
Figures and figure supplements

Relationship between cognitive abilities and mental health as represented by cognitive abilities at the neural and genetic levels of analysis

Yue Wang *et al.*

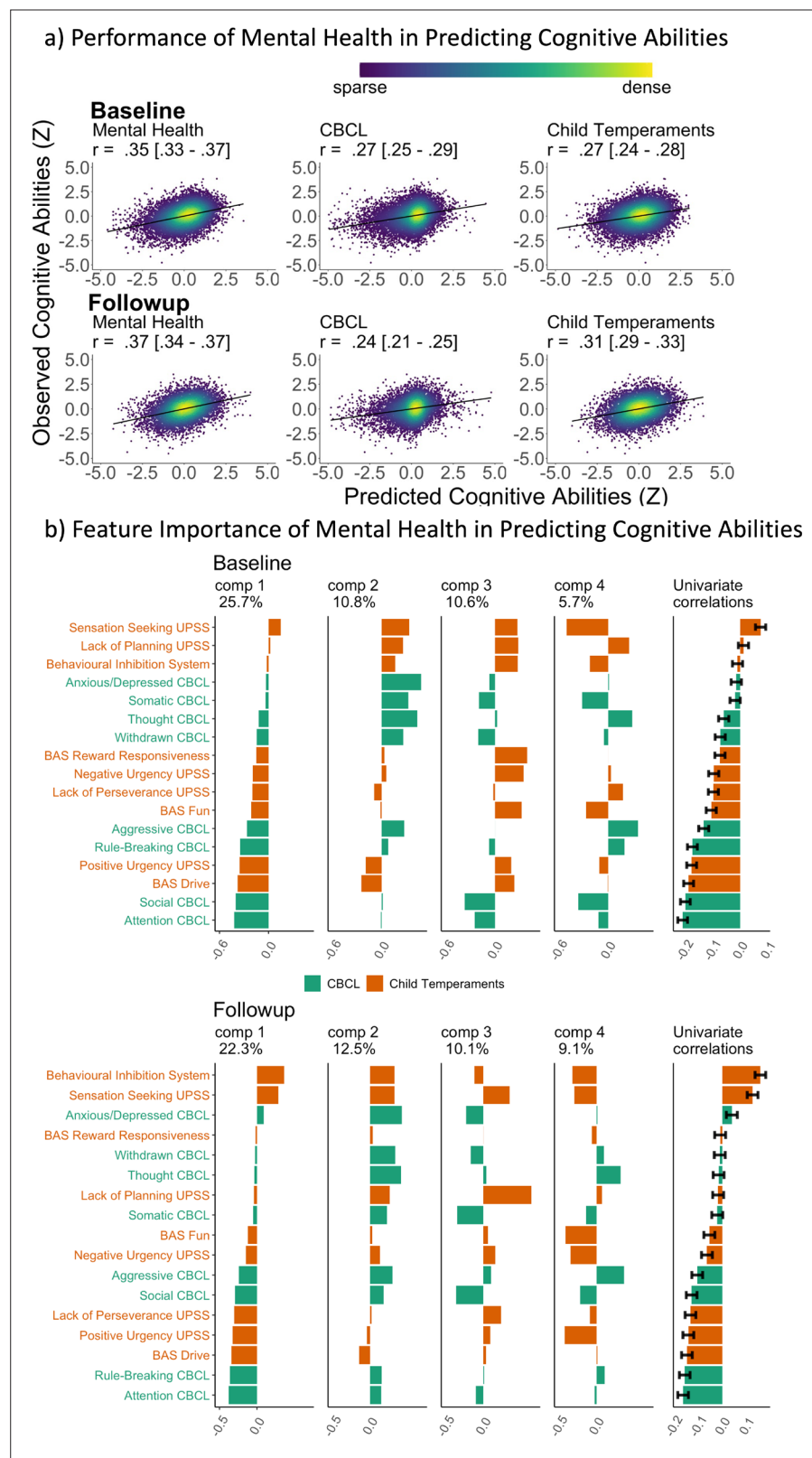


Figure 1. Predictive models, predicting cognitive abilities from mental-health features via Partial Least Square (PLS). **(a)** Predictive performance of the models, indicated by scatter plots between observed vs predicted cognitive abilities based on mental health. Cognitive abilities are based on the second-order latent variable, the g-factor, based on a confirmatory factor analysis of six cognitive tasks. All data points are from test sets. r

Figure 1 continued on next page

Figure 1 continued

is the average Pearson's r across 21 test sites. The parentheses following the r indicate bootstrapped 95% CIs, calculated based on observed vs predicted cognitive abilities from all test sites combined. UPPS-P Impulsive and Behaviour Scale and the Behavioural Inhibition System/Behavioural Activation System (BIS/BAS) were used for child temperaments, conceptualised as risk factors for mental issues. Mental health includes features from CBCL and child temperaments. **(b)** Feature importance of mental health, predicting cognitive abilities via PLS. The features were ordered based on the loading of the first PLS component. Univariate correlations were Pearson's r between each mental-health feature and cognitive abilities. Error bars reflect 95% CIs of the correlations. CBCL = Child Behavioural Checklist (in green), reflecting children's emotional and behavioural problems; UPPS-P = Urgency, Premeditation, Perseverance, Sensation seeking, and Positive urgency Impulsive Behaviour Scale; BAS = Behavioural Activation System (in orange).

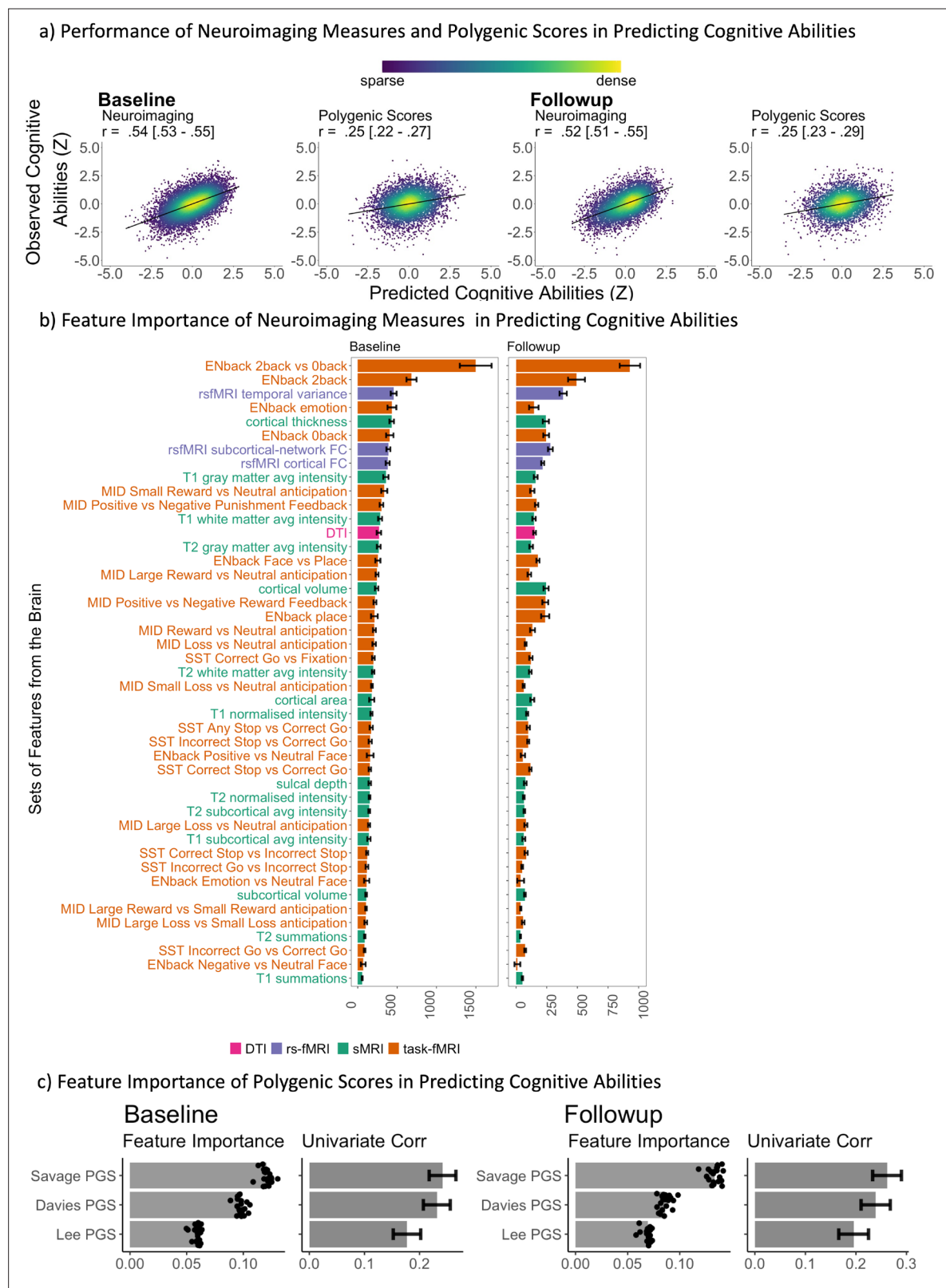


Figure 2. Predictive models predicting cognitive abilities from neuroimaging via opportunistic stacking and polygenic scores via Elastic Net.

(a) Scatter plots between observed vs predicted cognitive abilities based on neuroimaging and polygenic scores. Cognitive abilities are based on the second-order latent variable, the g-factor, based on a confirmatory factor analysis of six cognitive tasks. The parentheses following the r indicate the bootstrapped 95% CIs, calculated based on observed vs predicted cognitive abilities from all test sites combined. All data points are from test sets. r is

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Figure 2 continued

the average Pearson's r across 21 test sites. The parentheses following the r indicate bootstrapped 95% CIs, calculated based on observed vs predicted cognitive abilities from all test sites combined. **(b)** Feature importance of the stacking layer of neuroimaging, predicting cognitive abilities via Random Forest. For the stacking layer of neuroimaging, the feature importance was based on the absolute value of SHapley Additive exPlanations (SHAP), averaged across test sites. A higher absolute value of SHAP indicates a higher contribution to the prediction. Error bars reflect standard deviations across sites. Different sets of neuroimaging features were filled with different colours: pink for dMRI, orange for fMRI, purple for resting-state functional MRI (rsMRI), and green for structural MRI (sMRI). **(c)** Feature importance of polygenic scores, predicting cognitive abilities via Elastic Net. For polygenic scores, the feature importance was based on the Elastic Net coefficients, averaged across test sites. We also plotted Pearson's correlations between each polygenic score and cognitive abilities computed from the full data. Error bars reflect 95% CIs of these correlations.

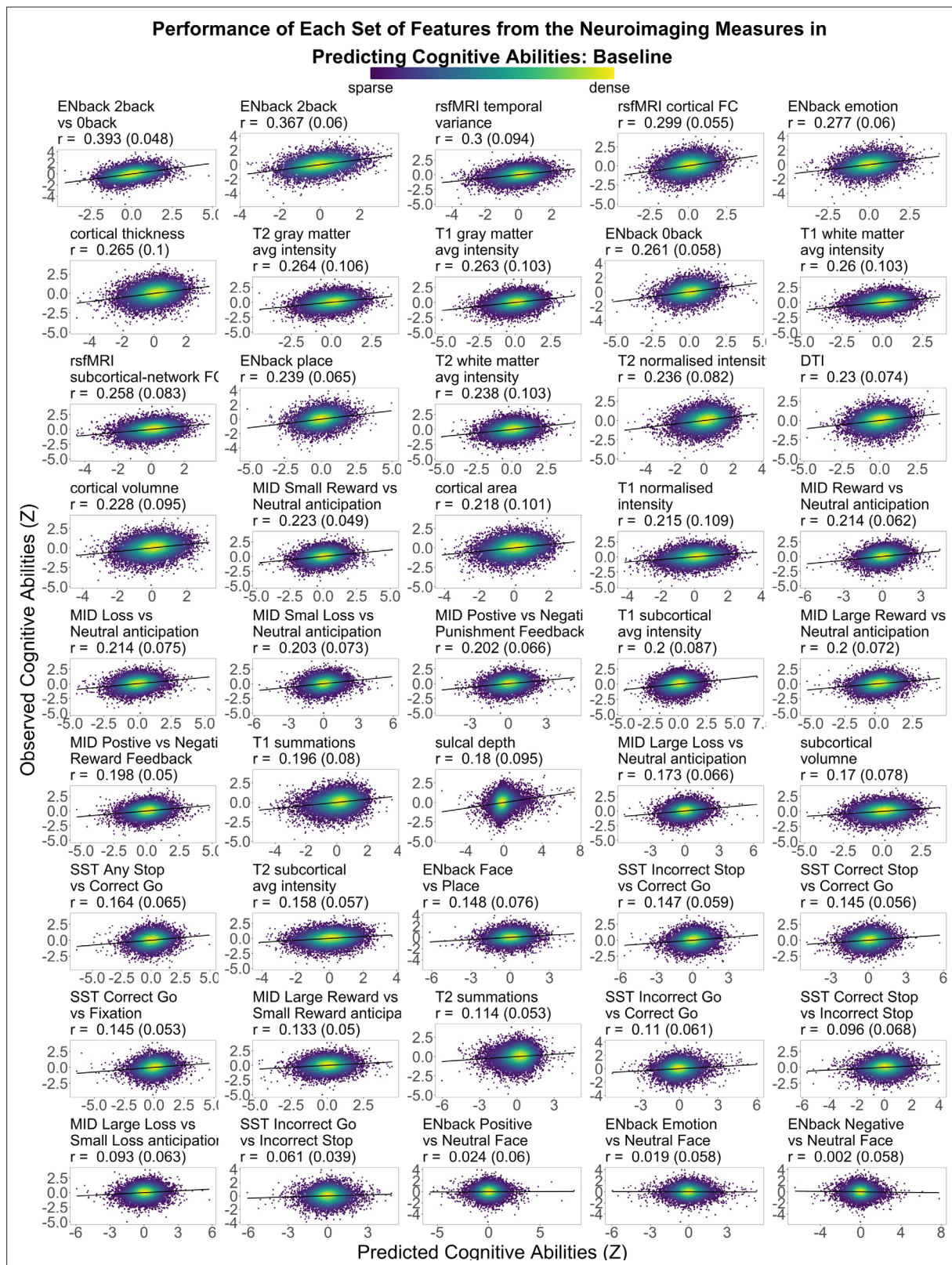


Figure 2—figure supplement 1. Scatter plots between observed vs predicted cognitive abilities based on each set of 45 neuroimaging features in the baseline data. All data points are from test sets. r is the average Pearson's r across 21 test sites, and the parenthesis is the standard deviation of Pearson's r across sites.

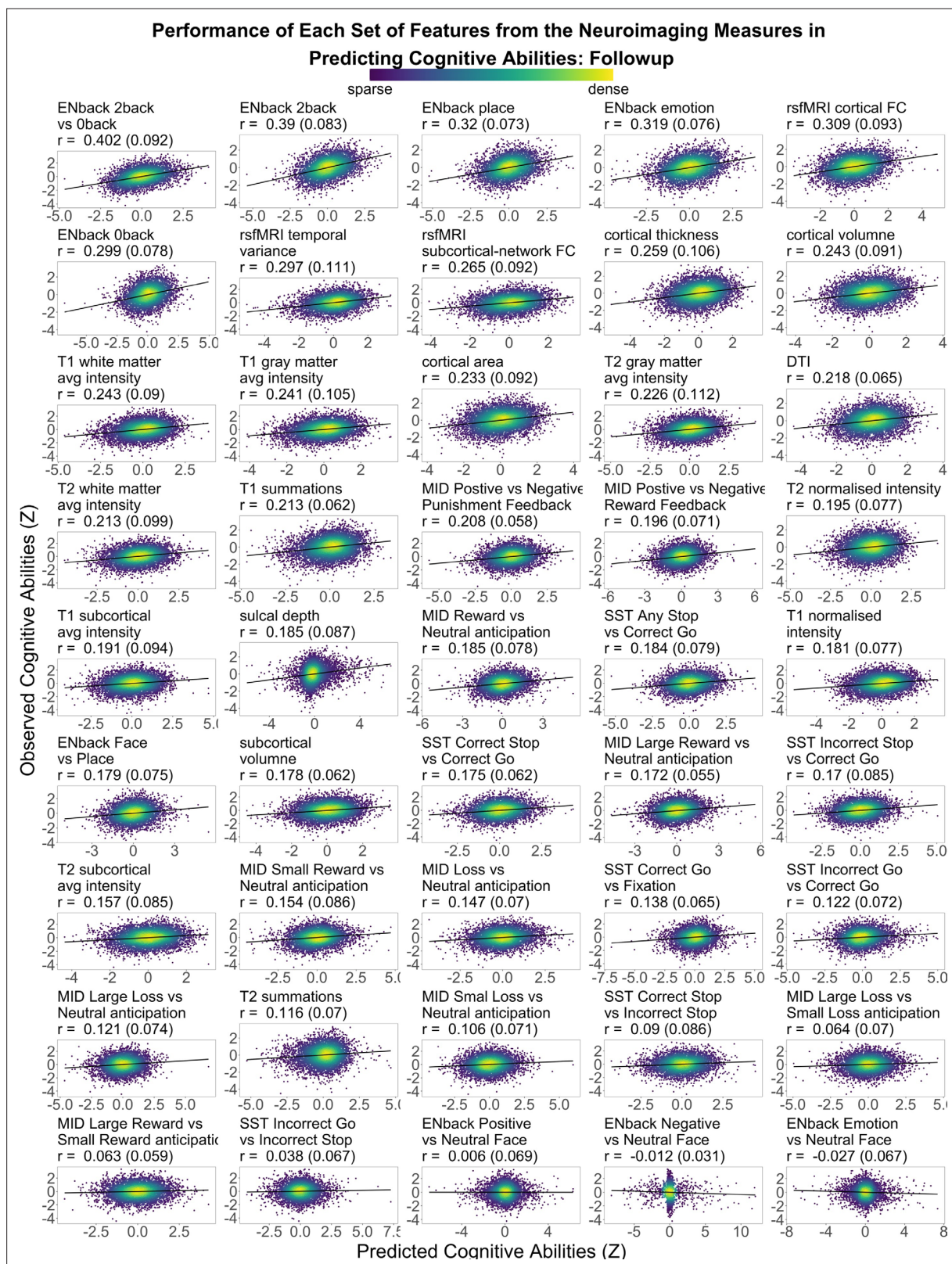


Figure 2—figure supplement 2. Scatter plots between observed vs predicted cognitive abilities based on each set of 45 neuroimaging features in the follow-up data. All data points are from test sets. r is the average Pearson's r across 21 test sites, and the parenthesis is the standard deviation of Pearson's r across sites.

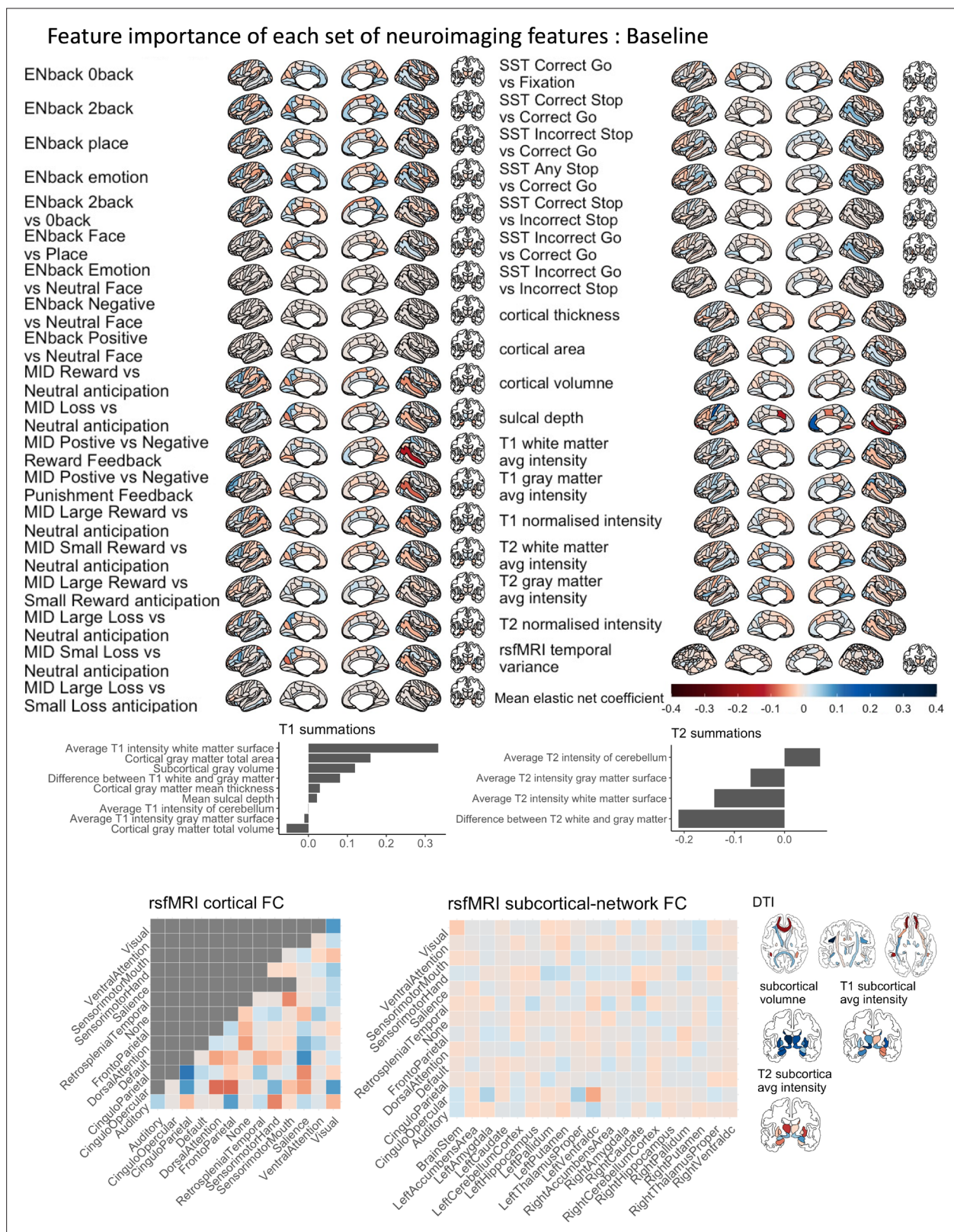


Figure 3. Feature importance of each set of neuroimaging features, predicting cognitive abilities in the baseline data. The feature importance was based on the Elastic Net coefficients, averaged across test sites. We did not order these sets of neuroimaging features according to their contribution to the stacking layer (see **Figure 2**). Larger versions of the feature importance for each set of neuroimaging features can be found in **Figure 3—figure supplements 1–11**. MID = Monetary Incentive Delay task; SST = Stop Signal Task; DTI = Diffusion Tensor Imaging; FC = functional connectivity.

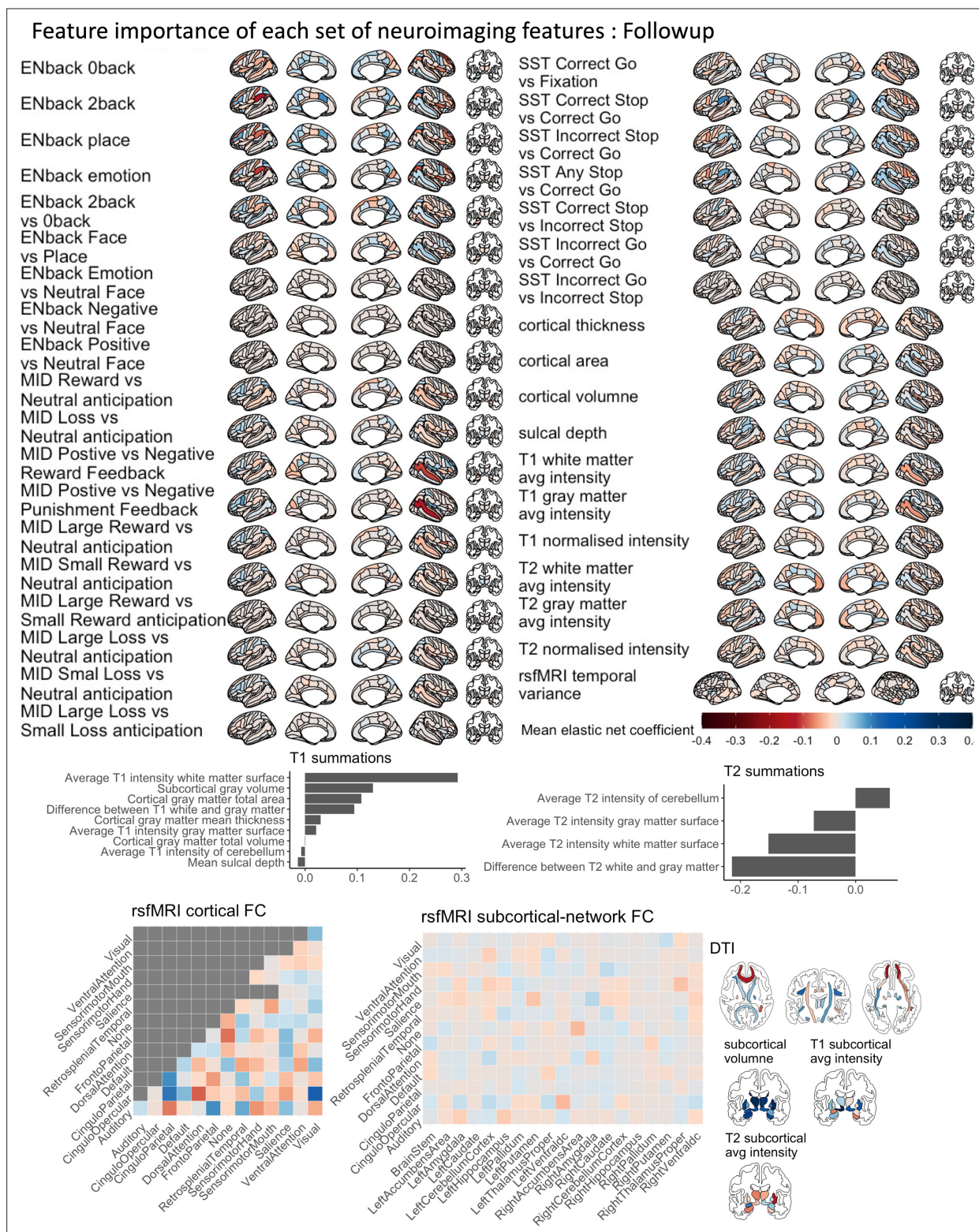


Figure 3—figure supplement 1. Feature importance of each set of neuroimaging features, predicting cognitive abilities in the follow-up data via Elastic Net. The feature importance was based on the Elastic Net coefficient, averaged across test sites. We did not order these sets of neuroimaging features according to their feature importance (see **Figure 2**). MID = Monetary Incentive Delay task; SST = Stop Signal Task; DTI = Diffusion Tensor Imaging; FC = functional connectivity. The brain plots were created via the *gseg* and *gsegExtra* packages (1).

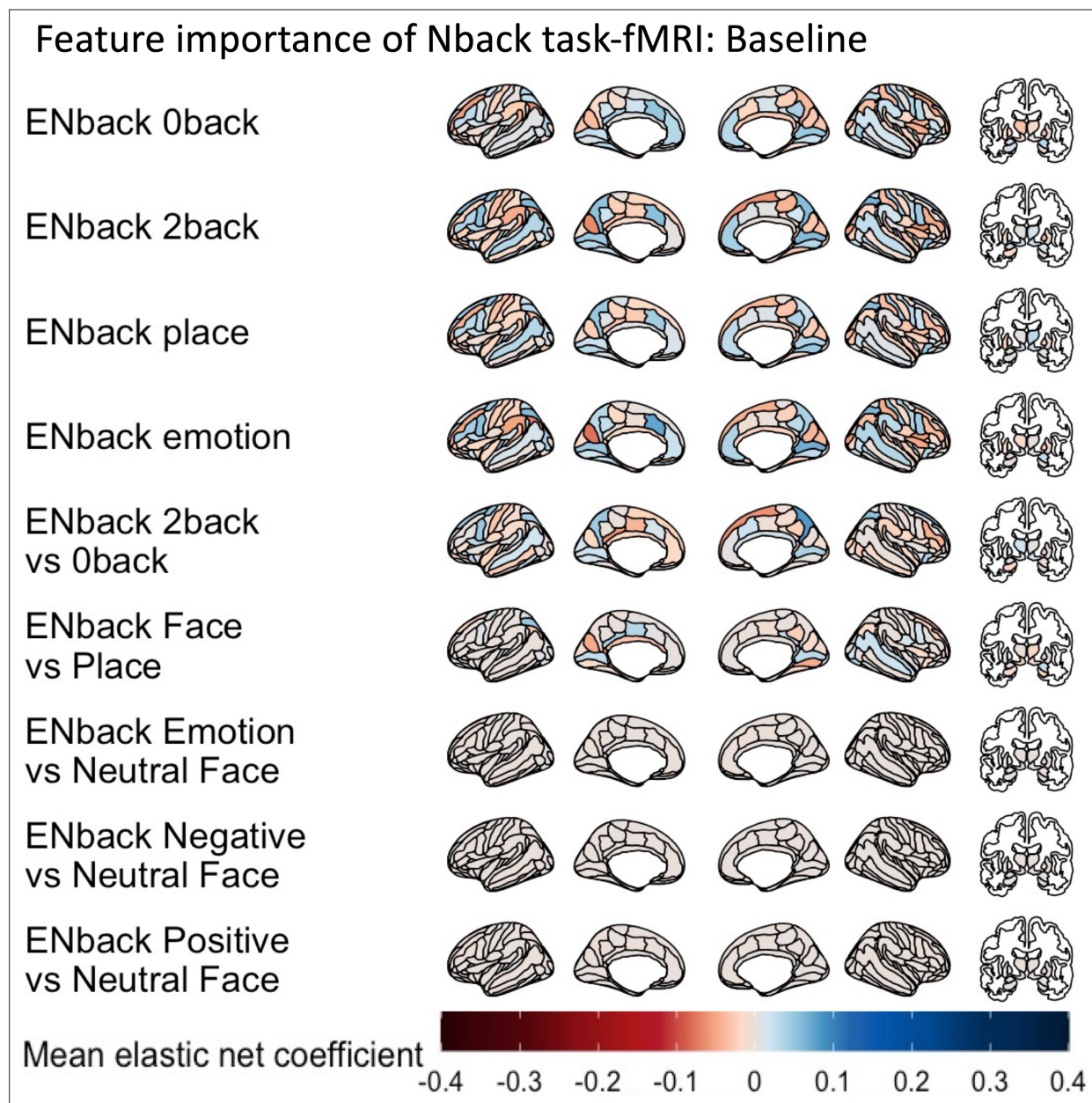


Figure 3—figure supplement 2. Feature importance of Nback task-fMRI features, predicting cognitive abilities in the baseline data via Elastic Net. The feature importance was based on the Elastic Net coefficient, averaged across test sites. We did not order these sets of neuroimaging features according to their feature importance (see **Figure 2**). The brain plots were created via the *ggseg* and *ggsegExtra* packages (1).

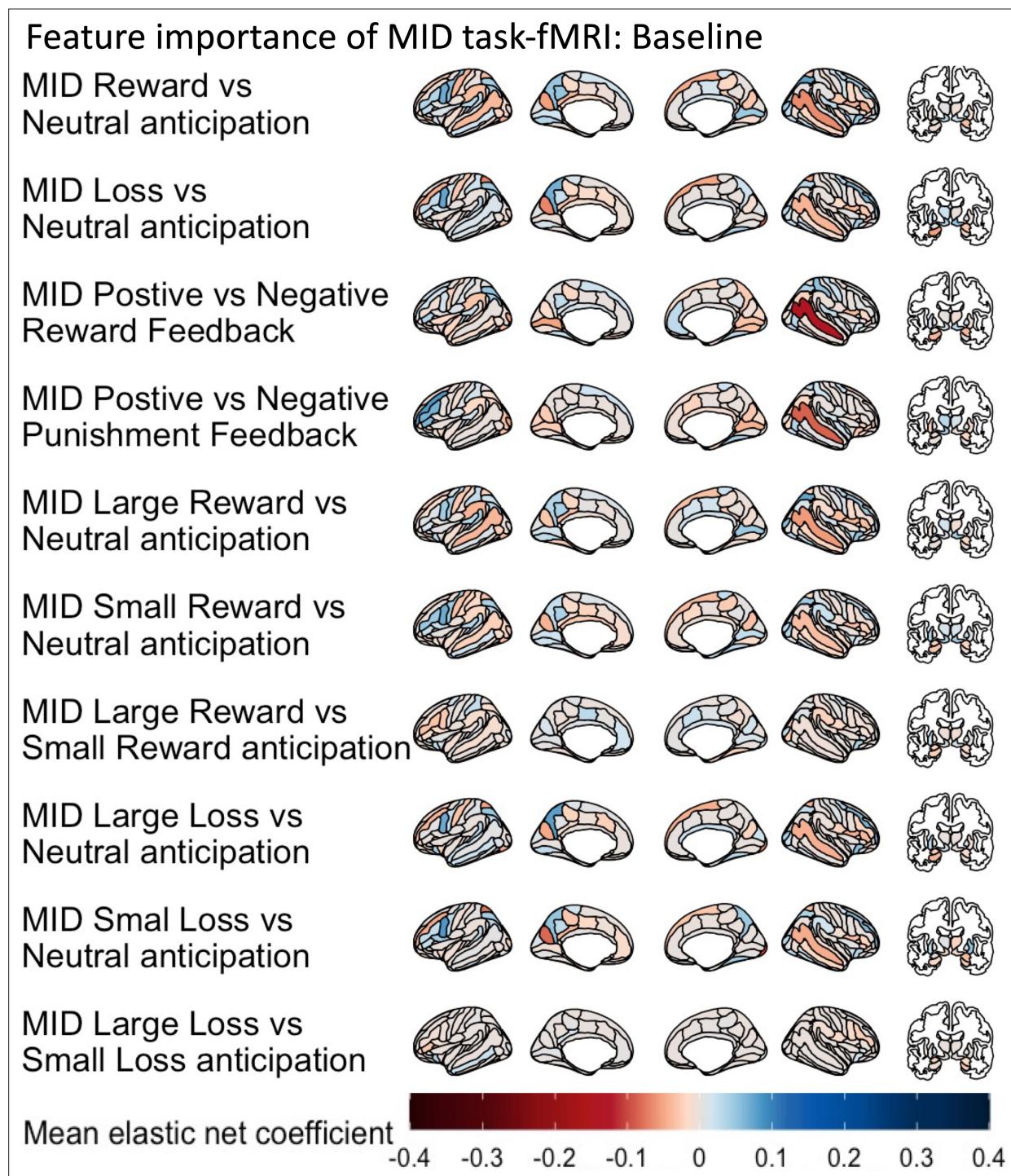


Figure 3—figure supplement 3. Feature importance of MID task-fMRI features, predicting cognitive abilities in the baseline data via Elastic Net. The feature importance was based on the Elastic Net coefficient, averaged across test sites. We did not order these sets of neuroimaging features according to their feature importance (see **Figure 2**). MID = Monetary Incentive Delay task. The brain plots were created via the *ggseg* and *ggsegExtra* packages (1).

Feature importance of SST task-fMRI: Baseline

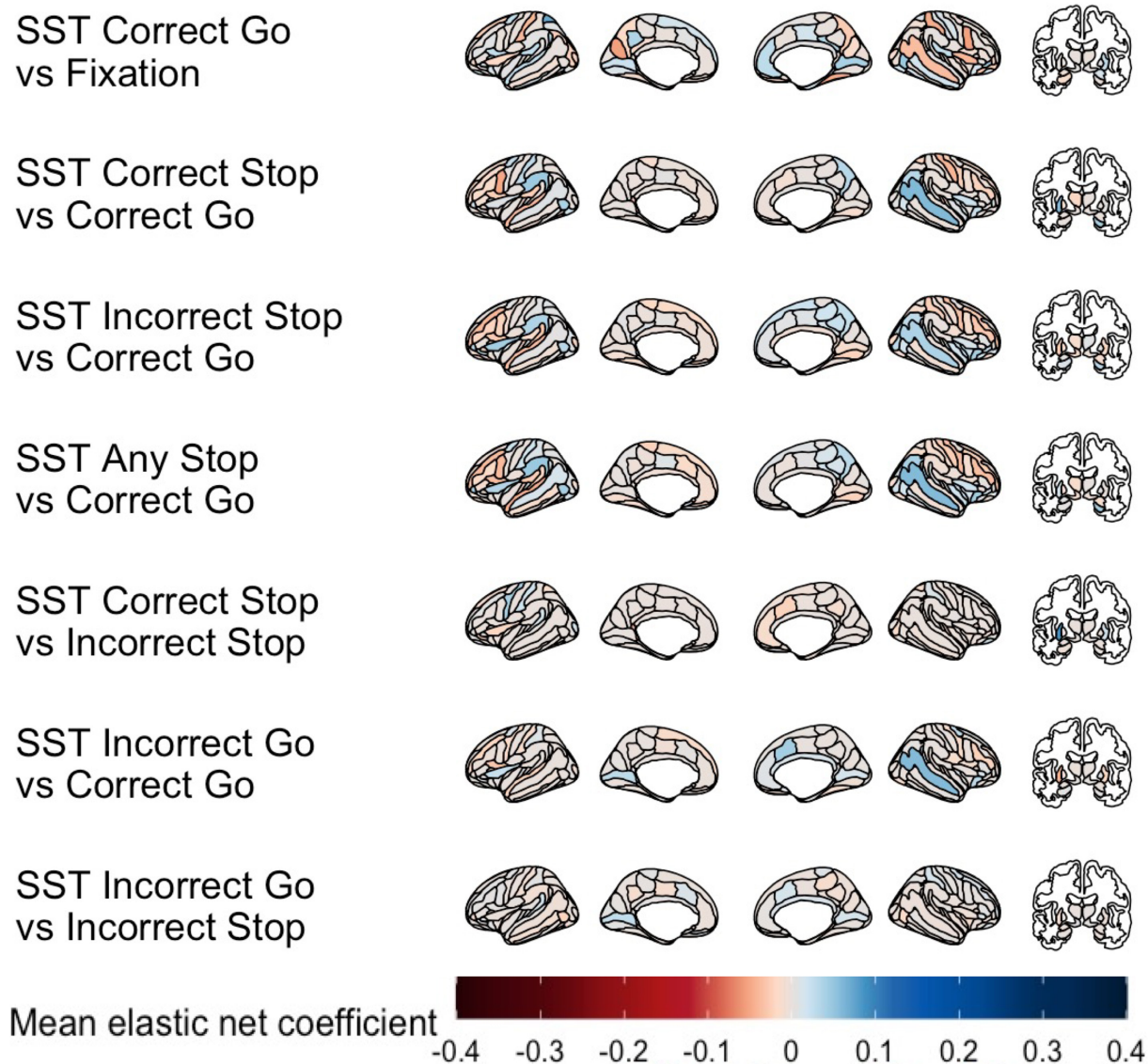


Figure 3—figure supplement 4. Feature importance of SST task-fMRI features, predicting cognitive abilities in the baseline data via Elastic Net. The feature importance was based on the Elastic Net coefficient, averaged across test sites. We did not order these sets of neuroimaging features according to their feature importance (see **Figure 2**). SST = Stop Signal Task. The brain plots were created via the *ggseg* and *ggsegExtra* packages (1).

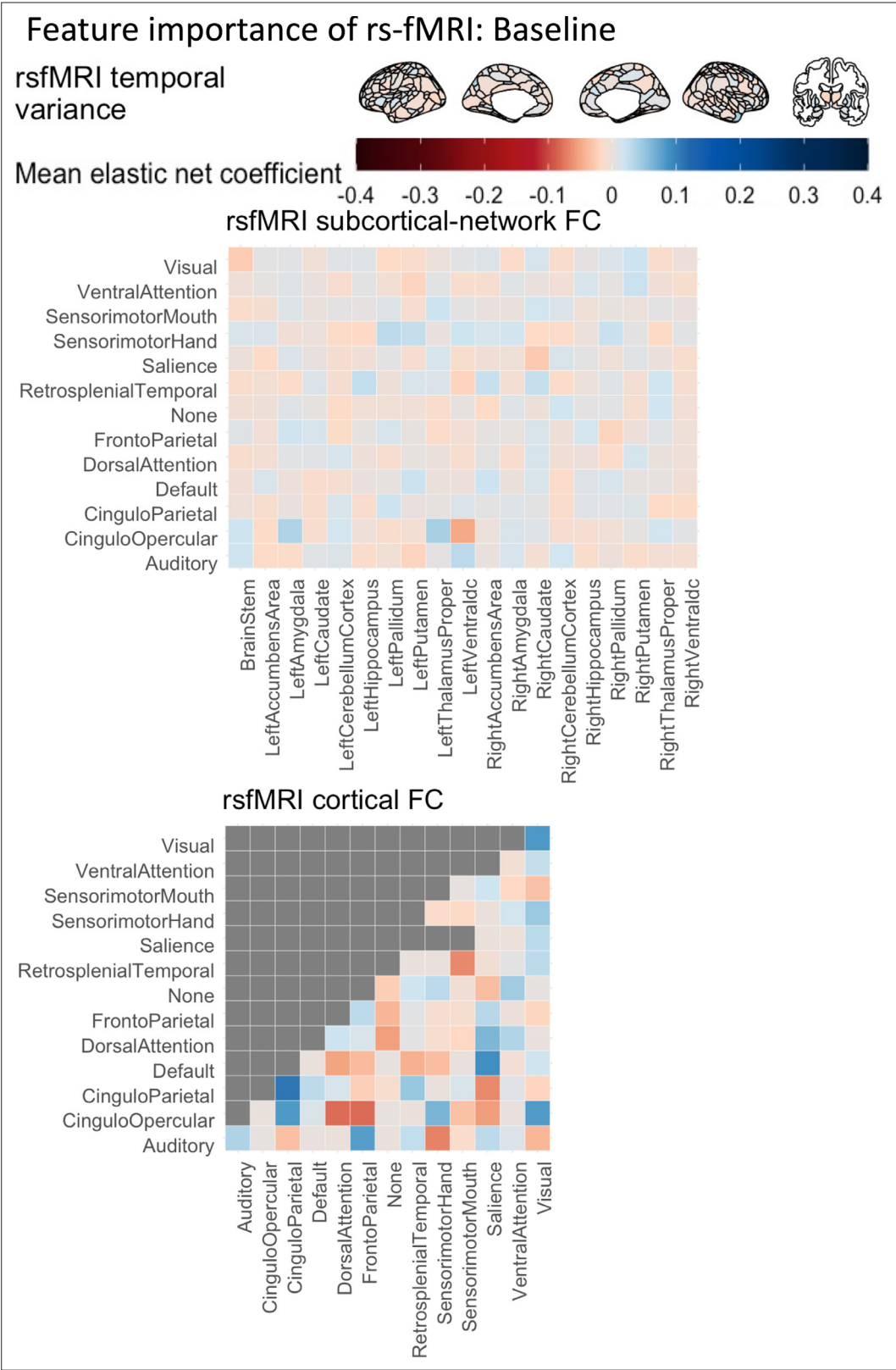


Figure 3—figure supplement 5. Feature importance of resting-state functional MRI (rs-fMRI) features, predicting cognitive abilities in the baseline data via Elastic Net. The feature importance was based on the Elastic Net coefficient, averaged across test sites. We did not order these sets of neuroimaging features according to their feature importance (see **Figure 2**). FC = functional connectivity. The brain plots were created via the *ggseg* and *ggsegExtra* packages (1).

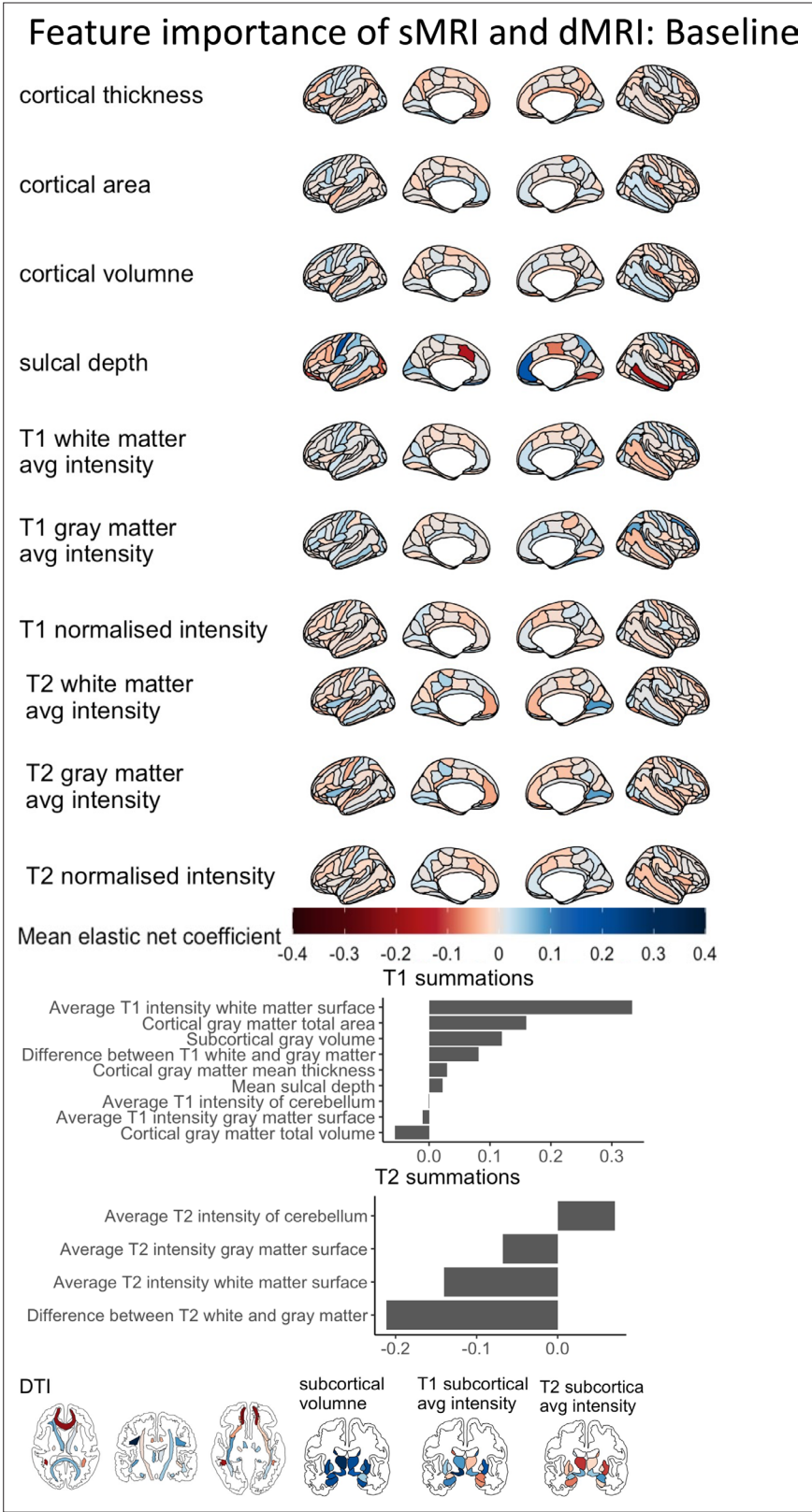


Figure 3—figure supplement 6. Feature importance of structural MRI (sMRI) and dMRI features, predicting cognitive abilities in the baseline data via Elastic Net. The feature importance was based on the Elastic Net coefficient, averaged across test sites. We did not order these sets of neuroimaging features according to their feature importance (see **Figure 2**). DTI = Diffusion Tensor Imaging. The brain plots were created via the *ggseg* and *ggsegExtra* packages (1).

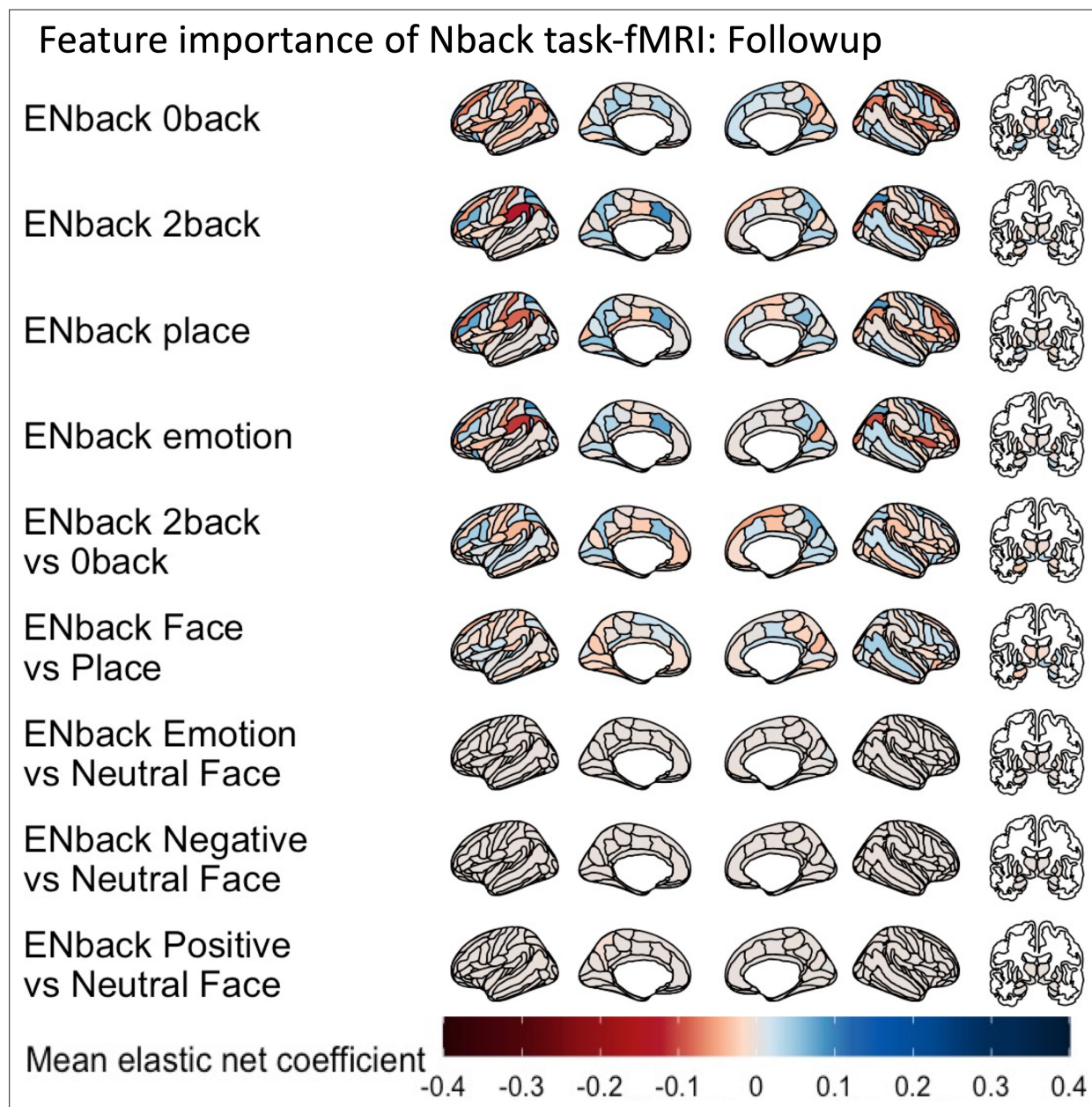


Figure 3—figure supplement 7. Feature importance of Nback task-fMRI features, predicting cognitive abilities in the follow-up data via Elastic Net. The feature importance was based on the Elastic Net coefficient, averaged across test sites. We did not order these sets of neuroimaging features according to their feature importance (see **Figure 2**). The brain plots were created via the *ggseg* and *ggsegExtra* packages (1).

Feature importance of MID task-fMRI: Followup

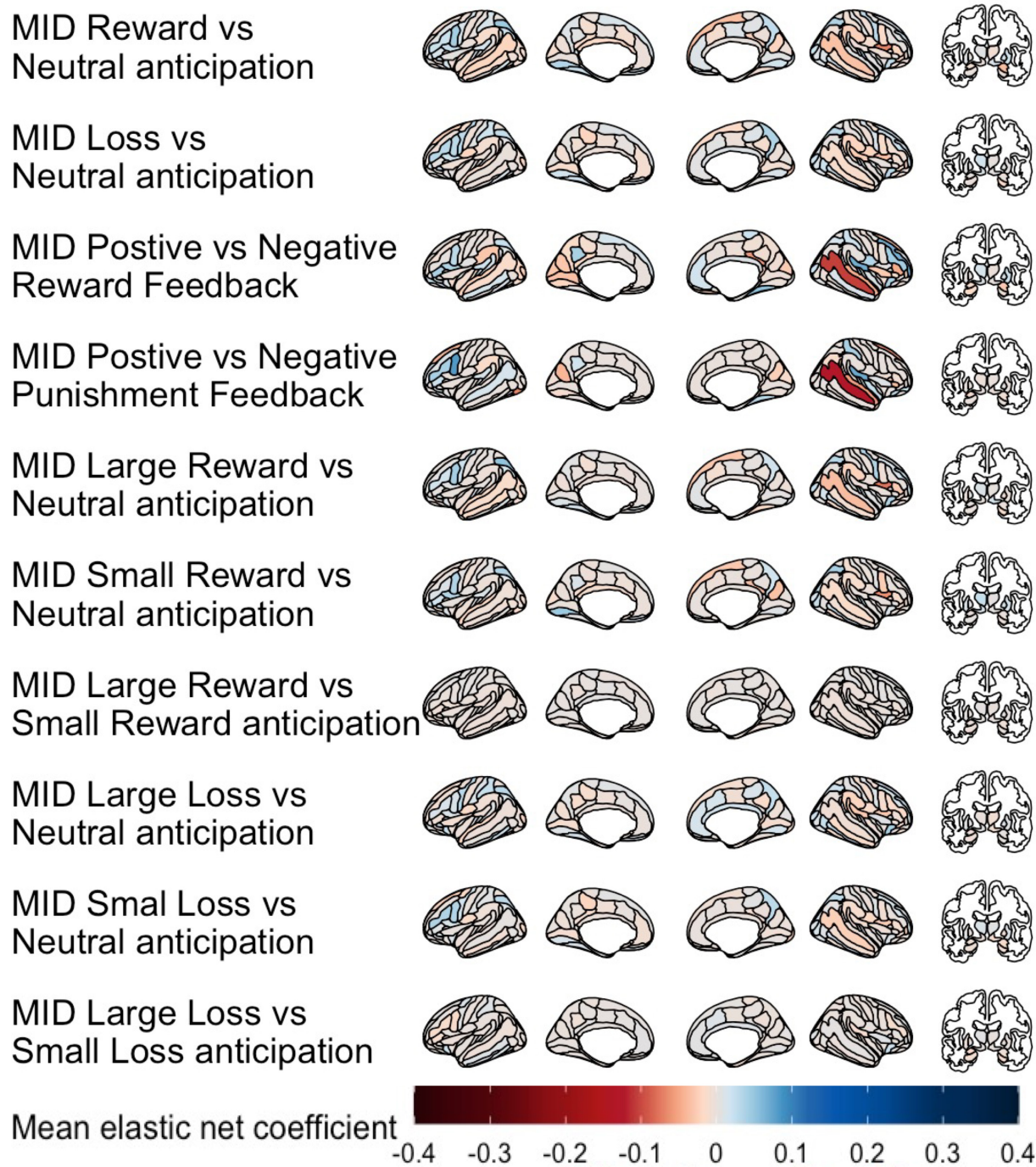


Figure 3—figure supplement 8. Feature importance of monetary incentive delay (MID) task-fMRI features, predicting cognitive abilities in the follow-up data via Elastic Net. The feature importance was based on the Elastic Net coefficient, averaged across test sites. We did not order these sets of neuroimaging features according to their feature importance (see **Figure 2**). MID = Monetary Incentive Delay task. The brain plots were created via the *ggseg* and *ggsegExtra* packages (1).

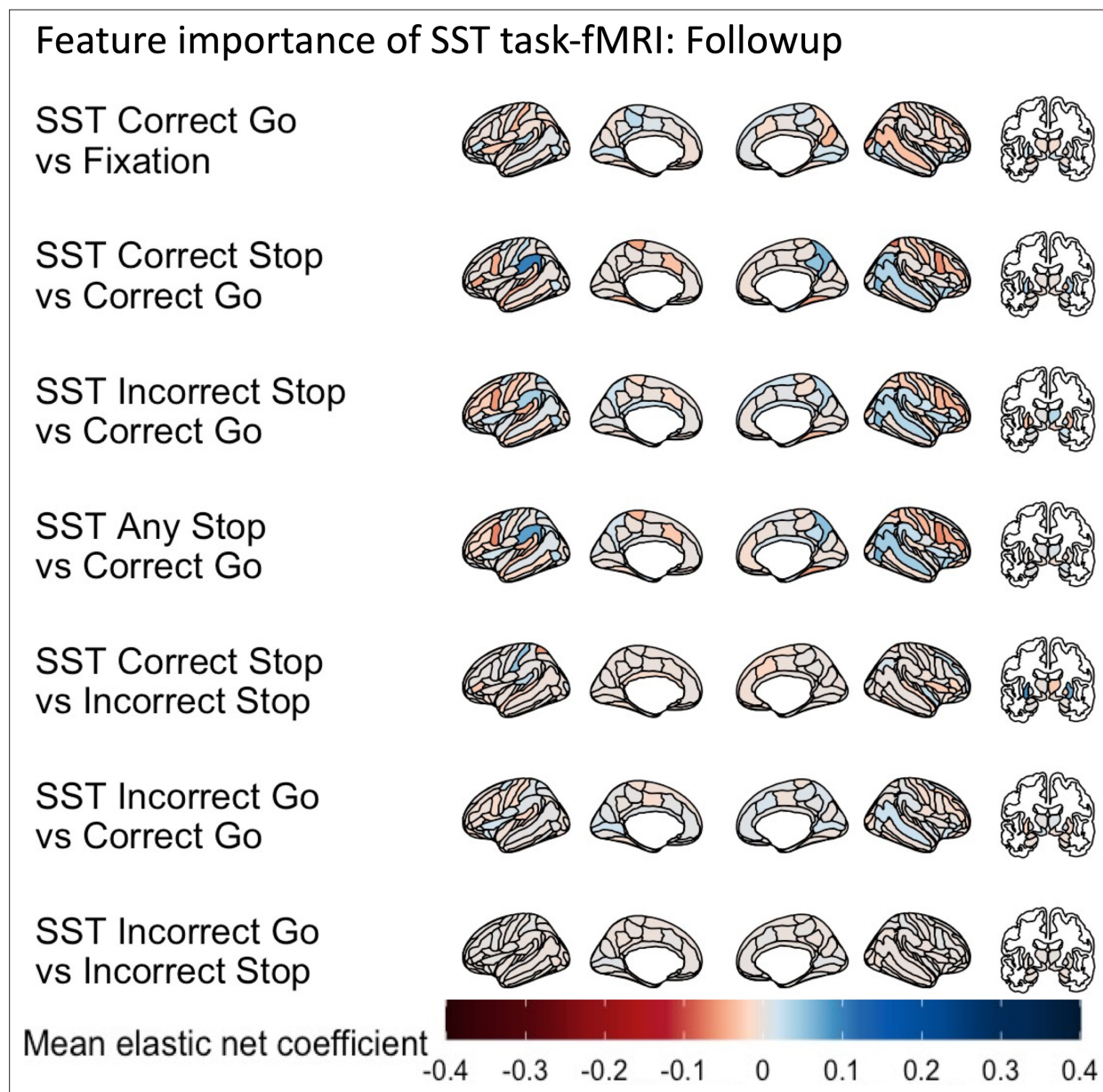


Figure 3—figure supplement 9. Feature importance of SST task-fMRI features, predicting cognitive abilities in the follow-up data via Elastic Net. The feature importance was based on the Elastic Net coefficient, averaged across test sites. We did not order these sets of neuroimaging features according to their feature importance (see **Figure 2**). SST = Stop Signal Task. The brain plots were created via the *ggseg* and *ggsegExtra* packages (1).

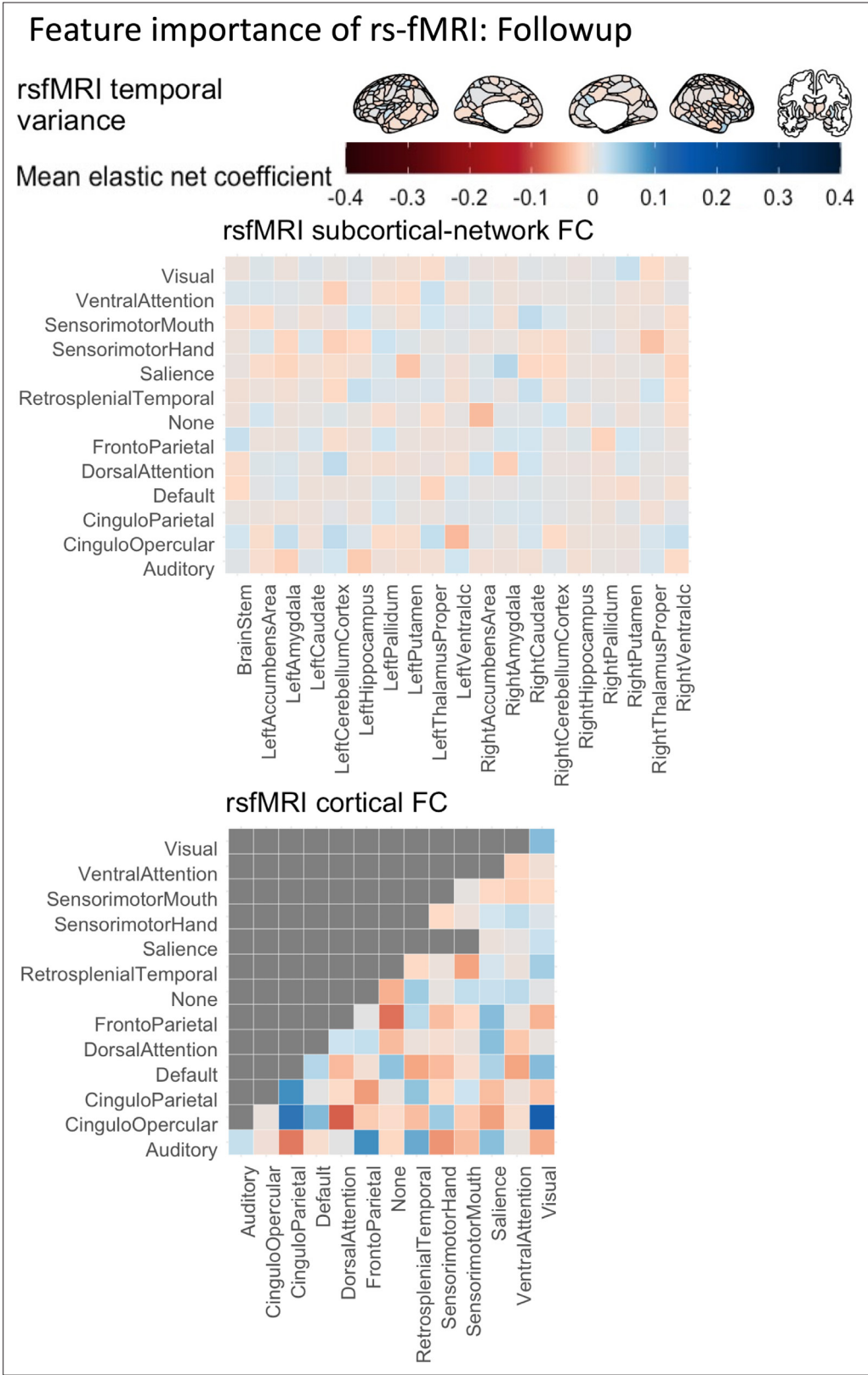


Figure 3—figure supplement 10. Feature importance of resting-state functional MRI (rs-fMRI) features, predicting cognitive abilities in the follow-up data via Elastic Net. The feature importance was based on the Elastic Net coefficient, averaged across test sites. We did not order these sets of neuroimaging features according to their feature importance (see **Figure 2**). FC = functional connectivity. The brain plots were created via the *ggseg* and *ggsegExtra* packages (1).

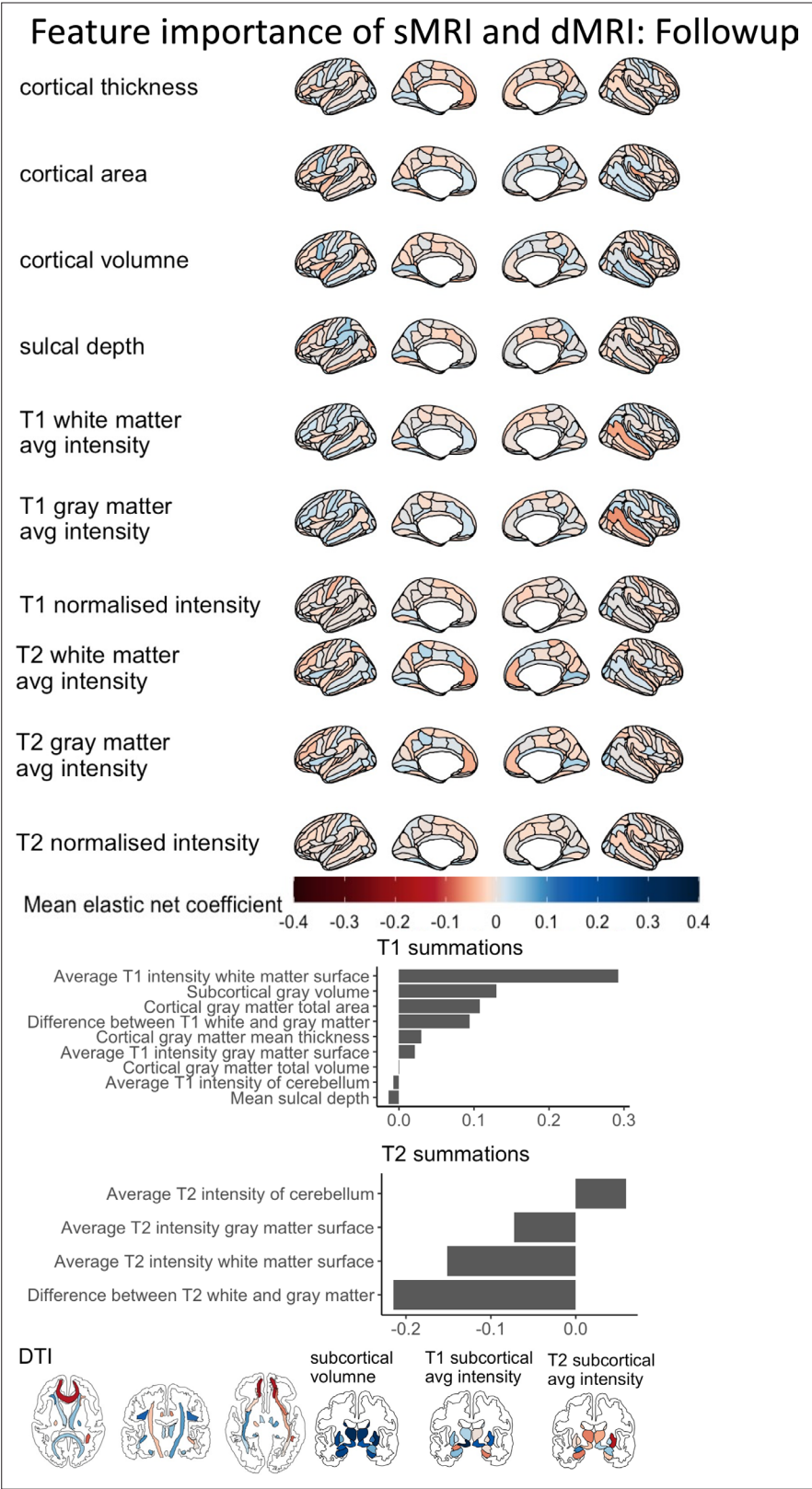


Figure 3—figure supplement 11. Feature importance of structural MRI (sMRI) and dMRI features, predicting cognitive abilities in the follow-up data via Elastic Net. The feature importance was based on the Elastic Net coefficient, averaged across test sites. We did not order these sets of neuroimaging features according to their feature importance (see **Figure 2**). DTI = Diffusion Tensor Imaging. The brain plots were created via the *ggseg* and *ggsegExtra* packages (1).

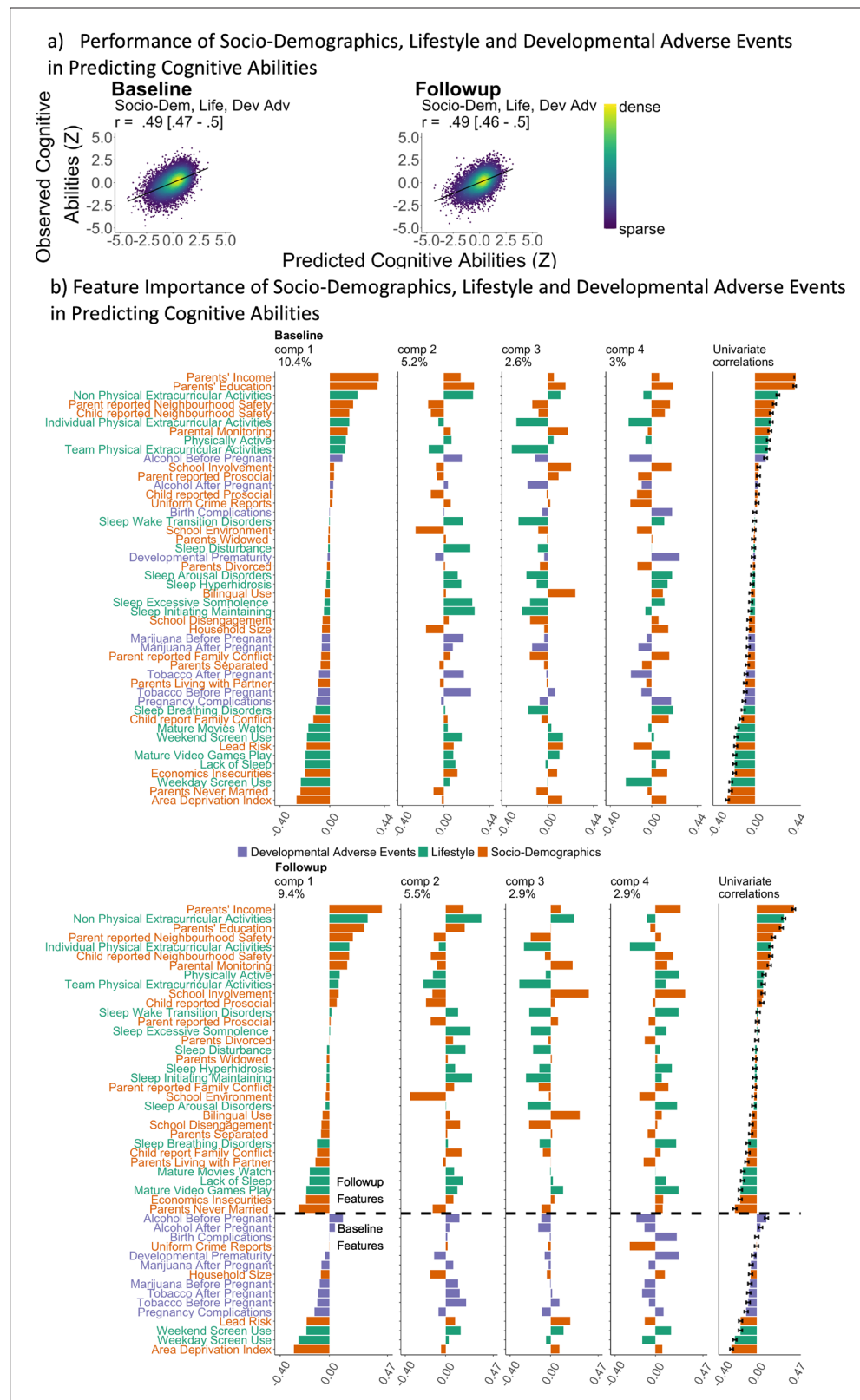


Figure 4. Predictive models, predicting cognitive abilities from socio-demographics, lifestyles, and developmental adverse events via Partial Least Square (PLS). **(a)** Scatter plots between observed vs predicted cognitive abilities based on socio-demographics, lifestyles, and developmental adverse events. Cognitive abilities are based on the second-order latent variable, the g-factor, based on a confirmatory factor analysis of six cognitive tasks. All data

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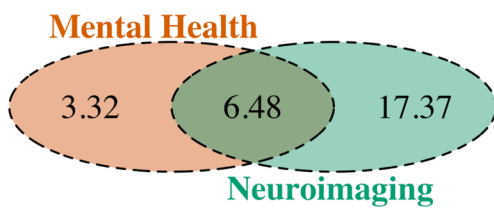
Figure 4 continued

points are from test sets. r is the average Pearson's r across 21 test sites. The parentheses following the r indicate bootstrapped 95% CIs, calculated based on observed vs predicted cognitive abilities from all test sites combined. **(b)** Feature importance of socio-demographics, lifestyles, and developmental adverse events, predicting cognitive abilities via Partial Least Square. The features were ordered based on the loading of the first component. Univariate correlations were Pearson's correlation between each feature and cognitive abilities. Error bars reflect 95% CIs of the correlations. Different types of environmental factors were filled with different colours: orange for socio-demographics, purple for developmental adverse events and green for lifestyle. A dashed horizontal line in the follow-up feature importance figure distinguishes whether the variables were collected at baseline or follow-up.

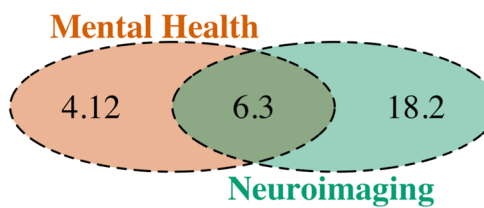
Commonality Analysis

Baseline

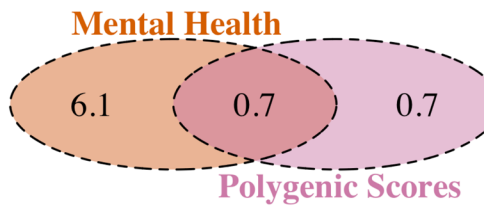
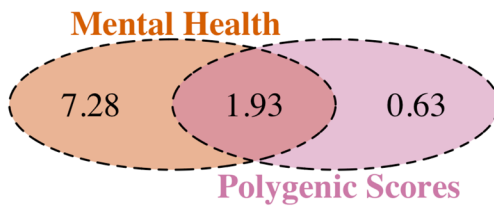
Cognitive Abilities ~ Mental Health + Neuroimaging



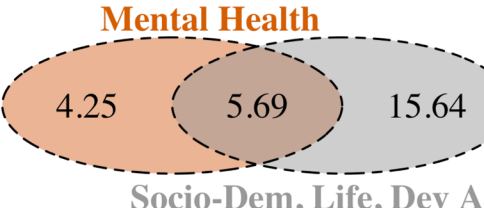
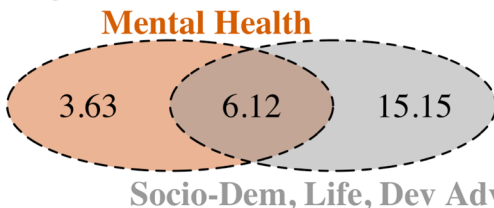
Followup



Cognitive Abilities ~ Mental Health + Polygenic Scores



Cognitive Abilities ~ Mental Health + Socio-Dem, Life, Dev Adv



Cognitive Abilities ~ Mental Health + Neuroimaging + Polygenic Scores + Socio-Dem, Life, Dev Adv

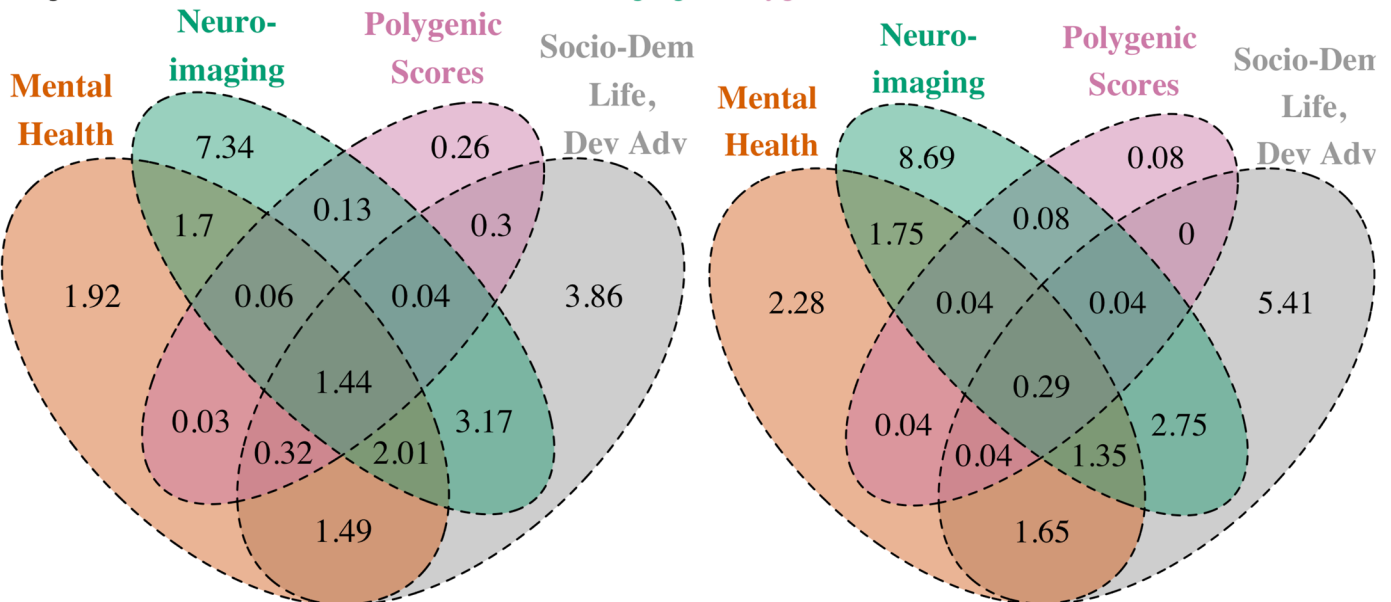


Figure 5. Venn diagrams showing common and unique effects of proxy measures of cognitive abilities based on mental health, neuroimaging, polygenic scores, and/or socio-demographics, lifestyles and developmental adverse events in explaining cognitive abilities across test sites. We computed the common and unique effects in % based on the marginal R^2 of four sets of linear-mixed models.

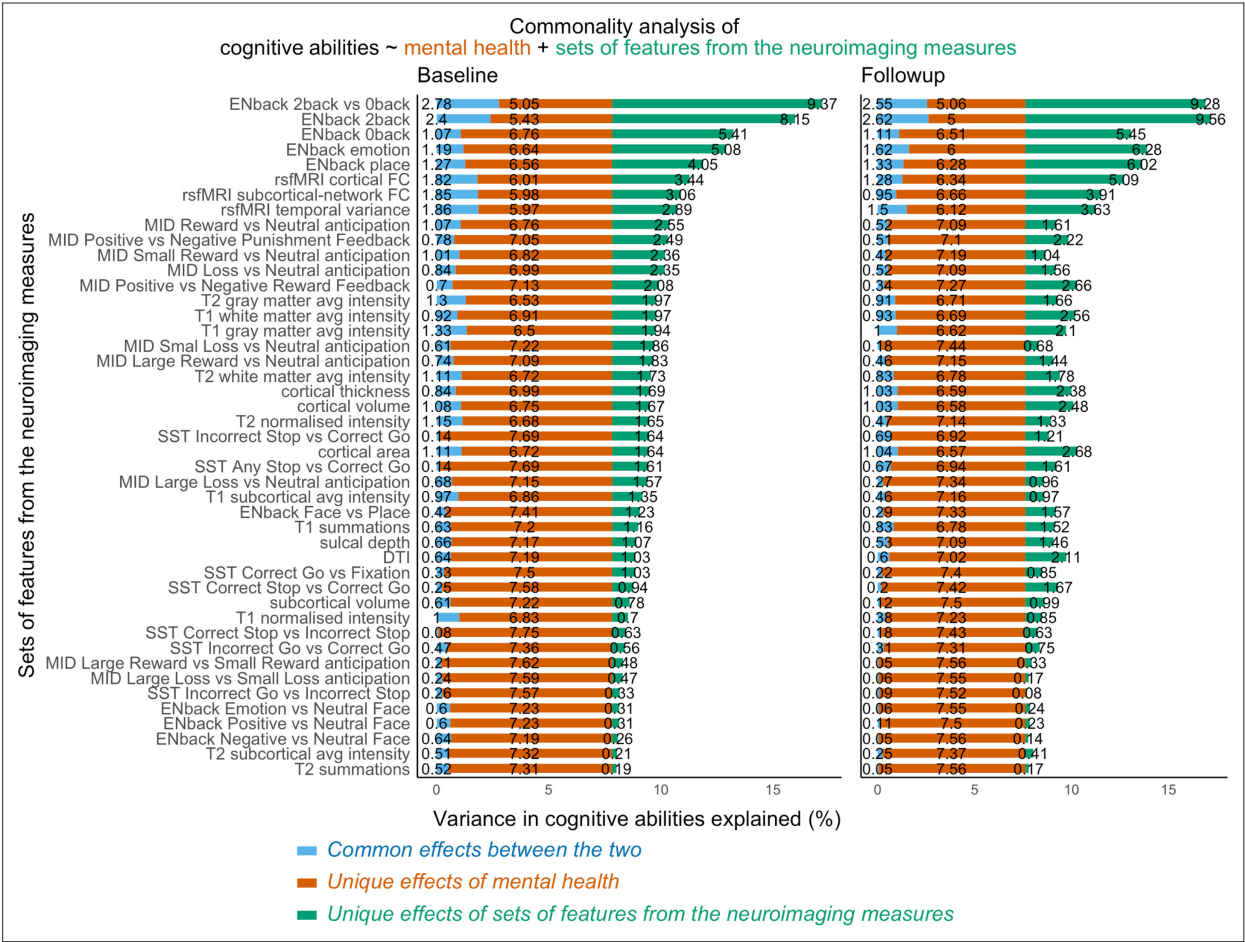


Figure 5—figure supplement 1. Stacked bar plots showing common and unique effects of proxy measures of cognitive abilities based on each set of neuroimaging features in explaining cognitive abilities across test sites. We computed the common and unique effects in % based on the marginal of linear-mixed models.

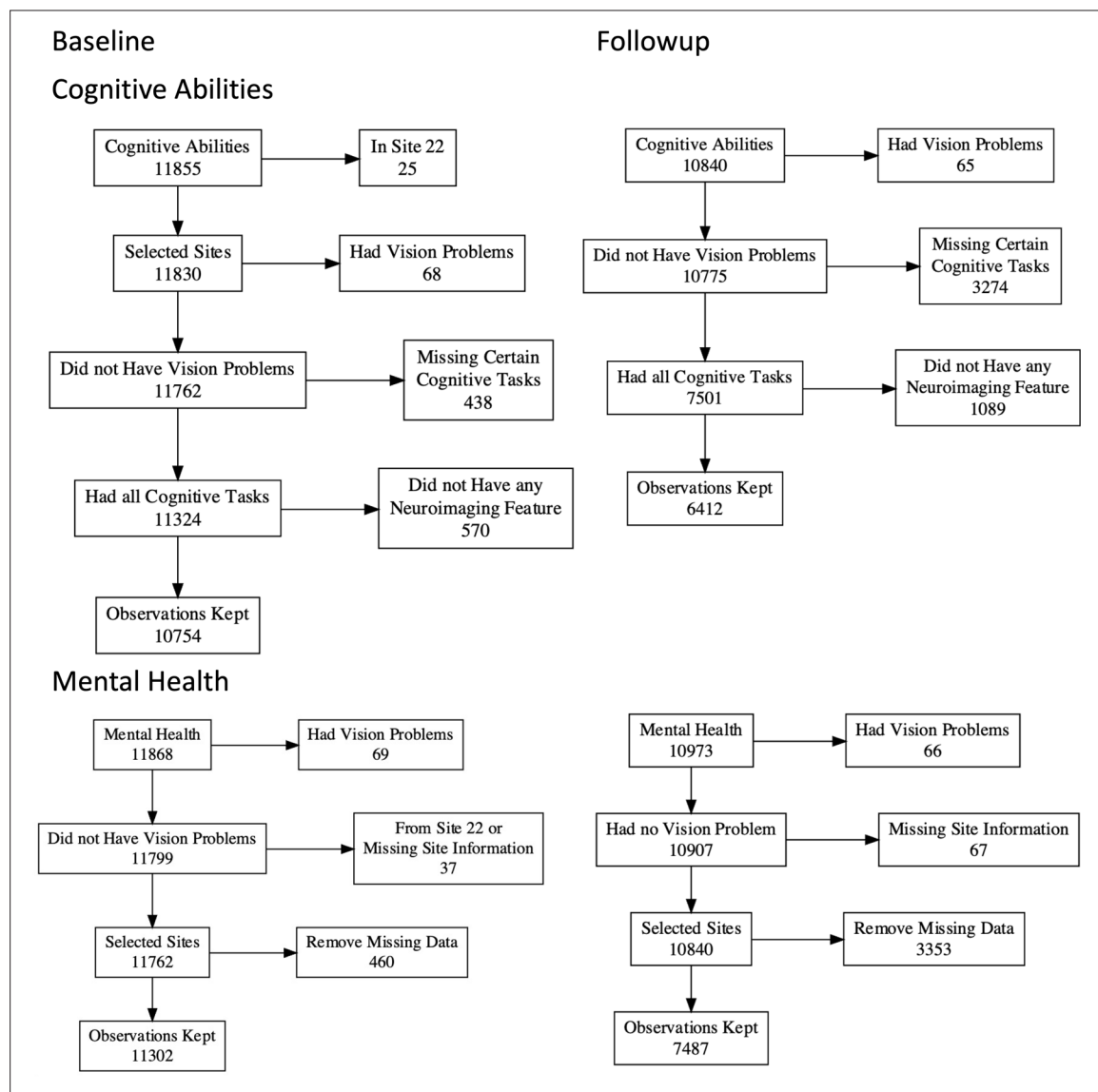


Figure 6. Flow diagram of participants' inclusion and exclusion criteria. Here, we show the criteria for cognitive abilities and mental health across the two time points.

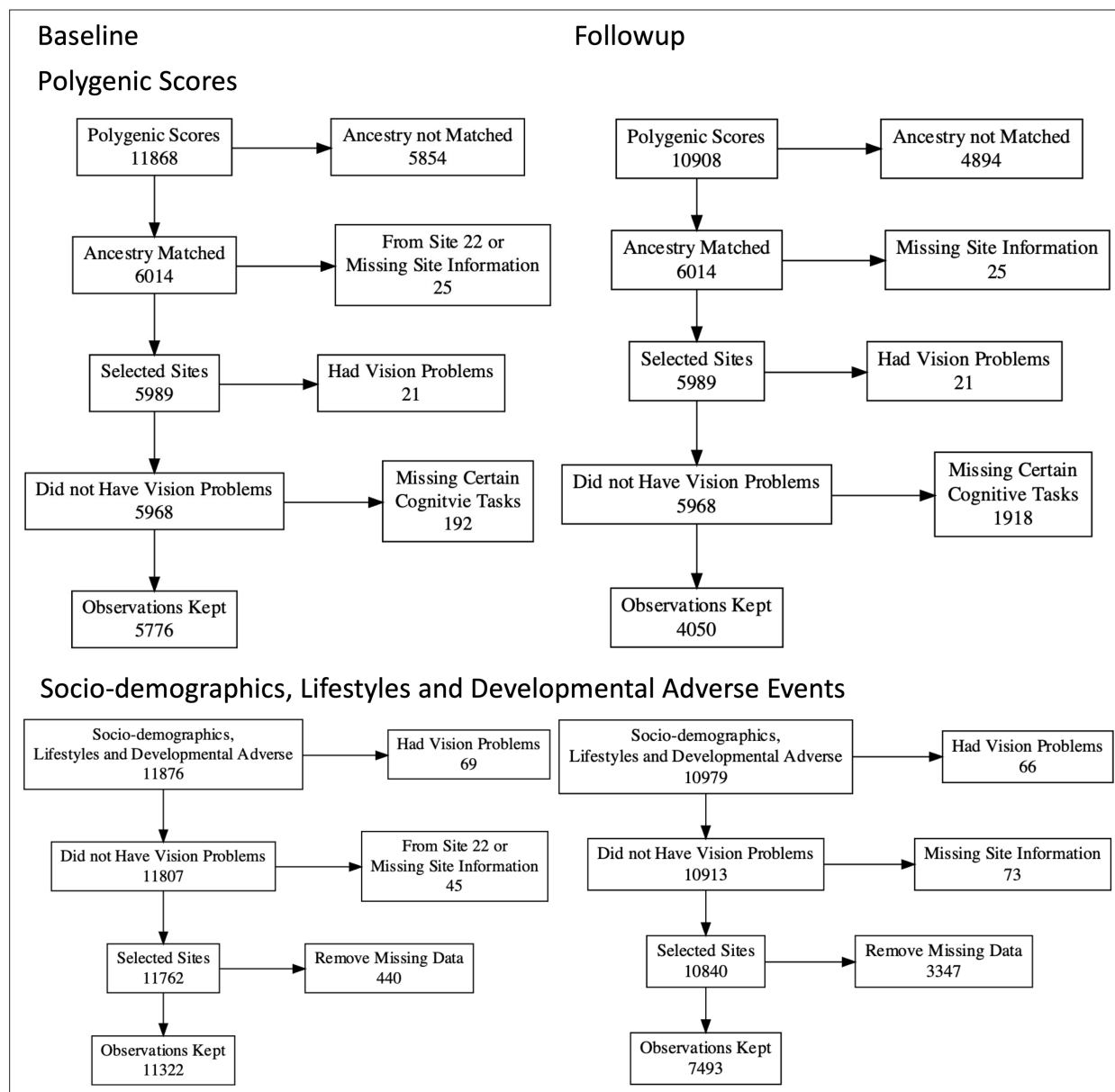


Figure 6—figure supplement 1. Flow diagram of participants' inclusion and exclusion criteria. Here, we show the criteria for polygenic scores and social demographics, lifestyle, and developmental adverse events across the two time points.

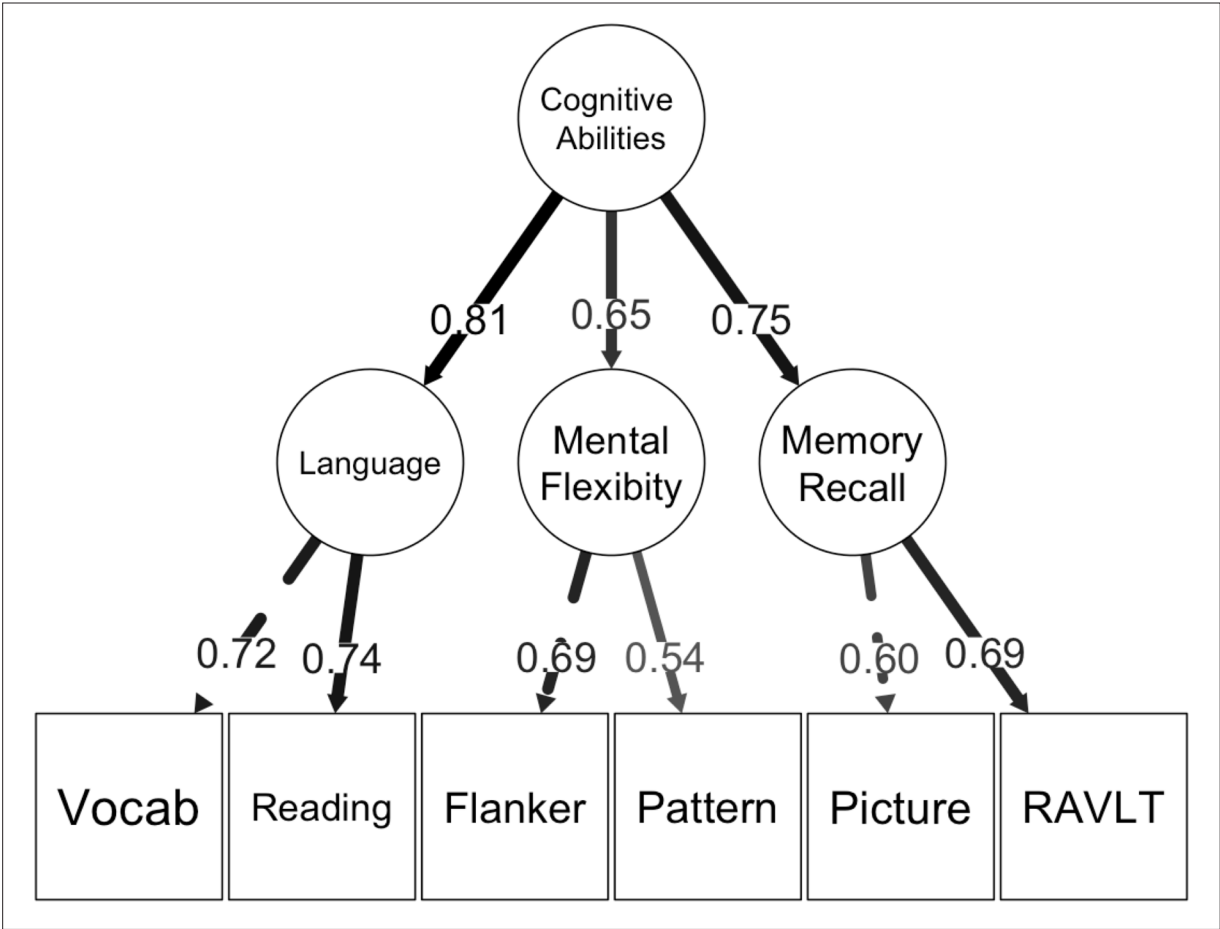


Figure 7. Standardised weights of the second-order 'g-factor' model. These weights were derived from confirmatory factor analysis, fitted on cognitive abilities across six cognitive tasks from the entire baseline dataset. The actual weights used for predictive modelling were slightly different, as the predictive modelling was based on leave-one-site-out cross-validation, which trained on data from all but one site.

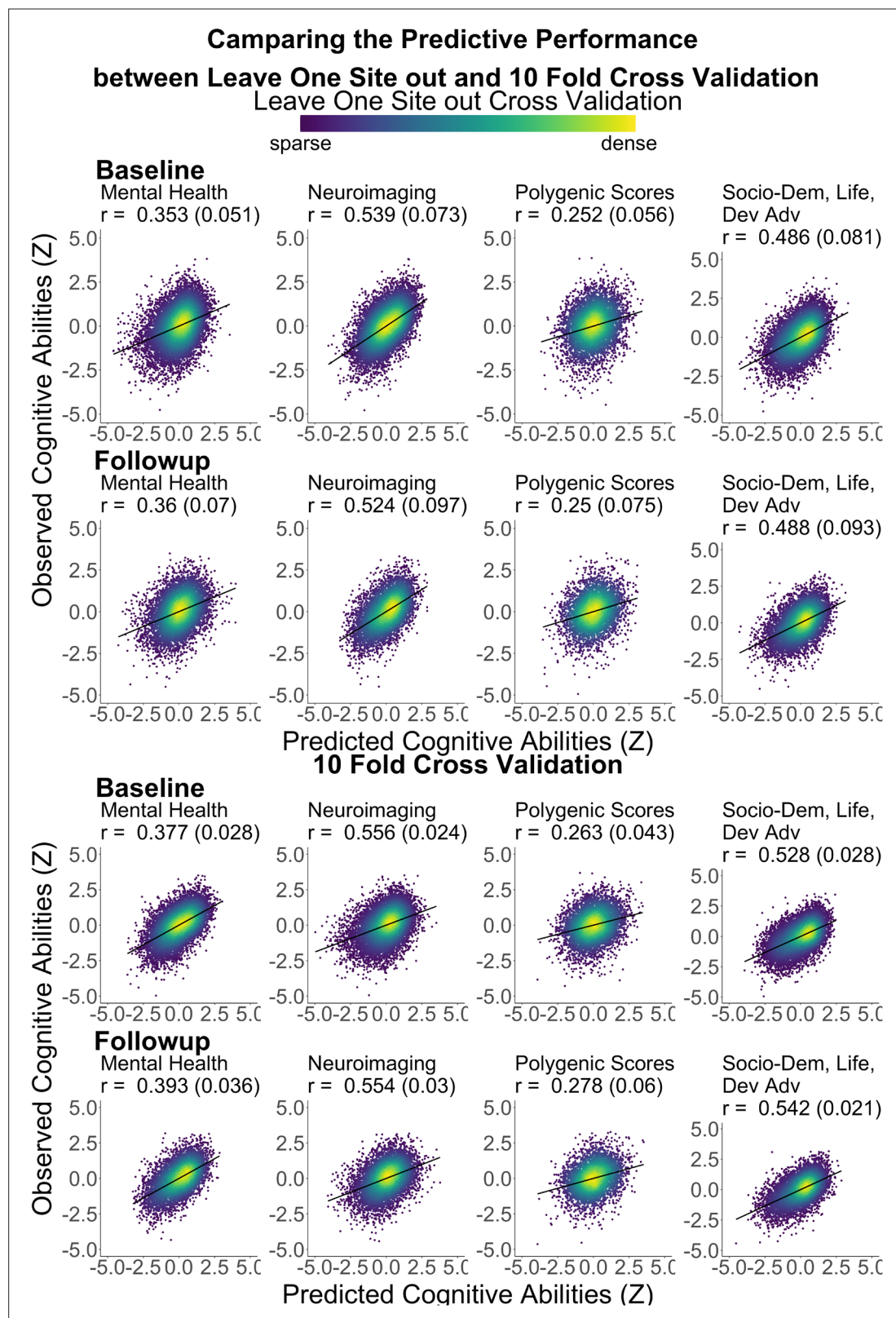


Figure 8. Predictive performance of leave one site out cross-validation vs 10-fold cross validation.

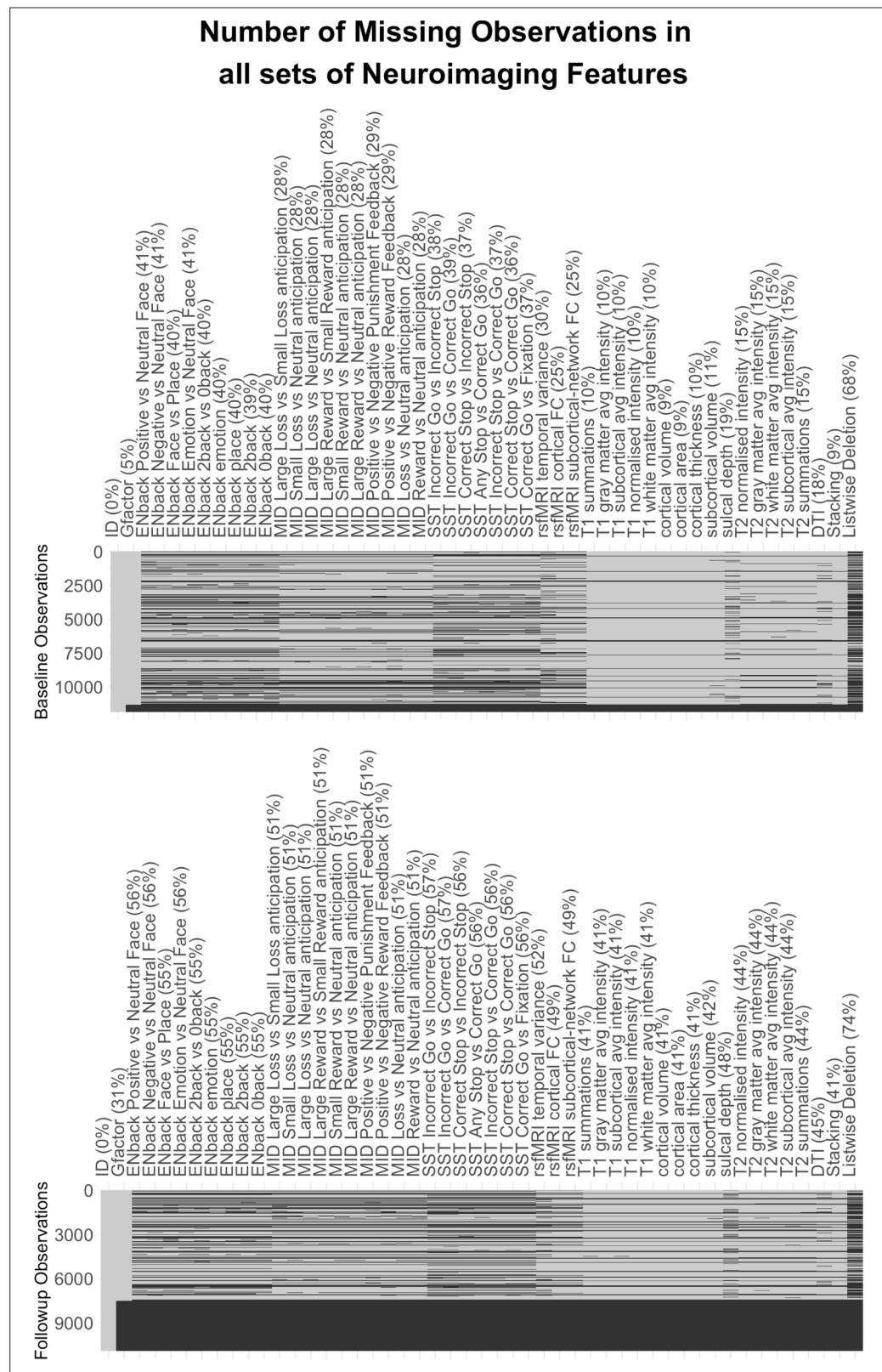


Figure 9. Illustration of data missingness (black) versus presence (grey) across different sets of neuroimaging features. This figure compares the number of observations in the analysis. Opportunist stacking (referred to as stacking here) requires only at least one neuroimaging feature to be present, thus allowing the inclusion of more neuroimaging features compared to listwise deletion.