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Visual deprivation induce cross-modal enhancement of olfactory perception

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ABSTRACT

The underlying mechanisms responsible for enhanced olfactory perception of congenital blind humans remain elusive so far. Here, animal behavioral test showed that congenital visual deprivation (from postnatal day 0–28) or one-week visual deprivation during juvenile stage (from postnatal day 21–28) could reduce the latency time of food-seeking but increase the odor discrimination performance of rodents. The enhanced olfactory perception induced by one-week visual deprivation could be returned to base level when visual input was recovered. Accordingly, local field potential (LFP) oscillation recording *in vivo* showed that the power of high-frequency β and γ oscillations were increased in olfactory bulb (OB) and anterior piriform cortex (aPC) of vision deprived animals. This research discovered the enhancement of olfactory perception and adaptive plasticity of oscillations in olfactory system of rodents induced by visual deprivation, which may facilitate better understanding of mechanisms underlying cross-modal plasticity.

1. Introduction

Both the juvenile and the adult brain were able to be shaped by developmental events, experience and environmental inputs [1]. Existing meritorious studies has documented striking effects of sensory loss in one modality on the development of other remaining modalities leading to extensive adaptation of brain circuits, which is broadly referred to as cross-modal plasticity [2]. For example, when vision input is lost or impaired, the adaptive reorganization associated with neuroplasticity affects remaining sensory modality [1]. Blindness offers a natural model to assess the effects of visual deprivation on the development of the human brain. Early blindness leads to behaviorally observed cross-modal benefits, such as improved hearing capability characterized by frequency discrimination performance and sound localization abilities testing [3,4]. Visual deprivation happened within the critical period of brain development profoundly affects the normal function of the brain. The central nerve system has the capability to adapt to the loss of one modality by undergoing plastic changes in its structural connectivity and neural interactions [5,6]. Cross-modal plasticity was first observed at the synaptic level as a global reduction in the postsynaptic strength of excitatory synaptic transmission in A1 cortex after visual deprivation [7,8]. The thalamocortical inputs to primary auditory cortex were potentiated by visual deprivation in both juvenile and adult animals [9].

Besides, visual deprivation could also affect other remaining sensory modality, such as somatosensory. Visual deprivation induced cross-modal facilitation of long-term potentiation at L4 to L2/3 synapses in somatosensory barrel cortex, suggested an enhancement of feed-forward sensory processing in the spared modality [10]. Depriving vision reduced AMPA receptor-mediated excitatory synaptic transmission in primary somatosensory cortex [7]. To date, neuroplastic changes have been well documented in visual deprivation individuals for the processing of auditory and tactile information. But few studies were involved in olfactory processing during the absence of vision. It is well known that human could use not only vision but also olfaction to enjoy desirable food, which might base on close association between visual and olfactory system. Visual cues such as colors [11,12], shapes [13], pictorial images [14,15] and abstract symbols [16] could modulate olfactory perception, suggesting the existence of cross-modal interaction between the two sensory modalities. Moreover, recent neuroimaging studies that activation of human visual cortex by repetitive transcranial magnetic stimulation could improve the performance of odor discrimination [17]. All these clues indicate

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that olfactory system is susceptible to cross-modal changes similar to those observed from the touch and auditory modalities in the absence of vision input. However, little is known about the underlying mechanisms of altered olfactory capabilities by losing vision. The present study was to investigate whether visual deprivation could enhance olfactory capability and how neural plasticity would change in olfactory system.

2. Materials and methods

2.1. Animal models

Sprague-Dawley rats and C57BL6 mice (purchased from SLAC Laboratory Animal Center, Shanghai) were reared in standard cage with *ad libitum* access to food and water. The congenital visual deprivation models at early stage were demonstrated by exposing rats (Postnatal day 0) to darkness for 28 days (DE rats). Control animals were performed by exposing rats with similar age and strain in normal visual experience with 12 h light/dark cycle (NR rats). On the other hand, the one-week visual deprivation models during juvenile stage were demonstrated by exposing mice (Postnatal day 21) to darkness (DE mice) for 7 days. Control animals were performed by exposing mice with similar age and strain in normal visual experience (NR mice) with 12 h light/dark cycle. The recovered mice (RE mice) were made by returning a subset of DE mice to the normal environment for 7 days with 12 h light/dark cycle. The investigation was approved by the Ethic Committee and the Committee of Animal Experimentation of Shanghai University and conformed to the Guidelines for the Care and Use of Laboratory Animals from the National Institutes of Health.

2.2. Behavioral testing

Based on the sniffing ability and olfactory sensitivity, which are important indicators of mammalian olfactory capability [18], food-seeking test and odor-avoiding test were demonstrated to detect olfactory metergasis induced by visual deprivation. All tests were performed in dark environments.

Food-seeking test: Two days before testing, each rat/mouse respectively received 3 g/1.5 g of powdered food pellets with water *ad libitum* each day. Twelve hours before testing, food was removed. When testing, rats/mice were placed individually into a clear cage (36 cm * 20 cm * 19 cm), in which a piece of food pellet (0.7 g) was randomly hidden under a 0.5 cm layer of standard bedding at one corner of the cage. The rat/mouse was placed in center of the cage and allowed to explore for 3 min. The latency for retrieving the hidden food pellet was recorded. After each experiment, the cage was cleaned with ethanol, then new food pellet and fresh bedding was added.

Odor-avoiding test: The apparatus used in odor avoiding test was standard cage (36 cm * 20 cm * 19 cm) divided into two parts by hardboard with a gate in middle-bottom. A piece of filter paper added 10 μL odor liquid (Diethyl phthalate (DEP) or 2-methylbutyric acid (2-MB)) was placed in smaller part (odor area) while animals can move towards and backwards the larger part (avoiding area) freely through the gate. All animals were tested twice. In first time, animal was set free in odor area while filter paper added odorless DEP. In second time, different concentration of 2-MB (0.1 M, 0.3 M and 1 M) was added, according to the subgroup, respectively. The time which animals stayed in avoiding area was recorded as baseline (the first test) or test value (the second part). Influence of 2-MB was showed as difference between test value and baseline.

2.3. In vivo LFP recording

The animals were anesthetized with chloral hydrate (10%, 4.5 mL/kg), placed in a stereotaxic frame and implanted with 16-channel nickel-chromium microelectrode array (impedance less than 1 MΩ). Neural data were acquired using a Plexon OmniPlex System (Plexon Inc., USA) as broadband signal (0.1 Hz~5 kHz). Probes were placed in olfactory bulb (lateral or medial part of OB at a depth that maximized the number of channels located in the mitral cell layer) and anterior piriform cortex (rats: 2 mm anterior to bregma, 4 mm lateral to the midline and 5–7 mm below the brain surface, mice: 1 mm anterior to bregma, 2 mm lateral to the midline and 3.0–4.5 mm below the brain surface) according to brain topography results. Brains were dissected, sliced and stained after recording in order to ensure that probes were located in correct position.

2.4. Data analysis

All subsequent data analysis steps were done off-line with custom written MATLAB scripts. After importing data into the MATLAB environment, a random 10s epoch was selected for each recording and were extracted to create a single file. LFP recordings were low-pass filtered with a cutoff at 300 Hz. Line noise artifacts were removed using a 50 Hz Butterworth notch filter. To reduce variability of individuals of each group, the recordings were normalized with total power. Power spectral density was computed using Welch technique, with Hamming windowing, and a fast Fourier transform segment length of 512 samples with 256-sample overlap. Changes in power were analyzed for five frequency oscillations (δ: ~1–4 Hz, θ: ~4–8 Hz, α: ~8–13 Hz, β: ~13–30 Hz, γ: ~30–90 Hz). Wavelet packet decomposition was used to extract these five frequency bands. These oscillations were chosen because preliminary analyses showed that specific spectral changes occurred in these frequency bands when animals were anesthetized. Power of each oscillation was computed separately. Data are expressed as mean ± SEM. Because of differences between individual, statistics were done separately for each animal. T-test was chosen using a significance criterion of $p < 0.05$.

3. Results

3.1. The enhanced olfactory perception of rats induced by congenital visual deprivation from birth

The food-seeking test showed that DE rats could finish the task faster than NR rats, the latency time of DE rats was significantly reduced (from 64.45 ± 4.35s to 44.13 ± 3.17s, $p < 0.001$) (Fig. 1A). The odor-avoiding experiment revealed that the staying time of NR rats in avoiding area was significantly increased in the concentration of 1 M 2-MB compared to DEP condition (from 75.76 ± 3.72s to 115.41 ± 3.57s, $p < 0.05$). The staying time of DE rats in the avoid area were remarkably increased in the concentration of 0.3 M and 1 M 2-MB compared to corresponding DEP condition (from 68.98 ± 8.39s to 117.88 ± 4.39s, $p < 0.01$; from 72.27 ± 6.39s to 114.17 ± 6.03s, $p < 0.05$) (Fig. 1B and C). These results suggested that DE rats could identify 2-MB at lower concentration and then do avoid behavior compared to NR rats.

3.2. The enhanced olfactory perception of mice induced by one-week visual deprivation during juvenile stage

In addition, the food-seeking test showed that one-week visual deprivation was sufficient to reduce the latency time of DE mice compared to NR mice (from 78.7 ± 4.62s to 60.11 ± 4.42s, $p < 0.05$).

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