external phasic input (J_{phasic}), and then send output to the PFC neurons to release DA. The DA release level in the PFC, $Z_{\mathrm{DA}}(t)$, is given by:

$$\tau_{\mathrm{DA}}\frac{dZ_{\mathrm{DA}}(t)}{dt} + Z_{\mathrm{DA}}(t) - F_{\mathrm{DA}}(Y_{\mathrm{mid}}(t)) = 0 \tag{1}$$

$$\tau_{\mathrm{P-M}}\frac{dY_{\mathrm{mid}}(t)}{dt} + Y_{\mathrm{mid}}(t) - B_{\mathrm{gain}}X_{\mathrm{PFC}}(t) - J_{\mathrm{phasic}} = 0 \tag{2}$$

$$F_{\mathrm{DA}}(Y_{\mathrm{mid}}(t)) = \frac{K}{1 + exp(-(Y_{\mathrm{mid}}(t) - sigm))} \tag{3}$$

where the parameters are defined in Table.2.

3. Results

Modulation of PFC neurons' activity via D1 receptor activation

While the D1 receptor activation level was in the optimum range, the model PFC neurons showed the delay-period activity owing to the recurrent excitation (Fig. 2B). However, the results in the cases of lower and higher receptor activation indicated suppressed firing of the PFC neurons (Fig. 2A,C). Moreover, unless the D1 receptor activation level was fixed in the optimum range, the PFC neurons did not show sustained activity. These results show clearly how D1 receptor activation modulates the memory fields. This modulatory effect is characterized by the biphasic modulation (Fig. 2D), which is consistent with experimental findings [1,12] and our previous study [13].

Regulation of DA release

As mentioned above, the model PFC has the inverted-U shaped property (Fig. 2D). With this issue in mind, we here investigate the mesencephalic DA unit and the DA release. In our simulation, the DAergic neuron shows two kinds of activity modes, which are the burst activity and the sustained activity at very low frequency (Fig. 3B). The burst activity occurred during the cue period in which the phasic input activated the mesencephalic DA unit. During the delay period, the DAergic neuron's activity was sustained but at a much lower firing rate than the initial bursting component. Nevertheless, the DA release level was stabilized in the optimum range (Fig. 3C). The DA release level was initially activated as the DAergic neuron exhibited the burst activity, and then this level was stabilized although the DAergic neuron's activity was fairly low during the delay period. As for the PFC neurons' activity, Fig. 3A and D show their well-tuned delay-period activity in this simulation.

4. Discussion

This study investigated the circuit properties of the cortico-mesocortical system. Our simulation shows that the DAergic neuron exhibits two kinds of activity modes (Fig. 3B). The cause of the burst activity of the DAergic neuron is the external phasic input. On the other hand, the sustained activity at low frequency resulted from the cortical feedback input. Because the feedback gain was fairly low in that case, the activity of the DAergic neuron was much lower during the delay period than the initial bursting component (Fig. 3B). The DA level was stabilized in the optimum range of the inverted-U shaped curve only when the cortical feedback input was present in the mesencephalic DA unit (Fig. 3C). Then the feedback input would be necessary to control the DA release level. Consequently, the sustained activity in the PFC was derived from such optimized DA release during the delay period. In conclusion, we suggest that the cortico-mesocortical closed-loop circuit regulates the DA release level in the PFC, and this system would then stabilize the sustained activity of

PFC neurons.

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References

[1] P.S. Goldman-Rakic, E.C. Muly, G.V. Williams, D1 receptors in prefrontal cells and circuits, Brain Research Review 31 (2000) 295-301.

[2] N.A. Gorelova, C.R. Yang, Dopamine D1/D5 receptor activation modulates a persistent sodium current in rat prefrontal cortical neurons in vitro, J. Neurophysiology 84 (2000) 75-87.

[3] M. Iida, S. Tanaka, Postsynaptic current analysis of a model prefrontal cortical circuit for multi-target spatial working memory, Neurocomputing 44-46 (2002) 855-861.

[4] D.A. Lewis, S.R. Sesack, Handbook of Chemical Neuroanatomy Vol.13, The Primate Nervous System, Part I (Elsevier Science, 1997) 263-375.

[5] K. Morooka, S. Tanaka, Correlation analysis of signal flow in a model prefrontal cortical circuit representing multiple target locations, Neurocomputing 44-46 (2002) 541-548.

[6] P. Pedarzani, J.F. Storm, Dopamine modulates the slow Ca^{2+}-Activated K^+ current I_{AHP} via cyclic AMP-dependent protein kinase in hippocampal neurons, J. Neurophysiology 74 (1995) 2749-2753.

[7] J.K. Seamans, D. Durstewitz, B.R. Christie, C.F. Stevens, T.J. Sejnowski, Dopamine D1/D5 receptor modulation of excitatory synaptic inputs to layer V prefrontal cortex neurons, Proc. Nati. Acad. Sci. USA. 98 (2001) 301-306.

[8] S. Tanaka, Computational approaches to the architecture and operations of the prefrontal cortical circuit for working memory [Review], Prog. Neuro-Psychopharm. Biol. Psychiat. 25 (2001) 259-281.

[9] S. Tanaka, Multi-directional representation of spatial working memory in a model prefrontal cortical circuit, Neurocomputing 44-46 (2002) 1001-1008.

[10] S. Tanaka, Dopamine controls fundamental cognitive operations of multi-target spatial working memory, Neural Networks 15 (2002) 573-582.

[11] S.M. Williams, P.S. Goldman-Rakic, Widespread origin of the primate mesofrontal dopamine system, Cerebral Cortex 8 (1998) 321-345.

[12] G.V. Williams, P.S. Goldman-Rakic, Modulation of memory fields by dopamine D1 receptors in prefrontal cortex. Nature 376 (1995) 572-575.

[13] K. Yamashita, S. Tanaka, Circuit simulation of memory field modulation by dopamine D1 receptor activation, Neurocomputing 44-46 (2002) 1035-1042.

Figure legends

Fig 1. (A) DAergic effects on the conductance values. (B) The DA-induces leftward shift of the persistent sodium V-I curve. (C) Architecture of the model network. The PFC network consists of 3 layers, and involves 360 pyramidal neurons in each layer and 240 inhibitory interneurons. The mesencephalic DA unit receives the feedback input from the deep layer pyramidal neurons (X_{PFC}), and then the DA release level (Z_{DA}) is calculated by Eqs. (1)-(3).

Fig 2. Activity of the deep layer pyramidal neurons at the low (A), optimum (B), and high (C) levels of D1 receptor activation. The time bin width is 10 ms. (D) Biphasic DAergic modulation of the PFC neurons obtained in this simulation.

Fig 3. (A) Firing rate of the pyramidal neurons in the deep layer of the PFC. (B) The activity of the DAergic neuron. The DAergic neuron shows the sustained activity at very low frequency after the burst activity. The time bin width is 10 ms. (C) The DA release level. The DA release was stabilized at the optimum during the delay period. (D) Activity profiles of the pyramidal neurons and the interneurons.

Table.1 Coefficients of the polynomials (Fig.1A)					
Conductance	A	B	C	D	E
$AMPA$	0.000	0.015	-0.033	-0.092	1.110
$NMDA(Py)$	0.000	0.351	-1.375	1.902	0.112
$NMDA(In)$	0.742	-2.278	2.190	0.333	0.000
$K(Ca)$	0.000	0.015	-0.033	-0.092	1.110

Table.2 Model parameters	
Symbol	Description
$\tau_{\mathrm{P-M}}$	time constant of the DA unit activation: 10 [ms]
B_{gain}	feedback gain (from the PFC to the the mesencephalic DA unit): 1.1 [a.u.]
J_{phasic}	amplitude of the external phasic input: 100 [a.u.]
K	maximum value of the sigmoidal function (DA neuron's activity): 87 [a.u.]
$sigm$	intermediate point of the sigmoidal function (DA neuron's activity): 43.5 [a.u.]
τ_{DA}	time constant of the DA release: 800 [ms]

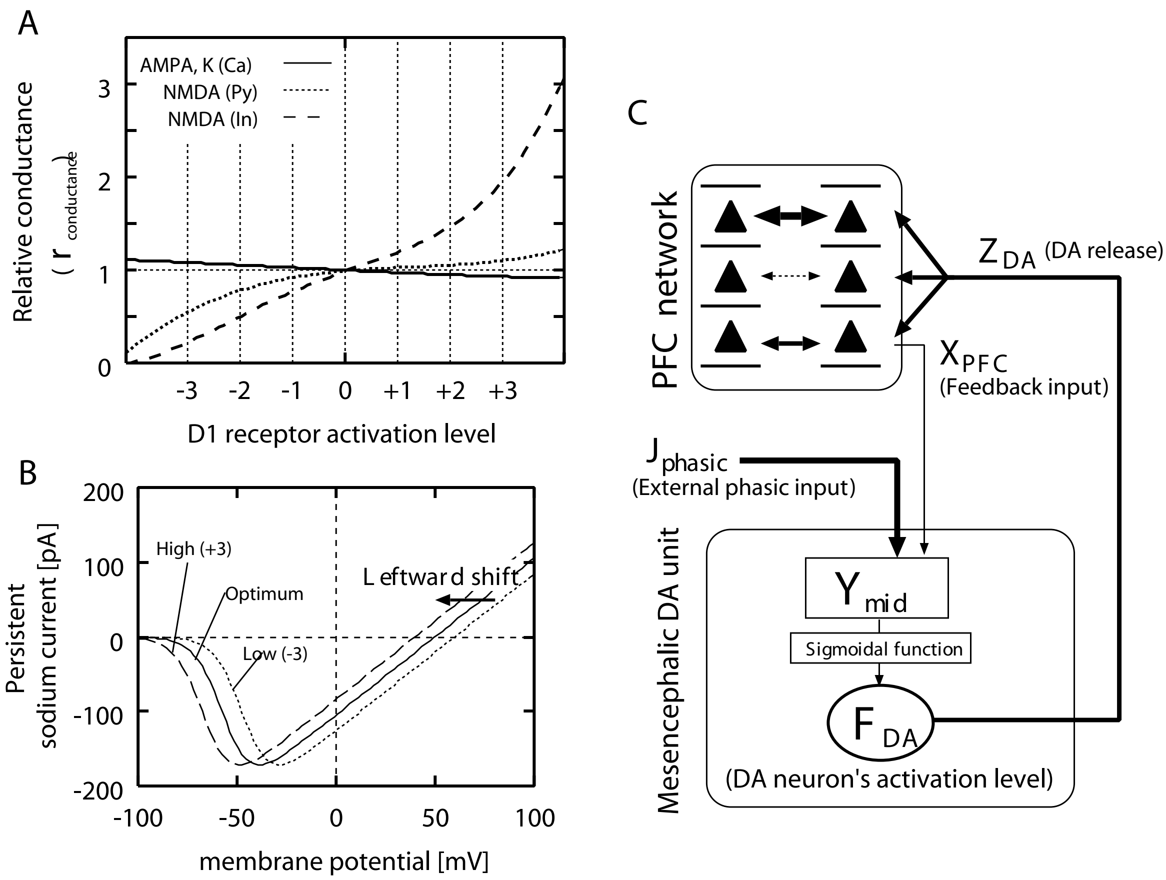

Fig.1 Yamashita & Tanaka

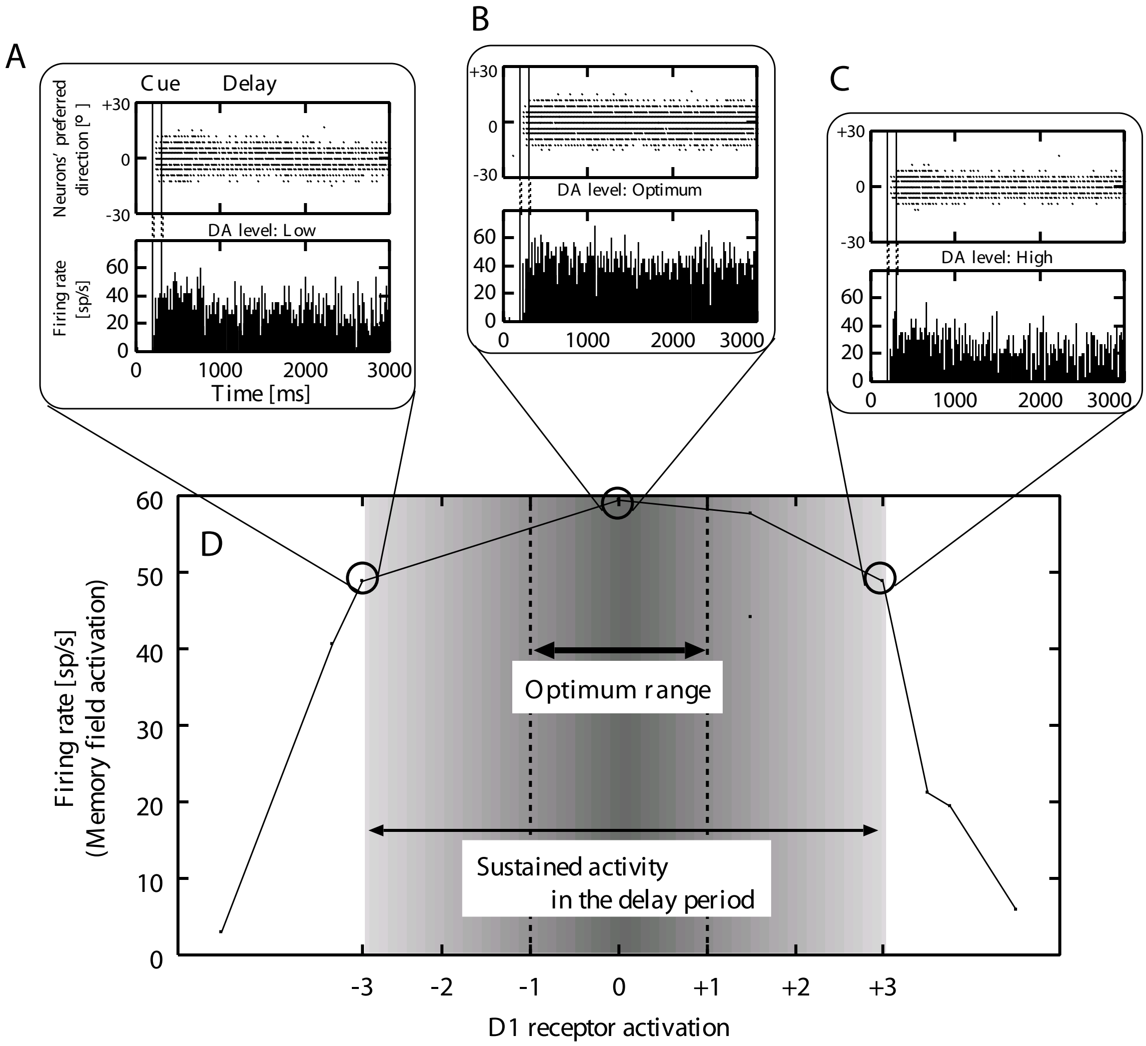

Fig.2 Yamashita & Tanaka

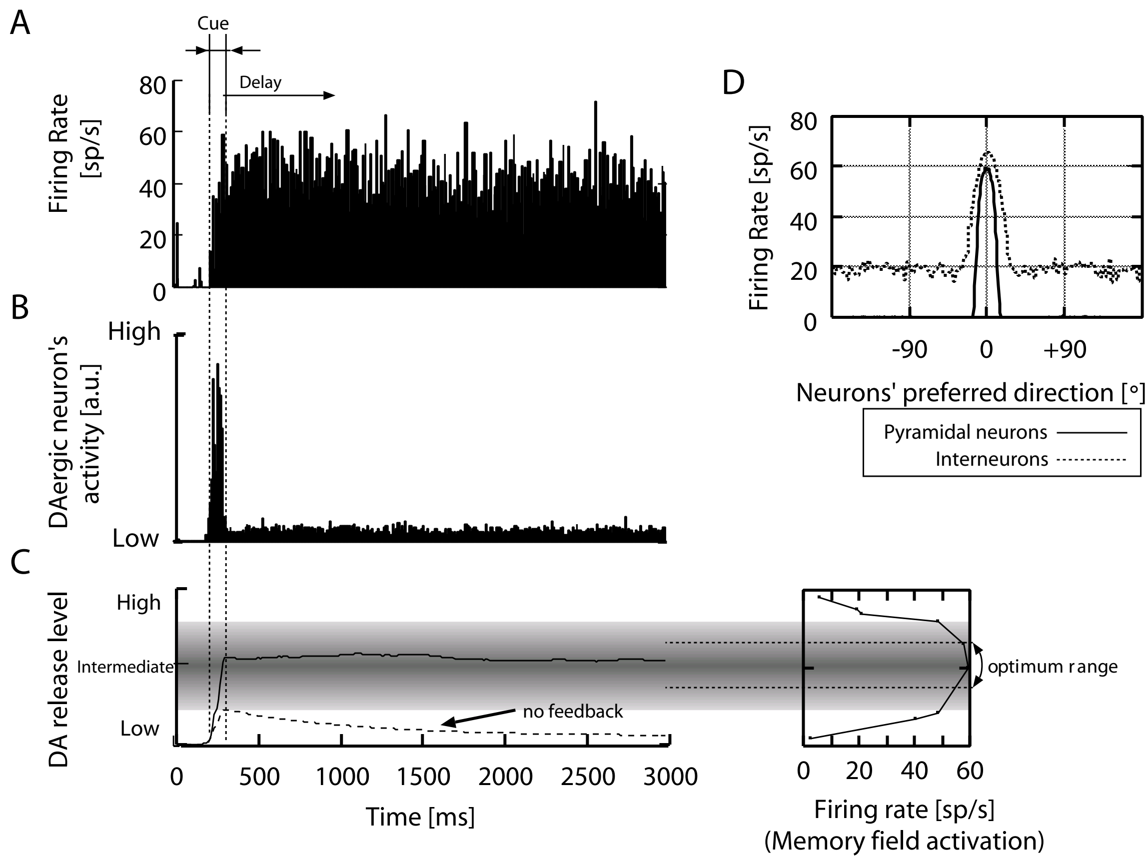

Fig.3 Yamashita & Tanaka