fMRI-guided MRS Studies of Cortical Reorganization Following Sub-cortical Stroke

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Introduction

Recovery of arm motor function following stroke occurs over weeks and months and is often attributed to neuronal reorganization. Functional imaging studies of the motor system in previous stroke survivors suggest that neuronal reorganization within remaining motor-related areas underlies this recovery. However, the relationship of this reorganization to motor recovery is less well understood.

Magnetic resonance spectroscopy (^{1}H-MRS) provides a non-invasive imaging probe of neuronal metabolic status through measures of N-acetylaspartate (NAA), a compound localized exclusively in neurons and their dendritic and axonal processes. Functional magnetic resonance imaging (fMRI) provides a means to identify the specific location of areas that are activated by a motor task that might be affected by stroke. The combined use of ^{1}MRS and fMRI provides a means for the detailed study of the relationship between functional and biochemical status of any cortical area in the intact as well as lesioned brain. In the current study we sort to characterize metabolism and function relationships in motor cortex of patients with subcortical stroke.

We assessed the following hypothesis: (i) how neuronal metabolic status (^{1}H-MRS) of remote primary motor cortex (M1) is altered after subcortical stroke; (ii) how neuronal metabolic status is related to functional (fMRI) status; and (iii) how neuronal metabolic alterations are related to the clinical level of arm paresis (motor impairment).

Methods

Five chronic subcortical stroke survivors (60.6±10.1 yrs, 2 male) and five age-matched healthy participants (53.0 ± 17.7 yrs; 3 male) were evaluated at 3 Tesla (structural MRI, fMRI, ^{1}MRS). In each subject, the spatial extent of bilateral M1 activation associated with a grip task executed with the impaired arm was determined with fMRI (BOLD, TR=2000ms; TE=50ms; 25 contiguous 5mm slices, 100 data points). A two dimensional MR spectroscopic imaging slab was then prescribed to include the three fMRI slices with maximal M1 activation (PRESS, TE=30ms, TR=1500ms, 15mm slice, outer voxel suppression, 16*16 phase partitions). Following zero-filling in both spatial directions, NAA concentrations were quantified using LCModel to analyze those spectra that corresponded to activated motor cortex as identified in post-processing from the fMRI data. We determined a spatial extent of activation measure from the fMRI data by calculating (number of activated voxels/ total number of voxels in the region of interest determined from the anatomic scans). Results from stroke survivors were compared with those from age- and sex-matched healthy subjects. The clinical Fugl-Meyer test was used to quantify arm motor impairment in stroke survivors.

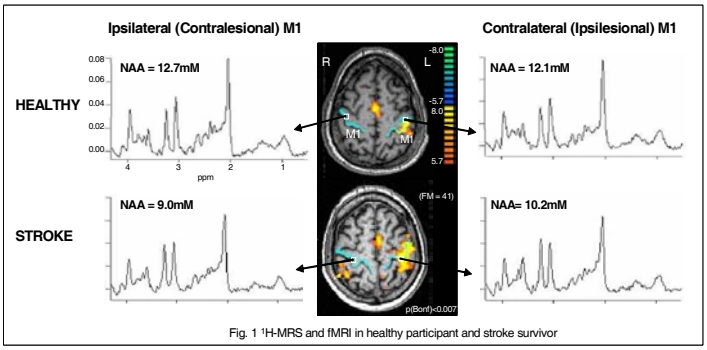

Fig. 1 ^{1}H-MRS and fMRI in healthy participant and stroke survivor

Results

Our data suggest that in stroke survivors, the NAA concentrations were decreased bilaterally compared to the healthy subjects (p=0.056, Fig. 1).

We found that decreased NAA concentrations were highly correlated with increased spatial extent of motor activation (R^2 =0.74, p<0.05) in the ipsilesional M1 (Fig. 2A). This correlation represents the first evidence for a relationship between the metabolic (lower neuronal metabolism, decreased NAA) and functional (greater spatial extent of motor activation) status in ipsilesional M1 remote from the site of the infarct in stroke.

Further correlation analysis suggested that decreased NAA concentrations in ipsilesional M1 were significantly correlated with the level of arm motor impairment evaluated by Fugl-Meyer test (R^2 =0.89, p<0.001, Fig. 3A).

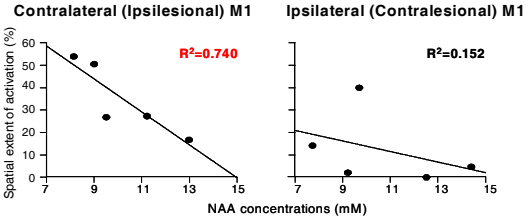

Fig. 2 Correlations between NAA concentrations and spatial extent of motor-related activation in stroke survivors.

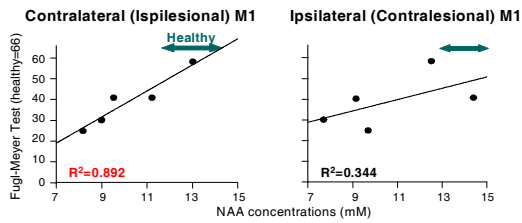

Fig. 3 Correlations between NAA concentrations and clinical level of arm motor impairment (Fugl-Meyer score) in stroke survivors. Doubled ended arrows indicate the range for healthy participants.

Conclusions

This is the first study in which combined neuronal biochemical and functional data are related to motor functioning and recovery after stroke. Lower NAA concentrations found in motor cortex remote from the site of subcortical infarct suggest that there is a metabolic impact on neurons mediated by connections through white matter perhaps by diaschisis. Such reductions in NAA are highly correlated with residual or recovered level of arm function indicating that the metabolic status of the neurons is at least partially responsible for the level of recovery of motor function. The strong correlation between residual NAA in M1 and spatial extent of activation suggests that processes that cause reduced metabolic state i.e., size of subcortical stroke, are also related to amount of recruitment of neighboring areas for motor tasks. These results indicate that integrated neuroimaging, particularly MRS and fMRI might play a valuable role in quantifying the extent of brain plasticity in stroke patients and in understanding plasticity processes. Such an understanding might be vital in assessing therapy, such as pharmaceutical, physical rehabilitation, or cortical stimulation, designed to modulate reorganization following stroke.