Fractal analysis of the brain blood oxygenation level dependent (BOLD) signal in the left putamen of mild traumatic brain injury (mTBI) patients

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Target Audience: Researchers and clinicians interested in mild traumatic brain injury (mTBI).

Purpose: Mild traumatic brain injury (mTBI) is a common condition that affects many people around the world. While some cases resolve without long-term side effects, others have to live with permanent disabilities such as learning difficulties, behavioral issues, and memory loss [1]. Conventional imaging techniques are unable to detect abnormalities in the brain of mTBI patients that have shown delayed functional response on neuropsychological evaluation. Therefore, the main objective of this study was to explore a novel analysis approach involving measurement of the temporal fractal nature of the resting state blood oxygen level depending (rsBOLD) signal.

Methods: Six subjects with mTBI (post-concussion symptom scale PCSS= 46±23) and 6 age-matched healthy controls were scanned at rest with eyes open using a GE MR750 3T MRI and 32 channel RF coil (General Electric Healthcare, Milwaukee, WI). Axial FSPGR 3D images were used to prescribe the rsBOLD (gradient echo EPI, flip angle = 90°, TE/TR = 35/2000ms, FOV = 22, 64x64 matrix, 31 continuous 4.5 mm slices, 180 temporal points acquired over 6 min). Motion correction was performed using the MCFLIRT tool from FSL [2]. The 3D data and BOLD images were aligned and spatially warped to the Harvard Oxford_sub_maxprob_thr50_2mm atlas from MNI using FSL (see Fig 1). The left putamen was selected as the region of interest (ROI) and the images were warped back to native space. Increased microglial activation in the putamen has been detected up to 17 years after TBI [3]. The fractal analysis of the BOLD signal over the entire putamen was assessed by calculating the Hurst exponent according to the procedure of Eke *et al.* [4] The statistical analysis was done using a two-tailed unpaired Student's t test to compare FD values between mTBI and control groups.

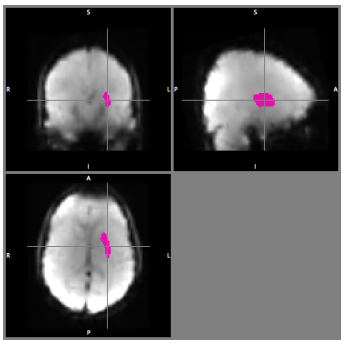

Fig 1. ROI registration on functional image.

Results and discussion:

Average fractal dimension (FD) and Hurst coefficient (H) in the left putamen comparing mTBI patients to controls is shown on Table 1. The mTBI patients had a significantly lower FD in the left putamen, compared to healthy controls ($P<0.05$). The mean FD for mTBI patients was 0.53 ± 0.69 compared to 1.38 ± 0.79 for healthy controls. The method described by Eke, characterizes the fractal signals according to two patterns they may exhibit. The FD is calculated depending on whether the signal fits the fractional Gaussian Noise (fGn) or the fractional Brownian motion (fBm). The BOLD data for controls mainly fitted the fBm model. fBm signals are non stationary and contain more low frequency components which could imply some contamination of the signal from brain CSF. Low FD characterizes less complex signals which has been previously associated with pathologies of the brain [5,6]. A decrease in signal complexity could be associated with lack of adaptability and decreased global connectivity in the brain. The results could possibly imply that the left putamen may have reduced connectivity with other parts of the brain due to subtle inflammatory processes. A recent paper [3] reported increased microglial activation in the putamen after mTBI. Chronically activated microglial cells secrete cytokines that could cause a permanent inflammatory response.

TBI	PCSS	H_{TBI}/R^2	FD_{TBi}	Controls	H_C/R^2	FD_C
1	78	0.1/0.94	1.90	1	0.08/0.99	1.92
2	57	2.03/0.55	0.03	2	0.11/0.92	1.89
3	48	2.19/0.56	0.19	3	2.44/0.56	0.44
4	43	2.48/0.57	0.48	4	0.08/0.95	1.92
5	0	2.72/0.62	0.72	5	0.19/0.94	1.81
6	51	1.88/0.55	0.12	6	2.27/0.61	0.27
Mean ±SD			0.53 ±0.69			1.38 ±0.79

Table 1. FD and H values and associated fit quality (R2) for each mTBI and control subject.

Conclusions: This preliminary study suggests that the analysis of the fractal dimension of the rsBOLD signal could possibly provide additional information in TBI. Additional studies should consider increasing the sampling rate and the number of temporal points in order to increase the accuracy of the FD. Additionally, extraction of CSF signal is recommended in order to limit the influence of the fractional brownian motion in the calculation of the fractal dimension.

References [1] J.J. Kim et al., *Neu. J Am. Soc.Exp. N.Th.*, vol. 8, pp. 39-53, 2011. [2] Jenkinson et al. NeuroImage, 17(2), 825-841, 2002. [3] Ann Neurol. 2011 Sep;70(3):374-83. [4] Eke et al. Eur J Physiol,(2000) 439:403-415.[5]. Goldberger et al. Proc Natl Acad Sci USA 99(Suppl):2466–2472 [6]. Suckling et al. J Neurosci Methods 174(2):292–300