Prediction errors of behavior in young populations: their associations with scan-related and sociodemographic variables

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Brain & Behaviour

Introduction

Neuroimaging-based prediction of human behavior serves as potential tools for individualized diagnosis and treatment in mental health.[1,2] However, the prediction power and generalizability, e.g. unfair prediction accuracy between ethnic groups[3], are concerning.[4,5]

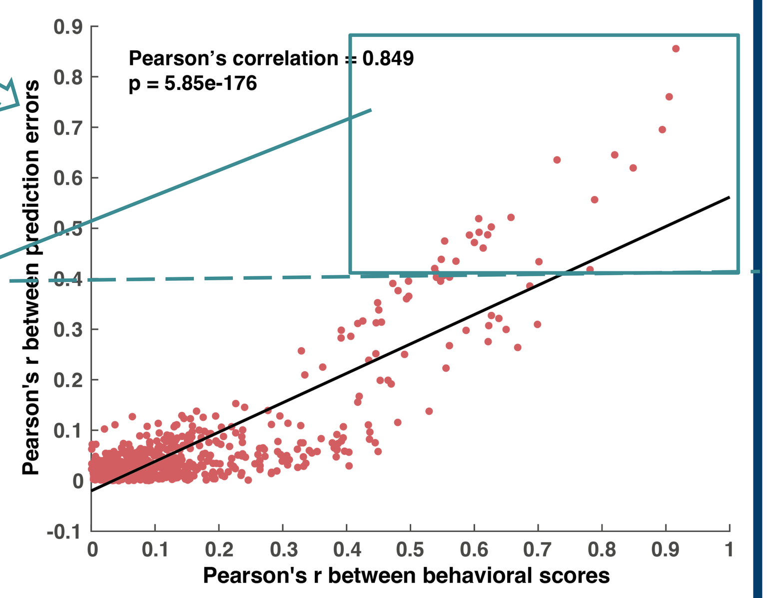
Greene et al. discovered that machine-learning models tended to classify a person's cognitive scores based on "stereotypes" in adult cohorts.[6] In other words, misclassified people tended to deviate from the stereotypical patterns observed in correctly classified participants, e.g. the higher education, the higher cognitive scores.

However, our understanding of prediction error in regression problems, in contrast to classification problems, especially in developing cohorts, is still limited. Furthermore, the association of prediction errors of behavioral measures beyond cognition with a broader range of covariates (e.g. head morphology) needs to be investigated. Therefore, we studied the associations in three young-population datasets and observed robust associations between prediction errors of multiple behavioral domains and many scan-related or sociodemographic covariates.

Methods

- Datasets
  - **Adolescent Brain Cognitive Development (ABCD)[7]:** *N = 5351, 9-11y, 36 behavioral measures*
  - **Human Connectome Project – Young Adults (HCP-YA)[8]:** *N = 948, 22-37y, 51 behavioral measures*
  - **Human Connectome Project – Development (HCP-D)[9]:** *N = 455, 8-22y, 22 behavioral measures*
- Preprocessing followed out previous works ([3] for ABCD & HCP-YA; [10] for HCP-D)
- Prediction methods
  - Machine learning algorithm: **kernel ridge regression** (ABCD & HCP-YA); **CBPP-SVR** (HCP-D)
  - Covariate regression before prediction: **age, gender, education** (parental education for ABCD), **intracranial volume, head movement** (& **household income** for HCP-YA).
  - Data split:
    - ABCD is multi-site. Hence (1) combine 19 sites to 10 bigger sets with similar sample size; (2) 7 sets for training, 3 sets for testing, in total 120 combinations.
    - HCP-YA: 10-fold nested cross-validation with 40 random repetitions
    - HCP-D only has 4 sites. 1 site = 1 fold (4-fold cross-validation). Random repetition not possible.
- Cluster behavioral measures based on similarity in prediction error, e.g., for ABCD:
- Scan-related covariates: Euler characteristic, head size, head motion
- Sociodemographic covariates: age, gender/sex, ethnicity/race, (parental) education, household income
- Statistical methods
  - Associations in full sample
    - Continuous covariates: Pearson's correlation
    - Binary covariates: two-sampled t test
    - Non-binary categorical covariates: one-way ANOVA
  - Robustness check: subsampling 100 times randomly (ABCD & HCP-YA; N = 455)
  - Handle collinearity across covariates: generalized linear model (GLM)

▪ Verbal Memory
▪ Cognition
▪ Mental Rotation
▪ CBCL (Child Behavior Checklist)
▪ Prodromal Psychosis

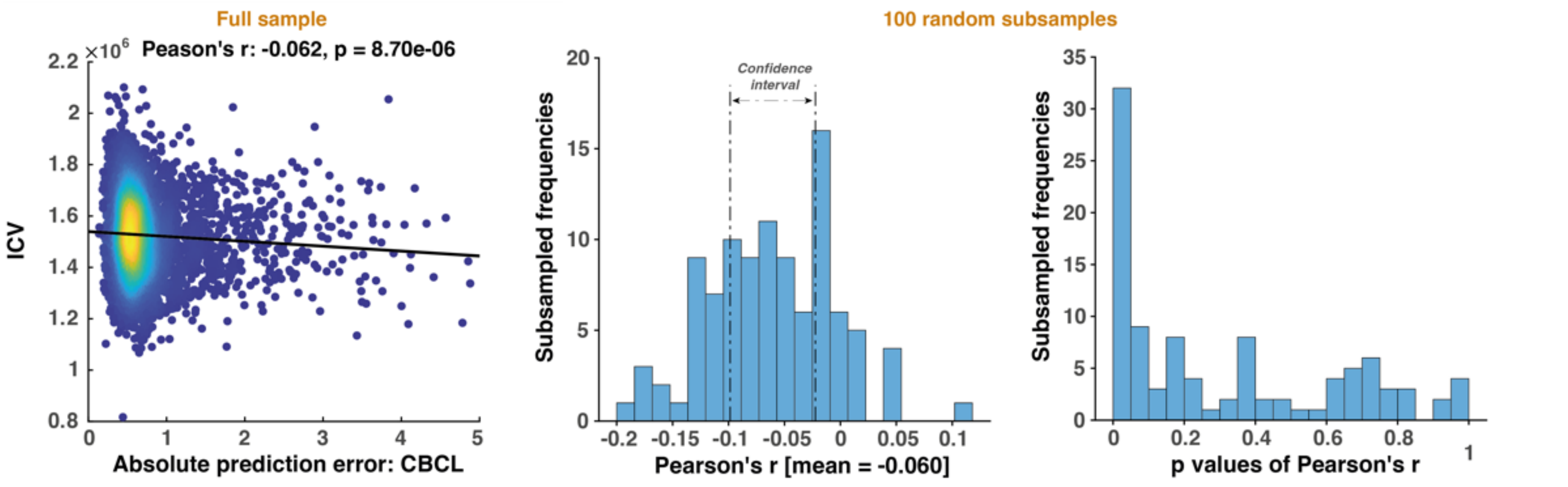


Results

❖ Exemplar association between prediction errors and scan-related covariates

ABCD: head size vs. prediction errors in CBCL.

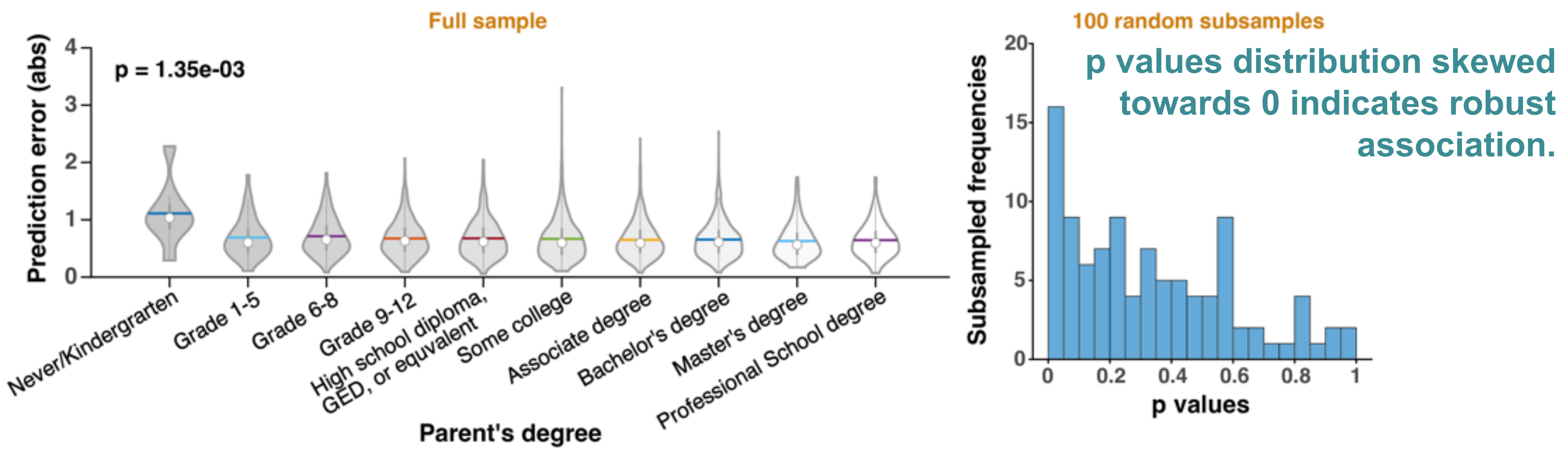
CBCL: Child Behavior Checklist, including Anxious/Depressed, Withdraw/Depressed, Social Problem etc.



A confidence interval not overlapped with 0 (middle) & p values distribution skewed towards 0 (right) indicate robust association.

❖ Exemplar association between prediction errors and sociodemographic covariates

ABCD: parental education vs. prediction errors in Cognition.



❖ Uni-covariate association summary

Prediction error (ABCD)	Associated covariates
Verbal Memory	Parental education, family income, age
Cognition	Euler characteristic, head motion, parental education, family income, ethnicity, age, sex
Mental Rotation	Ethnicity, age, sex
CBCL	Head size, head motion, parental education, family income, ethnicity, sex
Prodromal Psychosis	Head size, head motion, parental education, family income, ethnicity, age

Prediction error (HCP-YA)	Associated covariates
Social cognition	Head motion, education, family income, ethnicity
Positive/Negative Feelings	Head motion, education. family income, ethnicity
Emotion Recognition	Head motion, family income

Prediction error (HCP-D)	Associated covariates
Cognition	Education
Emotion Recognition	Euler characteristic, head size, education, age

❖ Multi-covariate GLM analyses

Goodness of full model: likelihood ratio test between full model and null model.

Full model: Prediction error ~ 1 + covariate 1 + covariate 2 + …; **Null model**: Prediction error ~ 1

Importance of a covariate: likelihood ratio test between full model and the model without this covariate

Scan-related full model: Prediction error ~ 1 + Euler characteristic + head size + head motion

		Full model	Euler characteristic	Head size	Head motion
ABCD	Verbal Memory	P = 0.0979	P = 0.649	P = 0.0448	P = 0.178
	Cognition	P = 0.0126	P = 0.0175	P = 0.969	P = 0.0586
	Mental Rotation	P = 0.330	P = 0.304	P = 0.168	P = 0.518
	CBCL	P = 6.90e-9	P = 0.261	P = 9.56e-6	P = 2.37e-5
	Prodromal Psychosis	P = 1.31e-13	P = 0.115	P = 2.26e-11	P = 1.99e-4
HCP-YA	Social Cognition	P = 5.56e-3	P = 0.345	P = 0.0563	P = 5.32e-3
	Positive/Negative Feelings	P = 0.0138	P = 0.384	P = 0.259	P = 3.63e-3
	Emotion Recognition	P = 2.11e-3	P = 0.954	P = 0.842	P = 1.37e-4
HCP-D	Cognition	P = 0.924	P = 0.521	P = 0.994	P = 0.664
	Emotion Recognition	P = 1.11e-6	P = 0.0115	P = 6.70e-6	P = 0.226

Sociodemographic full model:
Prediction error ~ 1 + age + sex/gender + ethnicity/race + (parental) education + family income

		Full model	Age	Sex/Gender	Ethnicity/ Race	(Parental) Education	Family income
ABCD	Verbal Memory	P = 2.77e-4	P = 0.0136	P = 0.927	P = 0.653	P = 0.0613	P = 2.08e-3
	Cognition	P = 8.71e-7	P = 0.00915	P = 6.82e-4	P = 0.0215	P = 0.0965	P = 0.300
	Mental Rotation	P = 1.05e-8	P = 5.19e-11	P = 8.15e-3	P = 0.0231	P = 0.607	P = 0.127
	CBCL	P = 5.75e-73	P = 0.564	P = 5.35e-16	P = 0.131	P = 5.66e-5	P = 4.77e-21
	Prodromal Psychosis	P = 1.86e-28	P = 1.03e-5	P = 0.393	P = 1.58e-4	P = 2.01e-3	P = 0.0109
HCP-YA	Social Cognition	P = 4.70e-6	P = 0.193	P = 0.864	P = 0.0209	P = 0.0487	P = 0.0829
	Positive/Negative Feelings	P = 1.35e-5	P = 0.759	P = 0.865	P = 1.09e-3	P = 0.0119	P = 0.246
	Emotion Recognition	P = 0.0906	P = 0.894	P = 0.0591	P = 0.773	P = 0.674	P = 0.0439
HCP-D	Cognition	P = 5.01e-4	P = 0.475	P = 0.722	P = 0.232	P = 1.04e-4	P = 0.464
	Emotion Recognition	P = 0.0165	P = 0.516	P = 0.283	P = 0.134	P = 0.326	P = 0.638

Discussion

1. Scan-related & sociodemographic covariates widely associated with the prediction errors of multiple behavioral domains in developing & young populations.
2. Such associations observed in full sample were confirmed by subsampling.
3. Subsampling in ABCD & HCP-YA to match the sample size of HCP-D also helped to control the effect of sample size across datasets.
4. After controlling the collinearity across covariates, majority of observed associations persisted.
5. Prediction errors of behavioral measures that were harder to prediction associated more strongly and widely with covariates.
   - Predictive models might tend to use covariate information to predict such behavioral measures
6. Richer associations were observed in the ABCD dataset compared to the other two datasets.
   - ABCD data is more diverse
   - Related to site? Prediction errors in ABCD were strongly associated with sites, but not in HCP-D.
     - Extended analysis: after controlling site, all associations of CBCL & Prodromal Psychosis preserved; associations of Verbal Memory, Cognition, Mental Rotation weakened. → consistent with Point 5.

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