Invasion of whisker cortical maps by adjacent forepaw representations visualized with BOLD fMRI

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Introduction: A large part of the neocortex is given over to topographic representations of sensory inputs and motor outputs termed cortical maps. Experience-dependent plasticity of cortical maps persists into adulthood, but at lower levels than during developmental critical periods (*1*). Reorganization in adult rodent somatosensory cortex has been visualized with blood-oxygen-level-dependent (BOLD) functional magnetic resonance imaging (fMRI) following whisker trimming (*2*). The representation of non-trimmed (spared) whiskers expands into cortex that has lost its normal whisker sensory input (deprived). Here, we induce plasticity in rodent somatosensory cortex with whisker trimming and use BOLD fMRI to determine whether reorganization is restricted to the whisker cortical map or whether the forepaw representation, which is adjacent to the deprived whisker representation, also expands into deprived cortex.

Methods: Male Sprague-Dawley rats (250 g) had all whiskers trimmed daily to the level of the fur except for C-row of whiskers on both sides of the snout. Control rats were sham-trimmed daily. After 7 days of trimming, rats were imaged with a 25 mm diameter surface coil (Varian, Palo Alto, CA, USA) in a 9.4T magnet (Oxford Instruments, Oxford, UK) while anaesthetized with α-chloralose (bolus of 65 mg/kg followed by an infusion at 30 mg/kg/hour). Rectal temperature was maintained at 37.0 ± 0.5 °C and respiration plus cardiac rate were monitored. The cortical representations of the right C-row whiskers and the right forepaw (n = 12) were imaged with BOLD fMRI. Each fMRI experiment comprised 50 ON blocks and 50 OFF blocks that were randomized. For C-row whisker representations, ON blocks involved mechanical deflection (3 mm rostro-caudally) of the right C1 – 4 whiskers by a purpose-built whisker actuator at 5 Hz. Forelimb representations were evoked by electrical stimulation (0.3 mA, 3 ms) at 3 Hz. The OFF block comprised no whisker deflection or no forepaw stimulation. Signal acquisition took 32.95 seconds per block. Anatomical spin-echo sequence: TR/TE = 1000/20 ms ; 10 x 0.5 mm thick slices; field of view, 32 x 32 mm; acquisition matrix 384 x 192 averaged 4 times. FMRI gradient-echo sequence: flip angle = 31 degrees; TR = 340 ms; TE = 4, 8, 12, 16, 20 ms acquired within a single TR; field of view, 32 x 32 mm; acquisition matrix = 192 x 96; single excitation; brain volumes comprised 10 x 0.5 mm thick slices. The contribution of large draining vessels was reduced by removing voxels with a BOLD signal that had a coefficient of variation greater than 15%. Probabilistic independent component analysis was performed using MELODIC (http://www.fmrib.ox.ac.uk/fsl/) to reduce coloured noise in the BOLD signal. Data were motion corrected, normalised to a template subject, smoothed with a 0.99 mm cubic kernel and modelled in SPM99 (http://www.fil.ion.ucl.ac.uk/spm/). The MarsBar tool (MARSeille Boîte À Région d'Intérêt) was used on single-animal statistical parametric maps to measure the: BOLD signal intensity; sizes of voxel clusters; and P values for voxels in regions of interest.

Results: Stimulation of the right forepaw in sham-trimmed rats evoked a positive BOLD response (PBR) in left somatosensory cortex that was maximal 1.0 mm rostral to bregma and extended over four contiguous slices in the group map (Fig. 1A) consistent with an activation in forepaw primary somatosensory cortex. Following one week of whisker trimming (see Methods), forepaw representations had expanded caudally into cortex normally subserving forelimb and whisker representations (Fig. 1B). Quantification of changes in the BOLD signal was based on single-animal maps. The volume of the forepaw PBR increased after 7 days of whisker trimming (trim, 78 ± 14 voxels, n = 8, control, 43 ± 9 voxels, n = 10; P = 0.039, t-test). In contrast, the amplitude of the forepaw PBR was not affected by whisker trimming (trim, 1.2 ± 0.2 %, n = 8, control, 1.0 ± 0.1 %, n = 10; P = 0.403, t-test).

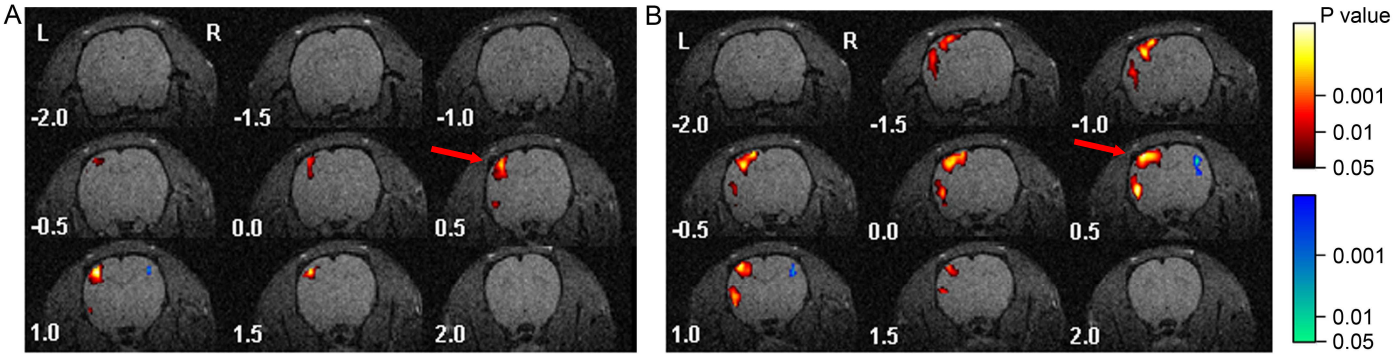

Figure 1 (A) Group map of BOLD response evoked by right forepaw stimulation in a sham-trimmed rat. (B) Group map of right forepaw representation in rats after 7 days of whisker trimming. Pseudo-coloured voxels have a BOLD signal significantly different from baseline. Red arrows indicate forepaw PBR in primary somatosensory cortex. Numbers denote the rostro-caudal distance (mm) of the image slice from bregma.

Discussion: Our data indicate that the forepaw cortical map expands into cortex normally subserving the trimmed whiskers. The lack of change in PBR amplitude in forepaw somatosensory cortex suggests that expansion of the BOLD signal is not an artefact of smoothing a higher amplitude BOLD signal. We concluded that plasticity is not restricted to the cortical map with altered sensory input, but instead occurs in representations at the boundary between deprived cortex and cortex with retained sensory input. Expansion of face representations into adjacent non-facial cortical maps has been documented electrophysiologically following forelimb deafferentation in monkeys (*3*) and rats (*4*). However, it remains unclear how much of the cortical reorganization is secondary to lesioning of the sensory system. Our findings indicate that non-traumatic sensory deprivation is sufficient to induce expansion of adjacent representations that are not directly modified by the deprivation protocol. This suggests that cortical representations compete with adjacent representations for cortical space in the normal brain.

References: (*1*) Buonomano, D.V. et al. Annu. Rev. Neurosci. (1998) 21:149-186. (*2*) De Celis Alonso, B. et al. Proc Int Soc Mag Reson (2007) 264. (*3*) Pons et al. Science (1991) 252:1857-1860. (*4*) Hickmott, P.W. & Merzenich, M.M. J. Neurophysiol. (2002) 88:1288-1301. **Acknowledgements:** Supported by the Wellcome Trust and MRC.