Adult deafening induces brain wide cross-modal plasticity in mice

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INTRODUCTION

Recent evidence suggests that sensory deprivation in adulthood can lead to substantial reorganizations across cortical regions. In sensory cortices, both “cross-modal recruitment’ (takeover of the deprived cortex by spared modalities) and “compensatory plasticity” (enhanced responses in spared modalities) have been reported. However, the extent and time course of this adult plasticity and the underlying neural mechanisms remain poorly understood. Here, we investigated the effects of deafening in adult mice, using 15.2T blood-oxygenation-level-dependent (BOLD) functional MRI (fMRI), which allows repeated brain-wide mapping of sensory responses before and after deafening in individual animals.

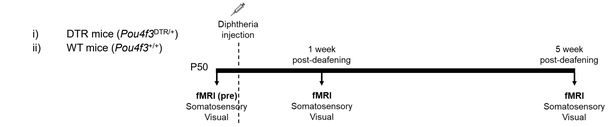
MATERIALS & METHODS

Animal preparation

Eleven adult Pou4f3$^{DTR/+}$ (B6.Cg-*Pou4f3*$^{tm1.1(HBEGF)Jsto}$/RubelJ) and eight wild-type (WT) mice were used for BOLD fMRI at 15.2T, five C57BL/6 mice were used for cerebral blood volume (CBV)-weighted optical intrinsic signal (OIS) imaging and nine VGAT-ChR2-eYFP mice were used for optogenetic fMRI with transient A1 suppression.

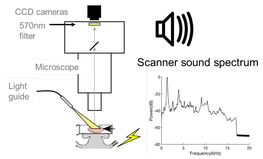
Experimental designs

1. BOLD fMRI Before vs After diphtheria toxin (DT) injection



- For *BOLD fMRI*, GE-EPI sequence, TE/TR = 16/1000 ms, resolution = 132x132x500 μm^3
- Forepaw stimulation (0.5 ms, 4 Hz and 0.7 mA) and visual stimuli (10 ms, 5 Hz and about 20 lux) was alternated
- Deafness confirmed by the absence of acoustic startle response (ASR)
- 125 ROIs were selected based on Allen brain atlas

2. CBV-weighted OIS imaging with scanner noise



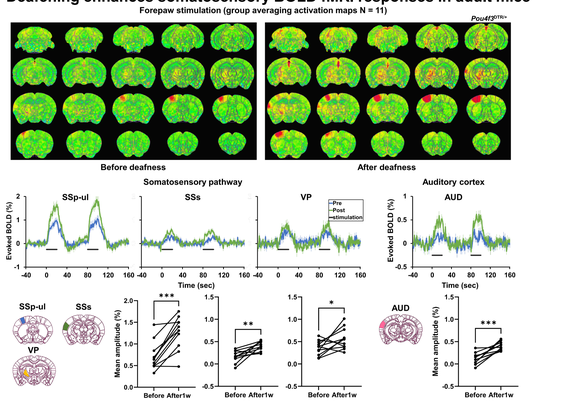
- For *OISI* , 572±15 nm filter (CBV-weighted), sampling rate = 2 Hz, resolution = 16x16 μm^2
- Forepaw stimulation was conducted on C57BL/6 mice while playing back scanner noise recordings (~115dB)
- Skull thinning was performed at least 1 week before the OIS experiment

3. BOLD fMRI with optogenetic A1 suppression

- *BOLD fMRI* at 15.2T
- Forepaw stimulation was conducted on VGAT-ChR2 mice while with or without bilateral A1 optogenetic suppression (473 nm, 10 ms, 20 Hz and about 3 mW)
- Optic cannulas were implanted on the bilateral A1 (AP: 2.6, ML: ±4.3)

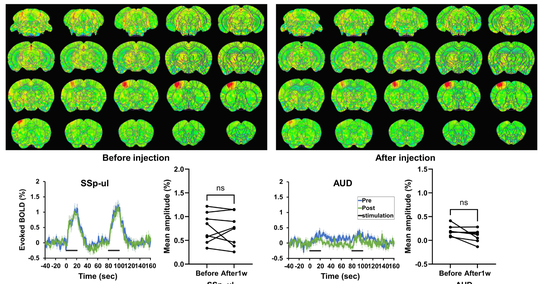
RESULTS

1. Deafening enhances somatosensory BOLD fMRI responses in adult mice

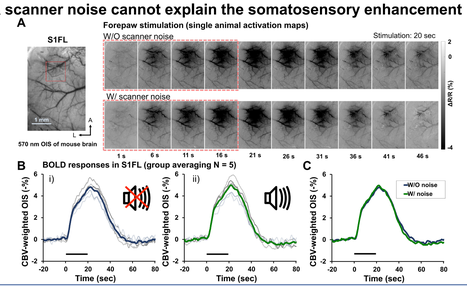


Acronym: Primary somatosensory area, upperlimb (SSp-ul), supplemental somatosensory area (SSs), ventral posterior complex of the thalamus (VP; VPL and VPM), auditory areas (AUD)

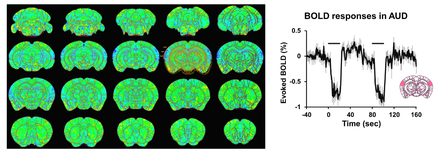
2. Diphtheria toxin in WT mice does not affect BOLD fMRI responses

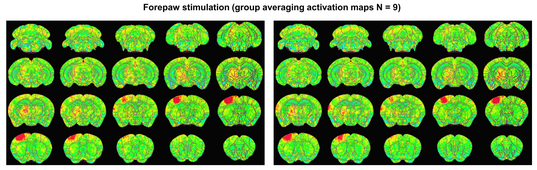


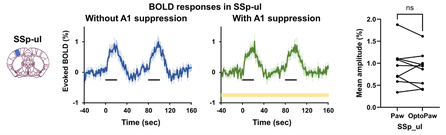
3. MR scanner noise cannot explain the somatosensory enhancement



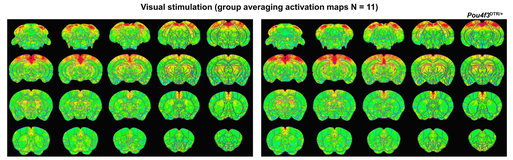
4. Acute inactivation of auditory cortex does not enhance somatosensory responses

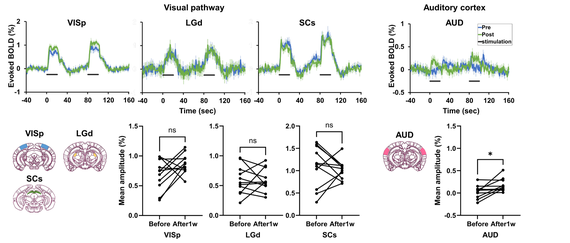






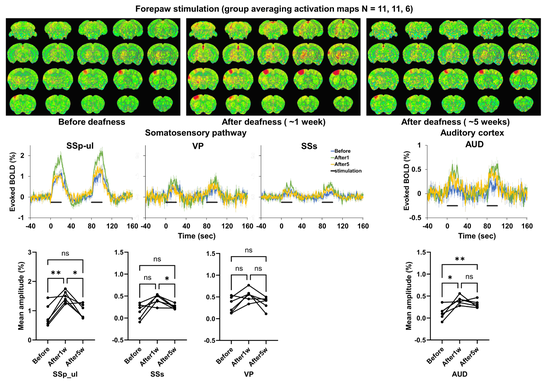
5. Deafening enhances visual BOLD fMRI responses in auditory cortex



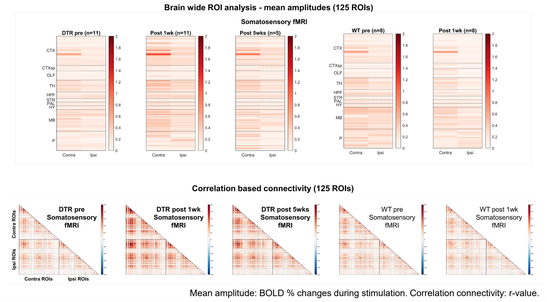


Error bars: SEM; *: p-value<0.05; **: <0.01; ***: <0.001; ns: significantly not different. Color scale of activation maps -1 < β < 1.

6. Repeated long term fMRI in adult mice after deafening



7. Adult deafening increases the correlation of somatosensory activation map



Mean amplitude: BOLD % changes during stimulation. Correlation connectivity: r-value.

CONCLUSION

- Deafening induces rapid compensatory plasticity and cross-modal recruitment in adult mice
- Some aspects of compensatory enhancement of the spared modalities (S1) may be temporary, while cross-modal recruitment may be long-lasting.
- The somatosensory pathway may be more strongly affected by deafening than the visual pathway
- Deafening induces a persistent enhancement in the pairwise correlations of BOLD responses across different regions of the brain
- Repeated brain-wide imaging using fMRI may reveal the neural mechanisms underlying cross-modal plasticity

ACKNOWLEGMENT

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