IC-P-133 MUSIC AS A PROBE OF DEFAULT MODE NETWORK FUNCTION IN YOUNG-ONSET ALZHEIMER'S DISEASE

Catherine F. Slattery[1], Jennifer L. Agustus[1], Ross W. Paterson[1], Mark J. White[1], Alexander J.M. Foulkes[1], Laura Mancini[1], Nick C. Fox[2], Jonathan M. Schott[1], Jason D. Warren[1], [1]*University College London, London, United Kingdom;* [2]*UCL Institute of Neurology, London, United Kingdom. Contact e-mail: c.slattery@ucl.ac.uk*

Background: Large-scale brain network disintegration is a unifying theme in neurodegenerative disease with converging lines of evidence implicating the default mode network (DMN) in Alzheimer's disease (AD). Most previous functional MRI (fMRI) work in AD has assessed the DMN role in memory but emerging evidence points to a much broader pathophysiological phenotype. Sound is an effective and clinically-relevant stimulus to address this: key DMN components are involved in sound decoding and patients with AD commonly experience difficulty perceiving complex auditory environments. In this activation fMRI study we used music as a model paradigm to assess changes in DMN function in young-onset AD. **Methods:** 32 patients fulfilling criteria for young-onset AD and 18 healthy age-matched controls underwent sparse-acquisition fMRI whilst passively listening to 8-second musical melodies in which key informational properties of temporal regularity (isochronous versus anisochronous) and familiarity (familiar versus novel) were manipulated in a factorial design. fMRI data were analysed in SPM8 and patient and healthy control groups were compared using 2nd-level t-tests. **Results:** Relative to healthy controls, AD patients showed enhanced activation of temporoparietal cortex for processing anisochronous versus isochronous melodies, but reduced activation of retrosplenial cortex, temporoparietal and medial prefrontal cortices for processing unfamiliar versus familiar melodies. **Conclusions:** Our findings delineate a novel pathophysiological phenotype of DMN dysfunction in this young-onset AD cohort. Relative to healthy individuals, these AD patients showed a complex profile of altered DMN activity during decoding of information in music, with both abnormally enhanced and reduced engagement of DMN components when processing particular musical properties. This work illustrates the potential of music as a novel probe of DMN dysfunction and the potential utility of fMRI in uncovering bidirectional network activity shifts in AD. Future work should assess the value of this paradigm as a sensitive disease marker, including during the presymptomatic phase of genetic AD.

IC-P-134 NEURITE ORIENTATION DISPERSION AND DENSITY IMAGING (NODDI) IN YOUNG-ONSET ALZHEIMER'S DISEASE AND ITS SYNDROMIC VARIANTS

Catherine F. Slattery[1], Jiaying Zhang[1], Ross W. Paterson[1], Alexander J.M. Foulkes[1], Laura Mancini[1], David L. Thomas[1], Marc Modat[1], Nicolas Toussaint[1], David M. Cash[1], John S. Thornton[1], Daniel C. Alexander[1], Sebastien Ourselin[2], Nick C. Fox[3], Hui Zhang[1], Jonathan M. Schott[1], [1]*University College London, London, United Kingdom;* [2]*Centre for Medical Image Computing, University College London, London, United Kingdom;* [3]*UCL Institute of Neurology, London, United Kingdom. Contact e-mail: c.slattery@ucl.ac.uk*

Background: Neurite orientation dispersion and density imaging (NODDI) is a novel MRI technique that provides more anatomically specific microstructural metrics of white matter damage than standard diffusion tensor imaging (DTI). In this study we aimed to compare neurite density index (NDI) using NODDI and DTI measures of fractional anisotropy (FA) in a cohort of patients with young onset Alzheimer's disease (YOAD). We also performed a preliminary exploratory comparison of the microstructural white matter signatures associated with the posterior cortical atrophy (PCA) and amnestic AD phenotypes. **Methods:** Twenty-six patients with YOAD (age: 61.0±5.5yrs, 33% male, age at symptom-onset 55.0±4.3yrs) and 19 controls (age=61.0±6.0yrs, 45% male), were imaged on the same 3T Siemens Trio scanner using a three-shell diffusion sequence optimised for NODDI (64, 32, and 8 diffusion-weighted directions at b=2000, 700 and 300 s/mm^2; 14 b=0 images; 55 slices; voxel size 2.5x2.5x2.5 mm^3; TR/TE=7000/92 ms; TA=15 mins). Images were corrected for motion and eddy-current distortion, NODDI parameters were estimated using NODDI Matlab toolbox, and FA estimated using Camino. Diffusion metrics were spatially normalized to the population-specific DTI template using DTI-TK. Tract-Based Spatial Statistics was used to detect group differences in FA and NDI, co-varying for age and gender (5000 permutations corrected for multiple comparisons with Threshold-Free Cluster Enhancement $p<0.01$). In a secondary, exploratory analysis we assessed NDI and FA in cohorts of PCA (n=7) and amnestic AD (n=7) versus controls. **Results:** Compared to standard FA metrics, NDI revealed more widespread white matter damage in the YOAD group (n=26). Within the patient cohort, PCA and typical AD subgroups had strikingly different patterns of decreased neurite density which in both cases broadly mirrored the FA changes but were more extensive. In PCA diffusion changes were localised to the right parieto-occipital region with very widespread changes seen in amnestic AD (figure 1). **Conclusions:** NODDI measures of neurite density provide additional and complementary information compared to standard diffusion metrics. NODDI imaging reveals widespread disruption to white matter architecture in AD and differential patterns of neurite loss in AD syndromic variants. NODDI is a powerful tool to investigate neuronal integrity in neurodegenerative diseases.

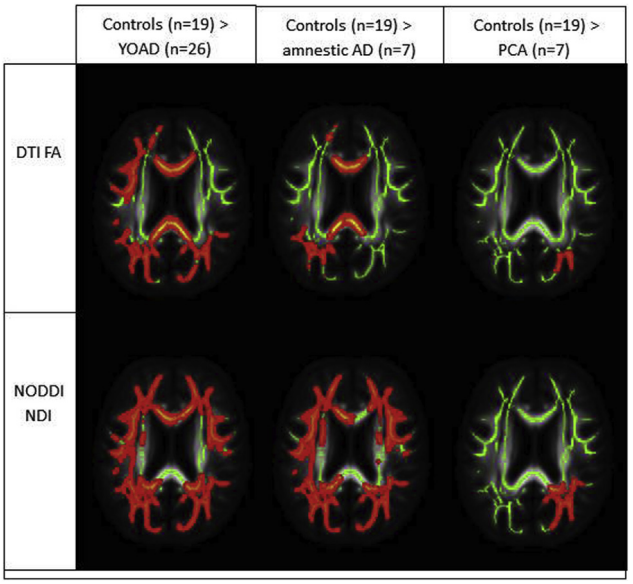

Figure 1. Fractional anisotropy (FA) and neurite density index (NDI) differences between YOAD patients and controls (red) shown on the group specific tensor template (green). Images corrected for multiple comparisons, $p<0.01$ ($p<0.05$ for FA in controls > PCA).