Does maximising connectome fingerprint identifiability improve connectome-based phenotype prediction?

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from molecules to mind

BACKGROUND

- Individual differences in functional connectivity (FC) patterns which are unique and stable like a "fingerprint", and have shown to predict individual differences in behaviour[1,2].
- We build on prior work identifying pre-/post-processing factors (See Methods) that improve connectome fingerprint-based identification and reduced the number of participants excluded from FC-based analyses due to excessive motion, by assessing whether the same factors can boost the robustness of connectome-based phenotype prediction.
- **To assess whether factors such as (1) dimensionality of parcellation schemes, (2) inclusion of cortical vs. subcortical regions, and (3) motion exclusion strategies such as scrubbing[3] and bagging[4,5] improve the predictive power of connectome-based predictive modelling (CPM) for the brain-behaviour relationships of age, general psychopathology [CBCL], and intellectual ability [FSIQ] in developing youths derived from the Healthy Brain Network[6].**

METHODS

- **Participants:** *N* = 540 Healthy Brain Network participants (198 F, 6-21yrs, M = 10.7±3yrs).
- **MRI data:** Siemens 3T Prisma scanner. T1-w MPRAGE (0.8 x 0.8 x 0.8 mm^3; 224 sagittal slices, TR = 2500 ms, TE = 3.15 ms, flip angle = 8°) and resting-state fMRI (EPI) data (60 slices; 2.4 x 2.4 x 2.4 mm^3, TR = 800 ms, TE = 30 ms, flip angle = 31°) were analysed.
- **Preprocessing:** Motion correction, grand mean scaling, linear & quadratic detrending, 36P confound regression (including GSR), spatial smoothing with σ = 6 mm, temporal filtering (0.009-0.1Hz). High-motion participants were defined as those with mean msFD[7] > 0.2 mm.

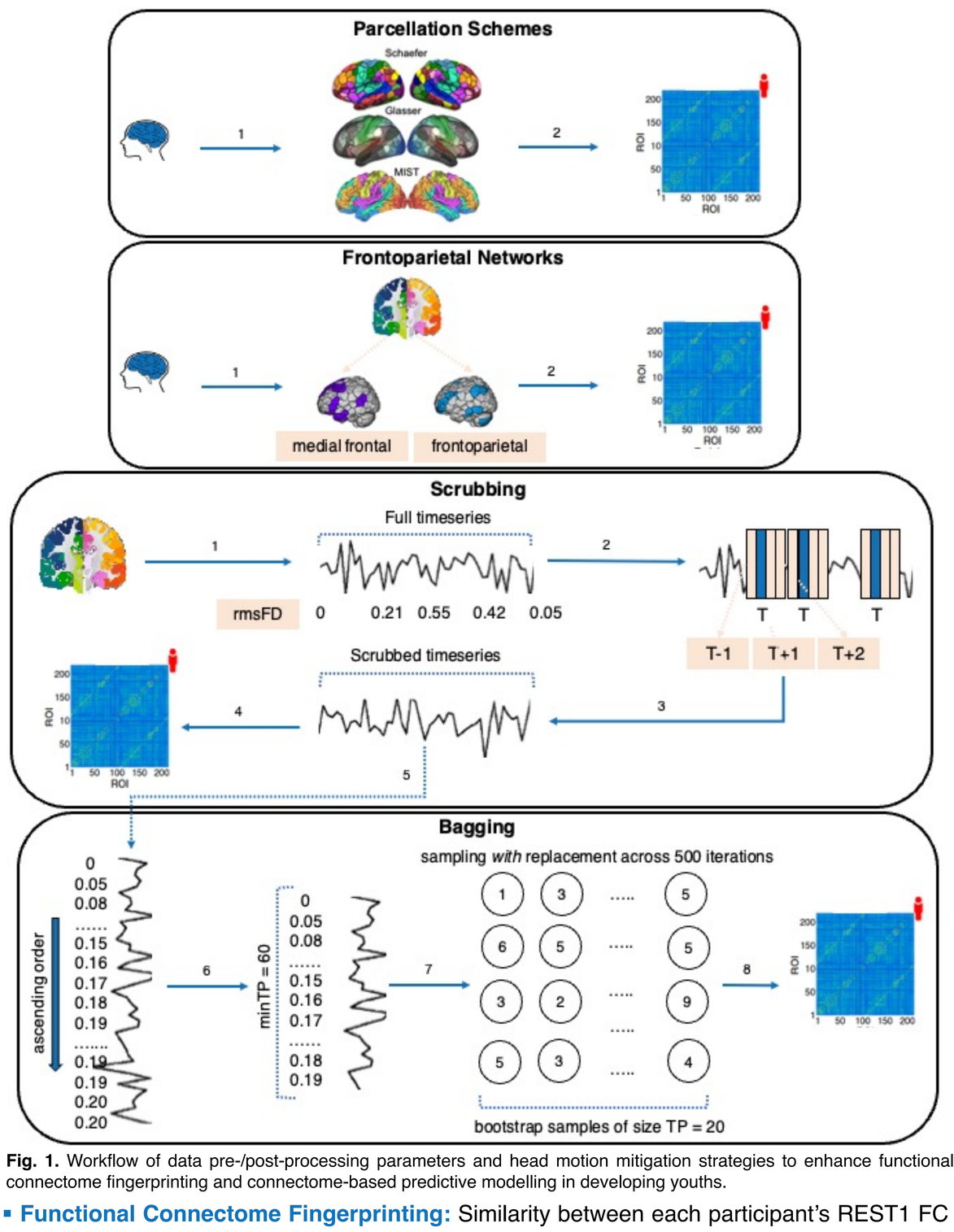

Fig. 1. Workflow of data pre-/post-processing parameters and head motion mitigation strategies to enhance functional connectome fingerprinting and connectome-based predictive modelling in developing youths.

- **Functional Connectome Fingerprinting:** Similarity between each participant's REST1 FC matrix and all REST2 FC matrices was derived using different configurations of FC estimates. ID accuracy was computed using binary identification (BID; i.e., 0/1 accuracy)[1,8].
- **Connectome-based Predictive Modelling:** CPM predicted the relationships between REST1 FC and behaviour using 95% of the significantly positively [POS] and negatively [NEG] correlated edges ($p < 0.01$) across a 10-fold CV over 100 iterations[2]. A sample of typically developing controls from the Autism Brain Imaging Data Exchange[9] [ABIDE] (*N* = 397, 6-57yrs, M = 16.5±7yrs) was used to test generalisation of CPM-based predictions.

RESULTS

1. Connectome-based fingerprint accuracy across parcellation schemes

- Baseline HBN-derived fingerprint BID accuracy was 78% which was obtained from the whole-brain Shen 268 parcellation scheme. The BID accuracies improved up to 90% when cortical parcellation schemes were employed at higher resolutions (e.g., ~500 parcels).

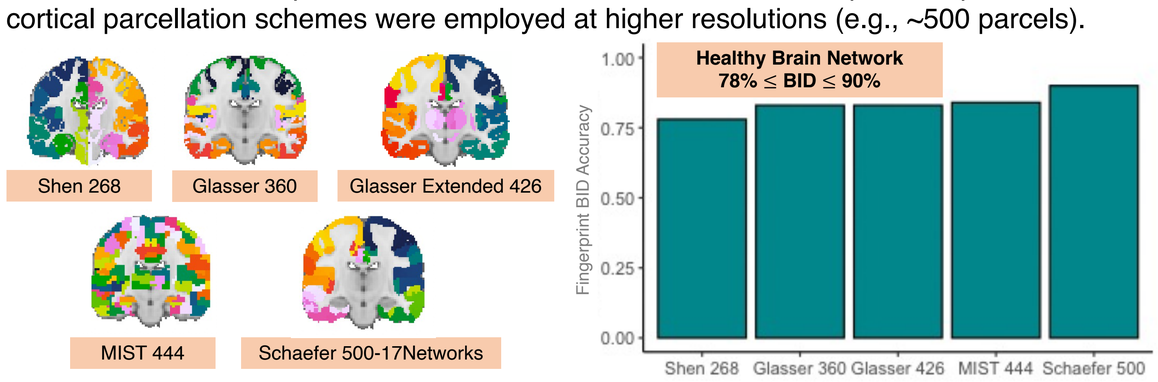

Fig. 2. Fingerprint BID accuracies derived from baseline Shen 268 parcellation scheme followed by finer cortical (e.g., Glasser 360, Schaefer 500-17Networks) and whole-brain (e.g., Glasser Extended 426, MIST 444) schemes.

RESULTS

2. Baseline connectome-based predictive modelling of age, CBCL & FSIQ

- Baseline CPM were predictive of age [POS: r = 0.61, p < 0.001; NEG: r = 0.57, p < 0.001], CBCL [POS: r = 0.16, p = 0.019], and FSIQ [POS: r = 0.16, p = 0.027].

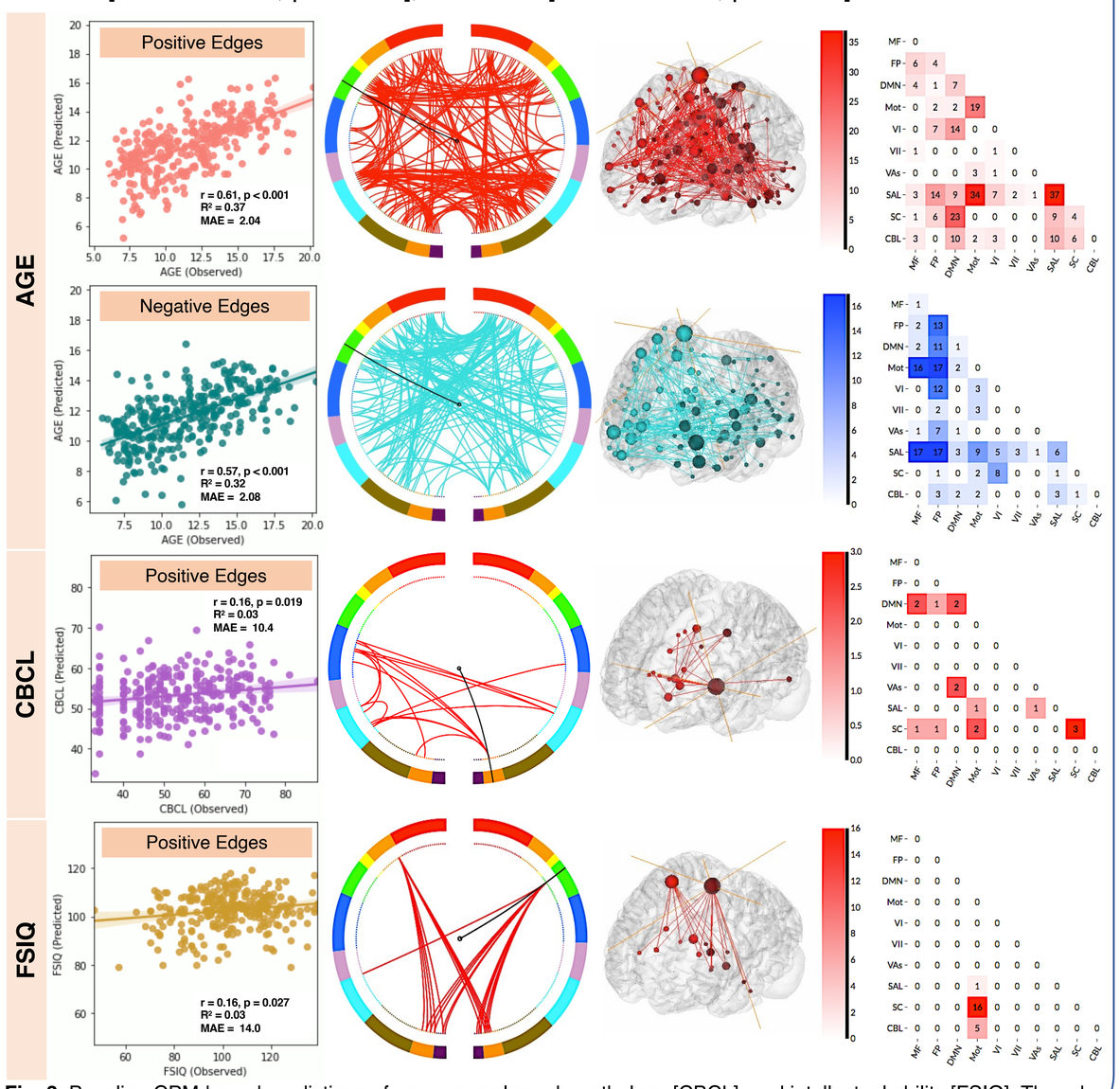

Fig. 3. Baseline CPM-based predictions of age, general psychopathology [CBCL], and intellectual ability [FSIQ]. The edge consistencies and contributions of the networks in predicting the behaviours are summarised using a 10-node definition[1].

3. Methodological implications on fingerprinting accuracy and CPM

- Relationships between observed and predicted behavioural phenotypes were maintained across several parcellation schemes and head motion mitigation strategies.
- Scrubbing preserved the CBCL associations whereas finer whole-brain parcellations and head motion exclusion strategies maintained the FSIQ relationships.

METHOD	BID	PATTERN	AGE	CBCL	FSIQ
Shen 268	0.78	Baseline	$r_P = 0.61^{**}$, $r_N = 0.58^{**}$	$r_P = 0.16^{*}$	$r_P = 0.16^{*}$
FP Networks	0.71	↓	$r_P = 0.40^{**}$, $r_N = 0.35^{**}$	$r_P = 0.03^{‡}$	$r_P = 0.03^{‡}$
Schaefer 500	0.90	↑	$r_P = 0.56^{**}$, $r_N = 0.58^{**}$	$r_P = 0.09^{‡}$	$r_P = 0.06^{‡}$
Glasser 360	0.83	↑	$r_P = 0.56^{**}$, $r_N = 0.53^{**}$	$r_P = 0.12^{‡}$	$r_P = 0.10^{‡}$
Glasser 426	0.83	↑	$r_P = 0.61^{**}$, $r_N = 0.53^{**}$	$r_P = 0.14^{‡}$	$r_P = 0.17^{*}$
MIST 444	0.84	↑	$r_P = 0.61^{**}$, $r_N = 0.60^{**}$	$r_P = 0.07^{‡}$	$r_P = 0.18^{*}$
Scrubbing	0.77	↓	$r_P = 0.60^{**}$, $r_N = 0.58^{**}$	$r_P = 0.18^{*}$	$r_P = 0.18^{*}$
Bagging (w/o high-motion)	0.69	↓	$r_P = 0.62^{**}$, $r_N = 0.53^{**}$	$r_P = -0.08^{‡}$	$r_P = 0.21^{*}$
Bagging (with high-motion)	0.68	↓	$r_P = 0.60^{**}$, $r_N = 0.50^{**}$	$r_P = -0.04^{‡}$	$r_P = 0.16^{*}$

Table 1. Relationships between observed and predicted behavioural phenotypes under different CPM configurations. $^{**}p < 0.001$. $^{*}p < 0.05$. $^{‡}p > 0.05$. r_P = positive edges. r_N = negative edges.

4. External validation of the CPM-based predictions derived from ABIDE

- HBN-derived CPM predictions generalised to an independent dataset: the observed and predicted relationships did not statistically differ from those obtained from ABIDE for age [$z_p = 1.91$, $p = 0.056$; $z_n = -0.20$, $p = 0.84$] and FSIQ [$z_p = 0.39$, $p = 0.70$].

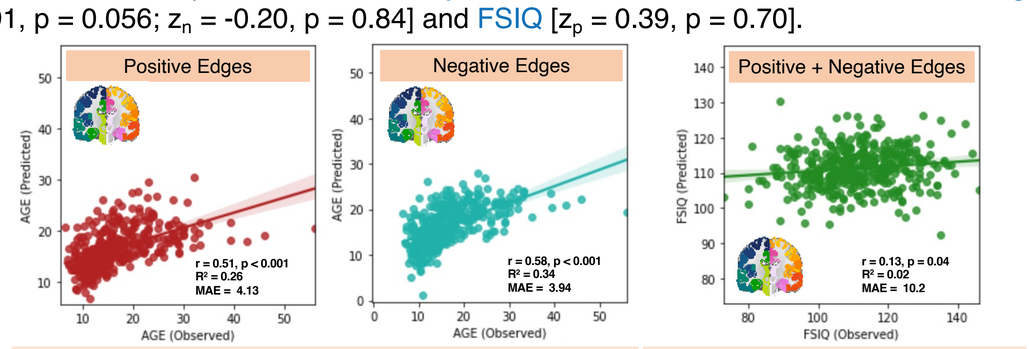

Fig. 4. Generalising the CPM-based predictions of age and FSIQ by employing typically developing controls derived from the ABIDE dataset. Fisher's z test was applied to compare the brain-behaviour relationships between HBN and ABIDE.

CONCLUSIONS

- Factors that boost the identifiability of individuals based on their functional connectome fingerprints do not appear to systematically improve connectome-based phenotype prediction, **suggests that more unique connectome fingerprints do not necessarily translate to better brain-behaviour relationships in developing populations.**

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