Unilateral Infraorbital Denervation Leads to Plasticity in the rat Whisker Barrel Cortex.

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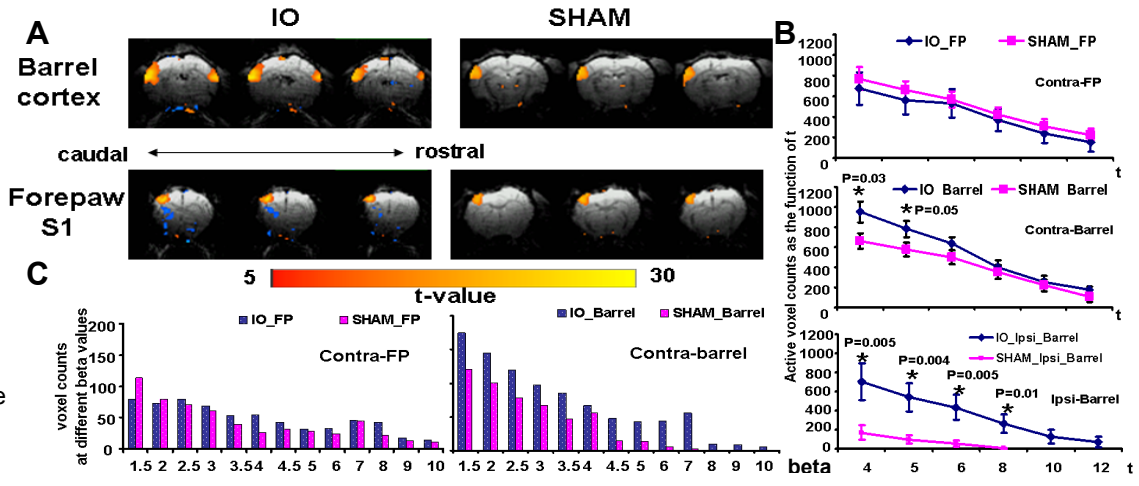
Introduction Plasticity after unilateral forepaw/hindpaw denervation has been shown to lead to detection of ipsilateral cortical fMRI responses to stimulation of the good paw in rats [1]. This ipsilateral activation is proposed to involve interhemispheric callosal connections and is relevant to some human studies that show similar plasticity after peripheral or central nervous system damage and may be important in predicting recovery from neuronal damage. Rats are very effective at integrating whisker information through interhemispheric interactions due to closely associated bilateral whisking that occurs [2]. Furthermore, there is abundant information about cortical processing in the whisker barrel, making this an excellent model to study interhemispheric plasticity following unilateral deprivation of the whisker sensation. Here, we used BOLD-fMRI to map the neuronal activity changes that occur in the barrel cortex after unilateral infraorbital denervation (IO). In the sham control group, bilateral activation following unilateral whisker stimulation was inconsistently observed (3 out of 7 rats) and was low in amplitude. Bilateral activation was detected in all six unilateral IO rats, showing a significantly increased ipsilateral fMRI response even compared to the 3 sham rats that showed bilateral activation. In addition, group analysis showed a significantly increased fMRI response in the contralateral barrel cortex of the unilateral IO rats. This work indicates that the unilateral IO denervation alters the whisker-barrel ascending pathway and interhemispheric neuronal interactions.

Methods BOLD-fMRI was performed in 13 rats anesthetized with α-chloralose at postnatal 6-7 weeks. IO and sham surgeries were performed on rats at postnatal 4 weeks after the early critical period for plasticity has passed [3]. Detailed procedures for imaging and animal preparation for fMRI were similar to those previously described [4]. Briefly, all images were acquired with an 11.7T/31cm horizontal bore magnet (Magnex, Abingdon, UK), interfaced to an AVANCE III console (Bruker, Billerica, MA) and equipped with a 12 cm gradient set. A custom-built, 9 cm diameter transmitter coil was used for transmit and a custom-built 4-array surface coil was used for receive employing a transmit/receive decoupling device. A 3D gradient-echo, EPI sequence was used for the fMRI studies. A single shot sequence with a 64 x 64 x 32 matrix was acquired with the following parameters: effective echo time (TE) 16ms, repetition time (TR) 1.5s, bandwidth 200kHz, filed of view 1.92 x 1.92 cm. This sequence gave isotropic resolution of 300 microns. A sub-skin electrical stimulation with 2.5 mA, 300μs pulses repeated at 3Hz was delivered to forepaw (FP) and whisker pads in a block design stimulation paradigm (30s on/off repeated 3 times). AFNI software was used for image analysis[5]. For group analysis, BOLD signals from the FP somatosensory (S1) area were used as the internal control to normalize the barrel cortex BOLD response level. This assumes that the IO did not alter the FP S1 response. Student's t test (two-tail) was used for statistical analysis.

Results Fig1A shows 2D t-maps overlaid on three consecutive coronal EPI images across the barrel cortex and the FP S1 cortex of two individual rats. Bilateral activation in the barrel cortex was observed in the IO rat (contra-barrel cortex, left; ipsi-barrel, right), while only contra-barrel cortex was activated in this sham rat. No contralateral activation was detected in IO rats when the affected pad was stimulated. Three out of 7 sham rats showed small activated regions in the barrel cortex ipsilateral to the stimulation (figure not shown). The lower panel in Fig1A shows the fMRI response of the FP S1 cortex (contra-FP, left). To examine the deprivation-induced functional alteration, active voxels were counted as the t-threshold varied from 4 to 12. There was no significant difference in number of voxels activating in the FP S1 as t-threshold varied, indicating no effects of IO on the forepaw response (Fig 1B top panel). A significantly increased number of active voxels was observed in the contra-barrel cortex of IO rats with t-threshold at 4 and 5 (Fig1B middle panel). As the t-threshold increased the number of active voxels in both IO and sham groups was similar, indicating that the extent of the strongest activation was similar and that the increased voxel number at lower thresholds most likely represents increased response in the barrel cortex due to plasticity. The histogram in Fig 1C shows the distribution of active voxels with different beta values, which has been used to estimate the BOLD signal change amplitude [4]. The number of active voxels and the voxel distribution as a function of beta in FP S1 cortex was not different in IO and sham groups indicating that the FP response is not altered due to IO. There are more voxels showing higher beta value fMRI responses in the contralateral whisker barrel in the IO compared to the sham rats indicating there has been an increase in response along the normal whisker pathway to the contralateral cortex. A significantly increased number of active voxels was observed in the ipsilateral barrel cortex of the IO group (Fig 1B lower panel).

Conclusions Unilateral IO denervation altered the whisker-barrel functional pathway and the interhemispheric neuronal connection. This altered interhemispheric connection leads to readily detectable ipsilateral activation when the good whisker pad is stimulated.



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