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Research report

Strengthening of non-NMDA receptor-dependent horizontal pathways between primary and lateral secondary visual cortices after NMDA receptor-dependent oscillatory neural activities

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Abstract

Emergence of oscillatory signal flows between the primary visual cortex (Oc1) and medial secondary visual cortex (Oc2M) was previously dynamically demonstrated in rat brain slices by us. Applying caffeine, a neural modulator, to the slices and using optical recording methods revealed this facilitation along horizontal intrinsic pathways in which initial forward propagation from Oc1 to Oc2M was dependent on both *N*-methyl-D-aspartate receptors (NMDARs) and non-NMDARs. Conversely, oscillatory backward propagation from Oc2M to Oc1 was entirely dependent on NMDARs. The present study examined: (1) whether the signal behavior between Oc1 and lateral secondary visual cortex (Oc2L) is based on the same mechanism with that between Oc1 and Oc2M; and (2) how non-NMDAR and NMDAR activities underlie opening of horizontal corticocortical pathways between Oc1 and Oc2. Under NMDAR blockade, signals elicited in the Oc1 either could not or only weakly penetrated the Oc2L, even in caffeine-containing medium. In contrast, once forward propagation from Oc1 to Oc2L and oscillatory backward propagation from Oc2L to Oc1 was established in caffeine-containing medium, signals elicited in Oc1 could strongly penetrate the Oc2 even during blockade of NMDA activities, when forward penetrating components were dependent on non-NMDARs. These findings suggest that: (1) signal behavior and its mechanism between Oc1and Oc2L are the same with those between Oc1 and Oc2M; and (2) NMDAR activation results in non-NMDAR activity, resulting in opening and strengthening of intrinsic signal pathways between Oc1 and Oc2. NMDAR-dependent forward and backward propagation might be involved in cortical reorganization of the visual cortex.

Theme: Excitable membranes and synaptic transmission
Topic: Postsynaptic mechanisms

Keywords: Primary visual cortex; Secondary visual cortex; Horizontal propagation; Oscillation; NMDA receptor; Non-NMDA receptor; Caffeine

1. Introduction

Functional linkage between the primary visual cortex (Oc1) and secondary visual cortex (Oc2) is critical to cognition of the visual world [1,4,11,12,24]. Specialization of receptive fields requires the development of functional intrinsic connections between two areas [3,14–16,28,29,39]. As animals mature, horizontal anatomical connectivity between the Oc1 and Oc2 is strengthened [10,15,19,30,33]. We recently reported enhancement of signal interactions along horizontal directions between Oc1 and the medial part of the secondary visual cortex (Oc2M) during development [38]. Dynamics of these developmental changes were successfully shown by applying the neural modulator, caffeine, to visual cortex slices of rats, and by using optical recording methods with voltage-sensitive dyes. Signal

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propagation elicited by Oc1 stimulation was restricted within Oc1 before caffeine application, while evoked signals spread from Oc1 to Oc2M by way of layer II/III principally after low-frequency stimulation to Oc1 on application of caffeine, and oscillatory signals emerged in Oc2M and spread back to Oc1. *N*-methyl-D-aspartate receptor (NMDAR) activation was required for oscillatory activities in Oc2M, but was not necessarily required for initial forward propagation from Oc1 to Oc2M. Focusing on initial forward propagation, initial horizontal components comprised fast non-NMDAR and slow NMDAR components.

Oc2 is located not only at the medial part of the Oc1, but also at the lateral parts, named Oc2L. Cytoarchitectural differences between Oc1 and Oc2M are also preserved between Oc1 and Oc2L [27,32,40]. If the manner of neural activity is dependent on cytoarchitectural features, signal penetration from Oc1 to Oc2L could generate neural oscillation in Oc2L, and oscillatory signals might spread back to Oc1, which may represent a similar pattern of propagation and oscillation to that between Oc1 and Oc2M. The present study examined whether the signal behavior between Oc1 and Oc2L is based on the same mechanism with that between Oc1 and Oc2M.

In general, activation of non-NMDARs and NMDARs is mutually controlled and is relevant to synapse plasticity in the central nervous system (CNS) [21,22]. In particular, the activities of NMDA receptors are indispensable for the induction of functional synapses mediated by non-NMDA receptors in the CNS [17,18,25]. In addition, a previous study predicted that intrinsic horizontal connections are concerned with remapping in the visual cortex [8]. Together, these findings suggest the possibility that NMDAR activities modify non-NMDAR activities, opening the horizontal intrinsic pathways to traffic. The aim of this study was to elucidate cause-and-effect during the process of establishing functional corticocortical interactions between Oc1 and Oc2.

2. Materials and methods

All experiments were performed in accordance with the guidelines for the ethical use of animals approved by the Japanese Physiological Society. Wistar rats (27- to 35-days-old) were decapitated under ether anesthesia, and the brains were quickly removed and soaked in cold medium (2–4 °C) comprising NaCl 124 mM, KCl 3.3 mM, NaH_2PO_4 1.25 mM, $MgSO_4$ 1.3 mM, $CaCl_2$ 2 mM, $NaHCO_3$ 26 mM, and D-glucose 10 mM, saturated with 95% O_2–5% CO_2. Visual cortex slices (350 μm thick) including the Oc1 and Oc2 were prepared using a slicer. Once cut, slices were left at room temperature for at least 1 h before starting the recording session.

To observe spatiotemporal dynamics of spreading neural activities, high-speed optical recording methods were used with voltage-sensitive dyes. Details of the optical recording system used in this study have been described elsewhere [13,23,26,31,34,37,38]. Slices were placed in a submerged-type chamber set on the stage of an IMT-2 upright microscope (Olympus, Tokyo, Japan) and perfused with medium (30 °C) at 5 mL/min. For optical recordings, slices were incubated with voltage-sensitive dye NK2761 (0.125 mg/mL; Nihon Kanko, Okayama, Japan) for 20 min, then transferred to the recording chamber. A bipolar tungsten electrode for stimulation was inserted into the border region between gray and white matter (WM) in Oc1 (WM stimulation). Duration and intensity of stimuli were 80 μs and 200–350 μA, respectively. Synaptic responses were elicited by WM stimulation at 0.03–0.3 Hz. Field potentials were recorded for monitoring electrical activities using a glass micropipette filled with 3 M NaCl, and

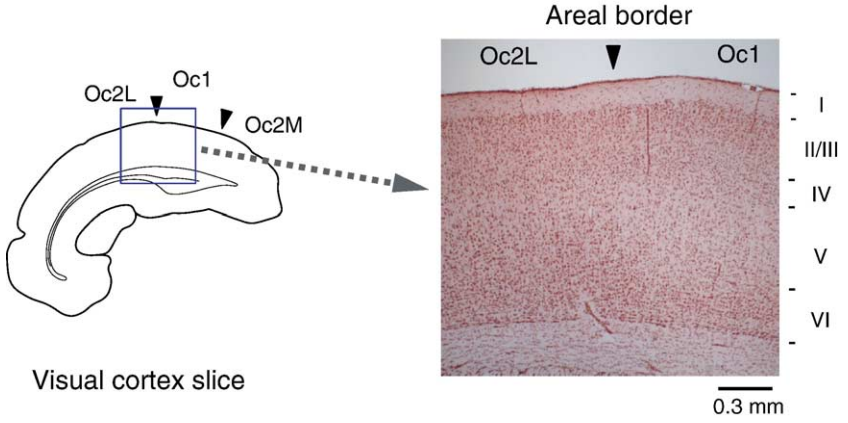

Fig. 1. Photomicrographs of a Nissl-stained visual cortex slice showing cytoarchitectonic features, in which the border of Oc1 and Oc2L is delineated. Photomicrographs were taken from the rectangular region indicated in the line drawing of the slice. Laminar borders of cortical layers and the Oc1/Oc2L border are indicated.