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Neural Correlates of Autobiographical Problem-Solving Deficits Associated with Rumination in Depression

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Abstract

Background—Analytical rumination can be characterized as negative thoughts focused on searching for answers to personal problems. Failure to think concretely during autobiographical problem-solving (APS) is hypothesized to drive the inability of ruminators to generate effective solutions. Clarifying the brain correlates underlying APS deficits in depressed ruminators may identify novel biological targets for treatment.

Method—Forty participants (22 unmedicated depressed and 18 never-depressed adults) ranging in rumination engaged in APS and negative self-referential processing (NSP) of negative trait adjectives during fMRI. We contrasted activation during APS with activation during NSP to isolate regions contributing to APS.

Results—Rumination was associated with having generated fewer solutions during APS and with a failure to recruit the angular gyrus (AG) and the medial frontal gyrus (MFG) during APS. Rumination was associated with greater MFG activation during NSP and stronger connectivity between the AG and the rostrolateral prefrontal cortex (RLPFC) during APS relative to NSP. Findings were not driven by clinical status.

Limitations—The use of an extreme groups approach can result in overestimation of effects sizes.

Conclusions—Ruminators fail to recruit regions with the default network (DN) that support APS. In particular, a failure to recruit the AG during APS may drive the abstract thinking style previously shown to explain depressed ruminator's difficulty generating concrete solutions. Targeting this mechanism directly may reduce rumination.

Keywords

Depression; Rumination; Autobiographical Memory; fMRI; Mental Simulation; Problem-Solving

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Introduction

The predominant motivations individuals give for engaging in repetitive negative thinking is to increase self-awareness and understanding of negative emotional states and to solve problems/prevent future mistakes (Watkins and Baracaia, 2001). This process can be adaptive (Matheson and Anisman, 2003; Treynor et al., 2003), but a subset of individuals appear to dwell on their problems and emotional reactions without generating or implementing effective solutions (Burwell and Shirk, 2007; Lyubomirsky and Nolen-Hoeksema, 1995; Lyubomirsky et al., 1999; Marx et al., 1992; Watkins and Baracaia, 2002). Thus, while these individuals believe they are engaging in adaptive autobiographical problem solving (APS), also referred to as self-reflection (Burwell and Shirk, 2007; Treynor et al., 2003), they are actually engaging in maladaptive rumination known to be associated with the onset, severity, and duration of depression (Abela and Hankin, 2011; Just and Alloy, 1997; Nolen-Hoeksema, 2000; Nolen-Hoeksema and Morrow, 1991; Nolen-Hoeksema et al., 1993; Spasojevic and Alloy, 2001). Behavioral evidence indicates that clinically depressed ruminators think abstractly rather than in concrete detail about their personal problems (Watkins and Baracaia, 2002; Watkins and Moulds, 2007) and recall non-specific memories during problem-solving that are devoid of relevant analogue situations (Goddard et al., 1996). Furthermore, this ruminative abstract thinking style partially explains why individuals diagnosed with major depressive disorder have difficulty generating effective solutions (Evans et al., 1992; Watkins and Moulds, 2005). To date, the brain regions underlying autobiographical problem-solving (APS) deficits in clinically depressed ruminators are not well understood. Clarification of these mechanisms could lead to the identification of novel biological targets for treatment.

Autobiographical problems tend to be ill-defined, or open-ended, such that the procedures for solving them cannot be readily stored and retrieved from semantic memory (Sheldon et al., 2011). Effective solution generation requires the recollection of specific analogue situations from memory that are relevant to the current problem (Evans et al., 1992; Goddard et al., 1996; Jing et al., 2016; Watkins and Baracaia, 2002) and the simulation of possible scenarios to determine the appropriate solution and/or solution paths (Sheldon et al., 2011). Successful APS has been shown to actively recruit portions of the default network (DN) coupled with the frontoparietal control network (FPCN) which may serve to maintain detailed internal trains of thought (Spreng et al., 2015; Spreng and Schacter, 2012; Spreng et al., 2010). These findings are consistent with accounts that APS involves both autobiographical memory retrieval and mental simulation, which are largely supported by both the DN and the lateral prefrontal cortex (Schacter et al., 2007; Schacter et al., 2012; Spreng et al., 2009). The DN contains subsystems that may contribute differentially to APS (Andrews-Hanna et al., 2010; Andrews-Hanna et al., 2014). Specifically, the midline core comprised of the anterior medial prefrontal cortex (amPFC), posterior cingulate cortex (PCC), and bilateral angular gyrus (AG), may support the processing of self-referential aspects of memories and the simulation of future social interactions (Andrews-Hanna et al., 2014; Szpunar et al., 2013). The left angular gyrus (AG), in particular, may support the ability to strategically access and attend to the specific details associated with a memory (Berryhill, 2012; Berryhill et al., 2007; Berryhill et al., 2010; Gorgolewski et al., 2014;

Spreng et al., 2015; Zhu et al., 2012) needed for successful APS. The medial temporal subsystem, which is comprised of hippocampus, parahippocampal cortex, retrosplenial cortex, posterior inferior parietal lobe (IPL), and the ventromedial prefrontal cortex, may support the ability to retrieve associative information from episodic memory and the construction of the coherent mental scenes needed to generate and simulate possible solutions (Andrews-Hanna et al., 2014; Szpunar et al., 2013).

Critically, greater activation and connectivity within the aMPFC and PCC has repeatedly been linked to the tendency to engage in maladaptive rumination in clinically depressed populations at rest (Berman et al., 2010; Hamilton et al., 2011a; Hamilton et al., 2011b; Zhu et al., 2012), which is thought to reflect increased self-referential and emotional processing (Fossati et al., 2003; Moran et al., 2006). These results suggest that depressed ruminators may activate regions in the midline core more when engaging in maladaptive negative self-referential processing (NSP) and less during adaptive analytical self-referential processing such as APS (Johnson et al., 2009). To date no published work has examined the neural underpinnings of APS deficits that are associated with rumination specifically among depressed individuals. Thus, it remains unclear the degree to which APS deficits associated with rumination in depression are associated with failure to recruit regions within the DN that facilitate adaptive APS. To test whether brain regions within the DN underpin APS deficits associated with rumination in the context of major depressive disorder (MDD), we created a novel problem-solving paradigm wherein participants were instructed to attempt to increase their understanding of and to generate solutions to their most pressing unresolved problems while undergoing a functional magnetic resonance (fMRI) assessment. We contrasted activation during adaptive APS with activation during maladaptive NSP to isolate regions contributing to APS (Moran et al., 2006; Yoshimura et al., 2013; Yoshimura et al., 2010; Yoshimura et al., 2009). We used an extreme groups approach to improve cost-efficiency without compromising statistical power (Preacher et al., 2005). The sample was comprised of never-depressed adults (healthy controls; HC, low rumination spectrum) and individuals diagnosed with MDD (high rumination spectrum). We hypothesized that rumination would be associated with decreased activation within the DN during APS relative to NSP; furthermore, we evaluated whether associations between rumination and regions identified within the DN midline core varied as a function of context (ASP vs. NSP). We also hypothesized that rumination would be associated with stronger functional connectivity between the angular gyrus and the right rostrolateral prefrontal cortex (r.RLPFC), given the demonstrated role of the r.RLPFC in the online maintenance and elaboration of emotional representations retrieved from memory (Daselaar et al., 2008).

Methods and Materials

Participants

Forty adults (age range: 18–48 years, $M_{\text{age}}=25.1$, $SD=7.1$ yrs., 70% females, 85% Caucasian, 7.5% African American, 2.5% Asian, 2.5% Hispanic/Latino, 2.5% Other) ranging in ruminative tendency ($M=3.1$, $SD=1.1$, range: 1.3 – 5) participated in the current study. The sample was comprised of twenty-two unmedicated adults diagnosed as having a current major depressive episode via a structured clinical interview (SCID-I; First et al.,

1996) and 18 never-depressed healthy controls (HC) with no current or past psychiatric diagnoses based on the SCID-I (First et al., 1996), and with no known first-degree relatives with psychiatric diagnoses. Seven participants were lost to analysis due to excessive sleepiness as indicated by prolonged eye closures observed via video-monitoring and behavioral non-responsiveness (MDD $n=4$; controls $n=1$) or due to technical difficulties during scan acquisition (MDD, $n=2$). The final sample was comprised of 33 adults (16 MDD; 17 HC; age range: 18–48 years, $M_{\text{age}}=24.9$, $SD=6.8$ yrs., 67% females, 91% Caucasian, 3 % African American, 3 % Asian, 3% Hispanic/Latino) ranging in ruminative tendency ($M=3.0$, $SD=1.2$, range: 1.3 – 5). Thus, we were adequately powered (80%) to detect a medium effect size ($r=.47$) setting $\alpha=.05$. All participants were required to have a Full Scale Intelligence Quotient Equivalent estimate (FSIQE) >80 based on the North American Adult Reading Test (NAART) (Nelson and Willison, 1991). All participants reported no significant health problems, psychoactive drug or alcohol abuse within the past 6 months, history of psychosis, or manic episodes and were not on psychotropic medications during the past month.

Procedure

Participants were recruited through flyers in the community and electronic postings. During an initial assessment, after providing written informed consent, all participants were screened using a SCID-I interview (First et al., 1996), completed a color-recognition test, and a cognitive screen. Participants were then trained on the APS task and completed a questionnaire battery assessing mood symptoms and rumination. Participants were scheduled for a second visit within two weeks. During this fMRI assessment visit, participants completed symptom questionnaires, practiced the task, and were asked to provide six personal problems that were used during the APS. Participants were then debriefed and compensated for their time. This study was approved by the University of Pittsburgh Institutional Review Board.

Self-Report Measures

The 12-item rumination subscale from the Rumination and Reflection Questionnaire (RRQ) was used to assess rumination prompted by threats, losses, and or injustices to the self (Trapnell and Campbell, 1999). As such, it encompasses primarily past-oriented self-focused recurrent thoughts associated with anxiety, depression, and anger, but without reference to emotional states or psychiatric symptoms. Thus, this measure—which loads highly on the same factor as the brooding and rumination subscales of ruminative response scale (Mandell et al., 2014; Nolen-Hoeksema et al., 1993; Siegle et al., 2004)—is not contaminated with items overlapping with depressive symptoms. Our extreme groups sampling approach was successful, the MDD group ($M=3.9$, $SD=0.7$) reported a greater tendency to engage in rumination relative to controls ($M=2.1$, $SD=0.8$; $t(31)=6.51$, $p<.001$, $d=2.39$). As shown in supplemental figure 1, we were able to capture the extremes of the rumination distribution, along with a small portion in the middle of the distribution.

APS Task

One hour prior to scanning, participants identified their six most troubling problems that they were currently trying to understand or solve. Participants then provided a brief

description of the problem (e.g., Getting laid off, not having work, not finding anything) and three cue words that when seen together prompted the recollection of the problem (e.g., Frustrated, Disappoint, Job). Acquiring cue words in close temporal proximity to the task was used to facilitate quick retrieval of the personal problem to allow more time for problem elaboration and problem-solving (Cabeza and St. Jacques, 2007; Daselaar et al., 2008). When in the scanner, participants were asked to develop a greater understanding of the problems and generate solutions. In order to differentiate APS from NSP, participants were also asked to view 18 negative adjectives presented in sets of threes (e.g., Fearful, Depressed, Unreliable) that were taken from a well-established list of personality trait words ranked based on their likeability (Anderson, 1968). Participants also rated 18 positive adjectives (positive self-referential processing, PSP) that were not the focus of the current investigation. Adjectives were selected from the top and bottom 20% of the list (Farb et al., 2007; Fossati et al., 2003). While in the scanner, participants were asked to think about what each word meant to them, and whether it described them or not. All trials in the APS, NSP, and PSP conditions included a fixation cue (1.67 sec); an introspective-period where three cue words—consisting of either participant-generated problem words or experimenter-selected trait adjectives—were presented (26.72 sec); a rating period, where participants indicated whether or not a solution was generated (used to calculate percentage of solutions generated) or whether one of the three presented words described them (3.34 sec); and a mask for the inter-trial interval (10.02 sec).

Post-Task Ratings

Following the scan, participants were audio recorded while they verbally recounted their thoughts as they had occurred during the problem-solving task for each of the six problems. Participants' narrative responses were transcribed and coded using a consensus approach with a team of two clinical psychologists (NPJ, LBS) and a research assistant to determine the severity of personal problems based on Likert scale ranging from 1 *Not at all Severe: Problems that impact convenience or luxury, e.g. mundane tasks, chores, etc.* to 5 *Very Severe: Problems that impact one's livelihood, e.g. providing basic needs, health issues*. Coders were blinded to rumination and clinical status. Problem severity was coded to be used as a control variable in supplemental analyses, given that more severe problems are likely more difficult to solve. The coding system is available in the supplementary materials. Participants also rated the degree of sadness and anxiety they experienced when trying to solve each of their problems on a Likert like scale ranging from 1 *not all* to 6 *a great deal*.

fMRI data Acquisition

fMRI data were collected using a 3.0-T Siemens Trio scanner. Each functional volume contained 32 oblique axial slices (TR=1.67, TE=29; FA=75°, FOV=205 mm, 3.2 mm thickness, 64 by 64 matrix, 3.2 × 3.2 mm in-plane resolution) parallel to the AC/PC plane. Axial anatomical images were acquired using a standard T1-weighted spin-echo pulse sequence using a finer in-plane resolution (1 mm thickness, FOV=25 mm, 256 by 256 matrix, 1 by 1 mm in-plane resolution). Preprocessing of the functional imaging data was completed using a variety of packages primarily including AFNI (Cox, 1996) and NIS (Fissell et al., 2003). Preprocessing included iterated least-square motion correction (AFNI 3dVolReg), realigning of volume slices to the same temporal origin (AFNI 3dTshift),

detrending and outlier correction (NISCorrect), temporal smoothing with a five-point middle-peaked filter (NISfilter), and voxelwise conversion to percent-change from the median of the data-set. Functional images were transformed into a common space using the parameters from co-registering the anatomical images to the MNI template (32 parameter non-linear warp to MNI brain),(Woods et al., 1992) and then spatially smoothed (6mm FWHM) to accommodate individual anatomical differences (NIS gsmooth).

Behavioral Data Analysis

Zero order correlational analyses were conducted to examine associations among rumination and subject rated percentage of solutions generated and emotional responses (i.e., subject rated anxiety and sadness) during APS.

fMRI Data Analysis

Whole-brain BOLD (Blood Oxygen Level Dependent) data analysis—A first-level GLM analysis was conducted using AFNI 3dDeconvolve which included: (1) the main effect of task which was modeled using a box-car function convolved with a single-gamma HRF with appropriately placed models of the HRF for the introspection period, and rating period for the problem-solving, negative-trait adjective, and positive trait adjective conditions; and (2) nuisance regressors which included the six motion parameters. The fixation cue and mask periods were included in the baseline. The main contrast of interest was the APS introspection period – negative trait adjective introspection period (APS -NSP). Whole brain analyses were conducted regressing rumination against level-1 estimates of brain activity for the APS-NSP contrast. Extracted brain regions surviving cluster thresholding for the APS-NSP contrast (described below) were probed to clarify the direction of associations between rumination and DN functioning under maladaptive and adaptive contexts. Specifically, a mixed effects analysis was used to examine condition (APS-Baseline, NSP-Baseline) x rumination interactions predicting activation within each region.

Functional Connectivity—We conducted a generalized context-dependent psychophysiological interaction analysis using activation from regions identified within the angular gyrus during the level 2 analysis described above as a seed region. Generalized PPI was conducted using previously published methods (Cisler et al., 2014; McLaren et al., 2012). In brief, activation within the identified seed regions was deconvolved using the hemodynamic response function (HRF) to obtain estimates of neural activity; (2) interaction terms for each condition were calculated by multiplying the vector of estimated neural activity with separate vectors of each conditions (APS, NSP, PSP) ON times and then convolving each interaction term with the HRF; (3) activation within the seed and the three generated interaction terms were subsequently added to the previously described level-1 model which was then re-estimated. Extracted brain regions surviving cluster thresholding (described below) were correlated with emotional responses during APS.

Familywise Error—The Type 1 error rate was controlled using AFNI's 3dClustSim -ACF option (Cox et al., 2016). Smoothness was estimated from the level 2 residuals for activity and connectivity analyses described above and a voxel-wise threshold of $p < .001$ was used

for cluster forming. These methods address issues raised by Eklund et al. (Eklund et al., 2016) and Woo et al. (Woo et al., 2014). Results indicated that an extent threshold of 38 voxels for activity analyses and 33 voxels for connectivity analyses corresponded to a cluster-wise familywise error rate of $p < .05$. For the main behavioral analyses, we used a Bonferroni correction to control the Type I error rate due to the number of correlational analyses conducted ($n=6$) which corresponded to effective $p < .008$ corresponding to $p < .05$ corrected.

Supplementary analyses

Finally, we also conducted specificity analyses to evaluate if rumination indeed accounted for unique variance in percentage of solutions generated and emotional responses during APS (sadness, anxiety) by conducting simultaneous regression analyses covarying for clinical status (MDD vs. HC) and problem severity in separate models. Similarly, we conducted simultaneous regression analyses to evaluate if rumination indeed accounted for unique variance in brain activity and brain connectivity indices over and above problem severity and clinical status. Given our extreme groups approach, this analysis provided a strict test of the hypothesis that brain activity and functional connectivity findings are being driven by rumination not clinical status.

Results

Behavioral Results

Rumination and Problem-Solving Ability—Rumination was associated with more severe problems ($r = .48$, $p = .004$) and having generated fewer solutions ($r = -.44$, $p = .001$). Furthermore, rumination was associated with greater sadness ($r = .69$, $p < .001$) and anxiety ($r = .66$, $p < .001$) during APS. The associations between rumination and percentage of problems solved, sadness, and anxiety remained significant after controlling for problem severity (see Table 1A). Simultaneous regression analysis indicated that rumination ($sr^2 = .11$, $p < .05$) was a stronger predictor of anxiety relative to clinical status ($sr^2 = .03$, $p > .10$; see Table 1B) and that clinical status ($sr^2 = .19$, $p < .01$) was a stronger predictor of problem severity relative to rumination ($sr^2 = .00$, $p > .10$). When combined in the same model neither rumination nor clinical status predicted sadness nor percentage of problems solved.

fMRI Results

BOLD Activation—As shown in Table 2, rumination was negatively correlated with activity within the medial frontal gyrus (Brodmann area; BA 10, Fig. 1A, 1B) and with activity within the AG (see Fig. 1C, 1D). As shown in Table 1B, rumination was a stronger predictor of MFG ($sr^2 = .31$, $p < .001$) and AG ($sr^2 = .41$, $p < .005$) activity relative to problem severity ($sr^2 = .00$, $ps > .10$). Critically, rumination was a stronger predictor of MFG ($sr^2 = .15$, $p < .05$) and AG ($sr^2 = .18$, $p < .01$) activity versus clinical status ($sr^2 = .00$, $ps > .10$) when both variables were included in the same model. The association between rumination and MFG activation varied as a function of context (ASP-Baseline vs. NSP-Baseline), $b = -.37$, $SE = .07$, $p < .001$ (Main effects: rumination: $b = 0.15$, $SE = .05$, $p = .005$; condition: $b = .18$, $SE = 0.08$, $p = .030$). As shown in Fig 1E, rumination was positively correlated with MFG activation during NSP ($b = 0.15$, $SE = .05$, $p = .005$) and negatively correlated with MFG activation during

APS ($b=-0.22$, $SE=0.05$, $p<.001$). The association between rumination and AG activation also significantly varied as a function of context, $b=-0.14$, $SE=.03$, $p<.001$ (Main effects: rumination: $b=0.04$, $SE=.02$, $p=.105$; condition: $b=0.00$, $SE=0.03$, $p=.926$). As shown in Fig 1F, rumination was not significantly correlated with AG activation during NSP ($b=0.04$, $SE=0.02$, $p=.105$), but was negatively correlated with AG activation during APS ($b=-0.10$, $SE=0.02$, $p<.001$).

Functional Connectivity—As shown in Table 2, connectivity analyses indicated that rumination was positively correlated with AG-r.RLPFC ASP vs. NSP connectivity (right middle frontal gyrus, BA10, Fig. 2A, 2B). As shown in Table 1B, rumination was a stronger predictor of AG-r.RLPFC connectivity ($sr^2=.35$, $p<.001$) relative to problem severity ($sr^2=.00$, $p>.10$). Critically, rumination was a stronger predictor of AG-r.RLPFC connectivity ($sr^2=.33$, $p<.001$) relative to clinical status ($sr^2=.03$, $p>.10$), when both variables were included in the same model. As shown in Fig 2C and Fig 2D, sadness ($r=.47$, $p=.006$) and anxiety ($r=.57$, $p<.001$) experienced during APS were positively correlated with AG-r.RLPFC connectivity.

Discussion

Using a novel APS paradigm, we demonstrated that rumination was associated with having more severe personal problems and with generating fewer solutions. Furthermore, rumination was associated with experiencing more sadness and anxiety during APS. Rumination was also associated with a failure to recruit the AG and MFG during APS and a greater tendency to activate the MFG during NSP. In addition, we observed that rumination was associated with stronger connectivity between the left AG and the r.RLPFC during APS relative to NSP, which was associated with negative mood. It is worth noting that, supplementary analyses indicated associations between rumination and problem-severity, percentage of problems solved, and sadness were likely confounded with or better explained by clinical status. However, given that rumination was a stronger predictor than clinical status for all other reported outcomes, the impact of rumination on APS warrants further investigation. Of note, high levels of rumination occurred almost exclusively within the MDD group; as such, our results more strongly reflect functional and connectivity abnormalities during APS that are associated with engaging in high levels of rumination in the context of MDD.

Our results support the hypothesis that rumination—occurring in this sample predominately in individuals diagnosed with MDD—is associated with a failure to activate regions within the midline core of the DN during APS. Depressed ruminators demonstrated decreased activation in the left AG during APS. Decreased angular gyrus activity is associated with the tendency to recall categories of events when asked to generate specific instances from memory (Zhu et al., 2012); recalling vague as opposed to specific thoughts at rest (Gorgolewski et al., 2014); and retrieving memories lacking in precision (Richter et al., 2016) as well as episodic detail (Daselaar et al., 2008). Thus, we hypothesize that decreased AG activity observed in the current context reflects an inability of depressed ruminators to access and attend to the full set of details associated with the problem and generate analogue situations from memory (Berryhill, 2012; Berryhill et al., 2007; Berryhill et al., 2010;

Gorgolewski et al., 2014; Spreng et al., 2015; Zhu et al., 2012) during APS. This would be consistent with past behavioral research indicating that ruminators think abstractly rather than in concrete detail about their personal problems (Watkins and Baracaia, 2002; Watkins and Moulds, 2007). As such, the angular gyrus may reflect the underlying neural mechanism that is likely targeted by concreteness training for rumination and depression which was designed to shift patients from engaging in an abstract thinking to a concrete thinking style (Watkins et al., 2009; Watkins and Moberly, 2009; Watkins et al., 2012). However, future research is needed to confirm this hypothesis. Depressed ruminators also demonstrated decreased activation in the MFG during APS. The aMPFC has been implicated in self-referential processing (Fossati et al., 2003; Moran et al., 2006); and the mental simulation of future social events (Addis et al., 2007; Szpunar et al., 2013) as well as the simulation of hypothetical scenarios that requires individuals to imagine themselves actively solving a problem (Gerlach et al., 2011). As such, one possibility is that depressed ruminators have a fundamental difficulty placing themselves in a hypothetical context in order to play out possible scenarios in the service of generating adaptive solutions to their problems (Schacter et al., 2008).

Interestingly, we observed that associations between rumination and aMPFC activation varied as a function of experimental context. Whereas, rumination was negatively associated with aMPFC activation during APS, rumination was positively associated with activation in the aMPFC during NSP. This later result is consistent with studies demonstrating that rumination is positively associated with greater activation and connectivity in aMPFC, at rest (Berman et al., 2010; Hamilton et al., 2011a; Hamilton et al., 2011b; Kucyi et al., 2014; Zhu et al., 2012).

As predicted, rumination was also positively associated with stronger functional connectivity between the angular gyrus and the r.RLPFC during APS relative to NPS, which was associated with negative mood during APS. Of note, the association between anxiety and r.RLPFC/angular gyrus connectivity held after controlling for clinical status, indicating that this association was not driven by clinical status. The r.RLPFC is uniquely sensitive to emotional intensity during memory access and the elaboration of autobiographical memories leading researchers to posit that it might serve as a form of affective working memory (Daselaar et al., 2008). Thus, we hypothesize that the r.RLPFC likely supports the ability of depressed ruminators to maintain a train of thought focused on abstract negative autobiographical information in the relative absence of generating effective solutions (Burwell and Shirk, 2007; Lyubomirsky and Nolen-Hoeksema, 1995; Lyubomirsky et al., 1999; Marx et al., 1992; Watkins and Baracaia, 2002). Future, research is needed to test the role of the r.RLPFC during ruminative processing.

Limitations

Several limitations of the current work warrant discussion. We used a highly novel idiographic problem-solving task; the main drawback to this approach is that stimuli were not standardized across participants. The use of such a relatively unconstrained task was chosen to examine the phenomena in question as naturalistically as possible. APS is predominately an intrinsically driven process that occurs without much external input. More

experimentally constrained tasks that promote externally focused attention are known to disrupt ruminative processing, making it difficult to study with standardized tasks (Spreng, 2012). A strength of the current methodology is that the debriefing interview increased our certainty that participants were actually engaging in APS and allowed us to characterize the severity of their problems. We also used an extreme groups approach which, while maximizing cost-efficiency and maintaining statistical power, can result in overestimation of effects sizes (Preacher et al., 2005). Future work is warranted that replicates our current findings in a large clinical sample of persons diagnosed with MDD varying in rumination.

Conclusion

The present study supports the conclusion that predominately depressed ruminators fail to recruit regions with the DN that support APS. A failure to recruit these regions, in particular, the angular gyrus, may drive the abstract thinking style that partially explains depressed ruminators difficulty in generating solutions to problems (Evans et al., 1992; Watkins and Moulds, 2005). Targeting angular gyrus functioning directly with novel treatments, such as transcranial direct stimulation, may improve our ability to address problem-solving deficits associated with ruminative processing.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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HIGHLIGHTS

- Rumination is association with poor autobiographical problem solving (APS).
- Rumination is associated with decreased activation in the angular gyrus during APS.
- Analyzing the content of rumination is needed to inform default network function.

Figure 1.

Sagittal and axial sections display the MFG (A) and AG (B) identified from whole brain regression of rumination against brain activity for the contrast of APS – NSP ($p<.001$ uncorrected, $p<.05$ corrected). Line graphs (C) and (D) display the correlation between the extracted MFG activity and AG for the APS-NSP contrast and rumination. Line graphs (E) and (F) display the interaction between rumination and condition (APS-Baseline and NSP-Baseline) predicting activation in the MFG and AG. MFG = medial frontal gyrus, AG = angular gyrus, APS = autobiographical problem solving, NSP = negative self-referential processing.

Figure 2.

A. Axial and Coronal sections display the rostralateral prefrontal cortex (BA10) identified from whole generalized context-dependent (APS vs. NSP) psychophysiological interaction analysis using the angular gyrus as seed region. Line graph (B) displays the correlation between rumination and the extracted AG-r.LPFC APS vs. NSP connectivity strength. Line graph (C) displays the correlation between anxiety generated during problem-solving and the extracted AG-r.LPFC APS vs. NSP connectivity.

Supplementary simultaneous regression analyses examining strength of prediction of behavioral and brain indices from rumination vs. problem severity and rumination vs. clinical status.

Table 1

A	Model			Rumination			Severity		
	<i>F</i> (2,30)	<i>R</i> ²		β	<i>SE</i>	<i>sr</i> ²	β	<i>SE</i>	<i>sr</i> ²
DV									
Percentage of Problems Solved	4.27	0.22	*	-0.53	4.15	0.22	**	0.18	9.30 0.03
Sad	15.46	0.51	****	0.52	0.16	0.20	**	0.30	0.35 0.07 *
Anxiety	14.00	0.48	****	0.72	0.17	0.40	****	-0.05	0.39 0.00
MFG (BA10)	9.60	0.39	***	-0.64	5.94	0.31	****	0.04	13.33 0.00
AG	13.96	0.48	****	-0.73	2.25	0.41	**	0.08	5.03 0.00
AG-RLPFC APS vs. NSP connectivity	14.54	0.49	****	0.67	0.14	0.35	****	0.05	0.32 0.00
B									
DV									
Problem Severity	11.19	0.43	***	-0.03	0.09	0.00		0.67	0.21 0.19 **
Percentage of Problems Solved	3.96	0.21	*	-0.31	5.62	0.04		-0.17	12.75 0.01
Sad	14.62	0.49	****	0.39	0.21	0.06		0.36	0.48 0.06
Anxiety	15.46	0.51	****	0.50	0.23	0.11	*	0.25	0.52 0.03
MFG (BA10)	9.75	0.39	***	-0.60	8.01	0.15	*	-0.03	18.15 0.00
AG	13.76	0.48	****	-0.66	3.03	0.18	**	-0.05	6.87 0.00
AG-RLPFC APS vs. NSP connectivity	16.00	0.52	****	0.88	0.18	0.33	****	-0.24	0.42 0.03

Table 2

Activation coordinates resulting from regressing rumination against brain activation and functional connectivity.

Anatomical Region	Centroid					MDD vs. HC	
	BA	k	Max t	x	y	z	R ²
Activation: APS vs. NSP contrast							
Angular Gyrus (AG)	39	104	-4.27*	-41	-68	40	.30
Medial Frontal Gyrus (MFG)	10	53	-4.85*	2	49	8	.24
Functional Connectivity: Seed AG, APS > NSP contrast							
Middle Frontal Gyrus (Rostrolateral Prefrontal Cortex)	10	36	4.64*	40	52	11	.18

Maximum t-values and centroid voxel coordinates for activation clusters, BA=Brodmann Area, k=cluster size in voxels ($3.2 \times 3.2 \times 3.2\text{mm}^3$),

* $p < .001$ uncorrected, $p < .05$ corrected.