Association of peri-infarct N-acetyl aspartate with recovery from stroke

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Introduction: Functional neuroimaging and transcranial magnetic stimulation studies suggest that peri-infarct tissue plays a crucial role in recovery following a stroke,[1-3] but much of the variability in recovery remains unexplained. We hypothesised that N-acetyl aspartate (NAA) can serve as a marker of neural integrity in the structurally intact peri-infarct region following stroke, with the potential to predict recovery. The purpose of this study was to measure NAA in a longitudinal MR spectroscopy cohort of stroke patients, and to correlate these findings with functional outcome.

Methods: Six patients (age 53±10 y) with a non-lacunar ischemic stroke in the left middle cerebral artery territory underwent MR spectroscopy at 3 and 15 weeks after stroke onset. MRS studies were performed with a 3T GE HDx TwinSpeed MRI scanner (GE Healthcare, Milwaukee, WI, USA). Proton spectra were acquired from the structurally intact peri-infarct thalamus, the contralesional thalamus, and the anterior cingulate cortex (ACC) using a point resolved spectroscopy (PRESS) sequence with an echo time of 30 ms and a repetition time of 3 seconds. Water-scaled NAA concentrations were calculated with LCModel[4] and corrected for partial volume CSF contamination. Clinical assessment included the Fugl-Meyer (FM) scale for the motor performance of the right arm and the NIHSS. Seven healthy controls (age 53±7 y) were also recruited and scanned at a single time point.

Results: At baseline, NAA was significantly lower in the patients than controls in the structurally intact ipsilesional thalamus (9.0±2.1 vs 11.3±1.2, p=0.030, figure 1), but not in the other 2 voxels. NAA decreased significantly between the 2 visits (9.0±2.1 vs 7.2±1.7, p=0.021, figure 2) in the patients, in the ipsilesional thalamus, but not in the other 2 voxels. The patients demonstrated significant clinical improvement during the course of follow up (median 15-point gain on the FM scale, p=0.042; and a 7–point decline on the NIHSS, p=0.026). NAA in the ipsilateral thalamus at baseline significantly correlated with the final FM (rs=0.81, p=0.025) and NIHSS scores (rs=-0.84, p=0.018).

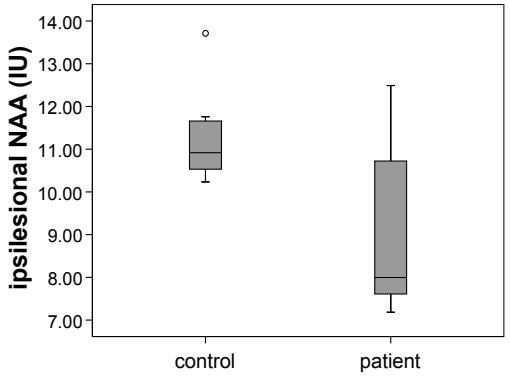

Figure 1. Water-scaled NAA concentration measured in the peri-infarct thalamus for the patients (at baseline) and the controls. Boxplots denote median and interquartile ranges.

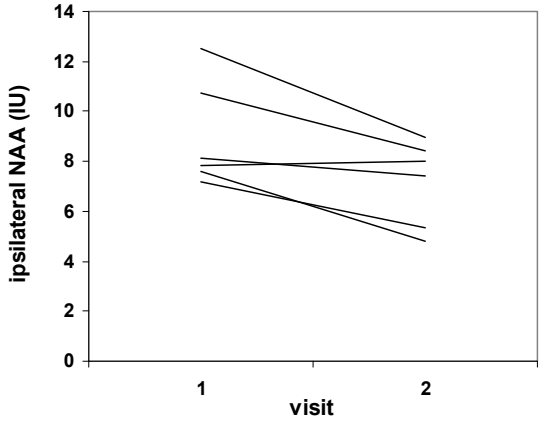

Figure 2. Change in peri-infarct NAA between 3 and 15 weeks post stroke.

Discussion: Stroke disturbs neuronal integrity in the structurally intact peri-infarct tissue. Despite clinical improvement, neural damage in the peri-infarct area appears to progress during the first 3-4 months following a non-lacunar ischemic stroke. This decreased neuronal integrity is associated with impaired recovery and may therefore represent a therapeutic target. Peri-infarct NAA is a potential biomarker not only for the prediction of recovery, but also for the monitoring of therapeutic interventions.

References: [1]Calautti et al., Stroke 34:1553-66 (2003), [2]Rossini et al., Lancet Neurol 2:493-502 (2003), [3]Ween et al., J Neuroimaging 18:227-36 (2008), [4]Provencher S. Magn Reson Med 30:672– 679 (1993).