Genetic ancestry and polygenic traits encoded in resting-state fMRI networks

W306

Andre Altmann[1], Sanjay M Sisodiya[2,3], Janaina Mourao-Miranda[4,5]

1 Computational Biology in Imaging and Genetics (COMBINE) Lab, Centre of Medical Image Computing (CMIC), Medical Physics and Biomedical Engineering, UCL, London, UK **2** Department of Clinical and Experimental Epilepsy, UCL Institute of Neurology, London, UK **3** Chalfont Centre for Epilepsy, Bucks, UK **4** Machine Learning and Neuroimaging Lab, Centre of Medical Image Computing (CMIC), Department of Computer Science, UCL, London, UK **5** Max Planck University College London Centre for Computational Psychiatry and Ageing Research, UCL, London, UK

Genetic ancestry can be read from rs-**fMRI networks.** Also increased polygenic scores for education, epilepsy and schizophrenia can be detected.

INTRODUCTION

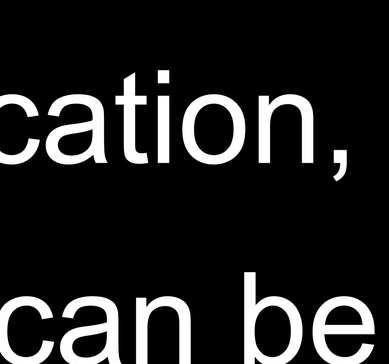
- Previous work showed that genetic ancestry had profound effects on brain morphology [1].
- We hypothesized that we can **predict genetic ancestry from rs-fMRI**
- We hypothesized that we can **predict polygenic scores** for traits such as education attainment and disease such as epilepsy **from rs-fMRI**

METHODS

1. N = 950 subjects from Human Connectome Project (HCP)
2. Partial correlation between ICA components (k=15, 50, 100, 300) [2]
3. Predicted genetic ancestry from genotyping data (SNPweights)
4. Polygenic scores (PGS) computed for (predicted) Central European participants
5. Use elastic-net classifier to predict ancestry (European vs. non-European) and polygenic scores (continuous)
6. Nested 10x5-fold CV repeated 100 times

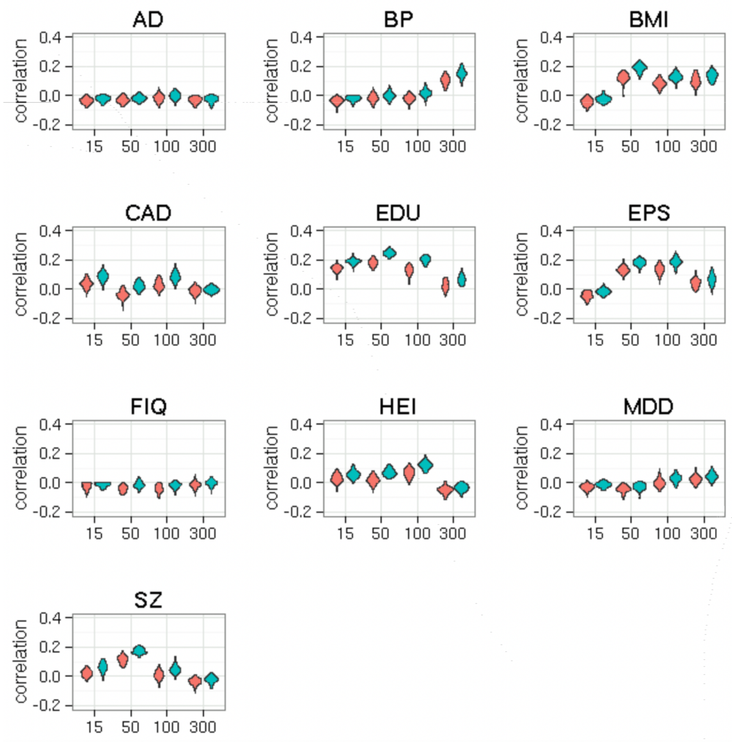
RESULTS

- 651 subjects were estimated to be of European ancestry based on DNA



Averaged ROC curves. Black, red, green and blue lines correspond to models based on 15, 50, 100 and 300 ICAs, respectively.

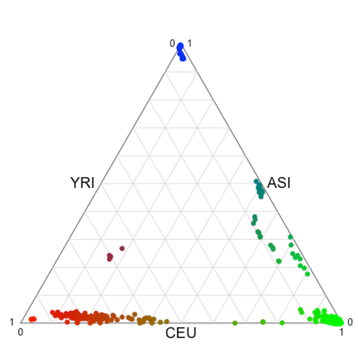
- Some of the PGS could be predicted at reasonable performance (max r 0.25)



Violin plots showing the correlation (r) between PGS derived from GWAS data and predicted from rs-fMRI data at different ROI parcellations (x-axis).

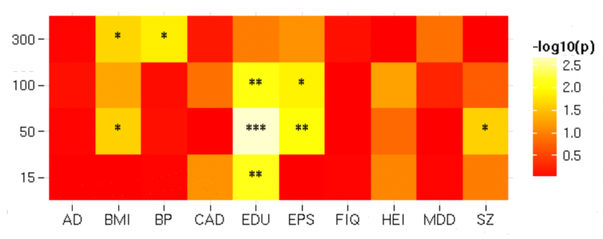
ADDITIONAL INFORMATION

- **Genetic ancestry distribution:**



Triangle plot showing the distribution of the three main genetic ancestries in the HCP dataset: European (CEU), African (YRI), Asian (ASI). The dimension for Native American (NAT) genetic ancestry was omitted from the plot.

- **Traits:** Alzheimer's Disease (AD; PMID: 24162737), Blood Pressure (BP), Body Mass Index (BMI), Coronary Artery Disease (CAD; PMID: 26343387), Education (EDU; PMID: 30038396), Epilepsy (EPS; PMID: 30531953), Fluid Intelligence (FIQ), Height (HEI), Major Depressive Disorder (MDD; PMID: 29700475) and Schizophrenia (SZ; PMID: 25056061).
- **Sampling schemes:** We compared two sampling schemes: a standard random sampling and a 'family-aware' sampling that placed all subjects belonging to a family into the same fold. **Standard nested CV showed consistently higher performance than family-aware nested CV** (largest Wilcox P < 4.3e-12).
- **Permutation test:** Statistical significance of median correlation of the family-aware nested CV result based on 1,000 random (family-aware) samplings of the output vector. Asterisks indicate significance levels: p<0.05 (*), p<0.01 (**) p<0.005(***).



References:

1. Fan, C. C. *et al.* Modeling the 3D Geometry of the Cortical Surface with Genetic Ancestry. *Curr Biol* **25,** 1988–1992 (2015).
2. Smith, S. M. *et al.* Resting-state fMRI in the Human Connectome Project. *Neuroimage* **80,** 144–168 (2013).

Contact: a.altmann@ucl.ac.uk

Follow us on twitter: @CombineLab