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Paralimbic and lateral prefrontal encoding of reward value during intertemporal choice in attempted suicide

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Abstract

Background—Alongside impulsive suicide attempts, clinicians encounter highly premeditated suicidal acts, particularly in older adults. We have previously found that in contrast to the more impulsive suicide attempters' inability to delay gratification, serious and highly planned suicide attempts were associated with greater willingness to wait for larger rewards. This study examines neural underpinnings of intertemporal preference in suicide attempters. We expected that impulsivity and suicide attempts, particularly poorly planned ones, would predict altered paralimbic subjective value representations. We also examined lateral prefrontal and paralimbic correlates of premeditation in suicidal behavior.

Methods—Forty-eight participants aged 46–90 years underwent extensive clinical and cognitive characterization and completed the delay discounting task in the scanner: 26 individuals with major depression (13 with and 13 without history of suicide attempt) and 22 healthy controls.

Results—More impulsive individuals displayed greater activation in the precuneus/posterior cingulate cortex (PCC) to value difference favoring the delayed option. Suicide attempts, particularly better-planned ones, were associated with deactivation of the lateral prefrontal cortex (IPFC) in response to value difference favoring the immediate option. Findings were robust to medication exposure, depression severity, and possible brain damage from suicide attempts, among other confounders. Finally, in suicide attempters longer reward delays were associated with diminished parahippocampal responses.

Conclusions—Impulsivity was associated with an altered paralimbic (precuneus/PCC) encoding of value difference during intertemporal choice. By contrast, better-planned suicidal acts were

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The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helinski Declaration of 1975, revised in 2008.

associated with altered LPFC representations of value difference. The study provides preliminary evidence of impaired decision processes in both impulsive and premeditated suicidal behavior.

Keywords

aging; suicide; impulsivity; discounting; neuroimaging

Suicide – the decision to forego one’s personal future – is sometimes perceived as the product of an impulsive, present-focused mind. Indeed, suicidal acts often involve little premeditation, and an important subgroup of suicidal individuals display high trait impulsivity and make shortsighted or negligent decisions (Gibbs *et al.* 2009; McGirr *et al.* 2009; Dombrovski *et al.* 2010, 2011; Clark *et al.* 2011). Yet, at another end of the spectrum we see carefully planned and executed suicidal acts, particularly, in older people (De Leo *et al.* 2001; Dombrovski *et al.* 2008, 2011). The psychological and cognitive underpinnings of premeditated suicidal behavior are less understood. Our earlier behavioral study found evidence that suicide attempters’ decision-making aligns with the profile of their real-life suicidal behavior (Dombrovski *et al.* 2011). Specifically, individuals with a history of poorly planned suicide attempts demonstrated a shortsighted preference for immediate over delayed rewards, echoing Baumeister’s conceptualization of a focus on immediate outcomes as a feature of the suicidal state (Baumeister 1990). In contrast, individuals who had carefully planned their suicide attempts demonstrated an intact ability to delay gratification. This study examines neural underpinnings of delayed gratification in suicide attempters in an attempt to further understand decision processes that lead to suicide.

Little is known about neural mechanisms of disadvantageous decision-making in suicidal individuals. One likely focus of individual differences is the mesostriatal-paralimbic reward system, thought to represent the subjective value of options (Bartra *et al.* 2013; Chase *et al.* 2015). Indeed, our earlier study suggested that impulsivity and poorly planned suicide attempts are paralleled by altered value signals in the paralimbic cortex, particularly the vmPFC (Dombrovski *et al.* 2013). A similar neural signature of impulsivity has been observed in problem gamblers (Miedl *et al.* 2012). It is not known, however, whether premeditated suicide attempts are similarly associated with alterations of value representations. The behavioral evidence of the ability to delay gratification in this group (Dombrovski *et al.* 2011) would suggest otherwise. Some studies have argued that the neural signature of this ability resides in cognitive control areas, such as the lateral prefrontal cortex (McClure *et al.* 2004; Tanaka *et al.* 2004; Wittmann *et al.* 2007). Taken together, these findings suggest different alterations of neural substrates in individuals with impulsive versus more premeditated suicide attempts.

The current study aimed to characterize these different alterations by examining neural correlates of value during delay discounting in suicide attempters. The delay-discounting task is ideal for examining how individuals track the values of options as they make choices between smaller immediate and larger delayed amounts of money. Choices on this task incorporate both reward magnitude and its time of delivery into the representation of subjective value (Frederick *et al.* 2002). Subjective value signals have been observed in medial orbitofrontal/ventromedial prefrontal cortex (mOFC/vmPFC), ventral striatum and

posterior cingulate cortex/precuneus (Kable & Glimcher 2007; Wittmann *et al.* 2007; Weber & Huettel 2008). We hypothesized that suicide attempts, particularly poorly planned ones, as well as trait impulsivity would predict altered value representations in the paralimbic cortex, consistent with Dombrovski et al. (2013). In addition, different functional mechanisms have been proposed for processing proximal versus distal delays in reward delivery (McClure *et al.* 2004; Wittmann *et al.* 2007), suggesting that delays surpassing some internal criterion, e.g., > 1 year, may result in the rewards being discounted more strongly than the more proximal rewards, e.g., 1 year. If suicidal behavior is accompanied by a more present-focused state (Baumeister 1990), this perspective may be reflected in altered temporal representations.

We attempted to characterize the mechanisms behind these alterations by employing two analytic approaches: isolating trial-by-trial value signals and contrasting value-guided choices when the delayed option is proximal versus distant (as in Wittmann *et al.* 2007). The latter approach examines more closely how incorporating temporal information into value representations may differ in our groups. In addition, we explored neural correlates of delay discounting as a function of degree of premeditation for the past suicide attempt to test if behavioral differences observed in Dombrovski et al. (2011) are paralleled by distinct patterns of neural activity. In addition to non-psychiatric controls, we included a group of depressed non-suicidal individuals to detect an association between decision-making and suicidal behavior beyond the effects of depression. We did not predict differences in discounting behavior between non-suicidal depressed and suicide attempter groups because of the aforementioned heterogeneity of the suicide attempters.

Methods

Participants—Forty-eight participants aged 46–90 years completed the study: 26 individuals with major depression (13 with and 13 without history of suicide attempt) and 22 healthy controls. All participants provided written informed consent. The University of Pittsburgh institutional review board approved the study. Their demographic, clinical and cognitive characteristics are described in Table 1.

Major depression was diagnosed by the Structured Clinical Interview for *DSM-IV* Axis I Disorders (SCID) (First *et al.* 1995). We excluded individuals with a diagnosis of clinical dementia and/or a score of less than 24 on the Mini-Mental State Examination. Further details on the recruitment of participants and exclusion criteria can be found in the Supplemental methods.

Suicide attempters engaged in self-injurious act with an intent to die; 5 made their first suicide attempt before 50 years of age, 2 after 50 years of age and 6 after 60 years of age. Medical seriousness of attempts was assessed using the Beck Lethality Scale (BLS) (Beck *et al.* 1975); for participants with multiple attempts, data for the highest-lethality attempt are presented. The suicidal intent of the suicide attempt was measured with Beck's Suicide Intent Scale (BSI) (Beck *et al.* 1974) ($M = 17.42$; $SD = 5.53$). The SIS-planning subscale (Mieczkowski *et al.* 1993) was used to assess the degree of planning of suicide attempts ($M = 6.85$, $SD = 2.73$). A study psychiatrist (A.Y. D. or K. S.) verified a history of suicide

attempts, based on the interview, medical records, information from family members and friends. We excluded participants with significant discrepancies between these sources.

Nonsuicidal depressed patients had no current or lifetime history of suicide attempts or suicidal ideation as established by clinical interview, review of medical records, SCID, and the Scale for Suicidal Ideation. Participants were excluded from this group if they had a current passive death wish or a history of indirect self-destructive behaviors.

Nondepressed controls were included as the benchmark group. They had no lifetime history of any psychiatric disorder as determined by SCID.

Clinical and cognitive assessments used to characterize the study groups are described in detail in the Supplemental methods.

Impulsivity, social problem solving, and attempt-related impulsivity

Impulsivity is a multifaceted construct (Sharma *et al.* 2013). In this study, we used a self-report measure sensitive to the aspects of trait impulsivity involved in suicidal behavior. The Impulsive/Careless Style subscale of the Social Problem-Solving Inventory (SPSI-ICS) (D’Zurilla & Nezu 1990; Gibbs *et al.* 2009) measures a narrow and hurried approach to social problem-solving situations.

The degree to which suicide attempts were planned (SIS-planning) captures preparation, premeditation, isolation, timing, and precautions against discovery (Mieczkowski *et al.* 1993). Our past research indicated that the planning of suicide attempts in the elderly is inversely related to the willingness to wait for larger rewards on a delay discounting task (Dombrovski *et al.* 2011) and to paralimbic expected value signals (Dombrovski *et al.* 2013). In the larger sample of suicide attempters, the SIS-planning subscale was found to be moderately correlated with the SPSI self-report measure of impulsivity.

Discounting task (modified from Wittmann *et al.* 2007)

On each trial, participants chose between an immediate smaller monetary reward and a larger delayed monetary reward. The delayed amount was presented in six possible delay conditions (5 day, 30 days, 90 days, 365 days or 1 year, 1095 days or 3 years, 3650 days or 10 years), blocked. The delayed amount remained constant mean = \$1000 within a block but varied between blocks (range \$976-\$1020) to prevent stereotyped responding. The immediate amount was titrated to the participant’s *indifference point* (Wittmann *et al.* 2007), i.e., the magnitude of the smaller immediate reward equivalent in value with the delayed discounted reward. This was done by re-specifying the lower and upper limits for the immediate prospect based on participants’ actions as follows (Figure 1). Initially, the interval between \$0 and the delayed prospect (e.g., \$1020) was divided in 3 parts. On the first trial, participants were presented with an immediate prospect with 1/3 magnitude of this interval (\$340) and on second trial with 2/3 magnitude of this interval (\$680). If the participant (1) rejected the first and second options, the upper interval was used (\$680-\$1020); (2) rejected the first but accepted the second option, the middle interval was used (\$340-\$680); (3) accepted both first and second options, the lower interval was used (\$0–

\$340). In the trials that follow, the range of the immediate prospect continues to narrow. Participants completed eight choices within each block, for a total of 48 trials.

The task necessitates making increasingly more difficult decisions based on computations that incorporate both magnitude and time into subjective value representations. The degree to which individuals value immediate versus delayed rewards, i.e., *discounting*, has been shown to be trait-like, stable within subjects, and scale with impulsivity (de Wit *et al.* 2007; Kable & Glimcher 2007; Peters & Büchel 2009; Miedl *et al.* 2012). For a given delay and a delayed reward of constant magnitude, more impulsive individuals tend to favor smaller immediate rewards before expressing preference for the delayed amount, resulting in an indifference point that is lower than for less impulsive individuals.

Data acquisition

Imaging data were collected with a 3-T Siemens Trio Tim scanner located in the MR Research Center at the University of Pittsburgh. For functional image alignment we used T2*-weighted image depicting blood oxygenation level-dependent (BOLD) contrast; TR = 1250ms, TE = 28ms, FOV = 24cm, flip = 60, 27 4mm slices). Stimulus presentation and response recording was controlled using the E-Prime software package (*E-Prime 2.0 software* 2002).

Image preprocessing

Functional images were preprocessed using tools from AFNI (Cox 1996) and the FMRIB software library (FSL; Smith *et al.* 2004). Functional volumes were aligned to the mean functional image using the FSL MCFLIRT program with sinc interpolation, and head motion parameters were estimated. Volumes with scan-to-scan movement over 0.7 mm in any dimension were censored from analyses (< 2%). Next, slice-timing correction was performed using FSL slicetimer. Non-brain voxels were removed from functional images by masking voxels with extremely low intensities and by a brain-extraction algorithm implemented in FSL's BET. Anatomical scans were registered to the MNI152 template (Fonov *et al.* 2009) using both affine transformation (FSL FLIRT) and nonlinear deformation (FSL FNIRT). The alignment of functional images to each subject's anatomical scan was computed using the white matter segmentation of each image and a boundary-based registration algorithm (Greve & Fischl 2009). Functional scans were then resampled into 3mm-isocubic voxels and warped into the MNI152 template's space using the concatenation of the functional-structural and structural-MNI152 transforms. Images were spatially smoothed using an 8mm full-width at half-maximum kernel (FSL SUSAN). A .008 Hz temporal high-pass filter was then applied to remove slow-frequency-signal changes. Finally, images were normalized to a global-median intensity of 10,000 to allow for comparability of parameter estimates across subjects.

Data analysis

Single subject analyses employed AFNI's 3dDeconvolve. To verify the presence of robust task-related activation, we contrasted task performance versus fixation by including an event regressor with a duration from the onset of reward options to the time of response

(Supplemental results). Two other models, described below, used parametric modulators convolved with response times.

Model 1: *value difference*.—One approach to modeling value is to assume hyperbolic discounting and calculate the difference between the smaller immediate (SIR) reward and the discounted delayed (DDR) reward for each trial, the latter being the subject's indifference point. This is appropriate for designs where trials with different delays are interleaved. In the current design, however, the trials were blocked by delay, resulting in the poor fit of the hyperbolic model. This led us to choose a modeling approach free of assumptions about hyperbolic discounting and equivalence of discount rates across blocks. We offer further illustrations of these issues and also describe converging findings from the conventional modeling approach in Supplemental methods.

Our *value difference* model included the following regressors: SIR, mean-centered for each block to account for between-block differences, as well as the block mean of SIR. Conceptually, the mean-centered SIR regressor captured trial-wise variation in relative value within each block. Higher values of the mean-centered SIR indicated that the immediate prospect dominated (relatively higher value of smaller immediate reward), while lower values indicated that the delayed prospect dominated (relatively higher value of larger delayed reward). The block mean represented the between-block variation in value differences, or block-wise scaling parameter of value. Since the SIR was titrated to the subject's indifference point, the block mean also approximated the value of delayed reward. Thus, the inclusion of both of these regressors permits disaggregation of within- and between-block effects of relative value on the neural response [see (Curran & Bauer 2011) for a related discussion of mean-centering to separate within- versus between-cluster variance in longitudinal models]. Delayed reward was constant and was thus not included in the model.

The performance of the value difference model was compared with the traditional model. While the parametric maps for these two models were qualitatively the same, we report the more robust findings from the *value difference* model. Note that by not incorporating choices, our approach also maintains the separation between value-related computations and subject's behavioral policy on the task, which may not always coincide. Model 2: the *longer versus shorter delays* model contrasted the blocks with longer (> 365 days) delays versus shorter (< 365 days) (adapted from Wittmann et al., 2007).

Each of the regressors was convolved with the canonical SPM5 double-gamma hemodynamic-response function. Voxelwise BOLD signal was regressed on these estimates in the single-subject analyses using AFNI's 3dDeconvolve (Cox, 1996). For group comparisons we used AFNI's 3dRegAna to regress the beta weights against predictors that included depression, history of suicide attempts and age (we verified that results were the same with and without co-varying for age). Results from these analyses were additionally verified by pairwise *t*-test comparisons.

The cluster threshold for whole-brain analysis was set with Monte Carlo simulations based on the residual spatial smoothness of the maps using the AFNI's 3dFWHM and 3dAlphaSim

programs (Forman *et al.* 1995; Cox 1996) ($p_{\text{voxelwise}} < .001$, 22 voxels, yielding $p_{\text{corr}} < .05$). Data from surviving clusters were extracted for further functional region of interest (ROI) analyses. We used the Talairach-Tournoux atlas for region identification.

Further, where multiple clusters were indexed by group analyses, we identified inter-correlated networks to reduce dimensionality and control type I error. These networks were identified through principal components analyses (using oblique promax rotation to allow for intercorrelation among components) on the cluster-wise beta coefficients from single-subject models. We used scree plots to find the number of networks that best account for cluster-wise variance in beta coefficients.

Results

Behavioral data is reported in the Supplemental results

Main effect of task—Task performance compared to fixation elicited a robust activation of visual areas, thalamus, striatum, and lateral frontoparietal and cingulo-opercular networks. The details and the correlations with task performance are included in the Supplemental results.

Value difference—In the entire sample, value difference favoring the delayed option elicited BOLD activity in the bilateral precuneus (BA 7) extending into the posterior cingulate cortex (PCC [BA 30–31]), shown in Figure 2A. No regions responsive to value differences favoring the immediate option were found at the pre-defined threshold. However at the lower voxelwise threshold of $p < .005$ ($p_{\text{corr}} < .05$), we observed activations in the right dorsolateral prefrontal cortex (Supplemental results). We performed an additional analysis with *trial difficulty* (Supplemental results), determined by how close the two prospects were in subjective value, and found that the response in the precuneus region was greater to easier choices. Hence, the precuneus appears to respond more as delayed prospect increases in subjective value.

Group comparisons: History of suicide attempts predicted a diminished response of the left dorsolateral prefrontal cortex (BA 9) to the increasing value difference favoring smaller immediate reward (Figure 2B).

The extent of this alteration was greater in patients with better-planned suicide attempts, measured by the SIS-planning subscale ($r[11] = -.56$, $p < .05$) (Figure 3A). These findings held when the data were analyzed using an alternate model of value difference (see Supplemental results for more details).

Correlations with Impulsivity Measures: A negative association of precuneus/PCC response with the SPSI-ICS subscale ($r[46] = -.33$, $p < .05$) suggested that in the more impulsive individuals this region that prospects favoring the delayed option elicited greater negative responses (Figure 3B). No other relationships, i.e. with geometric mean of the delay discounting parameter or degree of attempt planning, were significant.

Tracking value of choices with longer (>1 year, 1) versus shorter (1 year, 0) delays

Analyses in the entire sample identified 11 regions responsive to delays > 1 year (summarized in Table 2 and illustrated in Supplemental results).

PCA of cluster-wise individual beta coefficients identified four distinct networks of regions activated by longer versus shorter delays contrast. Longer delays were associated with increases in BOLD signal in visual (right lingual gyrus, right and left middle occipital gyrus [BA 18 and 19]), visual attention (left lingual gyrus [BA 18], thalamus, left fusiform gyrus [BA 19]) and motor/somatosensory (left superior parietal lobule [BA7], right precentral [BA 6], left medial frontal gyrus [BA 6]) networks, and with a diminished response in the right cuneus (BA 19). There was a modest positive correlation between the activity in the right cuneus and the geometric mean of the discount rate ($r[46] = 0.30, p < .05$), with more diminished responses for greater discounters (see Supplemental results for the illustration). The responses in these networks did not correlate with the impulsivity measures.

Group comparisons—History of suicide attempts was associated with the deactivation of the left parahippocampal gyrus (BA 35; MNI coordinates: $-24, -26, -16$; cluster volume: 594 mm^3 ; $t[44] = -4.36$) and left middle occipital gyrus (BA 37; MNI coordinates: $-47, -66, -13$; cluster volume: 1485 mm^3 ; $t[44] = -5.86$) to trials with longer delays.

Sensitivity analyses

Group differences for both models (value difference signals in the left dorsolateral prefrontal cortex and longer versus shorter delay signals in parahippocampal and left middle occipital gyri) were robust to the effects of possible brain damage from suicide attempts, burden of physical illness, depressive severity, co-occurring substance use and anxiety disorders, exposure to antidepressants, opioids and sedatives, lifetime exposure to electroconvulsive therapy, global cognitive functioning, variability in premorbid intelligence, and sex. No covariates were significant. We report the statistical results of these analyses in the Supplemental results.

Discussion

We investigated the functioning of neural systems that may underlie suicide attempters' myopia for future outcomes and the ability of some to delay gratification, as participants expressed their preferences for smaller immediate or larger delayed rewards. Choices on this task reflect subjective value comparisons that take into account both magnitude of the reward and its time of delivery (Frederick *et al.* 2002). Consistent with earlier studies (Kable & Glimcher 2007; Sripada *et al.* 2011; Manning *et al.* 2014), paralimbic cortex (precuneus/posterior cingulate [PCC]) was recruited as the larger delayed rewards increased in value. Additional analyses with trial difficulty suggested that the precuneus appears to respond more as delayed prospects increase in subjective value (thereby reflecting increasingly easier choices). The paralimbic response also scaled with impulsivity: greater difference in PCC responses between earlier and later prospects was seen in the more impulsive individuals. The dorsolateral prefrontal cortex (dlPFC) tracked the value difference for smaller immediate > larger delayed rewards, albeit only at a lower threshold. Unexpectedly, suicide

attempts, particularly, those that were well-planned, were associated with deactivation of dlPFC in response to increasing value of immediate choices. In addition, an exploratory contrast of blocks involving longer versus shorter delays identified visual, attentional, and motor/somatosensory networks partially replicating earlier reports (Wittmann *et al.* 2007). Suicide attempters displayed deactivation in parahippocampal and occipital cortices when a decision had to be made between rewards more than year apart or, alternatively, activation in these regions was higher when a decision had to be made between rewards a year or less apart.

Our predictions focused on regions in the *valuation* and *cognitive control* networks because altered functioning of these regions has been linked with suicidal behavior (Ernst *et al.* 2009; van Heeringen & Mann 2014). Our findings are consistent with the previously observed relationship between individual differences in self-reported trait impulsivity and those in paralimbic representations of subjective value during the discounting performance (Kable & Glimcher 2007; Peters & Büchel 2011; Sripada *et al.* 2011). Specifically, in the present study, trait impulsivity predicted greater negative responses of the precuneus/PCC as value difference increasingly favored the delayed prospect. This region was previously found to track the subjective value of intertemporal prospects (Kable & Glimcher 2007; Sripada *et al.* 2011). As shown by Kable and Glimcher (2007), impulsive individuals displayed steeper neurometric discounting curves than the more patient individuals. This was reflected in greater difference in PCC responses between earlier and later prospects in the impulsive than the more patient individuals. The current result is also consistent with our earlier report of blunted learned value signals in the paralimbic cortex (vmPFC and PCC/precuneus) of suicide attempters, particularly those with poorly planned attempts, and individuals high in trait impulsivity during a probabilistic reversal learning task (Dombrovski *et al.* 2013). Associations between impulsivity and responses to value difference during this task may be interpreted as a suboptimal integration of temporal information in the valuation network (Bechara *et al.* 2002; Miedl *et al.* 2012).

Value-based choices are also known to be modulated by the regions in the cognitive control network, i.e., lateral prefrontal cortex (PFC) (Hare *et al.* 2009), which also encodes decision-related information (Wallis & Miller 2003; Kennerley & Wallis 2009). This modulation has sometimes been described as top-down control that allows individuals to maintain and pursue goals (Wesley & Bickel 2014), for example, by continuing to choose a larger delayed reward, in spite of the relative increases in the value of the smaller immediate reward.

Although our findings are preliminary given the small sample size, this perspective suggests that altered representations of decision-related variables in the lateral PFC may underlie some aspects of anomalous decision-making in suicide attempters. In the present study, a high level of premeditation was paralleled by reduced dlPFC cortex responses to relative increases in value favoring immediate prospect. This result is consistent with our earlier behavioral finding that immediate rewards had less of an incentive value for individuals with a history of premeditated suicidal behavior (Dombrovski *et al.* 2011). It has been suggested that the dlPFC influences difficult choices, which require self-control (Hare *et al.* 2009; Cho *et al.* 2010; Figner *et al.* 2010; Manning *et al.* 2014). For example, Manning *et al.* (2014) demonstrate increased prefrontal activity during rational choices that are contrary to one's

dispositional tendencies. This was true among highly conscientious individuals who choose the immediate option. Further, extending behavioral evidence that the ability to delay gratification relies on cognitive control, dlPFC substrates of working memory and temporal discounting overlap, which points to its more general role in self-control and pursuit of goals (Wesley & Bickel 2014).

One factor at play in a suicidal crisis may be the individual's inability to represent personal future (Yufit *et al.* 1970; Brockopp 1971; Greaves 1971; Baumeister 1990; Williams *et al.* 1996). The contrast of prospects with longer versus shorter delays revealed deactivation in the parahippocampal region in suicide attempters. Parahippocampal gyrus is implicated in spatial navigation (Aguirre *et al.* 1996) but also in *prospection*, or mental representation of the future, and autobiographical memory (Spreng & Grady 2010). The blunted parahippocampal response to remote prospects may, therefore, represent a neural substrate of impaired *prospection* in suicidal individuals, (Schacter *et al.* 2007; Peters & Büchel 2010, 2011), potentially undermining the deterrents and alternative solutions during the suicidal crisis. Noteworthy, reduced specificity of autobiographical memories, as a consequence of retrieval difficulties, has been linked to diminished problem-solving abilities (Arie *et al.* 2008) and, separately, to suicidal behavior (Williams *et al.* 1996).

The main limitations of our study are the small sample size and cross-sectional case-control design. Independent of these limitations, our ability to rule out potential confounders (global cognitive function, depressive severity, medication exposure and possible brain injury from suicide attempts), as well as, replication of main neuroimaging findings using different modeling approaches add confidence in the findings.

In conclusion, our small cross-sectional case-control study uncovered three patterns of neural responses potentially underlying altered decision processes in suicidal behavior. First, suicide attempts, particularly better-planned ones, were associated with a lack of modulation of the dlPFC by increasing subjective value of immediate rewards. Second, paralimbic (precuneus/PCC) responses to value difference favoring the delayed option scaled with trait impulsivity, reflecting the individual differences in the steepness of discounting curves for subjective value. Finally, we found diminished parahippocampal responses in suicide attempters to temporally-remote prospects, which we interpreted as evidence of altered *prospection*. Taken together, these findings suggest that distinct alterations in the way time is integrated into decision-making in the brain may mark different cognitive pathways to suicidal behavior.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Illustration of the incremental narrowing of the interval for SIR choice as a function of participant's choices.

Figure 2.

Panel A shows the BOLD response in the whole sample to value difference in the precuneus (BA7)/posterior cingulate cortex (PCC [BA30–31]) at $p_{\text{voxelwise}} < .001$, $p_{\text{corr}} < .05$ (MNI coordinates: $-1, -61, 30$; cluster volume = 28764 mm^3 ; peak $t[47] = -6.66$). Panel B shows that the history of suicide attempts predicted a diminished response of the left dorsolateral prefrontal cortex (BA 9) to the increasing value difference favoring smaller immediate reward. (MNI coordinates: $-48, 10, 35$; cluster volume = 1107 mm^3 ; peak $t[44] = -4.60$). These findings held when the data were analyzed using an alternate model of value difference (see Supplemental results for more details).

Figure 3.

Panel A illustrates the correlation between SIS-planning and activity in the left dorsolateral prefrontal cortex (BA 9) derived from the value difference map. Panel B illustrates the correlation between Impulsive/careless subscale scores on Social Problem Solving scale and activity in the precuneus derived from the value difference map.

Table 1

Demographic, Clinical, and Cognitive Characteristics

Characteristic	Study Group					Statistic	p-value	Post-hoc Tukey HSD
	Non-psychiatric Controls (n = 22)	Non-suicidal Depressed (n = 13)	Depressed Suicide Attempters (n = 13)					
Male sex, No. (%)	7 (32)	3 (23)	8 (62)		$\chi^2 = 4.66$	.10		
Age in years (SD)	72.09 (10.6)	73.38 (5.5)	70.38 (8.9)		$F = 0.42$	.74		
White, No. (%)	20 (91)	7 (54)	10 (77)		$\chi^2 = 4.33$	.12		
Educational level, y	14.64 (2.5)	14.46 (2.3)	15.46 (3.3)		$F = 0.35$	.80		
Premorbid IQ, WTAR scaled (n = 41)	107.20 (9.4)	105.73 (17.3)	110.27 (14.7)		$F = 0.35$	.71		
Dementia rating scale (n = 47)	138.05 (2.7)	136.77 (4.3)	133.92 (7.8)		$F = 2.76$	.07		
Executive interview (n = 47)	6.50 (3.3)	6.77 (4.3)	8.08 (4.0)		$F = 0.71$	.50		
Physical illness burden (SD)	6.18 (2.9)	10.62 (2.7)	8.69 (5.9)		$F = 5.48$	.01		HC ¹ < D ²
Hamilton Rating Scale for Depression (without suicide item) (SD)	2.50 (2.2)	13.15 (6.9)	14.46 (8.0)		$F = 23.88$	.00		HC < D, SA ³
Beck Hopelessness Scale (SD)	1.05 (0.95)	8.15 (5.16)	11.62 (6.7)		$F = 25.86$	.00		HC < D, SA
Suicide Intent Scale: Planning subscale (SD)	NA	NA	6.85 (2.73)					
Social Problem Solving Inventory: Impulsive/Careless Style subscale	2.82 (2.58)	4.69 (2.75)	4.77 (3.24)		$F = 1.95$	.14		
Antidepressant exposure (n = 18)	NA	1.88 (1.8)	3.91 (3.2)		$F = 2.59$	.13		
Lifetime substance use disorders, No.	NA	4	7		$\chi^2 = 1.42$	.23		
Lifetime anxiety disorders, No.	NA	4	5		$\chi^2 = 0.17$	.68		

¹ HC = healthy controls;² D = depressed non-suicidal;³ SA = suicide attempters

Table 2

BOLD response to longer (> 1 year) versus shorter delays (≤ 1 year) contrast

Region	MNI Coordinates ^I	Peak <i>t</i> (47)	Cluster Size (mm ³)
[1] Left Middle Occipital Gyrus (BA 19/18)	−29, −89, 4	7.06	10422
[2] Left Superior Parietal Lobule (BA 7)	−30, −63, 47	5.73	8208
[3] Left Lingual Gyrus (BA 18)	−25, −79, −16	4.04	675
[4] Left Fusiform Gyrus (BA 19)	−41, −68, −20	6.05	1809
[5] Left Medial Frontal Gyrus (BA 6)	−3, 15, 52	5.40	2484
[6] Left Thalamus	−1, −18, −1	5.26	1431
[7] Right Lingual Gyrus/Cuneus (BA 17)	17, −92, −2	4.68	1782
[8] Right Middle Occipital Gyrus (BA 18)	25, −92, 18	5.11	2106
[9] Right Cuneus (BA 19)	8, −85, 32	−5.00	1134
[10] Right Middle Occipital Gyrus	35, −77, −14	4.57	1377
[11] Right Precentral Gyrus (BA 6)	43, −8, 61	4.82	675

^I We used Talairach-Tournoux atlas (TLRC) and the corresponding TLRC coordinates of the peak voxel to identify the region.