Diffusion anisotropy changes in comatose cardiac arrest patients

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Introduction: Assessing likelihood of recovery in patients who become comatose after cardiac arrest remains difficult. Diffusion-weighted imaging (DWI) has proven sensitive to brain injury after transient global ischemia. Severe reductions in ADC have been linked to poor clinical outcome. Studies involving small case series of cardiac arrest patients principally involved investigation of changes in the isotropic diffusion-weighted image or in the apparent diffusion coefficient (ADC). Early changes in the diffusion tensor in comatose patients after cardiac arrest have not been well studied. In studies of acute cerebral ischemia, both increases and decreases were found. We sought to determine whether similar changes exist after transient global ischemia and whether these changes are related to patient recovery as defined by eye opening (either spontaneous or in response to external stimuli) or modified Rankin (mRS) Scale scores at 6 months.

Methods: Comatose cardiac arrest patients who subsequently underwent MRI were retrospectively analyzed (N=80). All data sets were corrected for eddy current distortions. Five patients were excluded due to excessive motion artifact interfering with calculation of the diffusion tensor. ADC maps were calculated from the slope of the linear regression fit of the log of the DWI (b-value=1000 s/mm²) and b-zero (b-value=0 s/mm²) images. Fractional anisotropy values were derived from eigenvalues measured from the diffusion tensor calculated from the DTI dataset. The b-zero images were coregistered to the ICBM-452 T1 5th Order Polynomial Warps Atlas using a semiautomated program (MNI Autoreg). Using the ICBM probabilistic atlases, probability masks for the following regions were generated: white matter (WM), cerebellum, frontal, insula, occipital, parietal and temporal lobes, caudate, putamen, and thalamus, using a threshold of 50%. Median FA values were measured in these regions. To reduce effects from cerebral spinal fluid, analysis was limited to ADC values ≤ 1200×10⁻⁶ mm²/s. Spatial differences among the different regions were examined (ANOVA with post-hoc SNK test). Differences in patients with eye opening were compared (Wilcoxon-test) with no eye opening, a potential sign of poor recovery in patients who had life support withdrawn (and thus would die without the potential for demonstrating recovery at 6 months). We performed a similar analysis using mRS score >3 at 6 months representing poor outcome. Subset analysis was performed for patients imaged <3 days and ≥3 days.

Results: Median time to MR was 2 days, with a range of 0 to 10 days, for these 75 patients. As expected, FA in white matter (0.35±0.04) was significantly higher than all the other regions (P<0.0001), with insula the lowest (0.19±0.04). The values of FA in white matter are lower than typically reported in the literature due to partial voluming over a large region. Thirty patients experienced early eye-opening while 14 patients had 6 month mRS≥3 outcomes. For patients who did not experience eye opening, FA in white matter (0.36±0.05) was slightly elevated (P=0.06) compared to patients who experienced eye opening (0.34±0.03). Other regions did not show a difference (P>0.1). In terms of 6 month mRS, no statistical difference was found. Subset analysis was performed on studies <3 days (N=46) and ≥3 days (N=29). For early studies, 15 patients experienced eye opening and 6 patients had good outcome at 6 months. Again only WM was seen to be elevated in patients without eye opening (P=0.07). No statistically significant differences were seen between patients with good and poor mRS outcomes. For the late studies, 15 patients had eye opening and 8 patients had good 6 month mRS outcomes. Patients without eye-opening had significantly lower (P=0.01) FA values (0.2±0.05) than patients with eye opening (0.25±0.04) only in the putamen. FA values were also significantly lower (P=0.004) in the putamen in patients with bad outcome (0.21±0.05) compared to patients with good outcome (0.26±0.03). The caudate also showed slightly lower values (P=0.08) in patients with bad outcome (0.21±0.04) compared to those with good outcome (0.24±0.03). Interestingly, ADC was not significantly lower in the caudate (P=0.4) for these patients, despite being so for early studies (P=0.06).

Discussion: Our results suggest that monitoring changes in FA may be useful for understanding the pathophysiology of neuronal death after cardiac arrest. Changes in FA are highly dynamic, with both increases and decreases being indicators of severe ischemic injury. The exact mechanisms of increases in FA following an ischemic event is still ill-defined, with some positing increased anisotropy is due to cytotoxic edema. Coupled with changes in ADC, FA may provide insight into neuronal injury. Lack of differences in the caudate in terms of ADC as later time-points, despite notable changes in FA is suggestive of pseudo-normalization as a result of vasogenic edema. With the restoration of perfusion, it has been shown in animal models that brain tissue experiences rapid pseudo-normalization, only to deteriorate again at subsequent time points. A clear limitation of the study is its retrospective nature where patients were not imaged serially. This hampers our ability to better investigate the time-course of global ischemic injury. Nonetheless, our results suggest that multispectral MRI may be useful for investigating the pathophysiology of global cerebral ischemia.