Towards data salvage in high movement cohorts: bagging yields robust brain-behaviour relationships

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BACKGROUND

- The sharing of large consortia-level datasets has many advantages for the neuroimaging community, by providing opportunities for well-powered analyses of resting state fMRI data. One such analysis has revealed that very large sample sizes (N = ~2000) are required to achieve robust and reproducible brain-wide functional connectivity-phenotype associations[1].

- In typical functional connectivity (FC) brain-behaviour studies, many participants are often excluded due to excessive head motion, based on a head motion threshold (rmsFD)[2].

- Bagging (bootstrap aggregation) is a method applied in Machine Learning to reduce variance and increase the robustness of estimates derived from noisy data[3]. We assessed whether a bagging approach could be applied to estimate FC from a restricted number of timepoints sampled for each individual from those showing the least motion.

- **To assess the robustness of FC estimates computed using bagging from motion-limited time series, we computed (1) connectome fingerprint identification accuracy across within-session scans (REST1/REST2) and (2) confidence Intervals for FC-behaviour relationships computed for bagged FC estimates.**

METHODS

- **Participants:** N = 423 Healthy Brain Network[4] participants (153 F, 6-20yrs, M = 10.7±3yrs).

- **MRI data:** Siemens 3T Prisma scanner. T1-w MPRAGE (0.8x0.8x0.8mm^3; 224 sagittal slices, TR = 2500ms, TE = 3.15ms, flip angle = 8°) and resting-state fMRI (EPI) data (60 slices; 2.4 x 2.4 x 2.4mm^3, TR = 800ms, TE = 30ms, flip angle = 31°) were analysed.

- **Preprocessing:** Motion correction, grand mean scaling, linear & quadratic detrending, 36P confound regression (including GSR), spatial smoothing with σ = 6mm, temporal filtering (0.009-0.1Hz). *High-motion* participants were defined as those with mean rmsFD > 0.2mm.

- **Brain-behaviour relationships:** **Standard** – partial Spearman's Rank correlation (R) between standard (full timeseries) FC[5] and **age** at the edge level covaried for sex, rmsFD. **Bagging** – FC was first estimated based on the mean of 500 bootstrap (with replacement) samples (for a range of time series lengths) taken from motion-scrubbed timeseries (i.e., timepoints > 0.2mm rmsFD removed, plus 1 timepoint pre and 2 timepoints post)[6] such that samples comprised subsets of the **minTP** *least motion-contaminated timepoints,* where minTP ∈ {60, 200}. Partial Spearman's Rank correlations (R) were estimated between mean bootstrapped FC and **age** at the edge level covaried for sex, rmsFD.

- **Functional Connectome Fingerprinting:** Similarity between each participant's REST1 FC matrix and all REST2 FC matrices derived using standard/bagged FC estimates. ID accuracy was computed using binary identification (BID; i.e., binary 0/1 match accuracy)[7].

RESULTS

Standard and bagged brain-behaviour relationships as a function of N

- Following Marek et al. (2022), we examined the robustness of brain-behaviour relationships for FC-age using bootstrapped samples from N = 20 to N = 239 (full sample).

- We obtained comparable brain-behaviour associations using the standard approach ($|\bar{R}|$= 0.35) and bagging ($|\bar{R}|$= 0.37). Across both approaches, 95% CIs tightened as the sample size increased (Fig.1A; Fig.1B).

- The Area Under the Curve (AUC) of the 95% CIs was similar across the standard approach and bagging across three TP thresholds (Fig.1C).
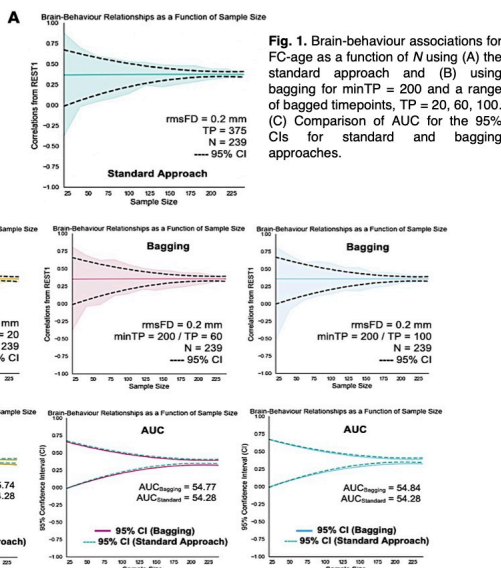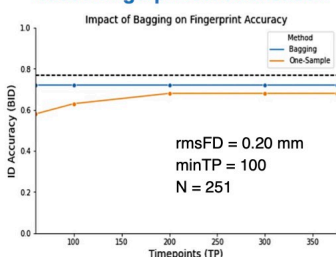

Fig. 1. Brain-behaviour associations for FC-age as a function of *N* using (A) the standard approach and (B) using bagging for minTP = 200 and a range of bagged timepoints, TP = 20, 60, 100. (C) Comparison of AUC for the 95% CIs for standard and bagging approaches.

Bagging yields reliable connectome-based fingerprint identification

- BID accuracy was optimal (77%) with the standard approach (full timeseries; 375 volumes) (Fig.2).

- Bagging with minTP = 100 and sampled TP ranging from 60 to 375 achieved near-ceiling BID accuracies from as few as 60 TP (BID accuracy = 72%; Fig.2).

- For comparison, when FC was computed on the basis of a single sample (i.e., not bootstrapped), BID accuracy was < 60% for TP = 60 (Fig.2).

Fig. 2. Impact of bagging on within-session fingerprint accuracy, relative to standard FC and single sampling.

RESULTS

Influence of minTP and TP on bagged brain-behaviour relationships

- By varying the minTP threshold, we observed a sigmoidal relationship between width of 95% CIs and sample size (Fig.3A). The widths of the 95% CIs were considerably large (width$_{minTP60}$ = 0.86; width$_{minTP100}$ = 0.83; width$_{minTP200}$ = 0.80) at smaller sample sizes but narrowed non-linearly (width = 0.01 for each minTP) with larger sample sizes.

- When we varied the TP thresholds, there was a similar relationship between width of 95% CIs and sample size (Fig.3B). The widths of the 95% CIs were large (width$_{TP20}$ = 0.86; width$_{minTP60}$ = 0.77; width$_{minTP100}$ = 0.80) at small sample sizes but tightened non-linearly (width = 0.01 for each TP) as the sample size became large.

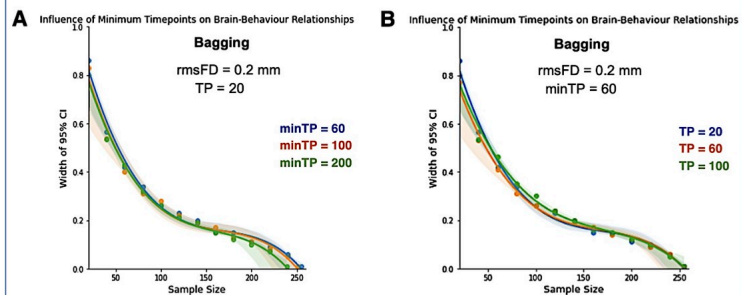**Fig.3.** (A) Influence of bagging minTP (∈ {60, 100, 200}) on the width of 95% CIs when TP held constant at 20. (B) Influence of TP (∈ {20, 60, 100}) on the width of 95% CIs when minTP held constant at 60.

Robust brain-behaviour associations with minimally bootstrap timepoints

- How few timepoints do you need? With minTP at only 60 and TP = 20, we observed robust brain-behaviour associations (Fig.4) for N = 255. Mean brain-behaviour $|\bar{R}|$ = 0.32 and 95% CIs narrowed with increasing sample size.

- Both the standard approach and bagging yielded comparable brain-behaviour associations as demonstrated by the AUC (Fig. 4B).

- For comparison, estimated brain-behaviour relationships were more variable when only a single sample of TP = 20 was used, rather than bagging (AUC = 71; Fig. 4C).
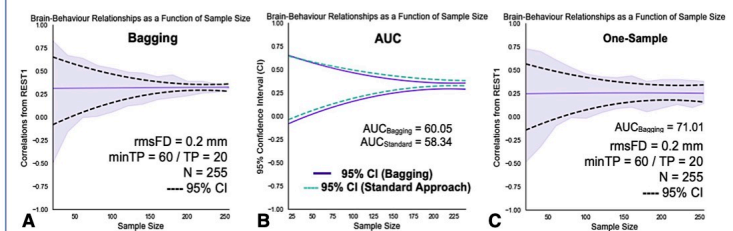

Fig. 4. Robust FC-Age associations for minTP = 60 and minimal number of bagged timepoints, TP = 20.

Salvaging "high-motion" participants for brain-behaviour associations

- To maximise sample size and the robustness and reproducibility of brain-behaviour relationships, we included even "high-motion" participants who had at least 60 timepoints with rmsFD ≤ 0.2mm in their scrubbed timeseries (i.e., minTP = 60) (Fig.4). This allowed for retention of ~90% of participants (N = 379; relative to N = 239 when mean rmsFD < 0.2mm threshold was applied).

- Using only 20 timepoints (TP = 20), brain-behaviour $|\bar{R}|$ = 0.24, and 95% CIs narrowed with increasing sample size (Fig.4A). For comparison, when FC was computed on the basis of a single sample (i.e., not bootstrapped), 95% CIs were wider (Fig.4B).
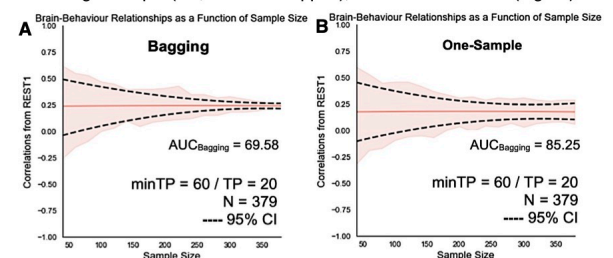

Fig.5. Bagging allows for salvage of "high-motion" participants to compute brain-behaviour associations.

CONCLUSIONS

- Bagging yields robust brain-behaviour associations as a function of sample size with as few as 20 timepoints bootstrap-sampled from 60 "lowest motion" scrubbed timepoints.

- Bagged data also enable high connectome-based fingerprint identification accuracy.

- Bagging offers a promising avenue to salvage "high-motion" participants that would otherwise be discarded, minimising data loss and wastage, and maximising sample sizes for robust and reproducible estimation of brain-behaviour relationships.

- Next steps: estimate the generalisability across brain-behaviour relationships, phenotypes and datasets, including ABCD dataset.

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