Task Difficulty Differences with Age in a Functional MRI Verb Generation Task.

M. S. Korgaonkar[1], S. Fiore[2], C. J. Perkins[2], N. K. Squires[3], Z. Yan[4], and M. E. Wagshul[1,4]

[1]Biomedical Engineering, Stony Brook University, Stony Brook, NY, United States, [2]Neurology, Stony Brook University, Stony Brook, NY, United States, [3]Psychology, Stony Brook University, Stony Brook, NY, United States, [4]Radiology, Stony Brook University, Stony Brook, NY, United States

Introduction

Why and how the human brain changes/compensates with age has always been an interest of the neuroimaging community. Studying changes in cognitive behavior and function with age has a number of implications in understanding brain plasticity and for evaluating the effects of pharmacological supplements working to compensate cognitive damage due to disease. Behavior, function and brain morphology using electroencephalography and MRI have been some of the markers to evaluate brain changes with age [1]. Previously, we have shown that subject-specific categorization of task difficulty can be used to identify differential recruitment in the standard language areas with change in difficulty, using a verb generation fMRI task [2]. The goals of this study were: 1. to evaluate the differences in functional recruitment with task difficulty, between younger and older subjects, and 2. to quantify between group and between individual variability of activation with task difficulty. Of particular interest is the quantification of individual subject task difficulty, which has specific implications for studying brain plasticity in stroke patients, where population-based inferences of task difficulty are likely to be inaccurate.

Methods

10 young (5 females; mean age, 24.4 ± 5.8yo) and 10 old (5 females; mean age, 57.8 ± 8.7yo) healthy volunteers participated in this study. All subjects were right handed and native English speakers. The fMRI paradigm was run on a Philips Achieva 3T scanner with the following imaging parameters: TE/TR= 30/2000, FOV=20 cm, matrix=96 x 96, ST=4 mm, voxel size=3.4 x 3.4 x 4 mm, SENSE factor 2, 187 frames, and total acquisition time=6:14. Subjects performed a simple verb generation task, in a jittered event related design, where nouns were flashed on the screen one at a time and the subjects were instructed to silently generate a verb associated with each noun. The subjects pushed a button immediately after generating the verb and response times (RT) were recorded. Response times were used to categorize task difficulty for each noun; nouns with longer RT's were classified as *difficult* and with shorter RT's as *easy* (For more details about the task and task difficulty categorization see [2]).

fMRI Data Analyses: The individual subject data analyses were done using SPM2. fMRI data was first corrected for motion between scans, variability in slice timing, differences in head sizes and variability in position of brain regions by normalizing to a standard brain template and smoothing with a 8mm Gaussian filter. We used two separate GLM (General Linear Model) [3] designs to model the individual subject data. These were designed to answer two separate questions: 1. Are there task difficulty differences between young and old subjects, and if so, which areas of the language network are recruited differentially? (using first GLM), and 2. To model the task difficulty effect over subsequent levels of difficulty, compare them over the two age groups and evaluate subject variability of task difficulty activation (using second GLM). For the first GLM, the two categories of stimuli (difficult and easy) were modeled as separate regressors. For the second GLM, all task stimuli were arranged in order of increasing RT and divided into four blocks, with each block defined as a separate regressor in the model. The BOLD response was modeled using the canonical hemodynamic response function and its temporal and dispersion derivates. We extracted the %BOLD signal change for the easy and difficult conditions (first GLM) and each block (second GLM) using a region of interest (ROI) analysis. Based on prior language functional neuroimaging studies, the following *apriori* cortical ROIs were used (left-L and right-R): BA44 (pars opercularis), BA45 (pars triangularis), BA47 (pars orbitaris), inferior temporal gyrus (ITG), middle temporal gyrus (MTG), superior temporal gyrus (STG), supramarginal gyrus (SMG), angular gyrus (AG) and the anterior cingulate cortex (ACC).

Statistical Analyses: A repeated measure analysis of variance (ANOVA), with age group as a between subject factor, was used to evaluate the significance of differences between the three conditions (easy, difficult and control) in the two age groups. %BOLD values for the four RT blocks, for all individuals were entered in separate linear mixed model analysis for the two groups to model the group linear relationship between RT and %BOLD. Individual subject regression analysis was also performed to obtain the regression line (%BOLD vs. RT) for each subject.

Results

Using the first GLM, a significant condition*group interaction was observed for L-BA45 (F=5, p=0.038) and R-BA47 (F=8.246, p=0.011) with larger changes in BOLD signal with difficulty in young subjects as compared to old subjects. Similar trends were observed for the L-BA47 (F=3.515, p=0.077), R-BA45 (F=4.242, p=0.055) and L-BA44 (F=3.953, p=0.062). The 4-block analysis yielded a significant linear relationship for young adults in left BA44-45-47, ITG, MTG, AG and right BA45-47 and SMG. For the older group, a significant linear relationship was modeled only in the left BA44 and ACC. The modeled relationship was significantly different between the groups for L-BA44-45-47, L-AG and for R-BA45-47. Table 1 summarizes the significant modeled linear relationship for the two groups. The p-value indicates the statistical significance of the modeled linear relation (over the 4 blocks) across individual subjects for the group and the effect defines the slope of the modeled linear relationship. Fig. 1 shows the %BOLD values in L-BA47 for each subject over the four RT blocks for both groups with their modeled linear relationship (bold line). Individual subject regression analysis modeled the task difficulty effect at an individual subject level.

Discussion

We found differential brain recruitment between the two groups in response to variations in task difficulty in a verb generation task. The task difficulty effect was much stronger in the younger group as compared to the old group, particularly in the L-BA45 and R-BA47. Using the mixed model analysis, we were able to model a stronger linear relationships between %BOLD and RT for the younger subjects, indicating that brain activity in younger subjects may be more sensitive to changes in task difficulty than their older counterparts. Improvements in language ability with age and experience may be one of the reasons for this reduced task difficulty effect observed in older participants, and will be important in consideration of task-difficulty-modulation effects in stroke patients.

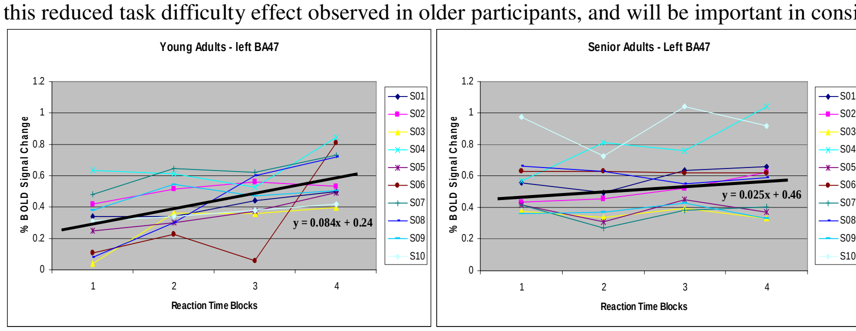

Fig 1: 4-block analyses for all subjects in L-BA47 (left-young, right-seniors). Modeled linear relationship is shown in bold.

ROI	Young		OLD	
	Effect ± SE	**p**	**Effect ± SE**	**p**
Left BA47*	0.084 ± 0.020	0.002	0.025 ± 0.013	0.083
RightBA47*	0.036 ± 0.009	0.003	0.003 ± 0.011	0.774
Left BA45*	0.100 ± 0.016	<0.001	0.021 ± 0.011	0.096
RightBA45*	0.030 ± 0.010	0.017	-0.009 ± 0.012	0.449
Left BA44*	0.067 ± 0.012	<0.001	0.025 ± 0.011	0.046
Left ITG	0.051 ± 0.005	<0.001	0.013 ± 0.014	0.379
Left MTG	0.047 ± 0.012	0.005	0.005 ± 0.007	0.556
Right SMG	-0.023 ± 0.005	0.002	-0.020 ± 0.012	0.149
Left AG*	0.070 ± 0.009	<0.001	0.000 ± 0.011	0.993
Left ACC	0.073 ± 0.036	0.089	-0.051 ± 0.015	0.02

Table1: Mixed model analyses for both groups.
*** indicates ROI with significant between-group differences**

References

1. Minati. L. *et al. J .Geriatr Psychiatry Neurol,* 2007; 20(1): 3-21.
2. Korgaonkar M.S. *et al. Proc. of ISMRM, Seattle,WA.* 2006; 5184
3. Friston K.J. *et al. Hum Brain Mapp.* 1995; 2: 189-210.