Joint activation of the SMA and pre-SMA during simultaneous motor and language tasks: a functional MRI study

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Introduction

The structure-function relationship of the supplementary motor area (SMA), traditionally defined as a single motor area, have been studied extensively in recent experiments utilizing functional magnetic resonance imaging (fMRI). As result of these experiments, the SMA has been dissected into two anatomically distinct regions, the rostral pre-SMA and the caudal SMA proper. The pre-SMA is involved in higher level cognitive processes, while the SMA proper is more closely tied to motor output (1,2). The importance of the SMA in the development of motor and language deficits after brain surgery has been highlighted (3,4). Rushworth et al., identified definite activation in a region on the border between the pre-SMA and SMA proper during a visual-switching fMRI paradigm (5). The purpose of this study was to extend our understanding of the structure-function relationship in the SMA. By using a more complicated task domain, we attempted to search for areas of overlap between the pre-SMA and SMA proper that may co-activate during simultaneous motor and language production tasks, and we compared the results with single individual tasks.

Subjects and Functional Tasks

Twelve healthy subjects (six males and six females), ranging in age from 21 to 31 years, without a previous history of neurological illness, were recruited for the study. Three different functional paradigms were used, including a motor task (finger tapping, Task A), a language task (verb generation, Task B) and simultaneous motor and language tasks (combined finger tapping and verb generation, Task C). These tasks were performed as block paradigms (6 cycles; 20 sec active period; 40 sec resting period). Self-paced sequential tapping of the thumb against each finger was used at a rate of approximately 2Hz to stimulate the SMA and primary motor cortex (PMC). During Task B, patients were presented with a noun (for example, "car") and asked to silently generate action words (for example, "drive, crash") associated with the noun. Four nouns were read over the course of 20 sec. There were 6 stimulation epochs, allowing for a total of 24 nouns. For Task C, subjects performed the finger tapping task while performing the silent verb generation task using different nouns. Task order was randomized individually. The subject's task performance and head motion were monitored using software (Brainwave, Medical Numerics) that permits brain activity to be observed in real time.

Method

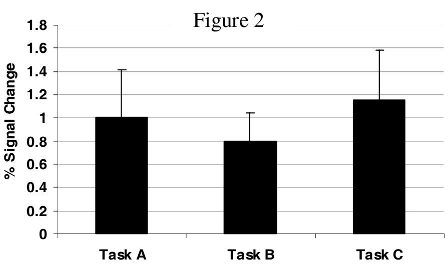
Twenty-six contiguous axial T1-weighted images were acquired for anatomical co-registration purposes. Functional images were acquired with a gradient echo EPI sequence (TR=4000 ms; TE=40 ms; 128×128 matrix; 240 mm FOV; 4.5 mm in thickness; repetitions=6) using a 1.5T GE scanner. 3D T1-weighted anatomical images were also acquired with a spoiled gradient-recalled acquisition in the steady state (GRASS) sequence. Subjects' head motion was minimized by using straps and foam padding. Image processing and statistical analysis were performed with AFNI software (6). The reconstructed fMRI data was aligned using a 3D rigid-body registration method and de-trended of low-frequency drifts. Spatial smoothing, using a gaussian filter of 4mm, as well as temporal filtering, reducing high frequency components in the time series, were performed. Individual functional activity during the three tasks was generated using cross-correlation analysis. To minimize the false positive activity due to large venous structures, larger vessel effects, or random signal fluctuation, we set voxels to zero when the standard deviation of the acquired time series exceeded 5 percent of the mean signal intensity. Caudal and rostral parts of the SMA were defined based on the VCA line (a vertical line passing through the anterior commissure, perpendicular to the anterior commissure–posterior commissure line) (7). Anatomical and functional images were converted to standard Talairach atlas space with $1mm^3$ voxels. For group analysis, a voxel-wise *t*-test was conducted comparing each experimental task to the baseline (white noise). The *t*-test generated *t*-value activation maps that were set to threshold at *t*-values corresponding to $p<0.001$. In addition to measuring the amplitude of the BOLD signal, ten of the voxels within the SMA, revealing the greatest activation during functional tasks, were used to generate corresponding percent signal changes, were averaged together, and were compared using a *paired t-test*.

Results

SMA Activation: Individual subject analysis indicated that significant SMA activation was observed during the three functional tasks in all 12 healthy subjects. Group analysis using a t-test generated statistically significant groups of activated voxels at different locations within the SMA with a correlation coefficient greater than 0.5 (Figure 1). *Percentage Signal Change (PSC)*: Averaged PSCs in the SMA were 1.0%, 0.8%, and 1.2% for tasks A, B, and C respectively (Figure 2). A *paired t-test* comparing the mean difference between tasks was used. Statistically significant differences in the PSC were found between Tasks C and B (p=0.01), suggesting that the PSC in the SMA due to activation during Task C is greater than that in the SMA during Task B. There was no statistically significant difference between Tasks A and B (p=0.11), nor between Tasks A and C (p=0.12).

Figure 1: Central areas of activation (arrows) in the SMA during (A) Task A, (B) Task B, and (C) Task C. Figure 1D represents the conjunction of activations in the SMA and the pre-SMA produced by manually combining A, B, and C. Significantly activated voxels in the SMA thresholded at p<0.0001 (correlation coefficient r>0.6) are displayed. Functional activity was overlaid onto an anatomical reference map in Talairach space.

Figure 2



Discussion

Shifts in the area of maximal SMA activation during performance of a single motor or language task to that of combined tasks permit the delineation of a centralized area at the pre-SMA/SMA border, an area previously shown to be involved in attentional set-switching within visual paradigms (5), imagining motor movements (7) and preparing motor responses (8). Surgical lesions of the SMA have shown to result in a characteristic SMA deficiency syndrome, ranging in severity from global motor and speech loss to mild reduction in spontaneous motor and speech output that may last for several weeks to months (3, 4). Additional functional studies are needed to further define this 'central SMA region' in order to better guide pre-operative planning efforts in patients with tumors in or adjacent to the SMA.

References **1**. Sadato N *et al., Jour of Neuroscience* (1997) 17:9667-9674; **2**. Alario F *et al., Brain Research* (2006) 129-143; **3**. Krainik A *et al., Neurology* (2003) 60:587-594; **4**. Krainik A *et al., Neurology* (2001) 57:871-878; **5**. Rushworth M *et al., J Neurophysiology* (2002) 87:2577-2592; **6**. Cox , R , *Comput Biomed Res.* (1996) 29:162-173; **7**. Stephan K *et al., J Neurophysiology* (1995) 73:373-386; **8**. Lee K *et al., Neuroimage* (1999) 9:117-123.