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BIOMARKERS

POSTER PRESENTATION

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NEUROIMAGING

Multimodal MRI reveals distinct patterns of vascular and microstructural disruption across disease stages in the Oxford Brain Health Clinic

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Abstract

Background: The Oxford Brain Health Clinic (OBHC) has assessed over 300 NHS memory clinic patients with a magnetic resonance imaging (MRI) protocol aligned with the UK Biobank. We also acquired the same data from over 100 healthy volunteers (HV) of a similar age range. This work explores multimodal patterns of imaging-derived phenotypes (IDPs) across diagnostic groups in a real-world memory clinic setting.

Method: Scans from 342 OBHC patients and 107 HV (demographics in Table 1) were processed with an integrated quality control-analysis pipeline optimised for memory clinic use (Gillis *et al.*, medRxiv, 2024). Subsequent diagnoses were extracted from electronic healthcare records and categorised as follows: dementia (ICD10 codes F00, F01, F02, F03), mild cognitive impairment (MCI - F06.7), and no dementia-related diagnoses (NDRD, including F10, F31, F32, F41). We performed ordinal regression analyses to test associations of IDPs with diagnoses, controlling for age, sex, head size, and applying hierarchical FDR correction.

Result: IDPs from all 6 MRI modalities significantly differed across groups (Figure 1). Pairwise post-hoc analyses revealed that healthy volunteers and dementia patients also significantly differed across all modalities (Figure 2A). In addition to structural changes, MCI patients had significantly higher cortical mean diffusivity, lower white matter integrity, and lower cerebral blood flow compared to HV (Figure 2B). Dementia patients had smaller volumes, localised increases in mean diffusivity, and more white matter hyperintensities (WMHs) than MCI patients (Figure 2C). Memory clinic patients who received no formal dementia-related diagnosis did not have significantly different brain volumes compared to HV, but the left hippocampal mean diffusivity was significantly higher (Figure 2D).

Conclusion: Thanks to the comprehensive multimodal MRI assessment offered in the OBHC, we observed distinct patterns of changes across the dementia spectrum. While structural IDPs may still provide best sensitivity, non-conventional MRI may give further insights on mechanisms of neurodegeneration. Microstructural and perfusion changes may precede the formation of overt WMH lesions, supporting the possibility of diffusion MRI and perfusion imaging as early signatures alongside structural imaging. Increased mean diffusivity in the left hippocampus in NDRD might explain memory problems that led to the referral to memory clinic.

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Table 1: Demographics of Oxford Brain Health Clinic (OBHC) patients and healthy volunteers (HV) of a similar age range. Patient diagnoses are stratified by diagnostic group with some patients missing a diagnosis since they have not yet attended their memory clinic appointment. MCI, mild cognitive impairment; NDRD, no dementia-related diagnosis; ACE-III, Addenbrooke's Cognitive Examination III; FT, full-time.

Characteristic	**Oxford Brain Health Clinic patients**					**Healthy volunteers (HV)**
	Total	**Stratified by diagnostic category**				
Sample Size	N=342	Dementia (N=149)	MCI (N=83)	NDRD (N=76)	Missing (N=34)	N=107
Age (years) – mean ± SD (range)	**77.4** ± 6.3 (65-101)	**79.8** ± 6.2 (65-101)	**76.3** ± 5.5 (65-88)	**73.9** ± 5.0 (65-85)	**77.9** ± 7.0 (66-94)	**75.2** ± 6.3 (60-92)
Sex - % F (M/F)	**48.2%** (177/165)	**46.3%** (80/69)	**48.2%** (43/40)	**48.7%** (39/37)	**55.9%** (15/19)	**54.2%** (49/58)
ACE-III Total Score – mean ± SD (range)	**75.5** ± 16.8 (9-100)	**64.4** ± 17.2 (9-98)	**81.2** ± 8.8 (55-97)	**89.8** ± 7.1 (63-100)	**74.9** ± 14.1 (42-99)	**95.4** ± 4.0 (78-100)
Years FT education – mean ± SD (range) [N]	**13.5** ± 3.9 (3-41) [N=309]	**13.0** ± 3.6 (3-25) [N=133]	**13.6** ± 4.7 (4-41) [N=78]	**14.4** ± 3.6 (9-30) [N=70]	**13.4** ± 3.8 (8-25) [N=28]	**15.9** ± 3.3 (10-25) [N=95]
Clinical Frailty Score – mean ± SD (range)	**3.0** ± 1.3 (1-7)	**3.3** ± 1.4 (1-7)	**2.8** ± 1.1 (1-6)	**2.5** ± 1.0 (1-6)	**2.9** ± 1.4 (1-7)	**N/A**

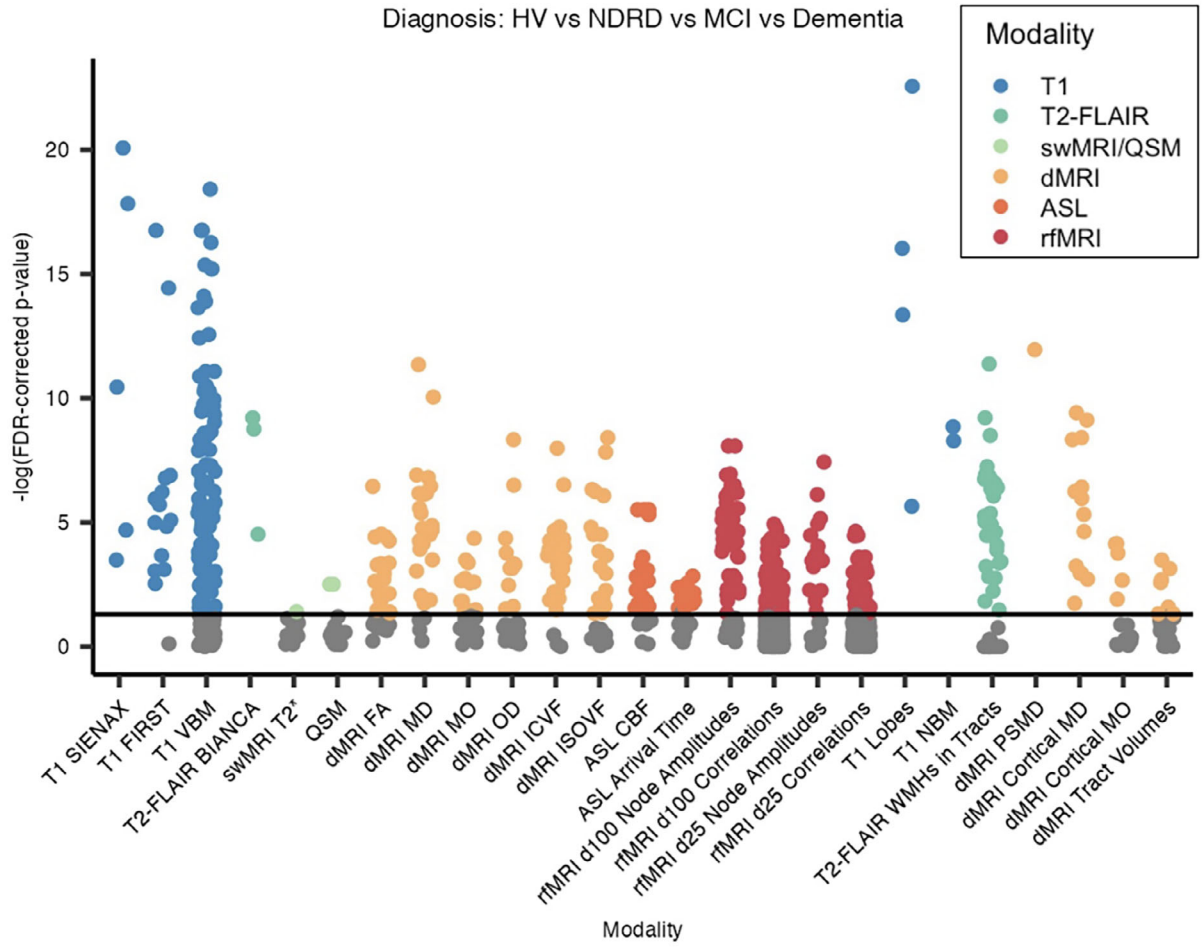

Figure 1: False discovery rate (FDR)-corrected p-values, hierarchical by modality, for associations between IDPs and diagnostic groups. Each dot represents one IDP, grouped by analysis tool/method and colour-coded by scan modality if significant. HV, healthy volunteer; NDRD, no dementia-related diagnosis; SIENAX, Structural Image Evaluation using Normalization of Atrophy (cross-sectionally); FIRST, FMRIB's Integrated Registration and Segmentation Tool; VBM, voxel-based morphometry; BIANCA, Brain Intensity AbNormality Classification Algorithm; FA, fractional anisotropy; MD, mean diffusivity; MO, mode of anisotropy; OD, orientation dispersion index; ICVF, intra-cellular volume fraction; ISOVF, isotropic volume fraction; CBF, cerebral blood flow; NBM, nucleus basalis of Meynert; WMH, white matter hyperintensity; PSMD, peak width of skeletonised mean diffusivity.

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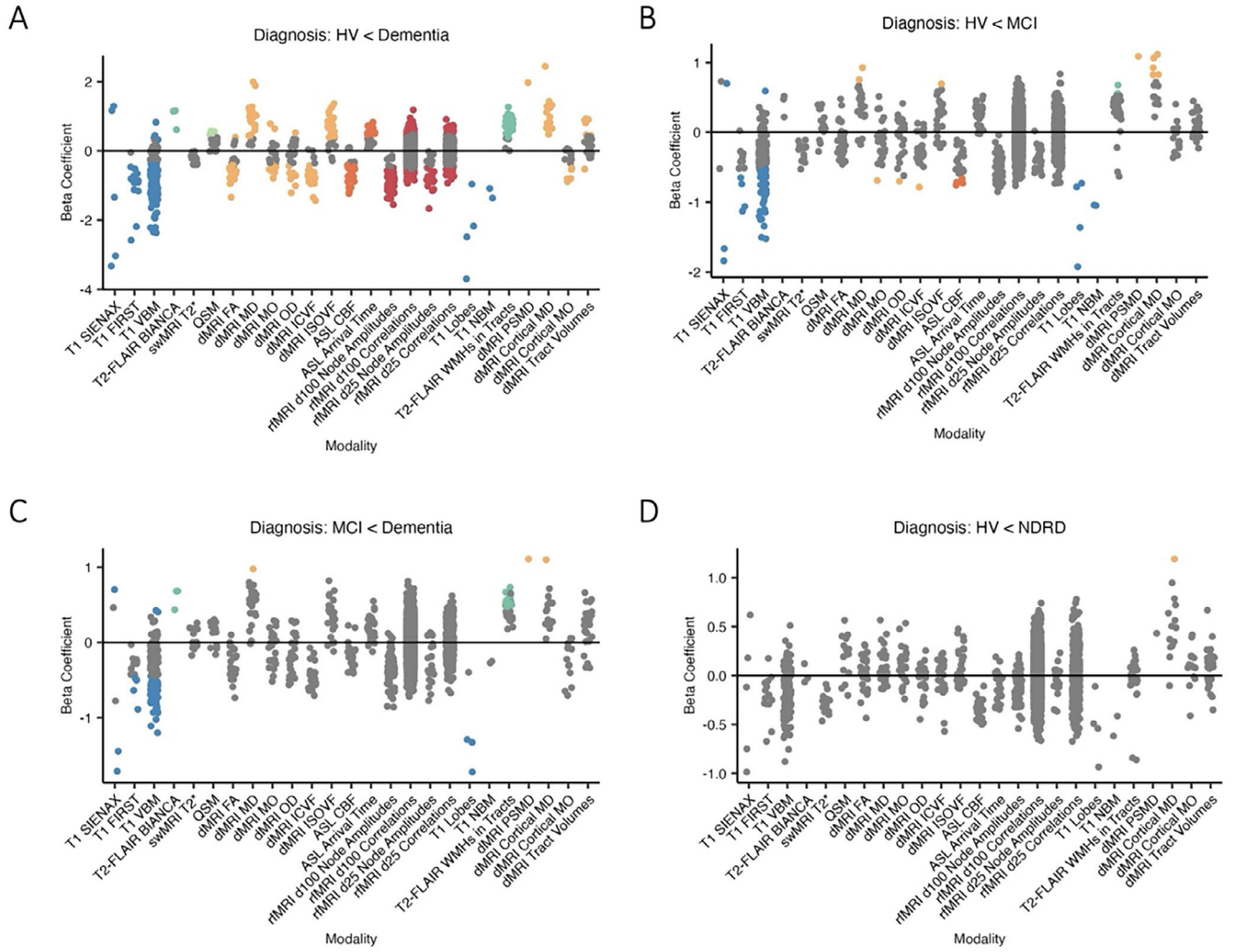

Figure 2: Beta coefficients for post-hoc associations between IDPs and pairs of diagnostic groups. All numeric variables are unit standardised, meaning that for a 1 standard deviation (SD) increase in an IDP value, the log-odds of receiving the more advanced diagnosis increases (or decreases if negative) by the β coefficient. Coloured dots indicate associations significant at the 5% FDR level, hierarchical by modality. HV, healthy volunteer; NDRD, no dementia-related diagnosis; SIENAX, Structural Image Evaluation using Normalization of Atrophy (cross-sectionally); FIRST, FMRIB's Integrated Registration and Segmentation Tool; VBM, voxel-based morphometry; BIANCA, Brain Intensity AbNormality Classification Algorithm; FA, fractional anisotropy; MD, mean diffusivity; MO, mode of anisotropy; OD, orientation dispersion index; ICVF, intra-cellular volume fraction; ISOVF, isotropic volume fraction; CBF, cerebral blood flow; NBM, nucleus basalis of Meynert; WMH, white matter hyperintensity; PSMD, peak width of skeletonised mean diffusivity.