Limited cortical thickness deficits across the psychosis spectrum

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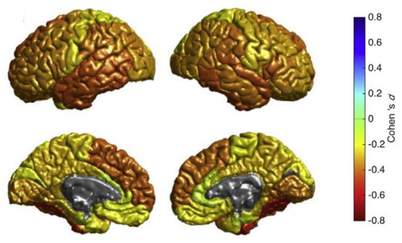
Background

- **Psychosis is thought to exist on a multidimensional spectrum** (positive, negative, disorganized, cognitive) (Guloksuz & van Os, 2017)
- Mapping **joint brain-behaviour dimensions** across a range of symptom severities may improve our understanding of how specific psychotic symptoms emerge (Cuthbert, 2015)
- Most psychosis imaging studies rely on case-control designs
- Replicated findings include lower cortical thickness (CT) in frontal/temporal regions
- **Aim:** comparing group-average and symptom-specific approaches to mapping CT deficits across the psychosis spectrum



van Erp et al., 2018

Methods

Sample: Prevention and Early Intervention for Psychosis, Douglas clinic

First episode of psychosis (FEP)	N = 69
Clinical high risk (CHR)	N = 40
Familial high risk (FHR)	N = 40
Healthy controls (HC)	N = 33
Total	**N = 182**

Age:
$\bar{x}$ = 24.14
s = 5.32
Range: 14-35

Sex:
61.5% males

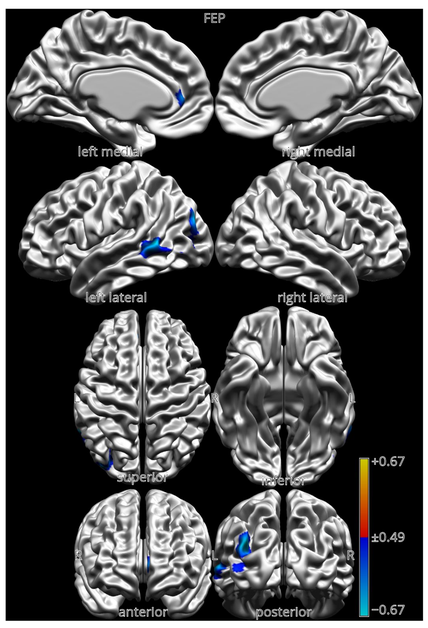
T1-w scans (MPRAGE) Quality controlled for motion artifacts → **minc-bpipe-library** Brain extraction, bias field correction → **CIVET** Vertex-wise (77 122) cortical thickness

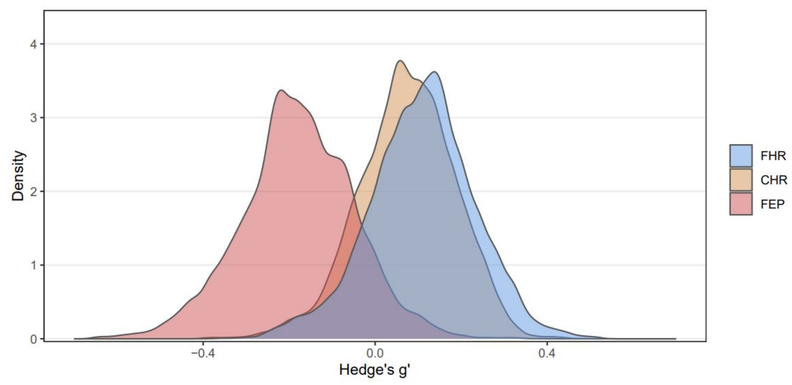
Final sample: 162/182 (89%) passed all pipeline stages

- No effect of quality control on age, t(180) = 1.528, p = 0.128
- No effect of quality control on sex, X^2 (1, N = 182) = 1.141, p = 0.286
- No differences in pass rates by group, X^2 (3, N = 182) = 4.014, p = 0.260

Univariate Analysis

Vertex-wise linear models: thickness ~ group + age + sex + handedness



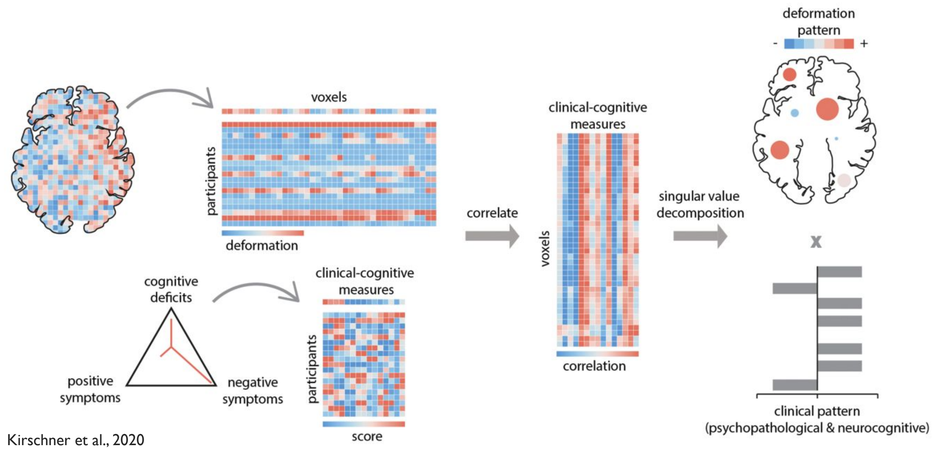


- FEP showed come CT reductions, only at 20% FDR
- Limited differences for other groups without thresholding
- No vertices passed at 5% FDR with models including intracranial volume, age^2, or an age * group interaction

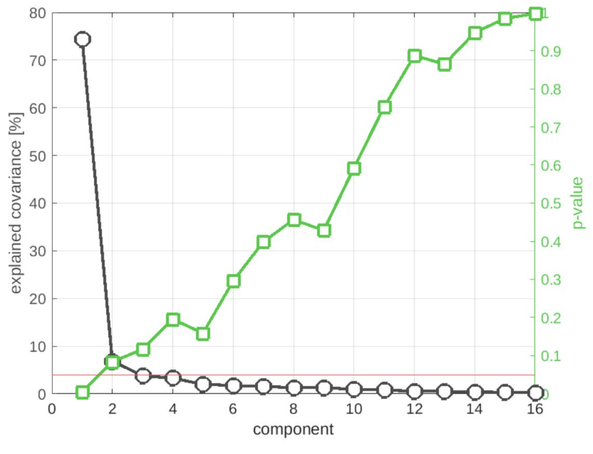
Limited evidence for group-level cortical thickness differences across the psychosis spectrum

Multivariate Analysis

Partial least squares correlation: mapping brain-behaviour latent variables (LVs)



Kirschner et al., 2020

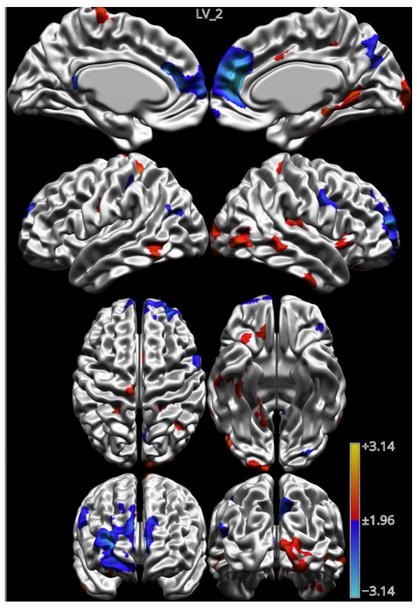


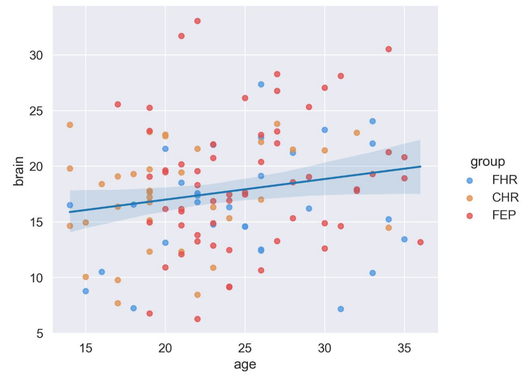
Brain: vertex-wise cortical thickness
Behaviour: SAPS, SANS, CogState
Subjects: N = 125

LV1: passed permutation test (p < 0.001)

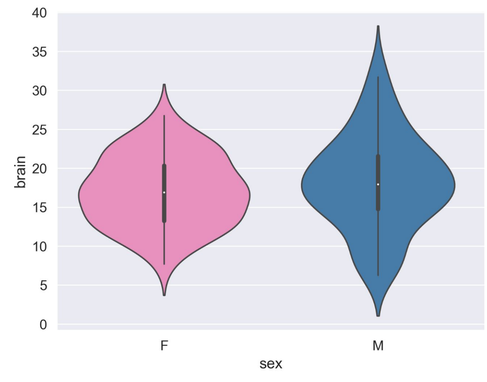
- Broadly lower cortical thickness
- Age-related, r(123) = 0.616, p < 0.001

LV2: permutation test approached significance (p = 0.08)





Age: relationship with LV2 brain scores
r(123) = 0.186, **p = 0.038**



Sex: no relationship with LV2 brain scores
t(123) = 1.169, p = 0.245

Some evidence for lower prefrontal cortical thickness related to positive/disorganized symptoms

Summary

- Limited group separability in cortical thickness measures
- Some support for specific CT deficits mapping to symptom dimensions (prefrontal, positive/disorganized)
- Can we validate this result (LV2) in a separate dataset?
- Does this generalize to other modalities?

Cuthbert BN (2015) Dialogues Clin Neurosc.
Guloksuz S, van Os J (2018) Psychol Med.
Kirschner et al. (2020) Schizophrenia Bulletin.
van Erp TGM et al. (2018) Biological Psychiatry.

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