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The mediating role of LPFC–vmPFC functional connectivity in the relation between regulatory mode and delay discounting

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HIGHLIGHTS

- We explored the effect of regulatory modes on delay discounting (DD) using RSFC.
- DD negatively correlated with assessment, but positively correlated with locomotion.
- Regulatory mode can be represented by LPFC–vmPFC functional coupling.
- Effect of regulatory mode on DD is mediated by LPFC–vmPFC functional coupling.

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ABSTRACT

Previous studies have shown that regulatory mode orientation can affect many human behaviors, such as risk-taking, counterfactual thinking and economic decision making. However, little is known about how regulatory mode affects delay discounting. To address this question, we used resting-state functional magnetic resonance imaging (rs-fMRI) to investigate whether regulatory mode orientations can be represented by functional connectivity and the influence of two regulatory modes (assessment and locomotion) on delay discounting. The behavioral results showed that delay discounting was negatively correlated with assessment scores but positively correlated with locomotion scores. Neuroimaging results indicated that the functional connectivity between lateral prefrontal cortex (LPFC) and ventromedial prefrontal cortex (vmPFC) was negatively correlated with assessment scores but positively correlated with locomotion scores. Furthermore, mediation analysis showed that the effect of regulatory mode on delay discounting is mediated by LPFC–vmPFC functional connectivity. These results suggested that people's regulatory mode orientation could predict delay discounting, which is mediated by LPFC–vmPFC functional connectivity. Therefore, the present study extends our perspective on regulatory mode and provides neural mechanism for understanding the link between regulatory mode and delay discounting.

1. Introduction

In goal-pursuit, people self regulate their behaviors through two essential orientations: assessment and locomotion [1,2]. Assessment constitutes the comparative aspect of self-regulation. It is concerned with critical evaluation of entities or states, such as goals or means in relation to alternatives in order to judge relative quality [2]. For example, an individual may assess preferences among alternatives, and how well he or she performed in the past. Individuals strong in assessment mode are preoccupied with these comparative judgments. In contrast, locomotion is the self-regulatory aspect concerned with movement from state to state and with committing the psychological resources that will initiate and maintain goal-directed progress in a straightforward and direct manner, without undue distractions of delays [2]. In the locomotion mode, individuals emphasize "doing", "getting on with it", "making something happen" rather than critical evaluation. Previous studies have shown that regulatory mode orientation can affect many human behaviors, such as risk-taking, counterfactual thinking and economic decision making [3–5]. However, little is known about how regulatory mode affects delay discounting.

Regulatory mode theory proposes that assessment and locomotion are independent and can be manifested chronically as a personality disposition [1,2,6]. The independence of the two modes allows for a possible predominance of one mode over the

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other. In the context of decision-making, regulatory mode has been included as individual characteristics, which may account for choice behavior [7]; but surprisingly, there is little empirical evidence on its relation with intertemporal choice. Higgins et al. [1] pointed out that individuals strong in assessment mode are more likely to critically evaluate options and relate future actions to critical standards in order to make the most appropriate decision. Such "evaluative criticism" leads assessors to make fewer impulsive choices, because they will compare current states to future outcomes to secure their interests in the long run. However, individuals with a strong locomotion tendency are motivated to quickly engage in activities, perceiving them as ends in themselves rather than means. Thus, they are presumed to live for the sake of the moment with less regard for future consequences of their actions. Furthermore, with respect to consuming behavior, locomotion (initiation and maintenance) prompts one to initiate compulsive or planned spending, presumably accruing less savings for the future. Assessment involves making budgets, keeping track of spending and setting financial goals, which can lead to increase in savings for the future by controlling overall spending. Thus, low locomotion and high assessment lead to more savings in the spending domain. In addition, the two different mode orientations induce distinctive preferences for decisional strategies: assessors prefer "full evaluation" strategy, whereas locomotors prefer "progressive elimination" strategy [8,9]. Hence, we expected that when assessment overrides locomotion, lower delay discounting would be in intertemporal choice; when locomotion overrides assessment, steeper delay discounting would be.

Generally, delay discounting is an important indicator of impulsivity of intertemporal choice, which refers to the degree of preference for smaller but immediate rewards over larger but delayed ones. The extent of preference for delayed rewards is captured by the discount rate, which expresses the subjective value of a delayed reward declines as a function of delay. Discounting rates vary between individuals, and are relatively stable over time [10]. Recently, functional magnetic resonance imaging (fMRI) studies have shown that the neural mechanisms underlying delay discounting mainly involved three distinct brain networks: valuation network (such as ventromedial prefrontal cortex, posterior cingulate cortex and ventral striatum), cognitive control network (such as lateral prefrontal cortex, anterior cingulated cortex), and prospection network (such as hippocampus, amygdala) [11–15]. Furthermore, some studies have suggested that the vmPFC plays a central role in intertemporal decision-making. First, neuroimaging studies of delay discounting have found that BOLD activity in vmPFC scales with the subjective value of the options being considered [13,14]. Second, values are assumed to be represented in vmPFC but are subject to top–down modulation by prefrontal control regions such as the lateral PFC in the self-control model [15,16].

Additionally, previous studies have found that assessment was positively related to the perceived value of the goals but negatively related to risk taking [4,17]. These results suggested that regulatory mode may be linked to the valuation and cognitive control network. Importantly, cognitive neuroscience research have suggested that successful self-regulation is dependent on top–down control from the prefrontal cortex over subcortical regions involved in reward and emotion [18,19]. Therefore, we anticipated that regulatory mode would be linked to coupling between the cognitive control and valuation networks.

Interestingly, Li et al. [20] found that the resting-state functional connectivity (RSFC) of the brain regions in delay discounting task (DDT) related networks was significantly correlated with participants' discounting rate among healthy individuals. This finding suggested that resting-state functional organization of the human brain may be a biomarker of impulsivity and can predict economic decision-making behavior. Therefore, RSFC may offer a valuable tool for analyzing the neural basis of individual variation in impulsive decision-making.

The present research was conducted to investigate the effect of regulatory mode on delay discounting using RSFC. We used the locomotion and assessment scale [2] to assess the individuals' chronic regulatory mode. Based on previous studies, we anticipated that assessment scores would be negatively related to delay discounting, whereas locomotion scores would be positively related to delay discounting. To identify the neural mechanism responsible for the influence of regulatory mode on delay discounting, we used a vmPFC mask from the meta-analysis on valuation [21] as seed to calculate the voxel-wise functional connectivity because vmPFC may have a crucial role in delay discounting. We first examined functional connectivity maps from the vmPFC correlated with delay discounting. We then used mediation analyses to test whether RSFCs plausibly contributed to the link between delay discounting and regulatory mode.

2. Methods

2.1. Participants and procedure

Eighty-two college students were recruited for the study, and they were paid for their participation. All subjects gave informed consent, and none had a history of neurological or psychiatric disorder. The experimental protocol was approved by the Institutional Review Board of the Southwest University. We removed eight participants due to excessive head movement in the resting-state fMRI analysis, and 74 subjects remained (38 female, 36 male; age range = 17–26, $M = 20.2$; all right-handed). All subjects completed the resting-state fMRI scan prior to behavioral measures, which contained the locomotion and assessment scales [2] and delay discounting task.

2.2. Measures

2.2.1. Regulatory mode

The locomotion and assessment scales [2] constitute two separate 12-item self-report measures designed to tap individual differences in these tendencies, which measures chronic individual differences in the strength of locomotion orientation and assessment orientation. Specifically, respondents rate the extent to which they agree with self-descriptive statements reflecting locomotion (e.g., "By the time I accomplish a task, I already have the next one in mind") or assessment (e.g., "I spend great deal of time taking inventory of my positive and negative characteristics"). Ratings are made on a 6-point Likert type scale with the response alternatives anchored at the ends with 1 (strongly disagree) to 6 (strongly agree). We computed assessment and locomotion scores separately by summing responses to each item. Previous studies have demonstrated that the locomotion and assessment scales have satisfactory reliability and validity [2,22]. In this sample, the two scales were not significantly correlated ($r = -0.075$, $p = 0.520$).

2.2.2. Delay discounting

We administered a modified version of delay discounting task [13], in which participants made a series of hypothetical choices between immediate rewards and delayed rewards. The small immediate amount was ¥20 on all trials. The larger delayed option was constructed using one of five delays (7, 15, 30, 60, 120 days) and one of ten add-percentages (10–500%) of the immediate reward, thus there were 50 unique choices. Participants were allowed as much time as they desired to make decision. Responses were made by pressing one of two buttons corresponding to immediate or delayed rewards.

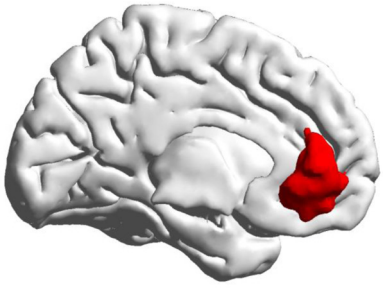

Fig. 1. vmPFC mask from the meta-analysis on valuation [21].

Delay discounting was taken as the area under the curve (AUC) because this measure has good psychometric properties [23–25]. This method involves determining, for each individual, the present value of the delayed option when paired with each immediate-reward amount (i.e., the estimated indifference point between the immediate and delayed rewards), plotting the resulting function, and calculating the proportion of total area falling under the curve. Smaller AUC values represent steeper discounting rates.

2.3. fMRI data acquisition

Images were acquired with a Siemens 3T scanner (Siemens Magnetom Trio TIM, Erlangen, Germany). A circularly polarized head coil was used, with foam padding to restrict head motion. Functional images were acquired with a $T2^*$-weighted echo-planar imaging sequence (echo time, 30 ms; repetition time, 2 s; field of view, 20 cm, matrix, 64×64) with 33 axial slices (slice gap, 3 mm; voxel size $3.1 \times 3.1 \times 3$).

During the resting state, subjects were instructed to keep their eyes closed, relax their mind, not to sleep, and remain motionless as much as possible. The resting scan lasted for 8 min. Corresponding high- resolution T1-weighted were recorded with a total of 176 slices at a thickness of 1 mm and in-plane resolution of 0.98×0.98 mm (TR = 2530 ms; TE = 3.39 ms; flip angle = 7°; FoV = 256×256 mm^2).

2.4. fMRI data analysis

Resting state fMRI data were preprocessed using the REST and DPARSF software [26,27]. Each participant's raw data were corrected for temporal shifts between slices, corrected for motion, and spatially smoothed with a Gaussian kernel (full width at half maximum = 4 mm). The T1-weighted images were co-registered to the EPI mean images and segmented into white matter, gray matter, and Cerebrospinal fluid (CSF). These images were then normalized to MNI space in $3 \times 3 \times 3$ mm^3 voxel sizes. To reduce the effect of head motion and obtain low-frequency fluctuation from resting-state fMRI data, we regressed the motion data out of the time series and then preformed bandpass temporal filtering (0.01–0.08 Hz) on the residual signals [28,29]. To further reduce nuisance signals, we regressed out the global mean signal, white matter signal and CSF signal [30]. The global signal is thought to reflect a combination of physiological processes (i.e., cardiac and respiratory fluctuations), and therefore, was treated as covariates to control for such factors [31]. The resultant resting-state fMRI data were then subjected to functional connectivity analysis.

To investigate functional network of delay discounting in resting-state, we used a vmPFC mask (see Fig. 1) from the meta-analysis on valuation [21] as seed to calculate the voxel-wise functional connectivity. In the first-level analysis, the average BOLD signal time courses within the vmPFC were correlated with every voxel in the whole brain for each subject using Pearson's correlation coefficient. Correlation coefficients were converted to normally distributed z-scores using Fisher's transform to allow for second-level random effects analysis. To determine brain regions significantly functional connectivity with the vmPFC, we performed random effect one-sample t-tests of individuals' z-valued functional connectivity maps in a voxel-wise manner. In this way, functional connectivity maps were obtained with a threshold of $p < 0.05$(FWE correction and cluster size ≥ 10). Further, positive and negative functional connectivity maps of the vmPFC were saved as masks for subsequent analyses. In the second-level analysis, to test the link between functional connectivity of the vmPFC and delay discounting, functional connectivity maps from the vmPFC were entered into a correlation analysis. Regions from the correlation analysis that survived a height threshold of $p < 0.05$ at the voxel level and an extent threshold of Alphasim correction (voxel size ≥ 85) at the cluster level were used as ROIs. In the following ROI analysis, we used Bonferroni correction to correct for multiple comparisons. To further examine the relation between regulatory mode and vmPFC seed functional connectivity which is significantly correlated with delay discounting, the connectivity value (Fisher's z-score) between the vmPFC and each ROI was extracted from the vmPFC connectivity map from each participant. We finally conducted mediation analyses to explore which functional connectivity between vmPFC and ROIs potential contributed to the link between delay discounting and regulatory mode.

3. Results

3.1. Behavioral results

As the reaction time in delay discounting task may be an important intervening variable, we first examined the relationship between regulatory mode and the reaction time. In order to compare the differences in reaction time, we split participants into two groups of assessors and locomotors according to relative strength of regulatory mode orientations [32]. Assessment and locomotion scores were first converted to normally distributed z-scores, respectively. We then regarded the subjects whose $Z_{\text{assessment}}$ scores are greater than $Z_{\text{locomotin}}$ as the assessors ($n = 33$), and other subjects as locomotors ($n = 41$). Results showed that assessors did not spend more time in making decisions than locomotors did ($T = 1.083$, df = 72, $p = 0.282$). Following cooper et al. [32], we used two different approaches to examine the link between regulatory mode and delay discounting. First, we computed the correlations between two regulatory mode scores and delay discounting. The AUC was positively correlated with assessment scores ($r = 0.296$; $p = 0.010$; see Fig. 2A) but was negatively correlated with locomotion scores ($r = -0.299$; $p = 0.010$; see Fig. 2B). Our second approach examined this effect in a categorical rather than a continuous manner. Locomotors showed a steeper delay discounting than assessors ($T = 3.175$, df = 72, $p = 0.002$; see Fig. 2C). The behavioral findings suggest that individual differences in regulatory mode orientation can predict delay discounting.

3.2. Resting-state functional connectivity results

First, we test whether delay discounting can be predicted by vmPFC seed functional connectivity. The correlation analysis showed that the AUC were negatively correlated with functional connectivity between vmPFC and left lateral PFC (LPFC), bilateral caudate, right medial frontal gyrus (MFG) and left temporal-parietal junction (TPJ) (see Fig. 3 and Table 1). Second, we further examined the relationships between regulatory mode orientations and vmPFC seed functional connectivity which are significantly cor-

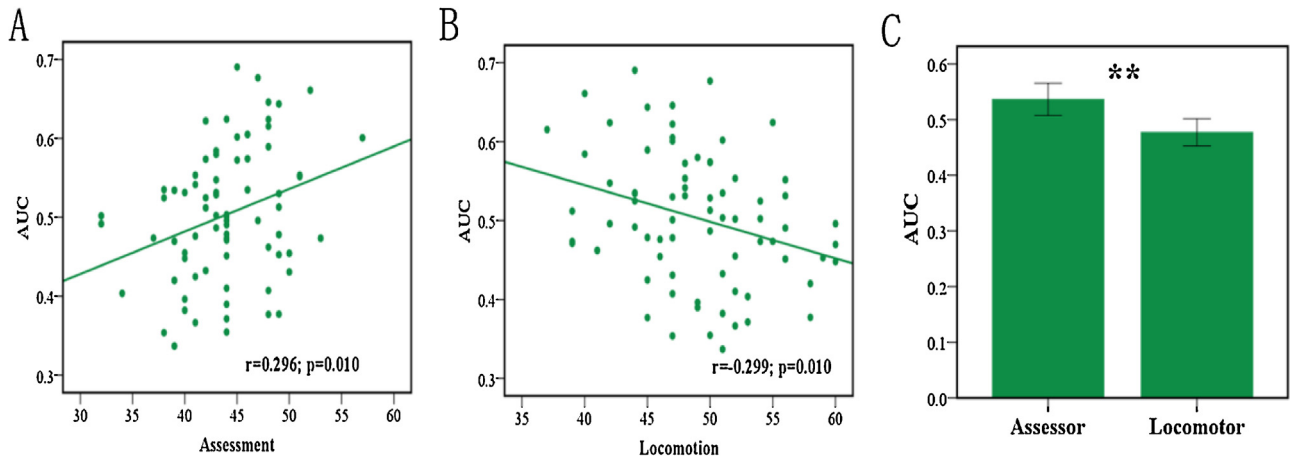

Fig. 2. Behavior results. A: significant positive correlation between area under the curve (AUC) and assessment orientation ($r = 0.296$; $p = 0.010$); B: negative correlation between AUC and locomotion orientation ($r = -0.299$; $p = 0.010$); C: Splitting all participants into two groups of assessors and locomotors, and locomotors showed a significantly lower AUC than assessors ($T = 3.175$, df = 72, $p = 0.002$).
$^{**}p < 0.01$.

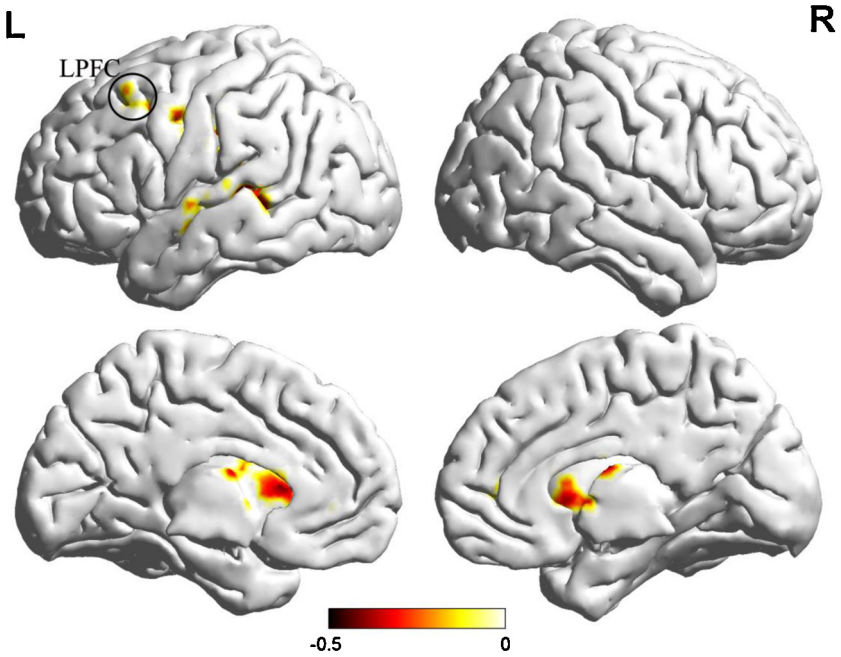

Fig. 3. Functional connectivity between vmPFC and other brain regions was significantly correlated with AUC ($p < 0.05$; Alphasim corrected, cluster size > 85).

related with delay discounting. The correlation analysis showed LPFC–vmPFC functional connectivity was negatively correlated with assessment scores ($r = -0.335$, $p = 0.004$), but positively correlated with locomotion scores ($r = 0.300$, $p = 0.009$). There was no other functional connectivity that was significantly correlated with regulatory mode orientations. These results also suggest that individual differences in regulatory mode orientation could be predicted by functional connectivity between left LPFC and vmPFC.

To further understand how regulatory mode affects delay discounting, we used the INDIRECT procedure in SPSS to test our mediation hypothesis [33–35]. The mediation model was estimated to derive the total, direct and indirect effects of regulatory mode on delay discounting through RSFC. Of these RSFCs, the functional coupling between LPFC and vmPFC was the only significant mediator. We estimated the indirect effect of assessment mode on delay discounting, quantified as the product of the OLS regression coefficient

Table 1
Areas of brain regions functional connectivity with vmPFC for correlated with AUC ($p < 0.05$; Alphasim corrected, cluster size > 85).

Region	BA	No. voxels	Peak *Z*-score	*x*	*y*	*z*
L. middle/inferior frontal gyrus	6/8/9	116	−0.335	−39	18	33
R. medial frontal gyrus	10/32	97	−0.433	33	30	12
Caudate/lateral ventricle	10	254	−0.504	0	−3	18
L. superior temporal gyrus/inferior parietal lobule	22/2/21	298	−0.429	−63	−39	0

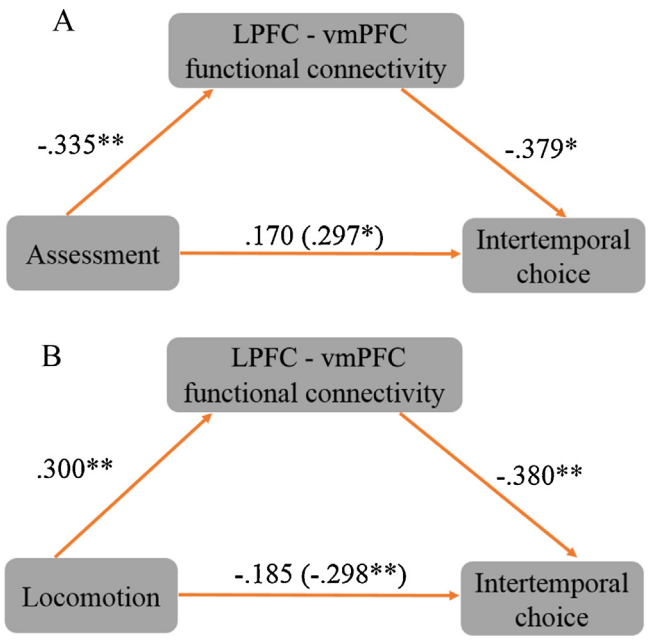

Fig. 4. Mediation results. Path analysis showed that the link between assessment mode and delay discounting is mediated by the LPFC–vmPFC functional connectivity (A), and the link between locomotion mode and delay discounting is mediated by the LPFC–vmPFC functional connectivity (B). *: $p < 0.05$, **: $p < 0.01$.

estimating LPFC–vmPFC functional connectivity from assessment mode, and the OLS regression coefficient estimating delay discounting from LPFC–vmPFC functional connectivity. A bias-corrected bootstrap-confidence interval (CI) for the product of these paths that does not include zero provides evidence of a significant indirect effect [34]. Using the INDIRECT procedure with 5000 bootstrap samples revealed a significant positive indirect effect of assessment mode on delay discounting through LPFC–vmPFC functional connectivity (point estimate = 0.127, 95% percentile CI = 0.032 to 0.282; see Fig. 4A). Similarly, the indirect effect of locomotion mode on delay discounting through LPFC–vmPFC functional connectivity was also significant (point estimate = 0.113, 95% percentile CI = −0.253 to −0.032; see Fig. 4B). Accordingly, these results showed that the effect of regulatory mode on delay discounting was mediated by the LPFC–vmPFC functional coupling.

4. Discussion

In the present study, we investigated the influence of self-regulatory orientation (assessment and locomotion concern) on delay discounting using RSFC. Behavioral data showed that delay discounting was negatively correlated with scores of assessment orientation, whereas positively correlated with scores of locomotion orientation. Neuroimaging results indicated that the LPFC–vmPFC functional connectivity was negatively correlated with assessment scores but positively correlated with locomotion scores. Furthermore, mediation analysis showed that the effect of regulatory mode on delay discounting was mediated by LPFC–vmPFC functional connectivity. Accordingly, our results suggested that individual differences in delay discounting were predicted by regulatory mode orientation. Importantly, mediation results indicated that LPFC–vmPFC functional connectivity is one of the neural mechanisms of the effect of regulatory mode on delay discounting.

Our findings showed that high assessment scores were associated with lower discounting rate, whereas high locomotion scores were associated with steeper discounting rate. These findings is consistent with the claim that assessors critically evaluate options and relate future actions to critical standards, while locomotors are motivated to quickly engage in activities perceiving them as ends in themselves rather than means. According to this argument, Mannetti et al. [36] found that when assessment overrides locomotion, people made more far-sighted choices; whereas when locomotion overrides assessment, people made more short-sighted choices. Our findings are consistent with previous researches' by showing that impulsive choices are characterized by low assessment and high locomotion orientation.

Even though the locomotion mode appears to be very similar to impulsivity, they are two distinct concepts. The notion of locomotion mode refers to moving from state to state and committing psychological resources to pursue goals in a straightforward manner [2]. This is motivated to goal-directed behavior. By contrast, the concept of impulsivity covers a wide range of actions that are poorly conceived, prematurely expressed, unduly risky, or inappropriate to the situation and often result in undesirable outcomes [37,38]. Deconstruction of this definition suggests that impulsivity could subsume behavior that has not adequately sampled sensory evidence ("reflection impulsivity"), a failure of motor inhibition ("impulsive action"), a tendency to accept small immediate or likely rewards versus large delayed or unlikely ones ("impulsive choice") and risky behavior, in the context of decision-making [38]. Impulsive behavior is often considered to be a product of impaired cognitive control and could potentially affect several aspects of the addictive process, including compulsive drug-seeking and relapse. Previous studies have suggested that deficits in self-regulation may be the core feature of a putative impulsive-compulsive disorder [39,40]. In the present research, we found that different functions (i.e., assessment and locomotion) of self-regulatory were uniquely related to delay discounting. The association between assessment and delay discounting may be explained, in part, by volitional inhibition (tapping such rumination and over controlled) [6,41]. These individuals will compare current states to future outcome to secure their interests in the long run. Additionally, Panno et al. [4] found that people with high assessment orientation have fewer risk-taking behaviors. A large number of studies have showed that risk taking is the product of a competition between the socioemotional and cognitive-control networks in many respects [42]. Other studies have indicated that the immaturation of cognitive-control system contributes to more risk-taking behavior [43,44]. Hence, these studies suggested that assessors perform better in cognitive control tasks than locomotors. The link between locomotion and delay discounting may be explained by behavioral activation system [6,41]. Specifically, individuals who report a locomotion mode are more inclined to act aggressively and behave impulsively without due deliberation.

Interestingly, we found that LPFC–vmPFC functional connectivity was positively correlated with assessment scores and negatively correlated with locomotion scores. Kruglanski et al. [17] found that assessment was positively related to the perceived value of the goals, while locomotion was positively related to the attainability of the goals. These results suggested that regulatory mode may be related to the valuation network in goal pursuit. Neuroscience studies have found that vmPFC is a major region that computes the value of various options, suggesting that vmPFC may be an important region that relates to neural representation of valuation in regulatory mode [13,45]. Additionally, cognitive neuroscience research has suggested that successful self-regulation is dependent on top–down control from the prefrontal cortex over subcortical regions involved in reward and emotion [18,19,46,47]. Our results suggested that the ability of LPFC to modulate vmPFC may be the neural representation of regulatory mode, which is consistent with these earlier studies.

Importantly, our mediation results suggested that the effect of regulatory mode on delay discounting was mediated by the LPFC–vmPFC functional connectivity. In delay discounting, the vmPFC is a major region that computes the subjective value of potential rewards to an individual [13,14,48]. The LPFC, however, is a crucial neural substrate for cognitive control processes in DDT, and the specific role of lateral PFC may play out by modulating activity in other areas [12,15,16,49]. Hare et al. [16] found evidence that LPFC influences self-control by modulating the value signal encoded in vmPFC. In line with this idea, a transcranial magnetic stimulation (TMS) study found that disruption of function of left, but not right, LPFC increased choices of immediate rewards over larger delayed rewards in DDT [15]. Importantly, TMS did not affect the valuation of decision options presented in isolation, which is compatible with the idea that LPFC modulates value signals in other regions rather than contributing to the actual valuation process. In addition, Camus et al. [50] found that applying inhibitory low-frequency TMS over LPFC caused a downmodulation of the computation of goal values at the time of decision-making. Recently, Hare et al. [45] proposed a model of the computational and neurobiological processes at work in self-control. In this model, vmPFC computes the value of options by identifying its various attributes, assigning value to them, and then integrating them into a net value for the option. A critical component of the model is that basic attributes (e.g., immediate monetary payoffs) are preferentially incorporated into the values computed in vmPFC. However, more abstract attributes (like delayed monetary payoffs) are generally given less weight unless left LPFC comes online and modulates activity in vmPFC, so that it weights all attributes according to the current goals (e.g., maximize monetary payoff). Our results support findings from previous research, which suggest that the ability of LPFC to modulate vmPFC may be a biomarker of cognitive control processing that biasing behavior towards choosing the far-sighted reward during intertemporal choice.. Therefore, our mediation results suggested that individuals with higher assessment orientation show smaller discounting rates in part, because they have stronger ability of cognitive control processing; whereas individuals with higher locomotion orientation show greater discounting rates probably because of impaired cognitive control.

Our findings could have important implications. The current study adds to the literature by examining different aspects of self-regulatory related to impulsivity. Specifically, results suggest that impulsive choices in delay discounting task are characterized by low assessment and high locomotion. The present study also provides an explanation for why regulatory mode affects delay discounting (differences in the ability of cognitive control). However, we should note that the results of this study do not in themselves provide evidence that the far-sighted choices made by assessors are associated with different levels of activity in the valuation and cognitive control brain networks. The findings may be limited as we only used RSFC. Future research is needed to examine which brain activities correspond to the differences in behavioral choices that arise from regulatory mode orientation.

In summary, we found that the influences of two distinct orientations of regulatory mode on delay discounting have different patterns, and were mediated by the ability of LPFC to modulate vmPFC. Considering the specific role of this modulation in cognitive control, our study suggested that individuals with higher assessment orientation prefer larger, later rewards to smaller, sooner ones in part because they are better at control process, whereas higher locomotion orientation prefer smaller, sooner rewards over larger, later rewards ones because they often employ impulsive process. Accordingly, the present study extends our knowledge on delay discounting, and provides neural mechanism for explaining the link between regulatory mode and delay discounting.

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