Evidence For Bias Of Genetics Ancestry In Resting State Functional MRI

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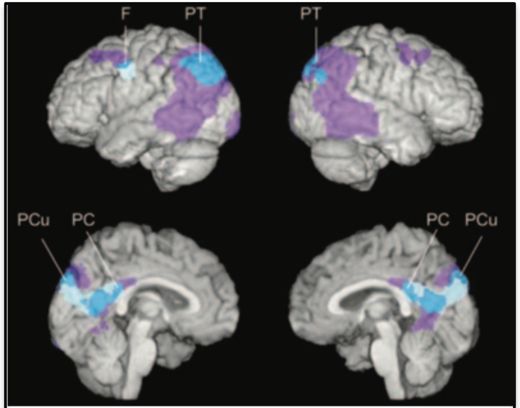
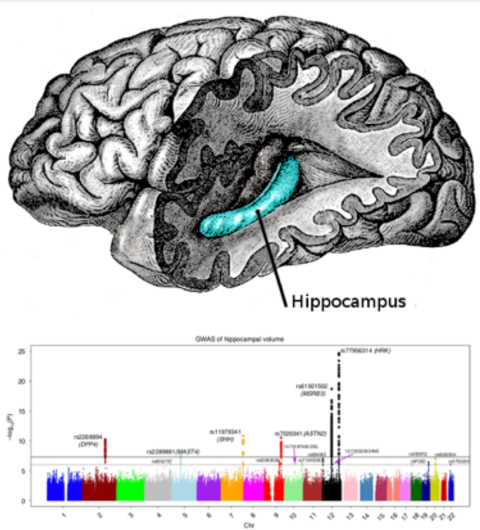
Topics in imaging genetics

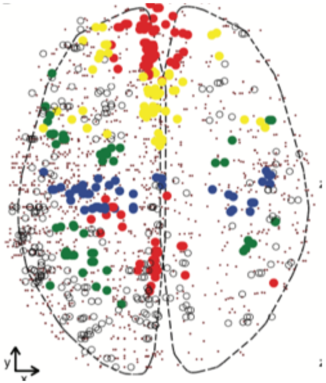


APOE-ε4 effect
on FDG-PET

Reiman et al., 2005, *PNAS* **102,** 8299–8302.



Hibar et al., 2017, *Nat Commun* **8,** 13624.



Which genes contribute
to functional connectivity?

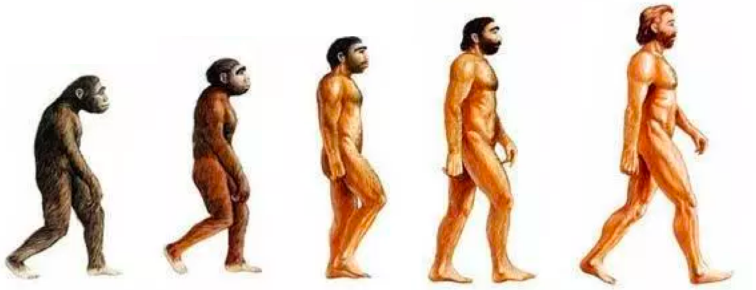
Richiardi et al., 2015, *Science* **348,** 1241-4.

Quantify genetic effects

Discover genetic effects

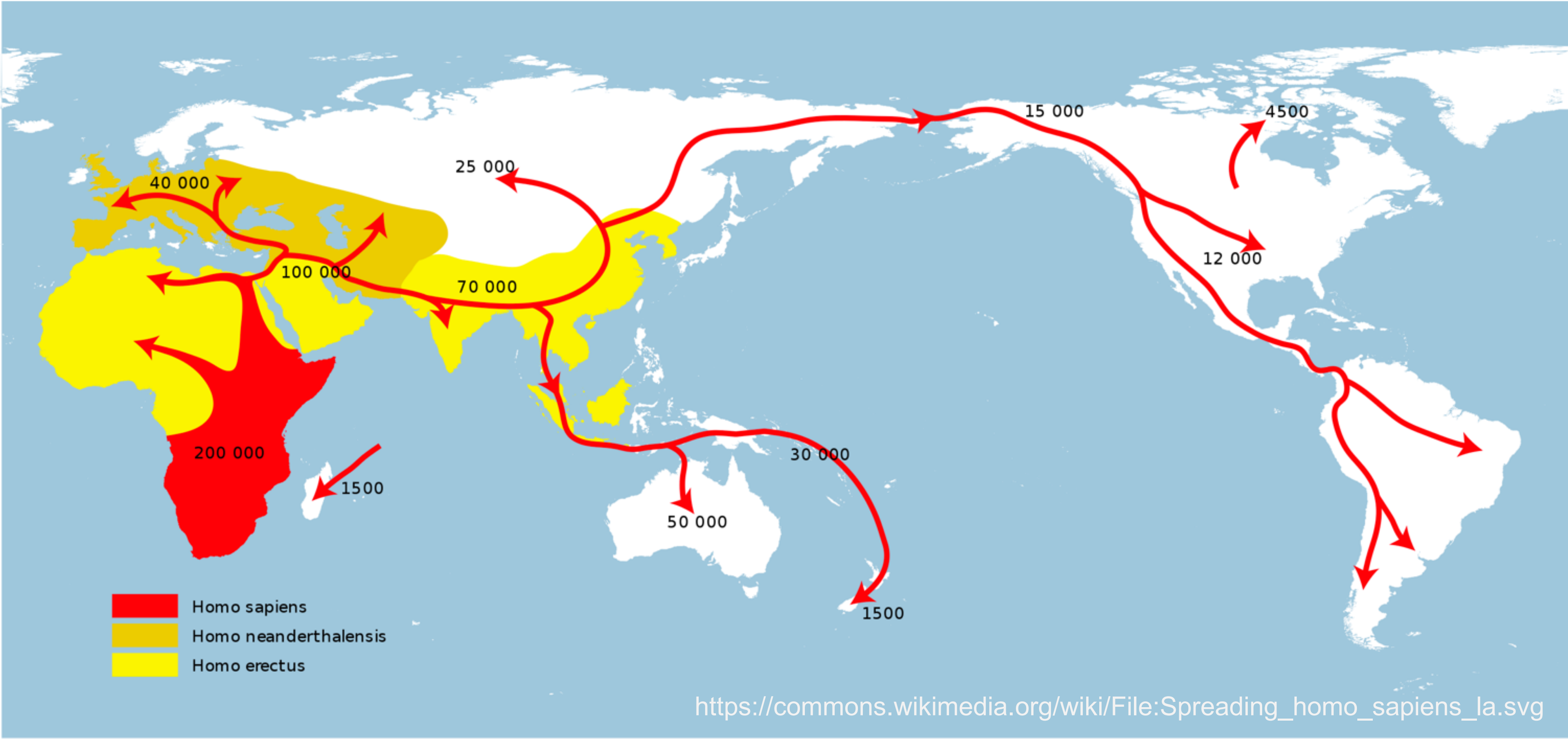
Understand organization

Genetics as 'historic baggage' in precision medicine



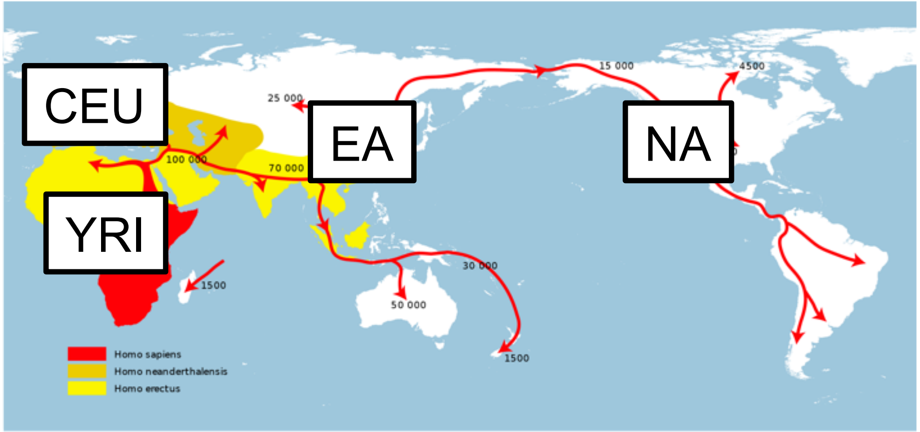
https://www.quora.com/

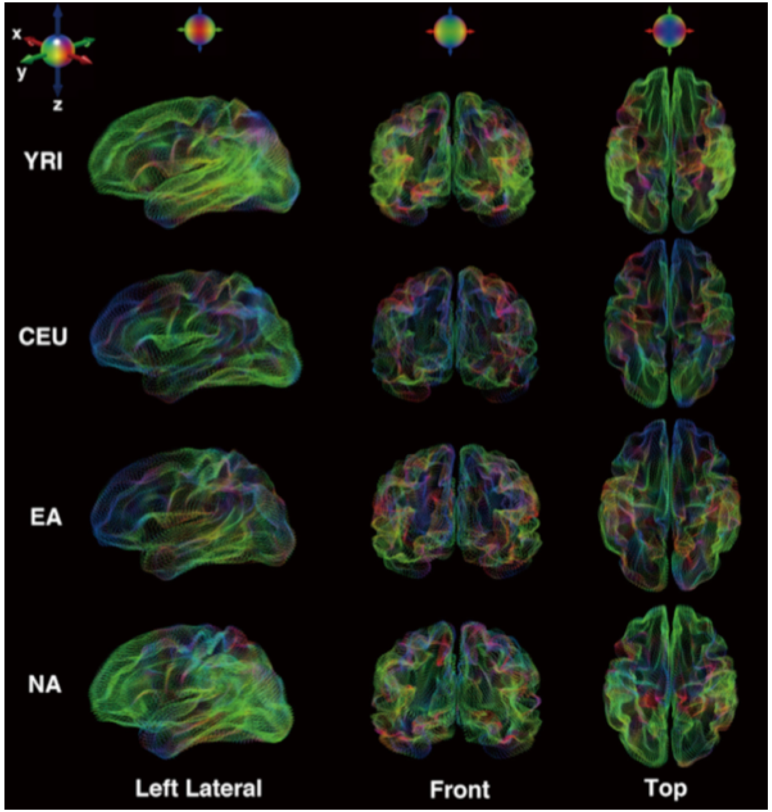
Human migration



https://commons.wikimedia.org/wiki/File:Spreading_homo_sapiens_la.svg

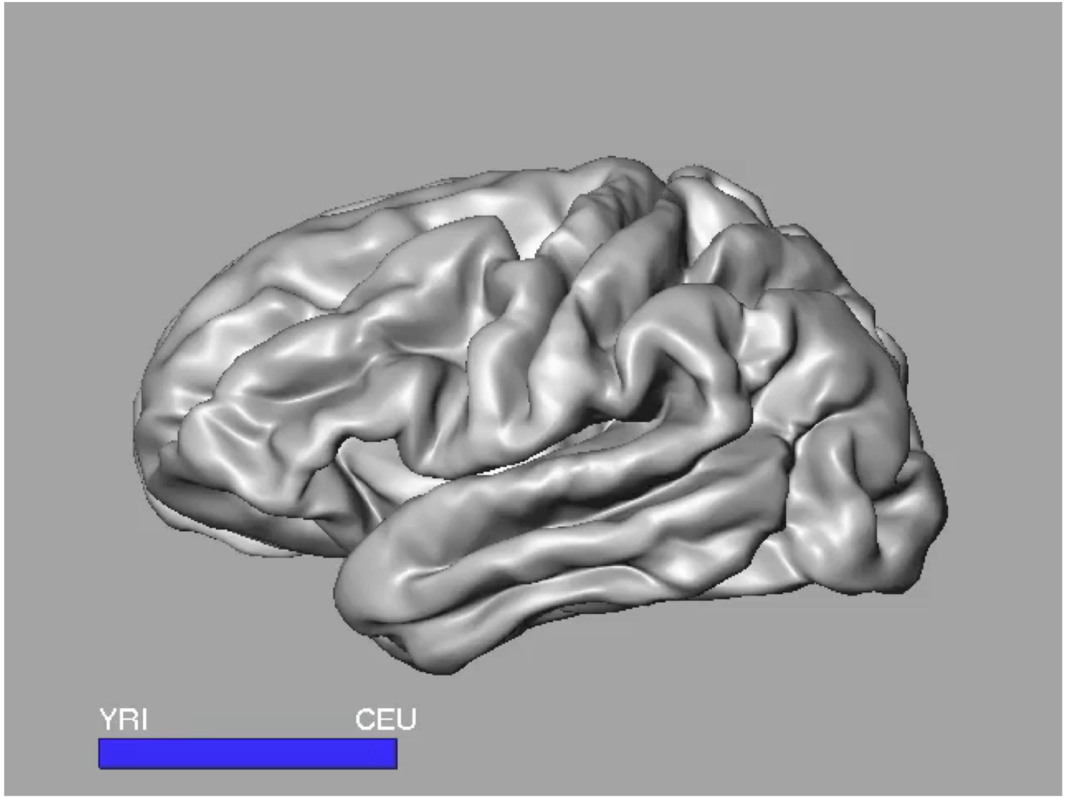
Genetic ancestry and brain morphology





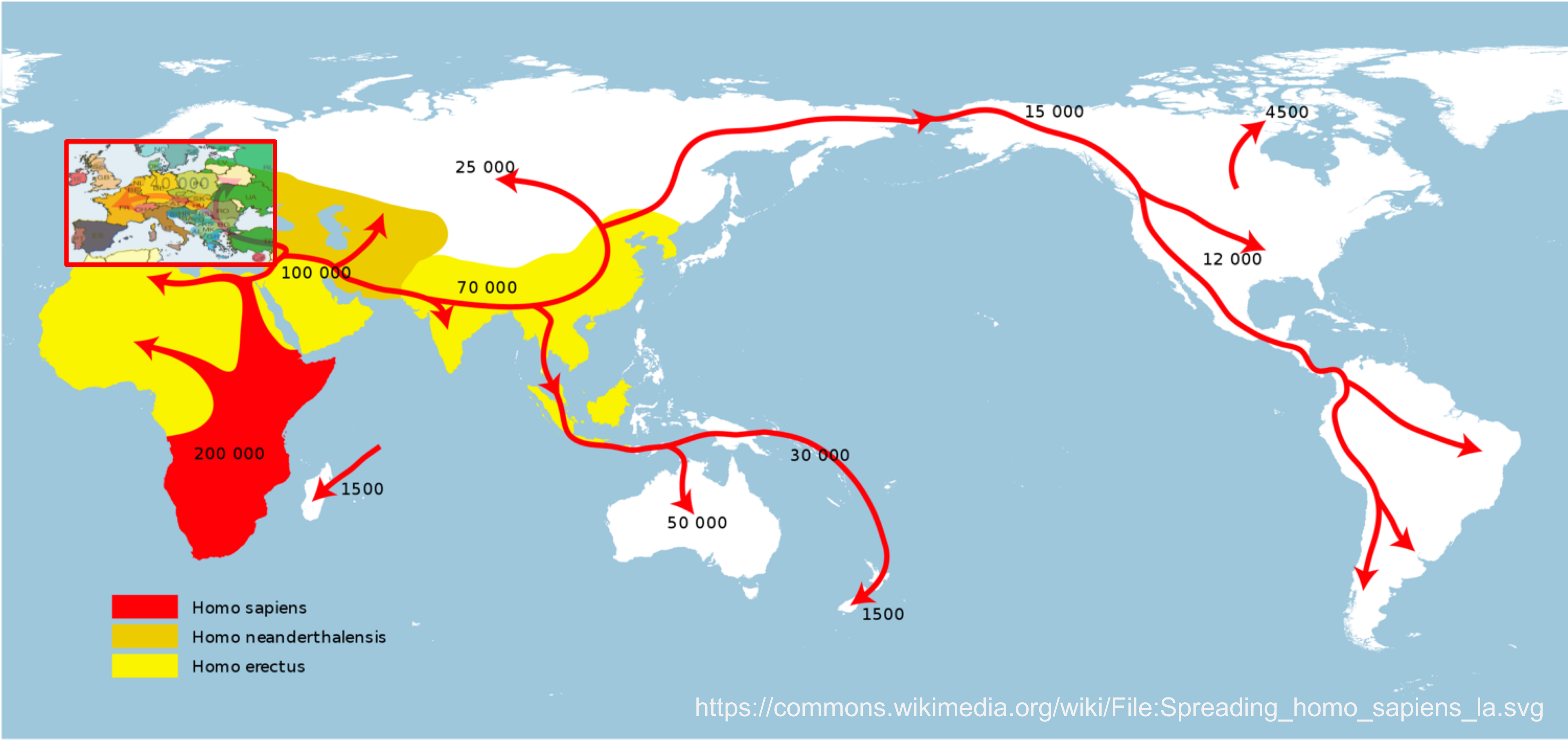
Fan et al., 2015, *Current Biology* 25, 1988–1992

Genetic ancestry and brain morphology



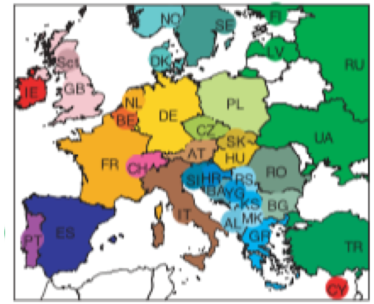
Fan et al., 2015, *Current Biology* 25, 1988–1992

Human migration



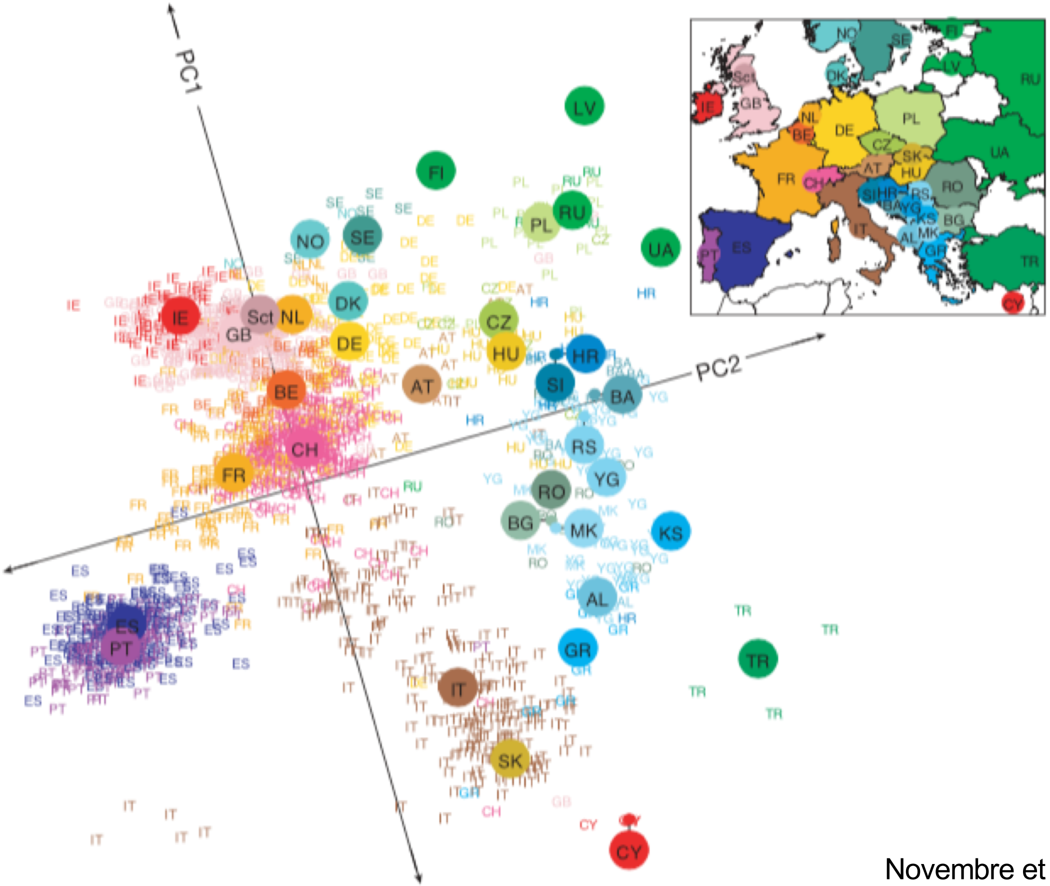
https://commons.wikimedia.org/wiki/File:Spreading_homo_sapiens_la.svg

Genes mirror geography within Europe



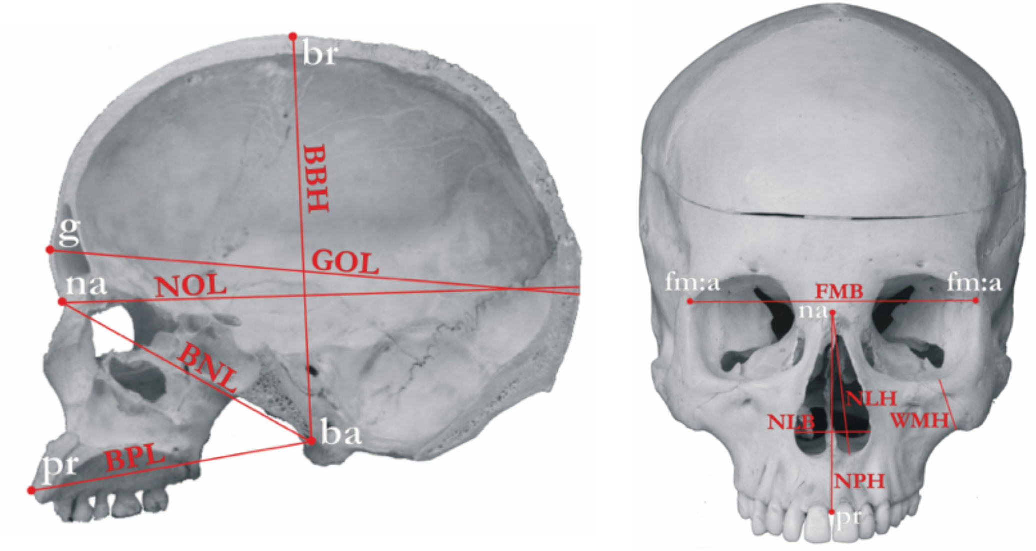
Novembre et al., 2008, *Nature* 456, 98–101

Genes mirror geography within Europe

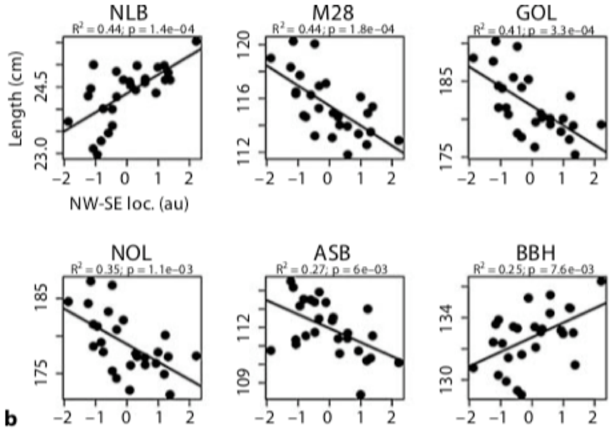


Novembre et al., 2008, *Nature* 456, 98–101

Geography cline of skull and brain morphology in Europe

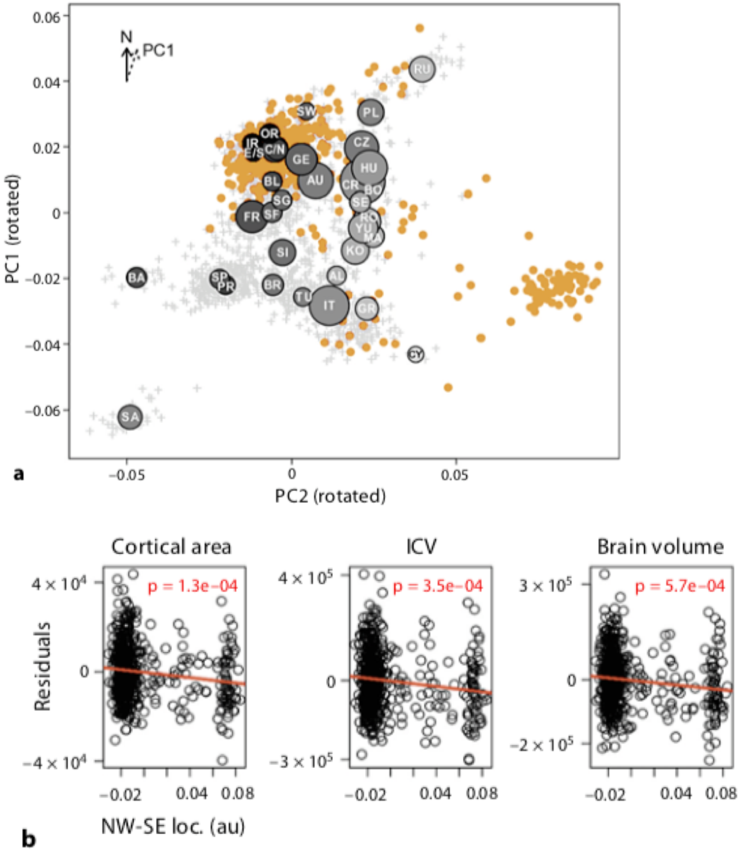


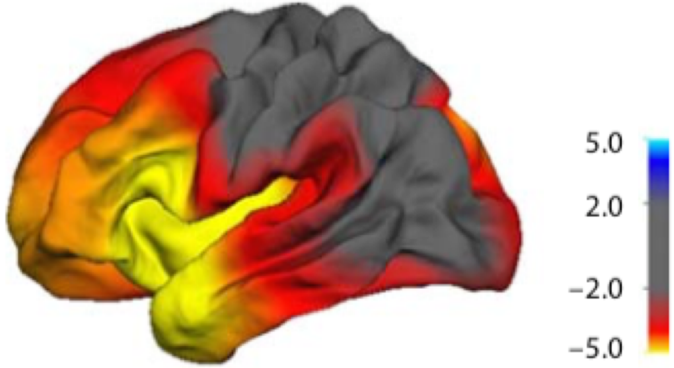
http://osteomics.com/cranExplr/



Bakken et al., 2011, *Hum Hered* 72, 35–44

Geography cline of skull and brain morphology in Europe





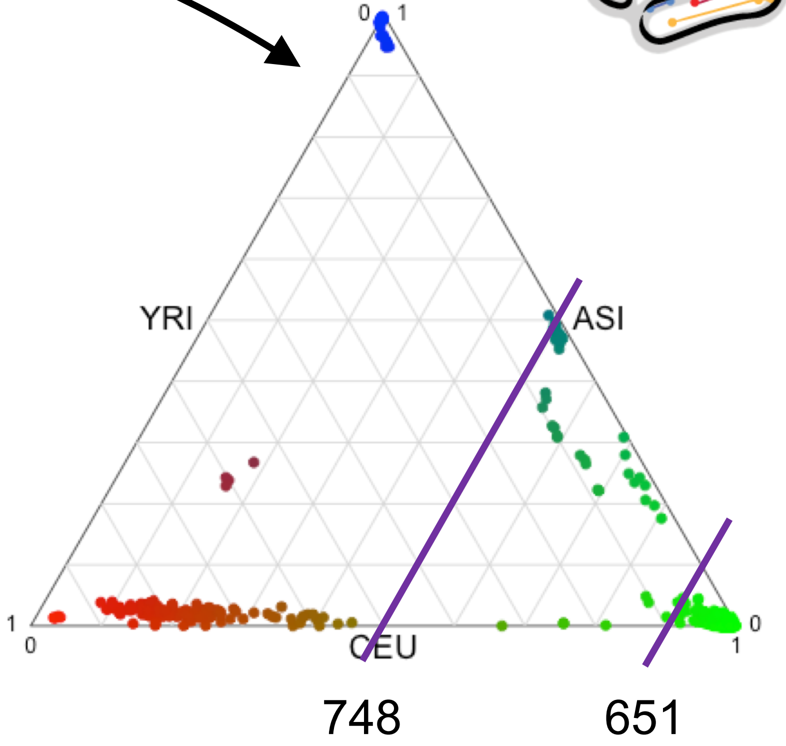
Bakken et al., 2011, *Hum Hered* 72, 35–44

Does this evolutionary bias extend to functional brain measures?

Genetic ancestry in HCP

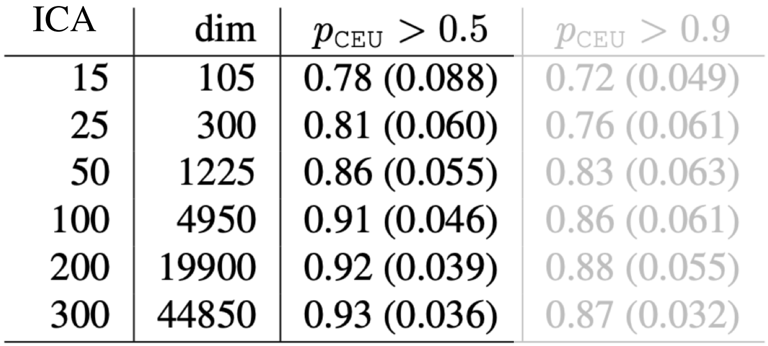
- 950 young adults with
  - Genome-wide SNP data
  - rs-fMRI (1h)

- Aim: classify CEU vs non-CEU
  - ICA: 15 to 300
  - Elastic net classifier
  - Nested CV
    - 10 outer folds (family aware)
    - 5 inner folds (optimize λ)
  - ROC curves

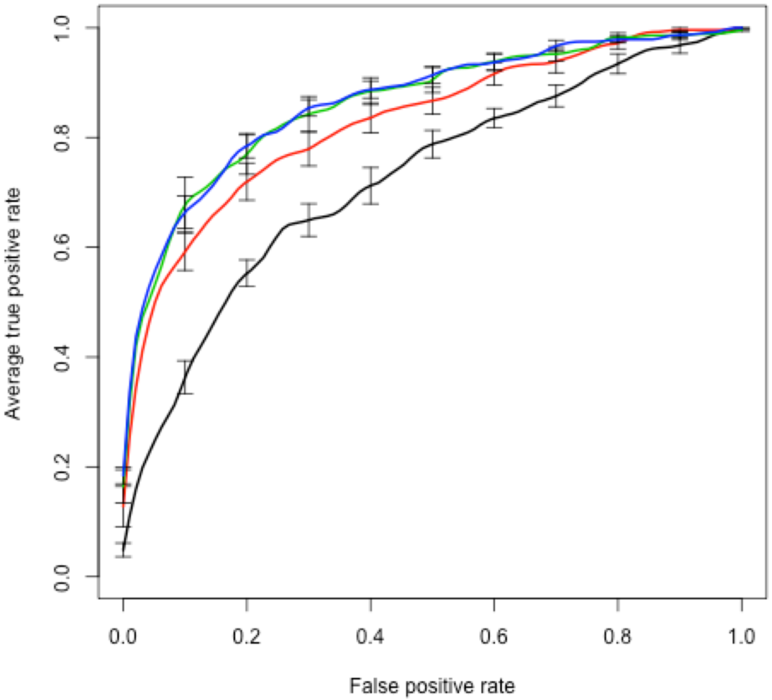


Genetic ancestry in HCP

- Genetic ancestry can be predicted from rs-fMRI
- Works best with ICA ≥ 100
- Works better for 0.5 cutoff

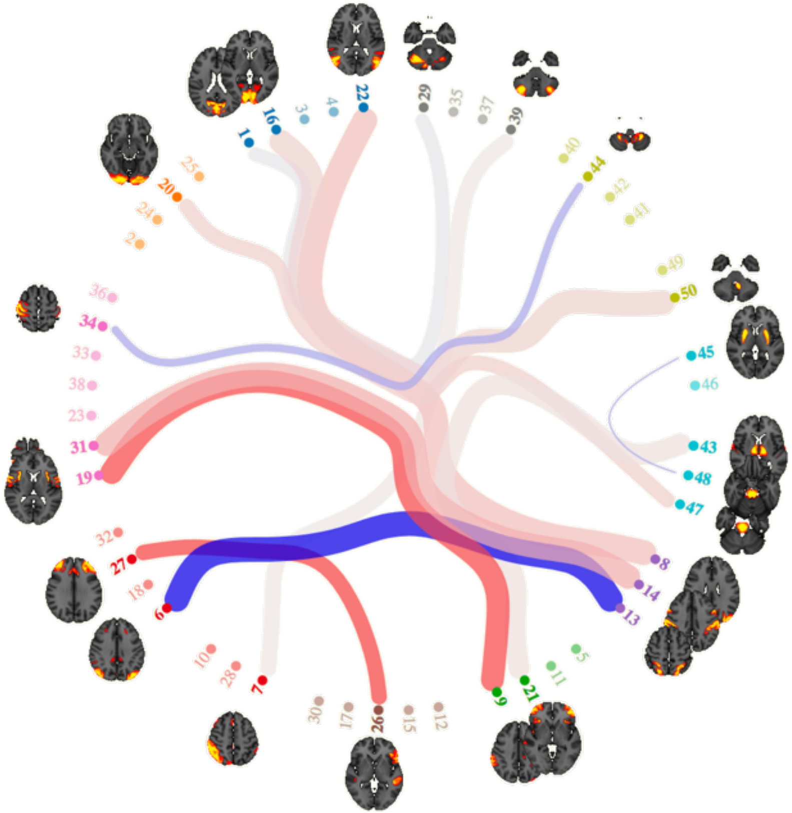


ICA	dim	$p_{\text{CEU}} > 0.5$	$p_{\text{CEU}} > 0.9$
15	105	0.78 (0.088)	0.72 (0.049)
25	300	0.81 (0.060)	0.76 (0.061)
50	1225	0.86 (0.055)	0.83 (0.063)
100	4950	0.91 (0.046)	0.86 (0.061)
200	19900	0.92 (0.039)	0.88 (0.055)
300	44850	0.93 (0.036)	0.87 (0.032)



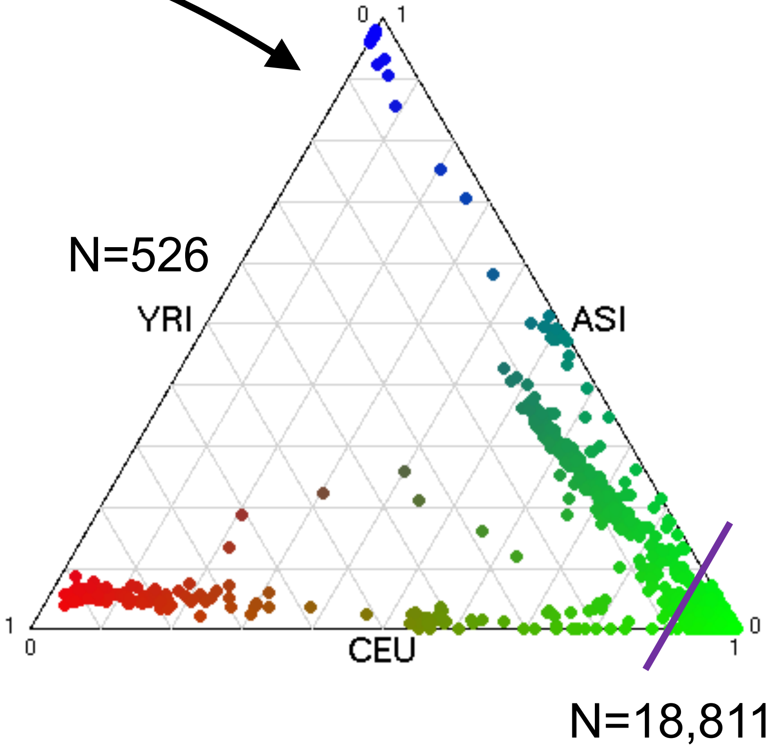
0.5 cutoff; ICA 15, 50, 100, 300

Which connections are important?



Genetic ancestry in UK Biobank

- 19,337 adults with
  - Genome-wide SNP data
  - rs-fMRI (6 min)
- Aim: classify CEU vs non-CEU
  - ICA: “25” and “100” (21 and 55)
  - Elastic net classifier
  - 100 bootstraps, subsample CEU (3:1)
  - Nested CV
    - 10 outer folds
    - 5 inner folds (optimize λ)
  - AUC



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ICA 25
- AUC 0.72

ICA100
- AUC 0.81

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Conclusions

- Genetic ancestry influences skull and brain morphology
  - Interpretation in precision medicine
- Genetic ancestry can be predicted from rs-fMRI
  - Presumably effects from brain normalization
- Consider to adjust brain imaging studies for genetic ancestry