Evaluating Harmonisation Methods for Multi-Site Psychosis MRI Data
Insights from the Psy-ShareD Resource

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Introduction

- MRI is widely used to study brain structure, but variability across scanners, sites, and acquisition protocols can introduce differences in the data, generating site-effects which can lead to biassed or inconsistent results and reduce reproducibility [1].

- Another challenge in MRI studies is the limited availability of large, diverse samples due to the high cost and logistical challenges of scanning. This issue is particularly challenging in studies of psychiatic disorders like schizophrenia, where sample sizes are limited [2, 3].

- Harmonisation methods aim to mitigate these differences, enhancing comparability of MRI data [1, 4, 5, 6]. They can be broadly divided in image-level and feature-level.

Objective: To compare different harmonisation techniques applied to T1w MRI data from the Psy-ShareD, specifically for individuals with schizophrenia and healthy controls. We assess their ability to perserve relevant biological information and mitigate scanner-related variability.

What is PsyShareD?
It is a free-to-acess database that hosts pre-existing structural MRI data (mainly T1-weighted images) collected from different sites around the world.
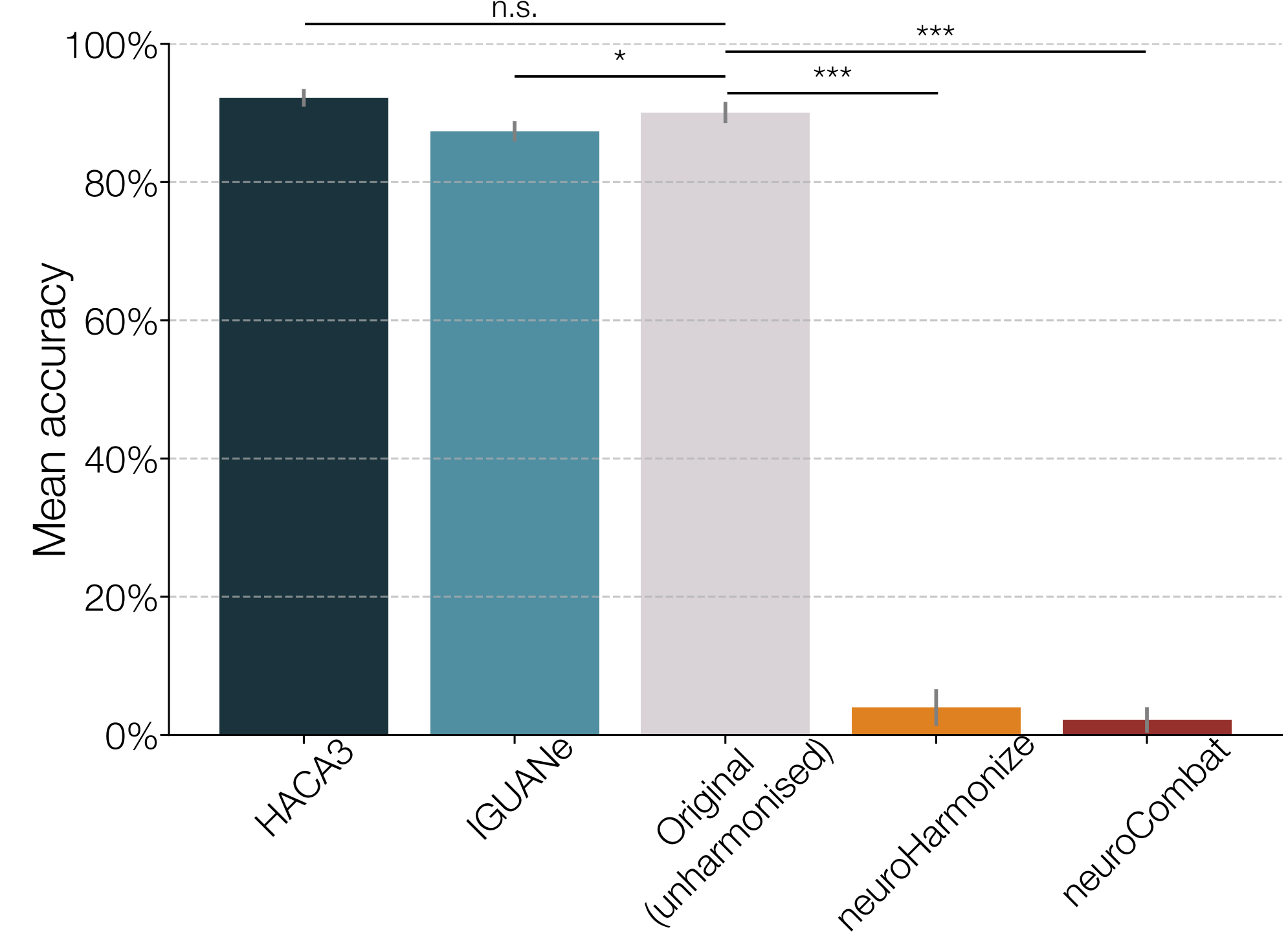
Methods
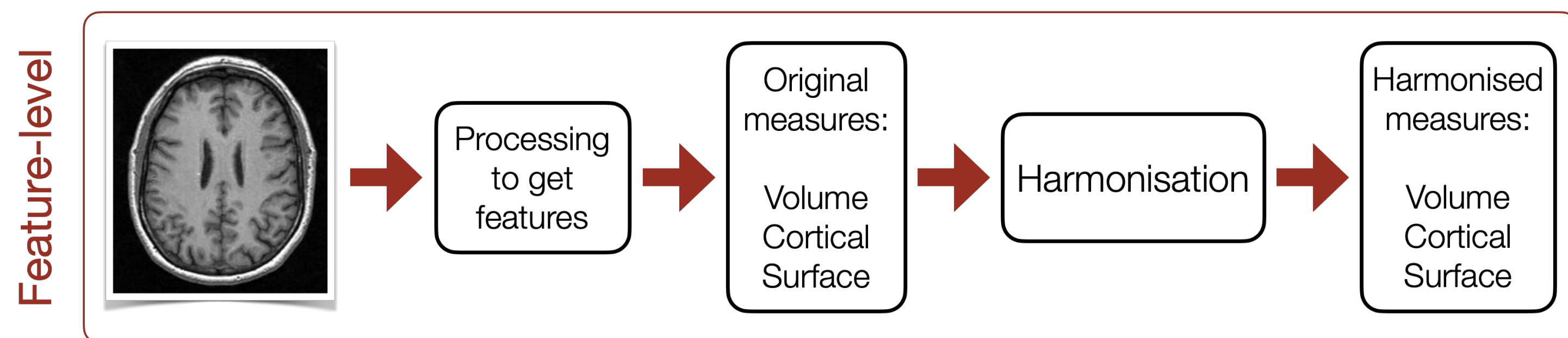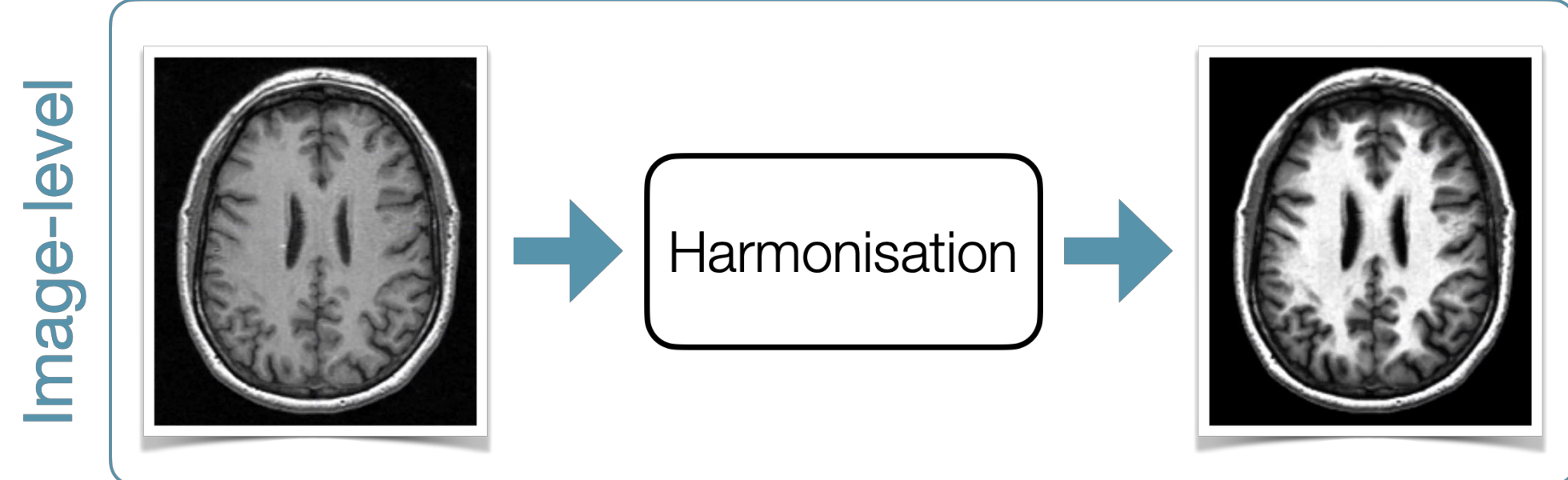
- Image-level harmonisation methods: HACA3 [5] and IGUANe [6]
- Feature-level harmonisation methods: neuroHarmonize [1] and neuroCombat [4]

- Data from 7 studies in 5 sites across 3 countries (UK, Italy and Japan)

- 269 healthy controls (101 females)
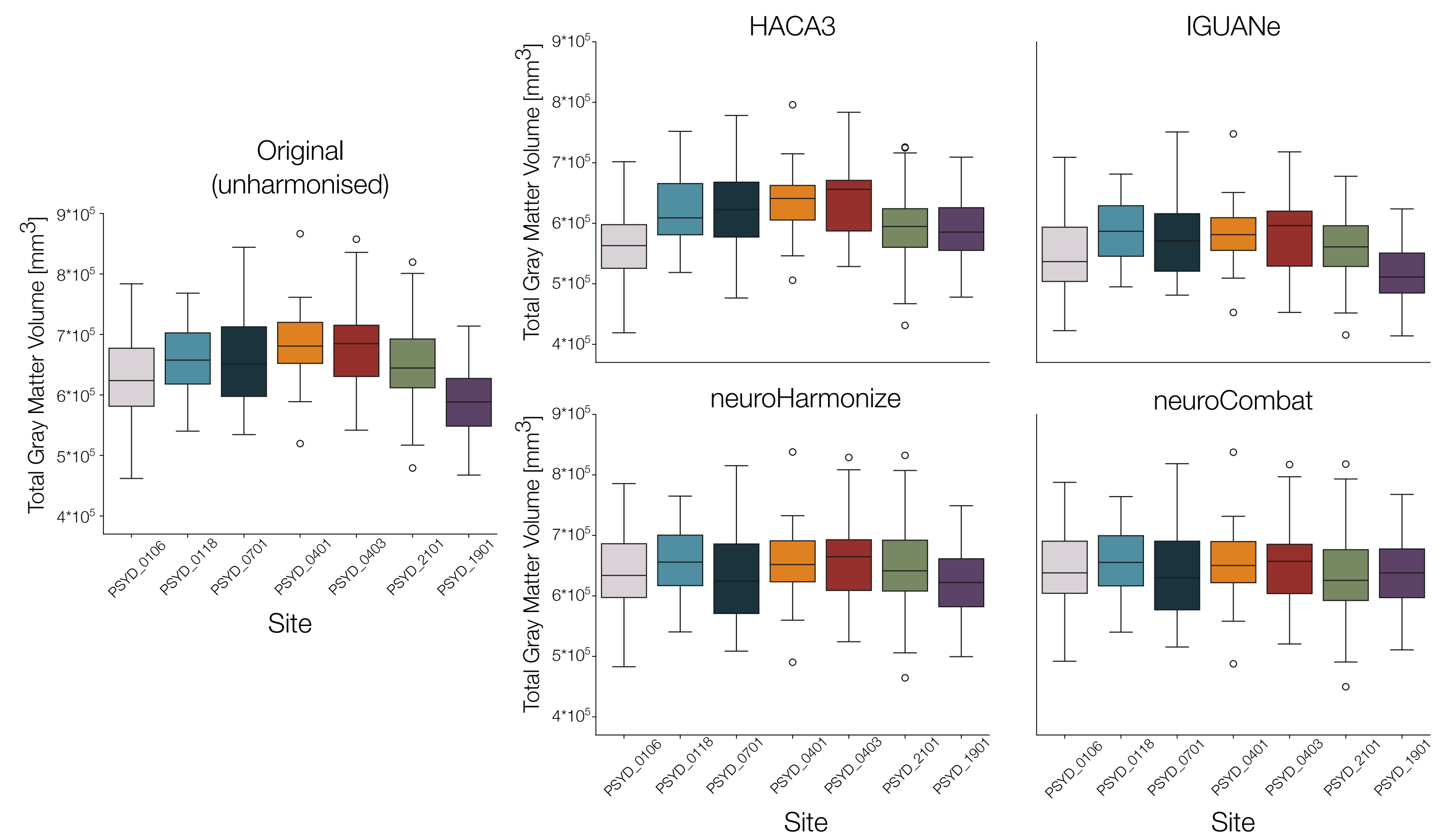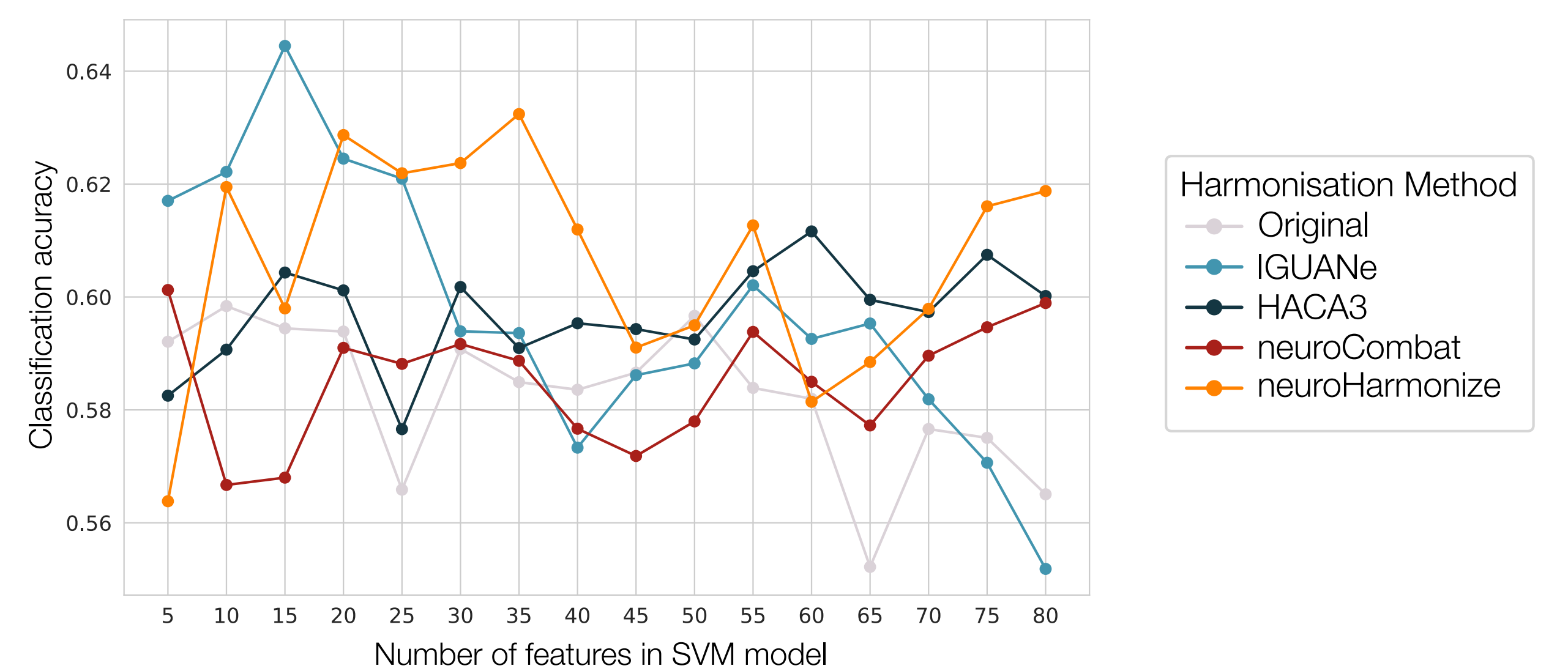- 295 individuals with schizophrenia (85 females)

Total PANSS distribution per site
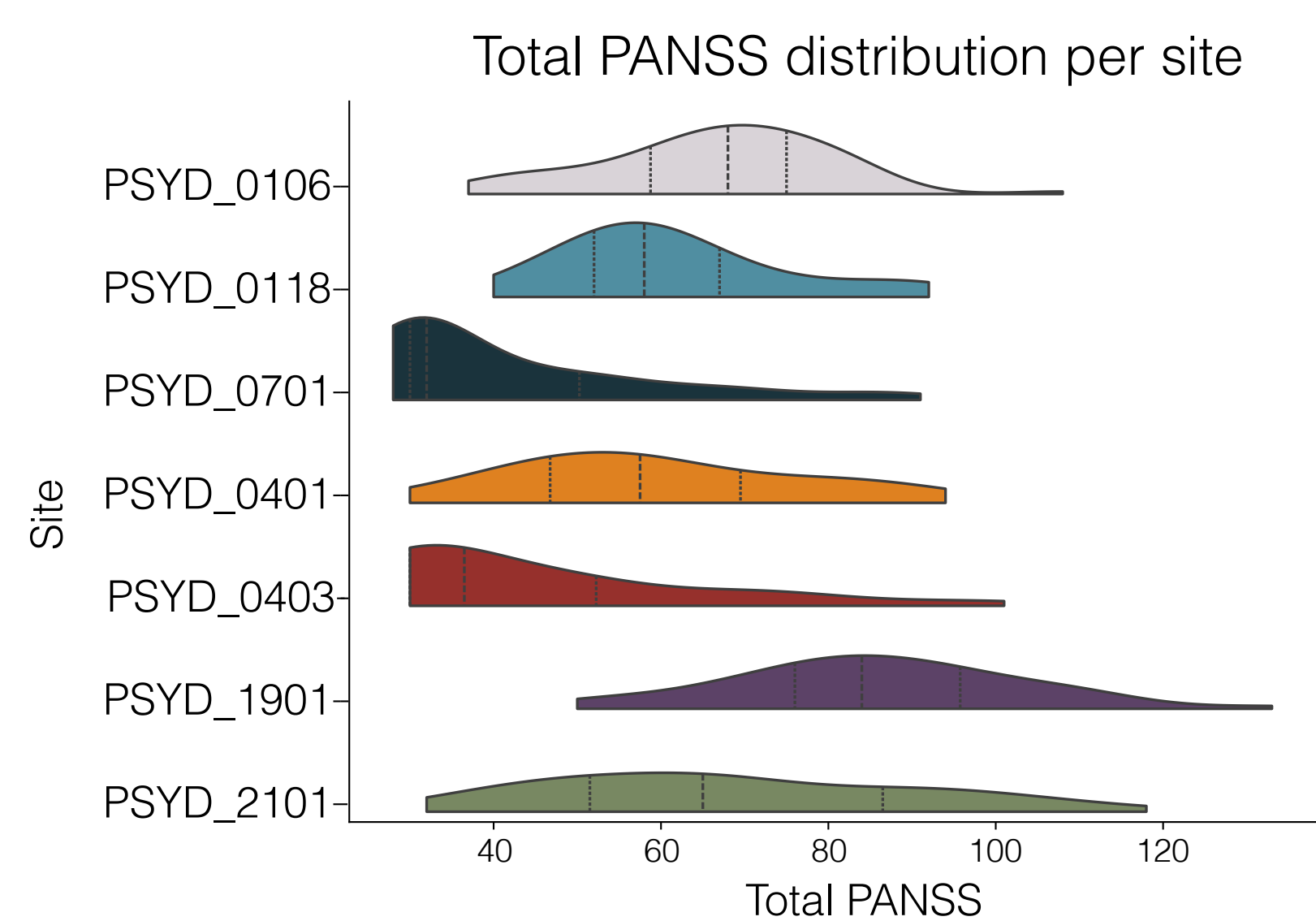
Results

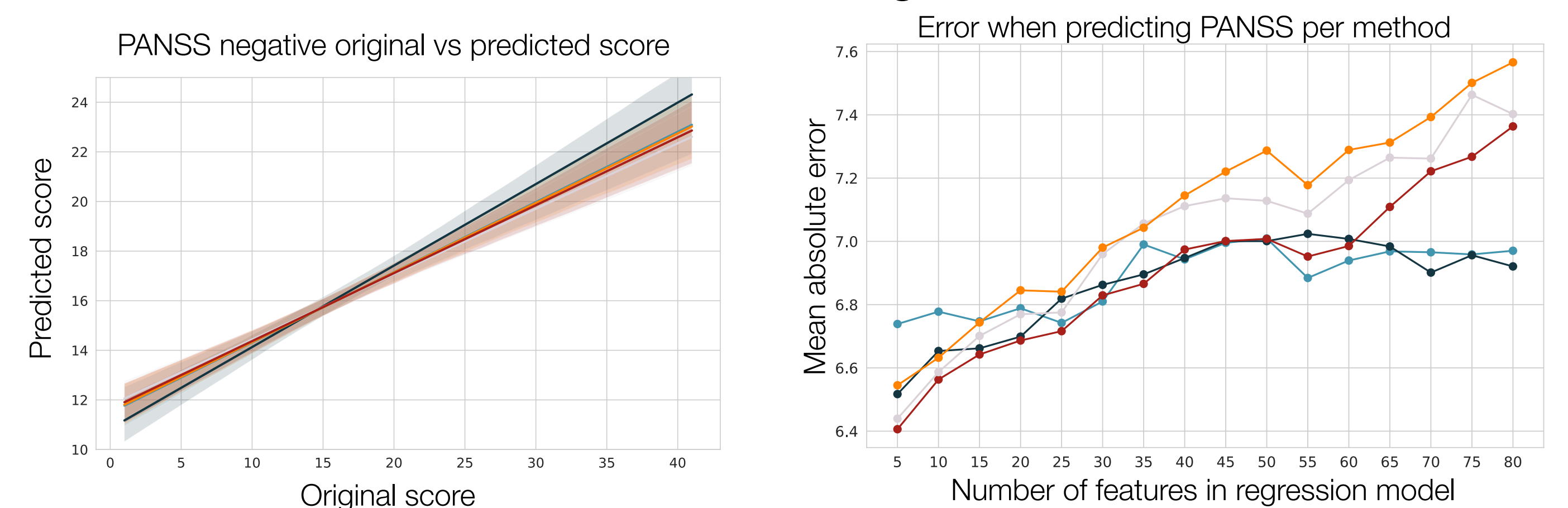### Site classification accuracies per harmonisation method

Mean total Gray Matter volume per harmonisation method

Classification accuracy of SVM into schizophrenia vs. control

Prediction of PANSS negative score

PANSS negative original vs predicted score

Error when predicting PANSS per method

Discussion

- Feature-level harmonisation methods effectively removes most site-related variance, as shown by site classifciation and total GM volume results.
- IGUANe image-level harmonisation significantly reduces site recognisability, though to a lesser extent than feature-based methods, while HACA3 does not reduce it.
- Harmonised images perform similarly to original images in schizophrenia classification and symptom prediction (PANSS negative).
- Reducing site-related variance is important, but it should not come at the cost of removing biologically relevant information. Image-level harmonisation methods, particularly IGUANe, show promising progress in achieving this balance.
- Careful selection of harmonisation methods is crucial and should align with the study's objective.

References: [1] Pomponio et al., (2020) NeuroImage; [2] Evans et al., (2025) Schizophrenia Research; [3] Allen et al., (2025) Human Brain Mapping; [4] Fortin et al., (2018) NeuroImage; [5] Zuo et al., (2023) Computerized Medical Imaging and Graphics; [6] Roca et al., (2025) Medical Image Analysis