Drumming training induces myelin remodelling in Huntington's disease: a diffusion MRI and quantitative magnetization transfer study

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Background

- Huntington's disease (HD) leads to debilitating cognitive and motor symptoms.
- Impaired myelination might contribute to HD pathology [1]. Myelin formation underlies motor skill learning [2].
- We tested whether motor training stimulated WM remodelling in HD patients, and induced motor and cognitive improvements.
- **Training-related changes in FA, RD, Fr, and MPF (fig.1)** were studied in left and right Supplementary Motor Area-Putamen pathways **(SMA-Putamen)**, and within three segments of the Corpus Callosum **(CCI, CCII and CCIII)**.
- **Baseline MPF differences** were assessed **to aid interpretation of the post-training microstructure changes.**

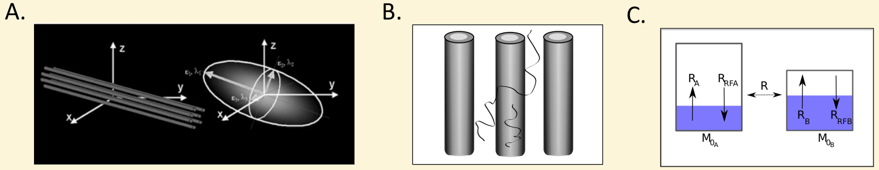

Figure 1. Schematic representations of the models of WM microstructure used in this study. A. The diffusion tensor model (DTI) [1] [2]. B. The Composite hindered and restricted model of diffusion (CHARMED) [3] [4]. C. The two-pool model of magnetization transfer (MT) [4].

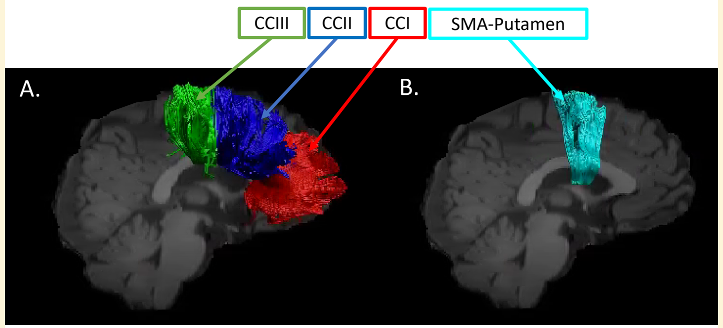

Figure 2. White matter regions of interest [6][7].

Methods

- **Subjects:** 8 HD patients and 7 age & sex-matched healthy controls.
- **Intervention:** 2 months of drumming training as previously described in [8]. Improvements were assessed for easy, medium and hard levels of difficulty.
- **MRI:** 3 Tesla General Electric HDx MRI system. Diffusion-weighted images were fitted to the **DTI** and the **CHARMED** diffusion models [3][4]. MT-weighted images were fitted to **Ramani's pulsed MT approximation** [5].
- **Tractography:** performed using the damped Richardson-Lucy algorithm [6]. Tract reconstructions were performed in ExploreDTI[7].
- **Analysis:** training effects on **drumming performance** were analysed with ANOVA. **Percentage change scores** were calculated for **MRI measures** in each tract & for **cognitive outcome measures**. **PCA** was utilised to reduce data dimensionality. **Group differences in training-associated microstructural and cognitive changes** were assessed with **permutation analysis. Correlations** were run to assess the relationship between training-associated changes in MRI measures, and changes in drumming and cognitive performance. **TBSS** [8] was run to investigate brain-wise patient-control differences in MPF before training.

Results & Conclusion

1. **Behavioural effect of the drumming training:** patients improved their drumming performance for the easy test pattern and controls for the medium difficult test pattern (Fig.3).
2. **HD patients presented significantly higher changes in MPF in response to training** in CCII [t(14) = -20.72, p=0.04], CCIII [t(14) = -25.87, p=0.04], and right SMA-putamen pathway [t(14) = -25.48, p=0.04] (FDR-corrected) (Fig.4).
3. **Changes** in MRI measures **did not correlate with changes in drumming and cognitive performance.**
4. **Baseline MPF reductions partly overlapped** with areas showing significant changes post-training (i.e. CCII and CCIII) (Fig.4).

➢ **Behavioural stimulation may result in neural benefits in HD that could be exploited for future therapeutics aiming to delay disease progression.**

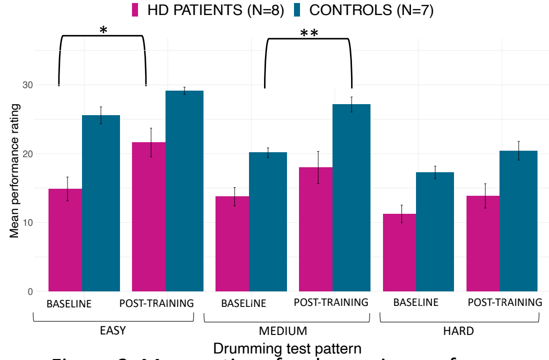

Figure 3. Mean ratings for drumming performance

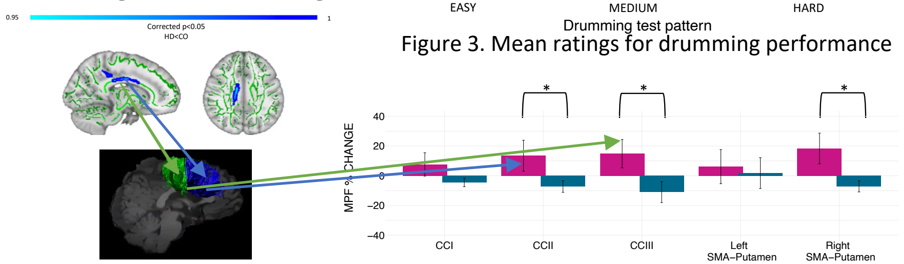

Figure 4. TBSS analysis of baseline MPF values & bar graph of the post-training percentage change in MPF across the inspected tracts (error bars represent the standard error).

[1] Bartzokis et al. (2007), *Neurochemical Research;* [2] Sampaio-Baptista et al. (2013), *The Journal of Neuroscience;* [3] Alexander et al. (2007), *Neurotherapeutics*; [4] Assaf & Basser (2005), *NeuroImage;* [5] Henkelman et al. (1993), *Magnetic Resonance in Medicine;* [6] Hofer & Frahm, (2006) *NeuroImage*; [7] Leh et al. (2007), *Neuroscience Letters*; [8] Metzler-Baddeley et al. (2014), *Journal of Huntington's Disease;* [7] Leemans et al. (2009), *Magnetic Resonance in Medicine*; [8] Schmierer et al. (2007), *Journal of Magnetic Resonance Imaging ;* [9] Ou et al., (2009). *NMR in Biomedicine*; Wheeler-Kingshott & Cercignani (2009), *Magnetic Resonance in Medicine*; [10] Fields et al. (2014), *The Neuroscientist*