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Dissociable Frontostriatal White Matter Connectivity Underlies Reward and Motor Impulsivity

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Abstract

Dysfunction of cognitive control often leads to impulsive decision-making in clinical and healthy populations. Some research suggests that a generalized cognitive control mechanism underlies the ability to modulate various types of impulsive behavior, while other evidence suggests different forms of impulsivity are dissociable, and rely on distinct neural circuitry. Past research consistently implicates several brain regions, such as the striatum and portions of the prefrontal cortex, in impulsive behavior. However the ventral and dorsal striatum are distinct in regards to function and connectivity. Nascent evidence points to the importance of frontostriatal white matter connectivity in impulsivity, yet it remains unclear whether particular tracts relate to different control behaviors. Here we used probabilistic tractography of diffusion imaging data to relate ventral and dorsal frontostriatal connectivity to reward and motor impulsivity measures. We found a double dissociation such that individual differences in white matter connectivity between the ventral striatum and the ventromedial prefrontal cortex and dorsolateral prefrontal cortex was associated with reward impulsivity, as measured by delay discounting, whereas connectivity between dorsal striatum and supplementary motor area was associated with motor impulsivity, but not vice versa. Our findings suggest that (a) structural connectivity can be associated with a large amount of behavioral variation; (b) different types of impulsivity are driven by dissociable frontostriatal neural circuitry.

Keywords

decision making; impulsivity; reward; ventral striatum; white matter

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Introduction

Self-control and inhibition are executive functions that are hallmarks of rational decision-making. Dysfunction of cognitive control often leads to impulsive behavior, which is symptomatic of disorders such as schizophrenia (Ouzir, 2013), bipolar disorder (Fortgang et al. 2016), drug abuse and addiction (Jentsch & Taylor 1999; Crews & Boettiger, 2009; Washio et al. 2011), pathological gambling (Dixon et al. 2006), and eating disorders (Manwaring et al. 2011; Lilienthal & Weatherly 2013).

Past research has yielded two distinct theories for the basis of such impulsivity. One suggests that a generalized cognitive “braking” mechanism underlies the ability to modulate various types of impulsive behavior (Band & Van Boxtel, 1999). This is supported by work in clinical populations, in which multiple subtypes of impulsivity were associated with a common biological factor: low dopamine D2 receptor function (Jentsch et al. 2014). A contrasting theory posits that multiple cognitive mechanisms underlie attentional, motor, and reward subtypes of impulsivity (Bari et al. 2013). Crucially, there is evidence that each of these different forms of impulsivity relies on distinct neural systems (e.g. Wang et al. 2016 In Press).

Impulsivity for rewards is commonly assayed via intertemporal choice tasks that quantify our propensity to favor larger rewards to smaller ones, and rewards that are delivered sooner rather than later. When reward magnitude and time delay are placed in tension, as they often are in real life, many people prefer a smaller-sooner reward, e.g. \$10 today, to a larger-later reward, e.g. \$15 in a week. In other words, they manifest delay discounting (Odum 2011), whereby they discount the subjective value of a reward if it is only available after a delay. In contrast, motor impulsivity refers to the ability to suppress a prepotent yet inapposite motor response (Chamberlain & Sahakian, 2007). Motor impulsivity is commonly measured with response inhibition tasks such as go/no-go, in which rapid motor responses are required in response to one stimulus, but inhibition of the same motor responses is required in response to a different stimulus (Ruchow et al. 2008).

Both types of impulsivity have been linked to a region of the basal ganglia called the striatum. The striatum is a complex structure that is highly interconnected with the cerebral cortex, projecting in “loops” to executive, motor, and limbic regions of the brain (Alexander et al. 1986; Choi et al. 2012). Research has increasingly parcellated the human striatum into subregions, both based upon cortical projections and psychological function (Pauli et al., 2016). Here we restrict the scope of our analysis to an a priori subset of these fiber pathways, as outlined below. These pathways are by no means exhaustive, and other possible pathways of interest are highlighted in the Discussion.

In cognitive neuroscience research, the striatum is often subdivided into the ventral and dorsal striatum. In non-human primates, the ventral striatum (vSTR) has long been implicated in reward sensitivity (Apicella et al. 1991; Schultz et al. 1992), reward anticipation across a delay (Cardinal et al. 2002) and reward prediction errors (Schultz et al. 1997). Human neuroimaging studies have consistently linked the vSTR to discounting behavior (Gregorios-Pippas et al. 2009; Christakou et al. 2011), with its activation varying

relative to inter-individual discounting rates (Hariri et al. 2006). The dorsal striatum (dSTR), though also implicated in intertemporal choice behavior (e.g. Tanaka et al. 2007) has more often been linked to motor behavior, including a type of motor learning called stimulus-response learning (Packard & Knowlton 2002). The dorsal striatum plays a key role in decision making, potentially through its role in action selection and initiation (Balleine et al. 2007; Cai et al. 2011). Activity in the dorsal striatum has been associated with go/no-go performance in non-human primates (Apicella et al. 1991) as well as in humans (Asahi et al. 2004).

Striatal regions act in concert with portions of the prefrontal cortex (PFC) to modulate impulsive behavior. Prior findings have specifically linked the ventromedial prefrontal cortex (vmPFC) to impulsivity, with some studies relating vmPFC gray matter volume to individual differences in impulsivity (e.g. Matsuo et al. 2009), and others finding associations with delay discounting (Peters & Büchel, 2011). Activity in additional regions of the cortex have been related to inhibition of a motor response, including the dorsolateral prefrontal cortex (dlPFC) and various motor cortices (Kawashima et al. 1996; Humberstone et al. 1997; Konishi et al. 1998; Garavan et al. 1999).

A small but growing literature of diffusion MRI studies such as diffusion tensor imaging (DTI) and probabilistic tractography suggests that individual differences in white matter connectivity correlates with impulsive behavior. For instance, Peper and colleagues (2012) found that white matter connectivity between the entire striatum and the entire PFC correlated with discounting behavior. Similarly, van den Bos and colleagues (2014) reported an association between increased striatal and dlPFC white matter connectivity and lower discounting, i.e. increased patience. In clinical populations, frontostriatal white matter connectivity correlates with go/no-go task performance (Casey et al. 2007) and also of self-reported impulsivity (Hoptman et al. 2004). Together this research suggests that some of the variance in impulsive behavior can be associated with variation in structural connectivity between portions of the frontal lobe and striatum.

Yet, the vSTR and dSTR are distinct in several ways. First, they differ in terms of cytoarchitectonic complexity: the vSTR is more histochemically heterogeneous and contains more cytoarchitectonic irregularities. This heterogeneity is partly the result of ventral striatal neurons higher proclivity for clumping, and partly due to the “intermingling” of medium-sized striatal neurons with larger pallidal neurons (Heimer et al. 2000). This intermixing also contributes to greater histochemical heterogeneity in the ventral striatum (Prensa et al. 2003). Given that the gray matter of the vSTR and dSTR are distinguishable, one might also expect distinct white matter connectivity to other brain regions. If such a distinction exists at the structural level, it is also likely that these white matter differences are borne out behaviorally, as has been shown in related domains (e.g. Leong et al. 2016).

Here, we tested the hypothesis that inter-individual variation in structural connectivity of the dorsal versus ventral striatum differentially relates to performance on tasks that tap into motor and reward impulsivity, respectively. We used probabilistic tractography of diffusion-weighted imaging data of healthy adults to test two hypotheses regarding the human striatum connectivity and impulsivity. First, we hypothesized that inter-individual variability in

structural white matter connectivity from the ventral striatum to areas of cognitive control, the vmPFC and dlPFC, would be associated with reward impulsivity as measured by a delay discounting task. Second, we predicted that structural white matter connectivity between the dorsal striatum and areas of response inhibition, supplementary motor cortex, would correlate with individual differences in motor impulsivity as assayed by go/no-go task performance. Finally, as we hypothesized that these white matter tracts relate to different functions, we sought to demonstrate a double dissociation such that the ventral tracts would not be associated with motor impulsivity and dorsal tracts would not correlate with reward impulsivity.

Methods and Materials

Participants

We recruited thirty participants from Temple University. All participants completed the behavioral and neuroimaging protocols. Four participants were excluded for failure to follow delay discounting task instructions. Statistical analysis confirmed that these participants had k values three standard deviations from the mean. The remaining twenty-six participants (12 female, $M = 20.10$, range 18 to 24) were used in subsequent analyses. All participants were native English speakers, right-handed (as ascertained by self-report), and had normal or corrected-to-normal vision. Participants had no history of psychological or neurological disorders and no MRI contraindications as ascertained by self-report. Participants were given flat rate compensation for their participation. Informed consent was obtained in accordance with the guidelines set forth by the Institutional Review Board of Temple University.

Study Design and Materials

All participants completed two tasks: delay discounting and go/no-go, described below.

Delay discounting task

The delay discounting task is identical to that used in O'Brien et al. (2011). Over a series of trials, participants are asked whether they would prefer a hypothetical larger, delayed reward or a smaller, immediate reward. Use of hypothetical choices in a delay discounting task has been shown to yield no systematic difference in discount rate compared to real choices, suggesting that hypothetical rewards are valid proxy for real rewards. In all trials, the value of the delayed reward is kept constant, at \$1000 (USD), and each trial begins with a starting value of the immediate reward value of either \$200, \$500, or \$800, randomly determined for each separate block. Each participant completes six separate trial blocks, one for each of six time delay intervals. If the immediate reward is chosen on a given trial, the next question will present an immediate reward halfway between the prior immediate reward value and zero (i.e. a lower amount). If the delayed reward is chosen, the next question is an immediate reward midway between the prior immediate reward and \$1000. This narrowing pattern continues, with all subsequent questions presenting immediate values midway between the reward rejected and the previously rejected higher or lower reward, until participants' choices converged on an indifference point (Ohmura et al. 2006), i.e. the value subjectively equivalent to the discounted delayed reward if the value were offered immediately (Green et

al. 2005). The individual's indifference point at each delay is then used to calculate their discount rate.

The discount rate (k) is an index of the degree to which an individual devalues delayed rewards as a function of the length of delay to receipt of the delayed reward (O'Brien et al. 2011; Ohmura et al. 2006). This k value is calculated using the hyperbolic function:

$$V = A / (1 + kD)$$

where V is the subjective value of the delayed reward (indifference point), A is the actual value of the delayed reward (in this case, always \$1000), D is the time delay interval, and k is the discount rate. Higher discount rates indicate increased devaluation of delayed rewards in favor of immediate rewards. In other words, higher discounting indicates higher reward impulsivity. We calculated participant's discount rates at each time delay and then averaged these rates to create a composite measure of discount rate for each participant.

Go/no-go

The go/no-go task assesses response inhibition abilities (Rubia et al. 2001). Participants focus on a central fixation cross while random letters are presented sequentially in the center of the screen. For go-trials, participants are instructed to press the space bar as quickly as possible whenever they see a letter appear on the screen. Conversely, for no-go trials in which the letter "X" appears on the screen, participants are told to withhold their response. The task consists of a total of 128 trials: 103 go trials and 25 pseudo-randomly interleaved no-go trials. Task performance is assessed by subtracting the normalized false alarm rate from the normalized hit rate in order to calculate a measure of discrimination sensitivity, d' . Higher d' indicates better performance and lower motor impulsivity.

Image Acquisition

MRI scanning was conducted at Temple University Hospital on a 3.0 T Siemens Verio scanner (Erlangen, Germany) using a conventional 12-channel phased-array head coil. DWI data were collected using a diffusion-weighted echo-planar imaging (EPI) sequence covering the whole brain. Imaging parameters were as follows: 55 axial slices, 2.5 mm slice thickness, Repetition Time (TR) = 9,900 ms, Echo Time (TE) = 95 ms, Field of View (FOV) = 240 mm², b-values of 0 and 1,000 s/mm², in 64 non-collinear diffusion directions. In addition to diffusion-weighted images, high-resolution anatomical images (T1-weighted 3D MPRAGE) were also acquired using the following parameters: 160 axial slices, 1 mm slice thickness, TR = 1,900 ms, TE = 2.93 ms, inversion time = 900 ms, flip angle = 9°, FOV = 256 mm².

Selection of Regions of Interest

For the seed regions, the vSTR and dSTR, lateralized masks were derived from the FSL Oxford-Imanova Probabilistic Connectivity Striatal Atlas (Tziortzi et al. 2013). In the 3-component atlas, the striatum is divided into limbic, sensorimotor and executive regions, corresponding approximately to ventral, dorsal, and medial striatum, respectively. We used the sensorimotor mask as our dSTR seed in this study. The executive and limbic masks

partially overlap in this atlas. To ensure maximal separation of our ventral and dorsal regions, we created our vSTR seed by subtracting the executive mask from the limbic mask, effectively excluding the more medial portion of the striatum. For the vmPFC, we used a normalized region of interest (ROI) from Bartra et al. (2013) and split it into left and right ROIs by subtracting a mask of the contralateral hemisphere. For the dlPFC, lateralized masks were constructed via Sallet Dorsal Frontal Connectivity Atlas (Sallet et al. 2013) using the cluster masks for Brodmann's areas 46 and 9. For motor ROIs, the Wake Forest Pick Atlas was used to create lateralized supplementary motor area (SMA) masks (Lancaster et al. 2000; Tzourio-Mazoyer et al. 2002; Maldjian et al. 2003) in SPM (Wellcome Trust Centre for Neuroimaging, University College, London). Seed and target ROIs are shown in Figure 1.

DWI Pre-Processing and Analysis

Diffusion-weighted images were pre-processed to correct for eddy currents and participant motion using an affine registration model. The b-vector matrix was adjusted based on rigid body registration, ensuring a valid computation of the tensor variables. Non-brain tissue was removed using an automated brain extraction tool (BET), and a least squares diffusion tensor fitting model was then applied to the data. All pre-processing was performed using FSL (Smith et al. 2004).

DWI tractography models the anisotropic movement of water molecules in restricted compartments, such as axons, to investigate white matter connectivity. Virtual reconstruction of the underlying tracts can be obtained from diffusion data, allowing for the assessment of specific white matter fasciculi, and their associated diffusion properties. In this study, we are particularly interested in specific white matter pathways. As such, we employed “seeded” tractography, with the dorsal and ventral striatum as seed regions—the starting locations for subsequent white matter tractography.

Seed and target ROIs were warped into subjects' native anatomical space, and subsequent tractography analyses were also performed in native space. Results were output in Montreal Neurological Institute (MNI) standard space according to transformation parameters. To achieve this, each participant's fractional anisotropy image was registered to an MNI template via a linear warping algorithm (Jenkinson et al., 2002). These transformation parameters were then used as a conversion matrix to transform from DWI to MNI space, and then inverted to allow for the reverse transformation. We conducted probabilistic tractography using the FDT Toolbox with a partial volume model, and up to two fiber directions in each voxel. Probabilistic tractography with dual-fiber models better account for crossing fibers and therefore yield more reliable results compared with single-fiber models (Behrens et al. 2007).

Five thousand sample tracts were generated from each voxel in the seed masks, either the ventral or dorsal striatum. For vSTR-seeded tractography, an exclusion mask was placed on the dSTR, and vice versa for dSTR-seeded tractography. This was done to exclude white matter connectivity to the target ROI from the striatum seed of non-interest for a particular tractography. We visually inspected tractography maps to ensure tractography was successful and acceptable for further analysis. All probabilistic tractography analyses were

conducted separately for each hemisphere such that for left hemisphere tractographies, the right hemisphere was excluded, and vice versa. Specifically, lateralized reconstructions were performed to isolate streamlines connecting the ventral/dorsal striatum to the vmPFC, dlPFC, and supplementary motor cortex, excluding the seed of non-interest as previously mentioned.

The resulting output of probabilistic tractography is the number of probabilistic connections, or “streamlines”, between the seed and target and from the target to the seed. Streamlines have previously been used to characterize the connective strength between two brain regions (e.g. van den Bos et al. 2014). Warping seed and target masks from standard to native space creates inter-individual variability in the size of the ROI, which could skew the relative number of connective streamlines. To correct for this, we divided the number of streamlines from seed to target by the number of non-voxels in the native space seed region, and divided the number of streamlines from target to seed by the number of non-zero voxels in the native space target region. Last, as the directionality between the regions in question is unknown, we averaged the afferent and efferent streamlines to create a composite measure of connectivity between the seed and target ROIs.

Results

Behavioral results

We assumed a hyperbolic delay discounting function, and calculated each participant’s best-fitting discount rate k ($M=0.02$, $k_{\min}=0.001$ and $k_{\max}=0.082$). Go/no-go d' values ($M=2.97$, $d'_{\min}=1.75$ and $d'_{\max}=3.99$) were normally distributed (Figure 2). Since the delay discounting k values (Figure 2) were not normally distributed, we log transformed the discounting rates, and used these values in subsequent analyses. Consistent with similar studies (e.g. van den Bos et al. 2015), go/no-go and discounting values were not significantly correlated, $r(24)=.07$, $R^2=.01$, $p=.73$. A bivariate Pearson’s correlation revealed that discounting rate varied with age, $r(24)=.48$, $R^2=.23$, $p<.05$, even in our relatively restricted sample. Go/no-go performance did not vary according to age, $r(24)=.11$, $R^2=.01$, $p=.61$. Therefore, we included age in subsequent analyses involving delay discounting, but not for go/no-go behavior. Independent sample t-tests showed that gender was not significantly associated with any behavioral or connectivity measure (all $p>.10$) and therefore was not included in any subsequent analyses. Due to the lack of correlation between discounting and go/no-go performance, we sought to understand if these two variables were associated with dissociable structural connectivity in the brain.

Brain-behavior Results

To examine the relationship between individual differences in delay discounting behavior and frontostriatal white matter connectivity, we built a series of multiple linear regression models. In each model, both the hypothesized striatal tract of interest, and the control tract were included. As age significantly correlated with discounting, age was also included in all discounting models. As mentioned above, age was not correlated with go/no-go behavior, and was therefore not included in any linear regression models relating to go/no-go.

Linear regression analyses were used to examine our hypothesis that white matter connectivity between the vSTR and vmPFC is associated with delay discounting performance, while controlling for connectivity from the dSTR and age. In the left hemisphere, there was a significant relationship between vSTR-vmPFC connectivity, delay discounting, and age, while controlling for dSTR-vmPFC connectivity. The overall regression model was significant ($F(1,23) = 5.04$, $p < .01$, adjusted $R^2 = .41$), such that both left vSTR-vmPFC connectivity ($\beta = .46$ $t(23) = 2.54$, $p < .05$) and age ($\beta = .47$ $t(23) = 2.82$, $p < .01$) was associated with discounting rate, while dSTR-vmPFC did not ($\beta = -.18$ $t(23) = -.99$, $p = .34$). That is, higher vSTR-vmPFC connectivity in the left hemisphere was associated with steeper discounting. In the right hemisphere, the variables mentioned above produced a non-significant model, with neither ventral ($\beta = .04$ $t(23) = .22$, $p = .83$), nor dorsal ($\beta = .21$ $t(23) = 1.16$, $p = .26$) white matter fibers to the vmPFC in the right hemisphere significantly associated with discounting. There was no significant association between ventral/dorsal white matter connectivity and the vmPFC and go/no-go performance in either hemisphere (all $p > .25$).

Next, regression analyses were used to examine the relationship between dorsal striatum white matter connectivity and go/no-go performance. For the left, the overall regression model was significant ($F(1,24) = 3.11$, $p < .05$, adjusted $R^2 = .17$), such that left dSTR to left SMA connectivity ($\beta = -.43$ $t(24) = 2.76$, $p < .01$) was associated with go/no-go performance. That is, higher dSTR-SMA connectivity in the left hemisphere was associated with lower go/no-go performance. Right-lateralized tractography between the same regions was not significantly correlated with go/no-go. In contrast, neither left nor right vSTR-SMA connectivity was associated with go/no-go performance (both $p > .70$).

Last, we examined the relationship between striatum-dlPFC connectivity and our impulsivity measures. Beginning with the vSTR, neither left nor right vSTR-dlPFC connectivity was associated with delay discounting rate ($p > .30$) or go/no-go ($p > .10$). Turning to the dSTR, for the left dSTR, the overall regression model was significant ($F(1,23) = 4.58$, $p < .01$, adjusted $R^2 = .32$), such that left dSTR to left dlPFC connectivity ($\beta = .41$ $t(23) = 2.29$, $p < .05$), as well as age ($\beta = -.61$ $t(23) = 3.47$, $p < .01$) was associated with discounting rate, but not go/no-go performance ($p = .85$). For the right dorsal striatum, the overall regression model was significant ($F(1,23) = 6.64$, $p < .01$, adjusted $R^2 = .40$), such that right dSTR to right dlPFC connectivity ($\beta = .53$ $t(23) = 3.04$, $p < .01$) and age ($\beta = .64$ $t(23) = 3.79$, $p < .001$) was associated with discounting rate, but not go/no-go performance ($p = .40$). That is, both higher left and right dSTR-dlPFC connectivity was associated with steeper discounting rates.

Given we created multiple models, we then corrected our model findings for multiple comparisons. To this end, we subjected the significance of each model to Benjamini-Hochberg correction (Benjamini & Hochberg, 1995). A summary of each model and the overall corrected significance values are depicted in Table 1.

Discussion

Each day we make thousands of decisions, some carefully considered, others impulsive. There has been debate as to whether a generalized cognitive control (Band & van Boxtel,

1999) or biological (Jentsch et al. 2014) mechanism underlies the ability to modulate all impulsive behaviors or if multiple cognitive and neural processes underlie various subtypes of impulsivity (Bari & Robbins, 2013). The present investigation sought to examine whether individual differences in structural connectivity of the ventral and dorsal striatum is associated with performance on tasks tapping into reward and motor impulsivity, respectively. To capture reward impulsivity, we measured individuals' rate of delay discounting, a ubiquitous (Kirby et al. 2002; Perry et al. 2005) phenomenon associated with substance abuse (Brody et al. 2014), pathological gambling (Dixon et al. 2006), and eating disorders (Manwaring et al. 2011). To assay response inhibition, we measured go/no-go performance, which is considered a marker of underlying genetic and neurological risk factor for several disorders, such as attention deficit hyperactivity disorder (Wilson et al. 2011) and schizophrenia (Heerey et al. 2007).

We found that, in our truncated college-age sample, that discounting increased with age. The direction of this relationship is at variance with a corpus of literature suggesting that discounting tends to decrease with age (e.g. Green et al. 1994). It is possible this difference is due to unmeasured participant characteristics such as future orientation (Steinberg et al. 2009) and drinking behavior (Smith et al. 2015), both known to affect discounting behavior, and to vary in this cohort. In addition, the decrease in discounting rates is most robust and precipitous during earlier adolescence, with declines attenuating at around 18 (Steinberg et al. 2009). Indeed, this large study found that persons 22 to 25 had numerically higher discounting rates than did 18 to 21 year olds (Figure 4, Steinberg et al. 2009). Though the findings of Steinberg and colleagues were not statistically significant, they are consistent with our results and underscore the possibility that the relationship between age and discounting may not be purely linear across lifespan.

We hypothesized that variability in ventral striatal connectivity to areas of cognitive control, namely the vmPFC and dlPFC, would be associated with reward impulsivity, whereas connectivity between the dorsal striatum and motor areas of response inhibition would be associated with individual differences in motor impulsivity. We also predicted a double dissociation such that the ventral white matter tracts would not be related to motor impulsivity and dorsal tracts would not be related to reward impulsivity. Our first finding was that greater connectivity between the vSTR and vmPFC was associated with higher delay discounting rates, while connectivity between the dSTR and vmPFC did not. That is, higher vSTR-vmPFC connectivity was associated with a decreased ability to delay gratification.

This finding supports, extends, and brings together several lines of research. At a broad scale, our finding corroborates research suggesting that hyperconnectivity among reward regions may underlie dysfunctional impulse control (e.g. Camchong et al. 2011). It is also consistent with research individually linking the vSTR (Christakou et al. 2011; Gregorios-Pippas et al. 2009; Hariri et al. 2006) and the vmPFC with discounting behavior (Cardinal, 2002; Matsuo et al. 2009). It extends previous research demonstrating a relationship between discounting and the structural connectivity of the entire striatum to vmPFC (e.g. Archterberg et al. 2016) by honing in on a specific subregion of the striatum and showing that vSTR-

vmPFC connectivity is likely key for reward-related impulsive behavior. The question then is why would connectivity between these two particular regions drive such impulsivity?

The delay discounting scenario mirrors real-world decisions that require weighing rewards across time, and may involve several cognitive processes. Specifically, the ability to delay gratification may depend partly on episodic future thinking, i.e. the ability to engage in prospective imagery to anticipate the future consequences of present behaviors. Indeed, behavioral research suggests that episodic future thinking reduces delay discounting (Atance & O'Neill, 2001; Suddendorf & Busby, 2005) according to the vividness of the imagery (Peters & Büchel, 2010). In the brain, the vmPFC seems to be key in mediating the impact of episodic future thinking on decisions that involve delay discounting (Benoit et al. 2011), and that entail projecting oneself into the future (D'Argembeau et al. 2008). Our finding supports the importance of the vmPFC in discounting, and indicates that hyperconnectivity between the vSTR and vmPFC may interfere with episodic thinking, thereby exacerbating discounting of future rewards.

Discounting rates were also associated with white matter tracts adjoining the dSTR and dlPFC. There is a sizable literature highlighting the role of the dlPFC in executive control (e.g. Tanji & Hoshi, 2008). Recent DWI research suggests that there is a relationship between striatum-dlPFC connectivity and reward impulsivity, with one study finding greater medial striatum–right dlPFC tract strength associated with less impulsive behavior, i.e., lower discounting rates (van den Bos et al. 2014). This association was replicated and extended by van den Bos and colleagues who found that greater connectivity of medial striatal fibers and the right dlPFC was associated with reduced discounting (van den Bos et al. 2015). In the present study we were interested specifically in a dissociation of ventral and dorsal striatal fibers, and therefore did not include medial striatum in our tractography analyses. We found that increased dSTR-dlPFC connectivity in both hemispheres was associated with increased discounting propensity.

In the context of the aforementioned findings, our results suggest the relationship between frontostriatal connectivity and discounting is complex, and it is unlikely that increased connectivity from every region of the striatum to every frontal region is “better”. To the contrary, the current findings indicate that connections to frontal cortices from the striatum may contribute to either increased or decreased impulsivity, depending upon where along the dorsal-ventral gradient they project. This notion is consistent with previous research (e.g. van den Bos et al. 2014) that has shown higher striatum white matter connectivity is associated with higher impulsivity or lower impulsivity, depending upon the connecting brain region.

Our results support the notion that the cognitive control required to delay rewards involves the dlPFC, and that individual reward impulsivity may be partly dictated by structural connectivity between the dlPFC and the dorsal region of the striatum. This fiber pathway may be particularly important for mediating reward impulsivity, as neither dorsal nor ventral striatum connectivity to the dlPFC was associated with go/no-go performance.

Lastly, we found that white matter tracts between the left dorsal, but not ventral, striatum and SMA was associated with go/no-go performance. Specifically, better performance on the go/no-go task was related to lower connectivity between the dSTR and SMA. Although go/no-go response inhibition tasks have been associated with activation of the SMA (Rubia et al. 2001) and dSTR (Aron et al. 2006), the role of structural connectivity between these regions and impulsivity was previously unexplored. Our results suggest that the structural neural circuitry underlying response inhibition is dissociable from other frontostriatal connections involving other types of impulsivity, and is likely driven partly by hyperconnectivity of the dSTR and the SMA.

Our diffusion MRI findings evince the importance of structural connectivity of specific tracts of the frontostriatal circuit, and raise questions as to whether functional connectivity of this circuit has comparable implications. Consistent with this perspective, one study using both structural and functional connectivity analyses found overlapping frontostriatal connectivity patterns (Jarbo & Verstynen, 2015). Another recent study examined similar brain regions using resting-state functional connectivity, and related this connectivity to analogous discounting and response inhibition tasks (Wang et al. 2016 In Press). Remarkably, their findings closely mirror our own: they reported that resting-state connectivity between the vSTR and vmPFC and frontal pole was associated with delay discounting, whereas pre-SMA connectivity was associated with motor impulsivity. Together with such functional connectivity research, our findings provide converging evidence that reward and motor impulsivity are driven by dissociable frontostriatal neural circuits. More broadly, our findings highlight the role of specific structural connections among brain regions in determining individual variability in complex behaviors such as impulsivity.

Together, this research suggests normative reward-based decision making likely results from an intricate balance of connectivity among the striatum and frontal regions that, if over-or under-connected, can result in suboptimal decision making, or potentially clinical disorders if severely unbalanced.

Limitations

In this study we examined the connectivity of the ventral and dorsal striatum. While our data and techniques did not allow for more segmentation of the striatum, future studies might use functional localizers and further parcellate the striatum on an individual basis. Further, the present study does not rule out the importance of other white matter tracts in impulsive behavior. Although we were able to account for a significant amount of the variance in performance, some variance was unaccounted for in our models. The addition of other behavioral variables, genetic markers, and white matter tracts might account for further variance.

Due to limitations in our sample size, and associated statistical power, we limited our evaluation of striatal connectivity to a subset of frontal target regions. Future studies with larger sample sizes could explore several other frontostriatal tracts that might also be important for individual differences in impulsive decision making behaviors. For instance,

the anterior cingulate cortex (ACC) sends projections to the ventral striatum and caudate nucleus (Haber and Knutson, 2010). This pathway may be important for impulsivity given its hypothesized role in supporting adaptive cognitive control (Shackman et al. 2011). In addition, aside from the dlPFC, other “stopping” regions of the brain such as inferior frontal gyrus (IFG) are known to have projections to the striatum and may therefore also be important for impulsive behavior, as recent research has suggested (e.g. van den Bos et al. 2014).

Other, non-striatal tracts may also relate to impulsive behavior, such as that connecting the vmPFC and hippocampus. We also did not examine any cortical-cortical connectivity, such as connectivity between the SMA and inferior frontal gyrus which may be linked to go/no-go performance (Aron et al. 2007). We urge future researchers to examine the relationship between these, and the many other, potentially-relevant white matter pathways that may contribute to complex impulsive behaviors.

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Highlights

- White matter connectivity associated with distinct impulsivity subtypes
- Ventral striatum-vmPFC connectivity specifically predicts delay discounting
- Dorsal striatum-SMA connectivity particularly predicts go/no-go performance
- Suggests distinct frontostriatal circuitry underlie motor and reward control
- Inter-regional structural connectivity seems key for complex behaviors

Fig 1. Seed and target regions of interest (ROIs) used for probabilistic tractography of diffusion weighted imaging (DWI) data to compute white matter connectivity of specific frontostriatal tracts.

Fig 2.

Top panel, from left to right: distribution of delay discounting k values across participants, arranged in ascending order; visualization of white matter connectivity target for a sample participant; linear regressions of k values and white matter connectivity. Bottom panel, from left to right: go/no-go d' values across participants, arranged in ascending order; visualization of white matter connectivity target from the dorsal striatum to the supplementary motor area for a sample participant; linear regression of go/no-go performance and white matter connectivity. Linear regressions with multiple regressors are plotted as residuals. vmPFC = ventromedial prefrontal cortex; dIPFC = dorsolateral prefrontal cortex; SMA = supplementary motor area; R=right; L=left.

Table 1

The relationship between structural frontostriatal white matter connectivity and reward versus motor impulsivity

	reward impulsivity			motor impulsivity		
	F	β	adjusted R^2	F	β	adjusted R^2
[R] vmPFC model	2.90		.19	1.49		.04
age		.48*				
vSTR		.04			-.15	
dSTR		.21			.33	
[L] vmPFC model	5.04*		.33	.48		-.03
age		.47*				
vSTR		.46*			-.21	
dSTR		-.18			.02	
[R] dlPFC model	6.64*		.40	.59		-.05
age		.64***			-	
vSTR		-.16			-.03	
dSTR		.53**			.22	
[L] dlPFC model	4.58*		.32	0.50		-.04
age		.61**			-	
vSTR		-.10			.20	
dSTR		.41*			.05	
[R] SMA model	2.89		.19	.15		-.11
age		.55**			-	
vSTR		.14			.07	
dSTR		-.21			-.08	
[L] SMA model	2.23		0.13	3.11*		.17
age		.48*			-	
vSTR		.04			.04	
dSTR		-.05			-.43**	

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Linear regression models examining the relationship between reward versus motor impulsivity and striatal white matter connectivity. Predictors were age, and white matter connectivity from either ventral striatum (vSTR) or dorsal striatum (dSTR) to respective target frontal region of interest (ROI). Reward impulsivity signifies logged delay discounting k values. Motor impulsivity signifies go/no-go d' values. vmPFC = ventromedial prefrontal cortex; dlPFC = dorsolateral prefrontal cortex; SMA = supplementary motor area; R=right; L=left. β is the standardized beta coefficient from linear regression. Significance at the model level was corrected using Benjamini–Hochberg false-discovery rate correction for multiple comparisons.

* $p < .05$.
** $p < .01$.
*** $p < .001$.