ARTICLE OPEN

Check for updates

Neuroanatomy reflects individual variability in impulsivity in youth

Elvisha Dhamala[1,2✉], Erynn Christensen[1], Jamie L. Hanson[3,4], Jocelyn A. Ricard[5,6], Noelle Arcaro[1], Simran Bhola[1], Lisa Wiersch[1], Katharina Brosch[1], B. T. Thomas Yeo[7,8,9,10,11,12], Avram J. Holmes[13] and Sarah W. Yip[14,15,16,17]

Individual differences in neural circuits underlying emotional regulation, motivation, and decision-making are implicated in many psychiatric illnesses. Interindividual variability in these circuits may manifest, at least in part, as individual differences in impulsivity. Impulsivity reflects a tendency towards rapid, unplanned reactions to internal or external stimuli without considering potential negative consequences, coupled with difficulty inhibiting responses. Here, we use multivariate machine learning approaches (brain-based predictive models) to explore the neural bases of impulsivity. We consider multiple impulsivity measures, neuroanatomical features (cortical thickness, surface area, and gray matter volume, as well as non-cortical gray matter volume), and sexes (females and males) in a large sample of youth from the Adolescent Brain Cognitive Development (ABCD) Study at baseline (n = 8630), two-year follow-up (n = 5998), four-year follow-up (n = 4844), and six-year follow-up (n = 3100). Using brain-based predictive models, we demonstrate that regional variations in cortical thickness, surface area, and gray matter volume significantly predict self-reported impulsivity measures, with associations varying across impulsivity dimensions and developmental timepoints. Impulsivity broadly maps onto default mode, limbic, ventral attention, and visual networks, as well as cerebellar and brain stem structures. While many relationships are stable across sexes and developmental time points, others exhibit sex effects and dynamic changes. These results suggest that neuroanatomy is linked to self-reported impulsivity in youth and highlight the complexity of these relationships across measures, features, sexes, and time points. This work also emphasizes the importance of adopting a multivariate and sex-specific approach in neuroimaging and behavioral research.

Molecular Psychiatry; https://doi.org/10.1038/s41380-026-03526-2

INTRODUCTION

Impairments in emotional regulation, motivation, and decision-making are prevalent across a range of psychiatric illnesses [1] and often emerge during early adolescence [2, 3]. These impairments contribute to the heterogeneity observed within psychiatric illnesses and may initially appear as more fundamental alterations in processes and behaviors such as impulsivity [4, 5]. Impulsivity reflects "a predisposition toward rapid, unplanned reactions to internal or external stimuli without regard to the negative consequences of these reactions to the impulsive individual or to others [6]." Changes in impulsivity are a normal part of development, but heightened levels of impulsivity may indicate increased risk for psychiatric illness [7–9]. Since adolescence is a period of significant brain plasticity, understanding brain-behavior relationships during this developmental window will be critical for future clinical research.

Although often treated as a single construct, *impulsivity* encompasses a variety of distinct but related functions that promote impulsive behavior [10]. These include an individual's (in) ability to consider the consequences of a behavior (lack of premeditation), tendency to disengage from tasks due to boredom or difficulty before completion (lack of perseverance), responses to emotional states (positive and negative urgency), and motivation to experience rewarding sensations (sensation seeking) [9]. Impulsivity can also be considered a product of two systems that promote impaired self-regulation: the behavioral inhibition and approach systems (BIS/BAS) [11]. The BIS prevents actions that may lead to a negative outcome [12], while the BAS encapsulates sensitivity to, and motivation for, reward/punishment, as well as escape from punishment, therefore encouraging incentive-motivated behavior [12]. These conceptualizations highlight the variability in how

[1]Institute of Behavioral Sciences, Feinstein Institutes for Medical Research, Manhasset, USA. [2]Department of Psychiatry, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Uniondale, Hempstead, USA. [3]Learning Research and Development Center, University of Pittsburgh, Pittsburgh, USA. [4]Department of Psychology, University of Pittsburgh, Pittsburgh, USA. [5]Stanford Neurosciences Interdepartmental Program, Stanford University School of Medicine, Stanford, USA. [6]Department of Psychology, Stanford University, Stanford, USA. [7]Centre for Sleep & Cognition & Centre for Translational Magnetic Resonance Research, Yong Loo Lin School of Medicine, Singapore, National University of Singapore, Singapore, Singapore. [8]Department of Electrical and Computer Engineering, National University of Singapore, Singapore, Singapore. [9]N.1 Institute for Health, National University of Singapore, Singapore, Singapore. [10]Integrative Sciences and Engineering Programme (ISEP), National University of Singapore, Singapore, Singapore. [11]Department of Medicine, Healthy Longevity Research Programme, Human Potential Translational Research Programme & Institute for Digital Medicine (WisDM), Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore. [12]Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Charlestown, USA. [13]Department of Psychiatry, Brain Health Institute, Rutgers University, Piscataway, USA. [14]Department of Psychiatry, Yale School of Medicine, New Haven, USA. [15]Child Study Center, Yale School of Medicine, New Haven, USA. [16]Center for Brain and Mind Health, Yale School of Medicine, New Haven, USA. [17]Wu Tsai Institute, Yale University, New Haven, USA. ✉email: elvisha@gmail.com

Received: 16 June 2025 Revised: 14 February 2026 Accepted: 10 March 2026
Published online: 24 March 2026

impulsivity is defined and measured, posing a challenge for research, and underscoring the need for greater conceptual clarity [6, 10]. Consequently, a crucial consideration is the extent to which different components of impulsivity may be driven by shared versus distinct neural features.

Foundational circuit-based research has established key neural substrates of impulsivity, particularly highlighting the role of corticolimbic and corticostriatal circuits [8, 13–16]. The corticolimbic system contributes to processing emotional salience and regulating emotional responses [17], while the corticostriatal system is involved in motivated behavior, reward processing, learning, and habit formation [18]. These systems mature throughout development [19] and this is accompanied by significant changes in synaptic connectivity and myelination [20–22]. This development is asynchronous. Limbic and striatal structures mature earlier than cortical structures, including the prefrontal cortex, resulting in heightened impulsivity during this period of 'mismatch' [21, 23, 24]. Behaviorally, emotional regulation, motivation, and impulse control evolve throughout development with rapid changes in early life followed by gradual changes during adolescence [25–29]. This is paralleled by changes in their neural substrates beyond corticolimbic and corticostriatal circuits, such as the insula and cingulate cortex [7, 29, 30]. Thus far, hypothesis-driven studies have provided crucial mechanistic insights into how specific brain regions and circuits contribute to impulsive behavior [31–35]. However, the extent to which distributed neuroanatomical features across the brain jointly predict individual differences in multidimensional impulsivity during development remains unclear.

Brain-based predictive models use machine learning to analyze whole-brain multivariate relationships [36], accounting for the interconnected nature of the brain. This data-driven approach complements hypothesis-driven research by characterizing population-level brain-behavior associations without a priori assumptions about which regions are most relevant. These models capture how regions jointly contribute to impulsivity rather than treating each region independently and can identify patterns that may not emerge from univariate or region-focused analyses. Importantly, distributed patterns identified through prediction models do not negate the importance of specific circuits established through mechanistic research; rather, they can reveal heterogeneity across impulsivity dimensions and generate empirical targets for subsequent mechanistic investigation. These models can also be used with longitudinal data to examine whether these relationships are consistent throughout development.

Neurodevelopmental processes and behavioral expressions vary between males and females, raising questions about the extent to which sex-specific neuroanatomical patterns contribute to observed differences in impulsivity. There are sex differences in the developmental trajectories of corticolimbic and corticostriatal systems [37, 38], although findings are inconsistent across studies. As an example, on average, females have greater relative volume in the prefrontal and orbitofrontal regions, while males have greater volume in ventral temporal and occipital regions [39]. Similarly, sex differences have been reported in impulsivity, but these results are also inconsistent [40]. Thus, it is plausible that sex differences exist across neuroanatomy, impulsivity, and their interrelationships, highlighting the importance of considering sex differences when studying impulsivity, particularly in youth. Furthermore, within the context of large data initiatives, it remains to be determined whether sex differences in impulsivity are driven by unique neuroanatomical substrates. This can be addressed by examining sex-specific relationships between neuroanatomy and impulsivity.

Thickness, surface area, and gray matter volume, reflect different aspects of neuroanatomy. Thickness (i.e., distance between the brain's outer surface and gray-white matter junction) reflects neuronal density and arrangement [41, 42]. It increases rapidly during the prenatal period, continues growing after birth, peaks in early childhood, and then gradually thins [43]. Surface area (i.e., area of the pial surface) is linked to the organization and complexity of cortical columns [41, 42] as well as neuronal proliferation [41, 42] and gyrification [44]. Surface area expands prenatally and through childhood, peaking in late childhood/early adolescence, and then gradually declines [43]. Gray matter volume, encompassing thickness and surface area, reflects the total amount of cells and synapses [41, 42], and follows a similar developmental trajectory as surface area [43]. Changes in these features reflect neurogenesis, synaptogenesis, synaptic pruning, cell death, and alterations in cell size and density, and are linked to various psychiatric conditions [41, 42]. These structural measures demonstrate high test-retest reliability within individuals [45], particularly when compared to functional measures derived from functional MRI [46]. While structural measures are not entirely insensitive to state-related factors [47], they show substantially less variability across scanning sessions than functional measures [45], making them better suited for capturing stable individual differences in brain-behavior relationships. A multimodal, whole-brain analysis considering these features is necessary to reveal their unique contributions to impulsivity.

Here, we investigated the neuroanatomical basis of impulsivity, across different neuroanatomical features and impulsivity measures, in a large sample of youth from the Adolescent Brain Cognitive Development (ABCD) Study at four time points. Using a data-driven, brain-based predictive modeling framework, we quantify multivariate associations between neuroanatomy and multiple dimensions of self-reported impulsivity, demonstrating that distributed cortical and subcortical features predict individual differences with modest but significant accuracy. While some of these relationships are shared, others vary across measures of impulsivity, morphometric features, and developmental time points. These findings highlight substantial individual variability in the neural basis of impulsivity in youth. Understanding these distinct markers of impulsivity is crucial for establishing normative developmental patterns and exploring how deviations may underlie psychiatric risk.

METHODS

Dataset

The ABCD Study is following a large community-based sample of children and adolescents throughout the course of development [48]. Participants are assessed on a comprehensive set of neuroimaging, behavioral, developmental, and psychiatric batteries. We used data from the ABCD 6.0 release. The research protocol for the dataset was reviewed and approved by a central Institutional Review Board (IRB) at the University of California, San Diego, and, in some cases, by individual site IRBs. Parents or guardians provided written informed consent, and children assented before participation.

We excluded participants with imaging data that was missing, as well as those not recommended for inclusion or with incidental MRI findings. We excluded participants with incomplete impulsivity data. Finally, we excluded related participants such that a single family member was included in the sample and others were dropped at random. We included 8620 participants at baseline (9–10 years old), 5998 at two-year follow-up (11–12 years old), 4844 at four-year follow-up (13–14 years old), and 3100 at six-year follow-up (15–16 years old; see Figure S1 for inclusion pipeline).

Neuroimaging

The imaging protocol and parameters for T1-weighted scans are detailed in previous publications [48, 49]. We used measures of cortical thickness (mean), surface area (total), and gray matter volume (total) for 68 regions (34 per hemisphere) from the Desikan-Killiany parcellation and measures of non-cortical gray matter volume (total) for 19 regions (8 subcortical and 1 cerebellar per hemisphere, and 1 brain stem) from the FreeSurfer automatic segmentation. Regional area and volume measures, but not thickness, were proportionally corrected for individual differences in intracranial volume [50] (see Figures S2-S4 for average measures and sex differences in the measures).

Impulsivity

We derived impulsivity measures from the self-report Behavioral Inhibition/Activation System (BIS/BAS) and the Modified Urgency, (lack of) Planning (or Premeditation), (lack of) Perseverance, Sensation Seeking, and Positive Urgency (UPPS-P [51]) Short Version scales, both of which have been validated in children [12, 52]. We focused on self-report measures because they capture trait-level impulsivity and show stronger predictive validity for real-world outcomes than task-based behavioral measures [53–55].

BIS/BAS. The BIS/BAS scale is a 20-item questionnaire used to measure individual differences in the behavioral inhibition and activation systems [56–59]. The behavioral inhibition system reflects motivation to avoid aversive outcomes, and the behavioral activation system reflects motivation to approach goal-oriented outcomes. There is one BIS-related scale (inhibition), and three BAS-related scales (reward responsiveness, drive, and fun seeking). Inhibition reflects sensitivity to punishment and is the sum of seven items. Reward responsiveness reflects reward anticipation, reward response, and reward satiation, and is the sum of four items. Drive reflects persistent pursuit of goals and is the sum of four items. Fun seeking reflects a desire for new rewards and a willingness to approach a potentially rewarding event and is the sum of five items. Participants respond to each item using a four-point Likert scale (ranging from 0–3), where higher values indicate higher levels of a given trait.

UPPS-P. The UPPS-P Short Version scale is a 20-item questionnaire used to measure five distinct impulsive personality traits: negative urgency, positive urgency, lack of planning, lack of perseverance, and sensation seeking [60–62]. Negative urgency is the tendency to act impulsively to negative emotions. Positive urgency is the tendency to act impulsively to positive emotions. Lack of perseverance is the tendency to give up or not complete tasks. Lack of planning is the tendency to act without considering the consequences. Sensation seeking is the tendency to pursue exciting or novel activities. Scores for each trait are based on the sum of four items each. Participants respond to each item using a four-point Likert scale (ranging from 1–4) where higher values indicate higher levels of a given trait.

Predictive modeling

We used a cross-validated brain-based predictive modeling framework [36] which we have leveraged in prior work [50, 63–67]. This framework avoids data leakage and minimizes overfitting to capture robust, reliable, and interpretable associations between imaging-derived measures and phenotypic data. For each pair of neuroanatomical features and impulsivity measures, we developed separate sets of sex-independent (i.e., including the entire sample) and sex-specific (i.e., in either females or males) linear ridge regression models at each of the time points to predict impulsivity based on neuroanatomical features (either thickness, area, or volume from 68 cortical regions or volume from 19 non-cortical regions). Using the same framework, we also examined whether longitudinal changes in neuroanatomy could predict changes in self-reported impulsivity measures. To maximize sample size, we considered changes from: baseline and (a) two-year follow-up, (b) four-year follow-up, and (c) six-year follow-up.

For each set of models, we randomly shuffled and split the data into 100 distinct training and test sets (at approximately a 4:1 ratio) without replacement. We accounted for potential variability introduced by imaging site by placing all participants from a given site in either the training or the test set but not split across the two. In doing so, we are able to test whether the brain-impulsivity relationship learned in a set of (training) sites generalizes to individuals from new (test) sites, despite potential MRI differences across sites. Within each training set, we optimized the regularization hyperparameter using three-fold cross-validation, ensuring participants from a given site were not split across folds. Once optimized, we trained the model on the entire training set using the optimized hyperparameter and evaluated model performance on the hold-out test set based on prediction accuracy (i.e., full correlation between observed and predicted values) [67–70]. We repeated this process for the 100 train-test splits to obtain a prediction accuracy distribution. We evaluated model significance by comparing these distributions to null distributions. We generated 1000 null models by randomly permuting the output variable within each site and then using those data to train and test a model using a randomly selected regularization hyperparameter from the set of optimized hyperparameters for the original model. We obtained the p-values for model performance by calculating the proportion of null models with accuracies greater than or equal to the corresponding original distribution. We corrected the p-values for multiple comparisons within the behavioral scales the Benjamini-Hochberg False Discovery Rate ($q = 0.05$) procedure [71].

Feature weights

We analyzed the feature weights for models capturing reliable brain-behavior relationships. We transformed the feature weights using the Haufe transformation [72] to increase their interpretability and reliability [68, 69, 73], and then calculated a mean feature importance for each set of models. We computed full correlations between the mean feature importance values to evaluate overlap. Lastly, we summarized the cortical feature weights to a network-level, as per the Yeo-7 parcellation [74], by taking the mean across all regions within a network.

RESULTS

Expressions of impulsivity vary across youth

Distributions of the self-reported impulsivity measures at each time point are presented in the Supplemental Materials (Figure S5). These distributions are consistent with prior work examining impulsivity in the ABCD Study [75, 76], indicating that our sample is representative of the cohort. Moreover, there are modest within-scale correlations of measures suggesting that they capture partially overlapping aspects of behavior, and significant but weak between-scale correlations indicating that the UPPS-P and BIS/BAS, while potentially related, measure somewhat independent constructs [77].

Neuroanatomy predicts impulsivity

Brain-based predictive models were used to quantify associations between neuroanatomy and impulsivity (Fig. 1, Tables S1-S4).

Models based on **thickness** accurately predicted drive, negative urgency, and positive urgency at baseline; drive and positive urgency at two-year follow-up; behavioral inhibition and drive at four-year follow-up; and behavioral inhibition at six-year follow-up.

Models based on **area** accurately predicted drive and lack of planning at baseline; positive urgency, lack of perseverance, lack of planning, and sensation seeking at two-year follow-up; sensation seeking at four-year follow-up; and behavioral inhibition and sensation seeking at six-year follow-up.

Models based on **cortical volume** accurately predicted behavioral inhibition, reward responsiveness, drive, fun seeking, positive urgency, and lack of planning at baseline; positive urgency, lack of planning, and sensation seeking at two-year follow-up; behavioral inhibition and sensation seeking at four-year follow-up; and behavioral inhibition at six-year follow-up.

Models based on **non-cortical volume** accurately predicted negative urgency, positive urgency, and lack of perseverance at two-year follow-up; and behavioral inhibition at four-year follow-up.

We used the same framework to examine sex-specific associations (Fig. 2, Tables S5-S12).

Female-specific models based on **thickness** accurately predicted reward responsiveness and drive at baseline; and drive, negative urgency, and positive urgency at two-year follow-up.

Female-specific models based on **area** accurately predicted drive at baseline; and behavioral inhibition at six-year follow-up.

Female-specific models based on **cortical volume** accurately predicted positive urgency at baseline; positive urgency and lack of planning at two-year follow-up; and behavioral inhibition and reward responsiveness at six-year follow-up. **Male-specific** models based on **cortical volume** accurately predicted lack of planning at baseline.

Female-specific models based on **non-cortical volume** accurately predicted lack of perseverance at baseline; negative urgency, positive urgency, and lack of perseverance at two-year follow-up; and sensation seeking at four-year follow-up. **Male-specific** models based on **non-cortical volume** accurately predicted negative urgency at two-year follow-up.

We also used the same framework to examine associations between changes in neuroanatomy and changes in impulsivity. These analyses largely yielded insignificant results.

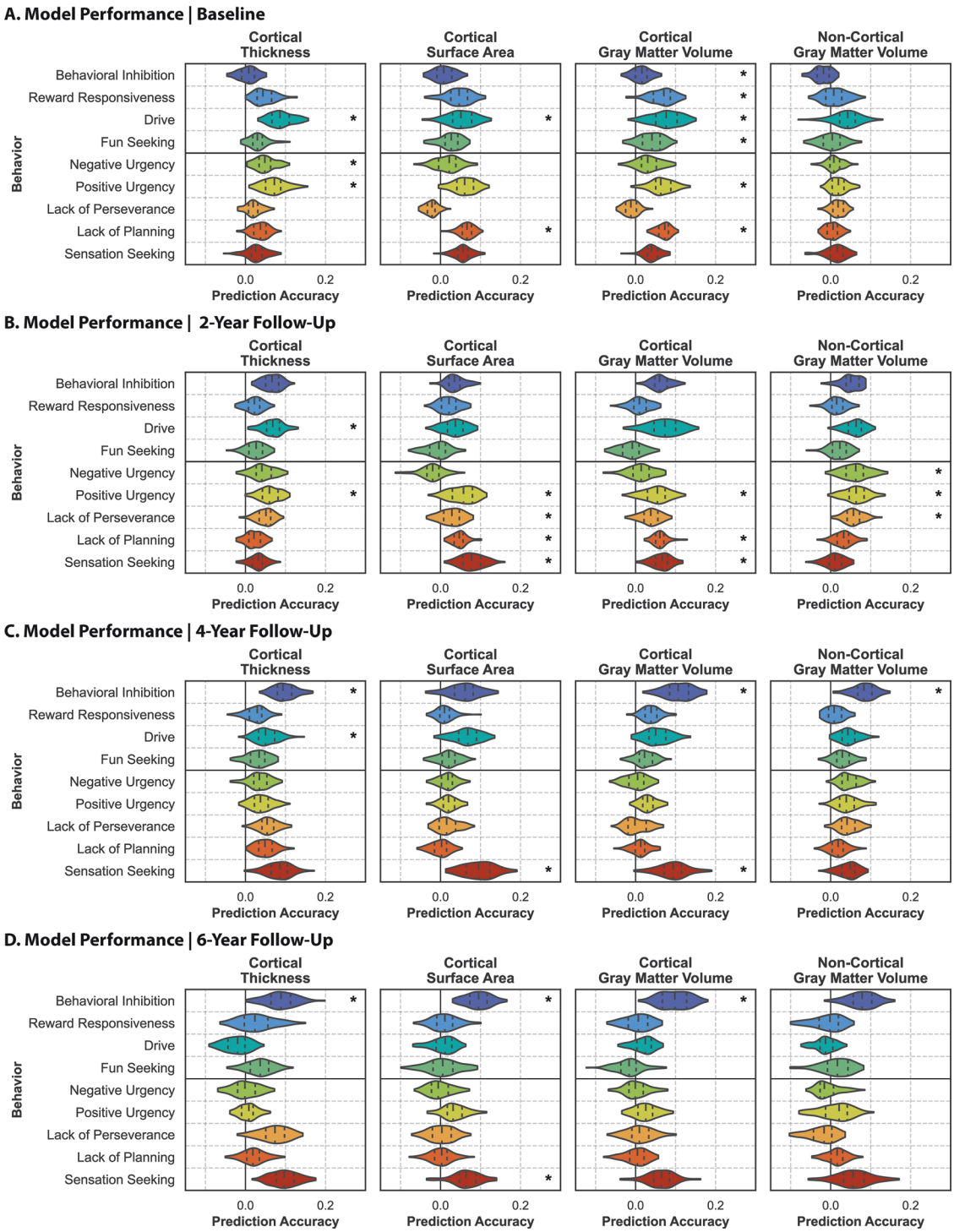


Fig. 1 Neuroanatomy reflects individual differences in impulsivity. Prediction accuracies (correlation between observed and predicted values) for models trained to predict self-reported impulsivity measures at baseline (**A**) two-year follow-up (**B**) four-year follow-up (**C**) and six-year follow-up (**D**). From left to right, cortical thickness, cortical surface area, cortical gray matter volume, and non-cortical gray matter volume results are shown. The shape of the violins indicates the distribution of values across 100 random splits of the data, the dashed lines indicate the median, and the dotted lines indicate the interquartile range. Asterisks indicate the model captured significant associations.

Changes in impulsivity are part of normative development and, at their extremes, are linked to the development of psychiatric illnesses later in life [78, 79]. We show that individual variations in neuroanatomy can predict impulsivity in youth. While certain measures can be predicted in both sexes, others yield significant results only in females, which may be due to the reliability of measures across sexes, reporting biases, and data quality, among other factors. In addition, while some self-reported impulsivity measures can be predicted across multiple time points, others are only predictable during earlier developmental periods, potentially due to reduced sample sizes at later time points or weakening brain-behavior relationships as development progresses.

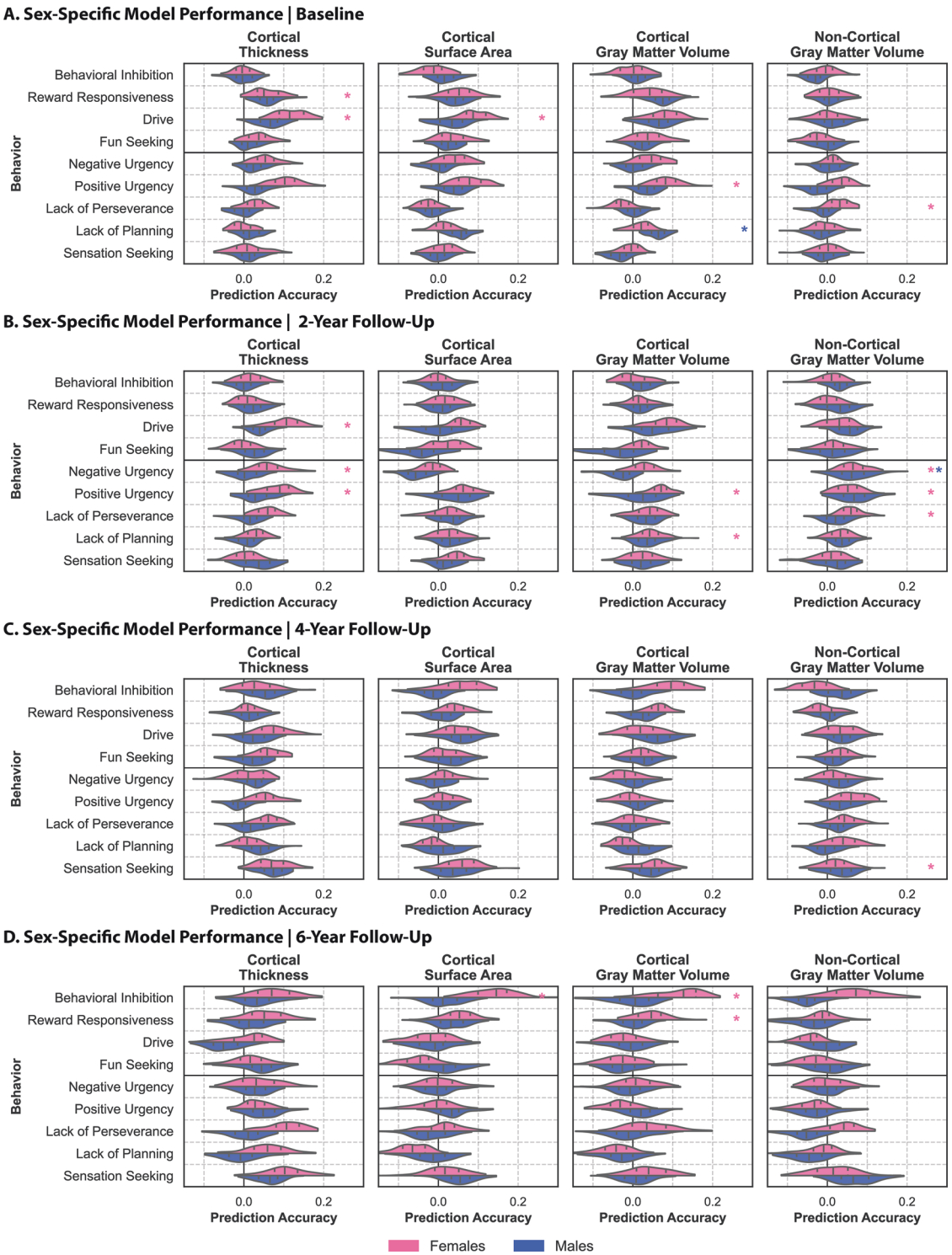


Fig. 2 Sex influences associations between neuroanatomy and impulsivity. Prediction accuracies (correlation between observed and predicted values) for sex-specific models trained to predict self-reported impulsivity measures at baseline (**A**) two-year follow-up (**B**) four-year follow-up (**C**) and six-year follow-up (**D**). From left to right, cortical thickness, cortical surface area, cortical gray matter volume, and non-cortical gray matter volume results are shown. The shape of the violins indicates the distribution of values across 100 random splits of the data, the dashed lines indicate the median, and the dotted lines indicate the interquartile range. Asterisks indicate the model captured significant associations.

Impulsivity maps onto shared and distinct brain regions

We derived the feature importance maps from the models and computed correlations to evaluate overlap, focusing on models that captured significant associations (Figure S6).

Models predicting measures from the same scale captured largely overlapping associations. As an example, associations between cortical volume and behavioral inhibition, reward responsiveness, drive, and fun seeking at baseline were highly similar. These included

widespread negative associations between volume and the impulsivity measures, particularly in limbic regions. Further, while some models predicting measures from different scales were similar, others were orthogonal or opposite. For example, cortical volume features associated with impulsivity measures from the BIS/BAS scales at baseline were positively correlated with those associated with urgency and negatively correlated with those associated with lack of planning. While the BIS/BAS measures and urgency showed broad negative associations with cortical volume, lack of planning showed positive associations, particularly in visual regions. These observed patterns were generally consistent across time points.

These analyses reveal that different dimensions of impulsivity map onto partially overlapping neuroanatomical patterns. The BIS/BAS and UPPS-P scales, though separable constructs, share some neuroanatomical underpinnings while also exhibiting distinct and even opposing features.

Neuroanatomical basis of impulsivity varies across measures of impulsivity

We examined the associations that exist between the neuroanatomical features and self-reported impulsivity measures, focusing on models yielding significant results (Fig. 3, S8-S9). Although associations between cortical features and impulsivity varied, regions within the default mode, limbic, ventral attention, and visual networks were consistently implicated. Non-cortical volume features associated with impulsivity were largely localized to the cerebellum and brain stem.

Behavioral inhibition exhibited varied associations with cortical features (Fig. 4). For **thickness**, associations were varied but primarily negative at four-year follow-up, but positive at six-year follow-up. For **area**, positive associations were present at the six-year follow-up. For **volume**, associations were negative at baseline, but positive at four-year and six-year follow-up.

Drive exhibited consistently negative associations with cortical **thickness, area**, and **volume** (Fig. 5).

Urgency exhibited varied but predominantly negative associations with cortical features (Fig. 6**)**. For **cortical thickness**, associations with negative urgency were primarily negative at baseline but associations with positive urgency at baseline were more mixed and became predominantly negative at the two-year follow-up. For **area**, associations with positive urgency were negative at two-year follow-up. For **volume**, associations with positive urgency were negative at baseline and two-year follow-up.

Lack of planning exhibited mixed associations with cortical features (Figure S9). For **area** and **volume**, associations were primarily positive at baseline, but negative at the two-year follow-up.

Sensation seeking exhibited varied associations with cortical features (Figure S10). For **area**, associations were primarily positive at two-year follow-up, mixed at four-year follow-up, and primarily negative at six-year follow-up. For **volume**, associations were primarily positive at two-year and four-year follow-ups.

Other impulsivity measures exhibited negative cortical and mixed non-cortical associations (Figure S11). Lack of perseverance exhibited negative associations with **cortical area**, but mixed associations with **non-cortical volume** at the two-year follow-up, showing positive associations in the cerebella and brain stem and negative associations in the bilateral caudate and putamen. Reward responsiveness and fun seeking exhibited negative associations with **cortical volume** at baseline.

These findings highlight the presence of multivariate relationships between neuroanatomy and impulsivity. While some associations are similar across impulsivity measures and developmental time points, others are more varied. These results suggest distributed brain networks encode individual differences in impulsive behaviors.

There are sex-specific associations between neuroanatomy and impulsivity

We evaluated sex-specific associations between neuroanatomy and impulsivity, focusing on models that yielded significant results (Figures S12-S13). These analyses provide a descriptive characterization of brain-impulsivity associations within each sex.

Females. Associations between cortical measures (thickness, area, and volume) and impulsivity were predominantly negative across all measures of impulsivity and time points, with one exception: reward responsiveness showed negative associations with cortical volume at baseline, but positive associations at six-year follow-up. Associations between non-cortical volume and impulsivity measures were sparse across all time points and localized to cerebellar regions and the brain stem, with primarily positive associations at baseline and negative associations at the two-year and four-year follow-ups.

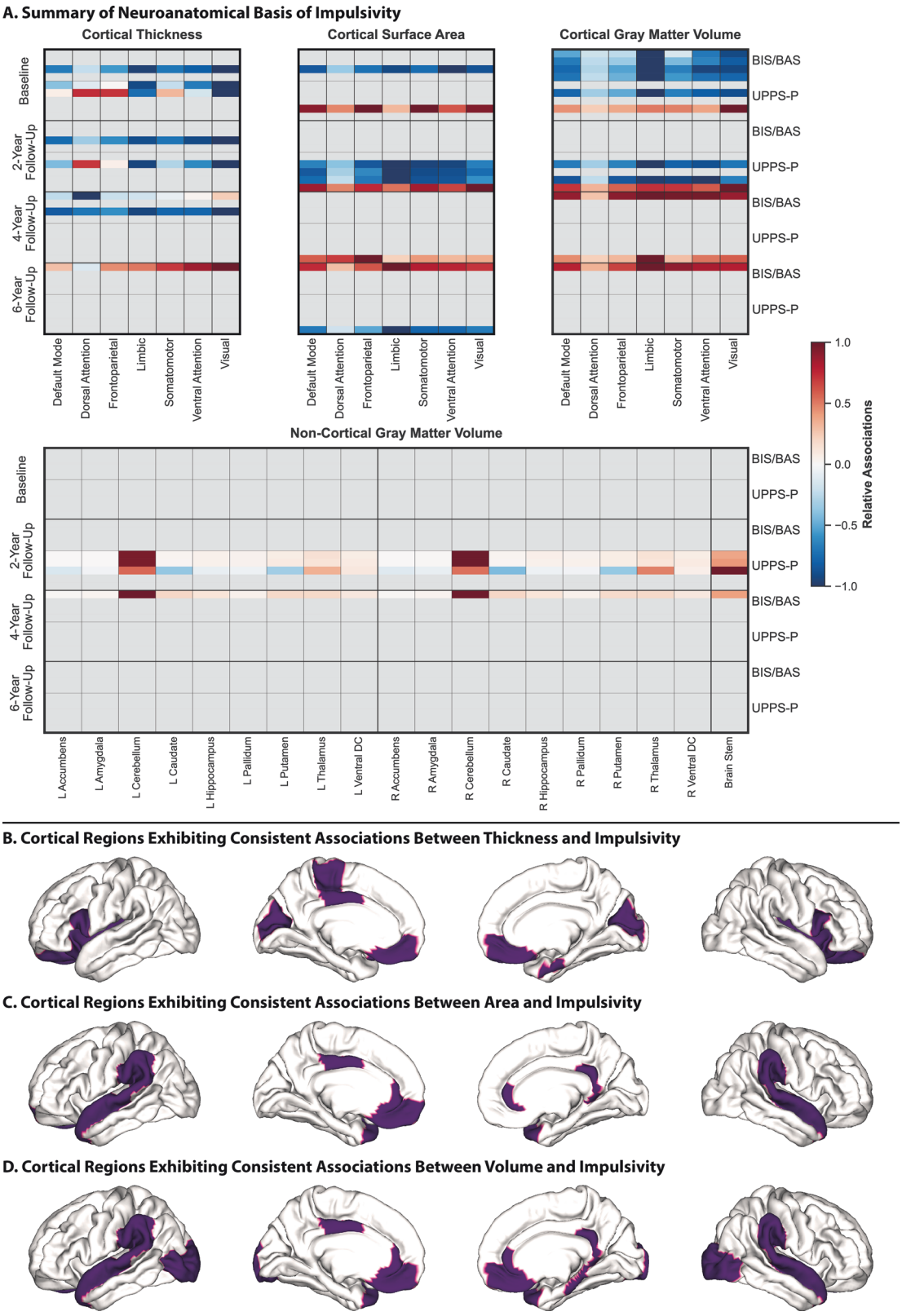
Males. Lack of planning showed positive associations with cortical volume at baseline. Negative urgency exhibited sparse positive associations with non-cortical volume in the cerebella and brain stem at two-year follow-up.

While many of these relationships are similar to those captured by the sex-independent models, there are also some differences suggesting there are sex-specific associations between neuroanatomy and impulsivity. These sex-specific relationships may, in part, explain observed sex differences in impulsive behaviors and vulnerability to impulsivity-related psychiatric illness.

DISCUSSION

In this study, we leveraged the large ABCD dataset and a data-driven analytical approach to examine the associations between neuroanatomy and impulsivity across development. First, we systematically quantified the extent to which different anatomical features predict distinct self-reported impulsivity measures, revealing that prediction accuracy varies substantially across impulsivity measures and providing an empirical benchmark for the degree to which impulsivity is linked to brain structure. Second, we demonstrated that different dimensions of impulsivity are predicted by both overlapping and dimension-specific anatomical features, supporting multidimensional conceptualizations of impulsivity and suggesting that different clinical presentations of impulsivity may have partially distinct neurobiological underpinnings. Third, we showed that these associations are not static but vary across development and sex, highlighting the importance of considering sample demographics when examining brain-behavior relationships. While our predictive models identify brain-behavior associations, they do not establish causal mechanisms. Rather, our findings provide a population-level, multivariate characterization of which structural features are associated with individual differences in impulsivity, complementing circuit-based mechanistic research and potentially informing dimensional approaches to psychiatric classification.

Impulsivity is, in part, driven by individual differences in corticolimbic, corticostriatal and motor-sensory circuits [8, 13–16, 80]. Recent advances in brain-based predictive modeling allow us to examine whole-brain multivariate relationships [36]. While traditional approaches test whether specific circuits are involved in impulsivity, whole-brain predictive modeling identifies distributed patterns that optimize prediction. These approaches provide complementary but distinct insights into brain-behavior relationships. In recent years, a few studies have used this approach to investigate the neural basis of impulsivity, although they have generally focused on a different set of imaging features and impulsivity measures, ignored sex effects, or considered individual time points [8, 69, 81–83]. Using a multivariate approach, we replicate certain univariate findings [84–86] and demonstrate that impulsivity maps onto a dispersed set of cortical networks and non-cortical regions. While some relationships are shared across networks and time points, others are distinct. The neuroanatomical basis of drive appears to be



particularly stable, exhibiting widespread negative associations across thickness, area, and volume measures at multiple time points. Conversely, lack of planning showed markedly different patterns, with cortical area and volume associations shifting from positive at baseline to negative at the two-year follow-up. In contrast, behavioral inhibition exhibited negative associations with cortical volume at baseline but positive associations at four-year and six-year follow-ups.

In line with prior work, we observe prominent associations with impulsivity in the default mode, limbic, ventral attention, and visual

Fig. 3 Default mode, limbic, ventral attention, and visual networks, as well as the cerebellum and brain stem are implicated in impulsivity. Relative associations (Haufe-transformed feature weights) between neuroanatomy and impulsivity (**A**) derived from the models based on cortical thickness (top right), cortical surface area (top center), cortical gray matter volume (top left), and non-cortical gray matter volume (bottom). To facilitate visualization, regional feature weights from the cortical models (top) were summarized to a network-level, and association values for each set of models were divided by the maximum value for that model. Warmer colors indicate a stronger positive association, cooler colors indicate a stronger negative association. Results are only shown for models that captured significant associations. Cortical regions (shown in purple) appearing in the top 20% most important features in ≥ 50% of all significant models predicting different impulsivity measures based on thickness (**B**) area (**C**) and volume (**D**). Lateral (outer) and medial (inner) surfaces for left (left) and right (right) hemispheres are shown.

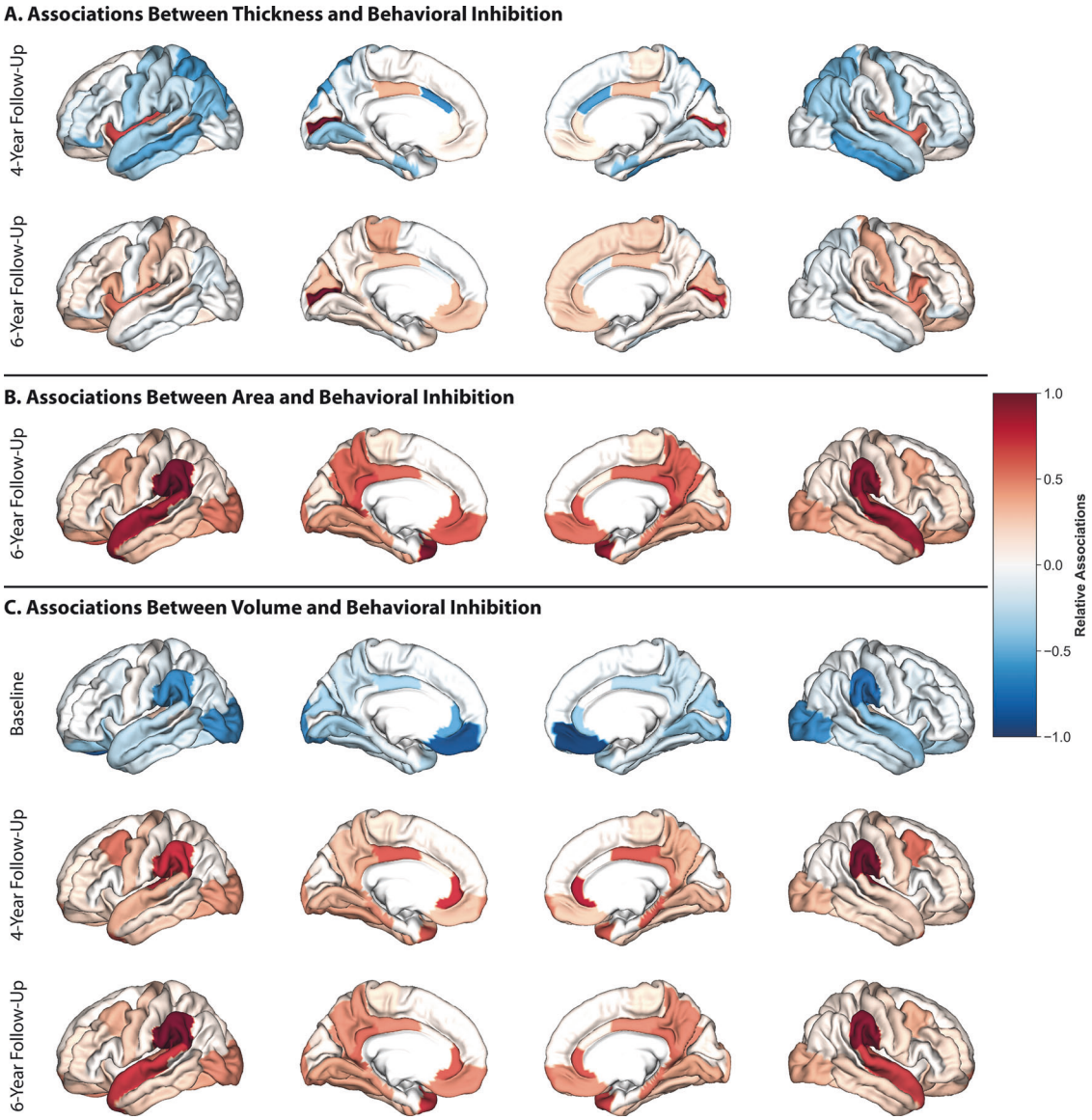


Fig. 4 Associations between neuroanatomy and behavioral inhibition vary across morphometric measures and time points. Relative regional associations (Haufe-transformed feature weights) from models trained on cortical thickness at four-year follow-up and six-year follow-up (**A**) cortical surface area at six-year follow-up (**B**) and cortical gray matter volume at baseline, four-year follow-up, and six-year follow-up (**C**) to predict behavioral inhibition. Lateral (outer) and medial (inner) surfaces for left (left) and right (right) hemispheres are shown. Warmer colors indicate a stronger positive association, cooler colors indicate a stronger negative association. To facilitate visualization, association values for each set of models were divided by the maximum value for that model.

networks, although the direction of these associations varied. Functional alterations in the default mode network, active during wakeful rest, have previously been observed in individuals with impulsivity-related disorders, including substance use and attention disorders [87–89]. The limbic network, which plays a crucial role in higher-order cognitive processes related to emotions, memory, and motivation, is related to impulsivity. While previous work has identified associations between impulsivity and dopamine receptor binding in limbic structures [90], as well as links between receptor density and altered functional connectivity patterns in substance use disorder [91], the relationship between these molecular processes and the macro-scale structural alterations we observe is likely complex and indirect. Cortical thickness in the ventral attention network, responsible for detecting unexpected stimuli

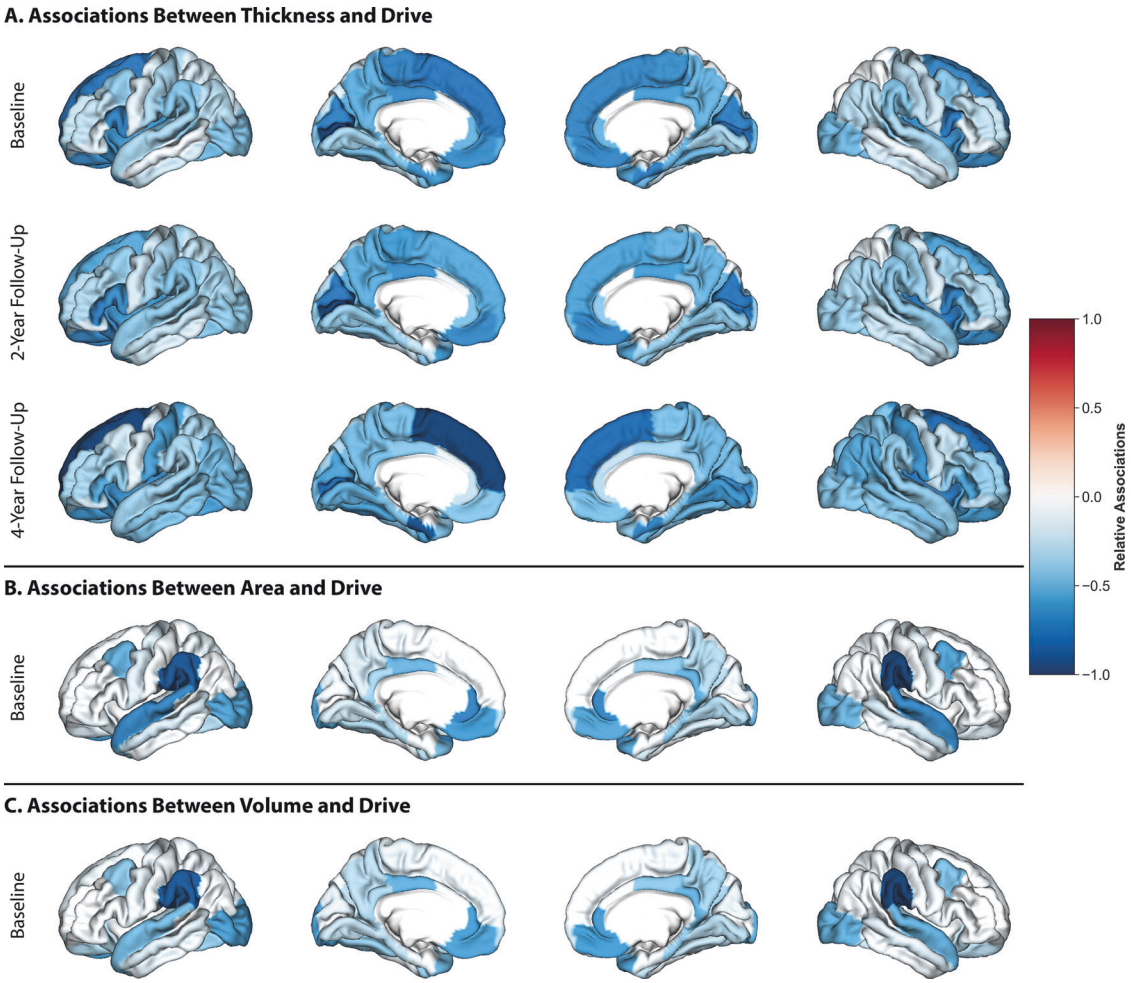


Fig. 5 Associations between neuroanatomy and drive are consistent across morphometric measures and time points. Relative regional associations (Haufe-transformed feature weights) from models trained on cortical thickness at baseline, two-year follow-up, and four-year follow-up (**A**) cortical surface area at baseline (**B**) and cortical gray matter volume at baseline (**C**) to predict drive. Lateral (outer) and medial (inner) surfaces for left (left) and right (right) hemispheres are shown. Warmer colors indicate a stronger positive association, cooler colors indicate a stronger negative association. To facilitate visualization, association values for each set of models were divided by the maximum value for that model.

and reorienting attentional processes, particularly in the temporoparietal junction, is negatively associated with impulsive behaviors in adolescents [92]. Finally, gray matter alterations in the visual network, responsible for the processing of visual stimuli, have been linked to impulsivity [93]. These associations may explain difficulties with visual attention and increased distractibility common in impulsive individuals [93]. The morphometric patterns we observe may reflect cumulative developmental processes including synaptic reorganization, myelination, and cellular changes that correlate with, but are not directly caused by, neurotransmitter system alterations. Our results also implicate the cerebellum and brain stem. Cerebellar abnormalities have been increasingly linked to psychiatric illnesses involving impulsivity [94], and functional connectivity studies have demonstrated important roles for both the cerebellum and brain stem in impulsivity [83, 95]. Our analyses found consistent associations in these regions, further emphasizing their contributions to impulsivity. These converging results also underscore the important of considering non-cortical structures when examining brain-behavior relationships in future research. Collectively, these findings demonstrate that impulsivity is associated with a complex pattern of neurobiological alterations across multiple networks.

There are ongoing theoretical debates about the nature of impulsivity. While some research has suggested a general "I" factor underlying impulsive behaviors [96], other work has challenged the idea of a unitary construct [10], instead proposing multidimensional models [51, 56–59]. Although no single neuroanatomical signature consistently predicts all self-reported impulsivity measures, we find that the default mode, limbic, ventral attention, and visual networks are repeatedly implicated across models, though with varying directionality. This suggests that different aspects of impulsivity map onto dynamic neuroanatomical patterns involving these networks rather than a single signature for impulsivity. This heterogeneity supports theoretical models that conceptualize impulsivity as a multidimensional construct and emphasizes the importance of examining specific impulsivity dimensions and developmental stages rather than assuming a common neuroanatomical substrate.

These findings have important clinical implications. Heightened impulsivity is a core feature of many psychiatric disorders [6]. While certain disorders are associated with broad impulsivity, others are linked to specific impairments. Individuals with a history of childhood trauma [97], depression [98, 99], bipolar disorder [98, 99], anorexia nervosa [100], or social anxiety [101] exhibit heightened levels of behavioral inhibition relative to controls. Individuals with bipolar disorder additionally exhibit greater behavioral activation relative to controls [98, 102], while those with depression [101], social anxiety [101], or schizophrenia [102]

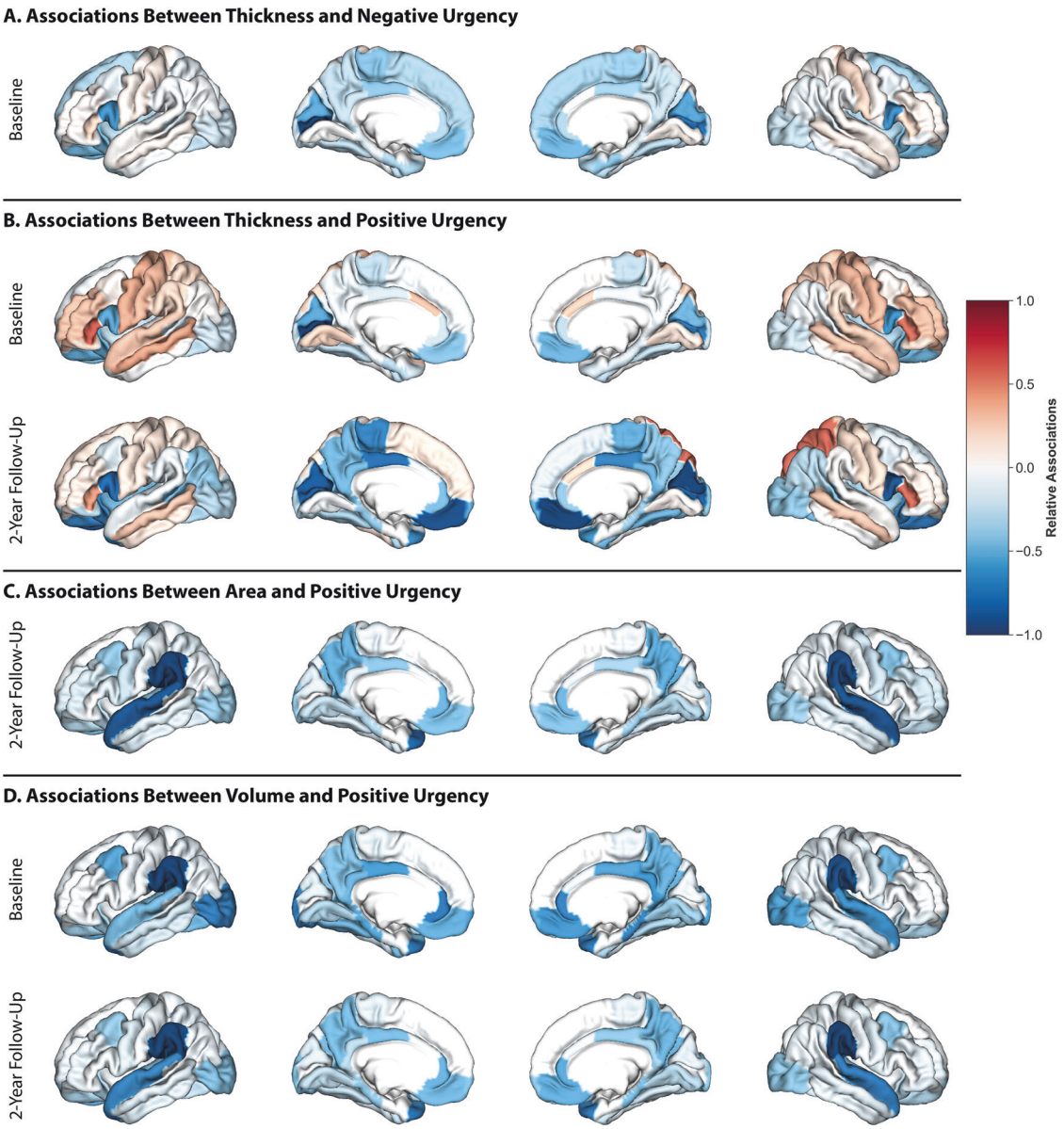


Fig. 6 Associations between neuroanatomy and urgency vary across morphometric measures but are relatively consistent across time points. Relative regional associations (Haufe-transformed feature weights) from models trained on cortical thickness to predict negative urgency at baseline (**A**) cortical thickness to predict positive urgency at baseline and two-year follow-up (**B**) cortical surface area to predict positive urgency at two-year follow-up (**C**) and cortical gray matter volume to predict positive urgency at baseline and two-year follow-up (**D**). Lateral (outer) and medial (inner) surfaces for left (left) and right (right) hemispheres are shown. Warmer colors indicate a stronger positive association, cooler colors indicate a stronger negative association. To facilitate visualization, association values for each set of models were divided by the maximum value for that model.

exhibit lower activation. Further, individuals with borderline personality [103], substance use [104], or attention deficit hyperactivity [105] disorders exhibit higher levels across the UPPS-P measures compared to controls. Finally, the onset of self-harm behaviors is linked to heightened sensation seeking, while the maintenance is linked to heightened lack of premeditation [106]. These behavioral differences may reflect disruptions in distinct brain networks and regions, highlighting why these dimensions should be studied and potentially treated as separate constructs rather than manifestations of a single underlying impairment.

Impulsivity follows a non-linear trend, increasing during childhood and adolescence and decreasing throughout adulthood [107–109]. This trajectory mirrors developmental changes observed in neuroanatomy. During adolescence and early adulthood, significant maturation occurs in the prefrontal cortex, a region critical for emotional regulation and impulse control [20–22]. This maturation involves synaptic pruning and increased white matter connectivity to refine neural circuits, leading to improved cognitive control and decreased impulsivity [22]. Our results show that the neural basis of impulsivity is not static, potentially reflecting these broader developmental changes. While some regions show consistent relationships, others are dynamic, suggesting that changes in impulsivity may be driven by shifts in the underlying neuroanatomical associations. Importantly, these changes are not consistent across time points. This may be due to several factors. First, our sample size decreased substantially at later time points, potentially limiting our ability to capture meaningful brain-behavior associations. Second, brain-behavior relationships may not follow linear developmental trajectories as

associations may strengthen, weaken, or reorganize as neural circuits mature. Third, the constructs captured by the self-report measures of impulsivity may shift across development as children's self-awareness mature.

Contrary to prior literature highlighting the broad involvement of subcortical structures in impulsivity [14–16, 18, 31, 35, 90, 110, 111], our analyses found that few models based on non-cortical gray matter volume yielded significant results. This pattern may reflect fundamental differences in the sources of individual variation during this developmental period. At ages 9–16, cortical structures, especially prefrontal regions, are undergoing rapid and heterogeneous maturation, with substantial individual differences in the timing and extent of synaptic pruning, myelination, and cortical thinning [112, 113]. In contrast, subcortical structures develop earlier and more uniformly, potentially exhibiting less inter-individual variability during this age range. Consequently, cortical regions may capture greater variance in impulsivity simply because they show greater structural variability across individuals in this sample. Additionally, different methodological considerations may contribute to these largely null subcortical results. First, we considered total regional volumes, rather than subregional segmentations, potentially missing localized effects. Second, since multivariate prediction models optimize predictions across all features, regions that exhibit strong univariate associations may not emerge as important predictors if their unique contribution is limited when considered alongside other regions. Critically, these findings do not necessarily mean that non-cortical structures are uninvolved in impulsivity, but rather that the models did not capture sufficient unique predictive information or that individual differences in subcortical structure contribute less to variance in impulsivity during this specific developmental window.

We did not capture significant associations between changes in impulsivity and changes in neuroanatomy. This finding aligns with emerging evidence suggesting that individual differences in brain organization may be more predictive of behavioral outcomes than developmental changes [114]. Several factors may explain our results. First, individual trajectories of brain and behavior development may be more heterogeneous than cross-sectional associations, with individual-specific factors (e.g., genetics, environmental influences) driving unique developmental processes that obscure group-level patterns. Second, the timing of brain and behavioral changes may not be aligned, such that neuroanatomical development precedes or follows impulsivity changes rather than occurring simultaneously. Third, functional reorganization, rather than structural changes, may be the primary driver of behavioral change. These results emphasize that cross-sectional brain-behavior associations may not fully capture the complexity of adolescent developmental processes.

Research on sex differences in impulsivity has produced mixed findings [40, 115]. The most consistent finding is that females exhibit greater behavioral inhibition and males exhibit greater sensation seeking [40]. Activation-related impulsivity is comparable across the sexes [40], though differences have been reported for specific rewards [116]. One study examining relationships between cortical thickness and a single global measure of impulsivity in the ABCD cohort reported significant associations in males but not the entire sample [117]. A separate study exploring the volumetric correlates of impulsivity in the same cohort found that lack of premeditation and sensation seeking were related to larger volumes in many cortical and subcortical regions, while positive urgency was related to smaller volumes in those same regions [118]. They also found that many of the relationships were stronger in females. These studies highlight the need for sex-specific investigations. Our analyses build on this work using a multivariate machine learning approach and show that while some sex-specific brain-impulsivity associations resemble corresponding sex-independent associations, others exhibit marked differences. In some cases, the same regions and networks even exhibit opposite relationships. Importantly, we did not statistically test whether the patterns observed in the sex-specific models differed from one another. Therefore, the divergent patterns described here should be interpreted cautiously as descriptive differences. A particularly interesting example is the associations between cortical volume and behavioral inhibition at the six-year follow-up, where sex-independent models captured dispersed positive associations and female-specific models captured dispersed negative associations. This suggests that the female-specific models may capture certain associations obscured in sex-independent models. This difference was observed broadly across cortical networks, many of which exhibit structural [39] and functional [119] sex differences coupled to regional expression of sex chromosome genes and show enrichment for distinct cell-type signatures [39, 120, 121]. These findings suggest that sex differences in impulsivity may have a strong biological basis, rooted in sex-specific patterns of gene expression and cellular organization within key brain networks.

There are several limitations to this work. First, we used a single dataset. Although participants reflect different demographic groups, income levels, and living environments, our findings may be limited in generalizability [122, 123]. Factors including age, pubertal status, genetics, socioeconomic status, education, and medication use, among many others, may influence both brain development and the expression of impulsivity-related behaviors. Second, we only considered binary sex and thus were not able to assess these relationships in other populations. We also did not consider the effects of gender, which influences neurobiology [63] and behavior [124]. Third, the brain continues to develop throughout adolescence, with females and males reaching developmental milestones at different times [125]. Here, we used data from four time points but did not include older ages. Although age-related variability in impulsivity measures did not meaningfully improve model performance in over 98% of models (Table S13), suggesting our models capture individual differences rather than age-related trends within each timepoint, the associations we report may continue to shift throughout later adolescence and into adulthood. Further, we assessed associations at discrete chronological age windows (9–10, 11–12, 13–14, and 15–16 years) but did not account for individual differences in biological maturation (e.g., pubertal stage). Adolescents of the same chronological age can vary substantially in their neurodevelopmental and pubertal status, which may influence neuroanatomy and impulsivity. If biological maturation were systematically related to impulsivity within our age-restricted samples, our models might partly capture maturational timing effects rather than purely individual trait differences. However, the age-restricted nature of our samples at each timepoint likely minimizes, though does not eliminate, heterogeneity in developmental stage. Future analyses within global open-access datasets that consider the effects of additional biological and environmental factors across longer timescales can address these limitations and provide additional evidence to confirm (or refute) these findings.

While our multivariate approach provides a population-level characterization of brain-impulsivity associations that enables individual-level predictions, the present findings also reveal critical gaps that can inform future mechanistic research. Hypothesis-driven studies examining subcortical developmental trajectories with denser temporal sampling could clarify how subcortical maturation relates to changes in impulsivity over time. Integrating additional data modalities, including behavioral assessments of impulsivity, environmental factors, and genetic information, would help disentangle their relative contributions to brain-impulsivity relationships. The neuroanatomical patterns we identify here also provide empirical targets for experimental manipulations or intervention studies designed to establish causal relationships between structural features and impulsive behaviors. In this way,

our data-driven findings can guide hypothesis generation about which circuits, timepoints, and populations to prioritize in future causal investigations.

Increases in impulsivity are typical during development, and, when significant, may indicate vulnerability to psychiatric illness. Understanding the neuroanatomical basis of impulsivity is essential for clinical discovery and the translation of neuroscientific findings into practice. This foundation enables the development of brain-based diagnostic tools and neurobiologically-informed early interventions to prevent mental illness. In this work, we demonstrate how neuroanatomy underlies the diverse expressions of impulsivity throughout development.

DATA AVAILABILITY

Data used in the preparation of this article were obtained from the Adolescent Brain Cognitive Development™ (ABCD) Study, held in the NIH Brain Development Cohorts Data Sharing Platform. This is a multisite, longitudinal study designed to recruit more than 10,000 children aged 9–10 and follow them over 10 years into early adulthood. The ABCD Study® is supported by the **National Institutes of Health** and additional federal partners under award numbers: U01DA041048, U01DA050989, U01DA051016, U01DA041022, U01DA051018, U01DA051037, U01DA050987, U01DA041174, U01DA041106, U01DA041117, U01DA041028, U01DA041134, U01DA050988, U01DA051039, U01DA041156, U01DA041025, U01DA041120, U01DA051038, U01DA041148, U01DA041093, U01DA041089, U24DA041123, U24DA041147. A full list of supporters is available at Federal Partners – ABCD Study. ABCD Consortium investigators designed and implemented the study and/or provided data but did not necessarily participate in the analysis or writing of this report. This manuscript reflects the views of the authors and may not reflect the opinions or views of the NIH or ABCD Consortium investigators. The ABCD data repository grows and changes over time. The ABCD data used in this report came from the ABCD 6.0 release.

CODE AVAILABILITY

Code used for the analyses are on GitHub: https://github.com/elvisha/neuroanat_impulsivity.

REFERENCES

1. Sloan E, Hall K, Moulding R, Bryce S, Mildred H, Staiger PK. Emotion regulation as a transdiagnostic treatment construct across anxiety, depression, substance, eating and borde rline personality disorders: a systematic review. Clin Psychol Rev. 2017;57:141–63.
2. Cáceda R, Nemeroff CB, Harvey PD. Toward an understanding of decision making in severe mental illness. J neuropsychiatry Clin Neurosci. 2014;26:196–213.
3. Lincoln TM, Schulze L, Renneberg B. The role of emotion regulation in the characterization, development and treatment of psychopathology. Nat Rev Psychol. 2022;1:272–86.
4. Sonmez AI, Garcia JQ, Thitiseranee L, Blacker CJ, Lewis CP. Scoping review: Transdiagnostic measurement of impulsivity domains in youth using the UPPS impulsive behavior scales. J Am Acad Child Adolesc Psychiatry. 2024;63:789–812.
5. Struijs SY, Lamers F, Vroling MS, Roelofs K, Spinhoven P, Penninx BW. Approach and avoidance tendencies in depression and anxiety disorders. Psychiatry Res. 2017;256:475–81.
6. Moeller FG, Barratt ES, Dougherty DM, Schmitz JM, Swann AC. Psychiatric aspects of impulsivity. Am J psychiatry. 2001;158:1783–93.
7. Chambers RA, Taylor JR, Potenza MN. Developmental neurocircuitry of motivation in adolescence: a critical period of addiction vulnerability. Am J psychiatry. 2003;160:1041–52.
8. Kohler R, Lichenstein SD, Cheng A, Holmes A, Bzdok D, Pearlson G, et al. Identification of a composite latent dimension of reward and impulsivity across clinical, behavioral, and neurobiological domains among youth. Biol psychiatry: Cognit Neurosci neuroimaging. 2024;9:407–16.
9. Swann AC, Pazzaglia P, Nicholls A, Dougherty DM, Moeller FG. Impulsivity and phase of illness in bipolar disorder. J Affect Disord. 2003;73:105–11.
10. Strickland JC, Johnson MW. Rejecting impulsivity as a psychological construct: a theoretical, empirical, and sociocultural argument. Psychological Rev. 2021;128:336.
11. Braddock KH, Dillard JP, Voigt DC, Stephenson MT, Sopory P, Anderson JW. Impulsivity partially mediates the relationship between BIS/BAS and risky health behaviors. J personality. 2011;79:793–810.
12. Pagliaccio D, Luking KR, Anokhin AP, Gotlib IH, Hayden EP, Olino TM, et al. Revising the BIS/BAS Scale to study development: measurement invariance and normative effects of age and sex from childhood through adulthood. Psychological Assess. 2016;28:429.
13. Jean-Richard-Dit-Bressel P, Killcross S, McNally GP. Behavioral and neurobiological mechanisms of punishment: implications for psychiatric disorders. Neuropsychopharmacology. 2018;43:1639–50.
14. Cardinal RN, Winstanley CA, Robbins TW, Everitt BJ. Limbic corticostriatal systems and delayed reinforcement. Ann N Y Acad Sci. 2004;1021:33–50.
15. Scheres A, Milham MP, Knutson B, Castellanos FX. Ventral striatal hyporesponsiveness during reward anticipation in attention-deficit/hyperactivity disorder. Biol psychiatry. 2007;61:720–4.
16. Piantadosi PT, Halladay LR, Radke AK, Holmes A. Advances in understanding meso-cortico-limbic-striatal systems mediating risky reward seeking. J neurochemistry. 2021;157:1547–71.
17. Kovner R, Oler JA, Kalin NH. Cortico-limbic interactions mediate adaptive and maladaptive responses relevant to psychopathology. Am J Psychiatry. 2019;176:987–99.
18. O'Hare J, Calakos N, Yin HH. Recent insights into corticostriatal circuit mechanisms underlying habits. Curr Opin Behav Sci. 2018;20:40–46.
19. Uhlhaas PJ, Davey CG, Mehta UM, Shah J, Torous J, Allen NB, et al. Towards a youth mental health paradigm: a perspective and roadmap. Mol Psychiatry. 2023;28:3171–81.
20. Casey BJ, Getz S, Galvan A. The adolescent brain. Dev Rev. 2008;28:62–77.
21. Casey BJ, Jones RM, Hare TA. The adolescent brain. Ann N Y Acad Sci. 2008;1124:111–26.
22. Luna B. The relevance of immaturities in the juvenile brain to culpability and rehabilitation. Hastings law J. 2012;63:1469.
23. Somerville LH, Jones RM, Casey B. A time of change: behavioral and neural correlates of adolescent sensitivity to appetitive and aversive environmental cues. Brain cognition. 2010;72:124–33.
24. Blakemore SJ. The social brain in adolescence. Nat Rev Neurosci. 2008;9:267–77.
25. Schweizer S, Gotlib IH, Blakemore S-J. The role of affective control in emotion regulation during adolescence. Emotion. 2020;20:80.
26. Young KS, Sandman CF, Craske MG. Positive and negative emotion regulation in adolescence: links to anxiety and depression. Brain Sci. 2019;9:76.
27. Silvers JA. Adolescence as a pivotal period for emotion regulation development. Curr Opin Psychol. 2022;44:258–63.
28. Ripke S, Hübner T, Mennigen E, Müller KU, Rodehacke S, Schmidt D, et al. Reward processing and intertemporal decision making in adults and adolescents: The role of impulsivity and decision consistency. Brain Res. 2012;1478:36–47.
29. Romer D. Adolescent risk taking, impulsivity, and brain development: Implications for prevention. Dev Psychobiol. 2010;52:263–76.
30. Casey B, Heller AS, Gee DG, Cohen AO. Development of the emotional brain. Neurosci Lett. 2019;693:29–34.
31. Dalley JW, Mar AC, Economidou D, Robbins TW. Neurobehavioral mechanisms of impulsivity: fronto-striatal systems and functional neurochemistry. Pharmacol Biochem Behav. 2008;90:250–60.
32. Hollander E, Evers M. New developments in impulsivity. Lancet. 2001;358:949–50.
33. Crews FT, Boettiger CA. Impulsivity, frontal lobes and risk for addiction. Pharmacol Biochem Behav. 2009;93:237–47.
34. Plaisance CJ, Ledet III LF, Slusher NJ, Daniel CP, Lee Z, Dorius B, et al. The role of dopamine in impulsivity and substance abuse: a narrative review. Health Psychol Res. 2024;12:125273.
35. Dalley JW, Robbins TW. Fractionating impulsivity: neuropsychiatric implications. Nat Rev Neurosci. 2017;18:158–71.
36. Dhamala E, Yeo BT, Holmes AJ Methodological considerations for brain-based predictive modelling in psychiatry. Biological Psychiatry 2022.
37. Matte Bon G, Kraft D, Comasco E, Derntl B, Kaufmann T. Modeling brain sex in the limbic system as phenotype for female-prevalent mental disorders. Biol Sex Differences. 2024;15:1–15.
38. Laakso A, Vilkman H, Örgen, Bergman J, Haaparanta M, Solin O, et al. Sex differences in striatal presynaptic dopamine synthesis capacity in healthy subjects. Biol psychiatry. 2002;52:759–63.
39. Liu S, Seidlitz J, Blumenthal JD, Clasen LS, Raznahan A. Integrative structural, functional, and transcriptomic analyses of sex-biased brain organization in humans. Proc Natl Acad Sci. 2020;117:18788–98.
40. Cross CP, Copping LT, Campbell A. Sex differences in impulsivity: a meta-analysis. Psychological Bull. 2011;137:97.
41. Rakic P. Evolution of the neocortex: a perspective from developmental biology. Nat Rev Neurosci. 2009;10:724–35.
42. Rakic P, Ayoub AE, Breunig JJ, Dominguez MH. Decision by division: making cortical maps. Trends Neurosci. 2009;32:291–301.

43. Bethlehem RA, Seidlitz J, White SR, Vogel JW, Anderson KM, Adamson C, et al. Brain charts for the human lifespan. Nature. 2022;604:525–33.
44. White T, Su S, Schmidt M, Kao C-Y, Sapiro G. The development of gyrification in childhood and adolescence. Brain cognition. 2010;72:36–45.
45. Buimer EE, Pas P, Brouwer RM, Froeling M, Hoogduin H, Leemans A, et al. The YOUth cohort study: MRI protocol and test-retest reliability in adults. Developmental Cognit Neurosci. 2020;45:100816.
46. Elliott ML, Knodt AR, Ireland D, Morris ML, Poulton R, Ramrakha S, et al. What is the test-retest reliability of common task-functional MRI measures? new empirical evidence and a meta-analysis. Psychological Sci. 2020;31:792–806.
47. Zahid U, Hedges EP, Dimitrov M, Murray RM, Barker GJ, Kempton MJ. Impact of physiological factors on longitudinal structural MRI measures of the brain. Psychiatry Research: Neuroimaging. 2022;321:111446.
48. Casey BJ, Cannonier T, Conley MI, Cohen AO, Barch DM, Heitzeg MM, et al. The adolescent brain cognitive development (ABCD) study: imaging acquisition across 21 sites. Developmental Cognit Neurosci. 2018;32:43–54.
49. Hagler DJ Jr., Hatton S, Cornejo MD, Makowski C, Fair DA, Dick AS, et al. Image processing and analysis methods for the adolescent brain cognitive development study. Neuroimage. 2019;202:116091.
50. Dhamala E, Ooi LQR, Chen J, Kong R, Anderson KM, Chin R, et al. Proportional intracranial volume correction differentially biases behavioral predictions across neuroanatomical features and populations. NeuroImage. 2022;260:119485.
51. Desikan RS, Segonne F, Fischl B, Quinn BT, Dickerson BC, Blacker D, et al. An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. Neuroimage. 2006;31:968–80.
52. Geurten M, Catale C, Gay P, Deplus S, Billieux J. Measuring impulsivity in children: adaptation and validation of a short version of the UPPS-P impulsive behaviors scale in children and investigation of its links with ADHD. J Atten Disord. 2021;25:105–14.
53. Duckworth AL, Kern ML. A meta-analysis of the convergent validity of self-control measures. J Res personality. 2011;45:259–68.
54. Moffitt TE, Arseneault L, Belsky D, Dickson N, Hancox RJ, Harrington H, et al. A gradient of childhood self-control predicts health, wealth, and public safety. Proc Natl Acad Sci. 2011;108:2693–8.
55. White JL, Moffitt TE, Caspi A, Bartusch DJ, Needles DJ, Stouthamer-Loeber M. Measuring impulsivity and examining its relationship to delinquency. J Abnorm Psychol. 1994;103:192.
56. Carver CS, White TL. Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment: the BIS/BAS scales. J personality Soc Psychol. 1994;67:319.
57. Demianczyk AC, Jenkins AL, Henson JM, Conner BT. Psychometric evaluation and revision of Carver and White's BIS/BAS scales in a diverse sample of young adults. J Personality Assess. 2014;96:485–94.
58. Leone L, Perugini M, Bagozzi RP, Pierro A, Mannetti L. Construct validity and generalizability of the Carver–White behavioural inhibition system/behavioural activation system scales. Eur J Personality. 2001;15:373–90.
59. Jorm AF, Christensen H, Henderson AS, Jacomb PA, Korten AE, Rodgers B. Using the BIS/BAS scales to measure behavioural inhibition and behavioural activation: Factor structure, validity and norms in a large community sample. Personality Individ Differences. 1998;26:49–58.
60. Whiteside SP, Lynam DR. The five factor model and impulsivity: Using a structural model of personality to understand impulsivity. Personality Individ differences. 2001;30:669–89.
61. Whiteside SP, Lynam DR, Miller JD, Reynolds SK. Validation of the UPPS impulsive behaviour scale: a four-factor model of impulsivity. Eur J personality. 2005;19:559–74.
62. McCredie MN, Harris B, Regan T, Morey LC, Fields SA. Development and validation of a validity scale for use with the UPPS-P and Short UPPS-P Impulsive behavior scales. J personality Assess. 2021;103:752–61.
63. Dhamala E, Bassett DS, Yeo BT, Holmes AJ. Functional brain networks are associated with both sex and gender in children. Sci Adv. 2024;10:eadn4202.
64. Dhamala E, Chopra S, Ooi LQR, Rubio JM, Yeo BT, Malhotra AK et al. Sex differences in the functional network underpinnings of psychotic-like experiences in children. bioRxiv 2024.2004. 2022.590660 [Preprint]. 2024. Avilable from: https://www.biorxiv.org/content/10.1101/2024.04.22.590660v1.
65. Dhamala E, Jamison KW, Jaywant A, Dennis S, Kuceyeski A. Distinct functional and structural connections predict crystallised and fluid cognition in healthy adults. Hum Brain Mapp. 2021;42:3102–18.
66. Dhamala E, Jamison KW, Jaywant A, Kuceyeski A. Shared functional connections within and between cortical networks predict cognitive abilities in adult males and females. Hum Brain Mapp. 2022;43:1087–102.
67. Dhamala E, Ooi LQR, Chen J, Ricard JA, Berkeley E, Chopra S, et al. Brain-based predictions of psychiatric illness-linked behaviors across the sexes. Biol Psychiatry. 2023;94:479–91.
68. Chen J, Ooi LQR, Tan TWK, Zhang S, Li J, Asplund CL, et al. Relationship between prediction accuracy and feature importance reliability: an empirical and theoretical study. NeuroImage. 2023;274:120115.
69. Chen J, Tam A, Kebets V, Orban C, Ooi LQR, Asplund CL, et al. Shared and unique brain network features predict cognitive, personality, and mental health scores in the ABCD study. Nat Commun. 2022;13:2217.
70. Li J, Kong R, Liegeois R, Orban C, Tan Y, Sun N, et al. Global signal regression strengthens association between resting-state functional connectivity and behavior. Neuroimage. 2019;196:126–41.
71. Benjamini Y, Hochberg Y. Controlling the false discovery rate - a practical and powerful approach to multiple testing. J R Stat Soc Ser B-Statistical Methodol. 1995;57:289–300.
72. Haufe S, Meinecke F, Görgen K, Dähne S, Haynes J-D, Blankertz B, et al. On the interpretation of weight vectors of linear models in multivariate neuroimaging. Neuroimage. 2014;87:96–110.
73. Tian Y, Zalesky A. Machine learning prediction of cognition from functional connectivity: are feature weights reliable? NeuroImage. 2021;245:118648.
74. Yeo BT, Krienen FM, Sepulcre J, Sabuncu MR, Lashkari D, Hollinshead M, et al. The organization of the human cerebral cortex estimated by intrinsic functional connectivity. J Neurophysiol. 2011;106:1125–65.
75. Owens MM, Hyatt CS, Gray JC, Miller JD, Lynam DR, Hahn S, et al. Neuroanatomical correlates of impulsive traits in children aged 9–10. J Abnorm Psychol. 2020;129:831.
76. Shao IY, Al-Shoaibi AA, Ganson KT, Testa A, Kiss O, He J, et al. From individual motivation to substance use initiation: a longitudinal cohort study assessing the associations between reward sensitivity and subsequent risk of substance use initiation among US adolescents. Addictive Behav. 2025;160:108162.
77. Akoglu H. User's guide to correlation coefficients. Turkish J Emerg Med. 2018;18:91–93.
78. Cardoso Melo RD, Groen RN, Hartman CA. Reward sensitivity at age 13 predicts the future course of psychopathology symptoms. Front Psychiatry. 2022;13:818047.
79. Read RW, Schlauch KA, Elhanan G, Neveux I, Koning S, Cooper T, et al. A study of impulsivity and adverse childhood experiences in a population health setting. Front Public Health. 2024;12:1447008.
80. Kebets V, Holmes AJ, Orban C, Tang S, Li J, Sun N, et al. Somatosensory-Motor dysconnectivity spans multiple transdiagnostic dimensions of psychopathology. Biol Psychiatry. 2019;86:779–91.
81. Ooi LQR, Chen J, Shaoshi Z, Kong R, Tam A, Li J, et al. Comparison of individualized behavioral predictions across anatomical, diffusion and functional connectivity MRI. NeuroImage. 2022;263:119636.
82. Ide JS, Li H-T, Chen Y, Le TM, Li CS, Zhornitsky S, et al. Gray matter volumetric correlates of behavioral activation and inhibition system traits in children: An exploratory voxel-based morphometry study of the ABCD project data. Neuroimage. 2020;220:117085.
83. Cheng A, Lichenstein S, Chaarani B, Liang Q, Babaeianjelodar M, Riley SJ, et al. Impulsivity and neuroticism share distinct functional connectivity signatures with alcohol-use risk in youth. Mol Psychiatry. 2025;31:1–10.
84. Rizzolatti G, Fogassi L, Gallese V. Motor and cognitive functions of the ventral premotor cortex. Curr Opin Neurobiol. 2002;12:149–54.
85. Holmes AJ, Hollinshead MO, Roffman JL, Smoller JW, Buckner RL. Individual differences in cognitive control circuit anatomy link sensation seeking, impulsivity, and substance use. J Neurosci. 2016;36:4038–49.
86. Levy BJ, Wagner AD. Cognitive control and right ventrolateral prefrontal cortex: reflexive reorienting, motor inhibition, and action updating. Ann N Y Acad Sci. 2011;1224:40–62.
87. Raichle ME, MacLeod AM, Snyder AZ, Powers WJ, Gusnard DA, Shulman GL. A default mode of brain function. Proc Natl Acad Sci. 2001;98:676–82.
88. Zhang R, Volkow ND. Brain default-mode network dysfunction in addiction. Neuroimage. 2019;200:313–31.
89. Uddin LQ, Kelly AC, Biswal BB, Margulies DS, Shehzad Z, Shaw D, et al. Network homogeneity reveals decreased integrity of default-mode network in ADHD. J Neurosci methods. 2008;169:249–54.
90. Barlow RL, Gorges M, Wearn A, Niessen HG, Kassubek J, Dalley JW, et al. Ventral striatal D2/3 receptor availability is associated with impulsive choice behavior as well as limbic corticostriatal connectivity. Int J Neuropsychopharmacol. 2018;21:705–15.
91. Ricard JA, Labache L, Segal A, Dhamala E, Cocuzza CV, Jones G, et al. A shared spatial topography links the functional connectome correlates of cocaine use disorder and dopamine D2/3 receptor densities. Commun Biol. 2024;7:1178.
92. Pehlivanova M, Wolf DH, Sotiras A, Kaczkurkin AN, Moore TM, Ciric R, et al. Diminished cortical thickness is associated with impulsive choice in adolescence. J Neurosci. 2018;38:2471–81.
93. Ide JS, Tung HC, Yang C-T, Tseng Y-C, Li C-SR. Barratt impulsivity in healthy adults is associated with higher gray matter concentration in the parietal occipital cortex that represents peripheral visual field. Front Hum Neurosci. 2017;11:222.

94. Miquel M, Nicola SM, Gil-Miravet I, Guarque-Chabrera J, Sanchez-Hernandez A. A working hypothesis for the role of the cerebellum in impulsivity and compulsivity. Front Behav Neurosci. 2019;13:99.
95. Hüpen P, Kumar H, Müller D, Swaminathan R, Habel U, Weidler C. Functional brain network of trait impulsivity: whole-brain functional connectivity predicts self-reported impulsivity. Hum Brain Mapp. 2024;45:e70059.
96. Huang Y, Luan S, Wu B, Li Y, Wu J, Chen W, et al. Impulsivity is a stable, measurable, and predictive psychological trait. Proc Natl Acad Sci. 2024;121:e2321758121.
97. Miu AC, Bîlc MI, Bunea I, Szentágotai-Tătar A. Childhood trauma and sensitivity to reward and punishment: Implications for depressive and anxiety symptoms. Personality Individ Differences. 2017;119:134–40.
98. Weinstock LM, Chou T, Celis-deHoyos C, Miller IW, Gruber J. Reward and punishment sensitivity and emotion regulation processes differentiate bipolar and unipolar depression. Cognit Ther Res. 2018;42:794–802.
99. Quilty LC, Mackew L, Bagby RM. Distinct profiles of behavioral inhibition and activation system sensitivity in unipolar vs. bipolar mood disorders. Psychiatry Res. 2014;219:228–31.
100. Jonker NC, Glashouwer KA, Hoekzema A, Ostafin BD, de Jong PJ. Heightened self-reported punishment sensitivity, but no differential attention to cues signaling punishment or reward in anorexia nervosa. PLoS one. 2020;15:e0229742.
101. Liu Q, Davey D, Jimmy J, Ajilore O, Klumpp H. Network analysis of behavioral activation/inhibition systems and brain volume in individuals with and without major depressive disorder or social anxiety disorder. Biol Psychiatry: Cognit Neurosci Neuroimaging. 2024;9:551–60.
102. Afshari B, Rasouli-Azad M, Ghoreishi FS. Comparison of original and revised reinforcement sensitivity theory in clinically-stable schizophrenia and bipolar disorder patients. Personality Individ differences. 2019;138:321–7.
103. Linhartová P, Látalová A, Barteček R, Širůček J, Theiner P, Ejova A, et al. Impulsivity in patients with borderline personality disorder: a comprehensive profile compared with healthy people and patients with ADHD. Psychological Med. 2020;50:1829–38.
104. Hildebrandt MK, Dieterich R, Endrass T. Disentangling substance use and related problems: urgency predicts substance-related problems beyond the degree of use. BMC psychiatry. 2021;21:242.
105. Haas SM, Derefinko KJ, Waschbusch DA. The use of multimethod impulsivity assessment in the prediction of ADHD, conduct problems, and callous-unemotional symptoms. Personality Individ Differences. 2017;116:289–95.
106. Lockwood J, Townsend E, Daley D, Sayal K. Impulsivity as a predictor of self-harm onset and maintenance in young adolescents: a longitudinal prospective study. J Affect Disord. 2020;274:583–92.
107. Betts MJ, Richter A, de Boer L, Tegelbeckers J, Perosa V, Baumann V, et al. Learning in anticipation of reward and punishment: perspectives across the human lifespan. Neurobiol aging. 2020;96:49–57.
108. Melo RDC, Schreuder MJ, Groen RN, Sarsembayeva D, Hartman CA. Reward sensitivity across the lifespan in males and females and its associations with psychopathology. Personality Individ Differences. 2023;204:112041.
109. Hammond CJ, Potenza MN, Mayes LC. *Development of impulse control, inhibition, and self-regulatory behaviors in normative populations across the lifespan*, 232. Oxford University Press New York, NY2012. https://psycnet.apa.org/record/2013-01231-019.
110. Seger CA. The involvement of corticostriatal loops in learning across tasks, species, and methodologies. In: Groenewegen, H., Voorn, P., Berendse, H., Mulder, A., Cools, A. (eds) *The basal ganglia IX*. Advances in Behavioral Biology, vol 58. Springer, New York, NY. pp 25-39.
111. Zhong G, Chen T, Zhong N, Rezapour T, Haghparast A, Jiang H, et al. Transdiagnostic neuromodulation of impulsivity: current status and future trajectories. Transl Psychiatry. 2025;15:209.
112. Blakemore SJ. Imaging brain development: the adolescent brain. Neuroimage. 2012;61:397–406.
113. Shaw P, Kabani NJ, Lerch JP, Eckstrand K, Lenroot R, Gogtay N, et al. Neurodevelopmental trajectories of the human cerebral cortex. J Neurosci. 2008;28:3586–94.
114. Xie Y, Zhang S, Orban C, Ooi LQR, Kong R, Floris DL et al. Convergent and divergent brain–cognition development. bioRxiv 2025.2006. 2006.658294 [Preprint]. 2025. Available from: https://www.biorxiv.org/content/10.1101/2025.06.06.658294v4.
115. Weafer J, de Wit H. Sex differences in impulsive action and impulsive choice. Addictive Behav. 2014;39:1573–9.
116. Barendse M, Swartz J, Taylor S, Fine J, Shirtcliff E, Yoon L, et al. Sex and pubertal variation in reward-related behavior and neural activation in early adolescents. Developmental Cognit Neurosci. 2024;66:101358.
117. Assari S. Sex differences in the association between cortical thickness and children's behavioral inhibition. J Psychol Behav Res. 2020;2:49–64.
118. Chen Y, Ide JS, Li CS, Chaudhary S, Le TM, Wang W, et al. Gray matter volumetric correlates of dimensional impulsivity traits in children: sex differences and heritability. Hum brain Mapp. 2022;43:2634–52.
119. Shanmugan S, Seidlitz J, Cui Z, Adebimpe A, Bassett DS, Bertolero MA, et al. Sex differences in the functional topography of association networks in youth. Proc Natl Acad Sci. 2022;119:e2110416119.
120. DeCasien AR, Guma E, Liu S, Raznahan A. Sex differences in the human brain: a roadmap for more careful analysis and interpretation of a biological reality. Biol sex differences. 2022;13:43.
121. Zhang X-H, Anderson KM, Dong H-M, Chopra S, Dhamala E, Emani PS, et al. The cell-type underpinnings of the human functional cortical connectome. Nat Neurosci. 2025;28:150–60.
122. Ricard J, Parker T, Dhamala E, Kwasa J, Allsop A, Holmes A. Confronting racially exclusionary practices in the acquisition and analyses of neuroimaging data. Nat Neurosci. 2022;26:4–11.
123. Dhamala E, Ricard JA, Uddin LQ, Galea LA, Jacobs EG, Yip SW, et al. Considering the interconnected nature of social identities in neuroimaging research. Nat Neurosci. 2024;28:222–33.
124. Wierenga LM, Ruigrok A, Aksnes ER, Barth C, Beck D, Burke S, et al. Recommendations for a better understanding of sex and gender in neuroscience of mental health. Biol Psychiatry Glob Open Sci. 2023;4:100283.
125. Marek S, Tervo-Clemmens B, Calabro F, Nichols T, Dosenbach N. Reproducible brain-wide association studies require thousands of individuals. Nature. 2022;603:654–60.

AUTHOR CONTRIBUTIONS

Conceptualization: ED; Methodology: ED; Software: ED; Validation: ED; Formal Analysis: ED; Investigation: ED; Resources: ED; Writing – Original Draft: ED, EC, JLH, JAR, NA, SB, SWY; Writing – Review & Editing: ED, EC, JLH, JAR, NA, SB, LW, KB, BTTY, AJH, SWY; Visualization: ED.

FUNDING

This work was supported by the following sources: Brain and Behavior Research Foundation (Young Investigator Grant to ED), Northwell Health Advancing Women in Science and Medicine (Career Development Award to ED and Educational Achievement Award to ED), Feinstein Institutes for Medical Research (Emerging Scientist Award to ED), NIAAA (R01AA027553 to SWY), NIDA (R01DA053301 to SWY), NIMH (2R01MH120080 to AJH and BTTY), Stanford University Knight-Hennessy Scholars Program (JAR) and the National Academies of Sciences, Engineering, and Medicine's Ford Foundation Predoctoral Fellowship (JAR). SWY is also supported by the Canadian Institute of Health Research (CIHR) and by Women's Healthy Research at Yale (WHRY). BTTY is also supported by the NUS Yong Loo Lin School of Medicine (NUHSRO/2020/124/TMR/LOA), the Singapore National Medical Research Council (NMRC) LCG (OFLCG19May-0035), NMRC CTG-IIT (CTGIIT23jan-0001), NMRC OF-IRG (OFIRG24jan-0006; OFIRG24jul-0049), NMRC STaR (STaR20nov-0003), Singapore Ministry of Health (MOH) Centre Grant (CG21APR1009), and the Singapore National Research Foundation (NRF) Investigatorship (NRFI10-2024-0014). Any opinions, findings, and conclusions or recommendations expressed here are those of the authors and do not necessarily reflect the views of the funders.

COMPETING INTERESTS

The authore declare no competing interest.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The research protocol for the dataset was reviewed and approved by a central Institutional Review Board (IRB) at the University of California, San Diego, and, in some cases, by individual site IRBs. Parents or guardians provided written informed consent, and children assented before participation.

ADDITIONAL INFORMATION

Supplementary information The online version contains supplementary material available at https://doi.org/10.1038/s41380-026-03526-2.

Correspondence and requests for materials should be addressed to Elvisha Dhamala.