Connectome Wide Intrinsic Functional Connectivity Associated With Delay Discounting in Adolescence

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**Abstract**

Impulsive risk-taking behavior is a major source of morbidity and mortality in adolescence and is frequently associated with psychopathology that emerges during that period. However, the neural mechanisms that underlie impulsive choice in adolescence remain poorly described. Here, we investigated how multivariate patterns of functional connectivity were associated with delay discounting (DD), a task that measures impulsive choice by comparing preferences for diminished immediate rewards over delayed but more substantial rewards. In a sample of 307 adolescent humans (ages 9-23 years; *M =*17.21years, *SD* = 3.08 years; 163 females), we conducted a connectome-wide analysis using multivariate distance-based matrix regression to examine the relationship between DD and functional connectivity (FC) measured at rest at using 3T fMRI. Two regions were identified as important drivers of functional connectivity patterns underlying individual differences in DD: the right temporal parietal junction (TPJ) and the dorsomedial prefrontal cortex (MFG). For the TPJ, greater DD was associated with greater connectivity with the dorsal attention network (DAN) and reduced connectivity with the default mode network (DMN). In contrast, for the MFG, greater DD was associated with greater functional connectivity with the DMN and reduced connectivity with the DAN. Taken together, these results suggest that impulsive choice in adolescence is associated with individual differences in the relationships between the DMN and the dorsal attention network.

**KEYWORDS**: delay discounting, impulsivity, adolescence, fMRI, functional connectivity, development

**INTRODUCTION**

Adolescence is a developmental period characterized by increased morbidity and mortality due to impulsive risk-taking behaviors (Casey et al., 2008; Romer et al., 2017). Furthermore impulsivity is a key feature of multiple clinical disorders, including substance abuse and attention-deficit hyperactivity disorder (Moeller et al., 2001; Bakhshani, 2014; Amlung et al., 2019). Impulsive choice is a key element of the broad domain of impulsivity and is frequently measured using delay discounting (DD). Impulsive individuals prefer smaller but immediate rewards over larger but delayed rewards(Kable and Glimcher, 2010). Studies using fMRI have revealed that DD engages a broad network of regions: the ventral striatum, ventromedial prefrontal cortex, posterior cingulate, and dorsolateral prefrontal cortex, medial prefrontal cortex, (Bartra et al., 2013; https://www.tandfonline.com/doi/full/10.1080/00952990.2018.1557675?casa\_token=u6tlVuE4i54AAAAA%3A-Gu6Hg6EpH8vIJyyJswILb77zs-hJ7J1m74-UfDVMiW9ks\_8K3RVO02uk4Z95xLTPuVsBZhshgoJ). Although task-based studies have yielded important insights into the underlying neural circuitry of impulsivity, DD is generally considered a stable personality trait that varies among individuals (Kirby, 2009). As such, investigators have increasingly sought to understand whether individual differences in DD are encoded by patterns of intrinsic functional connectivity (FC). Hence, resting state connectivity…

However, there are some studies that do use rsFMRI: <https://www.frontiersin.org/articles/10.3389/fpsyt.2020.618319/full> ; <https://pubmed.ncbi.nlm.nih.gov/16510242/>; https://pubmed.ncbi.nlm.nih.gov/27394716/- by and large they have much smaller samples, are focused on specific disorders; performed on adults/ limited by ROI approaches: https://www.sciencedirect.com/science/article/pii/S0306452220307430?casa\_token=XfxAitxxdD0AAAAA:pFLmkYFGXnAyKtuU8RCLQhlCbRk5ek4X4IIzIGyqsPf\_wws8YOwucrK7SVd0wZz4o0qaelheDQ

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Despite the importance of understanding delay discounting, particularly in youth due to susceptibility etc. , there has been more focus on adults.

Implicated regions:

* <https://www.sciencedirect.com/science/article/pii/S0028393220301639?casa_token=U8n1MP7C3gcAAAAA:EWgjNgi6N5sRthPdzwp5Cap1xwzzLLWxb1NvaU3ucvAFbGPP-6WehMQHf6y_eZ0vClBvOAFaPw>: caudate and ventral striatum, MFG, SMG
* https://www.sciencedirect.com/science/article/pii/S1878929321000335 : medial prefrontal/anterior cingulate, [posterior cingulate](https://www.sciencedirect.com/topics/neuroscience/posterior-cingulate" \o "Learn more about posterior cingulate from ScienceDirect's AI-generated Topic Pages), [precuneus](https://www.sciencedirect.com/topics/neuroscience/precuneus" \o "Learn more about precuneus from ScienceDirect's AI-generated Topic Pages), and inferior frontal gyrus (i.e., an immediacy effect).
* <https://www.nature.com/articles/s41598-017-11109-z> : DAC, dlPFC (large sample)
* <https://www.sciencedirect.com/science/article/pii/S1878929313000686> - left ventromedial caudate

Basically, not a lot of consensus.

However, it is notable that most prior studies have been limited by smaller samples that used seed-based analyses restricted to specific brain regions that were selected *a priori* see Wang et al 2017. As DD is a complex cognitive process that engages multiple brain networks, such studies may not capture important differences in connectivity that are distributed across the cortex (Wang et al., 2016; Korponay et al., 2017; Xu et al., 2019).

Accordingly, here we investigated how individual differences in DD are associated with differences in patterns of FC during adolescence. We capitalized on a large sample of 307 youths imaged as part of the Philadelphia Neurodevelopmental Cohort (Satterthwaite et al., 2014, 2016) that completed a DD task and were imaged using resting-state fMRI. To overcome limitations of region of interest and seed-restricted analyses, we conducted a connectome-wide association study (CWAS; Shehzad et al., 2014) which searches for changes in the multivariate pattern of connectivity at each location in the brain (Shehzad et al., 2014; Satterthwaite et al., 2015; Sharma et al., 2017). This fully exploratory approach allowed us to uncover novel associations between DD and FC in a large sample of youth.

Shehzad: connectivity data represents the next frontier in the neuroimaging connectomics era. Exploration of brain-phenotype relationships remains limited by statistical approaches that are computationally intensive, depend on a priori hypotheses, or require stringent correction for multiple comparisons.

Additional things to add:   
1. Background behind delay discounting and use

**Methods**

*Participants*

This study considered an initial sample of 1,601 youths recruited as part of the Philadelphia Neurodevelopmental Cohort (PNC) who underwent both neuroimaging (Satterthwaite et al., 2014, 2016) and neurocognitive assessment (Gur et al., 2010, 2012). Of these 1601 youths, 452 participants completed a behavioral delay discounting (DD) task outside of the scanning session. Of these, twenty-four participants were excluded for the following reasons: health conditions that could impact brain structure (n=19), scanning performed 12 months from the time of DD testing (n=1), inadequate structural image quality (n=3), missing imaging data (n=1), excessive in scanner motion (n=119), or poor quality behavioral data (n=11).

We applied previously defined procedures for procedures for quality assurance of behavioral data (Pehlivanova et al., 2018). Specifically, each participant’s responses were fit using a logistic regression model, with predictors including the immediate amount, delayed amount, delay, their respective squared terms, and two-way interaction terms. The goodness of fit of this model was assessed using the coefficient of discrimination (Pehlivanova et al., 2018); a value less than 0.20 indicated nearly random choices. Similarly, as described in previous work (Satterthwaite et al., 2013; Ciric et al., 2018) a resting-state fMRI data was excluded if mean relative root mean square (RMS) framewise displacement was higher than 0.2mm, or it had more than 20 frames with motion exceeding 0.25mm. Our final sample thus included 307 participants (163 females; age range: 9.67 - 23.58 years old, *M =* 17.21, *SD* = 3.08 years).

*Delay discounting task*

The DD task consisted of 34 self-paced questions where the participant chose between a smaller amount of money available immediately or a larger amount available after a delay (Senecal et al., 2012; Pehlivanova et al., 2018). The smaller, immediate rewards were uniformly distributed from $10 to $34, and the larger, delayed rewards were fixed at $25, $30, or $35 with equal frequency. The delays between reward selection and the rewards themselves ranged from 1 to 171 days. Trials and task procedures were identical in content and order for all participants. The DD task was administered as part of an hour-long web-based battery of neurocognitive tests (Gur et al., 2010), on a separate day from the imaging session. The mean interval between the DD task and imaging was 0.44 months with a SD of 1 month (range 0 – 8 months).

Discount rates from the delay discounting task were calculated with hyperbolic discounting model <add citation here for the Kable & Glimcher paper? > of the form: ,where *V* is the subjective value of the delayed reward, *A* is the amount of the delayed reward, *D* is the delay in days, and *k* is the subject-specific discount rate (Mazur, 1987) .As in previous work (Senecal et al., 2012; Pehlivanova et al., 2018), the *fmincon* optimization algorithm in MATLAB (MathWorks) was used to estimate the best fitting *k* from each participant’s choice data. A higher *k* value indicates steeper discounting of delayed rewards and thus more impulsive choices. As the distribution of estimated *k* parameters is right-skewed, we applied a log-transform (log *k*) prior to our analyses.

*Image acquisition*

All MRI scans were acquired using the same 3T Siemens Tim Trio whole-body scanner and 32-channel head coil at the Hospital of the University of Pennsylvania (HUP). Image acquisition protocols are described in detail by previous work (Satterthwaite et al., 2014).

The magnetization-prepared, rapid acquisition gradient-echo T1-weighted (MPRAGE) image was acquired with the following parameters: TR = 1810 ms; TE = 3.51 ms; TI = 1100 ms, FOV = 180 × 240 mm2, matrix = 192 × 256, effective voxel resolution = 0.9 × 0.9 × 1 mm3. Resting-state fMRI scans were acquired with a single-shot, interleaved multi-slice, gradient-echo, echo planar imaging (GE-EPI) sequence sensitive to BOLD contrast with the following parameters: TR = 3000 ms; TE = 32 ms; flip angle = 90°; FOV = 192 × 192 mm2; matrix = 64 × 64; 46 slices; slice thickness/gap = 3/0 mm, effective voxel resolution = 3.0 × 3.0 × 3.0 mm3. Resting-state scans consisted of 124 volumes. In addition, a B0 field map was derived for application of distortion correction procedures, using a double-echo, gradient-recalled echo (GRE) sequence: TR = 1000ms; TE1 = 2.69ms; TE2 = 5.27ms; 44 slices; slice thickness/gap = 4/0 mm; FOV = 240 mm; effective voxel resolution = 3.8×3.8×4 mm3.

*Image processing*

Before the processing of both structural and functional data, a custom adolescent template was created with Advanced Normalization Tools (ANTs; Avants and Gee, 2004; Avants et al., 2011a) The template was created to avoid registration bias and maximize sensitivity to detect regional effects that can be impacted by registration error (Avants et al., 2011a). Structural images were then processed and registered to this template using the ANTs cortical thickness pipeline (Tustison et al., 2014). This procedure includes brain extraction, N4 bias field correction (Tustison et al., 2010). Atropos probabilistic tissue segmentation (Avants et al., 2011b) and the top-performing SyN diffeomorphic registration method (Avants et al., 2008; Klein et al., 2009).

The fMRI data were processed with an empirically validated preprocessing pipeline implemented in the eXtensible Connectivity Pipeline (XCP) Engine (Ciric et al., 2018). Resting-state time series preprocessing included correction of distortion induced by magnetic field inhomogeneity using FMRIB Software Library (FSL)’s FUGUE utility (Jenkinson, 2003) realignment of all volumes to a selected reference volume using MCFLIRT (Jenkinson et al., 2002), interpolation of intensity outliers in each voxel’s time series using AFNI’s 3dDespike utility, and demeaning and removal of first- and second-order trends. After the despiking and detrending, the functional data were de-noised using a 36-parameter confound regression model that has been shown to minimize associations with motion artifact and other nuisance variables (Ciric et al., 2017). Specifically, the confound regression model included the six framewise estimates of motion, the mean signal extracted from eroded white matter and cerebrospinal fluid compartments, the global signal, the derivatives of each of these nine parameters, and quadratic terms of each of the nine parameters as well as their derivatives. To avoid frequency mismatch, both the BOLD-weighted time series and the confound regressor timeseries were temporally filtered simultaneously using a first-order Butterworth filter with a passband between 0.01 and 0.08 Hz (Hallquist et al., 2013). The confound regression was performed using AFNI’s 3dTproject. Denoised functional images were co-registered to the T1 image using boundary-based registration (Greve and Fischl, 2009) and aligned to the study-specific adolescent template using the ANTs transform for the T1 image as above. Functional images were resampled to 4 mm3 isotropic voxels in the template space before connectome-wide association study for computational feasibility (Shehzad et al., 2014). However, higher spatial resolution images (2 mm3) were used for follow-up seed-based analyses. Throughout, all transformations were concatenated so that only one interpolation was performed.

*Multivariate Distance Matrix Regression (MDMR)*

We performed a connectome-wide association study (CWAS) using MDMR as described in detail in previous studies (Shehzad et al., 2014; Satterthwaite et al., 2015; Sharma et al., 2017). A schematic of the CWAS procedure is depicted in **Figure 1**.

Graphical user interface

Description automatically generated

**Figure 1. Connectome-Wide Analysis using Multivariate Distance-Based Matrix Regression (MDMR)**. Template-space functional time series were resampled to 4 mm3 for computational feasibility. For each gray matter voxel (**A**), a connectivity map was created for each subject (**B**), and the maps were compared in a pairwise manner (using correlation) to create a distance matrix (**C**). MDMR used these distance matrices to evaluate the complex multivariate pattern of connectivity in association with delay discounting (DD) across subjects while controlling for age, sex, and in-scanner motion (**D**). Permutation testing yielded a pseudo-F statistic and a corresponding p value. This procedure was repeated for each gray matter voxel, yielding a voxel-wise statistical map (**E**).

First, the pre-processed participant BOLD timeseries were used to conduct seed-based connectivity analyses at each voxel within gray matter. Specifically, the Pearson’s correlation coefficient between each voxel’s time series and the time series of every other gray matter voxel (**Fig 1A-B**) was used to generate subject-level connectivity maps. Second, we summarized individual differences in functional connectivity maps by computing a distance matrix (also using Pearson’s correlation) between the connectivity matrices for every possible pairing of participants (**Fig. 1C**). Third, MDMR (**Fig. 1D**) was used to test how well our phenotypic variable, log(*k*), explained variation in the distances between connectivity matrices across participants. This provided a measure of how functional connectivity patterns across participants were impacted by individual differences in log(*k*), while controlling for the effects of age, sex, and in-scanner motion in the same model (Shehzad et al., 2014; Satterthwaite et al., 2015). MDMR yields a pseudo-F statistic for each voxel, whose significance was assessed using 5,000 iterations of a permutation test to generate a null distribution. The ultimate product of this procedure was a voxel-wise *Z*-statistic map describing the association between log(*k*) and the global pattern of connectivity for each voxel (**Fig. 1E**). Aligning with current recommendations to minimize false positives, (Eklund et al., 2016) the Type I error rate across voxels was controlled using cluster correction with a voxel height of z > 3.09 and utilized a cluster-extent probability threshold *p* < 0.05.

### *Seed-Based Analyses*

### MDMR identifies clusters where the overall multivariate pattern of connectivity is dimensionally related to DD, but it does not describe the specific pairwise FC patterns that drive the multivariate results. To characterize the direction of the effects, as in previous studies (Satterthwaite et al., 2015b; Sharma et al., 2017b), we conducted post-hoc seed-based descriptive analyses for each cluster returned by MDMR. Group-level seed analysis included age, sex and in-scanner motion as covariates and was computed using a general linear model (implemented in FSL’s *flameo*;Woolrich et al., 2004). These follow-up analyses were descriptive, as the seeds were selected on the basis of the significance of the MDMR result.

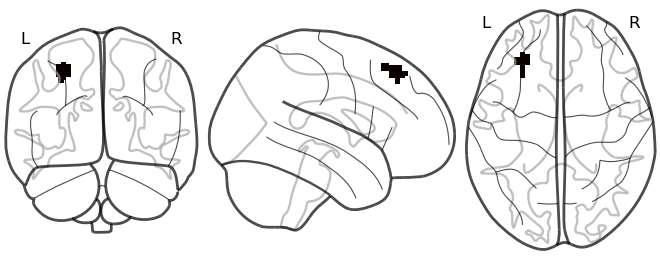
*Sensitivity Analyses*

To ensure that our results were not driven by confounding factors, we conducted several sensitivity analyses. First, to ensure that our results were not driven by socioeconomic status (SES), maternal education was included as a model covariate in addition to age, sex, and head motion. Second, our analyses were repeated while excluding participants who were taking psychotropic medication at the time of the scan (or whose medication status was unknown; N=30).

**Results**

*Connectome-wide analyses identify two distinct foci of connectivity related to delay discounting.*

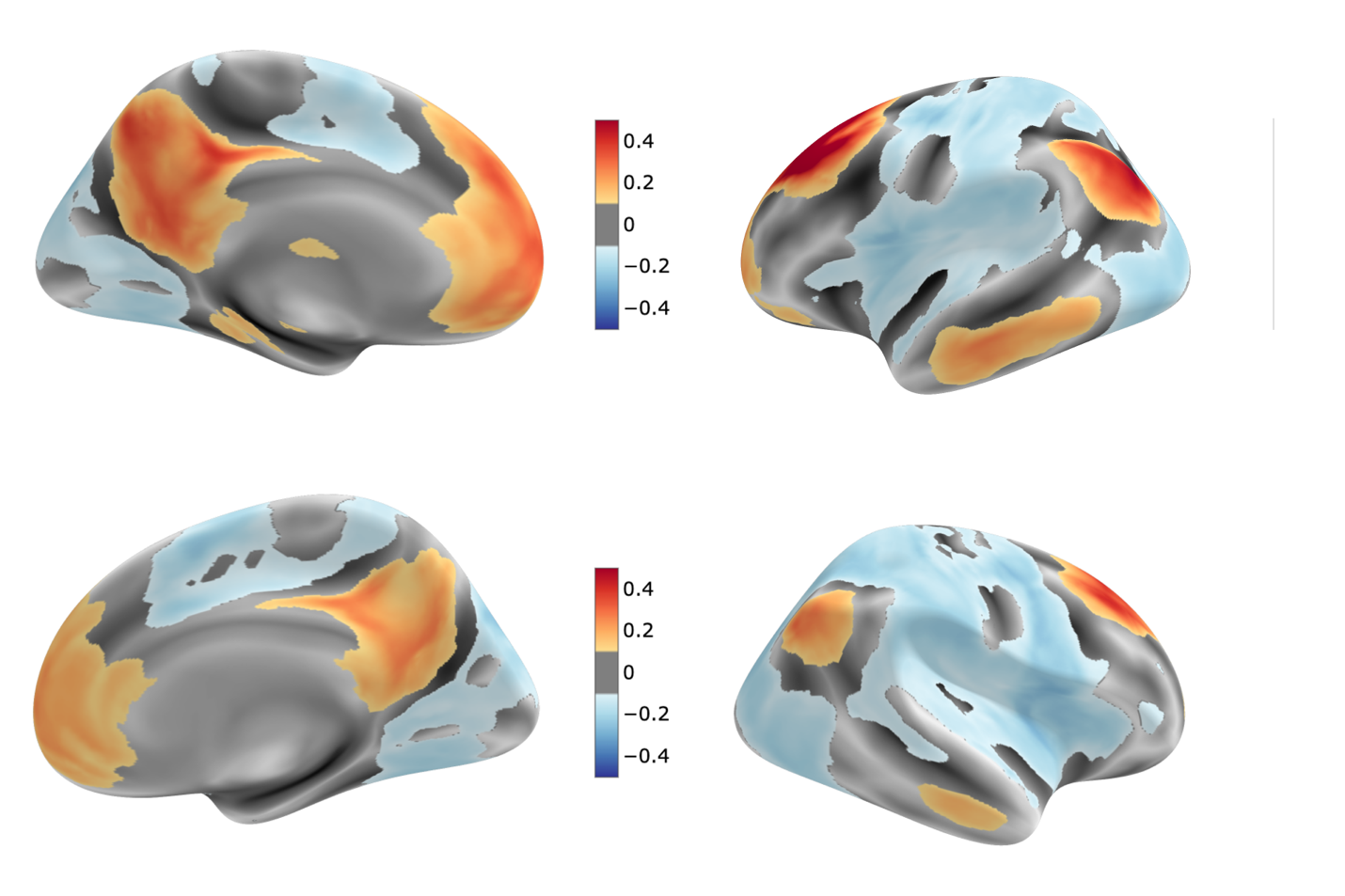
Connectome-wide analyses using MDMR revealed two foci where the multivariate pattern of FC was associated with delay discounting (**Figure 2**). The first cluster was located in the right temporoparietal junction (TPJ: x=48, y=-34, z=24; *k*=57 voxels). The second cluster was located in the left dorsomedial prefrontal cortex (dmPFC; x=-28, y=34, z=48; *k*=137 voxels). Having localized multivariate connectivity patterns associated with delay discounting to these two foci, we next sought to describe the specific connectivity pattern that drove the observed results. Accordingly, we next conducted standard seed-based connectivity analysis using both clusters identified in by MDMR.



**Figure 2**. **Connectome-wide analyses using MDMR reveals two clusters where DD is associated with a multivariate pattern of functional connectivity.** Cortical projection displaying two clusters identified by MDMR following cluster correction. The first cluster is the region at the right temporoparietal junction, and the second cluster is the region at left dorsomedial prefrontal cortex. All clusters corrected for multiple comparisons at z>3.09, p<0.05.

*Impulsive choice is related to individual differences in connectivity between attention and default mode networks*

As a first step, we evaluated the mean pattern of functional connectivity for each of the clusters identified by MDMR. Across the entire sample, the right TPJ cluster was strongly connected with regions in the cingulo-opercular network and somatosensory system. Specifically, these regions included insula and frontal operculum, anterior and middle cingulate cortex, posterior temporal cortex, and frontal pole (**Figure 3A**). In contrast, the left dmPFC seed was strongly connected to other elements of the DMN, including the posterior cingulate cortex, ventromedial prefrontal cortex, and inferior parietal cortex (**Figure 3B) – would add citations for this**.



**Figure 3. Mean connectivity of regions related to DD.** Each cluster identified by CWAS (Figure 2) was used as a seed i to understand the connectivity profiles of the regions related to DD. The right temporal parietal junction (TPJ; **A**) displayed functional connectivity to regions within the cingulo-opercular and somatosensory/sensorimotor networks. In contrast, the left dorsomedial prefrontal cluster (dmPFC; **B,**) had robust connectivity to other elements of the default mode network (DMN).

We next sought to determine how impulsive choice was associated with individual differences in functional connectivity from these seeds identified by MDMR. First examining the TPJ, we found that impulsive choice was associated with greater connectivity between the TPJ and elements of the dorsal attention network (DAN), including lateral occipital cortex, superior parietal lobule, and left? frontal eye field (**Figure 4A**)(cite?). Conversely, we found that greater delay discounting was associated with reduced connectivity between the TPJ and the elements of the DMN, including the ventromedial prefrontal cortex and posterior cingulate (cite?).

Graphical user interface

Description automatically generated with medium confidence

Chart, scatter chart

Description automatically generated

**Figure 4. Follow-up analyses reveal that individual differences in delay discounting are associated with functional connectivity between attention and default mode networks.** Having identified two clusters where multivariate patterns of functional connectivity are related to DD, we conducted seed-based analyses to understand what differences drove these results. Follow-up analyses using the TPJ cluster as a seed (**A**) revealed that greater discount rate was associated with increased connectivity between the TPJ and regions within the dorsal attention network (red), as well as decreased connectivity with major hubs of the default mode network (ventromedial prefrontal cortex and posterior cingulate cortex; blue). Similar follow up analyses from the dorsomedial PFC (**B**) revealed that increased discount rate was associated with increased connectivity with other elements of the default mode network (red) and diminished connectivity with elements of the ventral attention network. Maps represent feature importance driving MDMR rather than independent statistical tests; maps are FDR corrected at z>1.64, P<0.01. Should I be replicating the graphs?

Analysis of the cluster within the left dmPFC (**Figure 4B**) revealed that DD was positively associated with increased connectivity between the dmPFC and elements of DMN including the bilateral posterior cingulate, left orbital frontal cortex, and left lateral temporal cortex. In contrast, impulsive choice was associated with reduced connectivity between the dmPFC and regions within the ventral attention network (VAN), including the anterior insula, anterior cingulate, and TPJ. Together these results emphasize that impulsive choice in adolescence is associated with systematic alterations between the default mode and attention networks such as the DAN and VAN. – Not sure if all the anticorrelated parts were labelled?

*Sensitivity analyses provide broadly convergent results*

As a final step, we conducted two sensitivity analyses to evaluate potentially confounding variables. First, we included maternal education, a proxy of socioeconomic status, as an additional covariate in MDMR analyses. Second, we excluded participants (n=30) who were treated with psychotropic medication at the time of the scan, or whose medication status was not known. For both analyses, the dmPFC cluster identified in our main analysis remained significant. However, the TPJ cluster was no longer significant at our pre-defined significance threshold, due to a reduced cluster extent (i.e., cluster size reduced to 40 voxels above *z* >3.09 compared to 57 voxels in our main analysis). Overall, these results suggest that the dMPFC result is robust to important covariates, while the association of DD and FC from the TPJ cluster may be less specific.

**Discussion**

In this study, we used a data-driven approach to identify multivariate functional connectivity patterns that underlie delay discounting (DD) in a large developmental sample of adolescents and young adults. Our approach identified two distinct regions central to multivariate DD connectivity patterns: right TPJ within the somatosensory? sensorimotor network (SMN), and the left dmPFC? within the DMN – unclear, sounds like it’s within those networks rather than connected within those networks. Further analyses revealed that DD was associated with increased functional connectivity of the TPJ with elements of the DAN (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4107817/) and reduced functional connectivity between the TPJ and regions within the DMN (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3811106/). In contrast, DD was associated with increased functional connectivity of the dmPFC with other regions within the DMN and reduced functional connectivity between the dmPFC and regions within the DAN and cingulo-opercular network (CON). Taken together, these findings suggest that TPJ and dmPFC may be key nodes of a broader pattern of SMN, DMN and DAN connectivity that underlies individual differences in impulsivity during adolescence.

## rTPJ and MFG clusters Figure 2

Our results highlighting the role of the TPJ in DD align with prior literature demonstrating that the rTPJ communicates with other brain regions during intertemporal choices involving future rewards (Soutschek et al., 2020). These findings advance a growing understanding of the role of the rTPJ in functions beyond social processing and the attribution of mental states (refer back to this paper to elaborate: “Thus, the rTPJ appears to be a core node of a network that facilitates delaying gratification by enabling humans to take the perspective of their future selves.

In analogy to how the rTPJ may promote prosocial actions by overcoming a focus on the self [16,17], this view suggests that the rTPJ may reduce delay discounting by overcoming a focus on the present.”

Moreover, transcranial magnetic inhibition of the right TPJ was recently observed to produce steeper rates of discounting for both delayed and social rewards, potentially reflecting a common neurocognitive mechanism facilitating self-controlled and altruistic choices (Soutschek et al., 2016)

In contrast, low discount rates were associated with activity in the medial prefrontal cortex and right temporoparietal junction. This pattern may reflect biological mechanisms underlying behavioral heterogeneity in discount rates. (Neural congruence between intertemporal and interpersonal self-control: Evidence from delay and social discounting (2017))

); it is increasingly evident that the rTPJ also plays a role in the evaluation of future reward outcomes (Pehlivanova et al., 2018). For example, the rTPJ might facilitate delay during intertemporal choice by focusing attention on future events.

dmPFC

1. These results confirmed the important roles of DMPFC and FP in decision impulsivity(Activation patterns of the dorsal medial prefrontal cortex and frontal pole predict individual differences in decision impulsivity (2020))
2. Wang 2014 - that the dorsomedial prefrontal cortex represents the delayed reward size.( https://doi.org/10.1523/JNEUROSCI.0351-14.2014 ): "We found that activities in the posterior portion of the dorsal medial prefrontal cortex (DmPFC) were modulated by the value of immediate options, whereas activities in the adjacent anterior DmPFC were modulated by the subjective value of delayed options.”

## anticorrelation connectivity pattern figure 3

The two identified regions were found to be critical components of two distinct patterns of resting-state brain networks in DD. Seed-based connectivity of the rTPJ revealed high connectivity to somatosensory or sensorimotor (SMN) and CON regions and low connectivity to DMN regions. Contrastingly, seed-based connectivity of dmPFC revealed high functional connectivity to DMN regions and low connectivity to other resting-state networks, including the SMN. Although these networks have been previously associated with delay discounting, these anticorrelated patterns suggest that the rTPJ and dmPFC might serve as hubs in processing reward value during intertemporal choice. Importantly, the DMN is considered to be a “task-negative” network being engaged when an individual is not engaged in a specific goal-oriented task (Raichle et al., 2001; Fox et al., 2005). This pattern stands in contrast to “task-positive” resting-state networks that are engaged in response to specific tasks such as CON (executive control) and DAN (attention), all of which tend to be anticorrelated with the DMN (citation?).

##subsystems correlation with DD figure

## figure 4A rTPJ

In this study, rTPJ-coupled regions were predominantly task-positive control and attentional networks. The relative contributions of these task-positive networks such as SMN, DAN and CON at the time of decision making may influence the likelihood of selecting delayed reward, especially as expected value computation is increasingly cognitively demanding. The positive association between DD and connectivity between rTPJ and regions within DAN … The DAN has been shown to play a role in goal-directed attentional maintenance in situations in which an individual has to decide between immediate but smaller rewards over larger, delayed rewards (Corbetta et al., 2008). The DAN is also thought to be responsible for goal-directed top-down attention maintenance (Hartley and Somerville, 2015; Hansen et al., 2019). Thus, the positive association between rTPJ-DAN connectivity during successful DD could indicate that failures of DD in impulsive youth are a result of failure to fully integrate cognitive control systems when evaluating future outcomes in reward contexts (change acc. to comments). However, decreased connectivity of the rTPJ to DMN regions, including the dmPFC OR vmpfc? and the PCC, was also associated with successful DD. This negative association may stem from the fact that the rTPJ (an SMN/task-positive region) and DMN (task-negative) are functionally anticorrelated (Fox et al., 2005; Jack et al., 2013). We hypothesize that these anticorrelated functional patterns in the brain reflect competing network-level contributions to distinct cognitive domains. The association of DD with reduced connectivity between rTPJ to elements of the DMN may suggest that less DMN-driven cognition is required for intertemporal choice task. Reduced connectivity between TPJ and the DMN can also lead to temporary disengagement which may be imperative for WM (Anticevic et al., 2010).

“… the relationship between TPJ and DMN regions changes as different cognitive demands emerge. Therefore, we explored the relationship between TPJ and the DMN during the encoding and maintenance phases of a WM task.” – COULD BE TRUE FOR DD

## figure 4B ## role of dmPFC (move this first para up to the previous part? Not sure how much this adds)

The intrinsic interconnectivity of brain regions within the DMN is high, and we find that the degree of integration between the dmPFC and the rest of the DMN is important to DD. This is consistent with prior work linking the DMN to core processes of human cognition, such as the integration of cognitive and emotional processing, introspective thinking (Raichle et al., 2001; Gerlach et al., 2014; Vatansever et al., 2017), intertemporal choices, and value computation of various reward outcomes (McClure et al., 2004; Kable and Glimcher, 2007; Blakemore and Robbins, 2012). Specifically, the positive association between DD and increased functional connectivity of the dmPFC with these regions corroborates prior research implicating the necessity of these brain regions to decision-making processes (Li et al., 2013; Chen et al., 2017).

Functional connectivity of the dmPFC (a hub of the DMN) with regions within the DAN and CON networks was found to be negatively associated with DD. The functional roles of the DAN and COn are closely related. The CON and DAN networks are thought to be functionally involved in reallocating attentional resources (Sadaghiani and D’Esposito, 2015) and dynamically switching between other brain networks. In this context, functional connectivity between regions of the DMN, DAN, and CON network may reflect dynamic switching between large-scale networks during decision making and attention.

Limitations

Soon – Bailey et al

~~This preference for immediate reward is a sign of high impulsivity which is usually common in adolescence(O’Brien et al., 2011; Hansen et al., 2019)~~

1. Mechanisms underlying DD, but not necessarily impulsive decision making (this would call construct validity into question)
2. Correlational, not causational
3. Various results across such studies – delay discounting can be used in multiple ways (cite some studies) – difficult to generalize
4. First, examining whole-brain connectivity as we have done here may decrease sensitivity to highly localized sets of connections that relate to a phenotype. (Shehzad et al)
5. Third, because some of the identified neural networks play additional functional roles (e.g., general cognitive abilities for the frontoparietal network; Shamosh and Gray, 2008), the functional significance of these networks in the DDT is unclear. (Resting-State Functional Connectivity Predicts Impulsivity in Economic Decision-Making (2013))

Conclusions

* Hold off for now

Citations – fix after editingg

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