Effect of electric stimulus frequency on the activation of the secondary somatosensory cortex in BOLD fMRI

C. Del Gratta[1,2], A. Ferretti[2], C. Babiloni[3], M. Caulo[1], A. Tartaro[1,2], P. M. Rossini[4], G. L. Romani[1,2]

[1]Dipartimento di Scienze Cliniche e Bioimmagini, Università G D'Annunzio, Chieti, Italy, [2]Istituto di Tecnologie Avanzate Biomediche, Fondazione Università D'Annunzio, Chieti, Italy, [3]Dipartimento di Fisiologia Umana e Farmacologia, Università La Sapienza, Roma, Italy, [4]Dipartimento di Neurologia, Università Campus Biomedico, Roma, Italy

Introduction

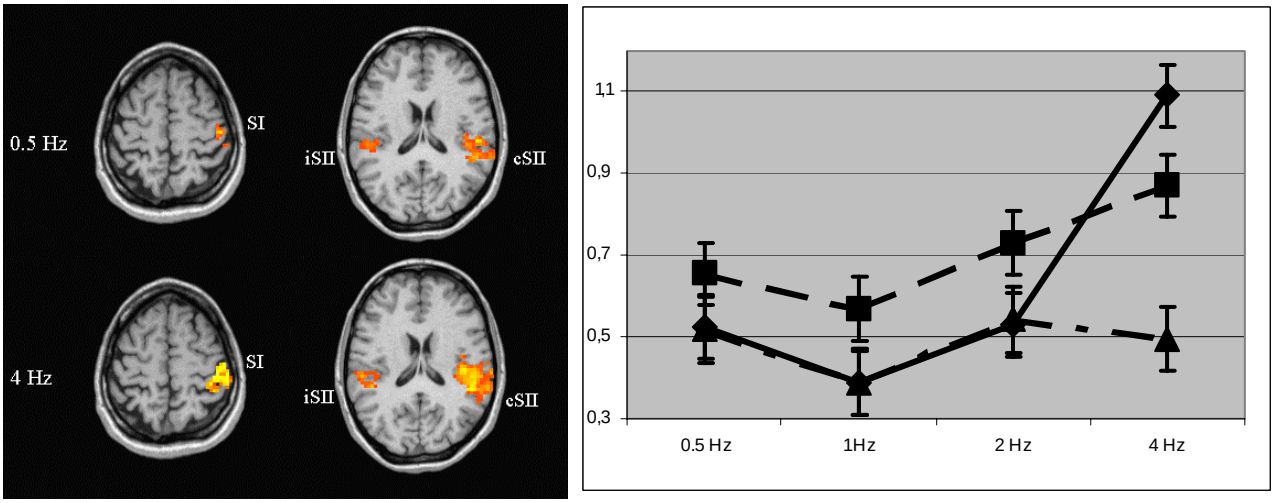
Functional magnetic resonance imaging (fMRI) during electrical nerve stimulation has become a widely used method for the mapping of the responses of primary (SI) and secondary (SII) somatosensory cortex. Previous evidence [1] indicates that SI presents an increase of the Blood Oxygen Level Dependent (BOLD) response with increasing stimulation frequency in the range 5-100 Hz. However, the responses of SI and SII to stimulations at lower frequencies are poorly known. This is an important gap, since the sensorimotor component due to the thumb twitch accompanying the median nerve stimulation affects low frequencies much less than high ones. The present study aims at investigating the BOLD response of SI and SII during the stimulation of the median nerve at frequencies in the range 0.5 Hz to 4 Hz.

Methods

Eight healthy right handed volunteers (age 18 to 22 y, 5 m, 3 f) were studied, who gave written informed conset. The protocol was approved by the local Institutional Ethics Committee. The electric stimulus was a rectangular pulse of 200 μs duration delivered to the right median nerve at the wrist via non magnetic electrodes at frequencies: 0.5 Hz, 1 Hz, 2 Hz, and 4 Hz. The stimulus intensity was assessed for each subject at a level eliciting a sustained thumb twitch, but avoiding any painful sensation. BOLD contrast functional images were acquired with a SIEMENS MAGNETOM VISION scanner at 1.5 T with the following EPI sequence parameters: TR 3 s, TE 60 ms, matrix size 64x64, FOV 256 mm, in-plane voxel size 4 mm x 4 mm, flip angle 90°, slice thickness 3 mm no gap. Functional volumes consisted of 22 transaxial slices parallel to the AC-PC line including the cortical regions of interest (SI, SII). The experimental paradigm was a block design alternating a state of stimulation of 36 s with a control state of the same duration. For each stimulus frequency a run of 100 volumes was acquired starting with a control period. A high-resolution structural volume was acquired at the end of the session via a 3D MPRAGE sequence with the following features: axial, matrix 256 x 256, FoV 256 mm, slice thickness 1 mm, no gap, in-plane voxel size 1 mm x 1 mm, flip angle 12°, TR = 9.7 msec, TE = 4 msec. Raw data were analyzed by means of the Brain Voyager 4.6 software (Brain Innovation, The Netherlands). Structural and functional volumes were transformed into the Talairach space [2] using a piecewise affine and continuous transformation. Functional volumes were resampled at a voxel size of 3mm × 3mm × 3mm. Statistical analysis was performed for individual subjects and stimulus frequencies using the general linear model (GLM) [3]. To account for the hemodynamic delay, the boxcar waveform representing the rest and task conditions was convolved with an empirically founded hemodynamic response function [4]. No spatial or temporal smoothing was performed in this analysis. To search for activated areas that were consistent for the entire group of subjects, a statistical group analysis was performed after the time series from each run and subject were z-normalized and concatenated. The normalized beta weights yielded by the GLM, expressing the variation of the BOLD signal between the rest and stimulation condition, were used to compare the effects of the different stimulation frequencies on the BOLD response. Individual and group statistical maps were thresholded at $p < 0.0004$ at the voxel level and a cluster size of at least four voxels was required, corresponding to a significance level of $p<0.05$ corrected for multiple comparisons. Individual thresholded statistical maps were then superimposed on the respective structural scans for the localization of significantly activated areas, while thresholded group activation maps were superimposed on the (Talairach transformed) structural scan of one of the subjects.

Results

The group analysis showed significantly activated areas in contralateral SI and bilateral SII at all stimulation frequencies. Results for the lowest (0.5 Hz) and the highest (4 Hz) stimulation frequencies are shown. The BOLD response increased in amplitude and spatial extension in SI and contralateral SII at the highest compared to the lowest stimulation frequency, but did not increase in the ipsilateral SII. To our knowledge this is the first case in which an asymmetry in the SII cortices is observed.



Left: Areas of activation (group analysis, $p<0.05$ corrected) during electrical stimulation of the right median nerve at different stimulus frequencies. Top: stimulation at 0.5 Hz. Bottom: stimulation at 4 Hz.Left is on the right. Right: BOLD response in the SI and SII cortices at the four stimulus frequencies. The response is represented by the normalized beta parameter derived from the GLM. Error bars are standard errors. SI diamonds, cSII squares, iSII triangles

Conclusions

The activity of the contralateral SI and SII but not of the ipsilateral SII increased as a function of the frequency rate. This represent the first evidence of a different functional role of the contralateral compared to ipsilateral SII in the processing of nonpainful stimuli features. Further experiments are worthwile in order to ascertain the existence of a spatial representation of different stimulus frequencies in the contralateral SII, as already observed for the coding of the stimulus intensity [6], as well as a strict functional coupling as revealed by brain rhythmicity of contralateral SI and SII in the coding of stimulus frequency.

References

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