Improved white matter microstructure after a novel drumming training in Huntington's disease

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Introduction: Huntington's disease (HD) is an inherited and progressive neurodegenerative disorder leading to cell loss in the basal ganglia and white matter degeneration in frontal motor pathways. Deficits in working memory/executive functions including multi-tasking, inhibitory control, motor sequence learning and timing, can be observed early, prior to the onset of clinical motor symptoms. This pilot study investigated for the first time the effects of a novel drum training paradigm and suggests improvements in white matter and working memory in HD.

Materials and Methods: N = 6 right-handed patients were recruited from local HD clinics [3 females, mean age = 52.2 years (range 42-64), mean dementia screening score = 23/30 (19-27), mean premorbid verbal IQ = 108 (100-121)]. **Baseline:** Working memory/executive function assessment in dual task (multi-tasking)[1], verbal trails (attention switching)[1], Stroop (suppression of conflicting information)[2] and verbal and category fluency [3]. Diffusion MRI Tractography: Data were acquired using a 3T GE HDx MRI system. Cardiac-gated HARDI diffusion MRI employed an optimised 60 direction gradient vector scheme and b-value 1200s/mm^2, 60 slices (2.4mm), FoV 24 cm, matrix 96x96, TE 87ms. Images were corrected for distortions and motion, with re-orientation of gradient directions [4], and damped Richardson-Lucy spherical deconvolution[5] used to extract peaks in the fibre orientational density function (fODF) in each voxel. Data were corrected for CSF partial volume artefacts with the Free Water Elimination method[6] Deterministic tractography was performed by seeding in all image voxels, and following peaks in the fODF, using *ExploreDTI* [7]. Putative 3D pathways belonging to the anterior corpus callosum (Segments 1 and 2 of Hofer & Frahm's midsaggital parcellation, 2006)[8], the anterior thalamic radiation, and the corticospinal tract (Figure 1) were selected from the whole brain tracking results using 'waypoint' regions of interest, using landmarking techniques shown previously to be reproducible for these tracts. Tract-specific measures of average fractional anisotropy, axial and radial diffusivity were subsequently generated. **Training**: Patients practised at home, 15 minutes per day for 2 months. They were provided with Bongo drums and a bespoke drumming training of 22 sessions on CDs which introduced patterns/ rhythms of increasing complexity and speed. Patients practised at their own individual pace and level of difficulty with each hand alone and both hands together. Training was recorded in a diary. **Outcome**: As baseline with parallel versions for working memory tests. Principal component (PC) analyses to derive the first principal component of all working memory measures and all white matter microstructural indices across tracts were conducted for pre- and post-training data.

Results:. Participants' working memory performance improved significantly after the training, $t(5) = 5.2$, $p \leq 0.007$, (see Figure 2A). Further, there was an increase in fractional anisotropy, $t(5) = 4.479$, $p \leq 0.007$, and axial diffusivity, $t(5) = 3.8$, $p \leq 0.013$, and a decrease in radial diffusivity, $t(5) = -3.4$ $p \leq 0.019$ after the training (see Figure 2B-D).

Conclusion: This study shows for the first time that not only is there an improvement in HD patients' working memory performance after a 2 months drumming training – but crucially, there is also **evidence of changes in white matter microstructure in frontal/motor pathways** which may underpin the improvements in cognitive performance. Determining whether this is due to alterations in myelin, axon density, axon diameter or some combination of all three is beyond the scope of the tensor model and so follow-up studies with multicomponent relaxometry and higher order models of diffusion are planned, in a larger cohort of patients.

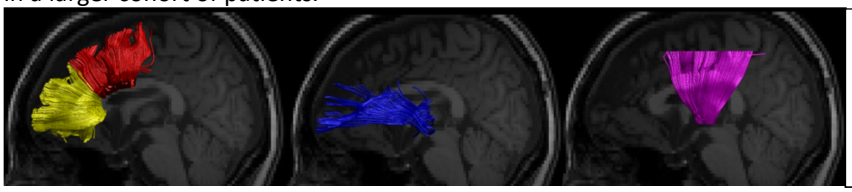

Figure 1: The pathways studied here: Corpus callosum (segment 1 in yellow, segment 2 in red), the anterior thalamic radiation (blue) and a segment of the corticospinal tract (pink). Tracts are overlaid on co-registered T1-weighted images.

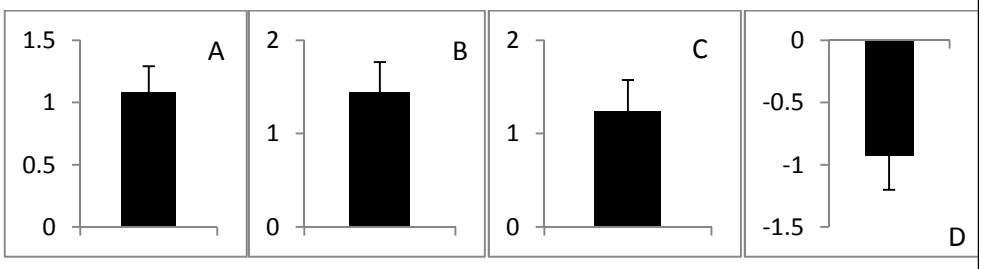

Figure 2: The y-axis plots the average difference score (standard error) between post- and pre-training principal component derived from A) working memory scores, showing significant cognitive improvement, and B) fractional anisotropy, C) axial diffusivity, D) radial diffusivity showing significant changes in white matter microstructure.

References: 1 Baddeley A 1996 *Q J Exp Psych* **49** A:5–28; 2 Trenerry M et al. 1989 *Stroop* Test. Odessa, FL: Psychological Assessment Resources; 3 Delis D et al 2001 *Delis–Kaplan Executive Function System*. Oxford: Pearson; 4 Leemans A, Jones D 2009 *Magn Reson Med* 61: 1336-1349; 5 DellAqua et al 2010 *NeuroImage.***49**:1446-58; 6 Pasternak et al 2009 *Magn Reson Med* **62**:717–730; 7 Leemans et al 2009 *ExploreDTI* In: *Proc ISMRM 17th Ann Meetg*, p. 3537, Hawaii, USA; 8 Hofer S, Frahm A 2006 *NeuroImage* 32: 989–994. **Target Audience**: Cognitive Neuroscientist, Clinicians, diffusion MRI scientists.