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Diffusion tensor brain imaging in forensic radiology

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ABSTRACT

Objectives: Evaluation of changes in DTI parameters in post-mortem (PM) cadaveric vs. antemortem (AM) healthy control brains based on eigenvalues at <24 h PMI.
Methods and materials: The in-situ DTI brain scans of 10 PM subjects were compared to 10 AM controls. DTI metrics were measured from 25 ROIs for each brain in the gray and white matter.
Results: PM eigenvalues ($\lambda 1$, $\lambda 2$, $\lambda 3$) were significantly lower than in the AM controls, independent of tissue type. Longitudinal diffusivity was more affected than transverse (control vs. PM, for $\lambda 1$, $\lambda 2$ and $\lambda 3$ in $mm^2/s \times 10^{-3}$: 0.96, 0.74, 0.58 vs. 0.27, 0.20, 0.15 for gray matter and 1.52, 0.44, 0.25 vs. 0.33, 0.10, 0.05 for white matter, $p<0.0001$). FA was significantly higher PM for gray matter (0.28 PM vs. 0.22 control, $p=0.003$) but similar for white matter (0.73 PM vs. 0.75 control, $p=0.4$). ADC values were lower for PM (0.73 control vs. 0.16 PM and 0.76 control vs. 0.21 PM, in white/gray matter respectively, $p<0.0001$; all units $mm^2/s \times 10^{-3}$).
Conclusion: Both longitudinal diffusivity, transverse diffusivity and ADC are reduced PM. The lack of FA changes in white matter PM implies that FA changes in stroke are due to the ischemic cascade rather than direct cell death. Gray matter of the caudate showed an increase in FA similar to what is seen in a number of both degenerative and inflammatory pathologies.

1. Introduction

Diffusion-tensor imaging (DTI) is an MR sequence that provides information on biological tissue activity at the microstructural level by quantifying water diffusion in various tissues. DTI assesses diffusion magnitude and diffusion directionality, and can elucidate fine fundamental details on both healthy and damaged neurological tissue. DTI enables the determination of three perpendicular eigenvectors, whose magnitudes are given by their three corresponding eigenvalues, $\lambda 1$, $\lambda 2$, and $\lambda 3$. The indices derived from DTI measurements such as fractional anisotropy (FA) and the apparent diffusion coefficient (ADC) are quantitative and objective measures of diffusion properties that can be measured in the human brain [1]. Decreased diffusivity has been described for cell death, particularly in cases of stroke.

Post-mortem (PM) DTI analysis is designed to compare and contrast MRI-derived data with histological and forensic findings. In the only such study to date, Scheurer et al. [2] analyzed MRI data from cooled, non-fixated brains using a clinical-standard MRI system (1.5 T). They found that the ADC values of the brain were significantly decreased compared to normal controls. Increasing the post-mortem interval (PMI) decreased the ADC values of gray matter, whereas the white matter showed no significant changes. ADC values were significantly lower in cases of mechanical and hypoxic brain injuries (caused by heart failure), compared to traumatic brain injury. Post-mortem FA was not significantly different from the FA of live brains, and showed little influence of PMI. The authors emphasized the importance of MRI in general, and ADC in particular, as a novel tool in forensic medicine that can help determine cause of death.

The present study expands upon by Scheurer et al. [2] by comprehensively evaluating changes in DTI parameters, and by including the eigenvalues, ($\lambda 1$, $\lambda 2$, $\lambda 3$), FA and ADC in cadaveric full brains at a relatively short PMI compared to antemortem (AM) controls. Assessment of the eigenvalue data determines the main directional changes in the PM brains. Unlike the longer and varied mean PMIs examined in Scheurer et al., our study examined the progression of early (<24 h) PM damage to brain tissue by comparing the extent of change in different areas and directions of diffusivity (longitudinal vs. transverse). The DTI parameters in both white and gray matter were measured and compared with the corresponding anatomical locations in healthy live controls and compared and contrasted the data with known DTI changes in

Abbreviations: ADC, apparent diffusion coefficient; DTI, diffusion-tensor imaging; DWI, FA, fractional anisotropy; MR, magnetic resonance imaging; ROI, region of interest; PMI, post-mortem interval; ES, effect size

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stroke (<24 h) and neurological disease.

2. Materials and methods

2.1. Subjects

The in-situ DTI brain scans of 10 post-mortem human cadavers were compared to a antemortem control group consisting of the DTI scans of normal brains of living patients with no known pathologies.

The 10 deceased cases, 3 females and 7 males, ranged in age from 30 to 62 years (mean 37.5 ± 10(SD)). Circumstances of death included natural death, disease, suicide, and homicide (Table 1). The average PMI was 12 ± 5.2 h. Prior to scanning, PM examination by a forensic pathologist was performed to ensure compliance with the inclusion criteria. Average core temperature before scanning was 14.8 ± 6.4 °C, measured rectally with a digital thermometer. The 10 control subjects, 5 females and 5 males, ranged in age from 24 to 39 (mean age 31 ± 5). The demographics are presented in Table 1. IRB approval was obtained.

2.2. Inclusion and exclusion criteria

The study included subjects with an intact cranium and PMI of less than 24 h. It excluded subjects with brain trauma, history of neurological disorder or findings of visible pathology as cause of death on conventional brain MRI. Antemortem controls were free of pathological findings.

2.3. MR imaging

Imaging of the in-situ brain was performed on a 1.5 T system (Siemens Megnaton Aera, Erlangen, Germany). Sagittal, axial and coronal T1, axial and coronal T2, axial FLAIR, GRE T2 and SWI were obtained. Axial DTI of the entire brain was done with pulsed gradient, spin-echo and echo-planar imaging: repetition time (TR) 6000, echo time (TE) 97, matrix 132×32, field of view 230 mm $\times$ 230 mm, contiguous slice thickness 3 mm, 2*b* values 0 and 1000 s/mm^2, acquisition time 3.26 min, pixel size 0.9×0.9 mm^2. Diffusion weighting was applied along 30 non-collinear axes.

2.4. Image processing

Quantitative analysis of DTI data and DTI maps were generated by the DTI task card using MRWP with a SyngoMR D11 imaging software platform (Siemens Medical Solutions, Erlangen, Germany).

Table 1
Subject demographics and clinical characteristics.

AM controls ($n=10$)	PM subjects ($n=10$)		
Age (years)	31(24–39)	37.5(30–62)	
Gender	$F=5$	$F=3$	
	$M=5$	$M=7$	
Circumstances of death	N/A	Unexplained sudden death	3
		Disease	2
		Suicide	4
		Murder	1
Clinical cause of death	N/A	Hypovolemic shock	2
		Suffocation	3
		Drug/alcohol abuse	1
		Pulmonary embolism	1
		MI or cardiac arrhythmia	2
		Acute pneumonia	1

2.5. Data collection

DTI metrics, including $\lambda 1$, $\lambda 2$, $\lambda 3$, ADC and FA were measured from 25 ROIs for each brain as presented in Fig. 1. From each hemisphere, 12 measuring ROIs were placed in consistent locations. Another single ROI was placed in the vermis for each brain. All measurement ROIs were of uniform size of 3 mm. Gray matter regions included the caudate, globus pallidum, motor cortex, and vermis (1 measurement per brain); the white matter included the midbrain corticospinal tract (CST), pons CST, corpus callosum-genu, body, and splenium, centrum semiovale, frontal white matter and internal capsule (anterior and posterior).

2.6. Data analysis

The data were categorized by anatomical region and as either white matter (WM) or gray matter (GM). The DTI values of WM and GM were analyzed separately as is typical in ischemia studies [3]. Because DTI values are temperature-dependent, DTI metrics ($\lambda 1$, $\lambda 2$, $\lambda 3$, and ADC) of the postmortem cases were also temperature-corrected to 38 °C by using a correction factor of 2% per °C according to the equation $ADC_{Tc}=ADC(100\%+2\%)^{(38\ °C\text{-}Tscan)}$ used by Scheurer et al. The body core temperature measured (anal probe) at the start of the scan (Tscan) was used for the correction [2].

2.7. Statistical analysis

All variables and derived parameters were tabulated by descriptive statistics. For all statistical tests, a *p*-value of 5% or less was considered statistically significant. The data were analyzed using the SAS® version 9.1 (SAS Institute, Cary, North Carolina).

3. Results

The DTI metrics measured in the different ROIs were categorized in terms of location, type of tissue (white/gray) and study group, and are presented in Table 2. Fig. 2 shows the DTI metrics for white/gray matter for the PM subjects vs. the AM controls, with and without temperature normalization.

Most DTI metrics for PM DTI values were significantly different from the DTI metrics of the AM controls.

All eigenvalues ($\lambda 1$, $\lambda 2$, $\lambda 3$) decreased significantly in the PM group, independently of the type of tissue analyzed. $\lambda 1$, $\lambda 2$, $\lambda 3$ were equal to 0.96 (Std, ± 0.17), 0.74 (Std, ± 0.15) and 0.6 (Std, ± 0.15) for gray matter controls vs. 0.27 (Std, ± 0.06), 0.20 (Std, ± 0.04), and 0.15 (Std, ± 0.03) for gray matter PM, respectively, and 1.52 (Std, ± 0.25), 0.44 (Std, ± 0.15), and 0.25 (Std, ± 0.14) for white matter controls vs. 0.33 (Std, ± 0.08), 0.10 (Std, ± 0.05), and 0.05 (Std, ± 0.03) for white matter PM, respectively. For all values (units measured in mm^2/s $\times 10^{-3}$), $p<0.0001$ (*T*-test).

The largest relative decrease from control subjects to PM subjects was found for the $\lambda 1$ of the white matter (1.52 vs. 0.33 mm^2/s $\times 10^{-3}$). In line with previous reports [9], in our study the ADC values were reduced post-mortem for both the white and gray matter. They dropped from 0.73 (Std, ± 0.09) mm^2/s $\times 10^{-3}$ to 0.16 (Std, ± 0.04) mm^2/s $\times 10^{-3}$ and 0.76 (Std, ± 0.15) mm^2/s $\times 10^{-3}$ to 0.21 (Std, ± 0.07) mm^2/s $\times 10^{-3}$, for the white and gray matter respectively ($p<0.0001$, *T*-test), as listed in Table 2.

The FA for the combined gray and white matter in our study (data not shown) did not differ significantly between the PM subject and the AM controls. In both PM subjects and AM controls, the highest FA was measured in the splenium of the corpus callosum with 0.87 (Std, ± 0.05), and the lowest in frontal WM with