Effect of Age on Visuomotor Functional MR Imaging[1]

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Rationale and Objectives. We sought to determine the effect of age on functional MR imaging experiments performed with visual and motor stimulation. We hypothesized that there would be a diminution in the amplitude of fMRI activation with increasing subjects' age.

Materials and Methods. We used fixed effects models to study the amplitude of activation during a block design visuomotor task in three different age groups: old (mean: 75 years; standard deviation: 6 years), middle-aged (mean: 52 years; standard deviation: 9 years) and young (mean: 29 years; standard deviation: 5 years). Each group included 7 subjects. Regions of interest (ROI) were left primary motor area (LM1), supplementary motor area (SMA), and right and left occipital (RO, LO) visual areas. Individual subjects and group statistical parametric maps (SPMs) were generated for each ROI, and then the mean amplitude of activation was compared using the group analysis and t test.

Results. The young age group showed higher amplitude of activation than middle and old age groups in all ROI ($P < 0.01$ uncorrected). Unpaired two tailed t test results between the groups showed significant differences between middle and young, and old and young age groups in all ROIs ($P \leq 0.05$), with the exception of old and young age groups in RO region ($P = 0.11$).

Conclusion. The group analysis, and unpaired t test results reveal higher amplitude of fMRI activation in the young versus the old and middle-aged groups.

Key Words. Amplitude; age; visuomotor task; functional MR imaging.

The effect of age has not been adequately addressed with visuomotor functional MR imaging studies in previous studies (1–4). The impacts of age in performing a task could reflect vascular or neuronal activity changes as one ages (5). Age-related increases in the winding, coiling, and number of "blind-ends" in the cerebral vascular microlattice may cause signal change in blood oxygenation level dependent (BOLD) functional MR imaging (fMRI) by affecting blood flow, blood volume, and oxygen consumption, all of which affect the oxygen concentration in the capillaries, venules, and arterioles (6,7). BOLD functional MR imaging is sensitive to these contributions from the vascular bed (4).

The effect of age using functional MR imaging (fMRI) has only been studied between widely disparate old and young age groups. We sought to determine the effect of age on fMRI experiments with visuomotor stimulation in old, middle-aged and young age groups. We debated whether the functional MR imaging correlate of aging would be a diminution in the amplitude of activation as

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subjects aged or a bell shaped curve with maximal amplitude in the middle-aged population.

MATERIALS AND METHODS

All subjects were recruited from an internal neuroradiology patient database or from the community by means of advertisements in the printed media and local flyers. Only subjects with no mass lesions or significant white matter changes (less than a grade of 4 on the Cardiovascular Health Study rating system) were included in the analysis. No subjects were taking medication that affected neurologic performance. Written informed consent from a protocol that was approved by the Johns Hopkins Institutional Review Board was obtained from all subjects.

Twenty-one healthy, right-handed subjects (12 females, and 9 males) were included in the study. There were 3 age groups, old (mean: 75, range: 69–85), middle (mean: 52, range: 42-61), and young (mean: 29, range: 26–33). Each group included 7 subjects; 4 females and 3 males.

Imaging was performed on a 1.5 T scanner (Gyroscan ACS-NT; Powertrak 6000, Philips Medical Systems, Best, The Netherlands) equipped with 2.3 G/cm gradients and echo-planar imaging. A standard head coil with foam padding to limit head motion was used. All patients underwent a screening T2-weighted scan (TR: 4000, TE: 102) to assess for masses as well as the presence and degree of white matter lesions. The functional MR imaging protocol employed a gradient echo blood oxygenation level dependent (BOLD) technique with a TR of 3000 ms, TE of 39 ms, 90 degree flip angle, 24 cm field of view, 60 time points in a 3 minute scan. Slices were acquired with a 5 mm thickness and an interslice spacing of 1 mm using a matrix of 128 $\times$ 128.

At the TE of 39 ms there is not enough time to sample the 128 $\times$ 128 k-space data matrix fully, hence partial acquisition of the k-space data (60%) was performed. Nonetheless, the spatial resolution remains 1.875 mm $\times$ 1.875 mm within the slice. Seventeen scan sections angled parallel to the intercomissural line and including both primary visual as well as sensorimotor cortices were obtained.

The block design was written in E-prime software (Psychology Software Tools, Inc., Pittsburgh, PA). The block design paradigm consisted of a round, multicolored visual cue appearing on the screen for 0.5 sec in a 30 second "off", and 30 second "on" paradigm. During the 30 seconds of "on" condition there were repetitive presentations of the visual cue presented to the subject at 3-second intervals, however random "blank screen" in which a cue was omitted were placed to prevent anticipatory responses. The "on" condition alternated with the "off" condition in which 30 seconds of a blank screen except for a fixation point was presented. The total scan time was 3 minutes with 3 off-on repetitions of the task. The subjects were asked to tap a finger press button with the index finger of their right hand as soon as they saw the visual cue. The functional data processing for each subject was performed on SUN Ultra workstations using SPM99 (Wellcome Dept. of Cognitive Neurology, London, UK) implemented in Matlab (Mathworks, Sherbon, MA, USA) (8). Realignment for motion correction was performed, followed by spatial normalization using the standard brain template from the Montreal Neurological Institute (MNI) and then converted to the standard stereotaxic atlas of Talairach space (9) using an algorithm developed by Matthew Brett (http://www.mrc-cbu.cam.ac.uk/Imaging/). Images were then smoothed at 5 mm full width half maximum Gaussian kernel. The model was created using a standard linear approach, in which the epochs are convolved with the hemodynamic function. All sixty time-points in the scan are used. This model was fit to the data and the percent signal change was computed for each voxel. Individual subject model estimation and thresholding using thresholds of $P < .01$ (uncorrected) were then performed. The subset of voxels within the region of interest (ROI) was defined for the individual statistical map, ie, voxels which were significant at the individual level and were within the ROI were used. Thus the number of voxels included for each subject was fixed. We computed the individual maps to be more sensitive to differences in activated voxels within the ROIs. In the same manner, the subset of voxels within the ROI was defined for the individual statistical map for each group for group comparisons. Then group analysis was done in each age group separately (old, middle, and young) utilizing the amplitude estimates (% signal change) of the 7 subjects in each group with a threshold of $P < .01$ (uncorrected).

Using an in-house developed "measure" program (10) and a canonical MNI normalized single-subject template, the masks for the 4 ROIs were drawn. Experts (NMB and MAM) determined ROI masks for the left primary sensorimotor area (LM1), right and left combined supplementary motor area (SMA), and left occipital (LO) and right occipital (RO) visual cortices