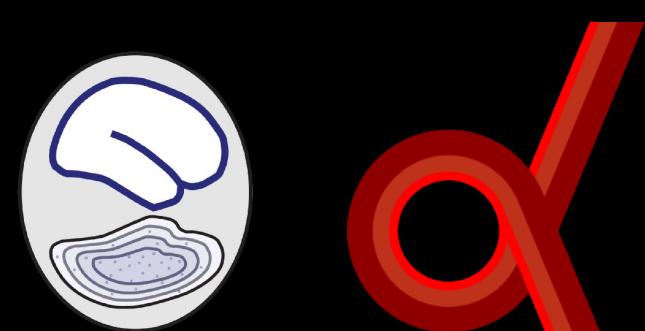


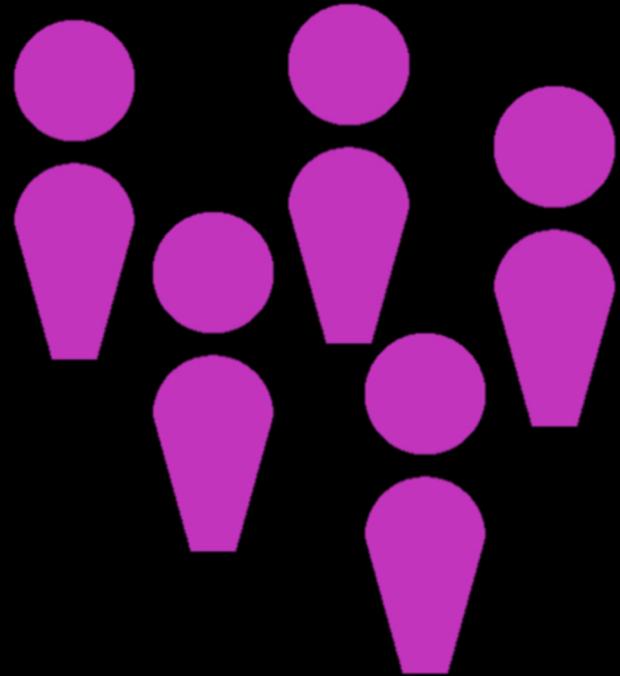
Normative modelling: the what, when and why

Hannah Savage & Charlotte Fraza

@DrHannahSavage
Post Doctoral Researcher
Predictive Clinical Neuroscience Lab



CHALLENGE:
HETEROGENEITY



Patients

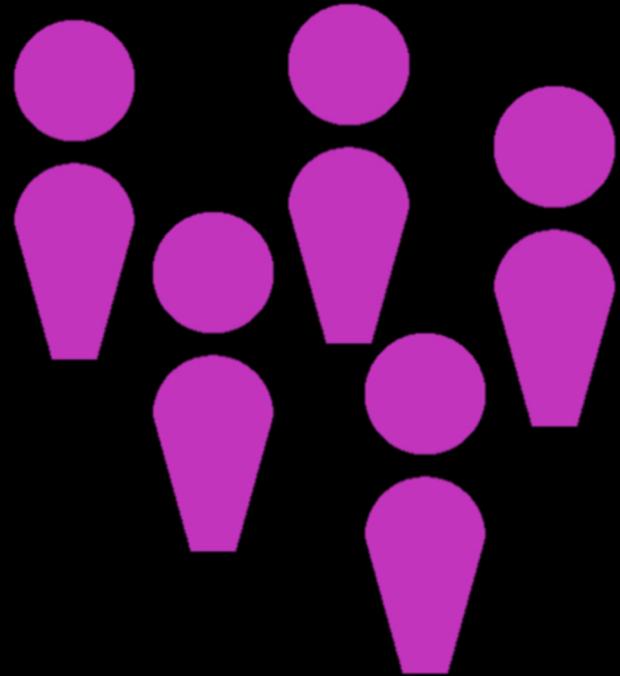


Unaffected controls

CHALLENGE:
HETEROGENEITY

CASE – CONTROL

CHALLENGE:
HETEROGENEITY

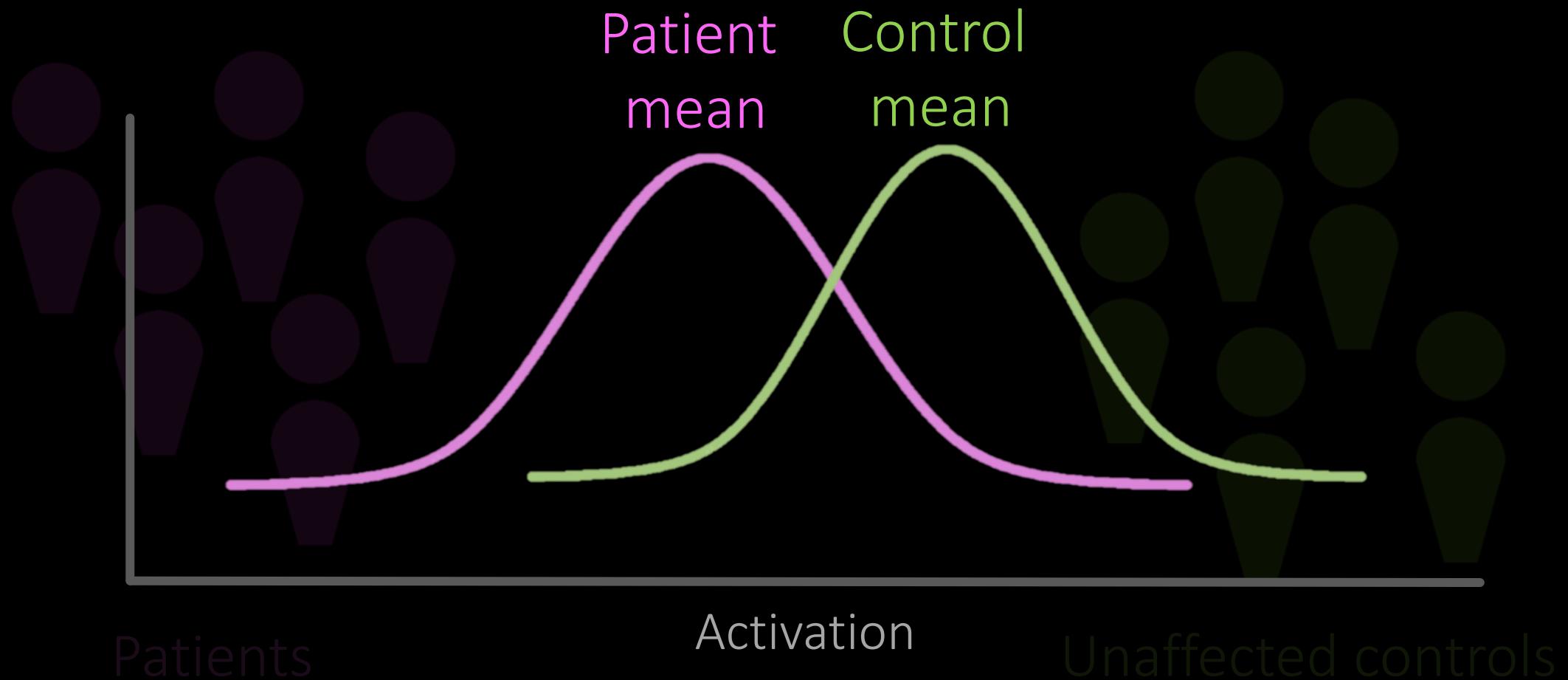


Patients

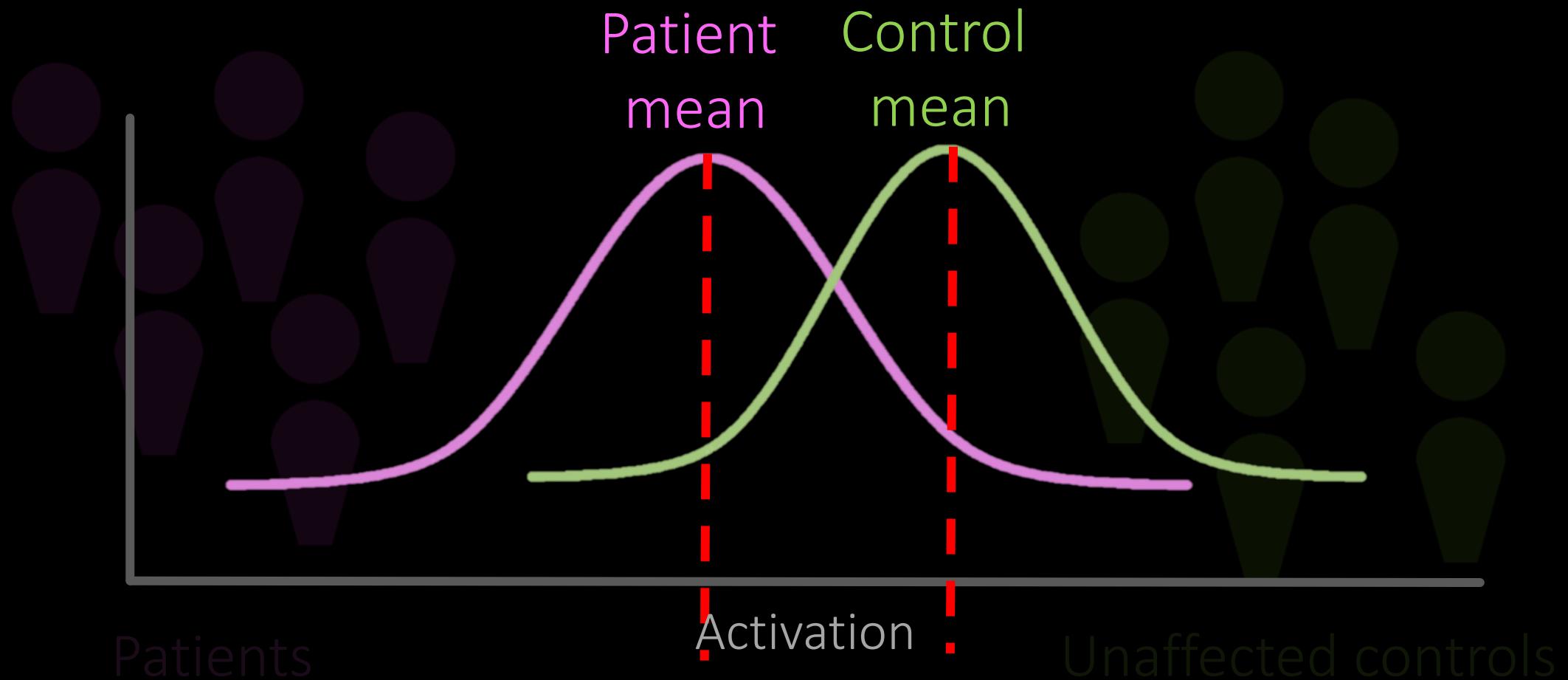


Unaffected controls

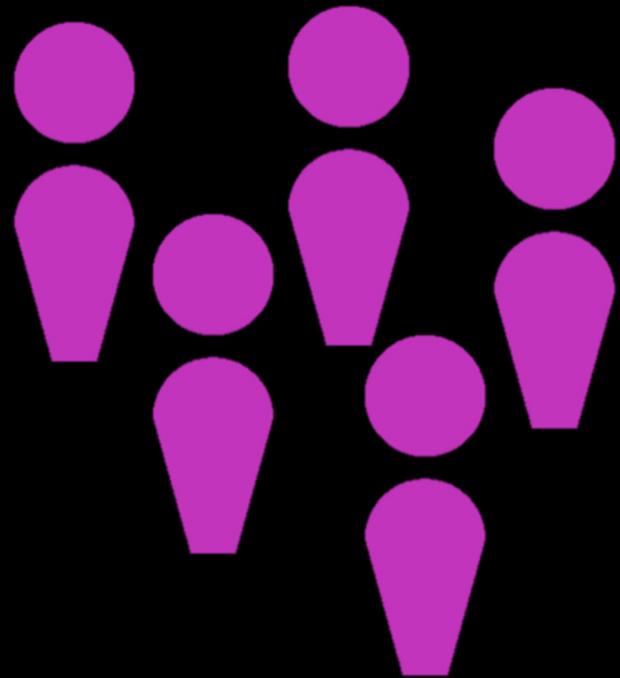
CHALLENGE:
HETEROGENEITY



CHALLENGE:
HETEROGENEITY



CHALLENGE:
HETEROGENEITY

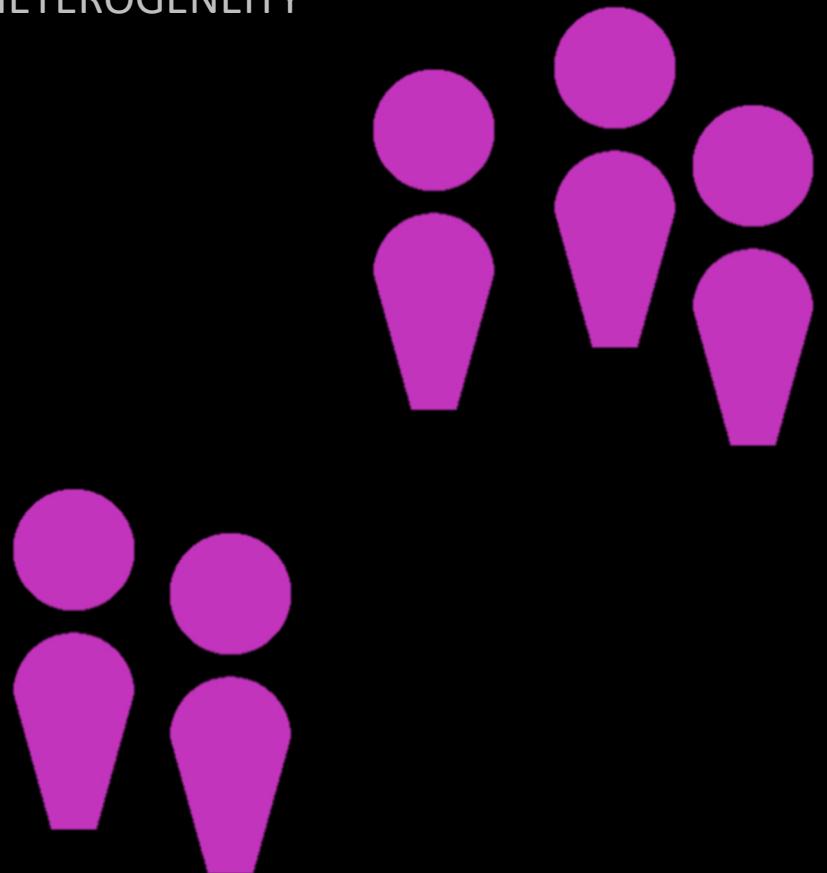


Patients

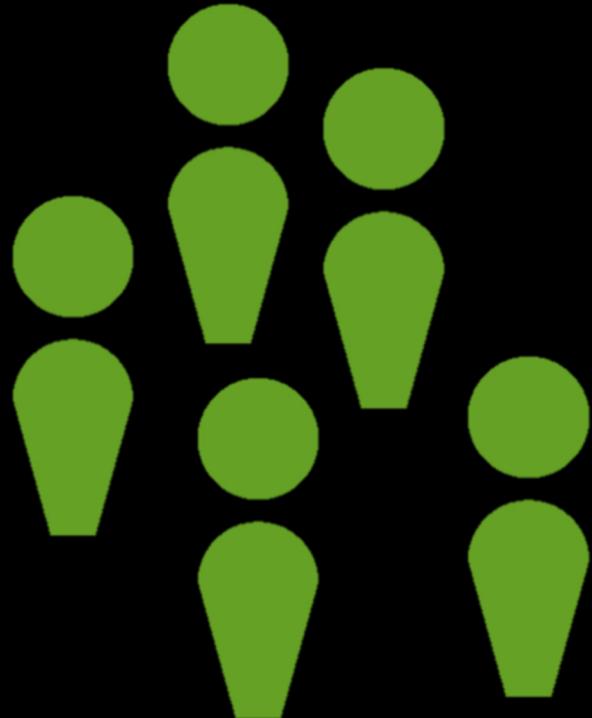


Unaffected controls

CHALLENGE:
HETEROGENEITY



Patients

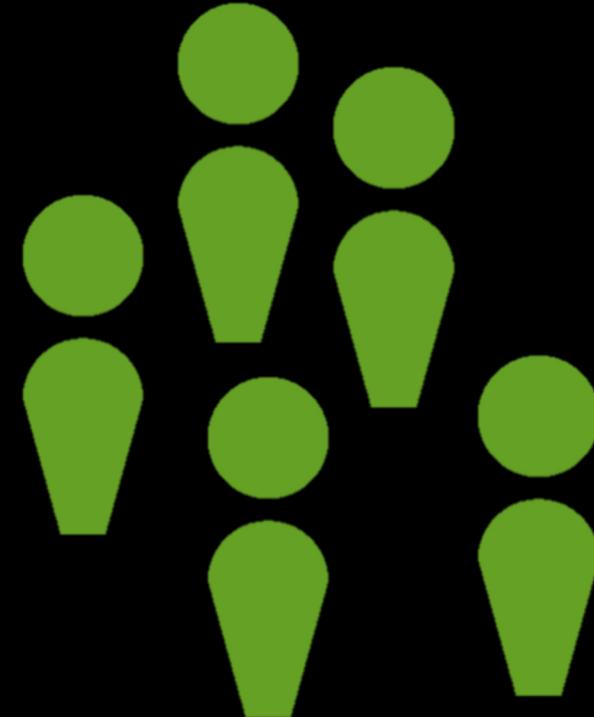
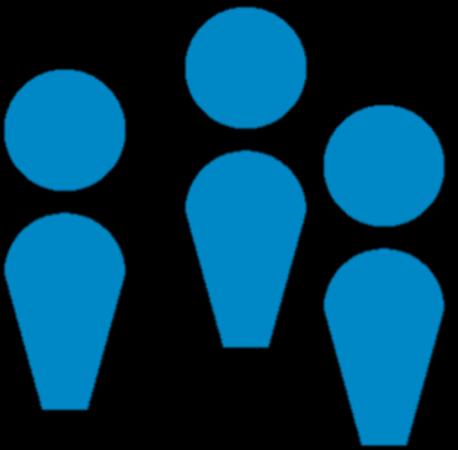


Unaffected controls

CHALLENGE:
HETEROGENEITY

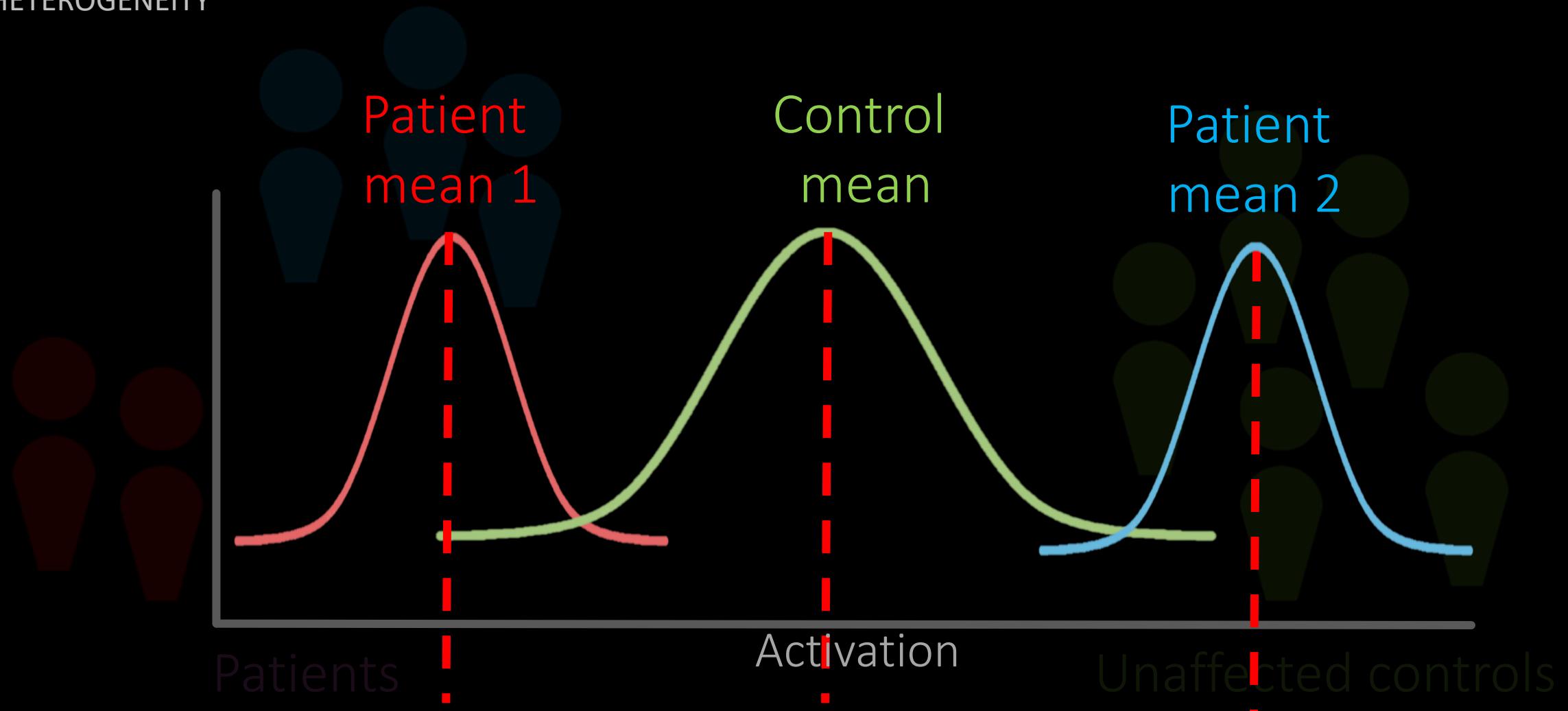


Patients



Unaffected controls

CHALLENGE:
HETEROGENEITY



CHALLENGE:
HETEROGENEITY



Patients

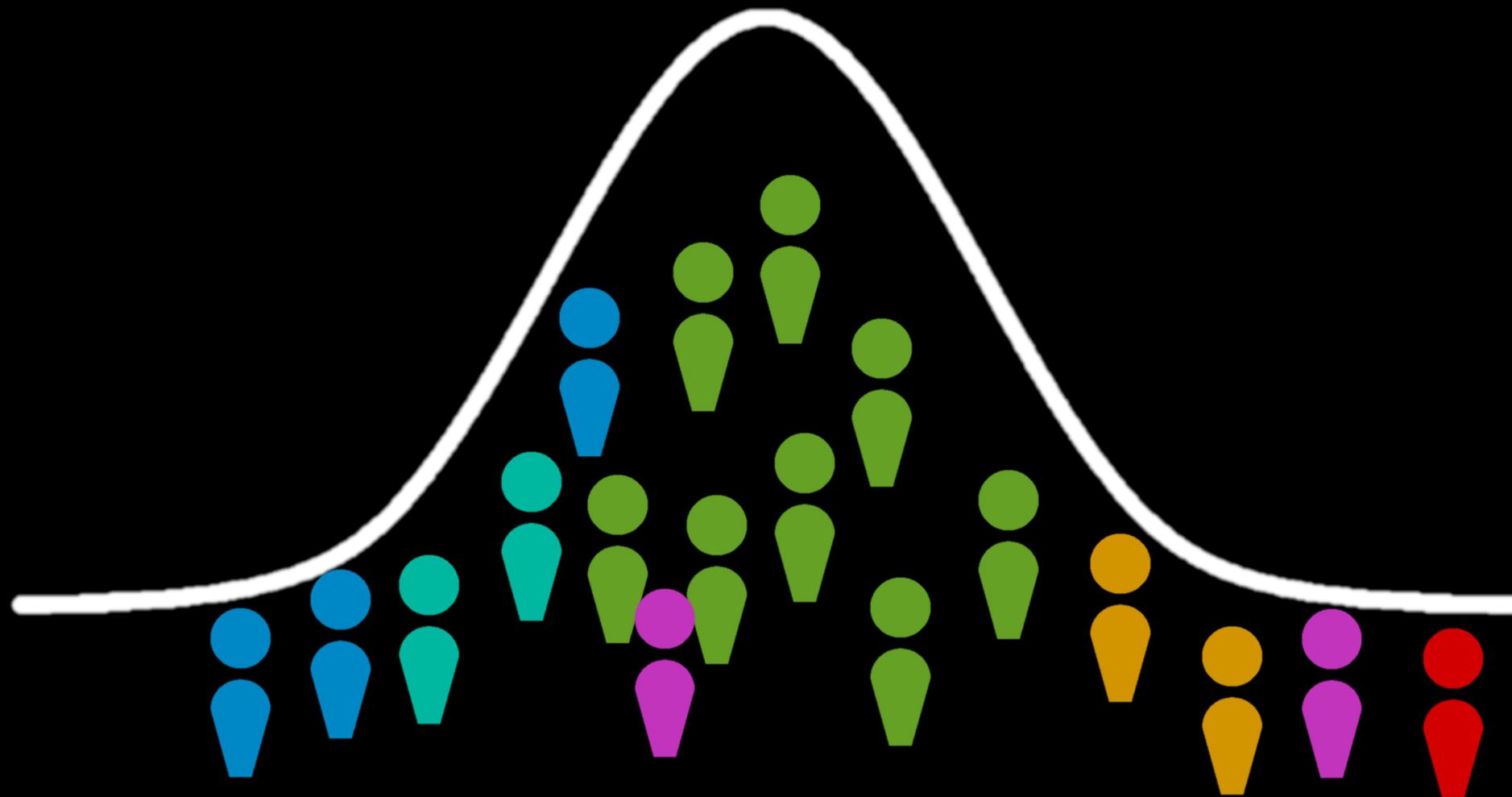


Unaffected controls

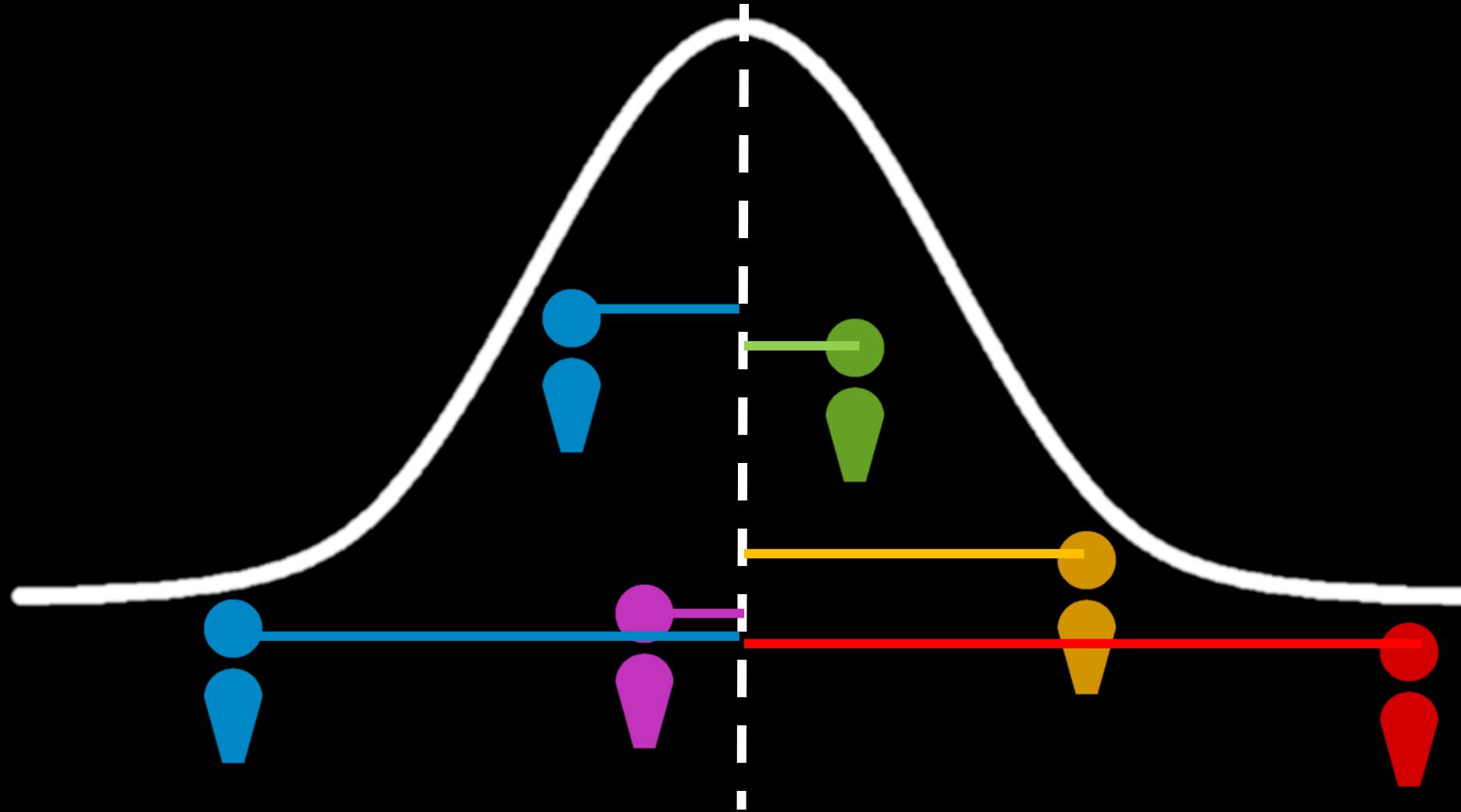
SOLUTION:
NORMATIVE MODELLING



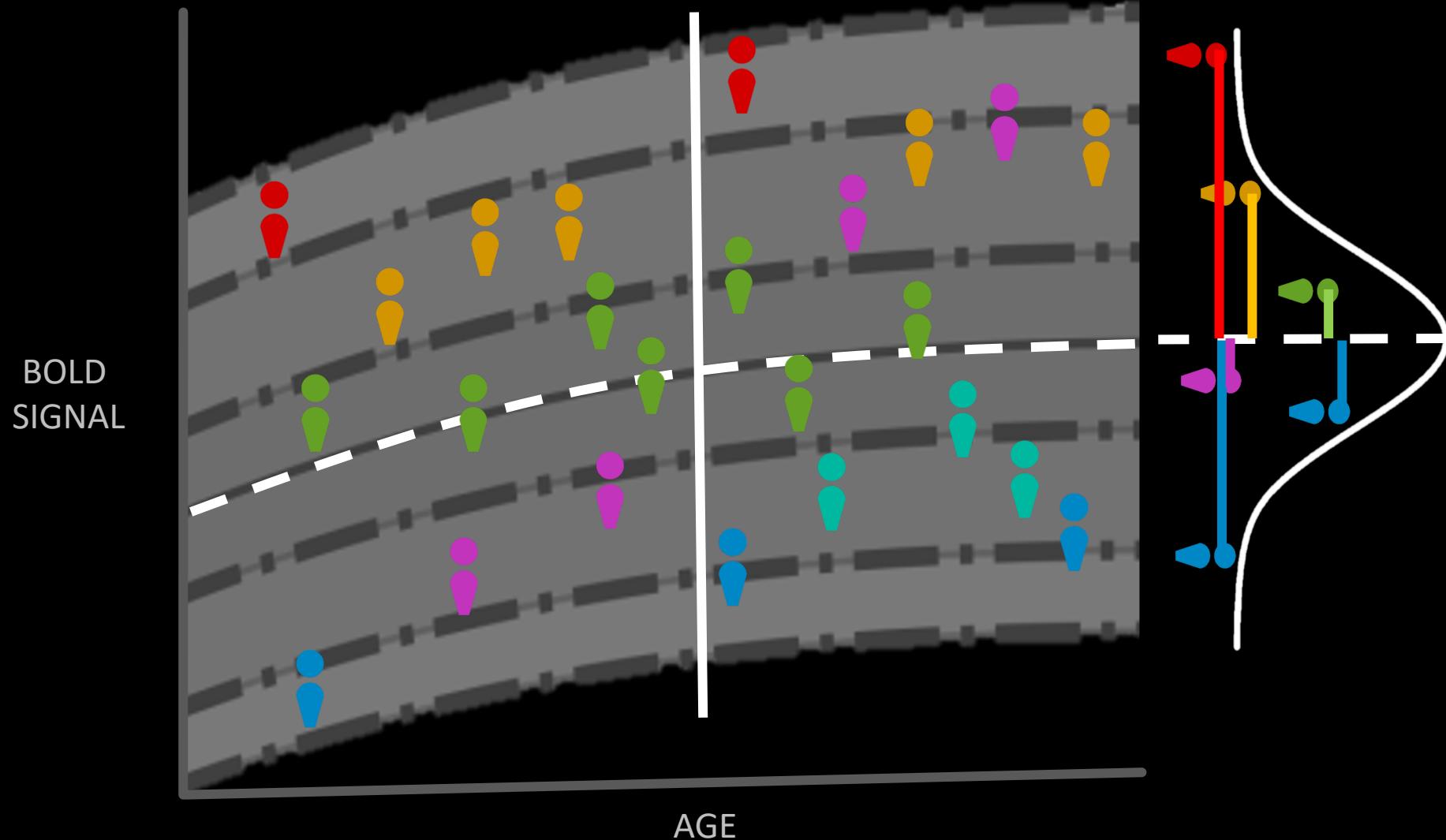
SOLUTION:
NORMATIVE MODELLING



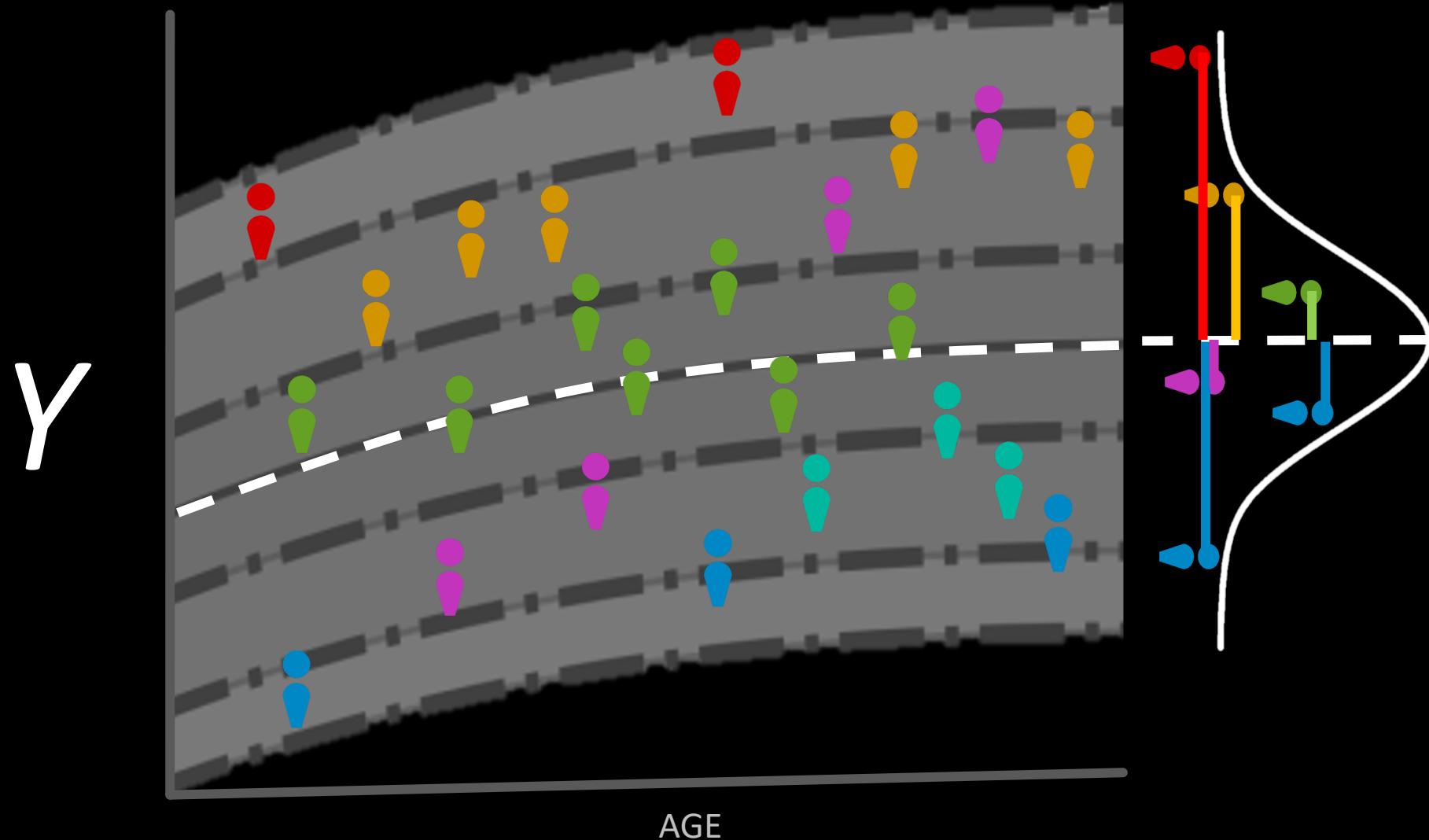
SOLUTION:
NORMATIVE MODELLING



SOLUTION:
NORMATIVE MODELLING



SOLUTION:
NORMATIVE MODELLING



SOLUTION:
NORMATIVE MODELLING

Y

Brain
(BOLD signal in
voxel, ROI)

SOLUTION:
NORMATIVE MODELLING

$$Y = f(X, \theta) + \epsilon$$

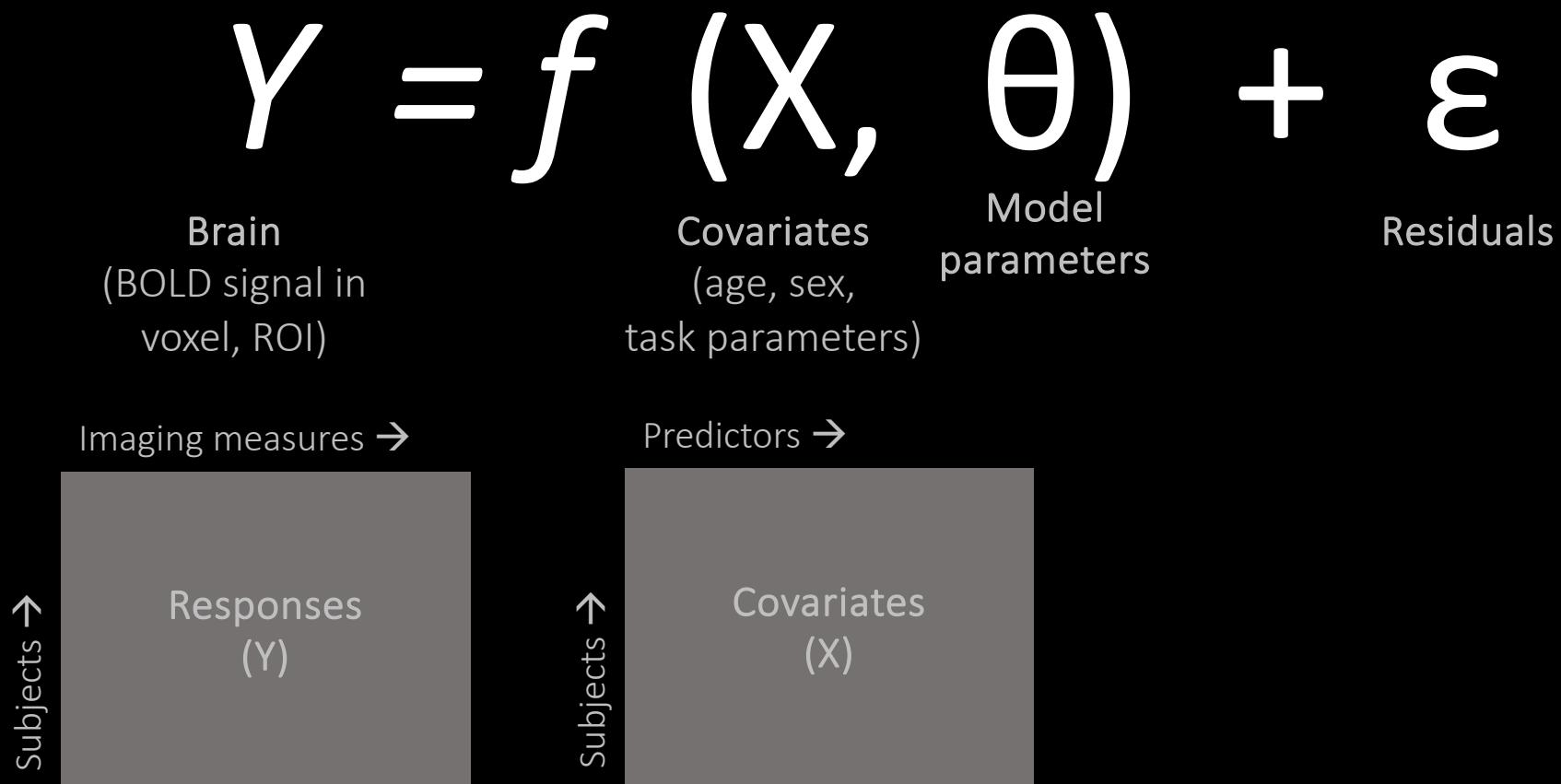
Brain
(BOLD signal in
voxel, ROI)

Covariates
(age, sex,
task parameters)

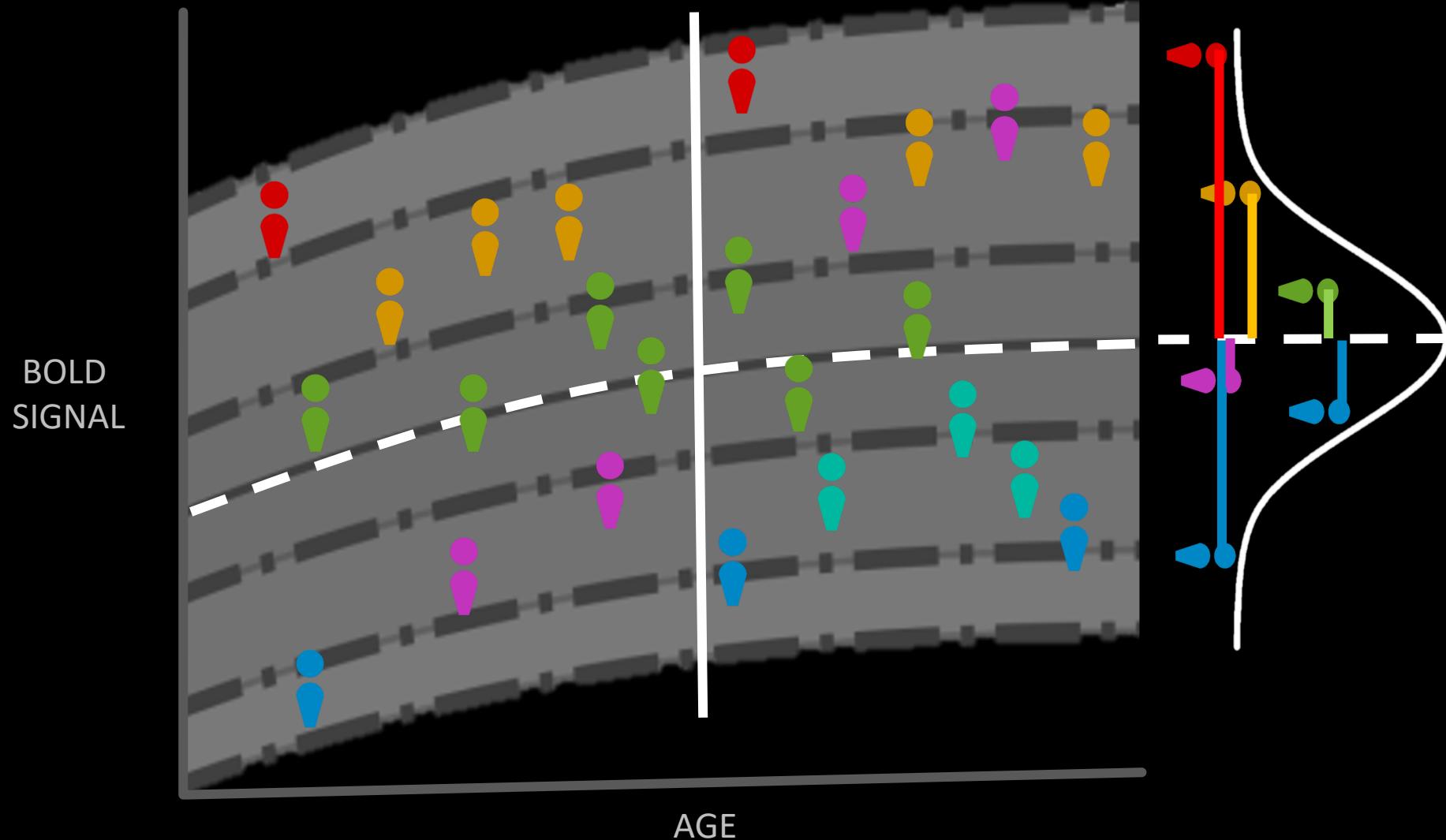
Model
parameters

Residuals

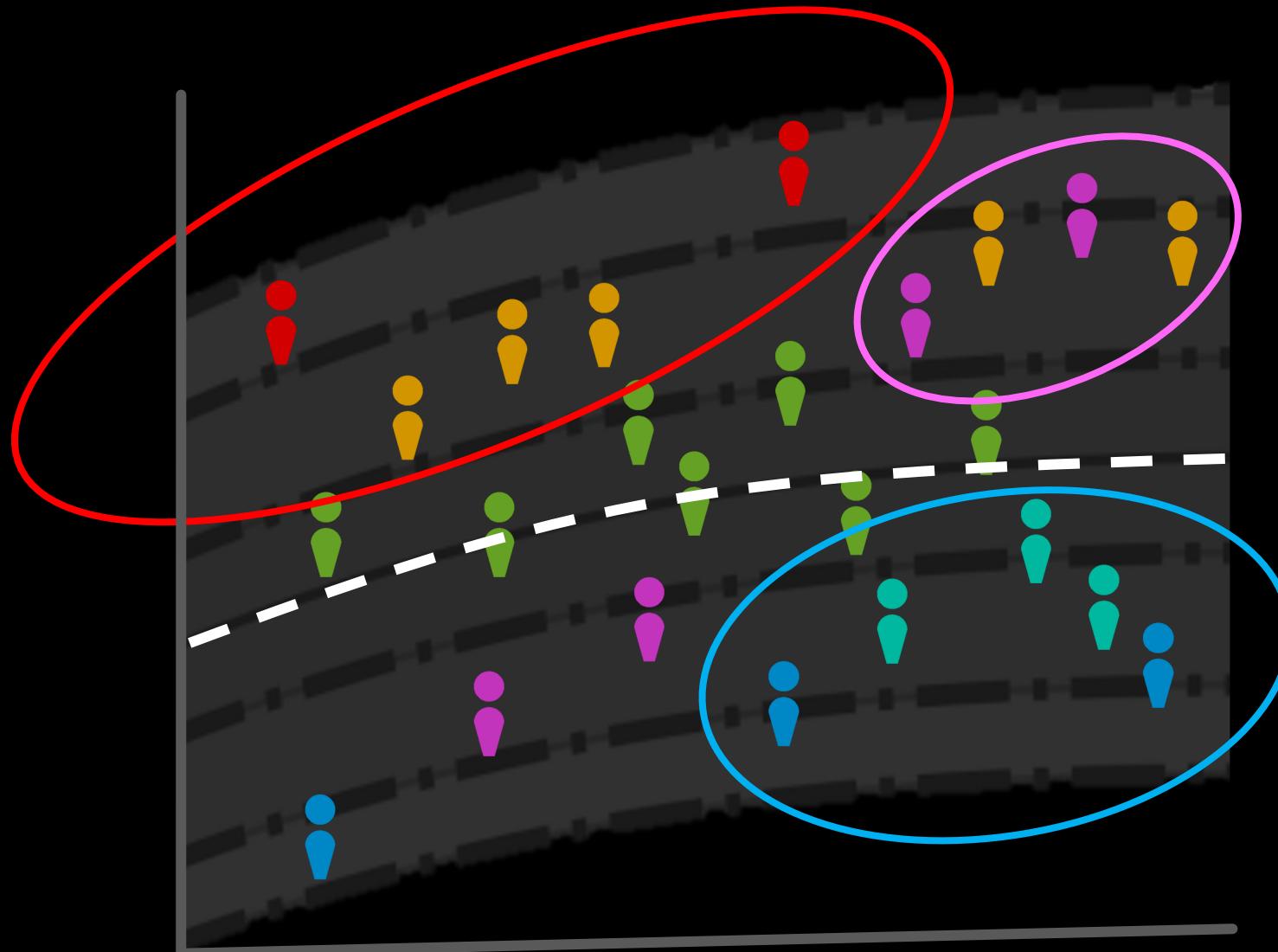
SOLUTION:
NORMATIVE MODELLING



SOLUTION:
NORMATIVE MODELLING



SOLUTION:
NORMATIVE MODELLING



Clustering/
Community detection

Regression model or
classification prediction
model

APPLICATION:

Structural:
Brain growth
and aging

Structural:
Clinical
Applications

Functional:
Emotional Face
Processing

**Future
Potential**

APPLICATION:

Structural:
Brain growth
and aging

Structural:
Clinical
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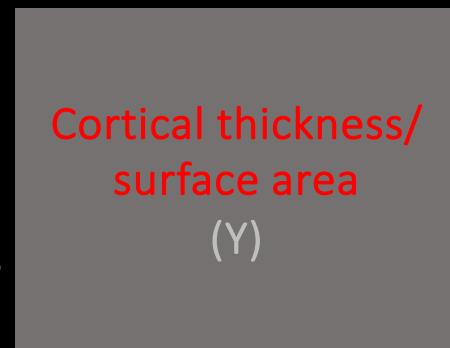
**Future
Potential**

APPLICATION:
STRUCTURAL

$$Y = f(X, \theta) + \epsilon$$

Cortical
thickness/
surface area

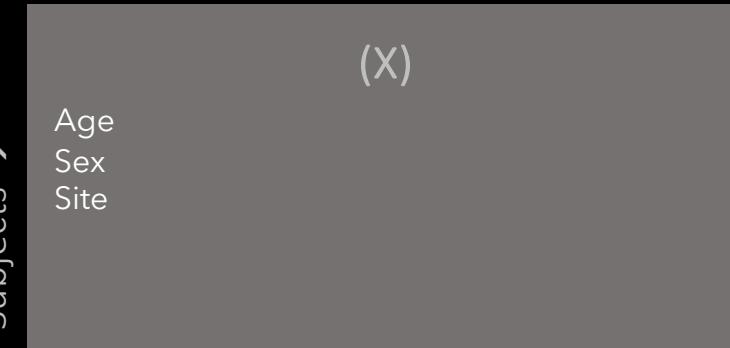
ROI/Voxels →



Subjects ↑

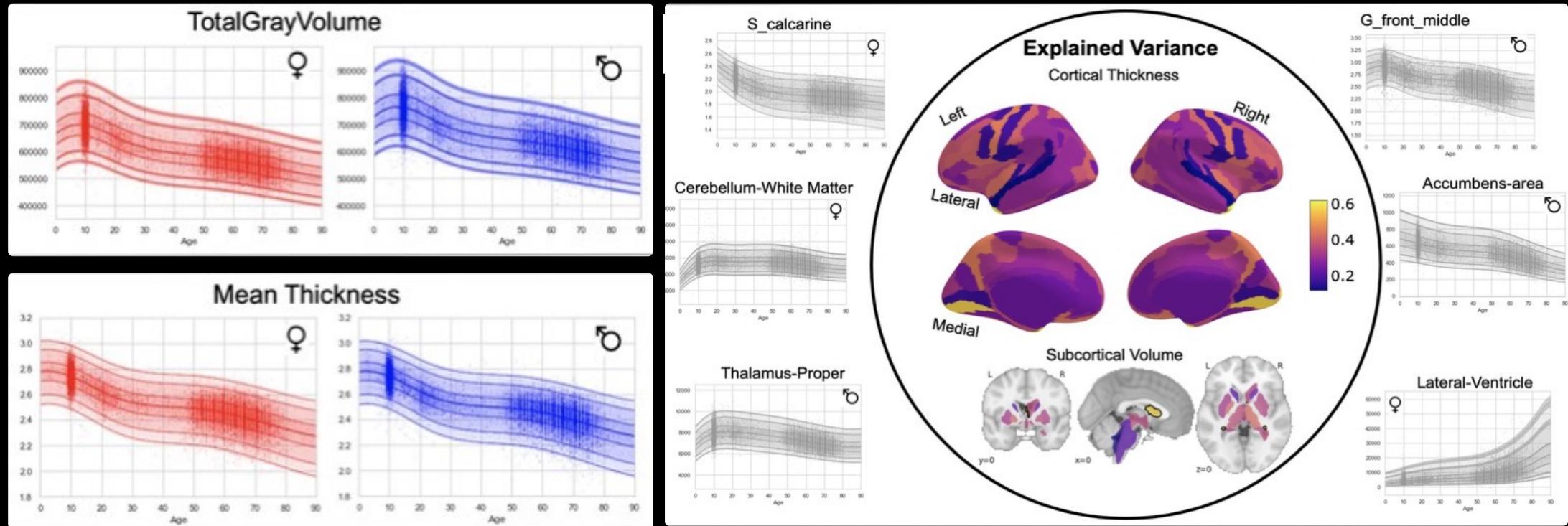
Covariates
(age, sex,
site)

Predictors →



Model
parameters

Residuals

APPLICATION:
STRUCTURAL DATA

58,836 individuals

82 scan sites

aged 2–100

Normative models for cortical thickness and subcortical volumes derived from Freesurfer



Saige Rutherford et al., (2022) Charting
brain growth and aging at high spatial
precision. *eLife* 11:e72904.

APPLICATION:

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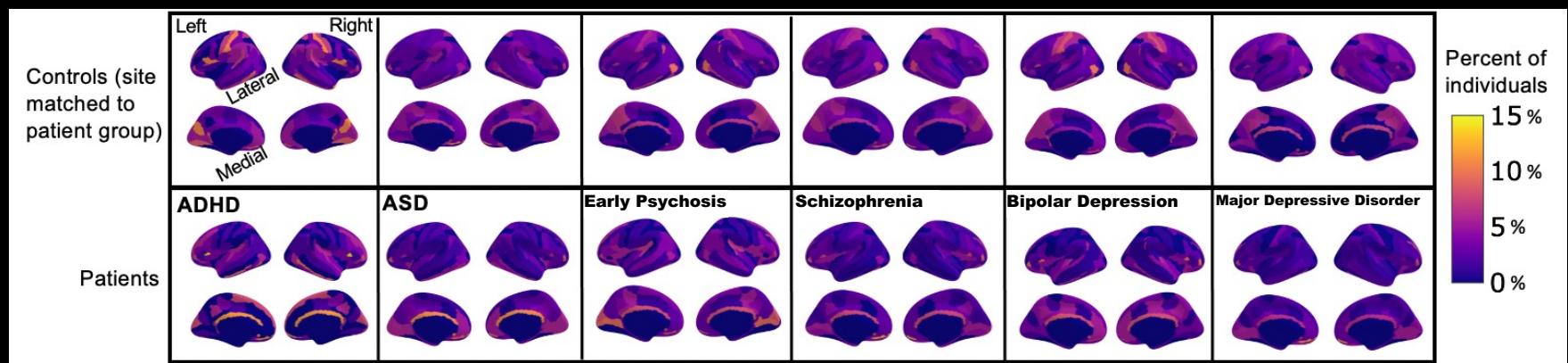
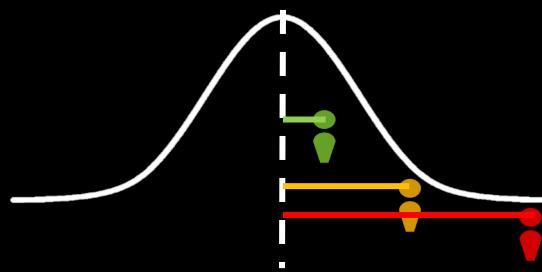
Structural:
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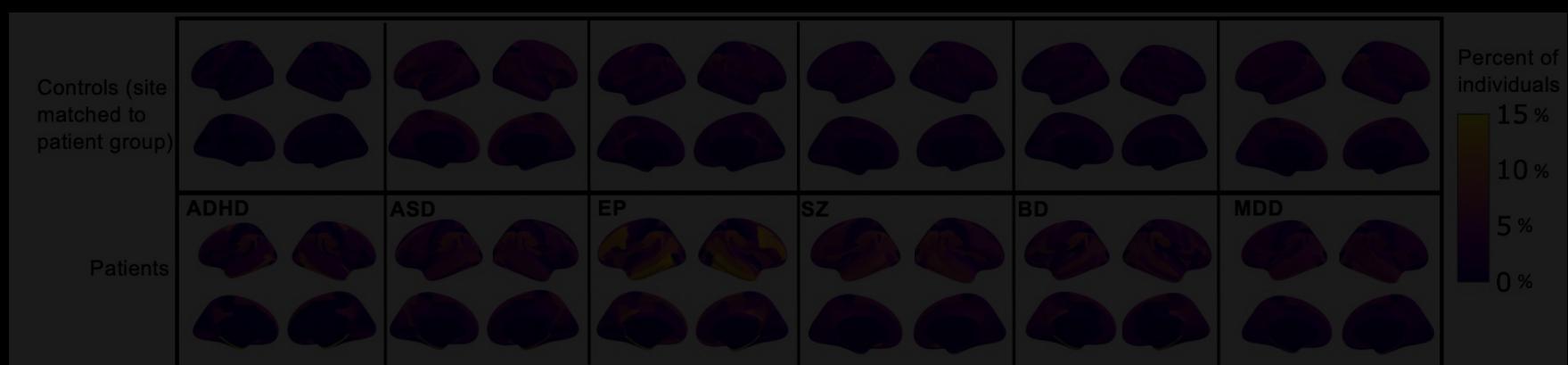
**Future
Potential**

APPLICATION: STRUCTURAL DATA

Positive deviations



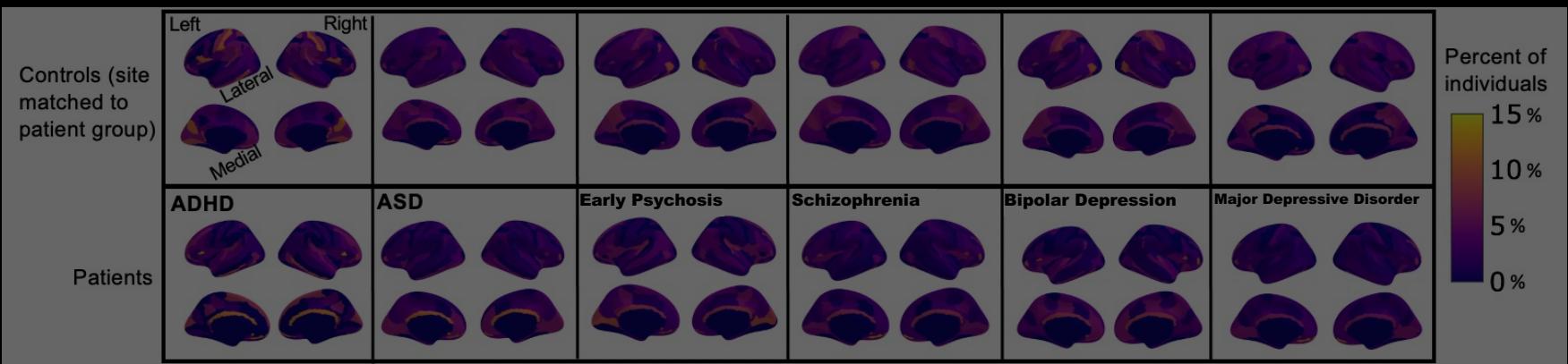
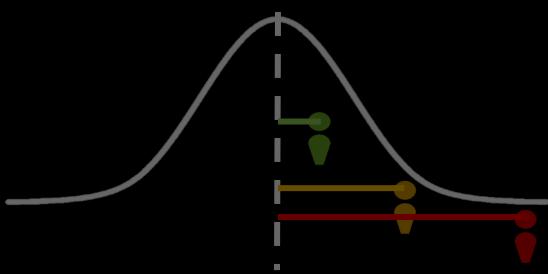
Negative deviations



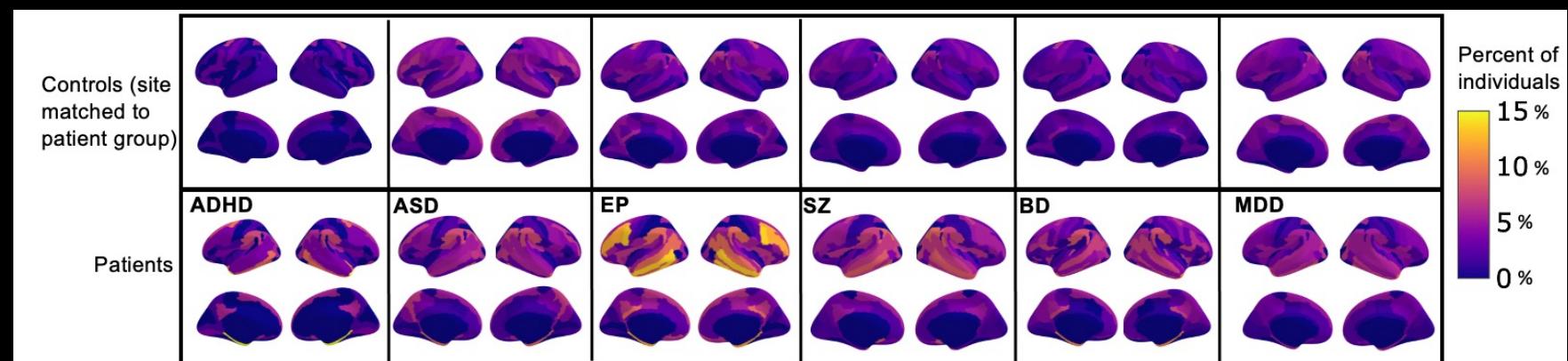
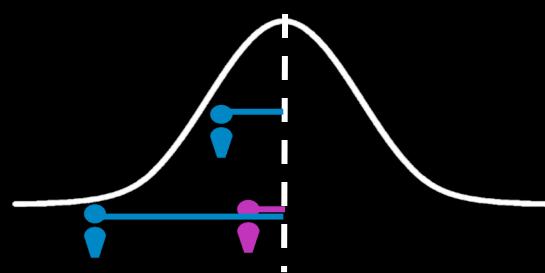
Saige Rutherford et al., (2022)
Charting brain growth and aging
at high spatial precision. *eLife*
11:e72904

APPLICATION: STRUCTURAL DATA

Positive deviations



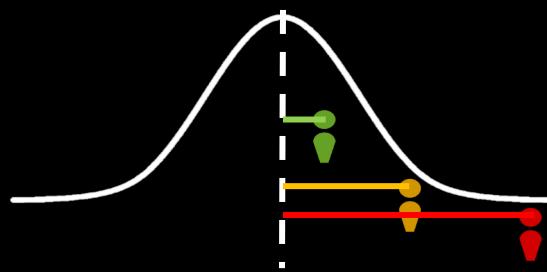
Negative deviations



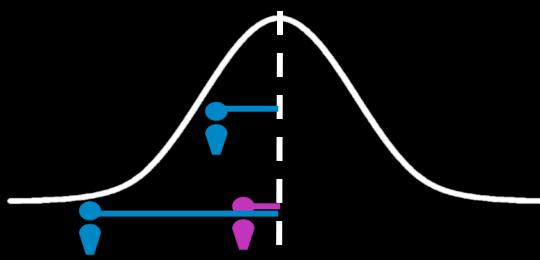
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Positive deviations



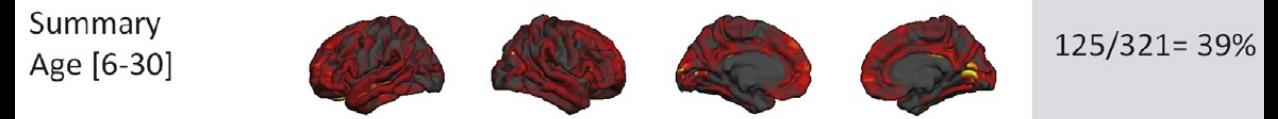
Negative deviations



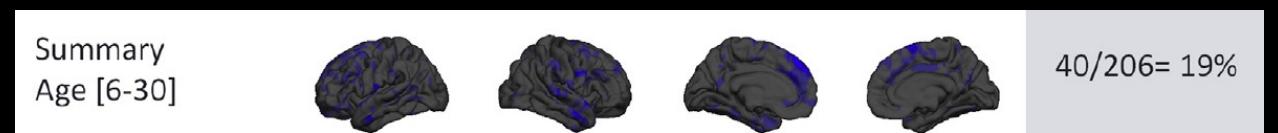
TD



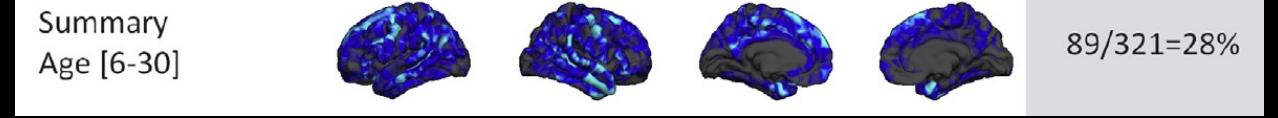
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TD

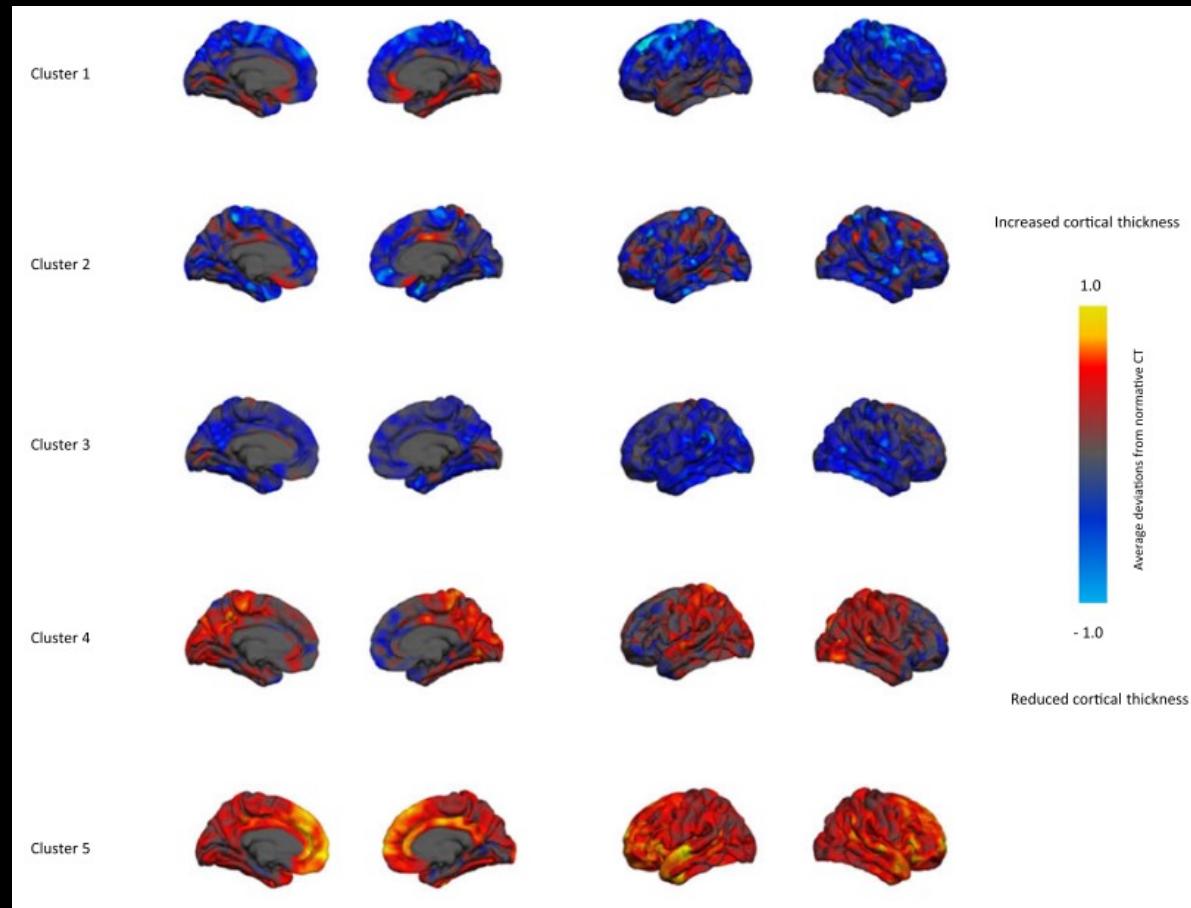


ASD



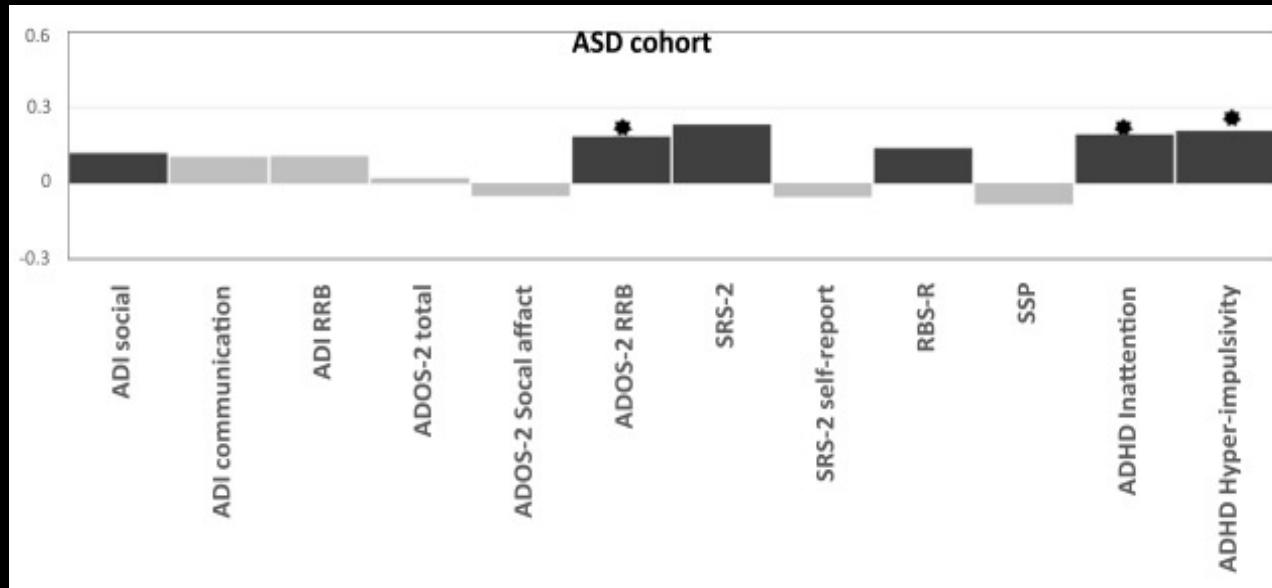
Zabihí, M., et al., (2019) Dissecting the Heterogeneous Cortical Anatomy of Autism Spectrum Disorder Using Normative Models. Biol Psychiatry Cogn Neurosci Neuroimaging, 4(6): 567-578.

APPLICATION: STRUCTURAL DATA



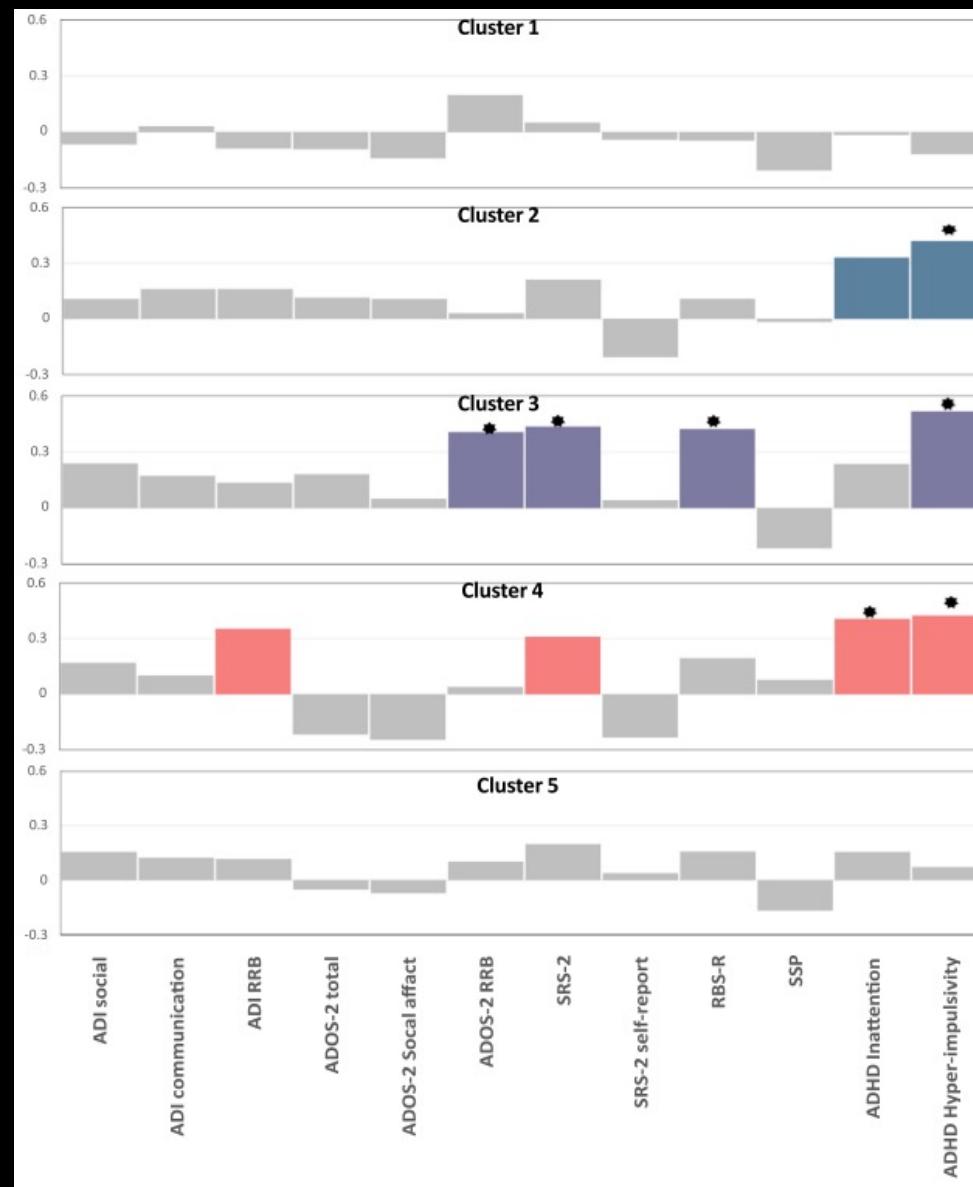
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STRUCTURAL DATA



Zabihí, M., et al., (2019) Dissecting the Heterogeneous Cortical Anatomy of Autism Spectrum Disorder Using Normative Models. Biol Psychiatry Cogn Neurosci Neuroimaging, 4(6): 567-578.

APPLICATION: STRUCTURAL DATA



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APPLICATION:
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$$Y = f(X, \theta) + \epsilon$$

Bold Signal

Covariates
(age, sex,
task parameters)Model
parameters

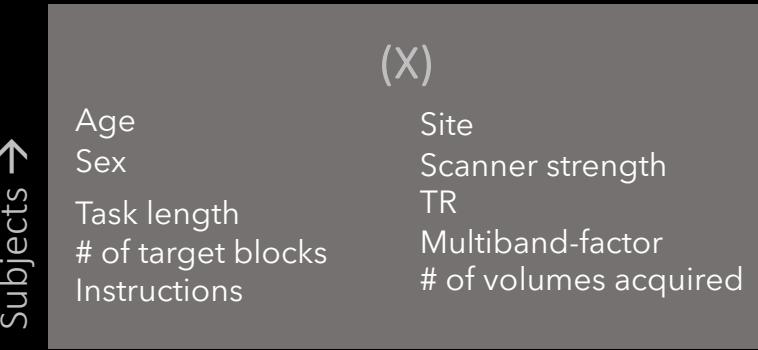
Residuals

Voxels →

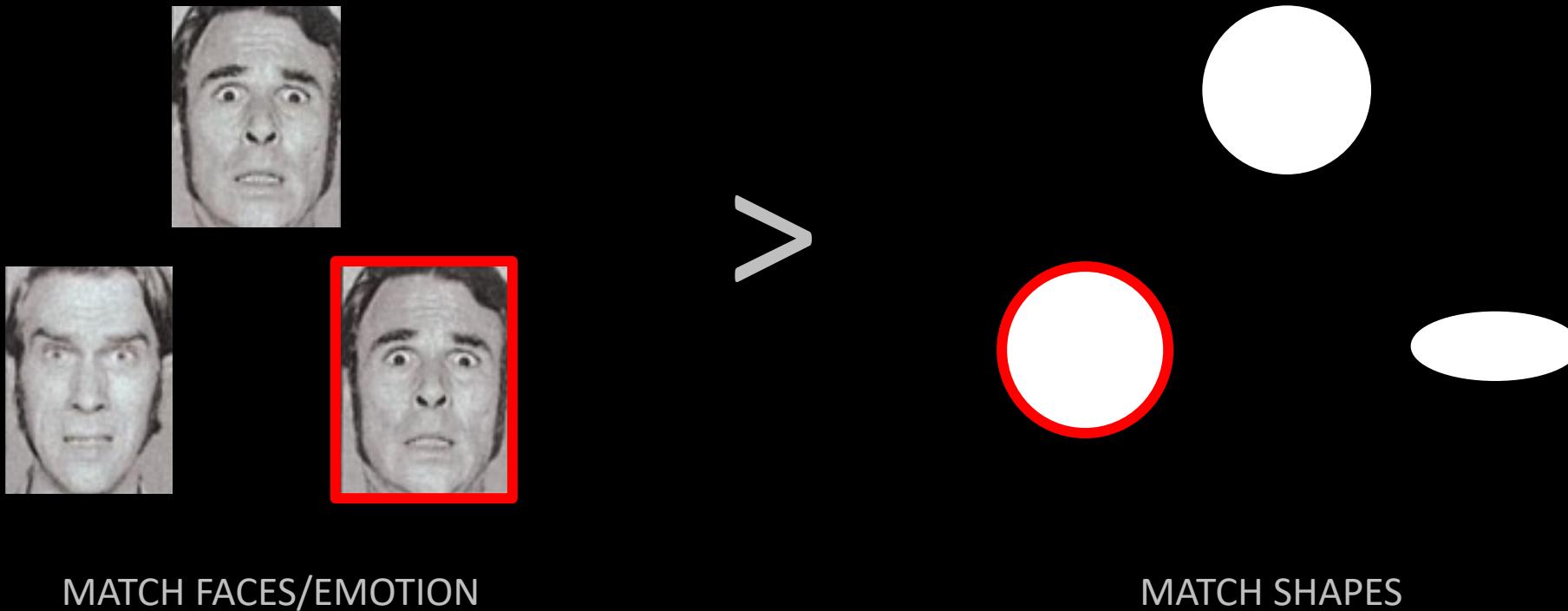


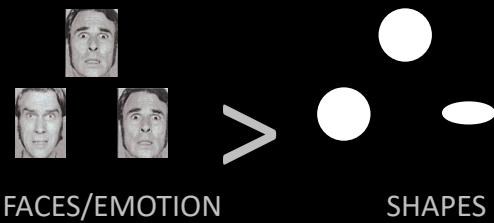
Subjects ↑

Predictors →

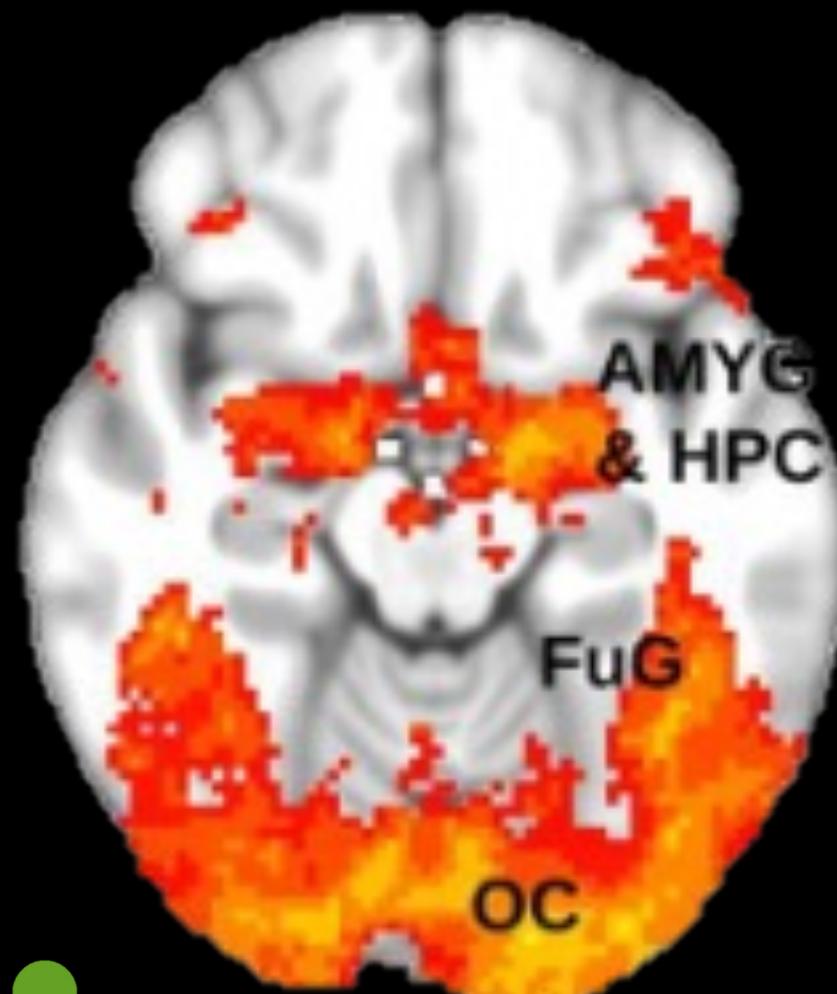


APPLICATION:
FUNCTIONAL

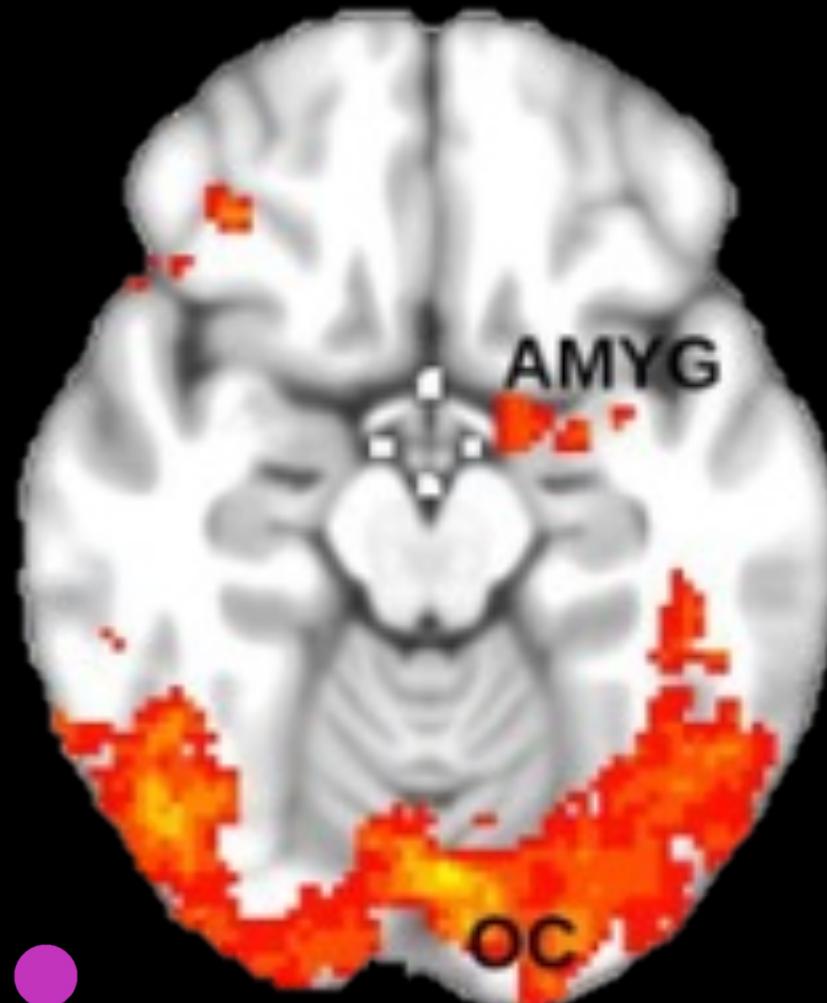
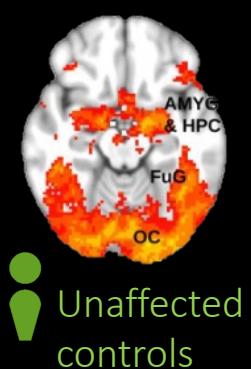
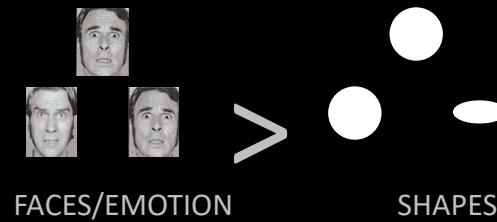




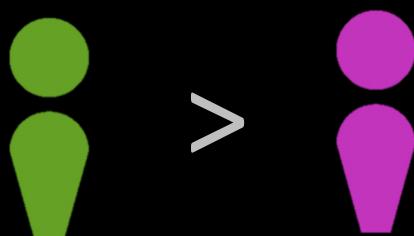
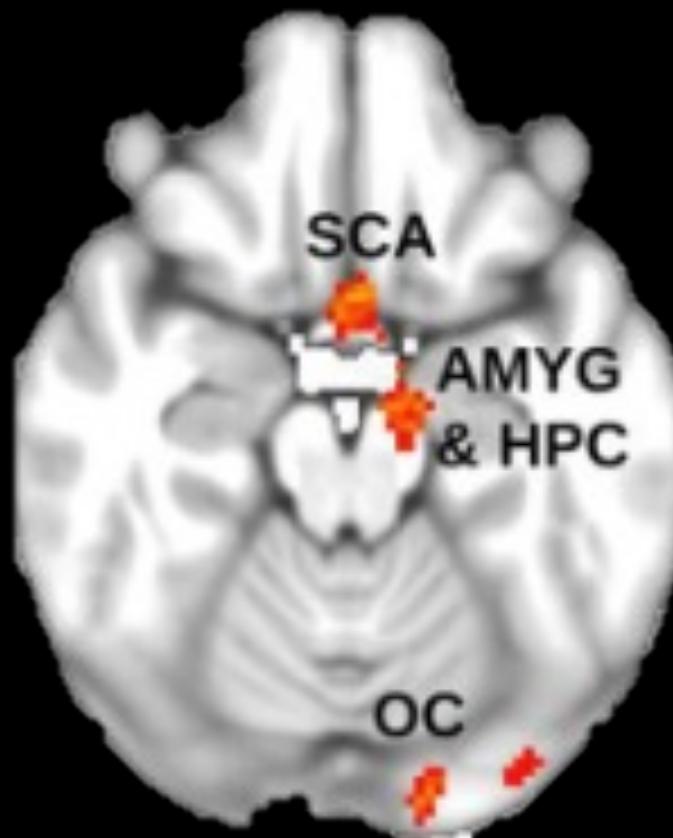
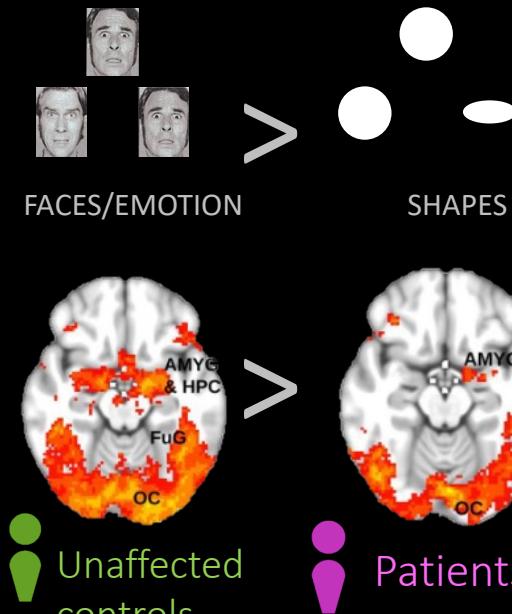
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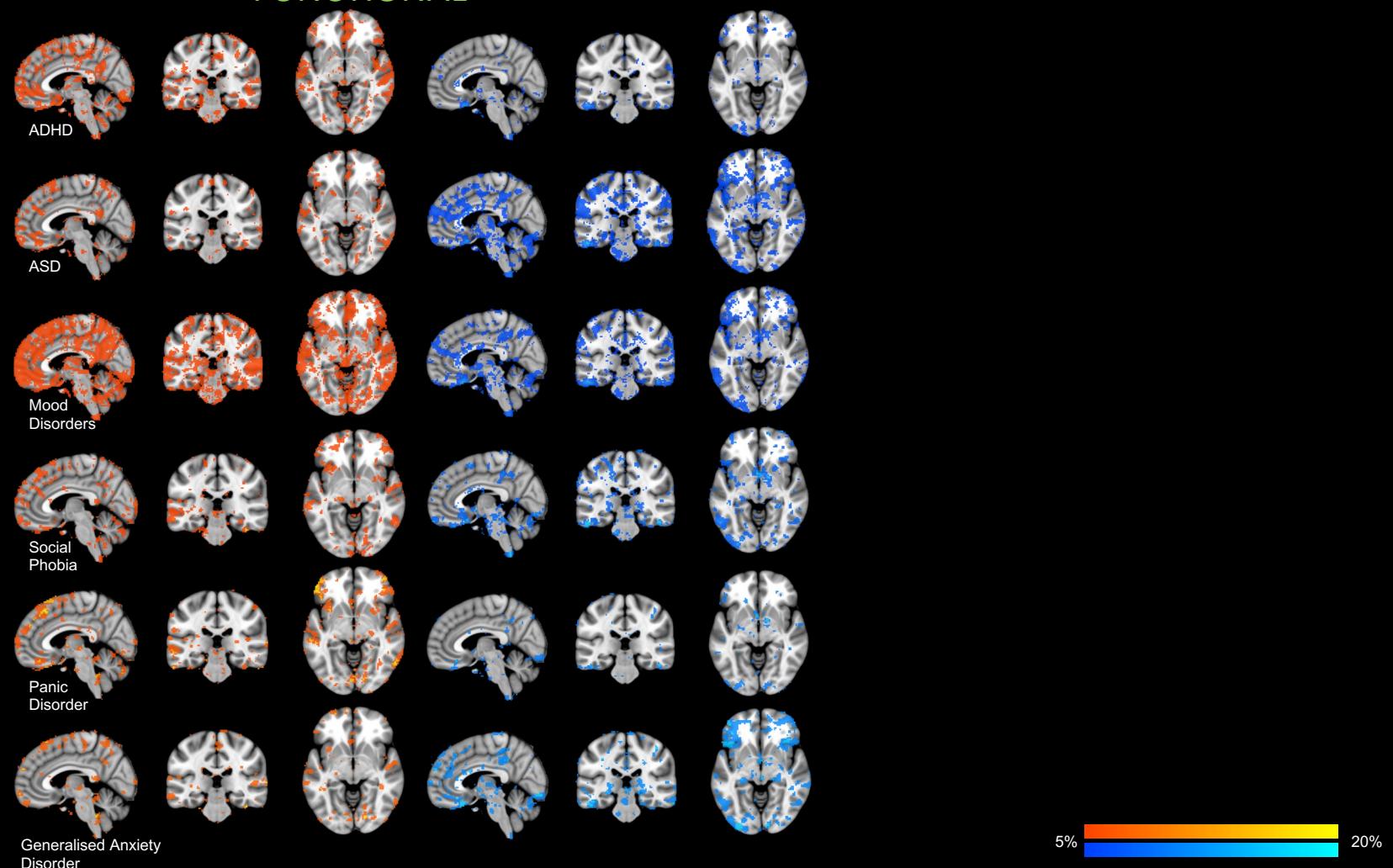


Unaffected controls

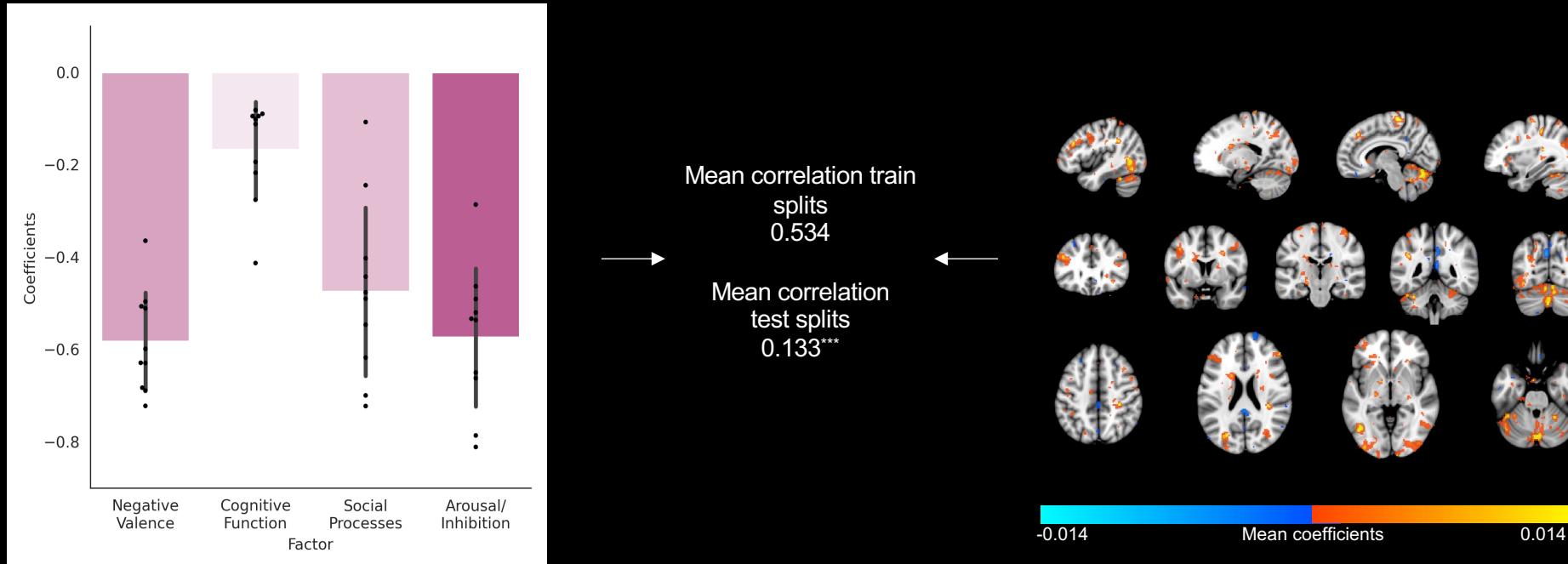
APPLICATION:
FUNCTIONAL

APPLICATION:
FUNCTIONAL



APPLICATION:
FUNCTIONAL

Savage H. et al., (2023) Unpacking the
functional heterogeneity of the Emotional
Face Matching Task: a normative modelling
approach. BioRxiv

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Savage H. et al., (2023) Unpacking the functional heterogeneity of the Emotional Face Matching Task: a normative modelling approach. BioRxiv

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Potential**

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**Future
Potential**

APPLICATION:
FUTURE POTENTIAL



DTI

Ramona Cirstian
ramona.cirstian@donders.ru.nl

APPLICATION: FUTURE POTENTIAL

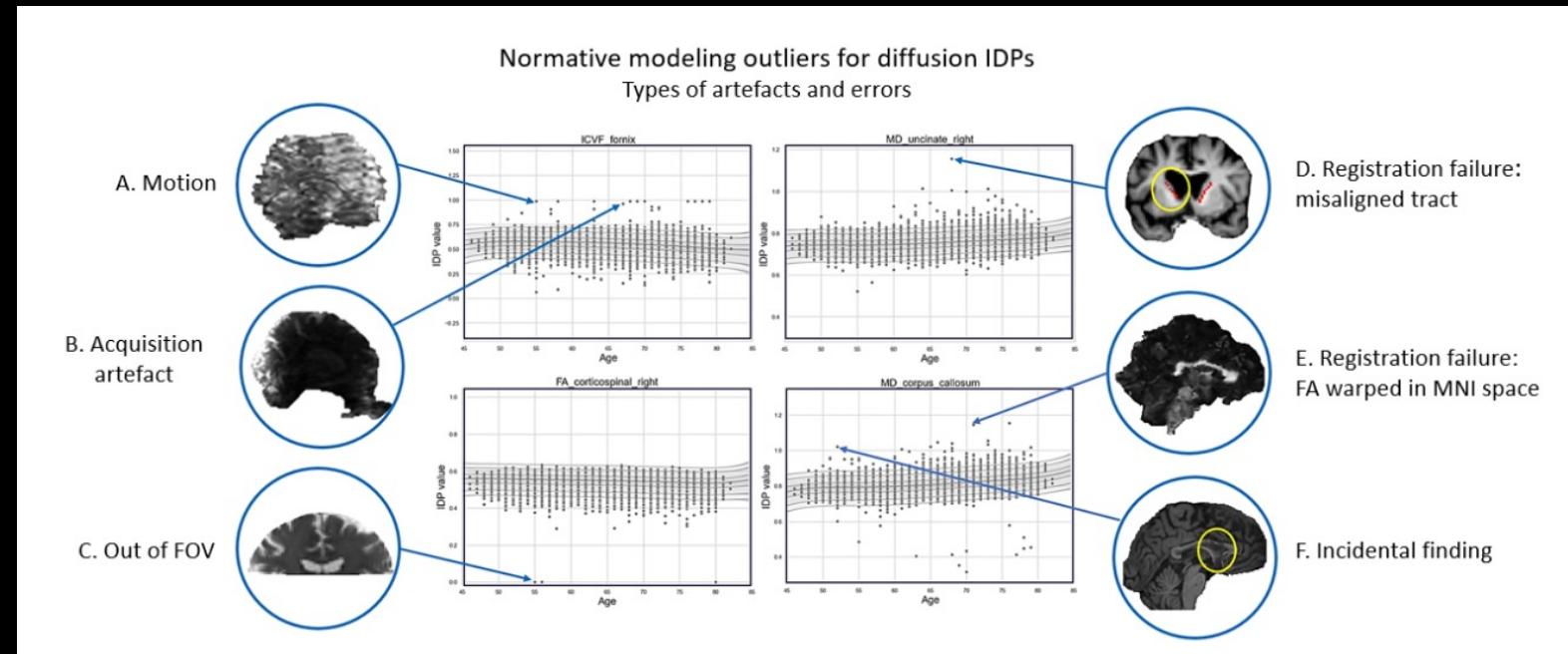


DTI

Ramona Cirstian
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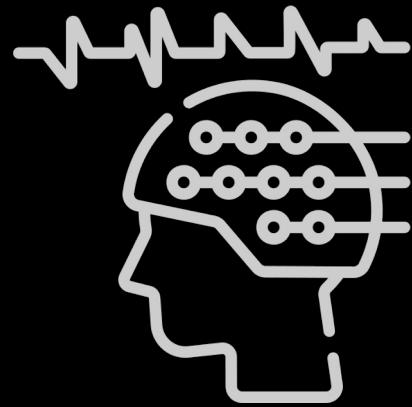
Cirstian R. et al., (2023) Objective QC for diffusion MRI data: artefact detection using normative modelling. BioRxiv



APPLICATION:
FUTURE POTENTIAL

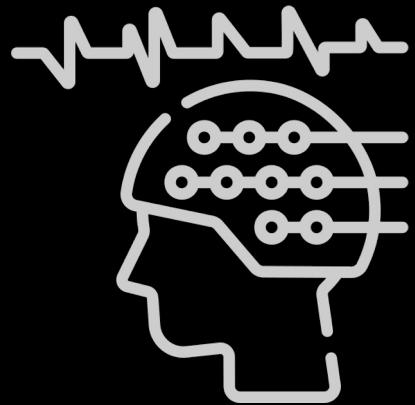


DTI



EEG

APPLICATION:
FUTURE POTENTIAL



DTI

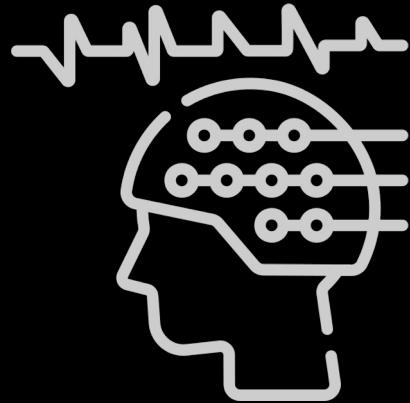
EEG

Psychometrics

APPLICATION:
FUTURE POTENTIAL



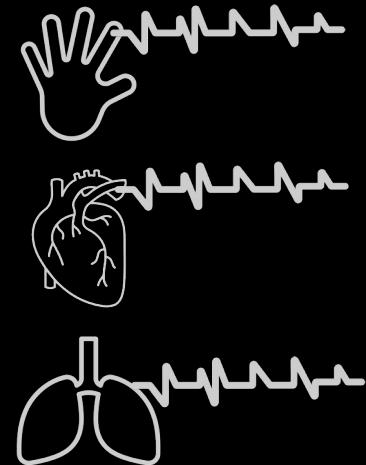
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EEG



Psychometrics

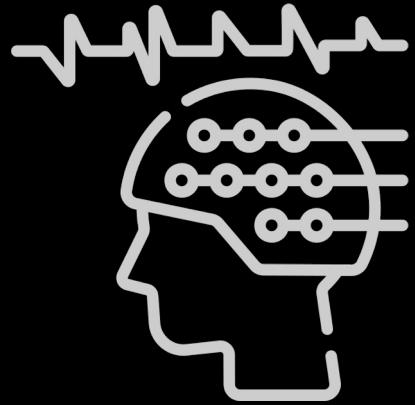


Physiology

APPLICATION:
FUTURE POTENTIAL



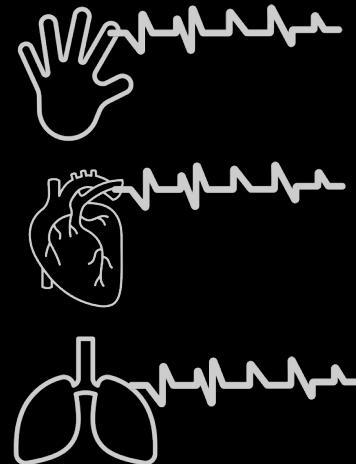
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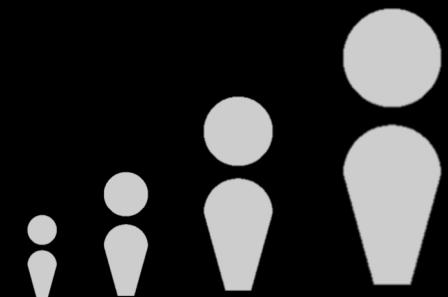
EEG



Psychometrics



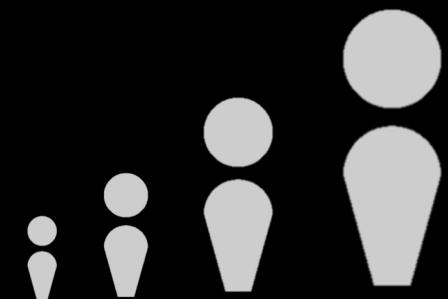
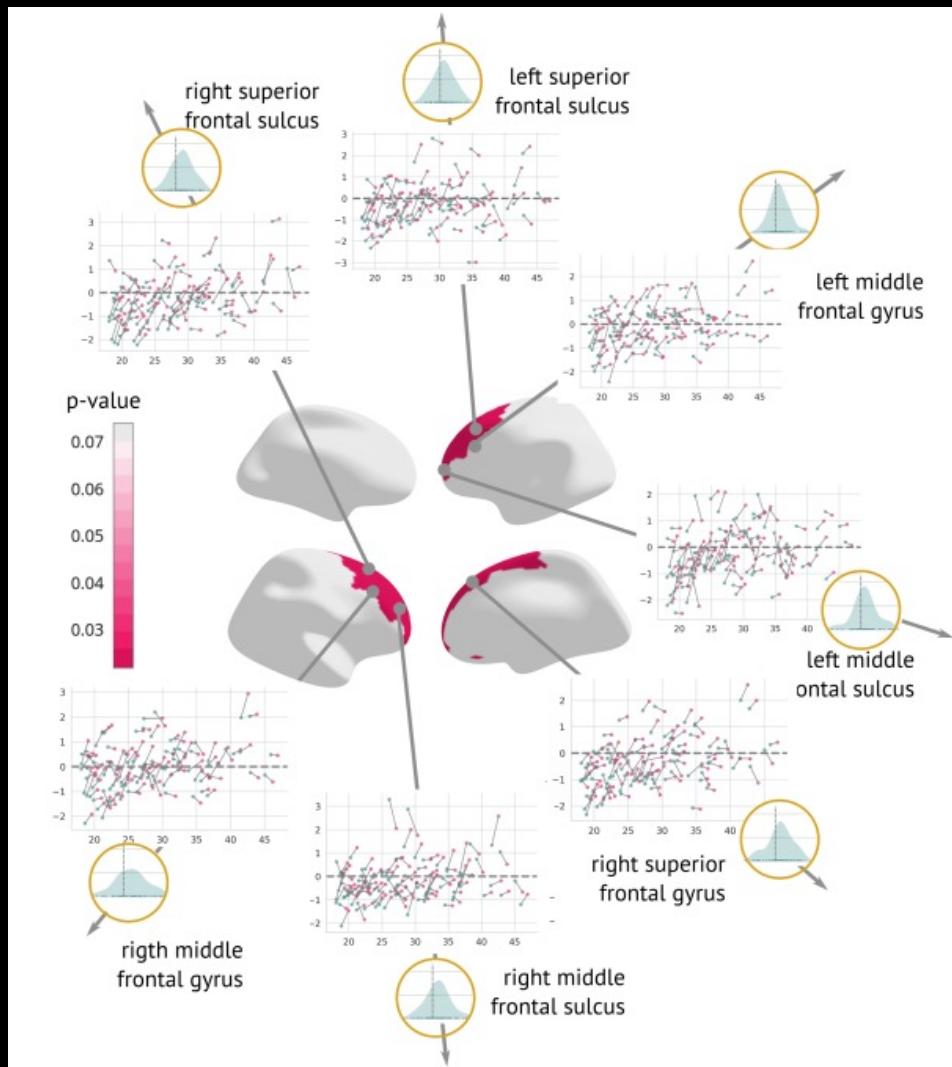
Physiology



Longitudinal

Barbora Bučková

APPLICATION: FUTURE POTENTIAL



Longitudinal

Barbora Bučková
barbora.buckova@donders.ru.nl

CONCLUSIONS

Structural:
Brain growth
and aging

Structural:
Clinical
Applications

Functional:
Emotional Face
Processing

**Future
Potential**

Changes across
the lifespan

Heterogeneity
within the
reference
populations

Heterogeneity
within and across
clinical conditions

Applications
in other
domains

CONCLUSIONS

THANK YOU!



Predictive Clinical Neuroscience Lab

Professor Andre Marquand

Radboudumc 



Download the toolbox
here:
github.com/amarquand



[pcnportal.dccn.
nl](http://pcnportal.dccn.nl)



<https://pcntoolkit.readthedocs.io>

Hannah.savage@donders.ru.nl
@DrHannahSavage

Charlotte.fraza@donders.ru.nl
@CFraza

TUTORIAL

https://github.com/CharFraza/CPC_ML_tutorial

Tasks

Task 1: Fitting normative models from scratch  [Open in Colab](#)

Task 2: Applying pre-trained normative models  [Open in Colab](#)

Task 3: Interpreting and visualizing the outputs of normative models  [Open in Colab](#)

Task 4: Using the outputs (Z-scores) as features in predictive model  [Open in Colab](#)

Task 1:

9:30 - 10:00

Task 2:

10:00 -10:30

Task 3:

10:30 -11:00

Task 4 :

11:00 - 11:30