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RESEARCH****Research Report****Neural mechanism of intertemporal choice: From discounting future gains to future losses**Lijuan Xu^{a,1}, Zhu-Yuan Liang^{b,1}, Kun Wang^a, Shu Li^{b,*}, Tianzi Jiang^{a,*}^aLIAMA Center for Computational Medicine, National Laboratory of Pattern Recognition, Institute of Automation, Chinese Academy of Sciences, Beijing 100190, China^bCenter for Social and Economic Behavior, Institute of Psychology, Chinese Academy of Sciences, Beijing 100101, China

ARTICLE INFO

Article history:

Accepted 23 December 2008

Available online 6 January 2009

Keywords:

Intertemporal choice

Discounting loss

Medial prefrontal cortex

Anterior cingulate cortex

Dorsolateral prefrontal cortex

ABSTRACT

Intertemporal choice, the tradeoff among outcomes occurring at different points in time, involves not only benefit options but also those associated with cost. Previous neuroimaging studies have primarily focused on discounting future gains; thus the neural mechanism underlying discounting future losses remains unidentified. Using event-related functional magnetic resonance imaging, we comprehensively investigated the neural mechanism of temporal discounting using two decision-making tasks with a symmetric pattern of gains and losses. Our results revealed that the lateral prefrontal and posterior parietal areas were activated in discounting both future gains and future losses, but their activations were stronger when discounting losses. Moreover, we found that the insula, thalamus and dorsal striatum were more activated during intertemporal choices involving losses, suggesting that the enhanced sensitivity to losses may be driven by negative emotions. In addition, whereas the posterior cingulate cortex and medial prefrontal cortex were activated when the choices included immediate options, extra regions including the anterior cingulate cortex, insula and superior frontal gyrus were preferentially activated when the choices involved immediate losses. Taken together, our findings suggest that a fronto-parietal network supports the common discounting process, and more importantly, discounting future losses and gains occurs asymmetrically in the brain. We speculate that this may provide a neural basis for the phenomenon that future losses are discounted less steeply than future gains.

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1. Introduction

Decisions about savings, work effort, education, and health all involve intertemporal choices, which refer to decisions involving tradeoffs among outcomes occurring at different points

in time (Frederick et al., 2002). People tend to discount future benefits/costs when facing decisions involving a smaller immediate gain/loss and a larger future one (Ainslie, 1975; Ainslie, 2001). Such a preference can be understood in terms of temporal discounting (Frederick et al., 2002). This phenom-

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Abbreviations: ACC, anterior cingulate cortex; CNY, Chinese Yuan; DLPFC, dorsolateral prefrontal cortex; fMRI, functional magnetic resonance imaging; G-TD, temporal discounting task of gains; L-TD, temporal discounting task of losses; LOFC, lateral orbitofrontal cortex; MOFC, medial orbitofrontal cortex; MPFC, medial prefrontal cortex; PCC, posterior cingulate cortex; PPC, posterior parietal cortex; SFG, superior frontal gyrus; VMPFC, ventromedial prefrontal cortex

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enon is ubiquitous in daily decision making, which involves not only positive, but also negative outcomes. Previous studies have proposed discounting functions to describe decreases in the subjective value of a delayed reward with increases in delay time (Loewenstein and Prelec, 1992; Myerson and Green, 1995; Raineri and Rachlin, 1993). Although similar discounting functions can be used to describe the discounting of delayed gains and losses (Estle et al., 2006; Murphy et al., 2001), behavioral evidence suggest that people usually discount delayed losses less steeply than delayed gains (Loewenstein, 1987; MacKeigan et al., 1993; Read, 2004; Thaler, 1981). This phenomenon, termed the sign effect (Loewenstein, 1987), is prevalent in daily decision-making as people prefer to incur a loss sooner rather than delay it. However, most previous studies focused on intertemporal choices of gains (Green and Myerson, 2004; Kable and Glimcher, 2007; McClure et al., 2004a; Takahashi, 2004; Wittmann et al., 2007) rather than on losses. In particular, whether discounting future losses and future gains share a common neural mechanism remains unclear.

Recent research on the neural mechanism of intertemporal choice has concentrated on whether behavior can be best explained by the interaction of multiple systems (Loewenstein et al., 2008). Evidence from neuroimaging studies has revealed that several systems in the human brain interact with each other when choosing between immediate and delayed gratification (McClure et al., 2004a; McClure et al., 2007; Wittmann et al., 2007). A functional magnetic resonance imaging (fMRI) study involving choices between rewards that varied by amount and the length of delay to delivery showed that immediate rewards recruited paralimbic areas, including the ventral striatum, medial orbitofrontal cortex (MOFC), and medial prefrontal cortex (MPFC); whereas the lateral prefrontal cortex and posterior parietal cortex were activated when making choices independent of delay (McClure et al., 2004a). Tanaka et al. (2004) also found that the lateral orbitofrontal cortex and the striatum were activated when subjects were presented with choices that would result in collecting immediate rewards; whereas the dorsolateral prefrontal cortex and inferior parietal cortex were activated when subjects acted in order to obtain large future rewards. These studies demonstrate that temporal discounting results from the combined influence of two neural systems: one involving the limbic and paralimbic cortical areas for evaluating immediate rewards and the other involving the frontoparietal areas for evaluating delayed gratification. This is consistent with the idea that several competing neural networks may be needed to complete a decision-making task (De Martino et al., 2006; McClure et al., 2004b; Sanfey et al., 2003; Sanfey et al., 2006). However, a recent study by Kable and Glimcher (2007) demonstrated that a single system tracks the subjective value of a delayed monetary reward, regardless of the time until delivery. Considering that discounting future losses is as prevalent as discounting gains in real-world decisions, it is necessary to search for the neural basis underlying intertemporal choices involving losses. Exploring whether choices between smaller immediate and greater delayed losses elicit activity in distinct neural systems should be especially interesting.

In the present study, we comprehensively investigated the neural basis of intertemporal choice from discounting

future gains to future losses by means of fMRI using two decision-making tasks with a symmetric pattern of gains and losses. Previous studies have indicated that a common temporal discounting process is involved in intertemporal choices of both gains and losses (Frederick et al., 2002; Green and Myerson, 2004). Therefore, we hypothesized that a neural network consisting of the lateral prefrontal and posterior parietal areas which have previously been revealed to be related to the cognitive process of evaluating future opportunities for gains (McClure et al., 2004a; Tanaka et al., 2004) would also be activated in discounting future losses. Because it has been shown that future losses are discounted less steeply than future gains (Loewenstein, 1987; MacKeigan et al., 1993; Read, 2004; Thaler, 1981), we speculated that the activity of these brain regions might be asymmetric in temporal discounting of gains and losses. Additionally, we suspected that there was a specific neural system that evaluates immediate losses as well as that the temporal discounting of losses was the result of interaction between two neural systems, when the choices contained an option of immediate loss.

2. Results

In this section, we first report statistics on task performance in temporal discounting tasks involving gains (G-TD) and temporal discounting tasks involving losses (L-TD). Using event-related fMRI in conjunction with a general linear model analysis, we subsequently documented that subjects encoded the G-TD as a temporal discounting of reward by replicating previously found activation patterns for temporal discounting. We then focused on the L-TD to find brain regions whose activity was modulated by temporal discounting of losses, and further to identify whether the process in L-TD was also the result of the interaction of multiple systems. Finally, we compared the brain activity in L-TD with that in G-TD to find out whether there were differences at the neural level in discounting future gains and future losses.

2.1. Behavioral results

In each trial, whether G-TD or L-TD, the subjects indicated whether they preferred a smaller/sooner option or a larger/later one. A paired t-test on the percentages of subjects' choices of smaller/sooner options in the G-TD and the L-TD revealed a significantly larger percentage of smaller/sooner choices in the L-TD ($p < 0.05$), suggesting a significant reduction in the discount effect for future losses compared with future gains (Fig. 1). This result is consistent with previous studies of temporal discounting (Frederick et al., 2002; Loewenstein, 1987; Read, 2004; Thaler, 1981).

2.2. Neuroimaging results

2.2.1. Identifying the neural basis of G-TD

Our whole brain analyses identified regions with significant activation across all decision epochs in G-TD. Foci of

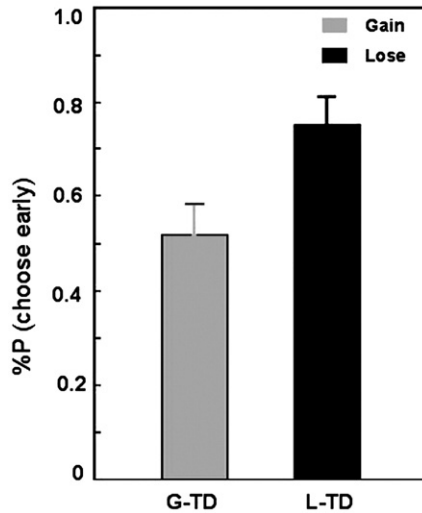


Fig. 1 – Behavioral results. Percentage of trials (P) in which subjects chose the smaller/sooner option in G-TD and L-TD. The results showed a significant discrepancy between the responses of the subjects to L-TD compared to G-TD in that they chose smaller/sooner options at a higher rate in L-TD ($p < 0.05$). Error bars indicate SEM.

significant activation were observed in the dorsolateral prefrontal cortex (DLPFC), lateral orbitofrontal cortex (LOFC), posterior parietal cortex (PPC), as well as in motor and visual regions (Fig. 2A; see Table S1 in the Supplementary data). When comparing choices that included an immediate option

with those that included only delayed ones, we observed that brain regions, including the medial orbitofrontal cortex (MOFC), medial prefrontal cortex (MPFC), posterior cingulate cortex (PCC), and ventral striatum, were more activated by choices involving an immediate outcome (Fig. 2B; see Table S2 in the Supplementary data).

2.2.2. Identifying the neural basis of L-TD

In the analyses of L-TD, decision-related activation was observed in the DLPFC, LOFC, PPC, and motor and visual regions across all decision epochs (Fig. 3A; see Table S3 in the Supplementary data), consistent with our findings from G-TD. However, brain regions, including the bilateral thalamus and dorsal striatum, also showed significant activation during all decision epochs in L-TD (Fig. 3A; see Table S3 in the Supplementary data). A comparison between choices involving an immediate option and those that included only delayed outcomes revealed a different activation pattern in the anterior cingulate cortex (ACC), insula, superior frontal gyrus (SFG), MPFC, and PCC (Fig. 3B; see Table S4 in the Supplementary data). These regions showed significantly more activation during choices involving an immediate outcome.

2.2.3. Comparison between G-TD and L-TD

Given that monetary gains and losses may differently influence the subjects' decisions, we evaluated whether the brain activity also showed different patterns in L-TD with those in G-TD. Relative to the G-TD, we found that the DLPFC, PPC, ventromedial prefrontal cortex (VMPFC), insula, thalamus, and striatum, showed greater activation during L-TD

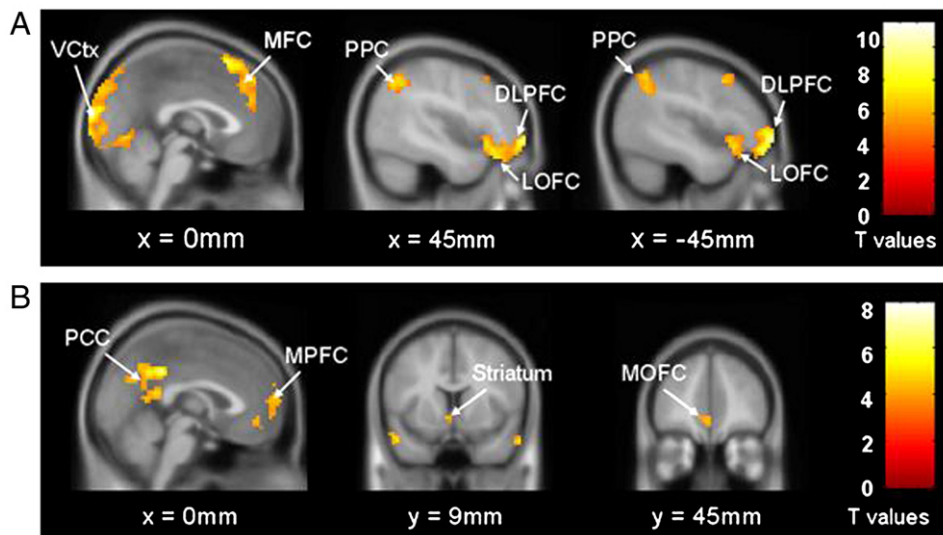


Fig. 2 – Brain regions activated in temporal discounting task of gains (G-TD) at a group level. (A) Brain regions activated for all choices independent of delay (with a combined threshold of $p < 0.001$, FDR corrected and cluster size ≥ 10 voxels). See Table S1 for details of MNI coordinates. Abbreviations: PPC, posterior parietal cortex; DLPFC, dorsolateral prefrontal cortex; LOFC, lateral orbitofrontal cortex; VCtx, visual cortex; MFC, medial frontal cortex. (B) Brain regions preferentially activated for choices in which money was available immediately (with a combined threshold of $p < 0.05$, FDR corrected and cluster size ≥ 10 voxels, except the striatum which with a combined threshold of $p < 0.05$, FDR corrected and cluster size ≥ 5 voxels). See Table S2 for details of MNI coordinates. Abbreviations: PCC, posterior cingulate cortex; MPFC, medial prefrontal cortex; MOFC, medial orbitofrontal cortex.

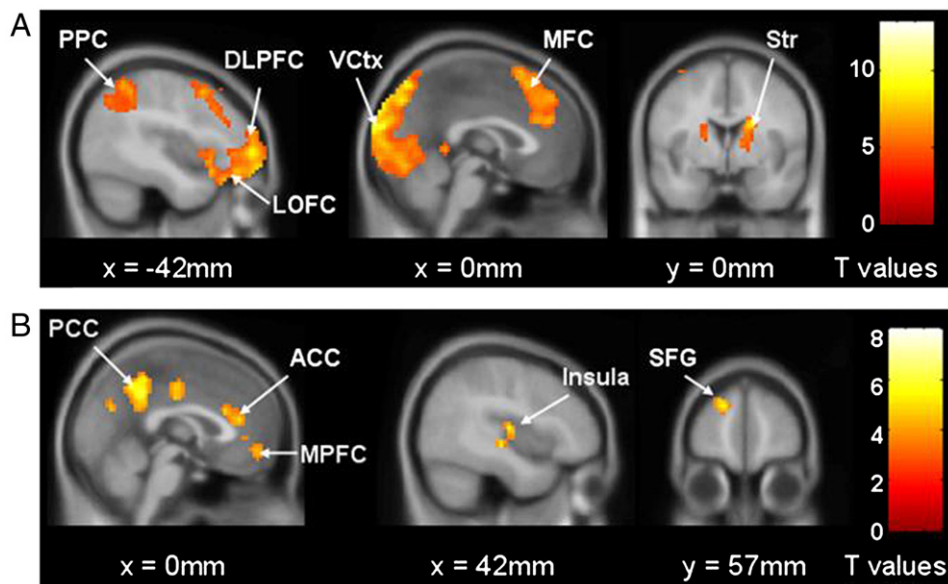


Fig. 3 – Brain regions activated in temporal discounting task of losses (L-TD) at a group level. (A) Brain regions activated for all choices independent of delay (with a combined threshold of $p < 0.001$, FDR corrected and cluster size ≥ 10 voxels). See Table S3 for details of MNI coordinates. Abbreviations: PPC, posterior parietal cortex; DLPFC, dorsolateral prefrontal cortex; LOFC, lateral orbitofrontal cortex; VCtx, visual cortex; MFC, medial frontal cortex; Str, striatum. (B) Brain regions preferentially activated for choices in which money was lost immediately (with a combined threshold of $p < 0.05$, FDR corrected and cluster size ≥ 10 voxels). See Table S4 for details of MNI coordinates. Abbreviations: PCC, posterior cingulate cortex; MPFC, medial prefrontal cortex; ACC, anterior cingulate cortex; SFG, superior frontal gyrus.

trials (Fig. 4). More specifically, the DLPFC and PPC were activated in both tasks but the activations were larger in L-TD; and the VMPFC, insula, and thalamus showed significant activation only in the L-TD. No region showed greater activation in the G-TD compared with the L-TD. Additional details can be seen in Table 1.

3. Discussion

Understanding how the brain processes intertemporal choice is perhaps one of the central motivating problems in neuroeconomics (Loewenstein et al., 2008). Our study provided novel

results for addressing these problems by exploring the neural mechanism of intertemporal choices, including discounting future gains and future losses. First, we identified brain regions that showed significant activation across all decision epochs in both G-TD and L-TD: the DLPFC, LOFC, and PPC, which are a subset of the regions usually activated in economic decision-making (Boettiger et al., 2007; Glimcher and Rustichini, 2004; Gold and Shadlen, 2007; Platt, 2002; Sanfey et al., 2006). Second, we showed that asymmetric neural mechanisms underlie the processes of gain- and loss-associated temporal discounting, with greater activation occurring mainly in the VMPFC, insula, thalamus, striatum, PPC, and DLPFC during L-TD. Finally, we identified brain regions that showed a selective increase in activation in response to choices involving immediate options,

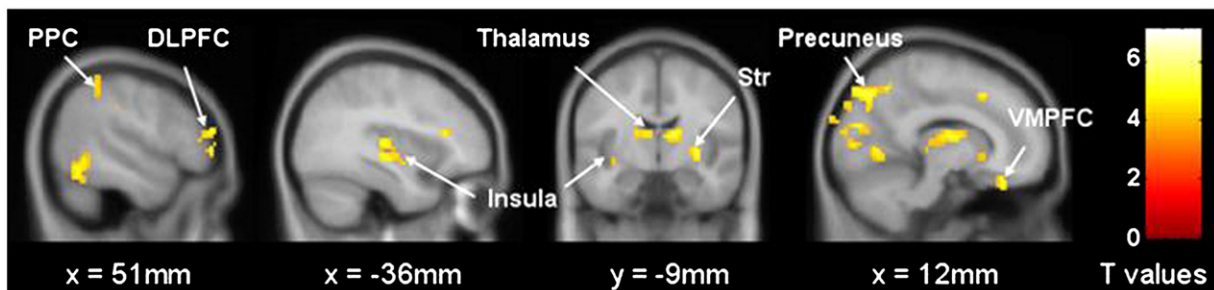


Fig. 4 – Brain regions showing greater activation in response to losses than in response to gains for all choices in temporal discounting task at a group level (L-TD > G-TD, with a combined threshold of $p < 0.05$, FDR corrected and cluster size ≥ 10 voxels). Random-effects analysis revealed regions that are differentially activated for choices in L-TD and G-TD. See Table 1 for details of MNI coordinates. Abbreviations: PPC: posterior parietal cortex; DLPFC, dorsolateral prefrontal cortex; Str, striatum; VMPFC: ventral medial prefrontal cortex.

Table 1 – Brain regions exhibiting greater activation for all choices independent of delay, when comparing losses with gains (L-TD>G-TD)

Brain regions	BA	Cluster size (voxels)	MNI coordinates			t_value
			x	y	z	
R dorsolateral prefrontal cortex	10/46	52	48	51	21	5.97
			54	39	21	4.2
R ventromedial prefrontal cortex	11/47	18	12	33	-24	5.37
R middle/inferior frontal gyrus	10/47	26	54	48	0	5.72
L middle/inferior frontal gyrus	46	21	-42	33	18	4.42
	46	24	-51	27	27	5.29
R middle/superior frontal gyrus	6/8	36	24	12	51	5.29
	6	19	42	9	57	4.89
	10	19	33	39	24	4.64
R thalamus/Striatum		430	12	-9	12	5.42
			30	-18	-6	5.98
R insula	13		27	18	-3	4.79
L thalamus		15	-24	-27	3	4.87
L striatum		107	-12	15	-3	4.4
L insula	13	57	-33	-18	6	5.55
R inferior parietal lobule	40	58	54	-42	48	5.25
	40	40	42	-57	45	5.2
L superior parietal lobule	7	35	-24	-72	60	5.23
B cuneus/R precuneus	17/18	611	6	-66	0	5.29
	7		15	-81	45	7.09
R middle/inferior temporal gyrus	37	111	54	-60	-12	5.37
L middle temporal gyrus	37	28	-51	-63	0	5.28

Coordinates of the peak voxel are reported in MNI space ($p < 0.05$, FDR corrected, cluster size ≥ 10 voxels). R, right; L, left; BA, Brodmann's area; (x, y, z), coordinates of primary peak locations in the Montreal Neurological Institute (MNI) space.

compared to those with only delayed ones. In addition to supporting the concept that separate neural systems value immediate and delayed monetary rewards (McClure et al., 2004a), we demonstrated for the first time that the valuation of immediate and delayed monetary losses also involves the engagement of distinct neural systems, which may well provide a mechanism for the loss-associated intertemporal decision-making process.

Consistent with our hypothesis, the lateral prefrontal and posterior parietal areas were activated during all decision epochs, not only in G-TD but also in L-TD. This implies that the neural basis underlying the intertemporal choices of gains and losses may share a common temporal discounting process. The lateral prefrontal and posterior parietal areas have been commonly observed to be activated in tasks involving high-level cognitive processes, such as abstract problem solving and exertion of control for long-term goals (Miller and Cohen, 2001; Platt and Glimcher, 1999; Tanji and Hoshi, 2001). Previous research on discounting future gains (Boettiger et al., 2007; McClure et al., 2004a; McClure et al., 2007; Monterosso et al., 2007; Tanaka et al., 2004) also found that the fronto-parietal network is important for temporal discounting, which accords well with its key role in executive control processes and future

planning (Baker et al., 1996; Cohen et al., 1997; Paulus et al., 2002; Tanaka et al., 2004). From these findings we suggest that the regions identified in our study are likely to be engaged in analyzing the quantities of the economic options and evaluating the future opportunities for both reward and cost.

Previous research has revealed that subjects discount delayed losses less steeply than they do delayed gains (Loewenstein, 1987; MacKeigan et al., 1993; Read, 2004), the sign effect. These findings are consistent with other studies which have reported asymmetry in decisions about gains and losses in discounting tasks (Baker et al., 2003; Thaler, 1981). Our neuroimaging results support the hypothesis that an asymmetric activity pattern underlies the process of discounting future gains and future losses. Brain regions of the insula, thalamus, VMPFC, and striatum showed greater activation in L-TD than in G-TD. The insula has often been noted as being associated with negative emotions, and is known to be particularly involved in the evaluation and representation of negative emotional states (Bechara, 2001; Kuhnen and Knutson, 2005; Sanfey et al., 2003). This accords well with its greater level of activation in L-TD because excessive sensitivity to losses is driven by negative emotions (Camerer, 2005; Tom et al., 2007). Activation of the thalamus in response to loss-associated temporal discounting is particularly interesting in light of this region's association with both primary and secondary aversive reinforcers such as noise blasts (Buchel et al., 1999), pain (Ploghaus et al., 1999; Wager et al., 2004), and losing money (Knutson et al., 2000). Recent research also found that the thalamus was activated during the experiencing of negative emotions (Damasio et al., 2000; Nummenmaa et al., 2008). Recruitment of these areas in response to monetary losses in L-TD is consistent with previous studies which showed activation of these same areas in response to cues which provoked a negative affect in response to aversive events (Wager et al., 2004). Therefore, our findings indicate that emotion, in particular the emotions subjects feel when they wait for some aversive outcome to occur, plays a role in decisions concerning time. Potential losses have a greater impact on preferences than do gains (Benzion et al., 1989; Tversky and Kahneman, 1991), and people often place disproportionate weight on losses relative to gains of equivalent value (Kahneman et al., 1991). The greater activation in the VMPFC in L-TD compared with G-TD, which has been found in coding for subjective value of both gains and losses (Breiter et al., 2001; Knutson et al., 2000; Tom et al., 2007; Wheeler and Fellows, 2008), indicates that the subjective value of losses was different from that of equivalent gains. Taken together, our findings suggest a role for activation in the insula, thalamus and VMPFC in processing losses. The greater activation in these regions may be caused by the subjects' enhanced sensitivity to losses compared to gains (Novemsky and Kahneman, 2005; Tversky and Kahneman, 1992).

The finding that the striatum showed greater activation in L-TD than in G-TD seemingly contradicts the observation that the striatum is mainly related to coding rewards and reward-related stimuli (Berns et al., 2001; Breiter et al., 2001; Elliott et al., 2000; O'Doherty, 2004). However, there is increasing evidence suggesting a more general role of the striatum in processing salient events, especially its role in

aversive events (Delgado et al., 2008; Jensen et al., 2003; Seymour et al., 2007; Tom et al., 2007; Zink et al., 2003). Making decisions about gains/losses is a common problem, but when decisions involve temporally delayed gains/losses, the problem becomes considerably more complex than simply choosing the course of action with the better expected outcome. During intertemporal choices involving losses, the interaction between loss aversion and temporal discounting may demand more attention and processing effort. Also, the distress people experience when losing an amount of money is suggested to be more intense than the joy they experience when gaining the same amount (Kahneman and Tversky, 1984). Hence, the greater activation level of the striatum in L-TD may indicate that options associated with intertemporal losses are perceived as being much stronger than those present in G-TD, adding support to the more general role that the striatum is involved in responding to salient stimuli (Delgado et al., 2008; Jensen et al., 2003; Zink et al., 2003). It is worth noting that recent studies have showed that during decision-making striatal activity is linked to the properties of the stimuli (Boettiger et al., 2007; McClure et al., 2007). Another study also showed that a secondary reward, such as money, may not provoke as intense a response in terms of activation in the ventral striatum, as a primary reward, such as juice (Delgado, 2007). We speculate that this might also account for the relatively low activation in the striatum in G-TD. Of course, it also suggests caution in the interpretation of striatal activity in human intertemporal decision-making since the differences people observed in temporal discounting of both gains and losses are still not well understood (Baron, 2008). Future research will be necessary to identify the specific role of the striatum.

In addition to the regions mentioned above, we also found that the DLPFC and PPC showed greater activation in L-TD relative to G-TD, although they were activated in both conditions. During intertemporal choices involving either gains or losses, activation in these regions may be related to the manipulation of cognitive processes associated with temporal discounting, namely evaluating future outcomes. However, in intertemporal choices about losses, sensitivity to losses and the discounting of future values interact with each other (Loewenstein and Prelec, 1991), and thus it may be more difficult to choose between a smaller/sooner loss and a larger/later one. In our experiment, subjects showed a shift toward preferring smaller, sooner losses, indicating that the fear of future losses is a greater motivator than the pleasure associated with future gains. In other words, the devaluation of larger losses caused by the delay was not sufficient to surpass the effect of loss aversion. Hence, the larger activation in the DLPFC and PPC observed in L-TD implies that greater cognitive demands were placed on the brain in order to compete with the strong emotional tendency to avoid larger losses.

With respect to our results when we compared choices that included immediate gains with choices that included only delayed ones in G-TD, activation in the MOFC, MPFC, ventral striatum and PCC was significantly greater when the choices involved immediate options. Our findings are in agreement with previous studies conducted by McClure et al. (2004a) on the comparison between immediate and delayed

rewards. The MOFC is involved in coding the relative value of different reward stimuli (O'Doherty et al., 2001; O'Doherty, 2004) and in updating the incentive value of outcomes in response to devaluation (Winstanley et al., 2004). Considering their association with limbic and paralimbic cortical structures, which are rich in dopaminergic innervation, these regions have consistently been implicated in impulsive behavior (Biederman and Spencer, 2002; Winstanley et al., 2004). Supported by earlier findings (McClure et al., 2004a; McClure et al., 2007; Tanaka et al., 2004), these corticolimbic regions, along with lateral prefrontal and posterior parietal areas, might process the twin demands that comprise temporal discounting tasks, that is, the emotional goal of getting immediate gratification and the cognitive goal of maximizing utility, respectively.

When comparing choices including immediate losses with those including only delayed ones, we found that the ACC, insula and SFG, along with the MPFC and PCC showed greater activation. Losses provoke emotional responses associated with fear or anxiety (Breiter et al., 2001; Camerer, 2005), so it is logical that previous studies have found that anticipated or experienced losses give rise to activation in regions that have been associated with negative emotions, such as the insula (Breiter et al., 2001; Kuhnen and Knutson, 2005). Our results are consistent with these earlier findings and indicate that subjects experience a greater degree of negative emotions associated with losses in the face of an immediate loss. The SFG has been found to be related to loss aversion (Tom et al., 2007); therefore greater activity in the SFG may reveal that subjects are motivated to avoid current losses. The ACC is associated with response conflict (Botvinick et al., 2001; Botvinick et al., 2004; Kuhnen and Knutson, 2005), and there is also evidence that the ACC responds to a variety of signals that indicate negative utility (Carter et al., 1998; Gehring and Willoughby, 2002; Peyron et al., 2000; Yeung and Sanfey, 2004). In this context, the involvement of the ACC may imply that decisions involving immediate losses are associated with greater conflict. Such findings may indicate that the paralimbic and fronto-parietal regions interact with each other during choices between smaller immediate and greater delayed losses. This supports a dual-system model of decision-making, in which emotion and cognition both guide decisions (De Martino et al., 2006; McClure et al., 2007; Sanfey et al., 2003). It should be noted that the involved neural networks were not exactly the same in processing immediate gains as in processing immediate losses. This may also support the notion that asymmetric activity patterns underlie the processes of gain- and loss-associated temporal discounting.

It should also be noted that this is a first step towards the analysis of the temporal discounting of losses, and our study, although promising, has several limitations that will be remedied in future studies. Although we found that the asymmetric neural mechanisms that underlie gain- and loss-associated temporal discounting correspond to significant differences in the size of the discount between gains and losses, we were unable to identify the neural activity which encodes the exact steepness of the discounting rate with the stimuli used in our study. This point should be further investigated in future studies if we are to draw more definitive conclusions. Also, as in a number of other studies (Kable and

Glimcher, 2007; McClure et al., 2004a; Moll et al., 2006; Preuschoff et al., 2008; Weber and Huettel, 2008), we only paid the participants for one of their choices from each of the two parts of the study, and the subjects were given an initial amount of money to play with in L-TD. These factors may have minimized the activation of loss- and gain-related brain areas so that the brain network that was active during the temporal discounting of losses could be a subset of the one that functions in real life. In future studies, an improved experimental design, in which loss and gain trials are presented in a single experiment in random order, could be adopted to increase our comprehension of the neural substrates of the temporal discounting of losses.

In summary, this study provides evidence that asymmetric neural mechanisms underlie the processes of gain- and loss-associated temporal discounting. Furthermore, we demonstrated for the first time that two distinct neural systems are involved in the valuation of immediate and delayed monetary losses. Additionally, the finding that the interaction of distinct neural systems forms the basis for both gain- and loss-associated temporal discounting may add evidence to the concept that reason and emotion come into conflict in making all kinds of judgments (Talmi and Frith, 2007). Overall, these findings may help to explain affect-related asymmetries in temporal discounting (Estle et al., 2006; Murphy et al., 2001; Thaler, 1981), and specifically, may provide neural evidence for the phenomenon that people usually discount future losses differently than future gains. More generally, our findings yield insight into the neural mechanism of intertemporal choice, which may provide

information that economists can use to build an empirical model of temporal discounting.

4. Experimental procedures

4.1. Subjects

Twenty healthy right-handed Chinese graduate students (ten female; mean age, 25; age range, 22–29) participated in this study. Two subjects were excluded from the analysis because of excessive head motion (absolute displacement with regard to the reference scan exceeded 2 mm). All subjects had normal or corrected-to-normal vision, and no history of psychiatric diagnoses, neurological or metabolic illnesses. They all gave full written informed consent to participate in the study. This study was approved by the Institutional Review Board of Beijing MRI Center for Brain Research.

4.2. Experimental design

The experiment was comprised of two parts: a temporal discounting task involving gains (G-TD) and a temporal discounting task involving losses (L-TD) (Fig. 5A). The tasks were similar to those employed by McClure et al. (2004a) but with a symmetric pattern of gains and losses. This allowed us to test neural responses during intertemporal choices involving losses and, more importantly, to perform a direct comparison between gain- and loss-associated temporal discounting. There were a total of 42 trials in each task, with

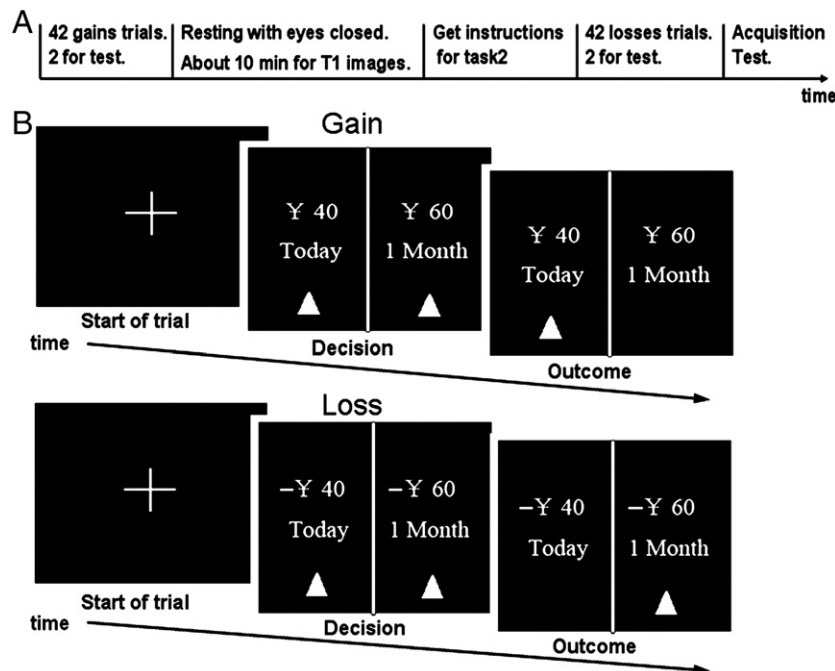


Fig. 5 – Experimental design (the actual time parameters were presented in Chinese during the experiment). (A) The timeline of the experimental procedure. (B) Trial structure for temporal discounting task of gains and losses. The gain session and the loss session had identical forms. The gain session was followed by the loss session after a 10-min interval. At the beginning of each trial, two options were presented and the subject indicated his/her choice by pressing a button. Then, the result was presented revealing one's choice.

the first two trials serving as task-check choices to ensure that the subjects were acclimated to the task performance. In G-TD, the subjects were instructed to choose between two monetary rewards (smaller/sooner and larger/later) available at different times (today, half a month from now and one month from now) and at different intervals (either half a month or one month after the earlier time) (Fig. 5B). The earlier reward was presented on the left with a smaller amount and the later reward on the right with a larger amount. The amounts of the monetary reward in the earlier choices ranged from Chinese Yuan (CNY) 13 to 110 (CNY $1 \approx \$0.15$) and were randomly drawn from a Gaussian distribution with a mean of CNY 50 and a standard deviation of CNY 25, with integer conversion. Meanwhile, the percent difference in amounts between the two rewards was selected from the set {5%, 10%, 15%, 25%, 35%, 50%}. The range of the trial associated discount rates (k) of the 40 formal trials, that is, the values of the discount rates at which the early and later options are perceived to be of equal value according to hyperbolic function proposed by Mazur (1987), is $0.003 \sim 0.035$, $Mean \pm Std = 0.016 \pm 0.001$, $Median = 0.017$ (the values of k are scaled by days). In L-TD, all trials were the same as those in G-TD (so the values of k in L-TD are the same as in G-TD), except for a “-” sign before the monetary amounts (Fig. 5B), indicating that the money would be lost at the corresponding time. All choices were randomly ordered.

Subjects were instructed about the task and tested for task comprehension prior to scanning. During the scanning, subjects viewed the screen by a mirror system attached to the head coil and were allowed to choose freely with no time limitation. They made their choices by pressing one of the two buttons corresponding to the location of the options on the screen. After the subject's response, the result would present for 2 s, followed by a black screen for 10 s until a 2-s fixation period was presented, indicating the next choice. There was a 10-min interval between the G-TD and L-TD trials for each subject. After the scanning, the subjects were asked to complete two check questions for each task using a five-point rating scale to determine their full engagement. These questions checked to determine that they had understood the instructions and believed they would gain or lose a certain amount of money at the corresponding time, as in the instructions. All subjects scored above 3 points on the rating scale.

An initial offer of CNY 150, which corresponded to the maximum amount they could lose in L-TD, was made available for each subject in the instructions about the L-TD. To ensure the subjects' engagement in the temporal discounting task, they were told that one trial would be randomly selected from each task after the experiment to count “for real”. Subjects were also paid CNY 100 in cash for participating, but they were not told about that until the experiment was completed.

4.3. fMRI data acquisition

Images were acquired with a 3.0 T Siemens MRI scanner. Whole-brain functional scans were collected in 26 axial slices using an echo-planar imaging (EPI) sequence (TR/TE=2000/30 ms, flip angle (FA)=90°, field of view (FOV)=19.2 cm, matrix=64×64, thickness=3 mm, gap=1 mm). For each subject, two functional runs were collected with a 10-min

T1-weighted anatomical scan intervening between the two runs. The first run was G-TD, and the second was L-TD.

4.4. fMRI data analysis

Analyses focused on changes in activation specifically during the decision epochs (corresponding to the time between presentation of the choice and the subject's recorded response) for both gains and losses trials. All analyses were conducted using statistical parametric mapping (SPM2, <http://www.fil.ion.ucl.ac.uk/spm>). The same analysis procedure was applied to both G-TD and L-TD. For preprocessing, images were first corrected for within-scan acquisition time differences between slices and then realigned to the first volume to correct for inter-scan head motions. Visual inspection of motion correction estimates confirmed that no subject's head rotated more than 2° or moved more than 2.0 mm in any dimension, relative to the first volume. We then spatially normalized the realigned images to the standard EPI template, resampled them to $3 \times 3 \times 3$ mm³, and smoothed them with an 8 mm full-width-at-half-maximum Gaussian kernel to decrease spatial noise. Subsequently, the functional images were detrended and high-pass filtered with a cut at 128 s for linear drift and low frequency fluctuations removal. Head movement estimates derived from the realignment step were included as regressors in the following analyses to help diminish the impact of any movement-related effects on the results. At the start of each functional scanning run, the screen remained black for 10 s to allow time for magnetization to reach the steady state and to allow for the subjects' adaptation to the situation. The first five images were discarded from the analyses. The duration of the experiment was variable because choices were self-paced. However, the majority of subjects completed each session within 15 min.

To identify activated brain regions, we used an event-related fMRI design. Our primary aim was to find brain activity patterns during the temporal discounting task of both gains and losses. For each condition presented to a single subject, a separate general linear model was defined which included the subjects' motion parameters and two task-related regressors: one for trials in which the early option was available immediately, the other for all trials. Each regressor was generated by convolving a γ -variate function that modeled a canonical hemodynamic response (Cohen, 1997) with a dummy variable that equaled 1 during decision epochs, and 0 for all other time points. For each subject, first-level contrasts were calculated voxel-by-voxel, identifying the corresponding activated regions for each regressor. A one-sample t-test was then used to determine where the second-level group contrasts values differed significantly from zero (a random-effects analysis).

Because the experiment consisted of two parts, another aim of our neuroimaging analyses was to determine which brain regions mediated the sign effect of temporal discounting, corresponding to a subject's behavioral tendency to discount future losses less steeply than future gains. A random-effect paired t-test analysis was performed to detect brain region activity that was significantly different in L-TD activities from that in G-TD activities.

Acknowledgments

We thank Yan-Mei Li, Jie-Hong Xu and Yan Sun for their help in experimental design; Zhendong Liu for helping in the data acquisition. We are thankful to Yuan Zhou, Yong Liu, and two anonymous referees for insightful comments on this manuscript. We also appreciate the assistance of Drs. Edmund F. and Rhoda E. Perozzi in correcting the English. This research was partially supported by the Natural Science Foundation of China, Grant Nos. 60675033, 30425004, 70701036 and 70671099, the National Key Basic Research and Development Program (973), Grant No. 2004CB318107, and the Knowledge Innovation Project of the Chinese Academy of Sciences, Grant No. KSCX2-YW-R-130.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.brainres.2008.12.061.

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