From the complexity of brain organization to challenges in brain-behaviour mapping

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Brain & Behaviour

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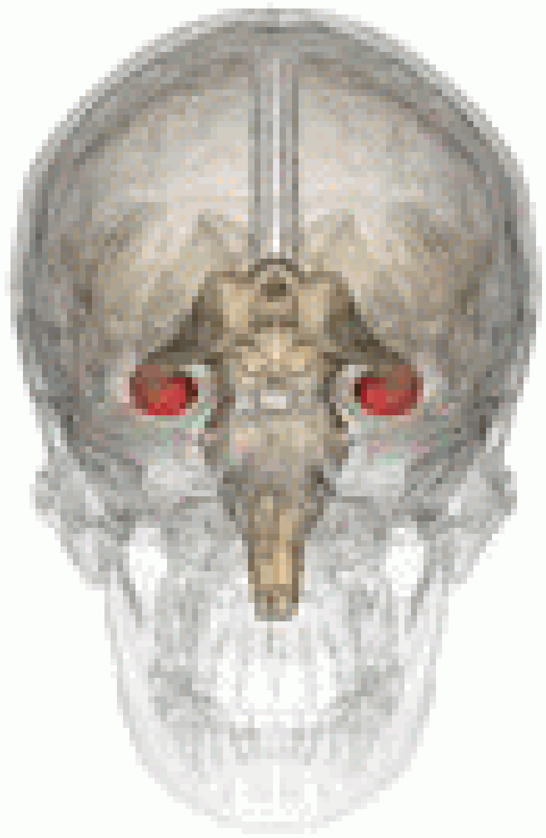
Understanding brain organization



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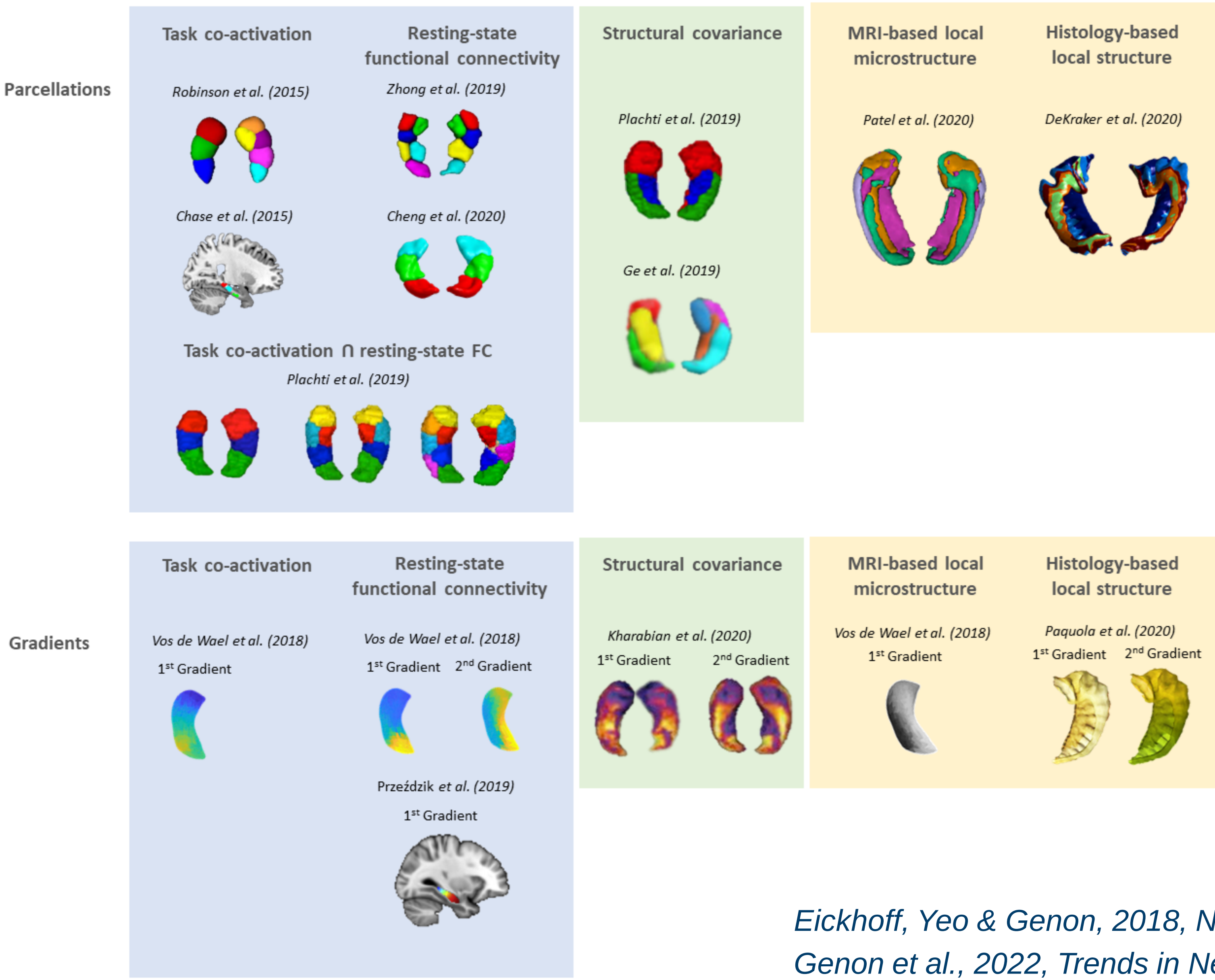
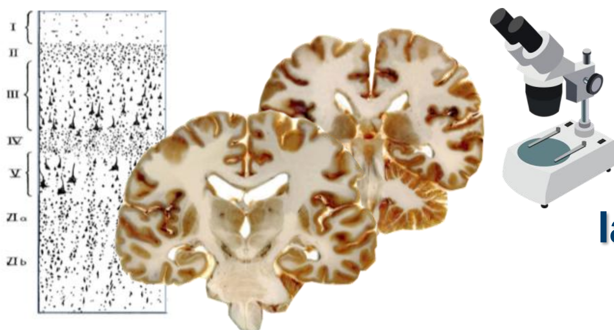
The complexity of brain organization

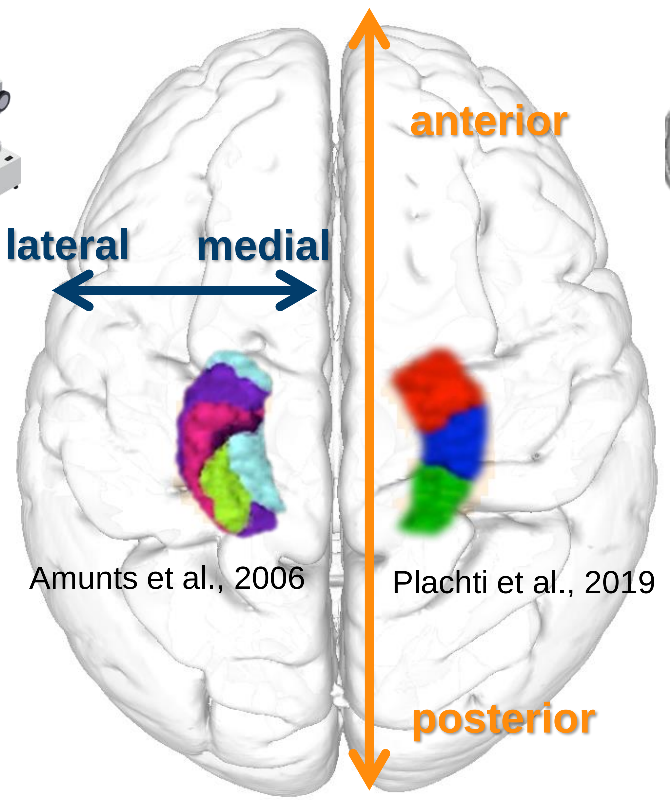


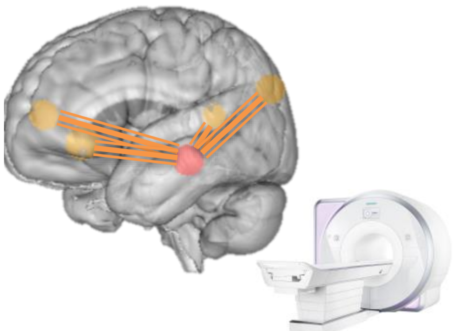
Eickhoff, Yeo & Genon, 2018, Nat. Rev. Neurosci.
Genon et al., 2022, Trends in Neuroscience

Local microstructure/processing VS large-scale functional integration



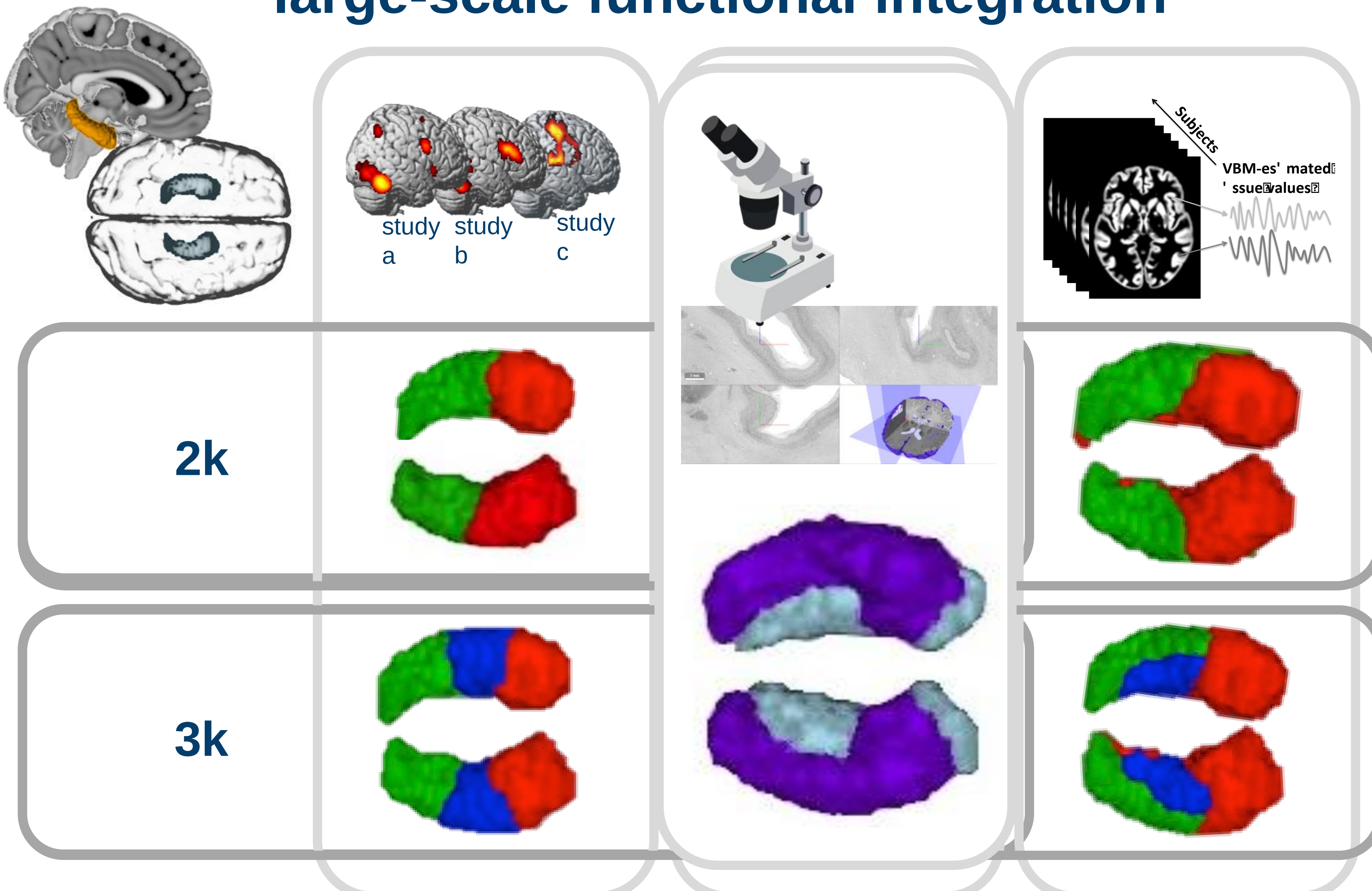
Local microstructure





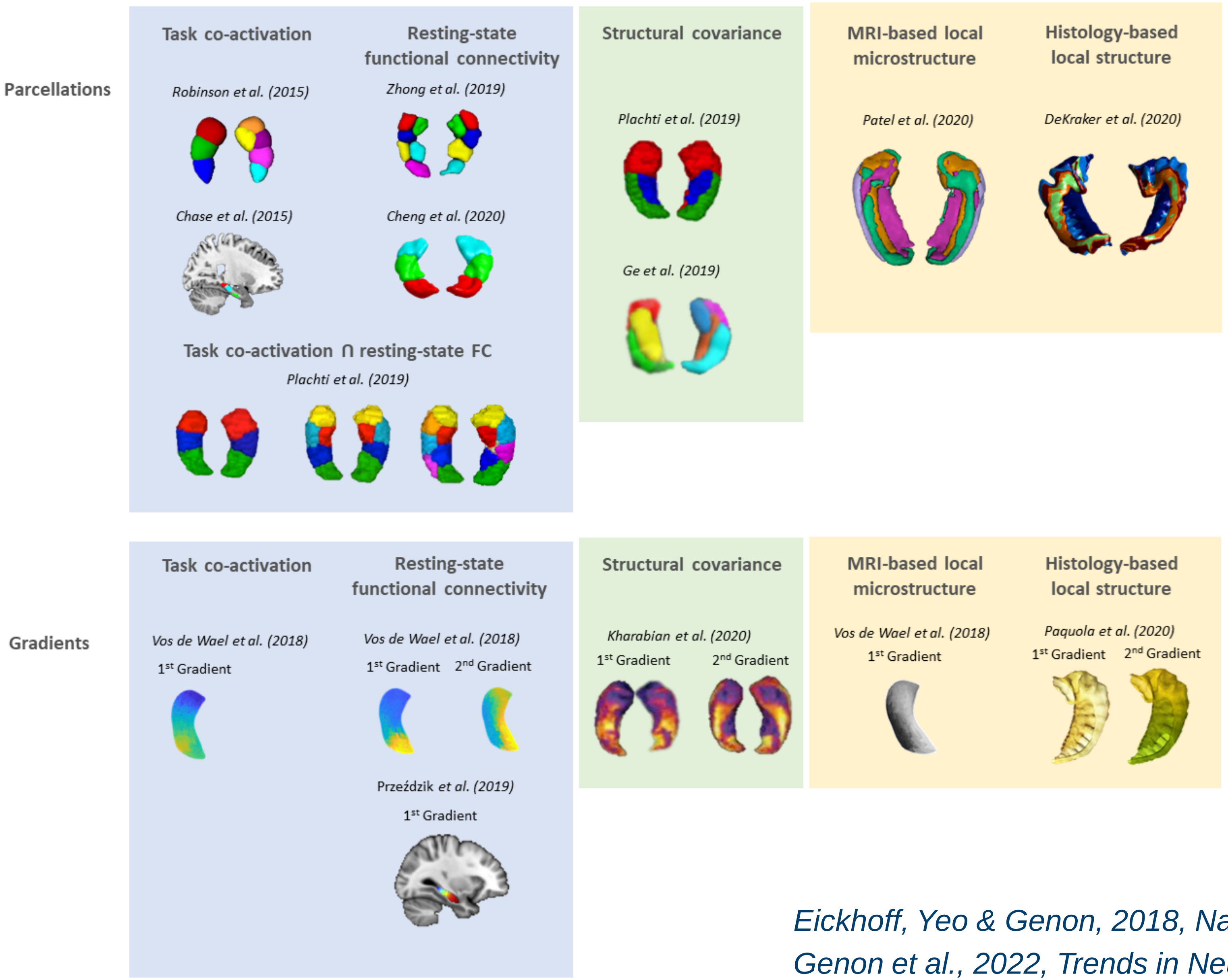
Connectivity markers

Local microstructure and large-scale functional integration



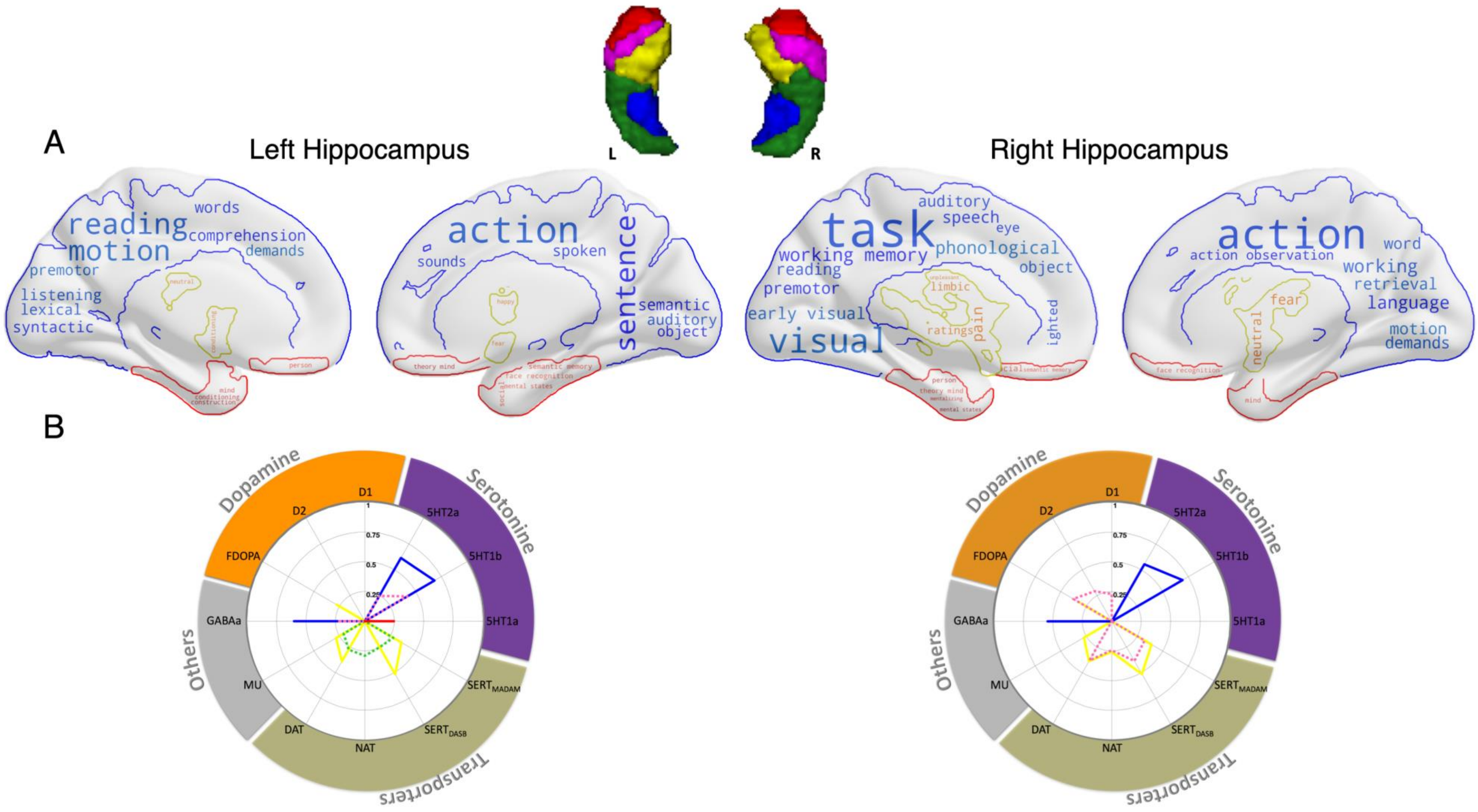
Plachti,…& Genon, 2019, Cerebral Cortex; Plachti,… & Genon, 2020, Brain

The complexity of brain organization



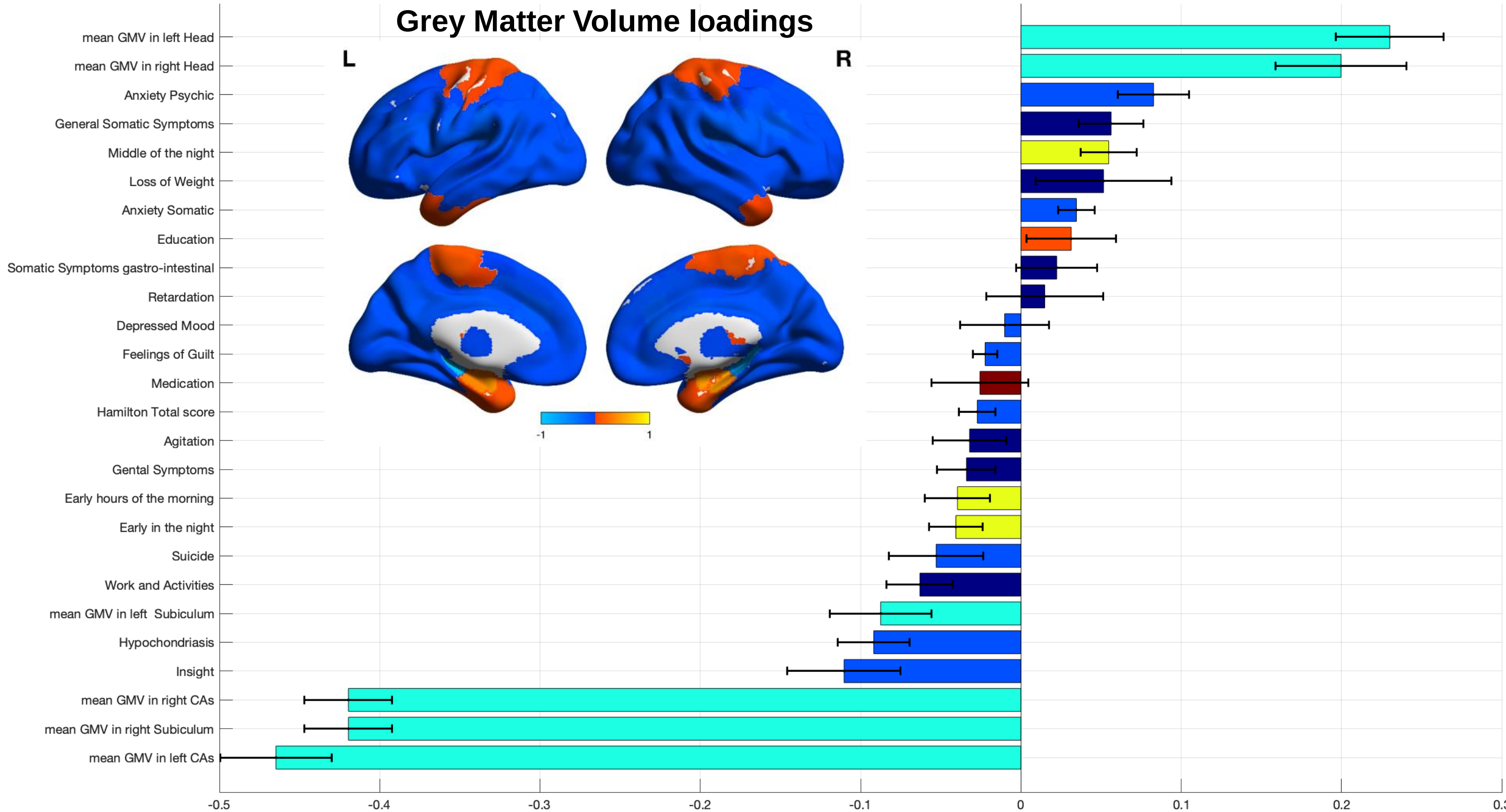
Eickhoff, Yeo & Genon, 2018, Nat. Rev. Neurosci.
Genon et al., 2022, Trends in Neuroscience

The complexity of brain organization: Hippocampal metabolic networks



Maleki Balajoo,…& Genon, under review

Hippocampal structural covariance networks in Major Depressive Disorders



Poster WTh591

Relating behavior to brain structure

OPINION

2011

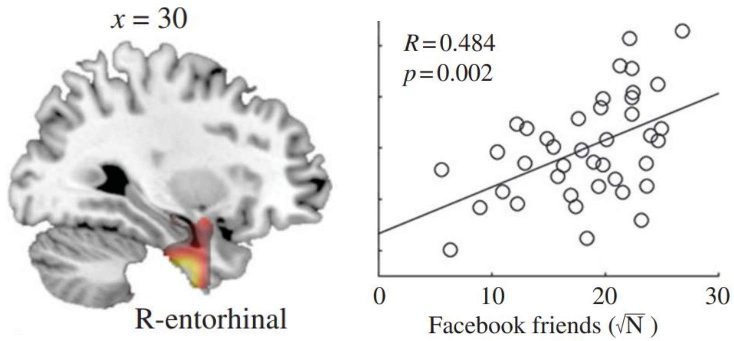
The structural basis of inter-individual differences in human behaviour and cognition

Ryota Kanai and Geraint Rees

Abstract | Inter-individual variability in perception, thought and action is frequently treated as a source of 'noise' in scientific investigations of the neural mechanisms that underlie these processes, and discarded by averaging data from a group of participants. However, recent MRI studies in the human brain show that inter-individual variability in a wide range of basic and higher cognitive functions — including perception, motor control, memory, aspects of consciousness and the ability to introspect — can be predicted from the local structure of grey and white matter as assessed by voxel-based morphometry or diffusion tensor imaging. We propose that inter-individual differences can be used as a source of information to link human behaviour and cognition to brain anatomy.

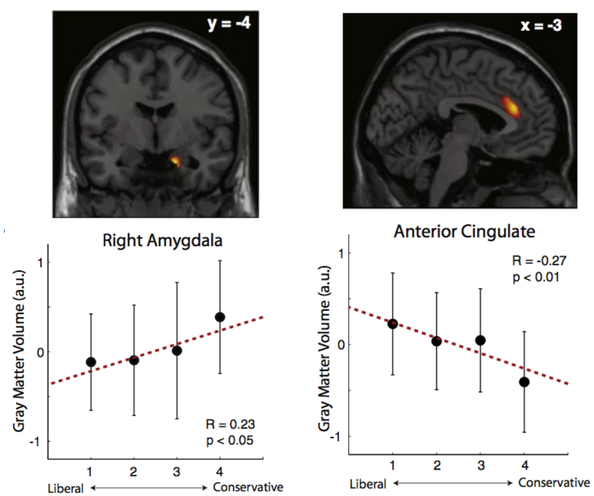
Relating behavior to brain structure

Number of facebook friends relates to local grey matter



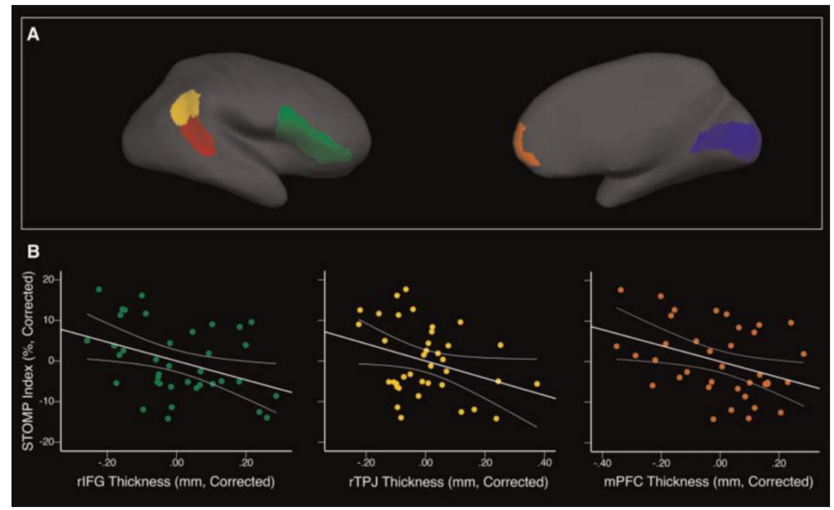
Kanai et al., 2012

Political orientation relates to local grey matter



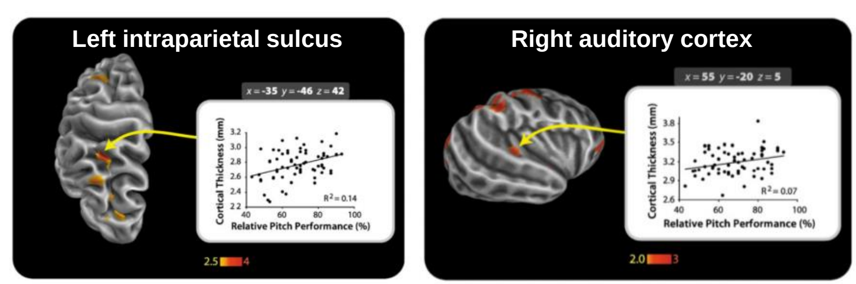
Kanai et al., 2011

Theory of mind performance relates to local cortical thickness



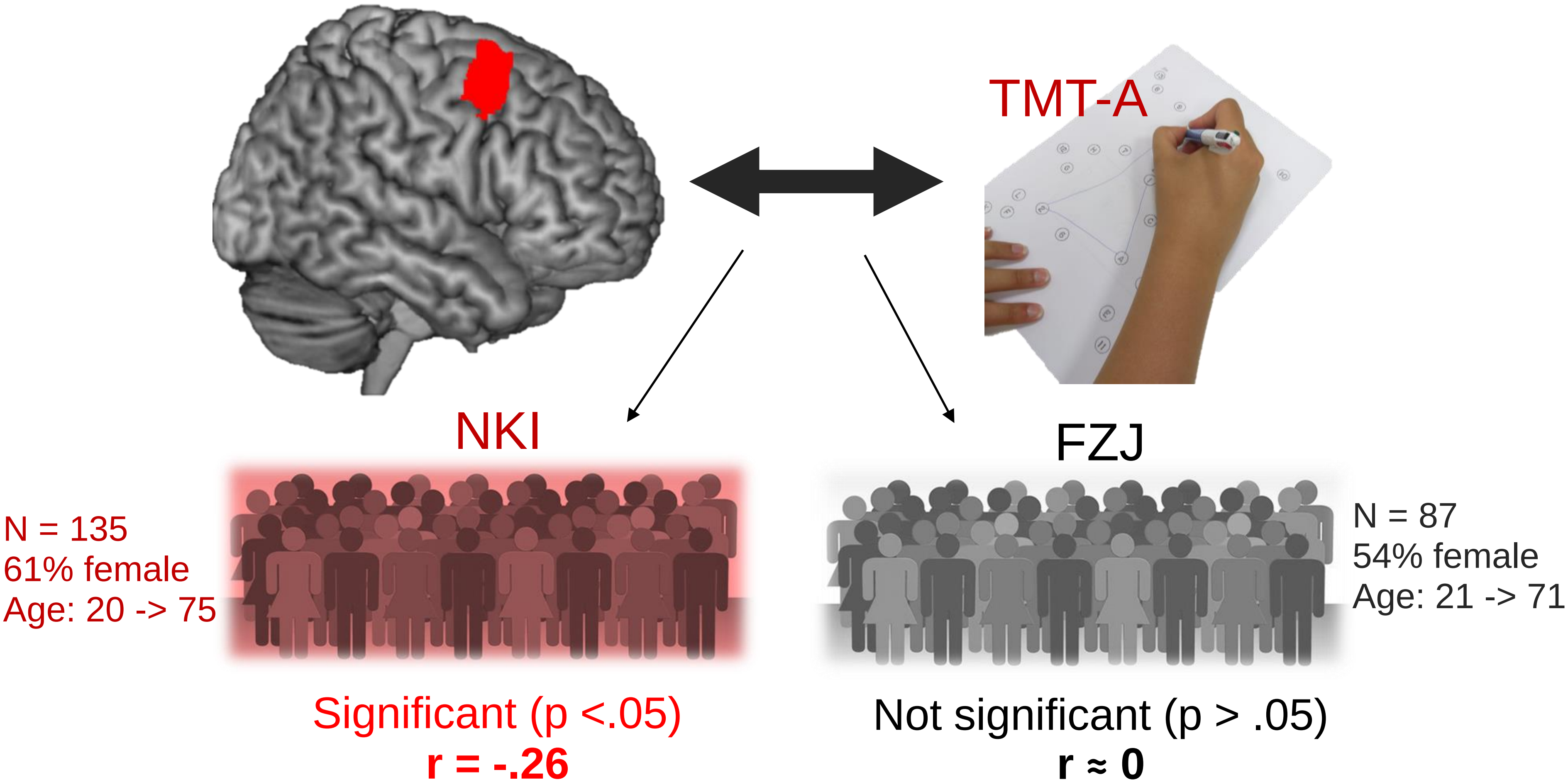
Rice & Redcay, 2015

Music pitch performance relates to local cortical thickness



Foster & Zatorre, 2012

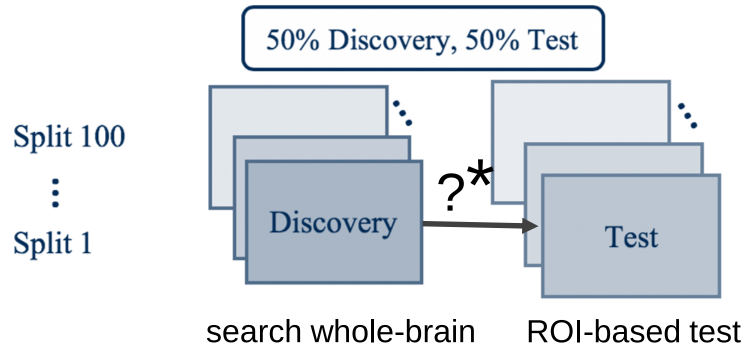
Mapping behavior to local brain morphometry: the replication crisis



Genon et al., 2017, NeuroImage

Which replicability for local GMV-behavior associations ?

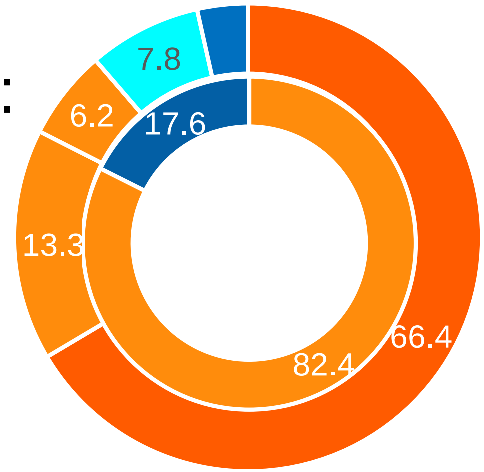
ROI-based confirmatory:



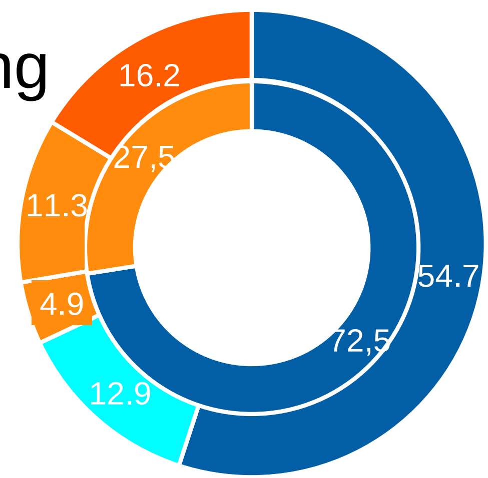
* Replication indexes:

Sign + p < .05	Replicate Not replicate
Bayes factor	Moderate-strong evidence H1 Anecdotal evidence H1 Anecdotal evidence H0 Moderate-strong evidence H0

Healthy adults cohort: (n = 466) Perceptual IQ



Clinical dataset: (n = 371) Verbal learning

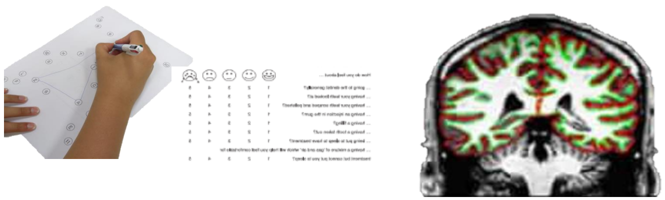


Kharabian,…& Genon, 2019, eLife

Which replicability for local CT-behavior associations ?

Young healthy adults N = 1206

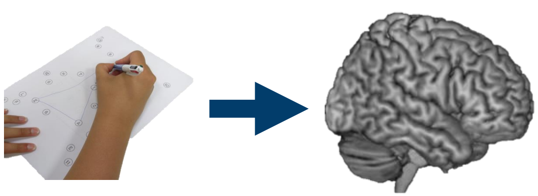
34 behavioral measures CT (Freesurfer)



Including composite score

Exploratory: spatial consistency

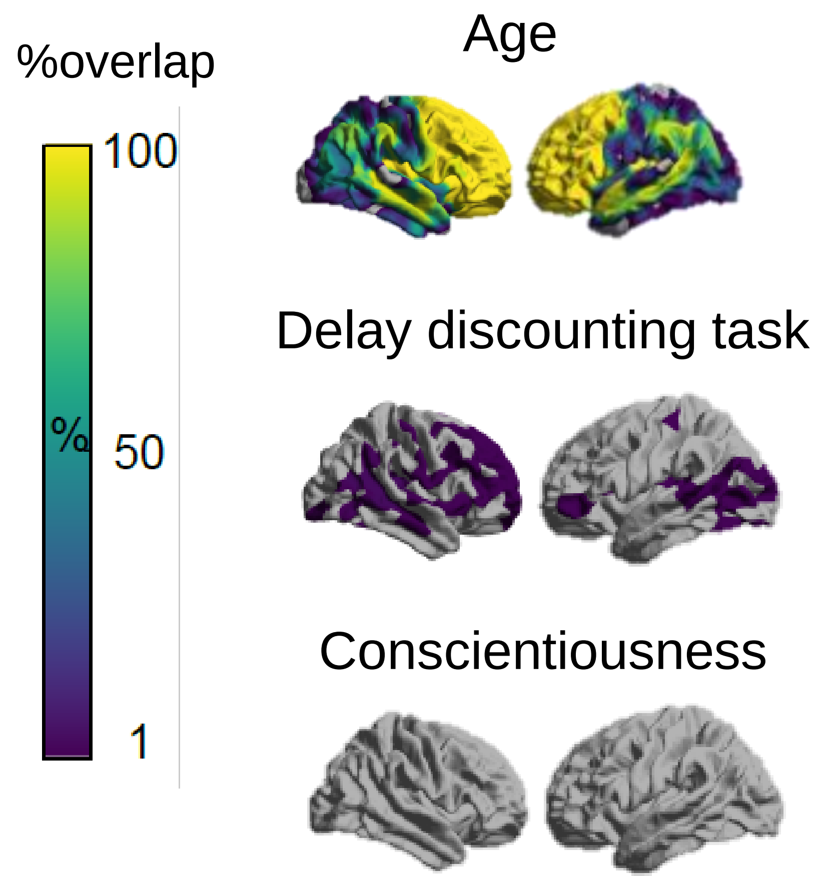
Search whole-brain, 100 split-half



<u>Benchmarks:</u>

Heathy adults data: <u>Age</u>

Spatial consistency:



Kharabian,…& Genon, 2020, BioRxiv

Relating brain structure to behavior

PERSPECTIVES 2022

Linking interindividual variability in brain structure to behaviour

Sarah Genon, Simon B. Eickhoff and Shahrzad Kharabian

- Large Datasets
- Confounds modelling
- Multivariate analyses
- Cross-validation scheme
- Out-of-cohort replicability

Relating brain structure to behavior

Brain structural data:
- *Cortical Thickness* (CT)
- *Surface Area* (SA)
- *Grey Matter Volume* (GMV)

Regularized Canonical Correlation Analysis (RCCA)

Behavioural data:
- *Alertness*
- *Cognition*
- *Emotion*

Machine Learning Framework: **Multiple Holdouts**

Within-dataset generalizability

1) Train set
2) Test
3) Optimisation set
4) Hold-out set

Code available at: https://github.com/anaston/cca_pls_toolkit

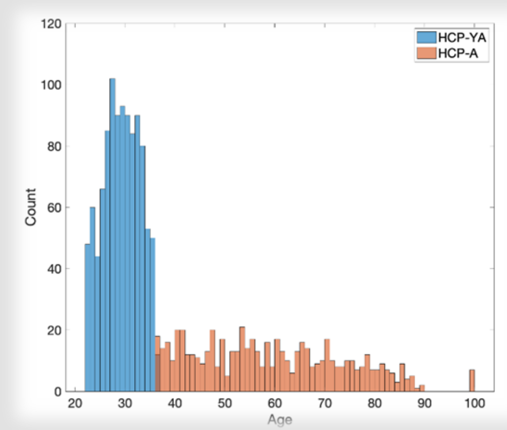
(Mihalik et al., 2020, Monteiro et al., 2016)

Cross-dataset replicability

Large datasets with **similar** brain and **behavioral measurments**

HCP young adults

HCP aging

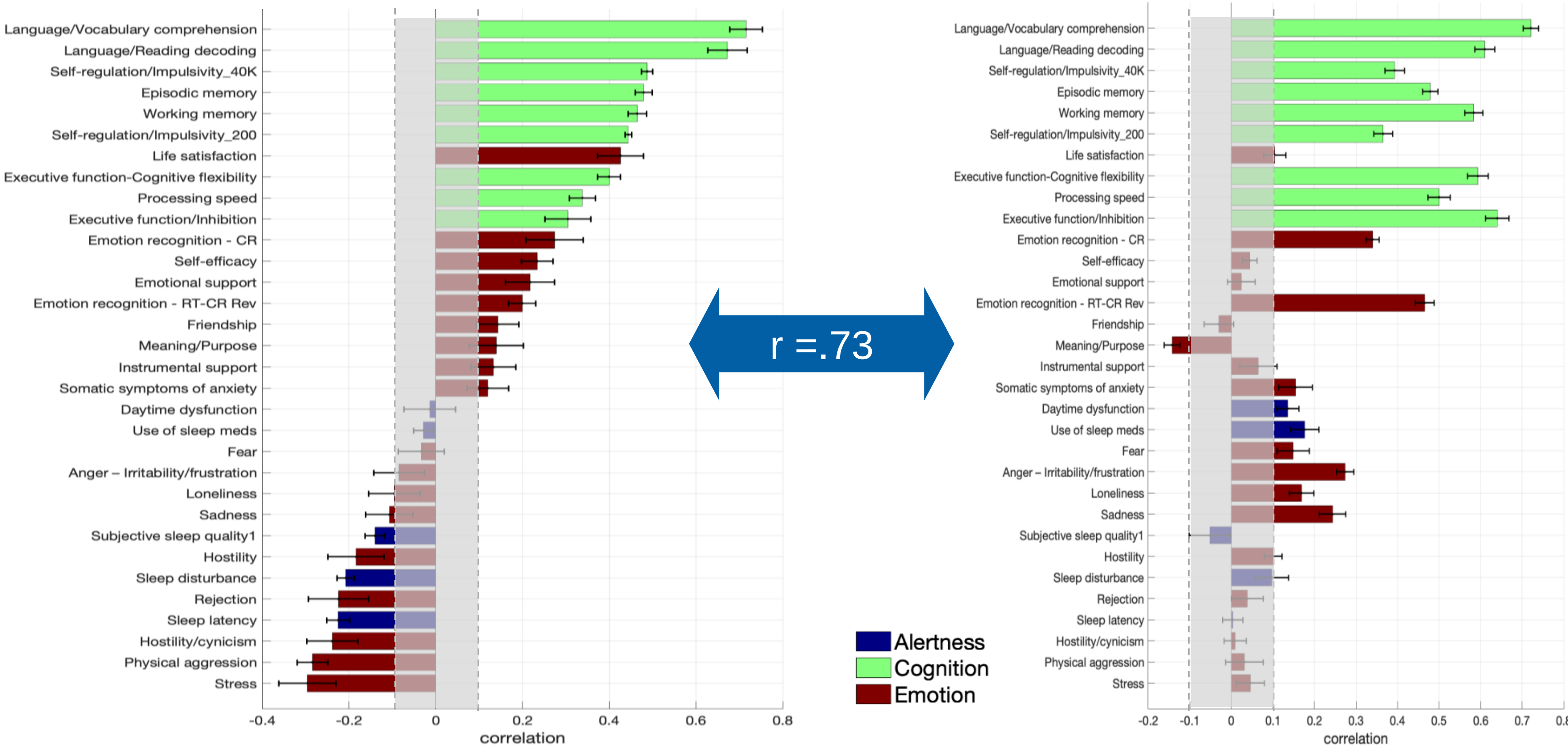


Nicolaisen-Sobesky,…,& Genon, under review

Relating brain structure to behavior

HCP young adults

HCP aging

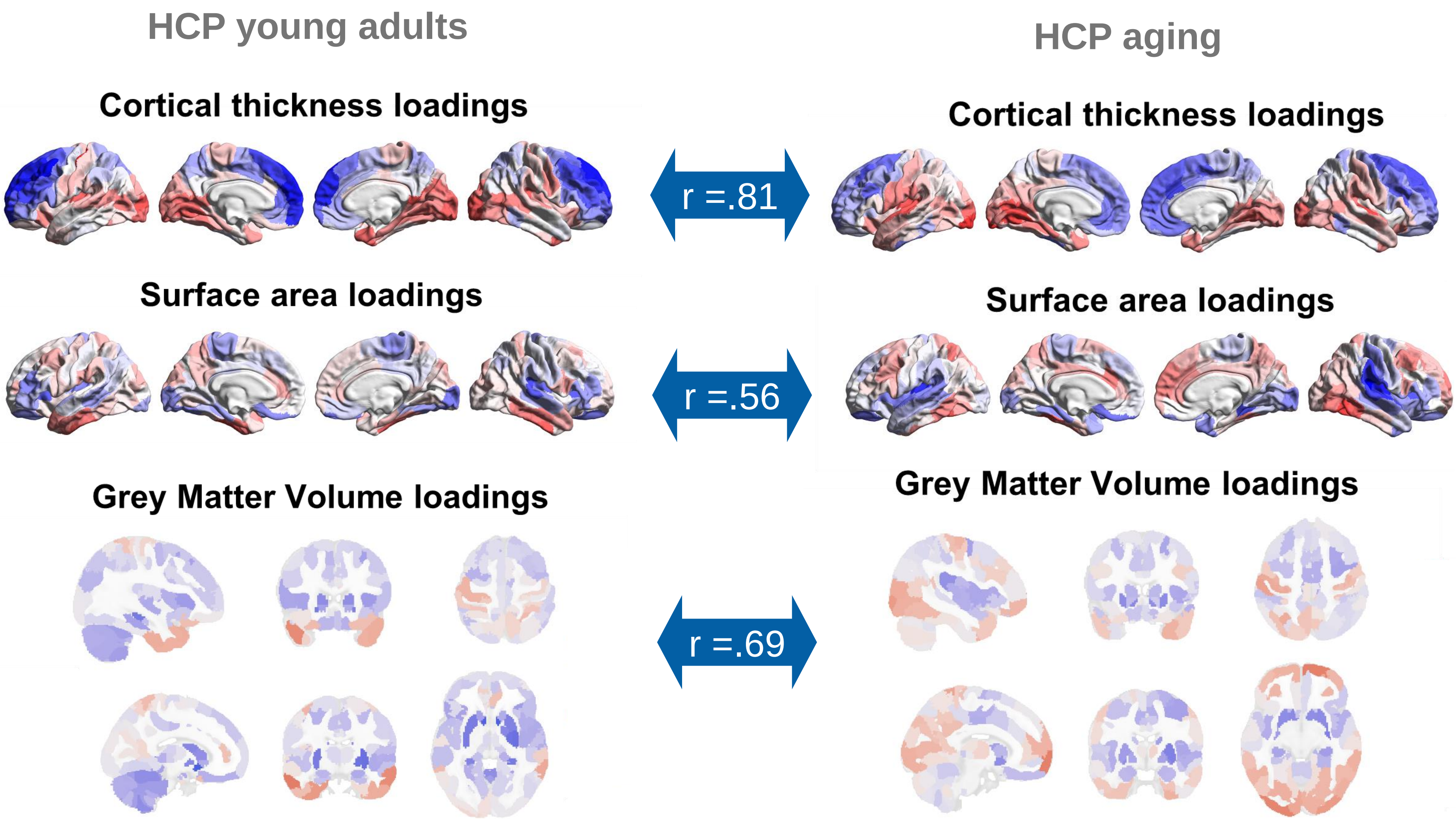


Member of the Helmholtz Association

Nicolaisen-Sobesky, …,& Genon, under review

Poster WTh595

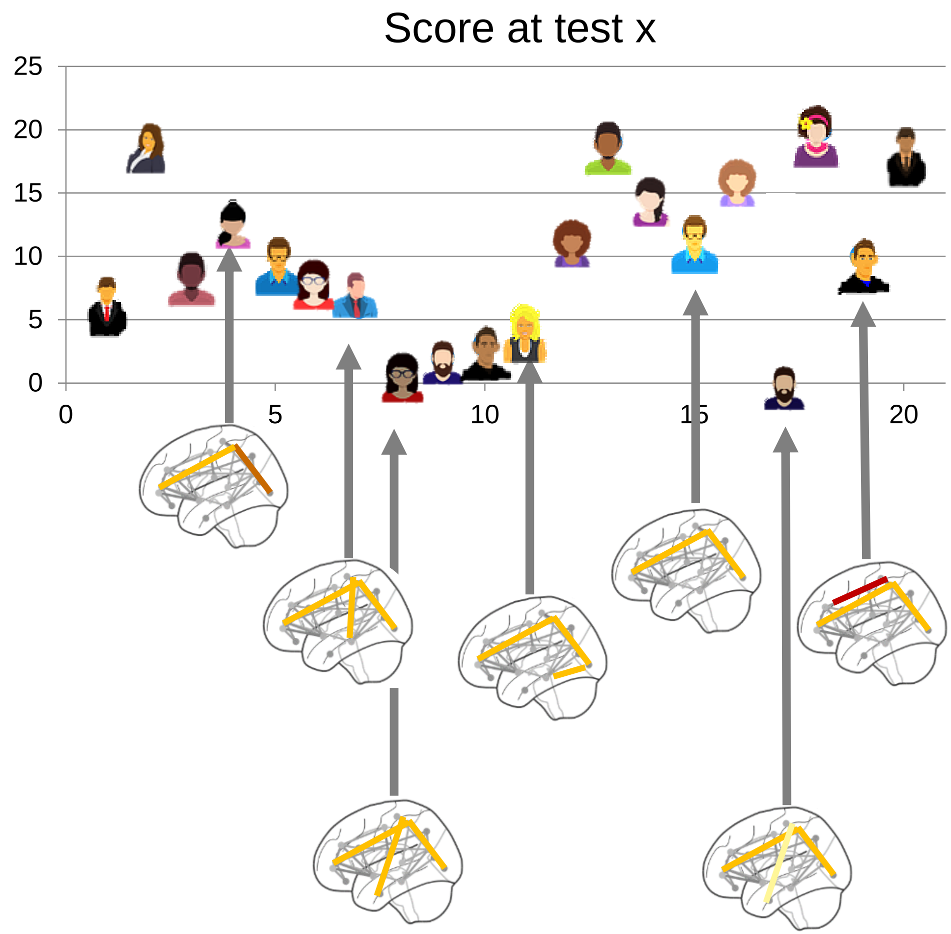
Relating brain structure to behavior



Nicolaisen-Sobesky,…,& Genon, under review

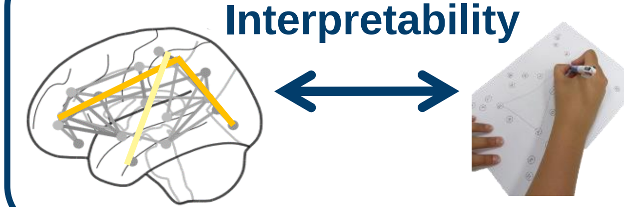
Poster WTh595

Connectivity-based psychometric prediction



Relating variability in performance to variability in brain functional connectivity

Interpretability



Replicability

Generalizability

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Predictive models of psychometric data

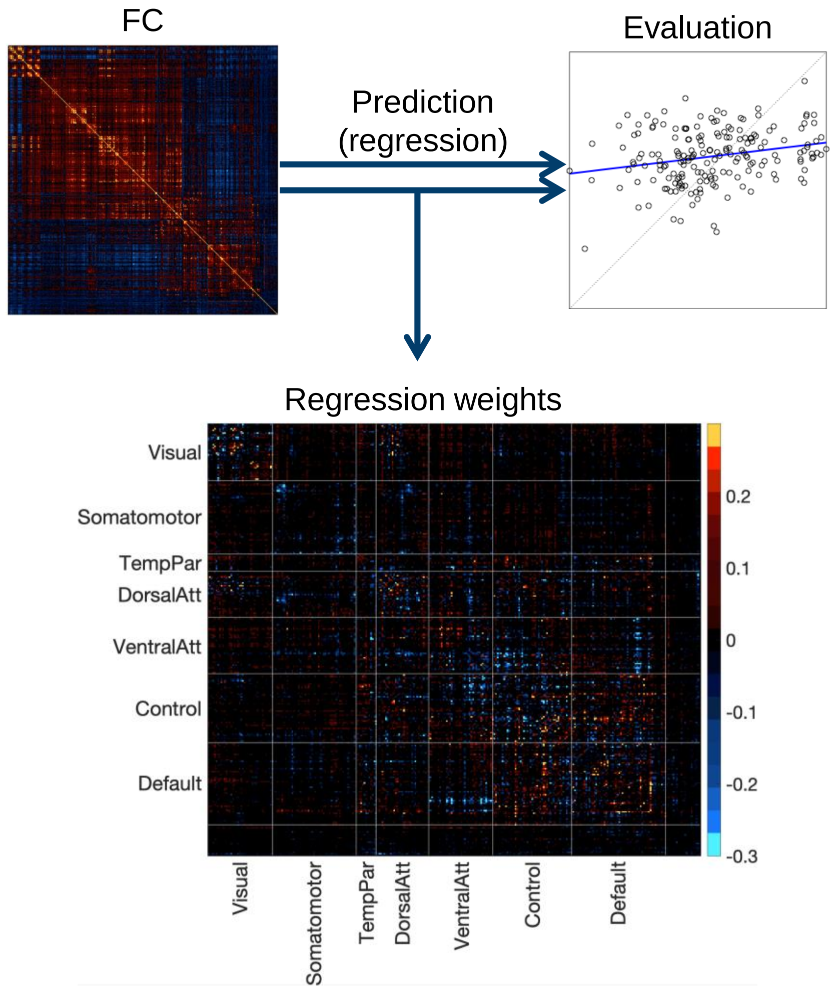
Interpretability /neurobiological validity issue

- Hypothesis-driven approach: a priori selection of specific regions/networks for the prediction

- **Data-driven approach**: How do we characterize each region/parcel's association to a psychometric variable?

- **Weight magnitude does not reflect** the regions' **association strength** with the psychometric variable

- Hard to get neurobiological insights

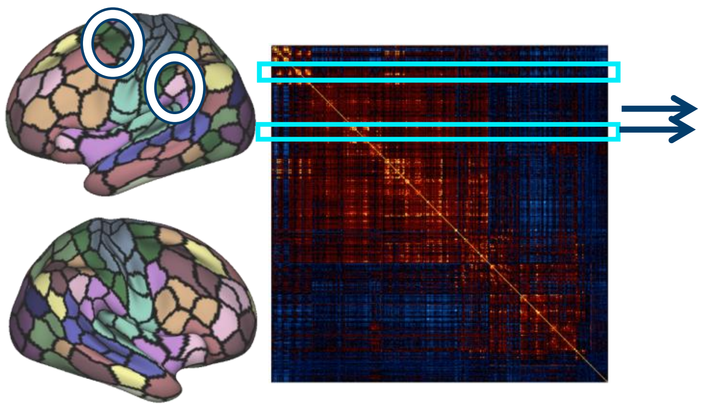


Wu,…,& Genon, 2021, Cerebral Cortex

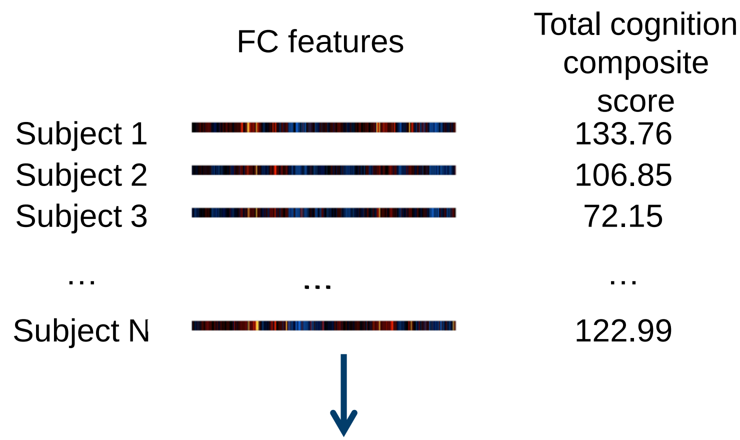
Predictive models of psychometric data: interpretability

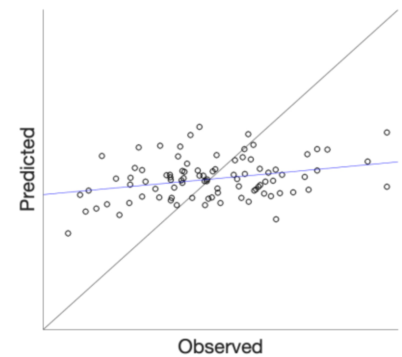
A region-based approach

- One predictive model for each brain region/parcel



(Schaefer et al., 2019)





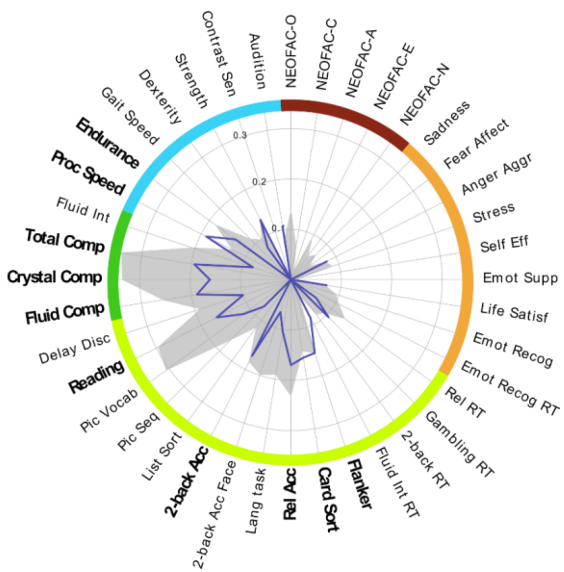
r = 0.32
r = 0.03

Wu,…,& Genon, 2021, Cerebral Cortex

Predictive models of psychometric data: interpretability

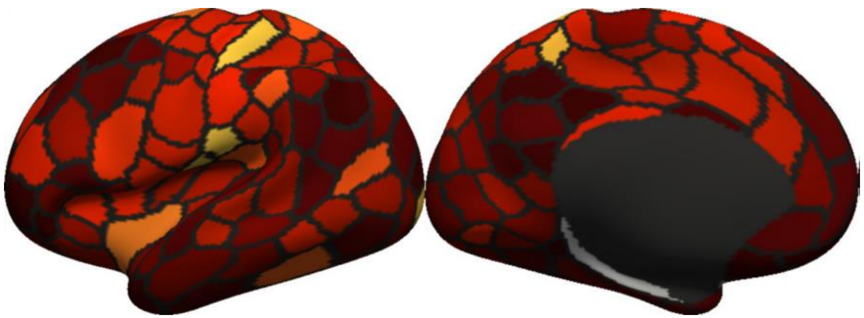
A region-based approach

1. **Brain region's perspective**: psychometric profile across psychometric variables



- Primary visual cortex
- Broca region
- Anterior hippocampus

2. **Psychometric variable's perspective**: prediction performance distribution across brain regions



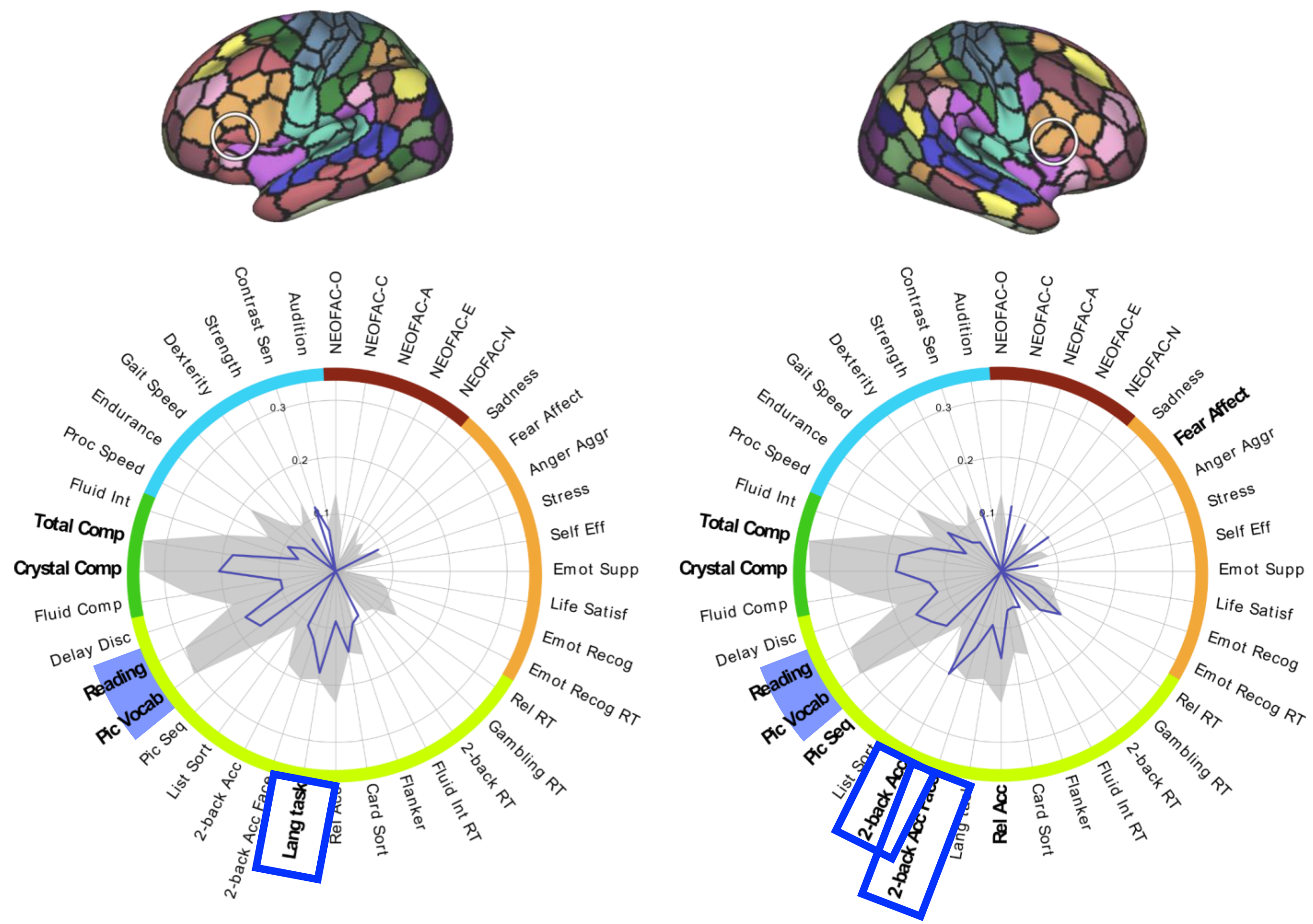
- Crystallized cognition composite score
- (Working memory) 2-back task accuracy
- (Working memory) 2-back face task accuracy

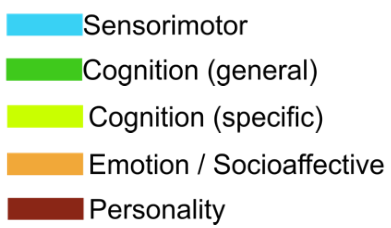
Wu,…,& Genon, 2021, Cerebral Cortex

Predictive models of psychometric data: interpretability

Psychometric Profile

Broca region



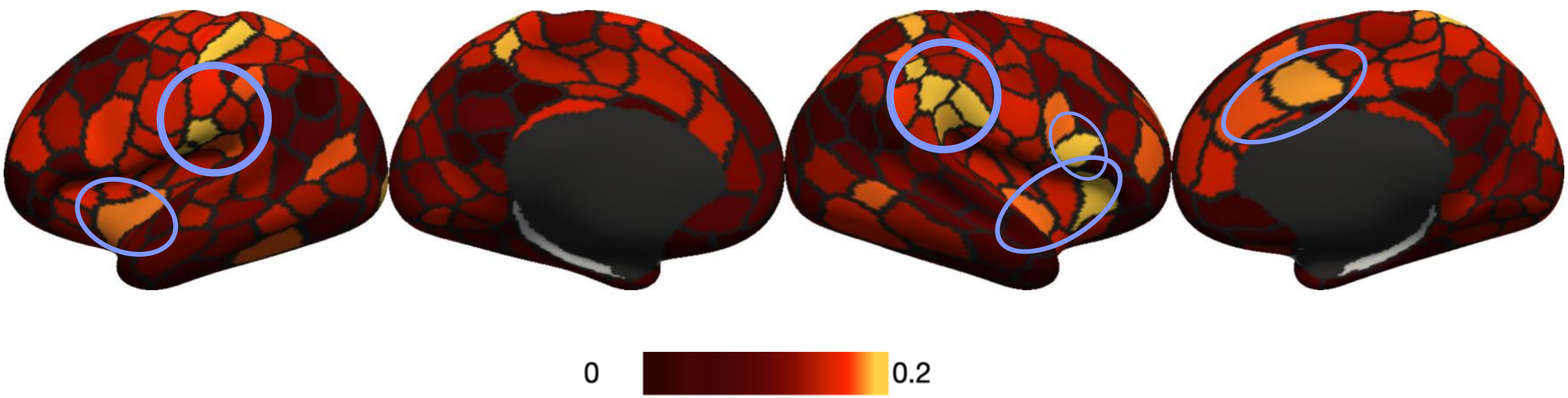


Wu,…,& Genon, 2021, Cerebral Cortex

Predictive models of psychometric data: interpretability

Prediction Performance Distribution

(working memory) 2-back task accuracy

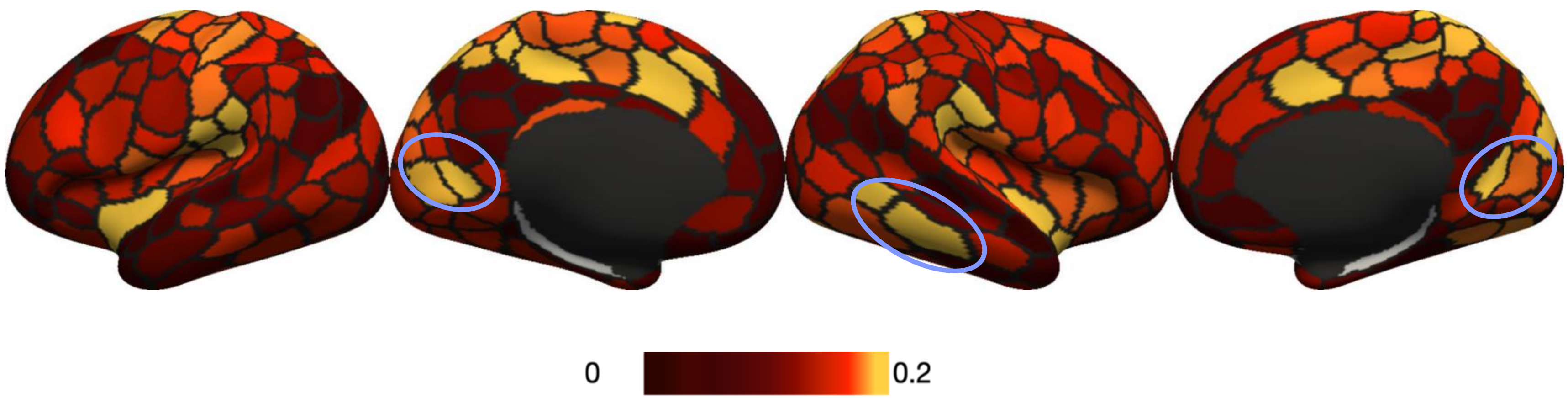


Wu,…,& Genon, 2021, Cerebral Cortex

Predictive models of psychometric data: interpretability

Prediction Performance Distribution

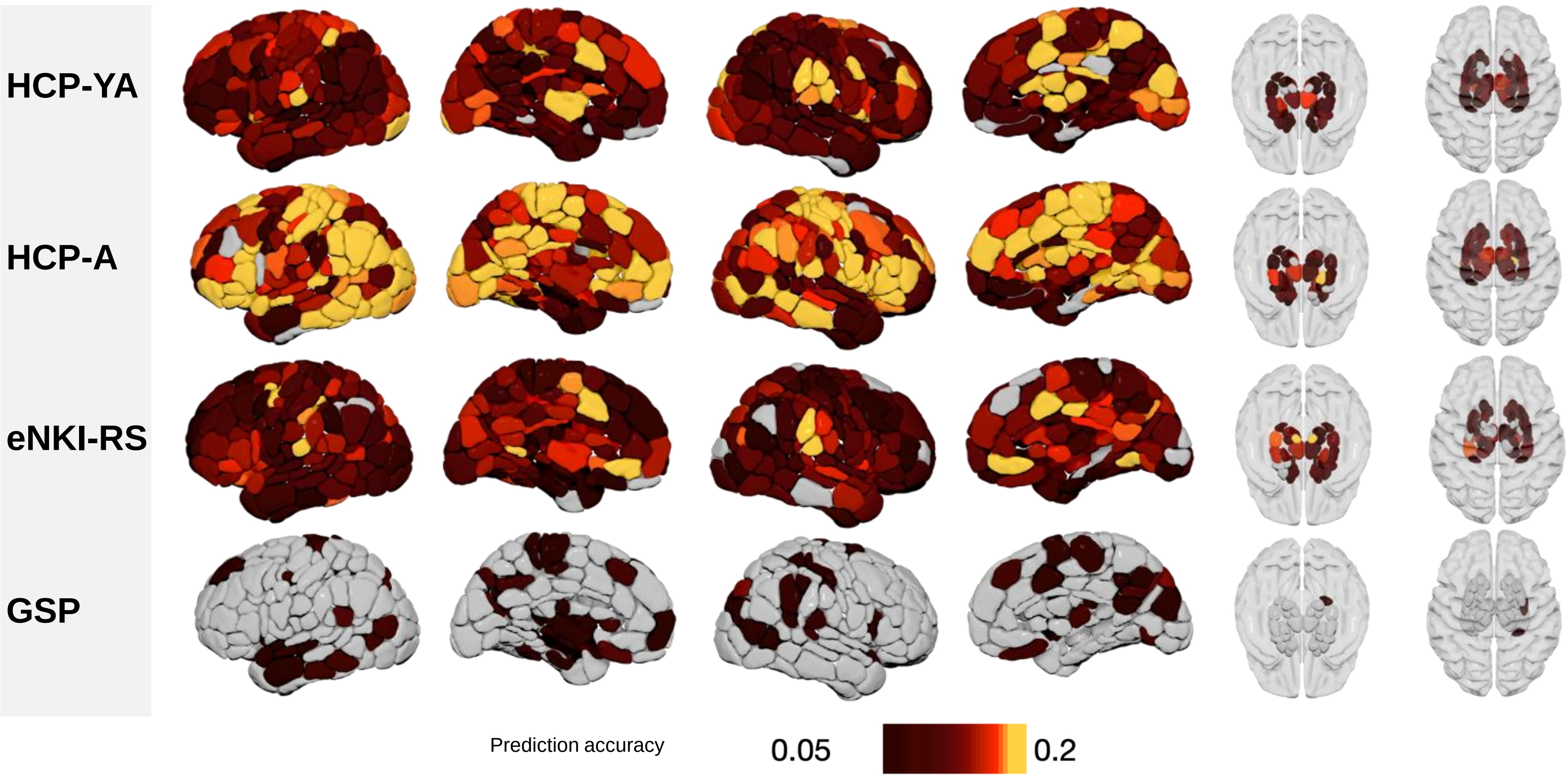
(working memory) 2-back **face** task accuracy



Wu,…,& Genon, 2021, Cerebral Cortex

Predictive models of psychometric data: replicability of brain-behavior patterns

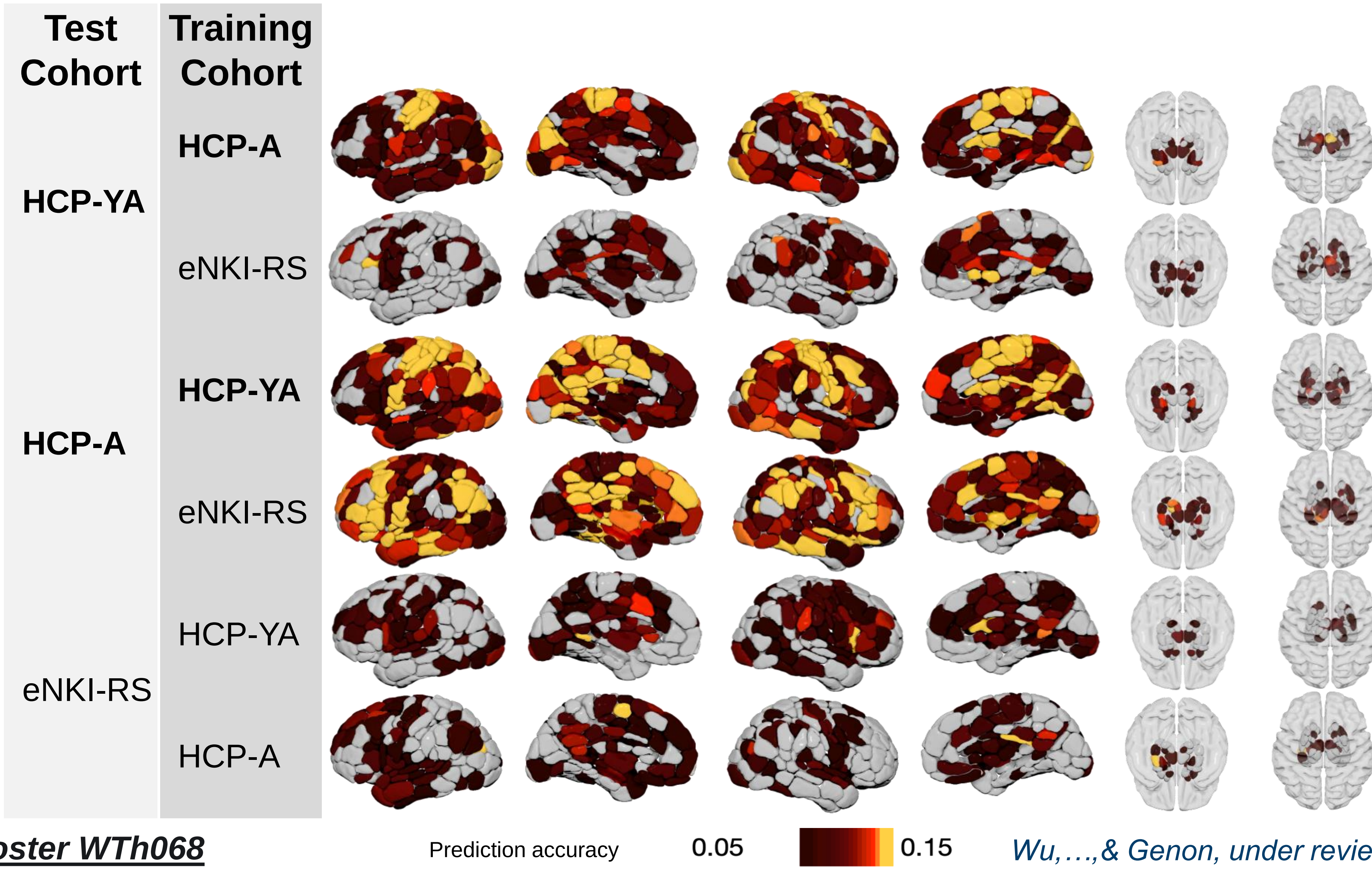
Cross-dataset replicability of brain predictive patterns for fluid cognition



Wu,…,& Genon, under review

Predictive models of psychometric data: cross-dataset generalizability

Cross-dataset generalizability of fluid cognition



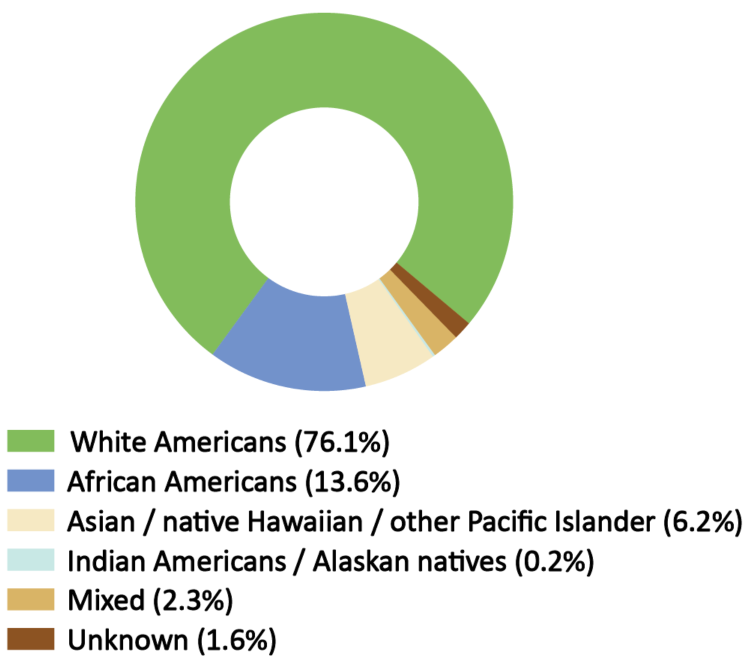
Poster WTh068

Wu,…,& Genon, under review

Predictive models of psychometric data: biases in population minority

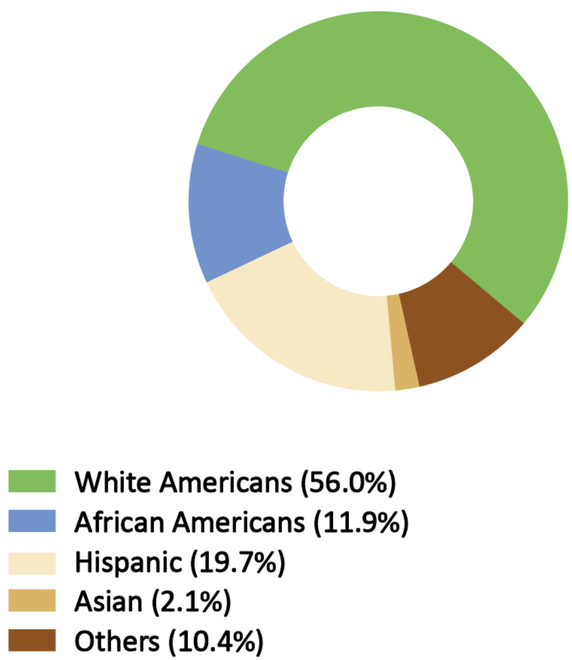
Human Connectome Project (HCP)

- N = 948; 22-37years
- 58 behavioral measures
- #WA = 721, #AA = 129



Adolescent Brain Cognitive Development (ABCD)

- N = 5351; 9-11years
- 36 behavioral measures
- #WA = 2997, #AA = 642

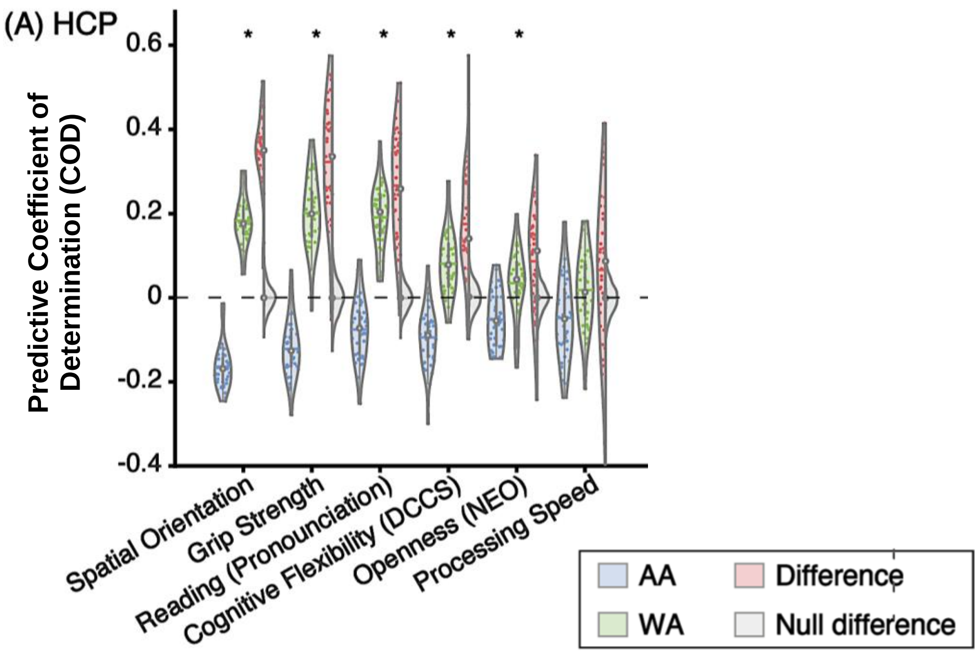


Li,…,Yeo & Genon, in press, Science Advances

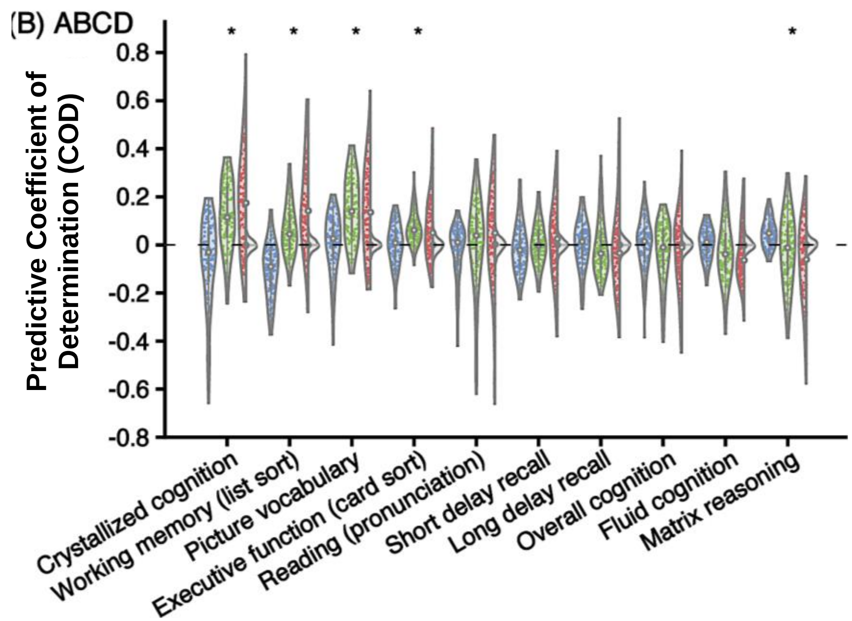
Predictive models of psychometric data: biases in population minority

LARGER PREDICTION ERROR IN AFRICAN AMERICANS THAN MATCHED WHITE AMERICANS

Human Connectome Project (HCP)



Adolescent Brain Cognitive Development (ABCD)



Only predictable behavioral measures are shown here.

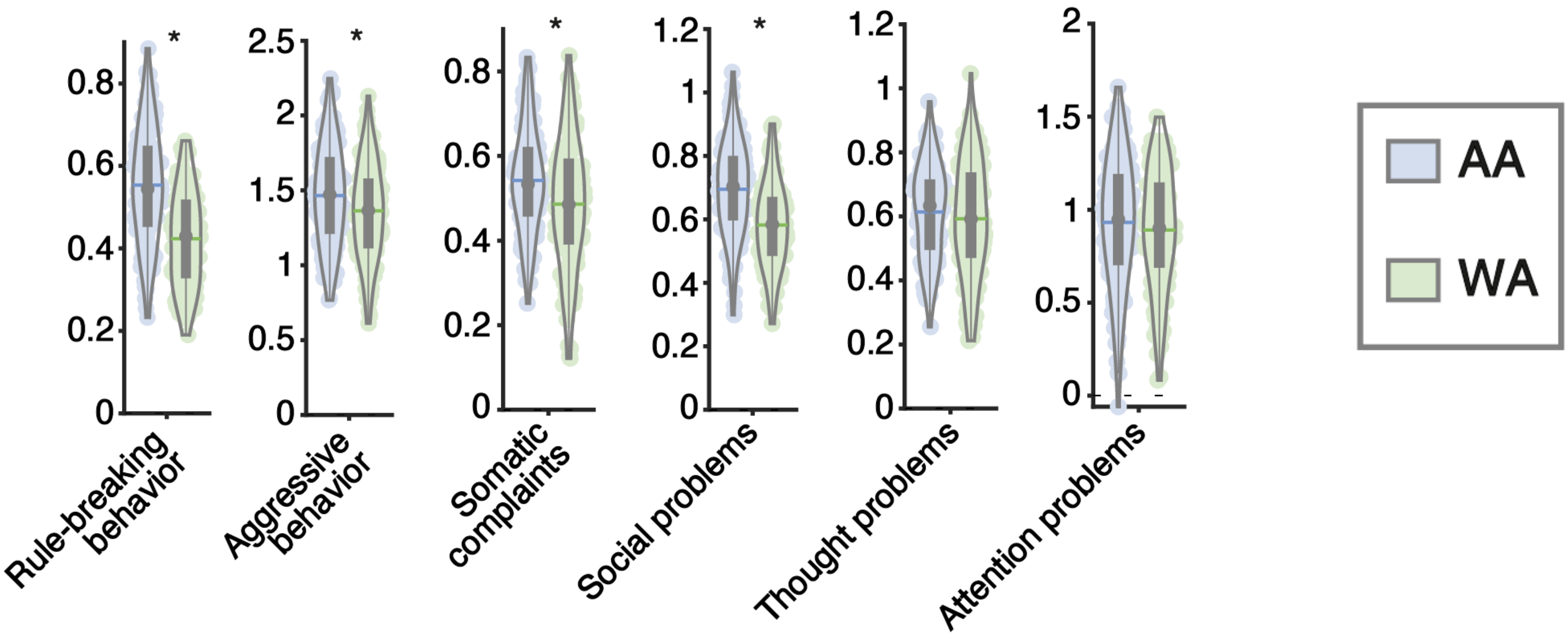
Similar pattern by looking into all behavioral measures, or regressing different confounds, or modelling with a different algorithm.

Li,…,Yeo & Genon, in press, Science Advances

Predictive models of psychometric data: biases in population minority

DIRECTION OF PREDICTION ERROR & POTENTIAL CONSEQUENCES

Predicted – observed behavioral scores



ABCD data - Achenbach Child Behavior Checklist

Li,…,Yeo & Genon, in press, Science Advances

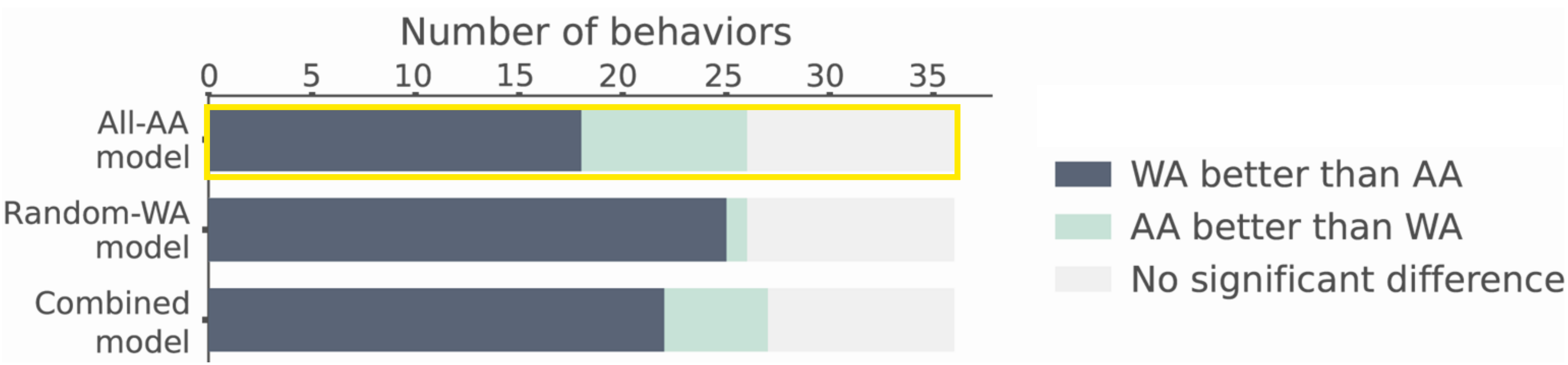
Predictive models of psychometric data: biases in population minority

EFFECTS OF TRAINING POPULATION

ABCD dataset

Compare 3 types of models, trained on:

a. AA only
b. WA only (same sample size as AA)
c. Half AA, half WA (combination of *a.* & *b.*)



Li,…,Yeo & Genon, in press, Science Advances

Conclusions

- Different brain parcellations reflect the complexity of brain organization
- Brain structural-behaviour (BSB) associations using traditional approaches show poor replicability
    - Multivariate BSB mapping reveals new global, robust and cross-cohort replicable patterns
- Connectivity-based predictions of behavioral phenotype
    - Benefit from frameworks promoting interpretability
    - Show limited cross-cohort replicability and generalizability
    - Show fairness issues for minority groups

$\Rightarrow$ More diverse datasets are needed to address replicability, interpretability and generalizability issues

Thank you

Düsseldorf (Germany)
- Katrin Amunts
- Svenja Caspers
- Simon Eickhoff
- Nicola Palomero-Gallagher

GIGA-ULiege (Belgium)
- Steven Laureys
- Gilles Vandewalle
- Eric Salmon
- Christina Schmidt

UCL Brussels (Belgium)
- Julie Duque

Neurospin/INRIA (France)
- Bertrand Thirion
- Demian Wassermann

UCL (UK)
- Janaina Mourao-Miranda
- Agoston Mihalik

WashU (USA)
- Aris Sotiras

Yale University (USA)
- Todd Constable
- Avram Holmes

NUS (Singapore)
- Thomas Yeo

Cognitive NeuroInformatics Lab

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