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Archival Report

A Developmental Perspective on Facets of Impulsivity and Brain Activity Correlates From Adolescence to Adulthood

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ABSTRACT

BACKGROUND: On a theoretical level, impulsivity represents a multidimensional construct associated with acting without foresight, inefficient inhibitory response control, and alterations in reward processing. On an empirical level, relationships and changes in associations between different measures of impulsivity from adolescence into young adulthood and their relation to neural activity during inhibitory control and reward anticipation have not been fully understood.

METHODS: We used data from IMAGEN, a longitudinal multicenter, population-based cohort study in which 2034 healthy adolescents were investigated at age 14, and 1383 were reassessed as young adults at age 19. We measured the construct of trait impulsivity using self-report questionnaires and neurocognitive indices of decisional impulsivity. With functional magnetic resonance imaging, we assessed brain activity during inhibition error processing using the stop signal task and during reward anticipation in the monetary incentive delay task. Correlations were analyzed, and mixed-effect models were fitted to explore developmental and predictive effects.

RESULTS: All self-report and neurocognitive measures of impulsivity proved to be correlated during adolescence and young adulthood. Further, pre-supplementary motor area and inferior frontal gyrus activity during inhibition error processing was associated with trait impulsivity in adolescence, whereas in young adulthood, a trend-level association with reward anticipation activity in the ventral striatum was found. For adult delay discounting, a trend-level predictive effect of adolescent neural activity during inhibition error processing emerged.

CONCLUSIONS: Our findings help to inform theories of impulsivity about the development of its multidimensional nature and associated brain activity patterns and highlight the need for taking functional brain development into account when evaluating neuromarker candidates.

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The ability to decide and act quickly without hesitation can be advantageous in some settings. However, when persistently expressed, this can also have negative consequences in many daily life situations and is then referred to as impulsivity (1,2). Impulsivity, often defined as action without foresight, is reflected in a lack of self-regulatory capacity associated with overt difficulties in response inhibition and altered reward processing (3). It underlies a broad range of human behaviors and a variety of different clinically relevant mental health conditions (4,5). Definitions range from rather general multifaceted personality accounts to more specific operationalizations, focusing, for example, on indices derived from neurocognitive testing (2). Impulsivity should thus be viewed as a multidimensional construct encompassing a broad variety of

components and facets (6,7). It is therefore not surprising that a range of methods exists to assess impulsivity (4,8). However, on an empirical level, it is still not clear if and how those different rather specific measures of impulsivity are related, and if and how associations change over time, particularly during critical developmental periods, such as adolescence. Furthermore, in this context, studies that relate different measures of impulsivity to brain activity patterns of related neural processes are lacking. This knowledge would empirically inform theoretical conceptualizations of the construct and enable a deeper characterization and understanding of its multidimensional nature, the various methods of assessment, associated neural processes, and developmental changes. Further, it might be relevant for potential clinical application

with regard to the identification of relevant biomarkers for indicating vulnerability or for predicting treatment response.

The current study addresses these open issues within a large-scale multicenter study exploring a population-based cohort of adolescents followed longitudinally into young adulthood (9). In line with Dalley and Robbins (6), for the multidimensional concept of impulsivity, we distinguished trait impulsivity assessed via self-report, questionnaire-based methods from more objective neurocognitive measures. Thereby, trait impulsivity is defined as a predisposition for rapid, but often premature actions without appropriate foresight (6), reflecting preferences for impulsive responding and immediate rewards (10,11). It tends to explain impulsive behaviors such as impaired response inhibition as a consequence of dysfunctional processing of delayed rewards (3). For objective neurocognitive measures of impulsivity, we differentiated between two indices of decisional impulsivity (6) assessing temporal discounting of delayed rewards (delay discounting) and delay aversion, respectively (12). Thereby, decisional impulsivity is reflected in a preference for smaller, immediate rewards over later but larger ones (13).

Whereas some component processes of impulsivity share common variance, thus suggesting overlapping psychological mechanisms, on the level of assessment, different measures of impulsivity often fail to intercorrelate substantially (14). Therefore, there might also be a nonoverlap (at least partially) between different facets of impulsivity representing rather distinct psychological component processes and/or distinct facets of the construct assessed via a specific method of measurement (6,15–17). Additionally, the period of time in the life span, and thus specific characteristics of the investigated samples, might have co-determined so far rather inconsistent previous results in this respect. Earlier studies on impulsivity mainly relied on adult samples and mostly used cross-sectional designs, while we still know very little about potential intercorrelations of different measures of impulsivity facets during critical maturational phases from a longitudinal perspective (18,19). Especially adolescence, with its often acknowledged substantial behavioral and brain changes (20,21), might be an interesting developmental period to focus on (22,23).

Within the last few years, research efforts have tried to unravel the neurobiological underpinnings of impulsivity and its latent phenotypes (24,25), resulting in a vast amount of literature on brain regions involved in aspects of the multifaceted construct. A prominent focus has been on the limbic corticostriatal systems (1). According to Kozak *et al.* (26), two of the relevant brain circuits involved in impulsivity are the cortical control system, including frontal regions for regulatory processes, and the reward system. Among potential brain correlates of interest, particularly the prefrontal cortex, the inferior frontal gyrus (IFG), the pre-supplementary motor area (pre-SMA), and further subcortical regions such as the striatum might play a role as indicated by previous studies [e.g. (18,22,27,28)]. For example, during inhibitory response control and inhibition error processing, those areas have been associated with neurocognitive measures of impulsivity (29–32). Further, during reward processing, frontostriatal deviations were related to measures of trait impulsivity previously (18). However, it is still unclear if and how those associations with neurobiological indices change over time, e.g., during

adolescence (33), and if those brain activity patterns have a predictive value for later changes in self-report and/or neurocognitive measures of impulsivity (35). Our study addressed these gaps by capturing brain activity data during inhibition error processing and reward anticipation and relating them to self-report measures of trait impulsivity and neurocognitive indices of decisional impulsivity. Associations were explored longitudinally during adolescence until young adulthood in a large population-based sample using cross-correlations, mixed-effect models, and predictive modeling.

METHODS AND MATERIALS

Participants

Anonymized data for the present study were obtained from the IMAGEN project (35), a multicenter study including 8 sites (London, Nottingham, Dublin, Mannheim, Dresden, Berlin, Hamburg, and Paris). Healthy participants were longitudinally assessed at baseline during adolescence (at around age 14) and reassessed at follow-up in young adulthood (at around age 19). Ethics approval was provided by the local ethical committees for each participating center, and written informed consent was obtained from parents or guardians. Furthermore, verbal assent was obtained from the adolescents. As young adults, participants provided written informed consent. Exclusion criteria were serious medical conditions, previous trauma with loss of consciousness, any magnetic resonance imaging (MRI) contraindications, or IQ <70. Details regarding the study protocol and data acquisition have been published previously (9). Participants were included in the current analyses if they had at least one facet of either trait impulsivity or decisional impulsivity assessed via self-report questionnaires or neurocognitive testing, respectively, and one functional MRI (fMRI) task of interest at baseline. Finally, data from 2034 healthy adolescents (mean [SD] age = 13.96 [0.45] years; IQ = 108.15 [13.53]; 49.4% male) and 1383 of these participants as young adults (age = 19.09 [0.77] years) were included.

Assessment of Trait Impulsivity and Neurocognitive Indices of Decisional Impulsivity

Trait impulsivity was assessed at baseline and follow-up using the following scales: the extraversion subscale from the Revised NEO Personality Inventory (36), the impulsivity subscale from the Substance Use Risk Profile Scale (37), and the impulsiveness versus reflection subscale from the Temperament and Character Inventory–Revised (38). To assess delay discounting as a facet of decisional impulsivity, the Kirby delay discounting task (39) was used at baseline and follow-up. Further, for measuring delay aversion, the Cambridge Gambling Task (CGT) delay aversion subscale from the Cambridge Cognition Neuropsychological Test Automated Battery (CANTAB) was included at baseline only. For more details on the scales and indices used, see [Supplement A](#).

Assessment of Related Neural Activity—fMRI Paradigms

The stop signal task (SST) (21,40) was implemented to assess neural activity related to inhibitory control, more specifically, inhibition error processing in pre-SMA and IFG (see

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Supplement B for a detailed description and Figure S1 for an example outline). The monetary incentive delay (MID) task (40,41) was used to explore striatal activity during reward anticipation (see Supplement B and Figure S2). Both tasks were assessed at baseline and follow-up.

For the current analyses, we focused on specific task contrasts and brain regions selected a priori based on previous findings [e.g., from the IMAGEN project (35,42)] for comparison purposes. In addition, the ventral striatum (VS) as a core region related to reward processing (anticipation) (43) has been the focus of a recent meta-analysis from Plichta and Scheres (18) exploring the relationship of brain activity in this region with trait impulsivity in adults.

Data Acquisition

Imaging data were acquired at each of the 8 sites with 3T MRI scanners by different manufacturers (Siemens, Philips Healthcare, GE Healthcare, Bruker). Full details of the MRI acquisition protocols and quality checks have been published previously (9). fMRI images were acquired using an echo-planar imaging sequence. For each subject, 444 volumes were acquired for the SST, and 300 volumes were acquired for the MID task. For both tasks, each volume consisted of 40 slices (2.4-mm slice thickness, 1-mm gap), and to provide reliable imaging of subcortical areas, echo time was optimized (echo time = 30 ms, repetition time = 2.2 s). The same scanning protocol was used at all sites.

Data Preparation

Data were z-standardized, and confirmatory factor analyses (44) were conducted on the indices for trait impulsivity (NEO Five-Factor Inventory, Substance Use Risk Profile Scale, Temperament and Character Inventory-Revised) and delay discounting K1–K3 values for the Kirby delay discounting task, respectively, to form one latent factor using the R software package lavaan, version 0.6-6 (<http://cran.uni-muenster.de/web/packages/lavaan/lavaan.pdf>). Predicted values were calculated for each participant estimating the factor scores on each construct. As only one value from the CGT delay aversion subscale was used, no factor analysis was conducted for this impulsivity index.

fMRI data were analyzed with SPM8 (<https://www.fil.ion.ucl.ac.uk/spm/>) and MATLAB, version 2011b (The MathWorks, Inc.). A detailed description of fMRI data preprocessing has been published previously (45) (see also Supplement B). The “stop failure versus stop success” contrast was analyzed for each participant to measure neural activity associated with unsuccessful stopping and inhibition error processing [inhibition error detection-related activity, in line with (42,46)]. This cognitive process is highly relevant for selecting adequate response tendencies and adapting goal-directed behavior (47) and thereby directly linked to the theoretical concept of impulsivity. For the MID task, the “anticipation hit big win versus anticipation hit no win” contrast was used for each participant as an index of neural activity associated with anticipation of a large reward (43). Region-of-interest (ROI) masks were derived from WFU PickAtlas, version 3.0.5 (48): the bilateral IFG and pre-SMA (separately) for the SST (49) and the bilateral VS for the MID task (50,51). Via the Region of

Interest Extraction Toolbox, version 2.1 (<https://www.nitrc.org/projects/rex/>), mean ROI activity values were exported for each participant. Analogous to the manifest variables assessing trait impulsivity and delay discounting, values were z-standardized, and a confirmatory factor analysis was conducted for the SST mean activity values to estimate predicted values for each participant forming one factor representing unsuccessful stopping activity related to inhibitory control in both ROIs. Only neuronal activity from the SST was included for the core analysis. Behavioral performance data were deliberately omitted, as behavioral and brain measures from the same task are per se dependent, and including both levels of data would have biased our data structure and analyses (nevertheless, descriptions and correlations with fMRI brain activity for the SST performance data are presented in Supplement B). Data distribution and the presence of extreme values were explored using Stem-and-Leaf plots in IBM SPSS Statistics for Windows, version 24 (IBM Corp.).

Statistical Analyses

To explore associations between measures of trait impulsivity and the two indices of decisional impulsivity (at baseline and follow-up, respectively) and their relationship with brain functional activity, linear partial correlation analyses were performed using IBM SPSS, version 24, controlling for age, sex, IQ, and site. As we explored associations between three or two facets/indices of impulsivity and with brain functional activity at baseline and follow-up, respectively, false discovery rate (FDR)-corrected *p* values are reported to address issues of multiple testing. As the CGT was assessed only at baseline, no correlational analyses could be conducted for follow-up data.

To assess changes in relationships from adolescence to young adulthood, linear mixed-effect models were fitted to the data using the nlme package in R software, version 3.5.1 (<https://www.r-project.org/>). Random intercepts and slopes were included. Measures of trait impulsivity and decisional impulsivity were entered as dependent variables separately. Brain functional measures (during inhibition error processing and reward anticipation, respectively) were used as independent variables. Of special interest for exploring developmental changes in associations was the interaction term between visit (baseline vs. follow-up) and brain activity. Furthermore, these models were subsequently used for prediction purposes. Baseline-corrected predictors were additionally entered into the model to explicitly control for confounding effects of previous measurements in longitudinal data.

Age, sex, IQ, and site were included as control variables of no interest for all mixed-effect model analyses. FDR-corrected *p* values (for each of the four interaction effects of interest and for the two models on predictive effects) are reported. Relevant effects of control variables on constructs of interest are presented in Figures S3–S6. As the CGT delay aversion subscale measuring probabilistic discounting was assessed only at baseline, models could not be fitted for this facet as dependent variable. For linear mixed-effect models, extreme values were not excluded owing to the possibility that they represent true random variation that might be of special interest with regard to implications for psychiatric populations. Measures analyzed in the current work have already been addressed in some

previous publications for different purposes. Thereby, often a cross-sectional approach was adopted, and variables were analyzed in association with further scales and tasks implemented within the IMAGEN project not included in the current work [e.g. (21,42,43,49,52–62)]. Therefore, no correction for multiple testing was applied with regard to those earlier studies but only for statistical tests conducted within the current work.

RESULTS

Descriptive Statistics

Descriptive statistics for included variables at baseline and follow-up are presented in Table 1. Furthermore, Figure S7 shows the distribution of (predicted) values for each of the constructs after z-score standardization. During adolescence, there was a significant positive association between all dimensions of trait impulsivity and decisional impulsivity: trait impulsivity and delay discounting ($r_{\text{partial}} = 0.094$, $p_{\text{FDR-corrected}} = .007$, $df = 1315$), trait impulsivity and delay aversion ($r_{\text{partial}} = 0.113$, $p_{\text{FDR-corrected}} < .007$, $df = 1105$), and delay discounting and delay aversion ($r_{\text{partial}} = 0.090$, $p_{\text{FDR-corrected}} = .011$, $df = 1102$). During young adulthood, a significant positive linear relationship was observed between trait impulsivity and delay discounting ($r_{\text{partial}} = 0.100$, $p_{\text{FDR-corrected}} = .009$, $df = 917$).

Neural Correlates of Trait Impulsivity and Neurocognitive Indices of Decisional Impulsivity at Baseline (Age 14)

During adolescence, higher brain activity in pre-SMA and IFG during inhibition error processing was related to lower trait impulsivity ($r_{\text{partial}} = -0.075$, $p_{\text{FDR-corrected}} = .042$, $df = 1063$) (Figure 1) (for nonsignificant associations, see Figure S8). A trend-level effect was found for delay aversion ($r_{\text{partial}} = -0.069$, $p_{\text{FDR-corrected}} = .091$, $df = 884$). Figures S10–S16 present the results for the relationships in adolescence excluding extreme values, resulting in similar associations.

Neural Correlates of Trait Impulsivity and Neurocognitive Indices of Decisional Impulsivity at Follow-up (Age 19)

During young adulthood, there was a trend-level effect (positive association) between brain activity in the VS during reward anticipation with trait impulsivity ($r_{\text{partial}} = 0.094$, $p_{\text{FDR-corrected}} = .092$, $df = 453$) (Figure 1) (for nonsignificant associations, see Figure S9). Again, a similar association was observed when extreme values were removed before analysis (Figures S17–S21).

Changes in Associations From Baseline (Age 14) to Follow-up (Age 19)

Changes in associations between brain activity and facets of impulsivity are displayed in Tables 2 and 3. There was a trend-level effect for the interaction between visit and reward anticipation activity in the VS for trait impulsivity ($F_{281} = 5.94$, $\beta = 0.12$, $p_{\text{FDR-corrected}} = .062$), but not for delay discounting ($p_{\text{FDR-corrected}} > .05$). No significant changes in association strength were observed for neural activity in pre-SMA and IFG during inhibition error processing either for trait impulsivity or for delay discounting ($p_{\text{FDR-corrected}} > .05$). Figure 2 shows the differences in associations at baseline and follow-up. Plots of residuals and plots of random effects for mixed-effect models are shown in Figures S22 and S23.

Predictive Value of Neural Activation Patterns at Baseline (Age 14) for Impulsivity at Follow-up (Age 19)

Using mixed-effect models, we explored whether brain activity during adolescence predicted either trait impulsivity or delay discounting during young adulthood. For delay discounting, a trend-level predictive effect of neural activity in pre-SMA and IFG during inhibition error processing was found ($F_{488} = 5.92$, $\beta = 0.12$, $p_{\text{FDR-corrected}} = .061$). Tables 4 and 5 present the results from the mixed-effect model analyses including baseline-corrected predictors.

Table 1. Descriptive Statistics for Analyzed Measures (All Available Data)

Scale	Baseline (Age 14)		Follow-up (Age 19)	
	<i>n</i>	Mean (SD)	<i>n</i>	Mean (SD)
NEO-FFI	2019	30.03 (5.60)	1448	29.44 (5.81)
SURPS	2014	2.44 (0.45)	1428	2.21 (0.43)
TCI-R	2011	26.03 (4.27)	511	25.54 (3.35)
Kirby DDT K1	2027	0.04 (0.04)	1434	0.04 (0.04)
Kirby DDT K2	2027	0.03 (0.03)	1434	0.02 (0.03)
Kirby DDT K3	2027	0.02 (0.03)	1434	0.02 (0.03)
CANTAB CGT Delay Aversion	1670	0.25 (0.14)	NA	NA
MID Task (ROI: VS) ^a	1430	0.26 (0.32)	749	0.22 (0.27)
SST (ROI: Pre-SMA) ^a	1609	-0.04 (0.75)	712	-0.05 (0.74)
SST (ROI: IFG) ^a	1609	-0.03 (0.64)	712	-0.04 (0.64)

CANTAB, Cambridge Cognition Neuropsychological Test Automated Battery; DDT, delay discounting task; CGT, Cambridge Gambling Task; IFG, inferior frontal gyrus; MID, monetary incentive delay; NA, not available; NEO-FFI, NEO Five-Factor Inventory; pre-SMA, pre-supplementary motor area; ROI, region of interest; SURPS, Substance Use Risk Profile Scale; SST, stop signal task; TCI-R, Temperament and Character Inventory-Revised; VS, ventral striatum.

^aWeighted mean ROI activity across all participants. Not all data were assessed for each subject included; see selection criteria in Methods and Materials (therefore, $N < 2034$).

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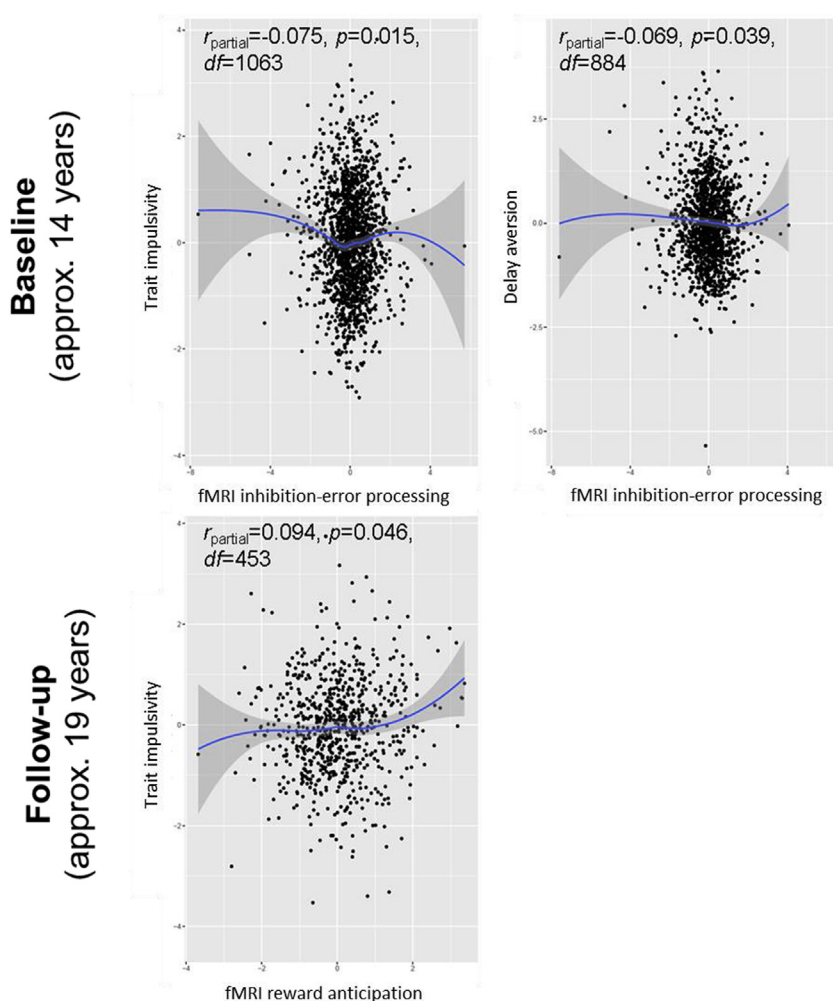


Figure 1. Significant brain responsivity impulsivity associations at baseline and follow-up. Functional magnetic resonance imaging (fMRI) reward anticipation represents mean region of interest activity in ventral striatum. fMRI inhibitory control reflects weighted mean region of interest activity (confirmatory factor analysis) in pre-supplementary motor area and inferior frontal gyrus.

Post Hoc Analyses

Simple-slope analyses were conducted for the four mixed models exploring changes from adolescence (baseline) to young adulthood (follow-up). Results indicate that decreases in impulsivity measures depend on fMRI brain activity during reward anticipation in the two respective models (Supplement H). In further post hoc analyses, partial correlations between baseline and follow-up measurements were calculated to explore associations across time controlling for age, IQ, sex, and site. Especially, we found low, nonsignificant correlations for neural activity measures between baseline and follow-up (see Supplement H for details).

DISCUSSION

Summary of Results and Interpretation

Within our large population-based sample of adolescents assessed longitudinally at age 14 and assessed again as young adults (age 19), we found significant associations between all measures of trait and decisional impulsivity (delay

discounting and delay aversion) in adolescence. In young adulthood, a significant correlation was identified for trait impulsivity and delay discounting, as delay aversion was not assessed at follow-up. In line with previous results (15,63,64), correlations between those measures of impulsivity were rather small, indicating that although different operationalizations of component processes of impulsivity share common variance, they are characterized by requiring distinct psychological processes reflecting different subdomains of impulsivity. This conclusion is further supported by the finding that measures of different facets of impulsivity distinguished within the current work show distinct patterns of associated brain activity. During adolescence, the exploration of the relationship between trait impulsivity and two indices of decisional impulsivity with neural activity resulted in a significant, but weak negative association between neural activity in pre-SMA and IFG during inhibition error processing and trait impulsivity. Further, a nominally significant negative correlation with delay aversion was identified. During young adulthood, we found a trend for a positive association between neural activity in VS during reward anticipation and trait impulsivity. As indicated by

Table 2. Linear Mixed-Effect Model Results for Change in Association Between Trait Impulsivity/Delay Discounting and Neural Activity During Inhibition-Error Processing

Effects	Trait Impulsivity							Delay Discounting (Decisional Impulsivity)						
	SD	<i>r</i>						SD	<i>r</i>					
Random Effects														
Intercept	1.61	–						1.43	–					
Visit	0.96	–0.90						0.87	–0.86					
Residual	0.54	–						0.51	–					
Fixed Effects	Estimate	SE	<i>df</i>	<i>t</i>	<i>p_t</i>	<i>F</i>	<i>p</i> Value	Estimate	SE	<i>df</i>	<i>t</i>	<i>p_t</i>	<i>F</i>	<i>p</i> Value
Intercept	0.02 ^a	0.98	1130	0.02	.99	3.41	.07	3.08	0.96	1126	3.22	<.01	1.77	.18
Visit	<0.01	0.05	347	0.18	.86	0.08	.77	0.07	0.05	340	1.41	.16	2.07	.15
fMRI Inhibition Error Processing	0.55 ^c	1.04	347	0.53	.60	9.09	.003	–0.78	1.00	340	–0.78	.44	2.05	.15
Age	<0.001	<0.001	1130	0.33	.74	0.02	.88	<–0.001	<0.001	1126	–2.03	.04	2.54	.11
Sex (as Factor)	–0.004	0.06	1130	–0.07	.95	0.09	.76	–0.18 ^c	0.05	1126	–3.36	<.001	10.43	.001 ^c
IQ	–0.002 ^b	0.002	1130	–0.93	.35	3.94	.05	–0.01 ^d	0.002	1126	–5.27	<.0001	27.00	<.0001 ^d
Site (as Factor)	– ^c	–	–	–	–	3.19	.002	–	–	–	–	>.10 ^e	1.26	.27
Site 2	0.09	0.10	1130	0.85	.39									
Site 3	0.15	0.13	1130	1.22	.22									
Site 4	–0.18	0.12	1130	–1.48	.14									
Site 5	–0.18	0.10	1130	–1.81	.07									
Site 6	–0.07	0.11	1130	–0.69	.49									
Site 7	–0.09	0.10	1130	–0.84	.40									
Site 8	–0.34 ^c	0.12	1130	–2.75	<.01									
Visit × fMRI Inhibition Error Processing	–0.01	0.06	347	–0.23	.82	0.19	.66	0.01	0.06	340	0.22	.83	0.002	.97
fMRI Inhibition Error Processing × Age	<–0.001	<0.001	347	–0.71	.48	0.12	.73	<0.001	<0.001	340	0.40	.69	0.01	.91
fMRI Inhibition Error Processing × Sex	0.03	0.06	347	0.50	.62	0.33	.57	0.06	0.05	340	1.10	.27	0.47	.50
fMRI Inhibition Error Processing × IQ	<0.001	0.002	347	0.29	.77	0.62	.43	0.003	0.002	340	1.40	.16	1.28	.26
fMRI Inhibition Error Processing × Site (as Factor)	–	–	–	–	>.10 ^e	0.41	.90	– ^b	–	–	–	–	2.17	.04
fMRI inhibition error processing × site 2								0.03	0.09	340	0.31	.76		
fMRI inhibition error processing × site 3								0.23 ^b	0.12	340	1.99	<.05		
fMRI inhibition error processing × site 4								0.21 ^a	0.12	340	1.78	.08		
fMRI inhibition error processing × site 5								–0.06	0.10	340	–0.54	.59		
fMRI inhibition error processing × site 6								–0.08	0.10	340	–0.81	.42		
fMRI inhibition error processing × site 7								0.06	0.11	340	0.59	.55		
fMRI inhibition error processing × site 8								–0.04	0.12	340	–0.32	.75		

Sex and site were included as factors with sex 1 and site 1 as reference, respectively.

fMRI, functional magnetic resonance imaging.

^a*p* ≤ .1 (based on *p* values from *F* statistic).

^b*p* ≤ .05 (based on *p* values from *F* statistic).

^c*p* ≤ .01 (based on *p* values from *F* statistic).

^d*p* ≤ .001 (based on *p* values from *F* statistic).

^eAll site effects not significant: *p* > .10 (based on *p* values from *F* statistic).

Table 3. Linear Mixed-Effect Model Results for Change in Association Between Trait Impulsivity/Delay Discounting and Neural Activity During Reward Anticipation

Effects	Trait Impulsivity							Delay Discounting (Decisional Impulsivity)						
	SD	<i>r</i>						SD	<i>r</i>					
Random Effects														
Intercept	1.52	–						1.61	–					
Visit	0.92	–0.89						0.90	–0.93					
Residual	0.52	–						0.47	–					
Fixed Effects	Estimate	SE	<i>df</i>	<i>t</i>	<i>p_t</i>	<i>F</i>	<i>p</i> Value	Estimate	SE	<i>df</i>	<i>t</i>	<i>p_t</i>	<i>F</i>	<i>p</i> Value
Intercept	1.14	0.99	1093	1.15	.25	0.94	.33	2.08	0.89	1091	2.33	.02	2.07	.15
Visit	–0.07 ^b	0.05	281	–1.33	.19	4.43	.04	–0.07 ^b	0.05	272	–1.41	.16	5.24	.02 ^b
fMRI Reward Anticipation	0.30	0.98	281	0.31	.76	1.00	.32	–0.54	0.90	272	–0.60	.55	0.75	.39
Age	<–0.001	<0.001	1093	–0.54	.59	0.30	.58	<–0.001	<0.001	1091	–0.87	.39	0.30	.58
Sex (as Factor)	–0.04	0.06	1093	–0.66	.51	0.41	.52	–0.23 ^d	0.05	1091	–4.58	<.001	20.27	<.0001
IQ	–0.004 ^c	0.002	1093	–1.98	<.05	8.95	.003	–0.01 ^d	0.002	1091	–5.55	<.001	32.69	<.0001
Site (as Factor)	– ^c	–	–	–	>.10 ^e	2.89	.005	–	–	–	–	>.10 ^e	1.11	.35
Visit × fMRI Reward Anticipation	0.12 ^b	0.06	281	2.12	.03	5.94	.02	0.10 ^a	0.05	272	2.06	.04	3.68	.06 ^a
fMRI Reward Anticipation × Age	<–0.001	<0.001	281	–0.59	.55	0.81	.37	<0.001	<0.001	272	0.33	.74	0.01	.92
fMRI Reward Anticipation × Sex	–0.07	0.05	281	–1.26	.21	1.37	.24	–0.06	0.05	272	–1.13	.26	1.26	.26
fMRI Reward Anticipation × IQ	0.001	0.002	281	0.65	.52	0.21	.64	<0.001	0.002	272	0.44	.66	0.06	.81
fMRI Reward Anticipation × Site (as Factor)	–	–	–	–	>.10 ^e	0.47	.86	–	–	–	–	>.10 ^e	0.60	.76

Sex and site were included as factors with sex 1 and site 1 as reference, respectively.

fMRI, functional magnetic resonance imaging.

^a*p* ≤ .1 (based on *p* values from *F* statistic).

^b*p* ≤ .05 (based on *p* values from *F* statistic).

^c*p* ≤ .01 (based on *p* values from *F* statistic).

^d*p* ≤ .001 (based on *p* values from *F* statistic).

^eAll site effects not significant: *p* > .10 (based on *p* values from *F* statistic).

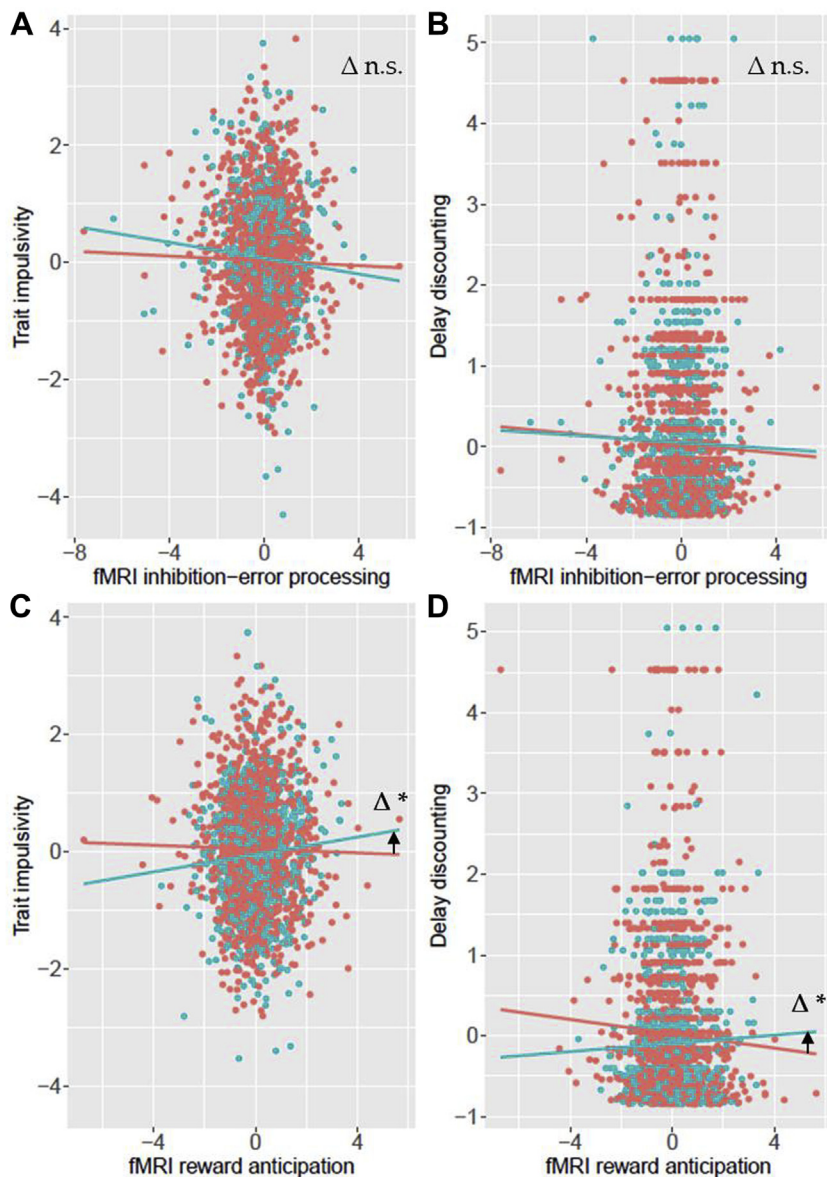


Figure 2. Plots of changes of brain responsivity impulsivity relationships from adolescence to young adulthood. **(A)** Association between trait impulsivity and functional magnetic resonance imaging (fMRI) inhibitory control. **(B)** Association between temporal discounting and fMRI inhibitory control. **(C)** Association between trait impulsivity and fMRI reward anticipation. **(D)** Association between temporal discounting and fMRI reward anticipation. Red dots and lines represent data in adolescence (baseline). Turquoise dots and lines show data in young adulthood (follow-up). Δ indicates change (in association), also highlighted by arrows; * $p \leq .05$, n.s., not significant (significance value refers to change in association).

these results, brain activity in pre-SMA and IFG during inhibition error processing might represent a possible candidate network for trait impulsivity in adolescence. However, neural correlates of inhibition error processing are not associated with the delay discounting subdomain of decisional impulsivity. This might be due to stronger associations of executive, higher-order cognitive processes of inhibition and error processing with trait-related aspects of impulsivity, rather than with cognitive aspects of decision making. Nevertheless, there is an association with delay aversion, which might be related to the fact that this construct reflects an aversion to delay owing to learned or expected negative emotions associated with waiting, thereby additionally involving affective components (12). Further replication is needed exploring the sensitivity and specificity of those associations in other longitudinal samples

(65) that also distinguish between delay discounting and delay aversion as two different expressions of decisional impulsivity and to prove whether they result from the same underlying neurobiological processes or also involve activity in distinct neural regions (66). As shown by the correlations with behavioral performance data from the SST, higher activity during inhibition error processing is associated with fewer omission errors (for both adolescence and young adulthood) and higher reaction times (go and stop signals) as well as more commission errors (for adolescence), especially with the latter being indicative of impulsive behavior.

Our findings indicate no relationship between facets of trait impulsivity and decisional forms of impulsivity with VS activity during reward anticipation in adolescence. However, we found a trend-level positive association between VS activity during

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Table 4. Linear Mixed-Effect Model Results for Predicting Trait Impulsivity Based on Neural Activity

Effects	Trait Impulsivity						
	SD	<i>r</i>					
Random Effects							
Intercept	0.64	–					
Visit	0.32	0					
Residual	0.24	–					
Fixed Effects							
	Estimate	SE	<i>df</i>	<i>t</i>	<i>p_t</i>	<i>F</i>	<i>p</i> Value
Intercept	3.35	1.46	500	2.29	.02	0.02	.89
Trait Impulsivity (Baseline)	0.25 ^b	0.04	500	5.93	<.001	40.89	<.0001
fMRI Reward Anticipation (Baseline)	–0.04	0.04	500	–0.86	.39	0.44	.51
fMRI Inhibition Error Processing (Baseline)	–0.07 ^a	0.05	500	–1.60	.11	3.61	.06
Age	<–0.001 ^a	<0.001	500	–1.98	<.05	3.58	.06
Sex (as Factor)	–0.07	0.08	500	–0.83	.41	0.45	.51
IQ	–0.006 ^a	0.003	500	–1.68	.09	3.31	.07
Site (as Factor)	–	–	500	–	<.10	0.43	.88

Sex and site were included as factors with sex 1 and site 1 as reference, respectively.

fMRI, functional magnetic resonance imaging.

^a*p* ≤ .1 (based on *p* values from *F* statistic).

^b*p* ≤ .001 (based on *p* values from *F* statistic).

reward anticipation and trait impulsivity in young adulthood, indicating a striatal hyperactivation with higher trait impulsivity scores. This finding is in line with previous meta-analytical results for healthy young adult populations (18), further supporting the validity of the current study results. Consequently, reward anticipation-related activity in the VS might represent a potentially relevant biomarker candidate for characterizing adult trait impulsivity. Especially, the facet of trait impulsivity is broadly associated with different brain activity patterns across the critical developmental period from adolescence to young adulthood. The current results indicate that trait impulsivity seems to represent a rather stable core construct within the broad and heterogeneous impulsivity concept.

An important objective of this study was to explicitly analyze developmental trajectories in the associations of interest. We

found that relationships between neural activity and measures of facets of impulsivity change across the developmental period from adolescence to young adulthood. Specifically, a trend-level significant change emerged for the association between reward anticipation activity in the VS with trait impulsivity from adolescence to young adulthood. These developmental effects are probably related to substantial changes on a neural level, whereas dimensions of trait impulsivity and decisional impulsivity remain relatively stable during the developmental period of interest as shown by post hoc simple-slope and correlational analyses. This finding is in line with results from previous studies that reported on ongoing developmental changes, especially with regard to neural reward processing, during the sensitive period of adolescence and young adulthood (23,67).

Table 5. Linear Mixed-Effect Model Results for Predicting Delay Discounting Based on Neural Activity

Effects	Delay Discounting (Decisional Impulsivity)						
	SD	<i>r</i>					
Random Effects							
Intercept	0.72	–					
Visit	0.36	0					
Residual	0.27	–					
Fixed Effects							
	Estimate	SE	<i>df</i>	<i>t</i>	<i>p_t</i>	<i>F</i>	<i>p</i> Value
Intercept	4.85	1.52	488	3.19	.002	0.76	.38
Delay Discounting (Baseline)	0.27 ^b	0.04	488	6.31	<.001	49.02	<.0001
fMRI Reward Anticipation (Baseline)	–0.003	0.05	488	–0.07	.94	0.04	.84
fMRI Inhibition Error Processing (Baseline)	0.12 ^a	0.05	488	2.56	.01	5.92	.02
Age	<–0.001 ^a	<0.001	488	–2.36	.02	4.53	.03
Sex (as Factor)	–0.23 ^a	0.09	488	–2.61	<.01	5.57	.02
IQ	–0.01 ^b	0.003	488	–3.37	<.001	13.36	<.001
Site (as Factor)	–	–	–	–	<.10	1.03	.41

Sex and site were included as factors with sex 1 and site 1 as reference, respectively.

fMRI, functional magnetic resonance imaging.

^a*p* ≤ .05 (based on *p* values from *F* statistic).

^b*p* ≤ .001 (based on *p* values from *F* statistic).

Finally, after controlling for multiple testing, a trend-level predictive effect of neural activity in pre-SMA and IFG during inhibition error processing in adolescence for delay discounting in young adulthood was found to have a potential practical value with regard to the prediction of development and treatment response.

Relevance of Results and Potential Clinical Implications

Impulsivity is a highly prevalent characteristic of normal as well as altered deviant human behavior, being implicated in a broad range of psychiatric disorders (1,2). Therefore, the current findings are of practical relevance—although the implications are restricted owing to the rather low effect sizes. Our results have implications for the conceptualization of the multidimensional nature of impulsivity, its developmental course, and associated neural activity patterns. Further, current findings might be relevant for our understanding of the etiology, diagnosis, and treatment of impulsivity-related behavioral problems and mental health disorders.

First, on a theoretical level, current results strengthen previous findings that impulsivity represents a rather heterogeneous construct being reflected in trait-focused self-report measures and further neurocognitive testing indices that on one hand share common variance, but nevertheless represent distinct psychological aspects (6,15–17). Although not all key subdomains of impulsivity have been addressed within the current work, these findings underline the need for an informed, theoretically driven fragmentation of the construct in future research and clinical practice, including detailed assessments, analyses, and comparisons of component processes of the complex concept.

Our study identified that brain activity in pre-SMA and IFG during inhibition error processing might be one candidate biomarker network characterizing the facet of trait impulsivity in adolescents. Furthermore, reward anticipated activity in the VS might possibly be a useful characteristic for characterizing adult trait impulsivity. Current results again underline the nonunitary of the concept of impulsivity and highlight that different facets of impulsivity are differentially related to distinct neural activity patterns depending on maturational stage. Relationships change substantially during the critical developmental period from adolescence to young adulthood, resulting in distinct patterns of associations at baseline and follow-up. The identified emergence of an association between reward anticipation activity in the VS and trait impulsivity in young adulthood is consistent with previous findings that report on ongoing dramatic changes with regard to neural processing until early adulthood (67) and results from an earlier meta-analysis (18). These findings highlight the need for taking maturational processes into account when assessing impulsivity within and across different developmental periods and when exploring biomarker candidates [in line with (68)].

However, given the small effect sizes identified, the current results suggest a rather restricted value for practical application with regard to clinical characterization. The identified neural correlates are not yet ready to be used for diagnostic purposes (i.e., for the characterization of behavioral symptoms) or as indices of vulnerability. Nevertheless, the neural

correlates identified within the current work might already be relevant for inclusion in machine learning approaches (69). With regard to the predictive value of neural activity for later impulsivity, results show only a trend-level effect after controlling for multiple testing not allowing for further conclusions either about early markers of vulnerability or about their sensitivity for predicting treatment response, especially as a healthy, community-based sample was analyzed.

Limitations and Future Directions

A few limitations of the current work have to be mentioned. First, healthy individuals were recruited for the sample, excluding patients with diagnoses of impulsivity-related disorders. Therefore, variance within the facets of trait and decisional impulsivity might be restricted. Associations might change in extreme ranges of impulsivity dimensions. Future studies are needed that include larger samples with individuals having more extreme and clinically relevant scores on impulsivity measures for broader conclusions that additionally explore nonlinearity in those relationships. In addition, other, probably more valid, scales would be available to assess aspects of trait impulsivity [for overview, see, e.g. (27)], which might in future studies add further relevant knowledge to the conceptualization of trait impulsivity by probing additional facets involving, for example, aspects of emotion processing and executive dysfunction. Further, effect sizes identified within current analyses are rather small (owing to the large sample size and high power), and results obtained within mixed-effect model analyses do not explain a substantial amount of variance, questioning the relevance of the biological characteristics explored in the sense of a biomarker. This needs to be taken into account when drawing conclusions for further clinical applications. Future studies are needed that replicate current findings while allowing for conclusions with regard to early vulnerability and predictive effects. Furthermore, identified associations are correlational in nature, not yet allowing for conclusions on causal relationships. Subsequent studies are warranted replicating current findings and explicitly proving biomarker criteria [as proposed by Thome *et al.* (65)]. In addition, in our study, there was a focus on specific, a priori defined neural processes of interest, also with regard to the fMRI contrasts and ROIs selected. However, others might be relevant [e.g. (34)]. Currently, this study should be seen as a starting point, and future studies extending these results are warranted. Furthermore, using confirmatory factor analyses, data were reduced by estimating predicted values. However, a higher validity of assessment might have been obtained by combining more than one measure per concept. Also, recent articles question the test-retest reliability of the fMRI blood oxygen level-dependent signal activity [e.g. (70–72)]. The resulting discussion is especially relevant when interpreting findings from longitudinal multicenter datasets focusing on developmental processes, and these should be addressed in future studies. These studies should explicitly assess test-retest reliability via adequate indices (e.g., intra-class correlation coefficient), compare indices, and then provide a framework for interpretation. Finally, earlier changes during the period from childhood to adolescence could not be analyzed. Future longitudinal projects should start assessing

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brain-behavior relationships in childhood (and continue assessment until late adulthood) to explore developmental trajectories across the life span.

Conclusions

The current study contributes important knowledge to our understanding of the multidimensional nature of the transdiagnostic impulsivity construct, various assessment methods, and associated neural and developmental processes. In this study, intercorrelations among measures of facets of impulsivity, developmental trajectories, and neurobiological correlates were explored. We found trend-level significant associations between measures of trait and decisional impulsivity as well as with brain activity in pre-SMA and IFG during inhibition error processing and in VS during reward anticipation from adolescence to young adulthood. Associations between self-report and neurocognitive measures of impulsivity with brain activity change substantially until young adulthood and are probably due to changes on the level of neural processing, resulting in distinct developmental patterns. These findings are relevant with regard to the conceptualization of the impulsivity construct and related neurobiological markers across the life span. The current results highlight the need for taking brain developmental processes into account when exploring brain activity correlates of different operationalizations of impulsivity. However, the relationships identified are rather small. Future studies are needed for replication and extension.

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