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Neuroanatomical foundations of delayed reward discounting decision making

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ABSTRACT

Resolving tradeoffs between smaller immediate rewards and larger delayed rewards is ubiquitous in daily life and steep discounting of future rewards is associated with several psychiatric conditions. This form of decision-making is referred to as delayed reward discounting (DRD) and the features of brain structure associated with DRD are not well understood. The current study characterized the relationship between gray matter volume (GMV) and DRD in a sample of 1038 healthy adults (54.7% female) using cortical parcellation, subcortical segmentation, and voxelwise cortical surface-based group analyses. The results indicate that steeper DRD was significantly associated with lower total cortical GMV, but not subcortical GMV. In parcellation analyses, less GMV in 20 discrete cortical regions was associated with steeper DRD. Of these regions, only GMV in the middle temporal gyrus (MTG) and entorhinal cortex (EC) were uniquely associated with DRD. Voxelwise surface-based analyses corroborated these findings, again revealing significant associations between steeper DRD and less GMV in the MTG and EC. To inform the roles of MTG and EC in DRD, connectivity analysis of resting state data ($N = 1003$) using seed regions from the structural findings was conducted. This revealed that spontaneous activity in the MTG and EC was correlated with activation in the ventromedial prefrontal cortex, posterior cingulate cortex, and inferior parietal lobule, regions associated with the default mode network, which involves prospection, self-reflective thinking and mental simulation. Furthermore, meta-analytic co-activation analysis using Neurosynth revealed a similar pattern across 11,406 task-fMRI studies. Collectively, these findings provide robust evidence that morphometric characteristics of the temporal lobe are associated with DRD preferences and suggest it may be because of their role in mental activities in common with default mode activity.

1. Introduction

Delayed reward discounting (DRD) refers to a person's preferences for smaller immediate rewards versus larger delayed rewards (i.e., how much a reward is discounted by virtue of its delay in time) (Bickel and Marsch, 2001; Madden and Bickel, 2009). Steep discounting of future rewards is considered a form of impulsivity and has been associated with a variety of different behaviors in normative samples, such as credit card debt (Meier and Sprenger, 2010) and completing regular health screenings (Bradford, 2010). Furthermore, precipitous DRD has been consistently associated with psychiatric disorders such as substance use disorders, gambling disorder, and attention deficit hyperactivity disorder (Amlung et al., 2016b; Jackson and MacKillop, 2016; MacKillop et al., 2011; Reynolds, 2006).

Two fMRI meta-analyses suggest that neural networks involved in cognitive control (e.g., dorsolateral prefrontal cortex, anterior cingulate cortex), valuation of reward (e.g., ventral striatum, orbitofrontal cortex, insula, ventral tegmental area), and self-reflective and future oriented thought (e.g., medial prefrontal cortex, posterior cingulate, temporoparietal junction, lateral and medial temporal lobe; referred to as the default mode network (DMN)) are activated by completing DRD tasks (Carter et al., 2010; Wesley and Bickel, 2014). However, in contrast to

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the relatively numerous fMRI studies on DRD, there have been surprisingly few studies on the relationship of brain structure with DRD. One modestly-sized study reported that DRD was associated with GMV in the ventromedial prefrontal cortex, the anterior cingulate, and the ventral striatum (Cho et al., 2013). This latter association was reported also in a subsequent study investigating only subcortical regions of the brain (Tschernegg et al., 2015). However, two other studies both found associations with the lateral prefrontal cortex, but not the medial prefrontal cortex (Bjork et al., 2009; Mohammadi et al., 2015). The largest study to date found DRD to be associated with GMV in the frontal pole, dorsolateral prefrontal cortex, medial orbitofrontal cortex, parahippocampal gyrus, striatum, temporal pole, precuneus, and precentral gyrus (Wang et al., 2016). Collectively, these initial studies suggest the brain regions in which structure is associated with DRD are those involved in subjective reward valuation (striatum, insula), self-reflective and prospective thought (DMN; medial frontal cortex, posterior cingulate, lateral temporal lobe), and cognitive control (dorsolateral frontal cortex, anterior cingulate cortex).

However, there are a number of inconsistencies across studies and limitations to the literature in general. To start, there has been limited investigation of whether aggregated neurostructural indices, such as total cortical or total subcortical GMV, are related to DRD. Instead, most studies have exclusively focused on *a priori* brain regions that are based on functional magnetic resonance imaging (fMRI) studies and do not consider the whole brain. This means that there may be other regions that are as important (or more) but are missed. In addition, because of high levels of correlation among cortical regions, *a priori* regions may be artifactually implicated because of interdependence with other unexamined regions, creating false positives. Additionally, the majority of previous studies have only investigated regions defined by an atlas, meaning that there may be relationships of brain structure and DRD that don't fit neatly within these frameworks. Finally, the vast majority of studies to date have been relatively small. Given the increasing acceptance of the potential pitfalls of small sample sized neuroimaging studies (Button et al., 2013), there is clearly a need to address these issues and systematically examine the morphometric correlates of DRD.

The goal of the current study was address a number of these limitations in a large cohort of healthy adults ($N = 1038$). Using data from the Human Connectome Project (Van Essen et al., 2013a) and a method that models boundaries between gray and white matter throughout the brain, we employed two strategies to characterize the relationship between GMV and DRD. The first strategy used cortical parcellation and subcortical segmentation, first examining total cortical and subcortical GMV in relation to DRD and then exploring neurostructural regions defined by the Desikan atlas (Desikan et al., 2006), which putatively reflect discrete areas of structural specialization. The second strategy used a voxelwise cortical surface analysis to test associations between GMV in individual voxels and DRD. The two strategies were considered complementary, as the cortical parcellation/subcortical segmentation approach emphasizes regional specialization, whereas the voxelwise approach is atheoretical and makes no assumptions about discrete structural subunits. Together, the two strategies balance the respective benefits and costs, and permit identifying both converging and diverging findings across methodologies. In addition to these primary aims, two follow-up strategies were used to inform the roles of the implicated regions: examination of the patterns of functional connectivity during resting state and generation of a co-activation meta-analysis from other fMRI studies.

2. Results

2.1. Cortical parcellation and subcortical segmentation analyses

In all instances of significant associations between gray matter volume (GMV) and mean area under the curve for both discounting tasks (mAUC, the primary metric of DRD used; see Methods, section 4.2; note that smaller AUC reflects more impulsive DRD), the relationship between GMV and AUC was positive, indicating that higher levels of GMV were associated with less steep DRD (i.e., more AUC, lower impulsivity). Partial correlations, incorporating demographic covariates, between total cortical gray and total subcortical GMV with mAUC indicated that mAUC was associated with total cortical GMV ($r = 0.124$, $p = 6E\text{-}5$; scatterplot in SI Fig. 1), but not total subcortical GMV ($r = -0.010$, $p = 0.748$). To confirm the lack of association between subcortical GMV and mAUC extended to individual regions (i.e., prevent type II error), we also tested the association of GMV with mAUC in each subcortical region using partial correlations without multiple comparison correction (SI Table 1). No significant associations were found between mAUC and any subcortical regions (all raw/uncorrected p-values > 0.05).

For completeness, when these analyses were completed with the two individual indices of DRD, area under the curve for $200 (AUC200) and area under the curve for $40,000 (AUC40K), the same general results were found. Both AUC200 and AUC40K were associated with total cortical GMV ($ps \leq 0.001$) and neither was associated with total subcortical GMV ($ps > 0.05$). Additionally, neither AUC200 nor AUC40K were associated with any individual subcortical region (all p-values > 0.05).

Significant partial correlations between cortical parcellation regions and mAUC following FDR correction are listed in Table 1 (associations between all regions and mAUC are listed in SI Table 2). AUC200 and AUC40K were associated with similar regions; regions associated with these indices and associated statistics can be found in SI Table 3. Effect sizes were slightly larger for AUC200 though the same general pattern of regions emerged as significant in both analyses.

In order to determine which regions contributed uniquely to DRD, regression analysis was completed for significant regions in partial correlations. Specifically, regions surviving FDR correction were added to a single regression model of age, sex, income, and intracranial volume to identify regions that were uniquely associated with mAUC. Regions were entered simultaneously and those uniquely predicting mAUC were retained. To evaluate the risk for multicollinearity within the regression models, bivariate correlations were conducted on the five sets of regions which were bilaterally related to mAUC (i.e., bilateral MTG, EC, precentral gyrus, inferior temporal gyrus, lateral orbitofrontal cortex). These revealed large and significant associations between right and left hemisphere in these regions ($rs = 0.57\text{-}0.86$, $ps < 0.001$; exact correlations reported in SI Table 4). As a result, bilateral regions were consolidated (i.e., summed) to avoid multicollinearity (the consolidated regions are henceforth referred to as bilateral [region name]).

In the regression, only bilateral MTG and bilateral EC were uniquely

Table 1
Partial correlations of a gray matter volume in segmented regions (based on Desikan atlas) with area under the curve controlling for gender, age, income, and total intracranial volume. Only regions with significant p-values after FDR are included (p < 0.05).

Rank	Hemi	Region	*R*	*p*
1	L	Entorhinal Cortex	0.151	1E-7
2	R	Middle Temporal Gyrus	0.141	1E-6
3	L	Middle Temporal Gyrus	0.140	1E-6
4	R	Entorhinal Cortex	0.125	.1E-5
5	R	Fusiform Gyrus	0.107	0.001
6	L	Lateral Occipital Cortex	0.101	0.001
7	R	Inferior Temporal Gyrus	0.098	0.002
8	L	Precentral Gyrus	0.098	0.002
9	L	Postcentral Gyrus	0.095	0.002
10	L	Precuneus	0.094	0.003
11	L	Inferior Temporal Gyrus	0.089	0.004
12	R	Banks of Superior Temporal Sulcus	0.087	0.005
13	L	Lateral Orbitofrontal Cortex	0.087	0.005
14	R	Lateral Orbitofrontal Cortex	0.086	0.006
15	L	Insula	0.083	0.008
16	L	Transverse Temporal Cortex	0.082	0.008
17	R	Superior Frontal Gyrus	0.080	0.010
18	L	Temporal Pole	0.079	0.011
19	R	Parahippocampal Gyrus	0.077	0.014
20	R	Precentral Gyrus	0.075	0.016