

Introduction

The cerebellum plays a critical role in behavior and motor control (Fox et al., 1985; Seitz et al., 1990; Sabatini et al., 1993; Ellerman et al., 1994). Here we wish to provide further evidence for cerebellar contribution to simple hand movements (sequential fist opening and closing), using functional Magnetic Resonance Imaging (fMRI). We hypothesize that blood-oxygenation level dependent (BOLD) signal will increase for the cerebellar hemisphere ipsilateral to the active hand.

Materials and Methods

Participants

One right-handed subject will participate in the experiment.

fMRI Task

The subject will lay supine on the scanner bed, and view visual stimuli back-projected onto a screen through a mirror. Foam pads will be used to minimize head motion. Stimulus presentation and timing of all stimuli will be achieved using Python and PsychoPy (Pierce, 2008). Subjects' eye movements will be monitored using an EyeLink 1000 Plus eye-tracker.

The experiment will consist of four 6 minutes experimental runs. The task will be presented in a block design (8 seconds task blocks alternated with 10 seconds of rest; 20 blocks per run). During experimental blocks an arrow will appear on the screen, to which the subject will be asked to react with sequential fist opening and closing of the appropriate hand (right or left, as indicated by the arrow direction), at her own pace. A fixation-cross will appear during rest periods. For each run, a right arrow will be presented in 10 blocks, and a left arrow will be presented in the other 10. The order of blocks will be randomized within and between runs.

2.3.3 MRI Data Acquisition

A Siemens 3-T Prisma scanner (located at the Edersheim-Levi Gitter Center for human brain imaging, Tel Aviv University, Israel) with a 64-channel Siemens Matrix head coil will be used to collect all functional and anatomical scans. A single high-resolution structural scan will be acquired using a magnetization-prepared rapid acquisition gradient echo (MP-RAGE) sequence (1 x 1 x 1 mm voxels). All functional

runs will be acquired parallel to the anterior-posterior commissure plane using the Center for Magnetic Resonance Research (CMRR) multiband accelerated gradient-echo EPI sequence (66 contiguous interleaved axial slices, 2 mm thickness, no gap; TR = 2000 msec; flip angle = 82; TE = 30 msec; in-plane resolution = 2 x 2 mm; matrix size = 96 x 96; multiband factor = 2; Ipat = 2).

Analysis

Image Preprocessing and Statistical Analysis

The acquired data will be analyzed using FEAT v6.00 (FMRI Expert Analysis Tool), part of FSL (FMRIB software library, version 5.0, www.fmrib.ox.ac.uk/fsl). Images will be realigned to the central volume of each run to correct for head movements, and spatially smoothed using a 5 mm kernel. The data will then be temporally filtered using both a high-pass filter with a cutoff of 50 seconds, and the FILM prewhitening tool. Functional images will be registered to the brain-extracted T1 image, using boundary based registration. The anatomical image will be registered to the standard MNI space (MNI152, 2mm) by first performing a linear registration with 12 degrees of freedom, and then using the FNIRT nonlinear registration tool with a warp resolution of 10 mm on the linearly registered image.

First level analysis will be executed using FILM. The model will include 4 regressors: right-hand and left-hand blocks will be modeled and convolved with a Double-Gamma HRF (Rh and Lh, accordingly). The temporal derivative of each of the resulting regressors will be added to the design matrix as a second explanatory variable to account for minor temporal offsets. The design matrix will then go through the same temporal filtering process as the empirical data, before beta values will be extracted for each voxel in the brain by fitting the model to the voxels time series. The four runs will be modeled as a fixed effect. A contrast between right-hand and left-hand regressors will be performed. We chose to restrict our analysis to the cerebellum, which was identified anatomically using the MNI atlas provided with FSL (MNI-maxprob-thr50-2mm). A small-volume false discovery rate (FDR) correction will be applied to the voxels within this region, using the Benjamini-Hochberg procedure (Benjamini & Hochberg, 1995).

Benjamini, Y., & Hochberg, Y. (1995). Controlling the false discovery rate: a practical and powerful approach to multiple testing. *Journal of the royal statistical society. Series B (Methodological)*, 289-300.

Ellerman, J. M., Flament, D., Kim, S. G., Fu, Q. G., Merkle, H., Ebner, T. J., & Ugurbil, K. (1994). Spatial patterns of functional activation of the cerebellum investigated using high field (4 T) MRI. *NMR in Biomedicine*, 7(1-2), 63-68.

Fox, P. T., Raichle, M. E., & Thach, W. T. (1985). Functional mapping of the human cerebellum with positron emission tomography. *Proceedings of the National Academy of Sciences*, 82(21), 7462-7466.

Peirce, J. W. (2008). Generating stimuli for neuroscience using PsychoPy. *Frontiers in neuroinformatics*, 2.

Sabatini, U., Chollet, F., Rascol, O., Celsis, P., Rascol, A., Lenzi, G. L., & Marc-Vergnes, J. P. (1993). Effect of side and rate of stimulation on cerebral blood flow changes in motor areas during finger movements in humans. *Journal of Cerebral Blood Flow & Metabolism*, 13(4), 639-645.

Seitz, R. J., Roland, P. E., Bohm, C., Greitz, T., & Stone-Elander, S. (1990). Motor learning in man: a positron emission tomographic study. *Neuroreport*, 1(1), 57-60.