## **Voxelwise DTI group analysis in professional fighter population**

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Target audience: Traumatic brain injury researchers

**Purpose:** The Professional Fighters' Brain Health Study (PFBHS) is a longitudinal study to monitor a cohort of active professional fighters annually over 4 years. From the initial data, ROI based DTI results have been published that show that the number of times a fighter has been knocked out (NKO) predicts DTI changes mainly in posterior corpus callosum (CC) in 74 boxers and 84 mixed martial art (MMA) fighters [1]. In this study, we included all the first year visit male fighters in PFBHS (N=305) and performed a voxelwise DTI group analysis using non-linear registration method to investigate if fight exposure history predicts DTI measures of white matter integrity in whole brain.

## Methods

<u>MR experiment:</u> MR scans were performed on a 3T Verio scanner (Siemens, Erlangen, Germany). A single-shot echo-planar imaging (EPI) scan was used to acquire high angular resolution diffusion images (HARDI) (TR/TE = 7000/91 ms; voxel size =  $2.5 \times 2.5 \times 2.5 \times 2.5 \times 2.5 \times 2.5$  mm<sup>3</sup>; 49 slices; 71 different diffusion direction with b = 1000 s/mm<sup>2</sup>, and 8 b=0 scans; total running time = 8:24).

<u>Subjects:</u> Three hundred and five male professional fighters (149/156 of boxers/MMA) participated in the first visit PFBHS. As described in ref [1], the individual fight related information and geographical information including number of professional fights (pNF) and NKO. Fighters with missing information were removed so that a total of 262 fighters (126/136 in boxers/MMA) were analyzed.

<u>DTI post-processing</u>: Field map-based distortion correction [2] was applied to unwarp EPI geometric distortion and an iterative motion and eddy current artifact correction method was employed [3] before DTI parameters calculation including longitudinal diffusivity (LD), transverse diffusivity (TD), mean diffusivity (MD) and fractional anisotropy (FA).

<u>Non-linear registration:</u> a typical brain was selected as a template. Individual T1w images were registered to a template using symmetric image normalization in Advanced Normalization Tools (ANTS) [4]. Then individual DTI maps were registered to a template using the ANTS transformation matrix.

<u>Statistical analysis</u>: voxel-wise multiple hierarchical linear regression analyses were performed to test the hypothesis that fight-related exposure, e.g. professional number of fight (pNF) and/or NKO, could predict DTI values (LD, TD, MD and FA) with a corrected p < 0.01, after controlling age and years of education effects [1].

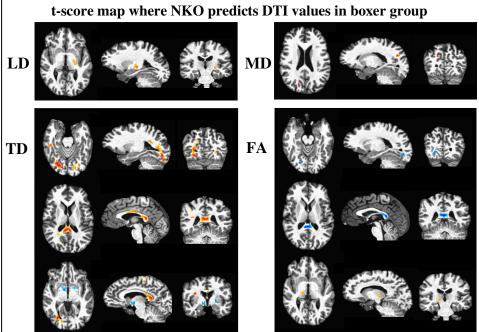
**Results:** There is no significant difference of age, years of education, pNF and NKO between boxer and MMA groups. Fig 1. shows that NKO predicts increased TD in the central and posterior CC, as well as the splenium of the CC, in boxers but not in MMA fighters. It is also observed that NKO predicts increased LD in part of the internal capsule in boxers but not in MMA fighters. NKO predicts increased LD in midline of the central CC with p < 0.05 in boxers (result not shown here). Increased TD and LD with NKO in those areas lead to decreased FA and increased MD in the corresponding areas of boxers. We found that NKO predicts decreased TD in palladium and the increased FA in thalamus proper area of boxer group. pNF does not predict DTI in either groups.

**Discussion:** We found that NKO predicts DTI changes after controlling for age and education effects, which shows good agreement with the previous finding [1]. This finding is observed only in boxers group, not in MMA. The boxer group shows increased TD in CC with NKO, which is commonly observed in mild TBI patients. The observation in boxers and not MMA may be explained by the fact that boxers mainly target the head of opponent, leading to higher risk of repetitive head blow exposure than MMA fighters who use grappling as well as striking. The decrease of TD with NKO in subcortical areas could be related to the repetitive pattern of injury and recovery, as discussed in ref [1].

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## Reference

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**Fig 1.** The areas in which NKO predicts TD values after controlling for individual variation factors (age and year of education) with p < .01 (corrected) are shown. Color represents student t-score, scaled from -5 (cool) to +5 (warm).