Evolution of Fractional Anisotropy in Hyperacute Ischemic Stroke

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Introduction

Diffusion imaging, specifically the apparent diffusion coefficient (ADC), is a highly sensitive method to detect hyperacute (<6 h from onset) ischemic stroke. In this phase of stroke, cytotoxic edema occurs and the ADC is reduced. Studies examining fractional anisotropy (FA) in hyperacute stroke have not thoroughly explained the evolution of FA. During hyperacute stroke, FA likely changes as evidenced by the combination of results in the literature. For example, one study within 24 h of stroke shows FA in WM is decreased and FA in GM is unchanged.[1] Others,[2,3] have shown a trend of increased FA in WM in less than 7 h of stroke onset. Also, individual FA changes have a range of -45% to +45%, while ADC changes were relatively consistent (-36% to -64%).[4] One explanation for this diversity of results is that FA changes during the first 24 h of stroke. Previously, three phases of ADC and FA evolution in ischemic stroke were proposed (phase 1: ADC decreased and FA increased; phase 2: ADC increasing and FA decreasing; phase 3: ADC increased and FA decreased).[5] This implies FA decreases simultaneously with the ADC increase; however, this is not completely supported by the literature, indicating changes in FA in hyperacute stroke cannot be attributed to the same mechanisms of ADC changes. The objective here was to perform a detailed investigation of the evolution of FA during hyper-acute ischemic stroke. We propose that FA may be useful to further characterize acute stroke lesions and potentially dichotomize patients for thrombolysis.

Methods

Ischemic stroke was induced in 8 canines using a previously described canine model,[6] with two modifications: (a) single clot injection was performed (indexed as time = 0 min) and (b) clots were double sieved in an attempt to cause more severe strokes. Pre-stroke imaging included 6 DTI acquisitions (TR/TE = 5500 ms/95.4 ms, 1 signal average, 1 $b = 0$ s mm^{-2} image, 15 directions of diffusion encodings at $b = 1000$ s mm^{-2}, 144 × 144 matrix, FOV = 24 cm × 14.4 cm). The injection of clot was indexed as time = 0 min and all subsequent imaging was referenced to this time. DTI imaging was initially performed every 5 min, which was then reduced in frequency to every 10 min and then to every 30 min. Following the imaging, the brain was extracted for histological assessment. H & E, Luxol fast blue, and MAP2 and albumin immunohistochemistry were performed to evaluate stroke severity.

ADC and FA maps were constructed using FSL (FMRIB, http://www.fmrib.ox.ac.uk/fsl/). Rigid-body registration was performed using the $b = 0$ s mm^{-2} images with SPM2 (Wellcome Trust Centre for Neuroimaging, http://www.fil.ion.ucl.ac.uk/spm/) to realign all diffusion maps to the first map. Tissue type was defined by the pre-stroke FA map; WM ≥ 0.31 GM < 0.24 and 0.24 ≥ MIX < 0.31. Time-to-infarct maps were constructed;[7] time-to-infarct maps are defined by the time at which the ADC for each voxel dropped below the 95% confidence interval threshold of the normal (pre-stroke) ADC. The time with the greatest infarct volume was selected for each tissue for each canine. These volumes were then analyzed using repeated-measures ANOVA examining canine and time for each tissue type. Following the repeated-measures ANOVA, the individual time changes were examined with a one-way ANOVA and Dunnett's tests as appropriate.

Results

The repeated-measures ANOVA indicated that both canine and time significantly affected the ADC and FA values in all three tissues. With the onset of stroke, ADC rapidly dropped and remained reduced throughout the experiment for all animals and all tissues. FA showed a more complex response. In 6 canines, FA in WM increased and then decreased below the normal baseline. These changes were significant all animals, but the magnitude and duration of these trends varied. More severe strokes showed earlier and shorter periods of the FA increase, while less severe strokes showed the FA increase later within the study. FA in GM increased in all canines. The magnitude of the GM FA increase was also related to the stroke severity, with more severe strokes showing greater increases.

Discussion

The two animals that did not show the early FA increase had more mild strokes, thus it may be postulated that the FA increase had not yet occurred, as evidenced by one of these animals whose FA at 330 and 360 min appeared to show an increasing trend. The two animals with the most severe strokes showed very rapid FA increases that did not persist for long (Fig). Similarly, animals with more severe strokes showed earlier significant FA increases in GM, while animals with mild strokes showed these increases at later time points. We propose that the changes in FA may assist in determining stroke treatment as it may assist in characterizing the blood brain barrier integrity.

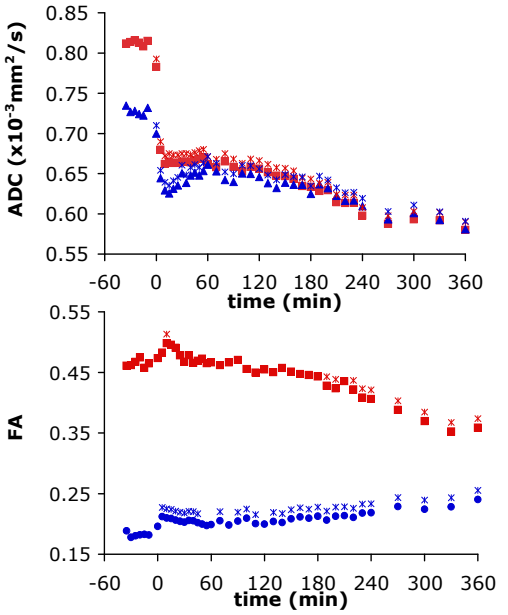

Fig. ADC and FA evolution for one canine over the 6 h study (blue circles = WM, red squares = GM). ∗ indicates significant difference from normal baseline according to the Dunnett's tests after the repeated-measures ANOVA.

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