# An fMRI study of cognitive functions in adolescents with spina bifida

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## Introduction

Spina bifida refers to conditions in which there is failure of fusion in the spinal column. Advances in surgical intervention for patients with spina bifida have significantly increased survival rate. However, questions concerning the long-term care of these patients persist as previous studies have demonstrated this population is at risk for cognitive difficulties as well as poor outcomes of measures of social/living independence.[1] Published studies provided comprehensive evidence to show impairment of executive processing skills for children/adolescents diagnosed with spina bifida, such as slower processing speed secondary to poor organizational skills and specific deficits with abstraction/problem-solving abilities.[2] In this study we investigated functional activity in adolescents with spina bifida when performing a response inhibition (go/no-go) task using fMRI and compared activation patterns with age matched controls.

## Methods

The Institutional Review Board (IRB) approved this study. Nine adolescents with spina bifida (7 male and 2 female, 15.1±1.5 years of age) and nine healthy controls (3 male and 6 female, 15.6±1.6 years) were recruited. All spina bifida patients were medically stable at the time of experiments. None of the control subjects had any history of neurological or psychiatric impairment. All participants were administered the Reynolds Intellectual Assessment Scale (RIAS IQ test), which consists of a Verbal and Nonverbal index scale and also yields a Composite measure.

MRI scans were performed on a 1.5 Tesla Philips MRI scanner. A 3D T1 weighted turbo field echo pulse sequence was used to acquire anatomical data. Parameters for this 3D T1 sequence include: 7.3 ms TR, 3.3 ms TE, 256 mm x 232 mm field of view, 1 mm x 1 mm x 1 mm isotropic voxel size, 160 contiguous sagittal slices, 8° flip angle, and 1 average. A single shot gradient echo EPI sequence was used to acquire fMRI data. Parameters for the fMRI sequence include: 2923 ms TR, 3.3 ms TE, 220 mm x 220 mm field of view, 2.4 mm x 2.4 mm acquisition voxel size, 5 mm slice thickness, and 156 repetitions with 2 dummy scans.

All participants were asked to perform a response inhibition task while being scanned during the fMRI experiment. An Eloquence fMRI system (Invivo Corp., Orlando, FL, USA) was used to assist fMRI data acquisition. The activation tasks were adopted from literature[3] with modifications and incorporated into an fMRI paradigm designed by E-Prime software (Psychology Software Tools, Inc. Pittsburgh, PA, USA). Both the baseline and activation stimuli were visual and included nine different shapes (i.e. combination of zero or one red triangle, four or five blue triangles, and four or five red trapezoids). In the baseline block, the participants were instructed to press right index finger whenever shapes appeared on the screen; in the activation block, the participants were instructed to press right index finger whenever shapes appeared on the screen and there was no red triangle. The finger press as well as response time were monitored by the Eloquence system.

After the scan, the EPI images were exported to a workstation with BrainVoyager software (Brain Innovation, Maastricht, the Netherlands) for fMRI data processing including slice scan time correction, 3D motion correction, spatial smoothing, linear trend removal, and temporal filtering. The EPI images were then co-registered to the T1 3D images which were then transformed to the standard Talairach Atlas to create a 3D-aligned time course dataset. A stimulation protocol was created to represent the block design (with hemodynamic response function refinement) used in the fMRI scans. General linear model (GLM) analysis was performed to calculate individual and average activation maps. The statistical threshold was set at $p < 0.001$ after bonferroni correction. A threshold of at least 50 voxels in a cluster was used to display the activation maps.

## Results

The mean Composite Index scores for the spina bifida and control subjects were not significantly different (92.00±8.60 vs. 96.56±8.14, $p > .05$). The differences in average response time (849±81 ms vs. 815±122 ms, $p > .05$) and average accuracy rate (82%±18% vs. 91%±7%, $p > .05$) for the fMRI task were also not statistically significant. Figure 1 shows the fMRI activation maps. Both controls and patients had strong posterior activation. For the controls, the activation was almost symmetrical, with clusters located in the posterior parietal, temporal, and occipital lobes as well as in the bilateral frontal lobes. For the spina bifida patients, the posterior activation in the right brain hemisphere was much stronger than that in the left, and there was only right but no left frontal activation.

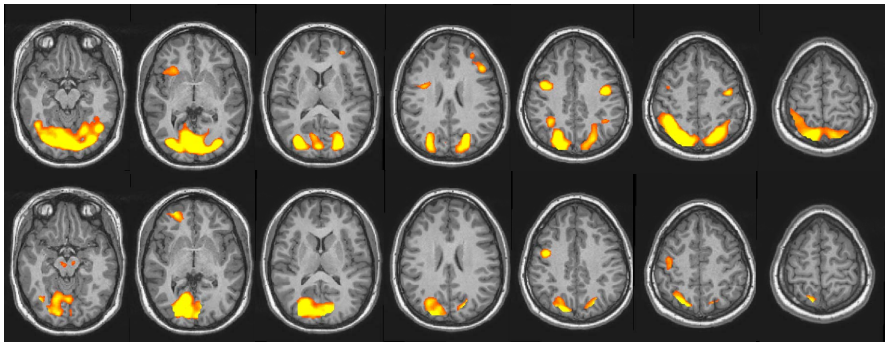

**Figure 1:** Average fMRI activation maps overlaid on normal axial T1 weighted images. Compared to controls (top row), the spinal bifida patients (bottom row) have weaker overall and asymmetrical activation (right hemisphere stronger than left). In addition, there was no activation in the left frontal lobe in spina bifida patients.

## Discussion

Our results indicated lack of activation in the frontal lobe for adolescents with spina bifida and may suggest poor frontal lobe functions which are consistent with literature. In addition, the control subjects had bilateral brain activation while the patients demonstrated primarily right hemisphere activation. This pattern was present in both posterior brain regions and frontal lobes, and may indicate decreased left hemisphere functioning in adolescents with spina bifida.

**References** 1. Hunt GM, Dev Med Child Neurol 1990; 32:108-118. 2. Snow JH et al, Archive of Clinical Neuropsychology 1995; 9:277-287. 3. Booth JR et al, Neuroimage 2003; 20:737-751

**Acknowledgements** This study was supported by the Children's University Medical Group (CUMG) award