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

Ruth L O'Gorman¹, Laszlo K Sztriha², Gareth J Barker³, Steven CR Williams³, and Lalit Kalra²

¹University Children's Hospital, Zurich, Switzerland, ²Clinical Neurosciences, Institute of Psychiatry, King's College London, United Kingdom, ³Centre for Neuroimaging Sciences, Institute of Psychiatry, King's College London, United Kingdom

**Introduction:** Functional neuroimaging and transcranial magnetic stimulation studies suggest that peri-infarct tissue plays a crucial role in recovery following a stroke,¹³ 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 LCModel⁴ 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](image-url)  **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](image-url)  **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.