A meta-analysis of neural systems underlying delay discounting: implications for transdiagnostic research

Min Kang Souther[1]*

Bema Boateng[1]

Joseph W. Kable[1]

[1] Department of Psychology, University of Pennsylvania

*Corresponding author:
Min Kang Souther, MA
Department of Psychology
University of Pennsylvania
3700 Hamilton Walk
Philadelphia, PA 19104
minskang@sas.upenn.edu

ABSTRACT

The National Institute of Mental Health launched the Research Domain Criteria (RDoC) initiative to identify common biological mechanisms underlying mental disorders. A central challenge for this approach is to identify reliable biobehavioral paradigms that engage specific neural circuits implicated across psychiatric disorders. Delay discounting paradigms have been proposed as a promising candidate because both excessive and insufficient tendency to discount future rewards have been reported across a wide range of diagnoses. Because delay discounting involves multiple facets of neurocognitive functions, identifying specific neural systems engaged during the task can inform ongoing efforts in clinical neuroscience to link neural patterns to a core symptom dimension. To this end, we conducted a meta-analysis of 72 fMRI studies of delay discounting by common analytic approaches (contrasts) to test the predictions of commonly proposed mechanisms underlying the decision-making process. Despite being widely used in previous studies, comparing impulsive and patient choices did not reveal any reliable clustering of effects. Our results instead revealed that the subjective value, magnitude, and delay contrasts reliably engage the valuation network, with the subjective value contrast eliciting more widespread activation. Furthermore, both the difficulty and task contrasts engage the frontoparietal network. Taken together, our findings suggest that both reward valuation and action selection are important but do not fully explain impulsive versus patient choices. Taken together, these results provide further support that delay discounting task is a promising measure of reward valuation that reliably activates the valuation network. In addition, we discuss implications for analytic strategies for future studies in clinical neuroscience.

In 2009, the National Institute of Mental Health launched the Research Domain Criteria (RDoC) initiative to identify common biological mechanisms for understanding mental disorders[1]. After over a decade of research, reliability remains a central challenge for identifying biobehavioral measures that provide novel insights into the core neurocognitive features exhibited across disorders[2]. Delay discounting, or the tendency to devalue rewards that are distant in the future, has been proposed as a promising candidate paradigm for shared reward-related changes across diagnostic populations[3]. Currently categorized as a subconstruct of reward valuation under positive valence systems, delay discounting has been implicated in a wide range of psychiatric disorders, as both excessive discounting (e.g., substance use disorder, depression, schizophrenia, binge eating disorder) and insufficient discounting (e.g., anorexia) can be highly maladaptive[4,5]. In addition to this dimensional feature that cuts across diagnoses, delay discounting has been shown to be a strong prognostic indicator of treatment response and relapse[6,7], and can be modified using pharmacological[8–10], neural[11], and behavioral[12,13] interventions, which demonstrates its potential for clinical utility. Coupled with its high test-retest reliability[14] and evidence for genetic basis[15,16], delay discounting indeed has many appealing features as a transdiagnostic construct. Moreover, delay discounting is thought to engage multiple key neurocognitive processes that are relevant to many psychiatric disorders, such as impulsivity, self-regulation, and valuation[17]. Given the multifaceted nature of neurocognitive processes likely engaged in this task, previous research has implemented a wide range of analytic approaches to neuroimaging analysis. Therefore, systematically evaluating the reliability of neural systems hypothesized to underlie these facets can provide important insights for future transdiagnostic research.

A prominent hypothesis for neural mechanisms underlying maladaptive decision-making across disorders is the Competing Neurobehavioral Decision Systems (CNDS) model[17]. This account draws upon one of the first neuroimaging studies of delay discounting that identified two separate neural systems in the healthy brain, one for impulsive, emotional choices that biases toward immediate reward and another that rationally weighs both options[18]. Therefore, the CNDS model posits that impulsive choices are driven by heightened sensitivity to bottom-up reward signals in the limbic areas in response to rewards that are available sooner. On the other hand, hyperactivation of the top-down inhibitory control signals in the frontal cognitive regions can override this sensitivity, leading to more patient choices. Taken together, both excessive and insufficient discounting can arise when competition between the bottom-up reward signals and top-down inhibitory signals is not balanced. Indeed, evidence consistent with this model has been reported across disorders. For one, patients with anorexia nervosa showed hyperactivations in the dorsal cognitive regions, whereas those with bulimia nervosa showed reduced activations during reward processing[19]. This framework has become instrumental for subsequent clinical neuroscience research, as numerous studies have compared neural activity by choice to dissociate the systems underlying impulsivity and self-regulation as a feature of various psychiatric disorders.

Another prominent framework for the neural systems underlying discounting behavior is the single valuation model[20]. Contrary to the CNDS, this hypothesis posits that, instead of two competing neural systems, there is a single system that tracks the subjective value of both options and people make choices that maximize subjective value[20,21]. Subjective value is an estimated value of the future reward after depreciation, which accounts for the objective amount (magnitude), devaluation from the waiting time (delay), and individual differences in one's

preference for the sooner option (discount rate). The rationale is that, within the same neural system, activation increases in response to greater reward amount and simultaneously decreases as the reward becomes more distant in the future. Under this framework, excessive discounting can be driven by exaggerated response to reward amount, heightened aversion to delay, or both. Conversely, insufficient discounting can be driven by a combination of dampened response to reward and reduced sensitivity to delay. This account is consistent with previous meta-analytic work which found that the same regions within the valuation network, consisting of ventral striatum and ventromedial prefrontal cortex (vmPFC), encode both positive and negative effects of subjective value[22]. Disruptions in value signals in either direction can be maladaptive. Reduced value response has been reported across disorders characterized by anhedonia or reduced motivation[23,24], whereas pathological gambling has been linked to exaggerated value signals[25]. Although the single valuation model has been widely examined in decision neuroscience, relatively fewer clinical neuroimaging studies of delay discounting have taken this approach[25,26].

Lastly, an emerging line of research in computational neuroscience calls for a third hypothesis, termed the evidence accumulation model[27]. This model draws upon previous findings of frontoparietal control activations during decision-making that do not require impulse control, such as perceptual judgment tasks[28,29]. This framework is complementary to the single valuation model but speaks to the post-valuation process, in which subjective values are evaluated and translated into decisions. This value accumulation and response selection process is believed to engage activations in the frontoparietal control areas including the dorsolateral prefrontal cortex (dlPFC), with increased activity when two options are highly conflicting. Applying this logic to delay discounting specifically, rewards that are similar in subjective value

are considered to be more conflicting and difficult, and thus would elicit greater activations in these regions. Indeed, increased frontoparietal activations as options become closer in value have been reported in delay discounting[30] and attenuated response to difficult decisions have been reported in patients with methamphetamine dependence[31].

In this study, we performed a series of meta-analyses of fMRI findings derived from analytic strategies grounded in the three prominent neurocognitive models of delay discounting with the goal of identifying the neural systems that are reliable and robust to individual study designs, including the presence of psychiatric diagnoses. Each model makes different predictions about the expected neural patterns. The CNDS model would predict greater fronto-striatal activations when presented with an immediate option ("immediacy bias") and greater frontoparietal activations for difficult decisions. Furthermore, the former regions would be more active for impulsive choices and the latter regions would be more active for patient choices. On the other hand, the single valuation model would predict activations in the valuation network as a function of subjective value, magnitude, and delay, and that these activations would occur in overlapping regions. An extension of this account by the value accumulation model would predict increased frontoparietal activations as a function of choice difficulty, which is consistent with the prediction made by the CNDS model. For each of these analytic contrasts, we conducted a multi-level kernel density analysis to quantify the proportion of studies that report consistent effects in a given anatomical location. We further tested the predictions of the three neurocognitive models by identifying unique and overlapping regions across analytic contrasts. We hope this work will shed light on the core neurocognitive processes underlying delay discounting behavior and contribute to building a strong foundation for future transdiagnostic research in clinical neuroscience.

Methods

Search strategy. Preregistration of the present meta-analysis is available on PROSPERO under protocol CRD42020150691. We conducted a systematic literature search on PubMed and PsycInfo (final search on February 2, 2021). Based on previous meta-analyses of delay discounting[4,32], we used the following search terms, which yielded 392 unique results:

> ((Delay discounting) OR (Temporal discounting) OR (Delay of gratification) OR (Intertemporal choice) OR (time discounting)) AND (fMRI OR functional magnetic resonance imaging)

We also reviewed the reference lists of previously published review articles and searches by frequently occurring authors (i.e., 10 or more unique articles in the initial search results), which identified 2 additional articles.

Study selection. All articles identified through the above search strategy were evaluated according to the preregistered inclusion/exclusion criteria. For inclusion, the study had to meet the following criteria: (1) English or an English translation is available; (2) human participants with no brain lesions; (3) fMRI data collected while the participants were completing a delay discounting task in the scanner; (4) the task included a delay of at least 1 day and used monetary rewards, regardless of payment contingency; (5) conducted a parametric or categorical contrast analysis across the whole brain; (6) spatial coordinates are available in Talairach or Montreal Neurological Institute (MNI) space, either reported in the manuscript or provided by the corresponding author upon request; and (7) diagnosis of psychiatric disorders can be present. Although existing meta-analyses of self-regulatory decision-making tend to focus on healthy adults or group comparisons[33–35], inclusion of individuals with psychiatric disorders achieves two goals. First, it allows greater variability of the clinical or cognitive constructs in question

(impulsivity, self-regulation, valuation, conflict monitoring, and action planning) and others that may be related to delay discounting. Second, given our ultimate aim to understand specific neural systems engaged during the task to inform its implications for transdiagnostic processes, inclusion of psychopathology without regard to specific diagnoses seemed critical. We excluded studies that (1) were not a primary source; (2) used non-monetary rewards; (3) had pharmacological manipulation unless they report effects in the placebo group; (4) resting-state or volumetric analyses; (5) connectivity and multi-voxel pattern analyses; (6) overlapping samples with another included study. In the event of overlapping samples, we included the largest sample. To ensure inclusion criteria are standard and to limit bias, all studies were reviewed using Rayyan (https://rayyan.qcri.org) by at least two independent reviewers (MSK and JWK, MSK and BB, or all three). The inter-rater reliability was high ($\kappa = 0.86$; 93.9% agreement) and all disagreements were discussed and resolved by a consensus decision. A total of 74 studies (1262 foci; 2911 participants) across were included in the quantitative meta-analysis (see Figure 1 for the PRISMA flow diagram; Table 1 for the list of studies and contrasts).

Coding contrasts. Following study selection, we coded the studies into the following contrast categories: general task-related activity (*Task*), choices involving an immediate reward (*Now*), choosing the smaller-sooner reward (*SSR*), choosing the larger-later reward (*LLR*), difficult decisions (*Hard*), easy decisions (*Easy*), subjective value (*SV*), objective amount (*Magnitude*), and length of delay (*Delay*). For *Task*, we included positive effects of comparing the delay discounting task to a fixation or implicit baseline or a control task (e.g., choose left/right, choose larger). We also categorized comparing a subset of the task to baseline (e.g., Hard > baseline) as *Task*. For *Now*, we included comparing trials involving an immediate reward to either all trials or trials involving delayed options only. *SSR* included direct comparisons

between the two choices (positive effects of SSR > LLR or negative effects of LLR > SSR) and *LLR* included the converse. As described earlier, trials in which the two options are closer in subjective value or near the indifference point are considered to be difficult, and studies categorize trials as hard or easy based on the value distance or distance from the indifference point. Therefore, *Hard* included direct comparisons between hard and easy trials (positive effects of Hard > Easy or negative effects of Easy > Hard) whereas *Easy* included the opposite effects. We also coded negative correlations with subjective value difference as *Hard* and positive correlations as *Easy*. For *SV*, we included brain regions showing positive correlation with the discounted value of the delayed reward. Although SV is frequently calculated using hyperbolic discounting[36], we deferred to the judgment of the original authors and reviewers and included all discounted value regressors regardless of how SV was calculated. For *Magnitude*, we included positive correlations with the objective amount of either the LLR or SSR, although all studies in our meta-analytic sample examined the amount of the delayed option except for one study[37], which examined varying amounts of the immediate option while keeping the amount of delayed reward constant throughout the task. For *Delay*, we included brain regions showing reduced activations as the delay increases (i.e., the negative effects of delay or positive effects of inverse delay). For studies that reported the peaks by comparison groups (e.g., young and older adults, healthy and psychopathology), we included them as separate studies rather than selecting a single group. After coding, there were 25 studies (250 foci) in *Task*, 8 (78 foci) in *Now*, 15 (95 foci) in *SSR*, 22 (171 foci) in *LLR*, 16 (112 foci) in *Hard*, 12 (95 foci) in *Easy*, 22 (263 foci) in *SV*, 9 (82 foci) in *Magnitude* and 9 (116 foci) in *Delay*.

Multilevel kernel density analysis. Multilevel kernel density analysis (MKDA) is a widely used technique for coordinate-based meta-analysis to quantify the proportion of studies that

report activation foci within a given radius, with the null hypothesis that foci are located randomly throughout the brain[22,38]. Unlike the traditional meta-analysis that examines the magnitude of effect sizes, here we aimed to identify anatomical locations where an effect is observed consistently across studies that used the same contrast. A previous meta-analysis from our group describes in detail the rationale for refining the MKDA procedure used in the present study[22]. We first converted all peak coordinates from each study into the MNI space using mni2tal to create a binary indicator map (IM)—for interpretability, we assigned 100 for voxels within 10mm of the peaks and 0 for others. We then averaged these maps across studies, resulting in the mean IM ranging from 0-100 that can be interpreted as the percentage of studies reporting a peak within a 10mm radius. For significance testing, we implemented permutation testing in Matlab by simulating a null-hypothesis that foci are randomly distributed, while maintaining the number of studies and number of foci per study. We also applied a cluster-forming threshold for each contrast to improve sensitivity. For each study, we first accounted for the probability of gray matter, where there is a higher probability of observing a positive IM value, by calculating the proportion of voxels with a positive IM value in the top quintile, as indicated by the ICBM tissue probability map (www.loni.ucla.edu/ICBM). These proportions were then treated as independent probabilities to derive the mean IM value that would be exceeded with a probability of less than 0.01 by chance alone. We applied this threshold to the results of each random permutation and recorded the largest cluster mass (sum of all IM values in a given cluster) in the null distribution. We also applied the same threshold to the real data, and the resulting clusters were assigned corrected p-values based on the frequency of equal or larger clusters in the null distribution. All reported results are based on 200 iterations of

permutations (one of which was the observed data) and a threshold of corrected p = 0.05 (one-tailed).

Spatial overlap. Lastly, a series of overlap analyses were performed using the maps obtained from the density analyses described above to reveal activity in unique and shared brain areas. Suprathreshold cluster mass were binarized and summed to create a conjunction map, which was generated and visualized in FSL. The centroid locations for overlapping clusters were identified and the number of contrasts that found significant clustering in a given voxel was examined.

Results

Individual contrasts. Significant clusters for each contrast are presented in Figure 2 and Table 2. We first examined general task-related activations (*Task*), which were significantly clustered in the superior frontal gyrus, inferior frontal gyrus, frontal pole, intraparietal sulcus, and insula. We also observed a cluster in the occipital pole, likely an effect of visual input from the task. We then examined specific contrasts, guided by different neurocognitive models of delay discounting. As previously described, the CNDS model predicts greater activations in the reward regions for choices involving an immediate option (*Now*) and choosing the smaller-sooner reward (*SSR*), as well as distinct, greater frontoparietal activations for difficult choices (*Hard*) and choosing the larger-later reward (*LLR*). Contrary to these predictions, we also observed no areas of significant clustering for *Now* and *SSR*, although the former null finding should be interpreted with caution as there were only 8 studies (78 foci) in this meta-analysis. For *LLR*, significant clustering occurred in the left precentral gyrus. Given this localization in motor cortex, we examined the studies that contributed to this cluster for motor confounds and found that they all instructed participants to choose the LLR using their right middle finger (and

SSR with the right index finger)[39–43]. Both the CNDS and anDDM models predict greater frontoparietal activation for difficult decisions (*Hard*). Significant clusters were found in the dorsomedial prefrontal cortex (dmPFC) and supramarginal gyrus for *Hard*, and in the posterior cingulate cortex (PCC) for *Easy* (i.e., negative effects of choice difficulty). The unitary valuation model predicts activations in the valuation network across *SV*, *Magnitude*, and *Delay* in overlapping regions. The highest meta-analytic statistics (i.e., percentage of studies reporting a peak within 10mm from a given voxel) were found in the striatum for *SV* (63.6%). Additionally, we observed significant clusters in the vmPFC, PCC, and middle temporal gyrus. Foci *Magnitude* were also clustered in the striatum. For negative effects of *Delay*, significant clustering was similarly found in the striatum, as well as medial prefrontal cortex, inferior frontal gyrus, and middle frontal gyrus.

Spatial overlap. We conducted an overlap analysis to identify unique and overlapping neural systems according to different neurocognitive models of delay discounting (Figure 3). Although the CNDS model would predict an overlap between *Now* and *SSR*, and between *Hard* and *LLR*, we did not conduct this follow up analysis because there were no significant clusters in the individual contrasts for *Now*, *SSR*, and *LLR* (other than motor activity). The single valuation model would predict an overlap among *SV*, *Magnitude*, and *Delay*. Consistent with this account, there was a considerable overlap among the clusters in the striatum, although there were no overlapping voxels shared by all three contrasts. The anDDM model would predict activations in the frontoparietal regions distinct from the valuation system. Contrary to this prediction, we found an overlap in the PCC for *SV* and *Easy*. We also explored overlapping clusters between task-related activations and individual contrasts, and found overlapping voxels between *Task* and

Hard in the medial prefrontal cortex, and between *Task* and *Delay* in the dmPFC and the right inferior frontal gyrus.

Discussion

In this paper, we report a series of meta-analyses examining neural effects predicted by existing models of delay discounting. Our first step was to identify general task-related activations, which revealed reliable clusters corresponding with the frontoparietal task control network[44]. We then tested the predictions of the CNDS model, single valuation model, and anDDM by examining individual contrasts. Contrary to the CNDS model, our meta-analysis did not reveal reliable effects of choice (impulsive or patient) at the neural level. Similarly, our results did not find neural effects of an immediacy bias, although this may be in part due to the small number of studies included in our analysis (n=8). Consistent with both the CNDS model and anDDM, our findings revealed significant effects of choice difficulty in the dmPFC, although we did not find clusters in the dlPFC as both models predict. Conversely, easy choices engaged the PCC, a node in the task-negative or default mode network[44], suggesting reduced cognitive engagement when the options have highly distinct values. In line with the unitary valuation model, the most reliable clusters were found throughout the valuation network as a function of subjective value, magnitude, and delay. Although we saw a more widespread engagement of the valuation network for subjective value than magnitude or delay alone, this comparison should be interpreted with caution given the relatively small sample sizes for magnitude and delay. Taken together, these results offer meta-analytic support for the unitary valuation model and anDDM, suggesting that both valuation and value accumulation processes are important for delay discounting. Although our findings may seem to contradict the CNDS model, the initial fMRI study that provided a foundation for this model in fact agrees that regions

activated by the task and value are distinct[18]. However, the interpretation that these networks are differentially associated with impulsive or patient choices is not supported by our work.

Similarly to the results of individual contrasts, our spatial overlap analysis suggests strong support for the unitary valuation model, as subjective value, magnitude, and delay were encoded in overlapping clusters of the striatum. Although not specifically predicted by any of the models of delay discounting, as one might expect, both the task and hard decisions engage the dmPFC, suggesting that difficult decisions require more task engagement. Our exploratory results also revealed overlaps between subjective value and easy choices in the PCC, and between task and delay in the dorsomedial prefrontal cortex. Although this finding was unexpected, we speculate that choices involving either extremely high values or extreme delays are easy and require less task engagement, indicated by deactivation of the task-positive network. Previous a meta-analysis which found similarities in the valuation network and default mode network also speculates a link between valuation and deactivation of task-related activity because value computation inherently involves episodic memory and mental simulations[45].

Since we began this work, a similar meta-analysis comparing a subset of these contrasts in healthy adults was published[33]. Because we included studies across the lifespan and psychiatric diagnoses, we had a much larger meta-analytic sample and therefore increased power to identify more clusters. Despite the differences in both study selection and meta-analytic approach (MKDA vs. activation likelihood estimation[46]), results are largely consistent for the valuation system (*SV*, *Magnitude*), frontoparietal control system (*Hard*), as well as task-related activations. However, our results did not replicate significant clusters previously reported in the

vmPFC for the immediacy bias (*Now*), and inferior frontal gyrus and insula for patient choices (*LLR*). They did not examine the *Delay*, *Easy*, and *SSR* contrasts.

Our ultimate goal for examining reliable neural effects by specific contrasts was to inform future transdiagnostic research. A sizable number of studies included in our quantitative analysis used delay discounting to investigate a wide range of psychiatric disorders and related symptoms – such as substance use[31,41,47–50], pathological gambling[25,26,40,51], obsessive compulsive disorder[39,52], ADHD[39], schizophrenia[53], major depressive disorder[54], obesity[55,56], prediabetics[57], and poor sleepers[58]. Although there were not enough studies for a meaningful quantitative meta-analysis for any given contrast, our work identified neural systems that are reliable across studies and robust to experimental variations, including psychiatric diagnoses. Among the studies with a psychiatric sample included in our analyses, *Task* and *SSR* were the most frequently used contrasts (n=8 for both), whereas only two studies[25,26] examined the *SV* contrast and only one study[54] examined the effects of *Magnitude* and *Delay*. While comparing choices is a logical approach to target neural systems underlying impulsivity, the hypothesis that there are distinct systems associated with impulsive and patient choices is not supported by our work. Based on our findings that the unitary valuation model yielded the most reliable effects, it would be worthwhile for future clinical neuroimaging studies to examine differential effects of magnitude and delay to characterize excessive or insufficient discounting, rather than choices per se.

There are several limitations to consider when interpreting our findings. Although our results suggest neural evidence for value computation and accumulation, neither account can yet fully explain how they ultimately translate to individual choices. It would be important for future research to focus on how valuation and value accumulation jointly shape discounting. Also, we

did not have enough studies for a categorical comparison between healthy volunteers and individuals with psychiatric disorders. However, we determined that inclusion of both healthy and psychiatric populations would be more in line with the goals of RDoC and relevant for future studies adopting this framework. Relatedly, because of the emphasis on including psychiatric populations, we coded studies that reported the effects of contrasts separated by comparison groups as independent studies, rather than selecting a single set of results to be included. Because these studies are not independent, our results may contain a bias for such studies that may not be present in other meta-analyses. It is also important to note that most studies contributed more than a single contrast, and these contrasts tended to go hand in hand (e.g., SSR and LLR, magnitude and delay, hard and easy), which could pose a confound for the spatial overlap results. Our work exclusively focused on monetary rewards, but there are a number of behavioral studies with paradigms using clinically relevant rewards (e.g., cigarettes for smokers[59], food for obese individuals[60,61]). Although we are cautiously optimistic about the generalizability of the present study given the evidence supporting a common neural valuation system across commodities[62], it is likely that there are commodity-specific activations that are not captured in our results. Lastly, because we were estimating the location of effects rather than the size of effects, there was no statical penalty for reported null reports. To this end, it is worth nothing that a large number of studies that used the choice contrast (LLR, SSR) reported no significant clusters for this contrast[20,31,43,48,50,56,58,63–70], whereas only two studies reported no significant effects of SV[71,72]. This comparison further highlights the importance for identifying and implementing more reliable analytic strategies for future research.

The present meta-analysis offers several exciting directions for future research. As data archiving becomes more common in the field, future meta-analysis can move beyond coordinate-

based meta-analysis and conduct image-based meta-analysis[73]. Unlike the coordinate-based methods, which only include the peak voxels, image-based methods can include the whole statistical map, allowing researchers to detect consistent but relatively weaker effects and to calculate effect sizes, which is a limitation of coordinate-based methods that only examines effect locations. In order to make image-based approach possible, it would be crucial for researchers to make whole-brain statistical maps publicly available in established archives, such as NeuroVault (https://neurovault.org/). Future meta-analytic work in delay discounting might also aim to examine the link between these neural effects and individual differences, such as discount rates, cognitive functioning, and psychopathology. As more neuroimaging studies of delay discounting in clinical populations become available, it would be worthwhile to conduct a future meta-analysis, both within specific disorders and across psychopathology in line with the RDoC framework. A practical goal of our work was to identify an analytic strategy that is reliable and robust to experimental variations. Given the high reliability and interpretability of effects produced by the subjective value contrast, our recommendation for future work is to use this contrast in the absence of specific hypotheses that call for a different approach. Another, also practical, outcome of our work is the generation of cluster maps that can be used as *a priori* ROIs for future research. This will be especially valuable for clinical neuroimaging studies of delay discounting that might be underpowered to detect modest effects using whole-brain approaches. All results will be made available in nifti format for this purpose.

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PRISMA 2009 Flow Diagram

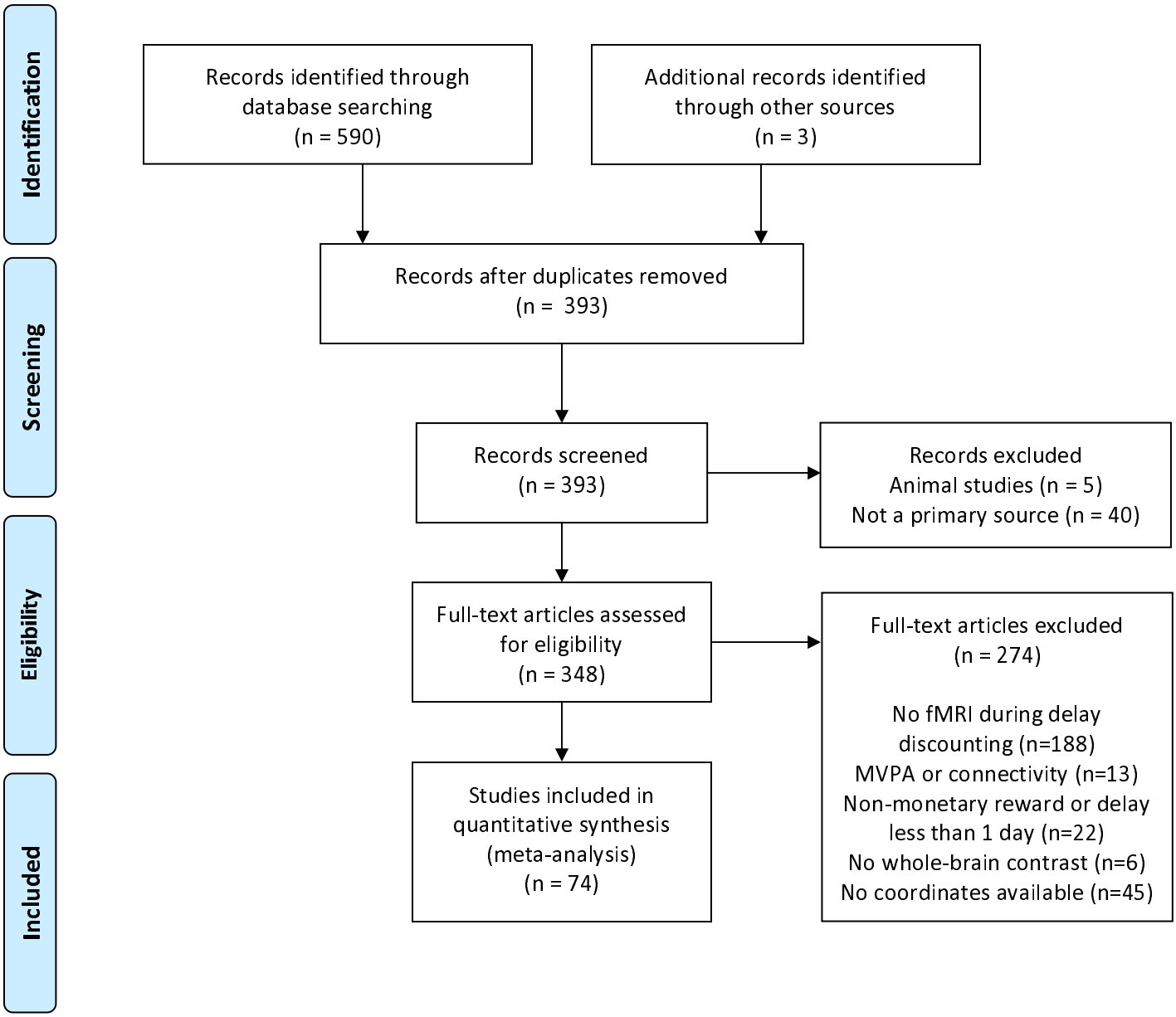
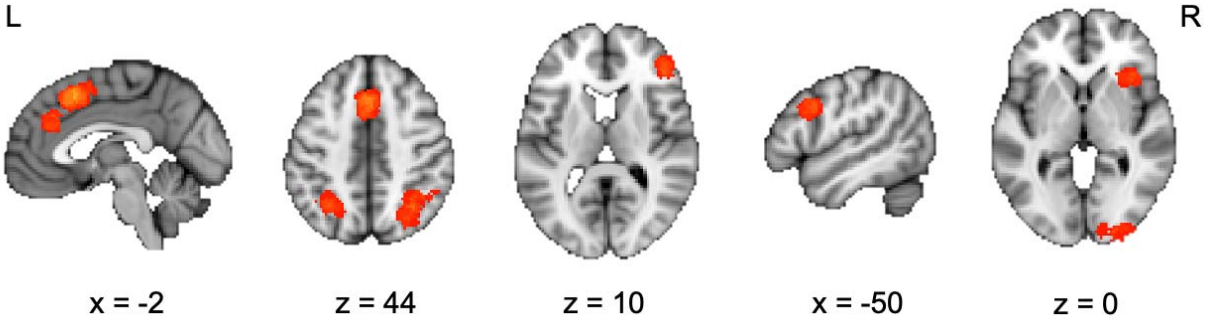
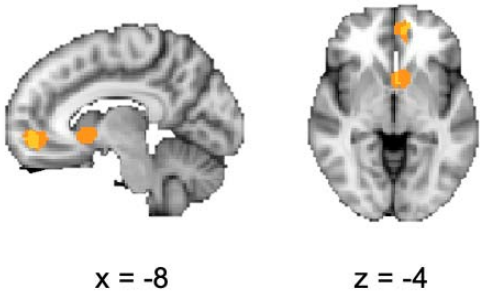


Figure 2. Whole-brain meta-analysis of common analytic strategies for BOLD signals during delay discounting task. There were no suprathreshold clusters for SSR > LLR and Now.

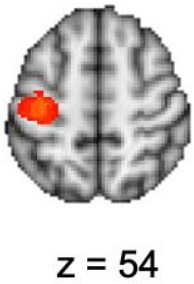
A Task



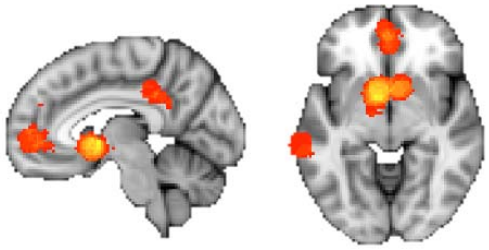
B Now



C LLR > SSR



D Subjective value

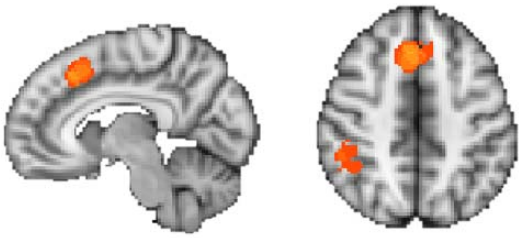


x = -6 z = -6

E Magnitude (red) and delay (blue)

x = 48 z = -6

F Hard (red) vs. Easy (blue)



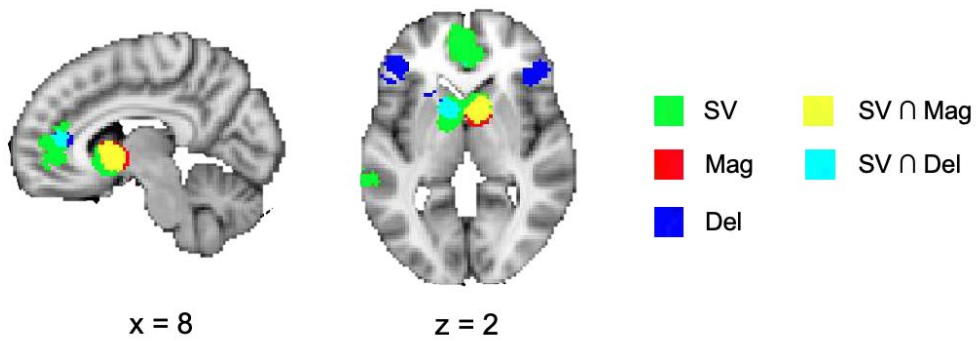
x = 8 z = 46

10% 64%

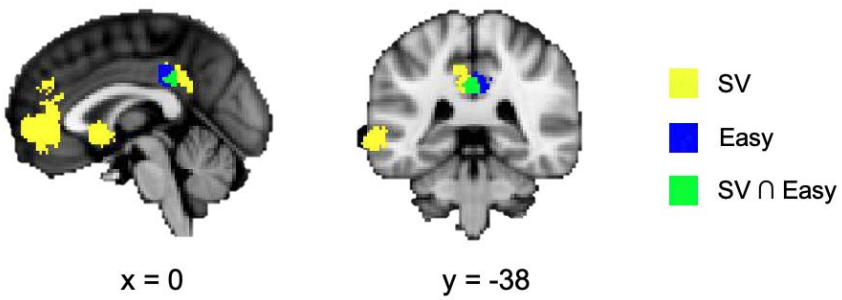
Notes: LLR = larger-later reward, SSR = smaller-sooner reward.

Figure 3. Spatial overlap analysis of clusters by individual contrasts.

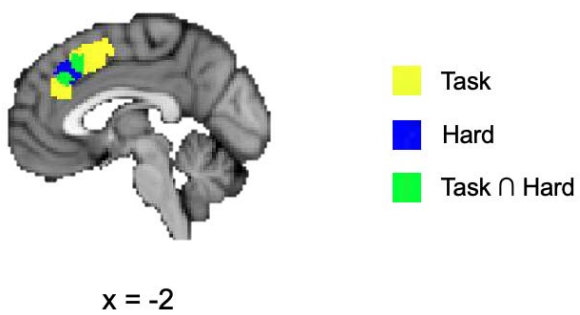
A Valuation system



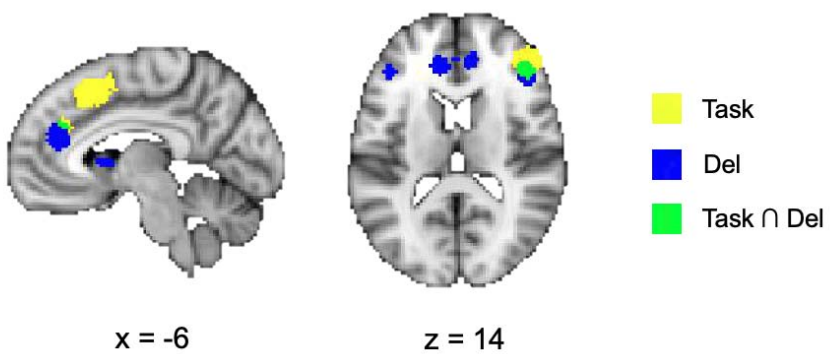
B SV and Easy



C Task and Hard



D Task and Delay



Notes: SV = subjective value, Mag = magnitude, Del = delay.

Table 1. Meta-analytic sample (N=72 studies; 136 contrasts).

				Number of foci								
Study	n	Diagnosis	Contrast	Task	LLR	SSR	SV	Mag	Del	Hard	Easy	Now
Albert et al., 2012[37]	40	NS	Choice evaluation > baseline Positive effects of differential magnitude	4				6				
Albrecht et al., 2011[74]	28	NS	Today trials > delay trials									18
Albrecht et al., 2013[75]	30	HC	SS > LL			3						
Avsar et al., 2013[53]	14	HC	Task > SMC trials Easy > hard	18							9	
	14	Schizophrenia	Task > SMC trials Easy > hard	8							9	
Ballard et al., 2009[76]	16	HC	Magnitude Negative effect of delay					3	3			
Banich et al., 2013[77]	29	HC	Task > fixation Now > later	22		17						
Bickel et al., 2009[78]	30	HC	Discounting > control (real money)	21								
Blain et al., 2019[79]	37	NS	Hard > easy							18		
Chantiluke et al., 2014[80]	18	HC	Delayed > immediate choices		2							
Christakou et al., 2011[42]	40	HC	Delay > immediate Immediate > delay		13	4						
Claus et al., 2011[41]	160	Heavy drinkers	Later > now Now > later		17	18						
Clithero et al., 2009[81]	11	HC	Delay task	3								
Cox et al., 2014[82]	20	HC	SV (narrow and wide)				4					
Deshpande et al., 2019[57]	54	Prediabetics (high BMI)	Hard > easy Easy > hard Immediate available vs. unavailable							6	11	18
Eppinger et al., 2012[83]	30	NS	All choice > baseline Immediate options > delayed options	5								2
Eppinger et al., 2018[84]	50	NS	SV Hard > easy Easy > hard				3			2	4	
Fröhner et al., 2019[85]	126	NS	SV				3					

				Number of foci								
Study	n	Diagnosis	Contrast	Task	LLR	SSR	SV	Mag	Del	Hard	Easy	Now
Gardiner et al., 2018[86]	177	NS	Hard > easy							4		
Hamilton et al., 2020[67]	27	HC	All choices vs. baseline	8								
Hare et al., 2014[87]	25	HC	SV Del > imm		24		11					
Hoffman et al., 2008[47]	36	Methamphetamine dependence[1]	DD task > magnitude estimation task	11								
Ikink et al., 2019[88]	24	NS	Conjunction of ambiguous and exact DD	7								
Kable et al., 2007[21]	10	NS	SV using HDR Objective value Inverse delay Delayed > immediate Negative effects of SVD		1		14	2	4	8		
Kable et al., 2010[20]	25	NS	NOW - 60 DAY									9
Kishinevsky et al., 2012[55]	19	Obese women	Hard > easy							2		
Koffarnus et al., 2017[89]	18	NS (excluded substance use disorder)	Hard > easy Easy > hard							1	5	
Laube et al., 2020[90]	70	HC	Delayed > immediate Immediate > delayed Now-Later options		8	8						8
Lempert et al., 2017[13]	35	NS	SV (memory and control choice)				24					
Lim et al., 2017[48]	17	Alcohol use disorder	SS > LL			3						
Liu et al., 2012a[91]	19	HC	Free choice > forced choice SV	11			17					
Liu et al., 2012b[92]	18	NS	Task > baseline during valuation	7								
Luo et al., 2012[93]	21	HC	LL > SS		7							

Study	n	Diagnosis	Contrast	Number of foci								
				Task	LLR	SSR	SV	Mag	Del	Hard	Easy	Now
Marco-Pallarés et al., 2010[64]	17	HC	Indifference > non-indifference Non-indifference > indifference							1	11	
Martin et al., 2015[58]	19	Poor quality sleepers[1]	Immediate > baseline	12								
Massar et al., 2015[94]	23	HC	SV Negative effects of delay level				21		12			
Mavrogiorgou et al., 2017[66]	20	HC	Immediate > delay			8						
Mavrogiorgou et al., 2018[52]	38	OCD[1]	Immediate > delay			7						
McClure et al., 2004[18]	14	NS	Delta system Beta system	8								5
Meade et al., 2011[49]	39	Cocaine dependence[1]	Task > baseline Hard > easy	1						9		
Meade et al., 2016[95]	35	HC	Task > baseline Hard > easy	8						8		
Miedl et al., 2012[25]	32	Pathological gamblers[1]	SV				25					
Miedl et al., 2015[40]	15	HC	LDR > SIR		2							
	15	Pathological gamblers	LDR > SIR		8							
	30	Pathological gamblers[1]	Indifferent > sure Sure > indifferent							20	13	
Monterosso et al., 2007[31]	29	Methamphetamine users[1]	Hard > easy	6						2		
Morys et al., 2018[56]	36	Obese[1]	Delay discounting > perceptual decisions SS > LL	7		4						
Murawski et al., 2012[96]	13	NS	Task > baseline SV Easy > hard	13			6				5	
Neukam et al., 2019[97]	90	HC	Parametric amount Negative effects of delay					7	32			

				Number of foci								
Study	n	Diagnosis	Contrast	Task	LLR	SSR	SV	Mag	Del	Hard	Easy	Now
Norman et al., 2017[39]	20	HC	Delay > immediate (both directions)		2	1						
	26	ADHD	Delay > immediate (both directions)		2	7						
	20	OCD	Delay > immediate (both directions)		2	3						
O'Connell et al., 2018[98]	26	NS	DEL > IMM Positive effects of net SV		3						14	
Peters et al., 2009	22	NS	SV Reward magnitude Inverse delay				25	15	13			
Peters et al., 2010[100]	30	HC	SV (control and episodic condition)				15					
Pine et al., 2009[101]	24	HC	Discounted utility (V) Undiscounted utility (U) Temporal discount factor (D) Hard > easy				7	16	22	7		
Pine et al., 2010[102]	14	HC	Discounted utility (V) Undiscounted utility (U) Temporal discount factor (D)				9	25	28			
Piva et al., 2019[103]	20	NS	Hard > easy Positive effect of relative SV							13	2	
Ripke et al., 2012[104]	222	HC	Task SV	18			19					
Samanez-Larkin et al., 2011[105]	25	NS	SV				19					
Sasse et al., 2015[106]	23	HC	SV (episodic condition)				12					
Sasse et al., 2017[107]	22	HC	SV				8					
Schneider et al., 2014[108]	48	HC	SV				4					
Sripada et al., 2011[71]	20	HC	LL > SS Immediacy		15							6
Stanger et al., 2013[50]	30	Substance abuse	LL > control task SS vs. LL	14		2						
Steinbeis et al., 2016[109]	20	HC	SV during valuation				4					
van den Bos et al., 2014[110]	22	NS	Choice > baseline LL-SS	7	5							

				Number of foci								
Study	n	Diagnosis	Contrast	Task	LLR	SSR	SV	Mag	Del	Hard	Easy	Now
van den Bos et al., 2015[69]	50	NS	LL-SS		4							
Vanyukov et al., 2016[54]	48	Major depression[1]	Task > fixation SIR-DDR Negative effect of longer vs. shorter delay Difficult > easy Negative effect of difficult > easy	11				1	1	3	1	
Vetter et al., 2017[111]	174	HC	Decision phase > baseline	1								
Waegeman et al., 2014[43]	41	HC	Delayed > immediate		41							
Wang et al., 2014[112]	28	HC	Amount of delayed reward Positive effects of SVD					7			11	
Wang et al., 2017[51]	21	HC	Delay - Immediate		3							
	18	Internet gambling disorder	Delay - Immediate		1	2						
Weber et al., 2008[68]	23	NS	Delayed > immediate		1							
Wiehler et al., 2017[26]	48	Pathological gamblers[1]	SV (conjunction of HC and gamblers)				3					
Wittmann et al., 2007[70]	13	HC	<1 versus >1 year Delayed vs. immediate		7				1			
Xu et al., 2009[113]	20	HC	Temporal discounting (gains) > baseline Available immediately (G-TD)	19								12
Zha et al., 2019[114]	46	HC	SV Difficulty				10			8		
Zhuang et al., 2020[115]	24	HC	Delayed > immediate Immediate > delayed		3	8						

Notes: HC = healthy controls, NS = not specified, Task = Task activations, LLR = larger later reward > smaller sooner reward, SSR = smaller sooner reward > larger later reward, SV = positive correlation with subjective value, Mag = positive correlation with objective (undiscounted) magnitude of reward, Del = negative correlation with delay or positive correlation with inverse delay, Hard = hard > easy, Easy = easy > hard, Now = trials with immediate option > trials with both options delayed. [1] includes HC (pooled across the entire study sample).

Table 2. Meta-analytic test statistic (% of studies that reported a peak within a 10mm radius).

#	Volume (mm^3)	MNI coordinates X	Y	Z	Value	Brain area
Task						
1	1222	-2	16	48	48.0	L. Superior frontal gyrus
2	671	34	-62	44	32.0	R. Intraparietal sulcus
3	486	-28	-60	46	32.0	L. Intraparietal sulcus
4	440	44	36	10	32.0	R. Frontal pole
5	476	-50	10	28	28.0	L. Inferior frontal gyrus
6	399	38	24	0	28.0	R. Insula
7	375	26	-94	-6	28.0	R. Occipital pole
Now						
1	232	-6	48	-12	50.0	L. vmPFC
2	253	-2	12	-8	50.0	L. Striatum
SSR > LLR						
No suprathreshold clusters						
LLR > SSR						
1	715	-34	-18	54	38.1	L. Precentral gyrus
Hard > Easy						
1	756	2	26	42	50.0	R. Superior frontal gyrus
2	342	50	-36	38	25.0	R. Supramarginal gyrus
Easy > Hard						
No suprathreshold clusters						
SV						
1	1452	-10	4	-6	63.6	L. Striatum
2	1333	-2	48	-4	45.5	L. vmPFC
3	400	-6	-40	34	36.4	L. Posterior cingulate
4	377	-58	-36	-6	27.3	L. Middle temporal gyrus
Magnitude						
1	490	14	4	-6	55.6	R. Striatum
Delay						
1	461	46	28	4	55.6	R. Inferior frontal gyrus
2	537	2	36	10	44.4	R. Medial prefrontal cortex
3	356	50	14	24	44.4	R. Middle frontal gyrus
4	346	-40	32	0	44.4	L. Inferior frontal gyrus
5	269	-12	4	2	44.4	L. Striatum

Notes: Task = Task activations, Now = trials with immediate option > trials with both options delayed, SSR = smaller-sooner reward > larger-later reward, LLR = larger-later reward > smaller-sooner reward, Hard = hard > easy, Easy = easy > hard, SV = positive correlation with subjective value, Magnitude = positive correlation with objective (undiscounted) magnitude of reward, Delay = negative correlation with delay or positive correlation with inverse delay, L = left, R = right.