Investigation of BOLD adaptation to hand tapping in healthy controls and patients with MS

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Introduction

The term "adaptation" is sometimes used in reference to changes in cortical activation after brain injury, due e.g. to multiple sclerosis (MS) or stroke[1,2,3,4]. However, the same term also refers to alterations in motor cortex excitability and/or changes in the location or extent of cortical representations with repeated movements, as has been demonstrated by transcranial magnetic stimulation[5,6]. In this study, we focused on this short-term adaptation. Our aims were to investigate if adaptation is demonstrable during repeated hand movements using fMRI, whether the activation decay is linear or exponential with time, and if it changes with the presence or progression of multiple sclerosis (MS) over a period of 1 year.

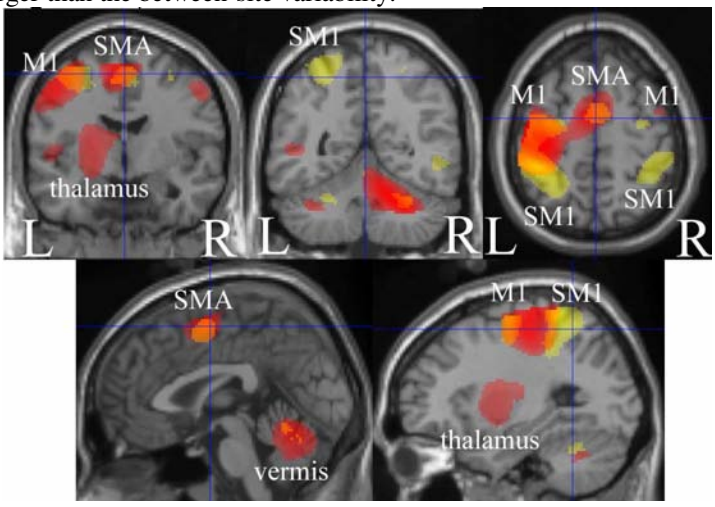
Methods

This study was conducted in 8 European sites using 1.5T MRI systems. Baseline: 4 fMRI data sets (runs) were acquired sequentially from 44 healthy controls, all right handed (median age 31 (range 19 to 54) years; 23 men; 21 women) and 37 MS patients with normal upper-limb function, all right-handed (14 men, 23 women, 30 relapsing-remitting and 7 secondary progressive; median age 35 (range 24 to 53) years; median expanded disability status score (EDSS) 2.5 (range 0.0 to 7.5)). 1-year follow up: 4 fMRI runs were acquired from a subset of the subjects (29 controls and 24 patients, 18 with EDSS assessments). Mean EDSS change between baseline and 1 year was 0.3 (standard deviation 0.5). fMRI parameters: gradient-echo echo-planar sequence, TE/TR=60/3000 ms, 3.75x3.75x6mm^3 resolution, 21 contiguous axial slices, 6.5 min per run. fMRI paradigm: "block" design alternating periods of 30s of rest to 30s of visually cued right-hand tapping (1 Hz). fMRI analysis: pre-processing + two-step statistical analysis (SPM5, www.fil.ion.ucl.ac.uk/spm/). First (**within-subject**) step: (1) for each subject a general linear model was inverted and three contrasts of parameter estimates were computed; summarizing linear adaptation, exponential adaptation and mean activation (**over runs**). (2) For those subjects examined at follow-up; a second model, including the baseline and follow-up runs, was inverted. Contrasts of differences between baseline and follow-up for the linear adaptation, exponential adaptation, and mean activation were computed. Second (**between-subject**) step: a two-factor ANOVA was performed to test differences between sites, and one- and two-sample t tests were used to perform within and between group (patient vs. control) comparisons. The SPM{t} were thresholded at a family-wise error of P<0.05 (corrected).

Results and Discussion

For controls, patients, and controls vs. patients, no statistically significant differences were found in linear or exponential adaptation between sites, suggesting that the between-subject variability was larger than the between-site variability.

As expected, in both controls and patients, there was significant mean activation in the left primary motor cortex (M1), right cerebellum, supplementary motor area (SMA) and left thalamus; smaller activations were observed in the right M1 and left cerebellum (the figure shows activation in controls in red).



Both linear and exponential adaptation were observed in controls (linear adaptation shown in yellow in figure) and patients, in the sensory-motor cortex (SM1) and cerebellum bilaterally, in the SMA, and in the contralateral M1. Less extensive adaptation was observed in the ipsilateral M1, in the fusiform gyrus, in the inferior prefrontal gyrus bilaterally, and in the vermis. Although all areas demonstrated both linear and exponential adaptation, the linear adaptation was a better model. No statistically significant differences were observed for either type of adaptation between baseline and follow-up in either control or patient groups, or patients vs. controls.

Conclusions

Our consistent multi-centre results showed that for 4 consecutive fMRI runs with right-hand tapping, a linear decay in activation over time was observed not only in the primary motor area, but also in the sensory-motor cortex, SMA and cerebellum. This adaptation appears to be a physiological process expressed in both controls and patients, and was not influenced by limited MS disease progression over a period of 1 year.

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References

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