Investigating metabolic and functional profiles of mild and moderate cervical spondylotic myelopathy: a MRS and fMRI study

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Purpose

The ideal timing of surgical intervention for cervical spondylotic myelopathy (CSM) patients, especially with early, mild symptoms, remains particularly controversial since select patients can stabilize clinically without operative intervention. Proton magnetic resonance spectroscopy (MRS) studies have demonstrated altered metabolite levels in the primary motor cortex (M1) of CSM patients suggesting mitochondrial dysfunction and/or neuronal death.[1] Functional MRI (fMRI) studies have provided evidence of cortical reorganization in response to spinal cord compression and surgery.[2] The purpose of this study was to compare the longitudinal effects of mild and moderate CSM on the injury and recovery of neuronal metabolism and function in the M1 prior to and following surgical intervention.

Methods

Fifteen mild CSM (50±12 years; 13 males) and thirteen moderate CSM patients (53±9 years; 8 males) were recruited. Ten healthy controls of similar age were also recruited (48±12 years, 5 males). Neurological and functional disability (and classification of CSM) was measured using the modified Japanese Orthopaedic Association (mJOA) scale. Mild CSM was defined by a score of >12 out of 18 (n=15) and moderate CSM by a score of 9-12 (n=13).[3] Each participant underwent two imaging sessions six months apart on a 3.0T Siemens Magnetom Tim Trio (Erlangen, Germany). Only the CSM group received decompressive surgery after the initial scan. Anatomical MPRAGE images (192 slices, 1mm isotropic, TR/TE = 2300/3.42ms, TI = 900ms) were acquired in each subject. Functional MRI scans of a right handed finger-tapping paradigm were acquired using an echo planar imaging sequence (FOV = 256x256mm, 45 slices, 3mm isotropic, TR/TE = 2500/30ms, flip angle = 90^o, iPAT=2). Functional images were analyzed using BrainVoyager QX software. For all contrasts, a volume of activation (VOA), corrected *p*-value, and Brodmann area were produced. A 20mm isotropic spectroscopy voxel was placed on the hand area[4] of the M1 contralateral to the greater deficit side in the CSM group and on both sides in the controls. Spectroscopic data were localized using PRESS (TR/TE =2000/135ms, 192 averages, voxel size = 8cm^3). The ratio of the levels of *N*-Acetylaspartate (NAA) and creatine (Cr) were measured.[5,6] Significant differences in metabolite ratios and functional activation between the controls, mild CSM, and moderate CSM groups at pre- and post-operative time points were identified. Paired t-test was used to detect the effects of surgery on the CSM group with an alpha error of 0.05.

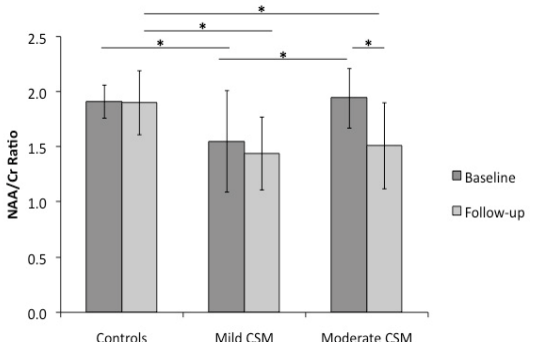

Figure 1: Average NAA/Cr metabolite concentrations at baseline and 6-month follow-up in the controls, and at pre- and post-operative time points in the mild CSM, and moderate CSM groups (error bars represent the SD; * represents significance p<0.05).

Results

At baseline we found a lower NAA/Cr ratio in the hand area of M1 in mild CSM (1.55 ± 0.46) compared to healthy controls (p<0.05) and moderate CSM (1.94 ± 0.27; p<0.05) suggesting neuronal loss or mitochondrial dysfunction (Figure 1). Following successful surgery and despite clinical improvement, NAA/Cr levels did not recover in mild CSM (1.44 ± 0.33; p=0.50; Figure 1). The moderate CSM patients, who had significantly worse pre-operative mJOA scores and demonstrated the largest interval functional improvement following surgery, demonstrated a *decline* in NAA/Cr levels following surgery (1.51 ± 0.39; p<0.05; Figure 1). The mild CSM group had a larger functional VOA in M1 than moderate CSM prior to surgery (p=0.05; BA 5; Figure 2). Following surgery, the VOAs were comparable between the mild and moderate CSM groups and had shifted towards the primary sensory cortex (p<0.001; BA 3; Figure 2). There was an increase in the VOA in moderate CSM following surgery using an uncorrected *p*-value, however the change did not reach the threshold for significance after correction.

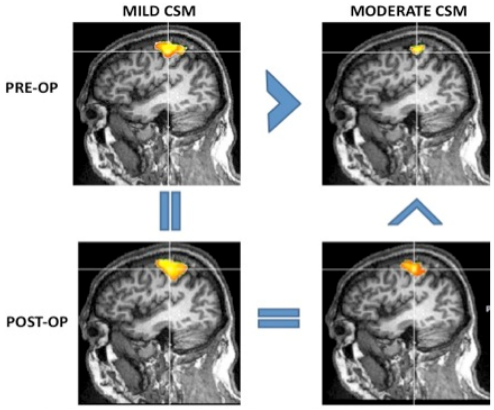

Figure 2: The volume of activation for the mild CSM (left) and the moderate CSM (right) patient groups are shown. The pre-op activation is displayed in the top row showing mild CSM had significantly larger activation near the primary motor cortex compared to moderate CSM. Following surgery, both groups had equal activation volume shifted towards BA 3, the primary somatosensory cortex.

Discussion

This study is the first to describe a clear distinction between mild and moderate CSM with respect to pre-operative NAA/Cr concentrations in M1. Our fMRI findings suggest that the mild CSM group has recruited surrounding cortex to enhance motor task performance prior to surgery. Surgical intervention did not reverse the low NAA/Cr levels in the mild CSM group, nor did it preserve the normal levels of NAA/Cr in the moderate CSM group. Following surgery, the neurological recovery experienced by the moderate CSM group despite decreased NAA/Cr could be associated with cortical reorganization since the VOA equalized to that observed in the mild CSM group.

Conclusion

NAA/Cr levels and the size of the VOA in M1 can be used to discriminate between mild and moderate CSM. Following surgery, the metabolic profile of the motor cortex did not change in either group, despite significant clinical improvement. We propose that metabolic impairment in M1 may trigger recruitment of adjacent healthy cortex to achieve functional recovery. Further work is needed to determine whether these distinct patterns of remote injury in the sensorimotor cortex in mild and moderate CSM patients could be used to determine the timing and need for intervention.

References

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