Experience-dependent plasticity of rat whisker cortical maps imaged with BOLD fMRI

B. de Celis Alonso[1], A. S. Lowe[2], J. P. Dear[3], K. C. Lee[4], and G. T. Finnerty[1]

[1]MRC Centre for Neurodegeneration, King's College London, London, United Kingdom, [2]Experimental Neuroimaging Group, University of Oxford, Oxford, United Kingdom, [3]Department of Mechanical Engineering, Imperial College London, London, United Kingdom, [4]Division of Engineering, King's College London, London, United Kingdom

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 is reduced during adulthood compared with developmental critical periods, but the capability for significant reorganization remains (1). Non-invasive techniques such as functional magnetic resonance imaging (fMRI) can detect reorganization in adult human motor cortex (2) and somatosensory cortex (3) following learning. However, much of our understanding of the cellular mechanisms underpinning experience-dependent plasticity has been obtained from animal models. These models allow detailed studies to be performed, but commonly only a small part of the brain can be investigated at any one time and the techniques used tend to be invasive (4). fMRI potentially offers significant advantages for the study of cortical map plasticity, but efforts to image map reorganization in animal models have met with mixed results (5). Here, we examine whether plasticity of rat whisker representations can be imaged in somatosensory cortex using blood-oxygen-level-dependent (BOLD) fMRI.

Methods: Male Sprague-Dawley rats (250 g) had all whiskers trimmed to the level of the fur except for C-row whiskers on both sides of the snout. Whisker trimming was performed daily for 7 days prior to imaging. Controls were sham-trimmed daily except immediately before scanning when all but the C-rows of whiskers were trimmed. Rats were imaged with a 25mm 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. An anatomical scan and an fMRI experiment were performed on every rat. This scan protocol takes 90 minutes. A randomized block design was used for fMRI experiments, which consisted of 60 ON blocks and 60 OFF blocks. During ON blocks, the right C1, C2 and C3 whiskers were mechanically displaced in a rostro-caudal direction at 5 Hz by a purpose-built whisker stimulator. The OFF block comprised no whisker movement. 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 = 28 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. Data were analyzed in SPM99 (http://www.fil.ion.ucl.ac.uk/spm/). The contribution of large draining vessels was reduced by removing voxels with signal variance greater than 15%. Probabilistic independent component analysis (PICA) was performed using MELODIC (http://www.fmrib.ox.ac.uk/fsl/) to reduce noise. Data were motion corrected, normalised to a template subject and smoothed with a 0.99 mm cubic kernel. Second level fixed-effect analysis was performed using scalp muscle as a covariate of no interest. Probability maps for each group were superimposed on the anatomical scans. We used the MarsBar tool (MARSeille Boîte À Région d'Intérêt) to measure the: sizes of voxel clusters; changes in BOLD signal intensity; and P values for voxels in regions of interest (ROI).

Results: Synchronous deflection of the right C1, C2 and C3 whiskers at 5 Hz evoked a positive BOLD response in left neocortex that was centred 2 – 3 mm caudal to bregma and extended over 3 contiguous slices of group maps (Fig. 1, white arrow). The location and rostro-caudal extent of the positive BOLD response were consistent with an activation in primary somatosensory cortex (SI). Quantification of changes in BOLD signal was based on single-animal maps. The area of activation in SI of trimmed rats was larger than the area of activation in sham-trimmed rats (trimmed = 48 ± 10 voxels, n = 9; non-trimmed = 20 ± 6 voxels, n = 8; p = 0.043, Mann-Whitney rank sum test). The peak change in BOLD signal for trimmed and sham-trimmed rats was not different (trimmed = 0.60 ± 0.11 %, n = 9; sham-trimmed = 0.67 ± 0.13%, n = 8: P = 0.67, t-test). A second positive BOLD response was present in the group map of trimmed rats in a location consistent with secondary somatosensory cortex (SII) (Fig. 1A, blue arrow). This activation was present in five of nine single animal maps. The peak BOLD signal change in SII of trimmed rats was 0.33 ± 0.15 % (n = 9) and mean size of the activation was 27 ± 9 voxels (n = 9).

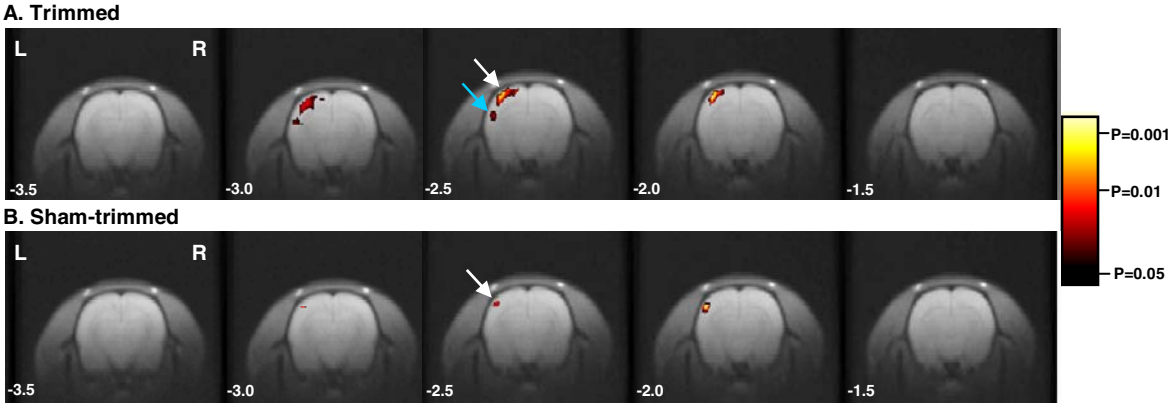

Figure 1: Group maps of the BOLD response evoked by 5 Hz deflection of right C-row whiskers in trimmed (A) and sham-trimmed (B) rats. Pseudo-coloured voxels have a BOLD signal that is statistically significantly different from baseline. The rostro-caudal distance (mm) from bregma is given for each slice. White arrows point to SI and the blue arrow denotes SII.

Discussion: Our data show that trimming whiskers of young adult rats for one week results in lateral expansion of the representation of spared C-row whiskers in SI that can be imaged with BOLD fMRI. Enlargement of the cortical representation of spared whiskers occurs without a corresponding increase in the maximum BOLD signal in SI. Human finger representations in both SI and SII enlarge following a coactivation protocol lasting hours (3). A whisker representation was not present in SII of the sham-trimmed group map, but was noted in the group map of trimmed animals. Our findings in somatosensory cortex contrast with a recent study of reorganization in monkey visual cortex, which found neither electrophysiological nor fMRI evidence for reorganization following bilateral retinal lesions in monkeys (5). Rats' whiskers go through repeated cycles of growth and loss during adulthood (6). Hence, it may be necessary for the rodent somatosensory cortex to remain plastic throughout life to enable sensory processing to adapt to normal, physiological changes in the biophysical properties of the whisker sensory transduction system.

References: (**1**) Buonomano, D.V. et al. Annu. Rev. Neurosci. (1998) 21:149-186. (**2**) Karni, A. et al. Nature (1995) 377:155-8. (**3**) Pleger, B. et. al. Neuron (2003) 40:643–53. (**4**) Fox, K. & Wong, R.O. Neuron (2005) 48:465-477. (**5**) Smirnakis, S.M. et al. Nature (2005) 435:300-7. (**6**) Ibrahim, L. et al. J. Embryol. Exp. Morphol. (1975) 33:831-44. **Acknowledgements:** Supported by the Wellcome Trust and MRC.