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Short communication

Short-term depression of synaptic transmission from rat lateral geniculate nucleus to primary visual cortex in vivo

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Abstract

Two forms of short-term synaptic plasticity, paired-pulse depression (PPD) and frequency depression, were prominent in the adult rat geniculo-cortical visual pathway in vivo. Iontophoresis of GABAa receptor antagonist (bicuculline methiodide) or GABAb receptor antagonist (2-hydroxy-saclofen) in the primary visual cortex significantly reduced the short-term synaptic depression. When NMDA or AMPA/kainate receptors were blocked, no obvious change of synaptic depression was observed. Application of high [Ca^{2+}] enhanced the short-term synaptic depression. Our results suggest that the presynaptic Ca^{2+}-dependent neurotransmitter depletion and postsynaptic GABAergic inhibition may be crucial for short-term synaptic depression in the geniculo-cortical pathway.

Theme: Sensory systems
Topic: Visual cortex: striate

Keywords: Short-term synaptic plasticity; Geniculo-cortical; Paired-pulse depression; Frequency depression; Rat

In the rat, as in other mammals, the projections from the dorsal lateral geniculate nucleus (dLGN) to the primary visual cortex are the major visual thalamocortical afferents [11]. These projections have been intensively studied and proved to play an important role not only in the relay of visual information from retina to visual cortex, but also in visual information processing and neuronal plasticity [10]. However, very little attention has been paid to the short-term synaptic plasticity of geniculo-cortical projections in rat before.

The transmission strength of a synapse is changed depending on the activity history of the synapse both in long term and in short term. Classic studies of synaptic transmission at the neuromuscular junction identified that short-term enhancement and short-term depression occurred over several time scales [20]. Repetitive activation of the excitatory synapses in the neocortex shows prominent frequency-dependent depression [6,15–17]. It is proposed that the frequency-dependent depression of the rat visual cortex provides an automatic, dynamic gain-control mechanism [1] and affects some of the specific temporal-filtering properties of the visual cortex [5]. In this study, we aimed to characterize two forms of short-term synaptic plasticity, paired-pulse depression and frequency depression of postsynaptic potentials (PSPs) in the rat geniculo-cortical pathway in vivo.

Adult Wistar rats (>2 months), weighing 200–300 g, were anaesthetized with urethane (20%, 1.2 g/kg, i.p.), and then were mounted in a stereotaxic apparatus. Body temperature was kept at 37 ± 0.5 °C. The eyes were covered throughout the experiment, except during positioning the stimulating electrode into dLGN [9]. Multibarrel glass electrodes (1.0–3.0 M when filled with saline, pipette tip size was about 2 μm) were introduced into the primary visual cortex (7.0 mm posterior to bregma; 3.0–4.0 mm lateral to the midline; 800–1000 μm ventral to dura). A concentric bipolar electrode (FHC, USA) was positioned 3.8 mm posterior to bregma, 3.5 mm lateral to stimulate the dLGN ipsilateral to the visual cortex recorded. To aid in the positioning of the stimulating electrode in the dLGN, visually driven multiunit activity was monitored as it was being tracked down through neocortex and overlying hip-

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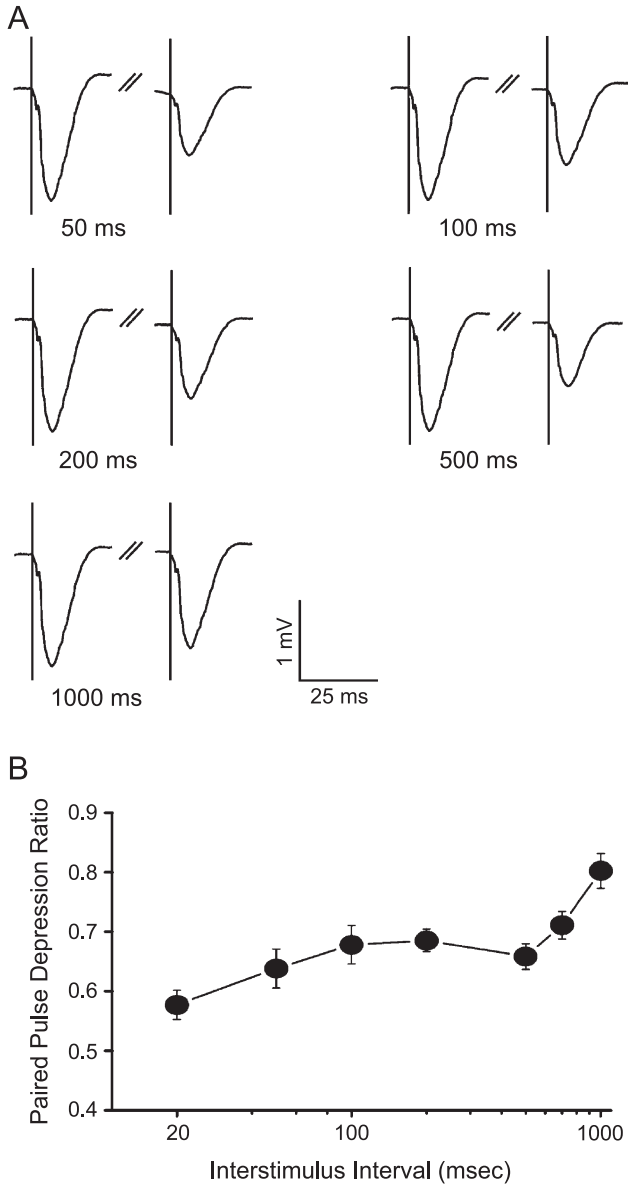

Fig. 1. Paired-pulse depression in rat geniculo-cortical pathway. (A) Typical field potentials induced by applying paired-pulse stimulation at stimulus interval of 50, 100 and 1000 ms. (B) Averaged paired-pulse depression ratio changes versus stimulus interval ($n = 30$).

pocampus. The final depth of the stimulating electrode tip was within 100–200 μm of first encountering visually responsive neurons. Histological analysis confirmed that the stimulating electrode tip was typically positioned within the first 200 μm of the dorsal surface of the dLGN. We positioned recording electrodes in the layer IV of the visual cortex (field potential with largest amplitude and shortest latency could be recorded in the layer IV of the visual cortex with electrical stimulation in the dLGN). Before the beginning of each experiment, full input–output series were performed, and a stimulation intensity yielding 50–60% of maximum was used for the remainder of experiment. Data are presented as means ± standard error of means (S.E.M.). Statistical significance was estimated by using paired *t*-test analysis. Drugs were held in the electrode barrel with a small negative retaining current (10–20 nA). Iontophoretic currents of 40–80 nA were employed.

With paired-pulse stimulation, the amplitude of the second field potential showed prominent depression, which is called paired-pulse depression (PPD). Fig. 1A shows typical field potentials induced by paired-pulse stimulation at the intervals of 50, 100 and 1000 ms. Paired-pulse stimulation with longer intervals usually caused less depression. Fig. 1B shows the relationship between the PPD ratio and interval of paired-pulse. The PPD ratio was expressed as the size of the second PSP amplitude relative to the first PSP amplitude. When the interval was less than 200 ms, larger interval stimulation induced bigger PPD ratio (less depression). However, the PPD was not restored monotonically as the interval of pared-pulse stimulation increased. At the interval of 200–500 ms, there was a second minimal peak of the PPD ratio.

As it is generally impossible to predict the steady-state behavior from the paired-pulse behavior [16], 15-pulse train stimulation at three different frequencies (10, 20, 50 Hz) were used to investigate the dynamic trend and steady-state behavior of this synaptic transmission. Fig. 2A shows typical evoked field potentials by 15 pulses at 50 Hz. The amplitude of the field potential decreased steeply at 50-Hz stimulation. The depression by repetitive stimulation is dependent on the frequency of stimulation (Fig. 2B). In contrast to paired-pulse effects, the steady-state depression

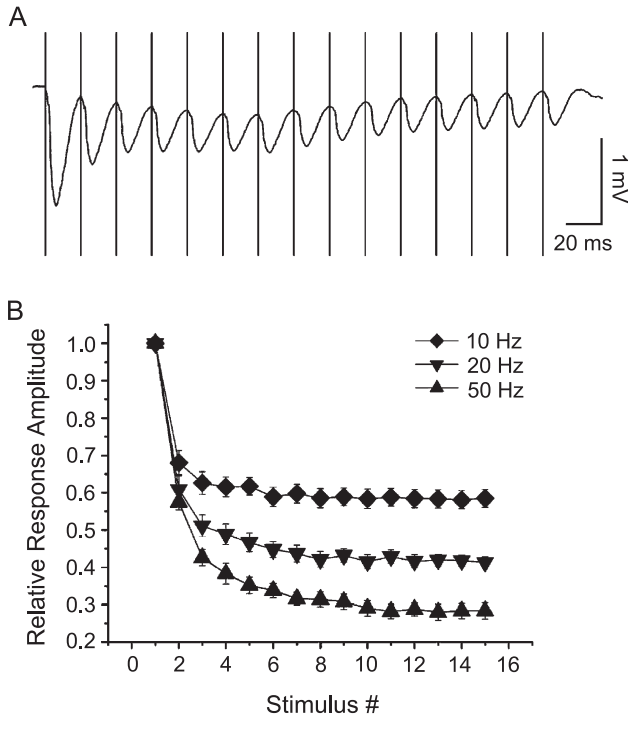

Fig. 2. Frequency depression in rat geniculo-cortical pathway. (A) Typical field potentials induced by applying 15-pulse train stimulation of 50 Hz. (B) Averaged relative amplitude of field potentials during three different frequency stimulation ($n = 29$).

increased monotonically across the measured range of frequencies. Higher frequency of stimulation will cause steeper depression and less amplitude of steady-state response. The steady-state depression ratio was expressed as the averaged size of the last three PSPs' amplitude relative to the first PSP amplitude.

Since factors modulating synaptic transmission and moreover the contribution of IPSPs were likely to influence the short-term depression in the geniculo-cortical pathway, we performed experiments utilizing drug iontophoresis. When GABAa-mediated inhibition was blocked by iontophoresis of bicuculline methiodide (BIM, 5 mM, pH 3), a prolongation of the field potential was found, indicating that a block of concomitantly activated inhibitory postsynaptic potentials. The amplitude of the field potential was increased to 166 ± 8%. Under these conditions, paired-pulse depression was significantly reduced for all stimulation intervals ($n = 12$; see Fig. 3). Frequency depression was significantly reduced by repetitive stimulation of 10 and 20 Hz ($n = 12$; see Fig. 4). When the specific GABAb receptor antagonist 2-hydroxy-saclofen (SAC, 25 mM, pH 3.5) was applied, field potential's amplitude was 101 ± 4% of control, paired-pulse depression was significantly reduced for stimulation intervals between 200 and 700 ms ($n = 10$; see Fig. 3). Frequency depression was significantly reduced by repetitive stimulations of 10 and 20 Hz ($n = 10$; see Fig. 4).

The amplitude of the field potential was increased by iontophoresis of high [Ca^{2+}] solution (3 M $CaCl_2$) (156 ± 7%) probably due to the increase of presynaptic transmitter release. Under these conditions, paired-pulse depression was significantly enhanced for all stimulation intervals ($n = 17$; see Fig. 3). Frequency depression was also significantly

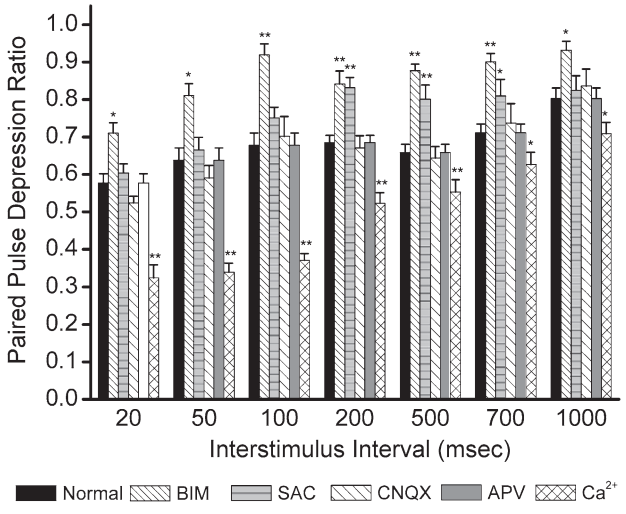

Fig. 3. Drug effects on paired-pulse depression (PPD). PPD was reduced in presence of bicuculline methiodide (BIM, $n = 12$) or 2-hydroxy-saclofen (SAC, $n = 10$), while the presence of high [Ca^{2+}] ($n = 17$) enhanced PPD. Iontophoresis of D-2-amino-5-phosphonopentanoate (APV, $n = 10$) and 6-cyano-7-nitroquinoxaline-2, 3-dione (CNQX, $n = 11$) had no significant effect on PPD. *$P < 0.05$, **$P < 0.01$; paired t-test, compared with normal adult rat groups.

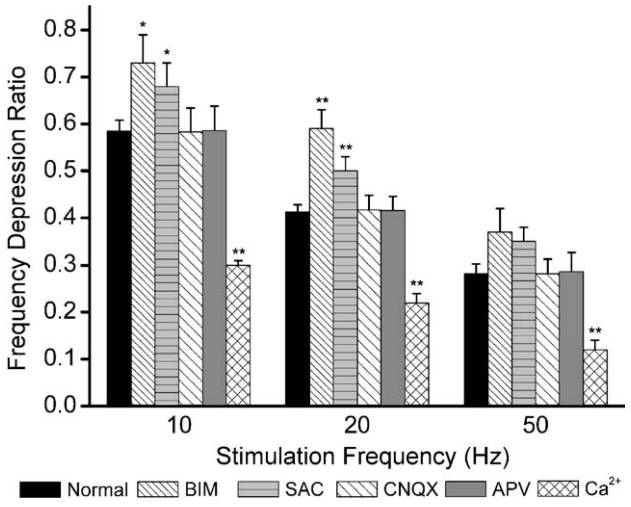

Fig. 4. Drug effects on frequency depression. Frequency depression was reduced in presence of bicuculline methiodide (BIM, $n = 12$) or 2-hydroxy-saclofen (SAC, $n = 10$), and was enhanced in presence of high [Ca^{2+}] ($n = 17$). Iontophoresis of D-2-amino-5-phosphonopentanoate (APV, $n = 10$) and 6-cyano-7-nitroquinoxaline-2, 3-dione (CNQX, $n = 11$) had no significant effect on frequency depression. *$P < 0.05$, **$P < 0.01$; paired t-test, compared with normal adult rats group.

enhanced for all stimulation frequencies ($n = 17$; see Fig. 4). The contributions of NMDA and AMPA/kainate receptors to short-term synaptic plasticity were investigated by iontophoresis of D-2-amino-5-phosphonopentanoate (APV, 50 mM, pH 8) and 6-cyano-7-nitroquinoxaline-2,3-dione (CNQX, 10 mM, pH 9.8), respectively. The amplitude of field potential was 35 ± 3% of control by CNQX and 98 ±4% of control by APV. No significant effect on paired-pulse depression or frequency depression was observed under these conditions (APV, $n = 10$; CNQX, $n = 11$; see Figs. 3 and 4).

Short-term synaptic plasticity was originally described in simple circuits, such as the neuromuscular junction, and its classical forms seem to arise from presynaptic-mediated changes of neurotransmitter. It is proposed that Ca^{2+} influx through voltage-gated Ca^{2+} channels is the key signal that dynamically regulates the refilling of the releasable pool of synaptic vesicles [21]. Differences in release probability may explain the pathway-specific variance in short-term synaptic plasticity [4]. Since the release probability at thalamocortical synapses is quite high [3,7,8], it is not surprising to observe prominent depression in this study. Similar depression was also observed in former in vitro studies on thalamocortical synapses [7,8] and geniculocortical synapses [13]. Our results may reflect that Ca^{2+}-dependent depletion of presynaptic neurotransmitter plays an important role in short-term synaptic depression of geniculo-cortical pathway. Under high [Ca^{2+}] condition, the neurotransmitter release probability was increased, which caused the presynaptic neurotransmitter to be depleted more rapidly. Thus, the degree of short-term depression increased. Some other presynaptic factors [19], such as the activation of GABAb autoreceptor may also contribute to

PPD. Similar regulation by GABAb receptors was reported on thalamocortical slices [3,7].

On the other hand, it is known that postsynaptic elements and circuit properties are important to short-term synaptic dynamics [2,18]. There are both physiological and anatomical evidences that thalamocortical afferent synapses strongly and monosynaptically excite GABAergic inhibitory interneurons in the cortex [12,14]. When the GABAergic inhibition was weakened, the strong disynaptic inhibitory inputs that shunt excitatory postsynaptic potentials were also weakened. It is also possible that IPSPs reduce field potentials by simple summation with EPSPs. Thus, under these conditions, short-term depression was reduced.

The prominent short-term synaptic depression observed in the present study may be the mechanism of visual pattern adaptation, which is much more salient in neurons of primary visual cortex than of lateral geniculate nucleus. Short-term synaptic depression may also contribute to the visual information gain-control mechanism and temporal-filtering properties as suggested in the intracortical synapses [1,5,15]. It plays an important role in the nonlinear temporal dynamics of visual cortex neurons that leads to enhancement of nonlinear temporal summation, orientation selectivity, and direction selectivity [5].

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References

[1] L.F. Abbott, J.A. Varela, K. Sen, S.B. Nelson, Synaptic depression and cortical gain control, Science 275 (1997) 220–224.
[2] J.X. Bao, E.R. Kandel, R.D. Hawkins, Involvement of pre- and postsynaptic mechanisms in posttetanic potentiation at Aplysia synapses, Science 275 (1997) 969–973.
[3] M.A. Castro-Alamancos, B.W. Connors, Thalamocortical synapses, Prog. Neurobiol. 51 (1997) 581–606.
[4] M.A. Castro-Alamancos, B.W. Connors, Distinct forms of short-term plasticity at excitatory synapses of hippocampus and neocortex, Proc. Natl. Acad. Sci. U. S. A. 94 (1997) 4161–4166.
[5] F.S. Chance, S.B. Nelson, L.F. Abbott, Synaptic depression and the temporal response characteristics of V1 cells, J. Neurosci. 18 (1998) 4785–4799.
[6] M. Galarreta, S. Hestrin, Frequency-dependent synaptic depression and the balance of excitation and inhibition in the neocortex, Nat. Neurosci. 1 (1998) 587–594.
[7] Z. Gil, B.W. Connors, Y. Amitai, Differential regulation of neocortical synapses by neuromodulators and activity, Neuron 19 (1997) 679–686.
[8] Z. Gil, B.W. Connors, Y. Amitai, Efficacy of thalamocortical and intracortical synaptic connections: quanta, innervation, and reliability, Neuron 23 (1999) 385–397.
[9] C. Rozas, H. Frank, A.J. Heynen, B. Morales, M.F. Bear, A. Kirkwood, Developmental inhibitory gate controls the relay of activity to the superficial layers of the visual cortex, J. Neurosci. 21 (2001) 6791–6801.
[10] J.A. Saez, J.M. Palomares, F. Vives, I. Dominguez, I. Villegas, R. Montes, D.J. Price, J.M. Ferrer, Electrophysiological and neurochemical study of the rat geniculo-cortical pathway. Evidence for glutamatergic neurotransmission, Eur. J. Neurosci. 10 (1998) 2790–2801.
[11] K.J. Sanderson, B. Dreher, N. Gayer, Prosencephalic connections of striate and extrastriate areas of rat visual cortex, Exp. Brain Res. 85 (1991) 324–334.
[12] J.F. Staiger, K. Zilles, T.F. Freund, Distribution of GABAergic elements postsynaptic to ventroposteromedial thalamic projections in layer IV of rat barrel cortex, Eur. J. Neurosci. 8 (1996) 2273–2285.
[13] K.J. Stratford, K. Tarczy-Hornoch, K.A.C. Martin, N.J. Bannister, J.J.B. Jack, Excitatory synaptic inputs to spiny stellate cells in cat visual cortex, Nature 382 (1996) 258–261.
[14] H.A. Swadlow, Influence of VPM afferents on putative inhibitory interneurons in S1 of the awake rabbit: evidence from cross-correlation, microstimulation, and latencies to peripheral sensory stimulation, J. Neurophysiol. 73 (1995) 1584–1599.
[15] M.V. Tsodyks, H. Markram, The neural code between neocortical pyramidal neurons depends on neurotransmitter release probability, Proc. Natl. Acad. Sci. U. S. A. 94 (1997) 719–723.
[16] J.A. Varela, K. Sen, J. Gina, J. Fost, L.F. Abbott, S.B. Nelson, A quantitative description of short-term plasticity at excitatory synapses in layer 2/3 of rat primary visual cortex, J. Neurosci. 17 (1997) 7926–7940.
[17] L.Y. Wang, L.K. Kaczmarek, High-frequency firing helps replenish the readily releasable pool of synaptic vesicles, Nature 394 (1998) 384–388.
[18] J.H. Wang, P.T. Kelly, Regulation of synaptic facilitation by postsynaptic Ca2+/CaM pathways in hippocampal CA1 neurons, J. Neurophysiol. 76 (1996) 276–286.
[19] K.S. Wilcox, M.A. Dichter, Paired pulse depression in cultured hippocampal neurons is due to a presynaptic mechanism independent of GABAB autoreceptor activation, J. Neurosci. 14 (1994) 1775–1788.
[20] R.S. Zucker, Short-term synaptic plasticity, Annu. Rev. Neurosci. 12 (1989) 13–31.
[21] R.S. Zucker, Calcium- and activity-dependent synaptic plasticity, Curr. Opin. Neurobiol. 9 (1999) 305–313.