Estimating Brain Maturation in Developing Adolescents with Multicontrast MRI

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Abstract Submission

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Introduction:

Predominant models of human cognitive development hypothesize developmental trajectories of brain structure and activity underly the timing of social, emotional and cognitive skill attainment. The adolescent brain, in particular, is characterized by heightened reward responsivity, fast incorporation of negative reinforcers for reforming behavior, and the ongoing refinement of action inhibition, which is reflected as lower levels of risk aversion and greater impulsivity in high reward contexts. Charting the time course of brain maturation can reveal the undefined temporal boundaries of adolescent brain development and identify individuals with lagging or advanced maturational trajectories. Here regularized regression models were trained on multicontrast MRIs at time k, and coefficients used to predict age at k+1 across ages 11-18. A quantitative metric of brain maturation is defined as the error between actual and predicted age and used to explore relationships between developmental delays in specific brain regions and behavior.

Methods:

Subjects. Youths aged 11-14 (N=143; right-handed) from the Washington, D.C. area participated in a longitudinal brain imaging study investigating the precursors and effects of early substance use. Participants had no history of mental disorders, serious head injury, or substance use at baseline. MRI data were collected at three ~18 month intervals. Youth with complete structural, diffusion and resting-state (rs) MRIs at each visit were retained for analysis (N=134/103/99 @ 0/18/36 mos, 336 total, 141 unique subjects).
Data Acquisition. A 3T Siemens Tim Trio with a 12-channel head coil was used to acquire whole-brain resting state functional (rsfMRIs; eyes open, TR/TE=2280/30ms, 3mm3 voxels, 5:49m), diffusion weighted (dwMRIs; TR/TE=7500/87ms, 2.5mm3 voxels) along 10, 10, 60 diffusion weighted A->P gradients for b = 0, 300 and 1100 ms/um & structural MPRAGE MRIs (sMRIs; TR/TE/TI/=1920/2.52/900ms, 1mm3 voxels).
Preprocessing. A multicontrast study specific template was generated with ANTs from tensor metric maps derived from dwMRIs, time-averaged rsfMRIs and denoised sMRIs of 175 sessions selected for image quality. Subject-specific brain segmentation and morphometrics were generated from sMRIs with FreeSurfer v6.0. dwiMRIs were denoised, motion/eddy current corrected, and fractional anisotropy (FA) maps calculated in mrtrix3.
Age Prediction. The least absolute shrinkage and selection operator (LASSO) implemented in glmnet was used to build a regularized regression model of age using a feature vector composed of gray matter volume, fractional anisotropy (FA) maps and subject-specific functional network maps sampled with the FreeSurfer anatomical parcellation. Leave-one-out cross-validation was used to estimate LASSO hyperparameters. The coefficient of regression using timepoints 1 and 2 were used to predict age at timepoint 3. The error between predicted and actual age was used as a metric of brain maturity.

Results:

The predicted age at the final visit was correlated with actual age at that time point (r = 0.40). The average error between predicted age and actual age was 25 months and showed a variance across subjects of 9.45 months. LASSO variable selection identified 62 structural features predictive of age. Of those features, 28 were volumetric, 25 derived from FA maps and 9 related to curvature changes. Regions such as the middle frontal gyrus and basal ganglia exhibited both volumetric and microstructural changes related to age. Decreases in folding related to age were observed predominantly in inferior frontal gyrus and temporal gyri.

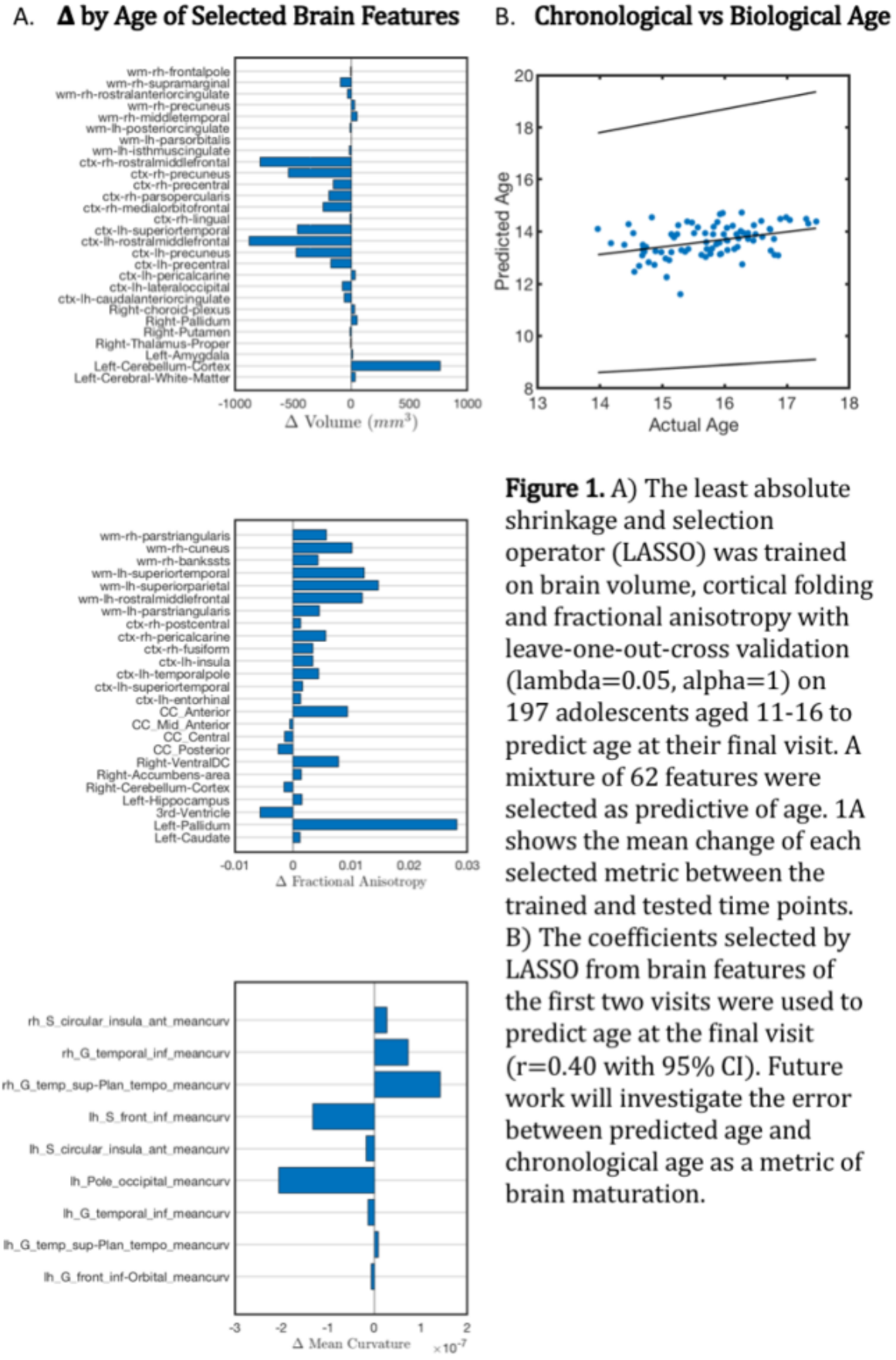

Figure 1. A) The least absolute shrinkage and selection operator (LASSO) was trained on brain volume, cortical folding and fractional anisotropy with leave-one-out-cross validation (lambda=0.05, alpha=1) on 197 adolescents aged 11-16 to predict age at their final visit. A mixture of 62 features were selected as predictive of age. 1A shows the mean change of each selected metric between the trained and tested time points. B) The coefficients selected by LASSO from brain features of the first two visits were used to predict age at the final visit (r=0.40 with 95% CI). Future work will investigate the error between predicted age and chronological age as a metric of brain maturation.

Conclusions:

Our results show brain maturation as measured with multicontrast MRI evolves with chronological age. Microstructural features and size/shape morphometrics contribute unique sources of variance in models of biological age. Future work will include functional MRI as an additional predictive feature and correlate brain maturation with behavior.

Lifespan Development:

Normal Brain Development: Fetus to Adolescence [1]

Modeling and Analysis Methods:

Classification and Predictive Modeling [2]
Multivariate modeling

Keywords:

Development
STRUCTURAL MRI
White Matter
Other - Adolescence, Prediction, Lifespan Development

[1|2]Indicates the priority used for review

My abstract is being submitted as a Software Demonstration.

No

Please indicate below if your study was a "resting state" or "task-activation" study.

Other

Healthy subjects only or patients (note that patient studies may also involve healthy subjects):

Healthy subjects

Are you Internal Review Board (IRB) certified? Please note: Failure to have IRB, if applicable will lead to automatic rejection of abstract.

Yes

Was any human subjects research approved by the relevant Institutional Review Board or ethics panel? NOTE: Any human subjects studies without IRB approval will be automatically rejected.

Yes

Was any animal research approved by the relevant IACUC or other animal research panel? NOTE: Any animal studies without IACUC approval will be automatically rejected.

Not applicable

Please indicate which methods were used in your research:

Functional MRI
Structural MRI
Diffusion MRI
Behavior

For human MRI, what field strength scanner do you use?

3.0T

Which processing packages did you use for your study?

AFNI
FSL
Free Surfer
Other, Please list - mrtrix3, ANTs

Provide references using author date format

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