Functional MRI activation patterns based on subject's reaction times in a verb generation task

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Introduction

In our previous study we had designed and implemented a simple picture naming task to elicit functional activity information using both functional Magnetic Resonance Imaging (fMRI) and Event Related Potential (ERP) [1]. The motivation behind developing such a task was to develop an assessment tool which could be used over the course of therapy of stroke induced aphasic patients. Using this task we saw differences in functional activation and level of recruitments of brain networks when identifying less familiar stimuli. However we were not able to acquire an accurate estimate of the temporal properties of the BOLD activity in the different brain networks recruited when identifying different types of stimuli using fMRI alone.

Verb generation task have been exclusively used in the past to study neural activity associated with language processing [2]. Visual presentation of verb generation task has also shown to be a reliable predictor of laterality in contrast to either a simple picture naming task or word reading task [3]. The goal of this study is to develop another task which could be used as an effective measure to understand differences in brain areas recruited in identifying less familiar stimuli, which once developed for healthy subjects, will be used to evaluate and understand the course of therapy of aphasic patients. In this study we implemented a verb generation task with the fMRI paradigm more on the lines of an ERP/EEG design. Such a design has been shown to give accurate estimation of the time course of the BOLD activity in addition to the patterns of activity which can be obtained using a block design [4].

Methods

Five healthy participants (3 females; mean age, 25; range, 20-39), right handed and native English speakers participated in this study. All the participants performed a simple verb generation task 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 once they had thought of the verb associated with the noun and their response times were recorded. In contrast to a block design we had used earlier for the picture naming fMRI paradigm [1], a jittered event related design (70 nouns with an inter-stimulus interval varying from 1-12 sec) was implemented. During the inter-stimulus intervals, the participants passively viewed a fixation cross and were instructed to focus on the cross without thinking about anything else. For analysis, the nouns were categorized into "easy" and "difficult" groups based on two criteria: 1) reaction times were recorded for the entire set of nouns from a group of 10 healthy individuals and 2) based on the reaction times for the individual subject recorded during the paradigm.

The fMRI paradigm was run on a Philips Achieva 3T scanner. Imaging parameters were: 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. The individual subject and group analyses were done using Statistical Parametric Mapping software (SPM2) and was performed for both the precategorized stimuli as well as the categorization of stimuli based on the individual response times. The functional images were spatially normalized to a standard reference EPI template in order to evaluate the group effects using a random effects analysis. Average t-maps were generated for difficult minus easy, easy minus rest and difficult minus rest contrasts at a significance level of $p = 0.01$ and only clusters of activation with more than 10 voxels were considered significant and reported.

Results

The reaction time tests collected on 10 healthy individuals prior to the study enabled us to group the original set of 152 nouns into 4 main groups: reaction time less than 1120 ms, reaction times between 1120 and 1400 ms, reaction times from 1400 ms to 1630 ms and reaction times greater than 1630 ms. Nouns with reaction times over 1630 ms were rejected as being too difficult, and those with reaction times between 1120 and 1400 ms were judged as being ambiguous as to their categorization. Thus, we were left with a set of 35 nouns with reaction time < 1120 ms, which were categorized as "easy" and 35 difficult nouns with reaction times between 1400 ms and 1630 ms, which were categorized as "difficult". There was a 68% agreement of the categorization of "easy" stimuli & about 61.5% with the "difficult" stimuli i.e. between the individual response times collected during imaging and the pre-categorization of the stimuli.

The group-mean t-maps showed a clear pattern of left-lateralized activation in the inferior frontal gyrus (Broca's area, BA 45), middle temporal gyrus and inferior frontal gyrus (BA 13) for the Difficult vs. Easy stimuli (Figure 1). This was also verified by the plot of the hemodynamic response averaged over the trials of the two types of stimuli for the individual subjects and also averaged over all the subjects in the inferior frontal gyrus area. Figure 2 shows the average of the hemodynamic response plot for all the subjects in the inferior frontal gyrus area. The plot indicates that the hemodynamic response associated with the less familiar or "difficult" trials took a longer time to return to the baseline as compared to the more familiar trials. This was verified for the individual subjects as well. At this level of sensitivity ($p < 0.01$), no activity was seen in the other language associated areas.

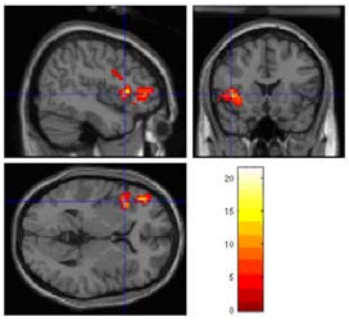

Figure 1: Group activation for Difficult vs. Easy contrast (Inferior frontal gyrus – BA45) ($p<0.01$; clusters of 10 voxels)

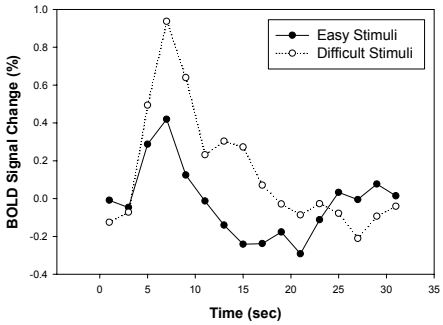

Figure 2: Comparison of average hemodynamic responses of "Easy" & "Difficult" trials over all the subjects.

Discussion

The activation maps indicate the differential levels of recruitment of the inferior frontal gyrus (BA45) for difficult to generate verbs as compared to the easy to generate verbs. The longer hemodynamic response for the difficult category of stimuli as compared to the easier stimuli indicates a different level of neural processing taking place when processing language information of varying difficulty in the case of healthy humans. Our next step will be to record event-related potentials with the same paradigm to detect temporal differences between the stimuli.

References

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