Research paper

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. Ruminators were 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.

1. 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 (DN coupled with the frontoparietal control network).
network (FPCN) which may serve to maintain detailed internal trains of thought (Spreng et al., 2015, 2010; Spreng and Schacter, 2012). 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, 2012; Spreng et al., 2009). The DN contains subsystems that may contribute differentially to APS (Andrews-Hanna et al., 2010, 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 (Berrylhill, 2012; Berryhill et al., 2007, 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, 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, 2010, 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).

2. Methods and materials

2.1. Participants

Forty adults (age range: 18–48 years, \( M_{\text{age}} = 25.1, SD = 7.1 \text{ yrs.}, 70\% \) females, 85% Caucasian, 7.5% African American, 2.5% Asian, 2.5% Hispanic/Latino, 2.5% Other) ranging in ruminative tendency (\( M = 3.1, SD = 1.1, \text{ range: } 1.3 – 5 \)) 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, \( M_{\text{age}} = 24.9, SD = 6.8 \text{ yrs.}, 67\% \text{ females, } 91\% \text{ Caucasian, } 3\% \text{ African American, } 3\% \text{ Asian, } 3\% \text{ Hispanic/Latino} \)) ranging in ruminative tendency (\( M = 3.0, SD = 1.2, \text{ range: } 1.3 – 5 \)). Thus, we were adequately powered (80%) to detect a medium effect size (\( r = 0.47 \)) setting \( \alpha = 0.05 \). 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.

2.2. 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.

2.3. 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 injustices to the self (Trappell 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; Sileo 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 fig. 1, we were able to capture the extremes of the rumination distribution, along with a small portion in the middle of the distribution.

2.4. 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
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