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Microglial removal of inhibitory synapses unleashes the multi-sensory potential in the association cortex

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Sensory inputs are essential to detect the external environment, but a part of them is disturbed in the blind and deaf. Traditionally, the concept of cross-modal plasticity has been raised, which an impaired sensory input is compensated by the other sensory systems and even promote the remained sensory abilities. Previous study showed whisker-dependent activation of visual cortex in the eye enucleated mice. However, the mechanism of cross-modal plasticity has not been shown yet. In this research, we unravel the effect of early visual deprivation on the activation of the visual association cortex with whisker stimulation. We first visualized the axonal projection from S1 (primary somatosensory cortex) to V2 (extrastriate cortex), which showed whisker-evoked responses both in normal sighted and monocular deprived mice (MD). Moreover, the axons are predominantly projecting to anterolateral visual cortex, which is previously known as the multisensory projected cortex in V2. Then we detected clear differences of neuronal activity of V2 between MD and control when touched with sandpaper; normal sighted mice showed strong suppression while MD promoted. This suggests that visual deprivation triggers the removal of the inherited system which the other modality suppress the cortex. We hypothesized that microglia, mediators for experience-depended synaptic plasticity, can play a part in remodeling of the circuits of V2. In fact, the depletion of microglia with Pexidartinib reduced the activation with whisker stimulation in MD. With immunohistological and electrophysiological methods, we revealed that microglia in MD wrap the soma of pyramidal neurons and cut the inputs from Parvalbumin-expressing interneurons that receive a projection from barrel cortex. Furthermore, interrupting the remodeling of extracellular matrix by inhibiting matrix metalloproproteinase-9 lessens the cross-modal effect. Thus, visual deprivation induces the microglial interruption of inhibitory synapses in a higher visual cortex, resulting in the acquisition of the responsiveness to the tactile sensation. This study will be an important clue to understand the physiological function of multi-sensory cortex and the microglial experience-depended synaptic plasticity.