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BACKGROUND

- **Population-scale resources such as UK Biobank (UKB)**¹ provide unparalleled statistical power, multimodal neuroimaging, and genetic data, enabling discovery of brain-disease associations. However, their clinical characterization of dementia is limited, reducing relevance to real-world patients.
- **Memory clinic cohorts** capture clinically meaningful, heterogeneous presentations of cognitive impairment but have limited participant numbers and data availability, constraining generalisability and discovery potential.
- **The Oxford Brain Health Clinic (OBHC)**², a real-world memory clinic cohort with brain MRI data matched to UKB, offers a unique opportunity to link clinically grounded dementia phenotypes to population-scale imaging and genetic data.

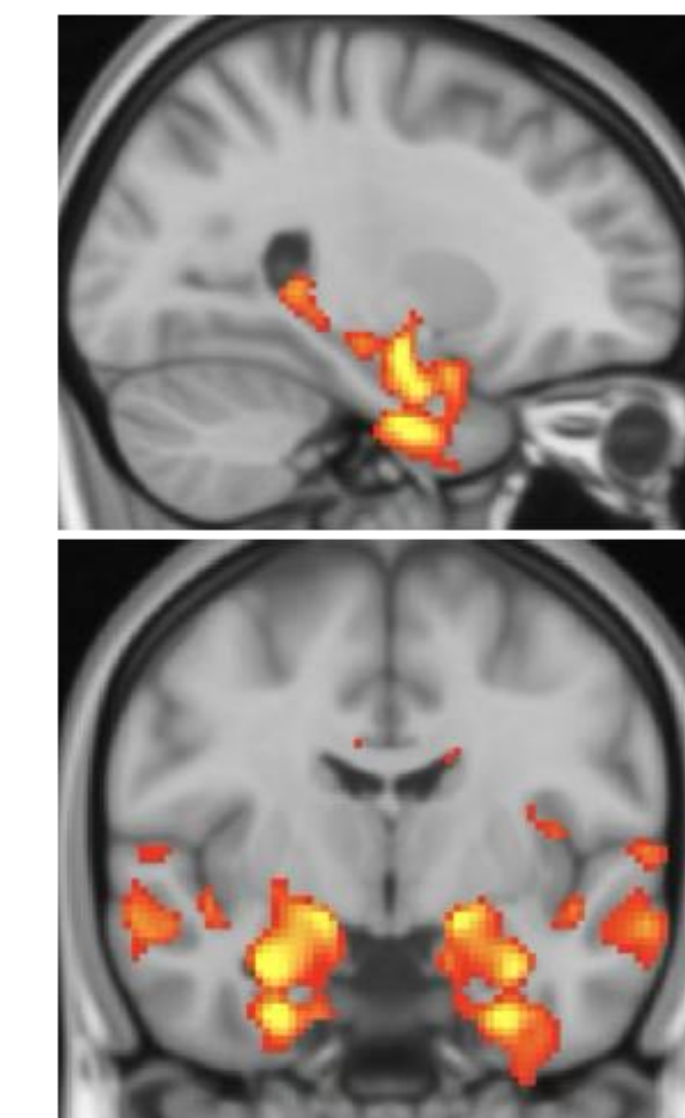
METHODS

- Structural T1-weighted MRI from 85 OBHC patients with a dementia diagnosis and 93 age- and sex-matched cognitively unimpaired controls analysed using a UKB-aligned analysis pipeline optimised for memory clinic^{3,4}.
- VBM was used to generate a **dementia-related spatial map** of grey matter differences between patients and controls. This map was applied within **PANDORA**⁵ (Figure A), which aggregates voxelwise neuroimaging data from 82K UKB participants.
- Using PANDORA's voxelwise regression tool, the OBHC dementia map was projected onto UKB imaging data (10K supervoxel version) to generate an **individualised dementia score** for 82K UKB participants.
- This score was used for validation against dementia status in UKB, **genome-wide association analyses**⁶, and **interrogation of imaging modalities not used for the original map**.

RESULTS

- Projection of the dementia-related map produced a continuous dementia score across the UKB population. **UKB participants with recorded dementia diagnoses showed elevated scores** (Figure B, black dots), supporting the validity of translating clinically derived patterns into population data.
- Genome-wide association analyses using the dementia score as a quantitative phenotype identified **genetic variants associated with dementia-related brain structural changes** (Figure C).
- Application of the dementia score to additional UKB imaging modalities revealed **associated effects beyond grey matter**, including alterations in white matter tracts involved in cognitive pathways, exemplified by associations with diffusion MRI tensor mode (Figure D).

A) Dementia-related map: grey matter differences between 85 OBHC dementia patients vs 93 matched controls.

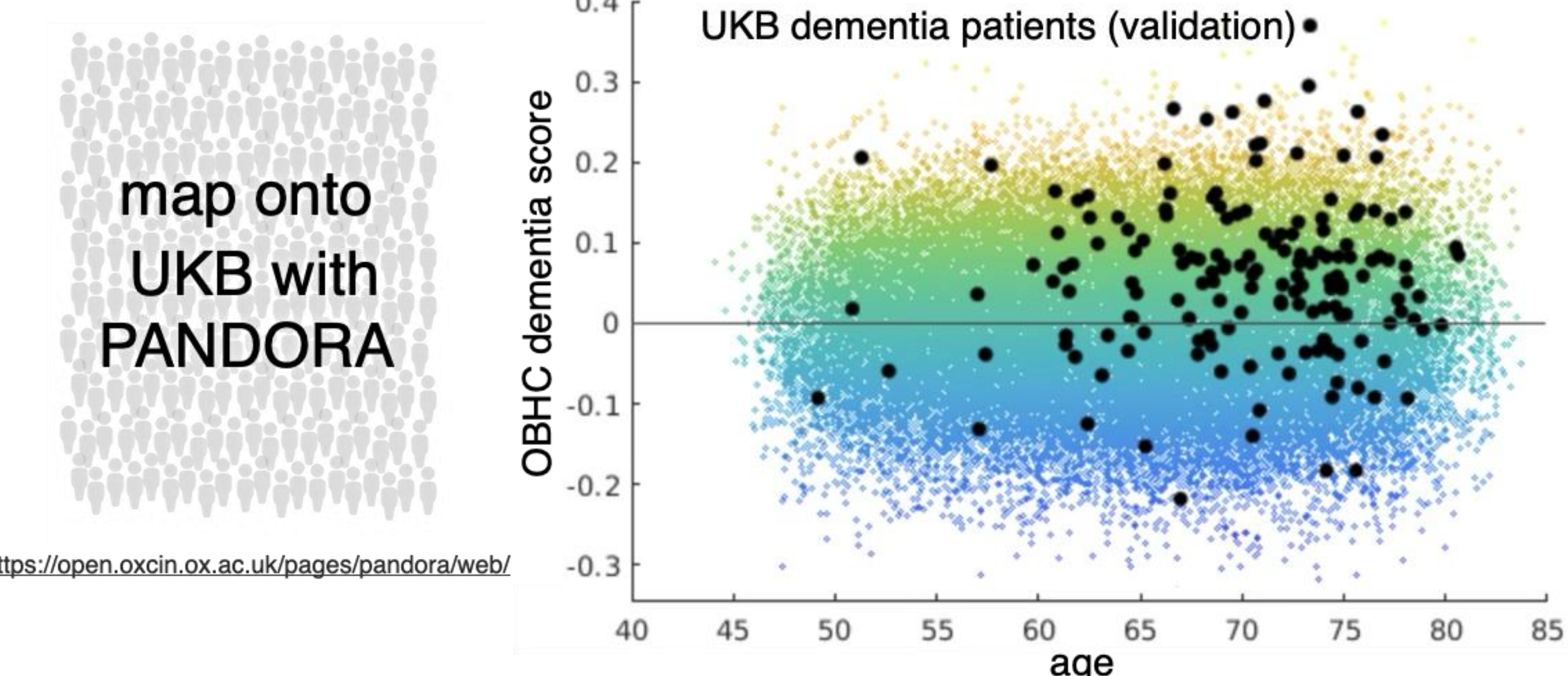


Oxford Brain Health Clinic

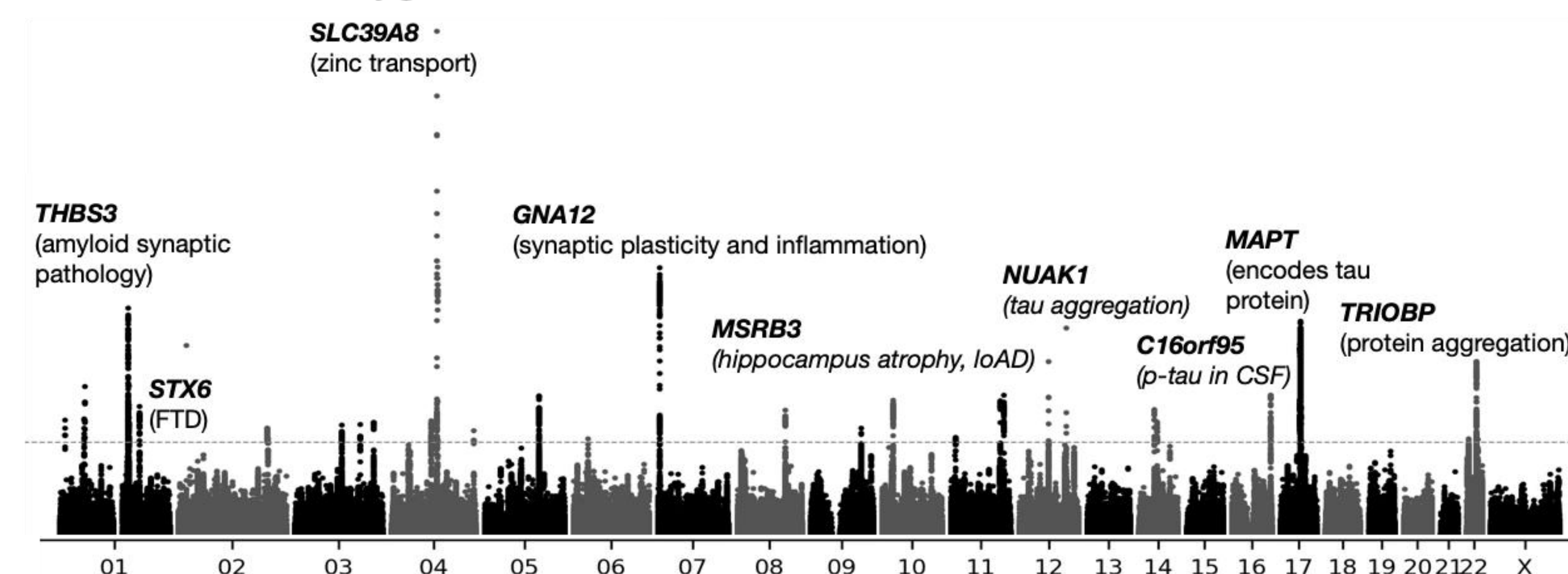


<https://tinyurl.com/OBHC-website>

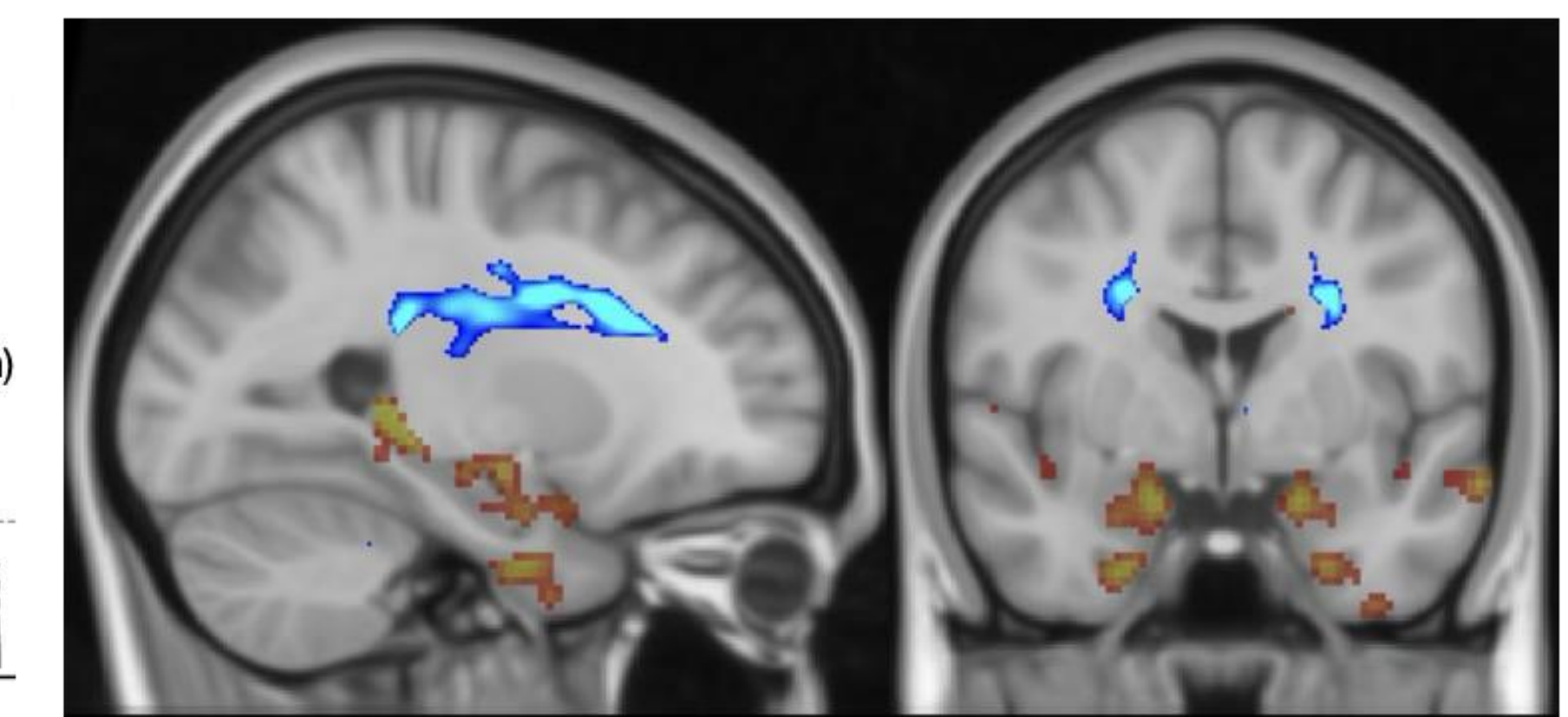
B) PANDORA framework: Structural differences from OBHC are mapped onto UKB to derive a custom dementia score for each UKB participant. As validation, UKB dementia patients (black dots) score highly



C) Genetic associations: GWAS of the OBHC dementia score, which can be turned into a Polygenic Risk Score.



D) Biomarker discovery: Dementia score mapped into other UKB modalities with PANDORA, here showing changes in a long-range white matter tract from Diffusion MRI.



CONCLUSION

By bridging population-scale imaging with real-world memory clinic data through harmonised imaging and PANDORA, dementia-related information from brain scans can be validated, genetically interrogated, and extended to imaging modalities not available for all individuals, enhancing **translational relevance** and **discovery potential**.



References

- ¹Miller et al., 2016, Nature Neuroscience; ²O'Donoghue MC. et al, 2023, BMJ Open (<https://www.psych.ox.ac.uk/research/research-groups/translational-neuroimaging-group/team/oxford-brain-health-clinic>)
- ³Griffanti et al., 2022, Neuroimage Clinical; ⁴Gillis et al., 2025, Human Brain Mapping
- ⁵Abivardi et al., 2026 - <https://doi.org/10.64898/2026.01.05.26343425> (<https://open.oxcin.ox.ac.uk/pages/pandora/web/>)
- ⁶Elliott et al, 2028 Nature