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An ERP study of multidimensional source retrieval in depression

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ABSTRACT

We collected event-related potentials (ERPs) from 24 unmedicated adults with Major Depressive Disorder (MDD) and 24 controls during source memory retrieval. Words were encoded on the left or right during animacy and mobility judgments. Mobility judgments were slower than animacy judgments, suggesting deeper encoding. Participants then recalled the encoding judgment (Question cue) and position (Side cue) for each word. Depressed adults, but not controls, showed better accuracy for words from the mobility task presented under the Question vs. Side Cue. Furthermore, depressed adults showed larger left parietal ERPs to words from the mobility task presented under the Question vs. the Side Cue from 400 to 800 ms and 800–1400 ms. This ERP effect was negatively correlated with sleep quality. Thus, deep encoding followed by retrieval of the encoding judgment supported memory in MDD and augmented left parietal ERPs that have been linked to recollection and that appear sensitive to sleep disturbance.

1. Introduction

Major Depressive Disorder (MDD) is associated with poor episodic memory (Airaksinen, Larsson, Lundberg, & Forsell, 2004; Burt, Zembar, & Niederehe, 1995; Rock, Roiser, Riedel, & Blackwell, 2014; Zakzanis, Leach, & Kaplan, 1998). Importantly, the extent of the memory deficit appears to vary with the degree of support provided at encoding. For example, Zakzanis et al. (1998) found that depressed adults performed worse when the encoding tasks provided less structure (e.g., memorization of uncategorized vs. categorized word lists). The cognitive initiative framework can account for such results (Hertel, 1997; Hertel & Hardin, 1990). The framework's core hypothesis is that depressed individuals can control attention and use strategies to enhance encoding and improve memory but that, in the absence of external support or emotionally compelling material, they often fail to do so.

To test this hypothesis, Hertel & Rude (1991) had depressed and healthy adults encode neutral words in a task with focused and unfocused conditions. Specifically, participants were asked to judge whether single words (e.g., "artist") fit well into sentence frames (e.g., "The young man's portrait was painted by the __"). In the focused condition, each word was shown for one second and disappeared when the sentence was presented (for eight seconds), such that the participant had to keep the word in working memory in order to respond accurately. Furthermore, participants in the focused condition could only respond when prompted, and they did so by repeating the word and then verbally indicating whether or not it fit into the frame. By contrast, in the unfocused condition the word remained onscreen while the sentence frame was presented, the participant could respond at any time, and the response consisted only of indicating whether or not the word was a quality fit. Thus, the focused condition made more demands on attention and working memory than the unfocused condition. This manipulation was designed to test the hypothesis that if depressed participants had to devote sufficient resources to encoding each word, they would be less likely to ruminate or otherwise engage in off-task thinking and memory would be enhanced. Consistent with this prediction, a *Group* x *Task* interaction emerged for free recall: relative to controls, depressed adults recalled fewer words from the unfocused condition, but there was no difference for words from the focused condition. Thus, depressed adults performed well when the encoding task demanded sustained engagement.

The cognitive initiative framework has also been applied to retrieval. Depressed adults typically show larger deficits for recall than for recognition (Burt et al., 1995), and when recognition is analyzed to estimate contributions made by recollection vs. familiarity, depression impairs the former more than the latter (Hertel & Milan, 1994; MacQueen, Galway, Hay, Young, & Joffe, 2002). The cognitive initiative framework explains these data by pointing to the greater need for controlled attention, effortful searching, and post-retrieval monitoring during recall vs. recognition, and in support of recollection vs. familiarity. Importantly, the results of Hertel & Rude (1991) suggest that depressed adults should show improved recollection if the task used to probe retrieval helps them focus their attention appropriately.

Given the elegant behavioral work on these issues, the paucity of relevant neuroscientific data is surprising. In particular, although there

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are many studies of hippocampal volume in depression (for review, see MacQueen & Frodl, 2011) and some functional imaging investigations of encoding (Bremner, Vythilingam, Vermetten, Vaccarino, & Charney, 2004; Dillon, Dobbins, & Pizzagalli, 2014; Dillon & Pizzagalli, 2013; Hamilton & Gotlib, 2008), there are remarkably few neuroscientific studies of memory retrieval in MDD. Over a decade ago, the National Institutes of Mental Health, Aging, and Neurological Disorders and Stroke called for neuroscientific research on depression and memory (Steffens et al., 2006). However, despite dozens of event-related potential (ERP) and functional magnetic resonance imaging (fMRI) studies of episodic retrieval in healthy adults (e.g., Eichenbaum, Yonelinas, & Ranganath, 2007; Rugg & Curran, 2007; Rugg & Vilberg, 2013), no similar literature has emerged in MDD.

The current study was designed to address this gap. Because depression affects recollection more than familiarity—and given the difficulties associated with imaging free recall—we elected to conduct an ERP investigation of source memory in MDD. Source memory refers to conscious retrieval of the spatiotemporal details that define an encoding episode (Johnson, Hashtroudi, & Lindsay, 1993). It depends heavily on recollection, and there is evidence that source memory is disrupted in depressed adults (Degl'Innocenti & Bäckman, 1999). We used a design that recruits neural systems engaged during conceptual and perceptual retrieval (Bergström, Henson, Taylor, & Simons, 2013: Dobbins & Wagner, 2005; Simons, Gilbert, Owen, Fletcher, & Burgess, 2005). At study, participants viewed neutral words shown on the left or right above a question specifying an animacy or mobility judgment. At test, they were cued to recall the presentation side (perceptual source, "Side" cue) and encoding task (conceptual source, "Question" cue). We used neutral words rather than emotional words to limit mood-congruency effects (Watkins, Mathews, Williamson, & Fuller, 1992), as these might obscure a more fundamental impact of depression on the neurocognitive processes that mediate source memory.

A recent fMRI/ERP study in healthy adults (Bergström et al., 2013) found that both conceptual and perceptual retrieval elicited the most well-studied ERP marker of recollection, which is a positive deflection over parietal scalp that extends from about 400–800 ms post-stimulus, typically with a left hemisphere maximum (Rugg & Curran, 2007). Both forms of retrieval also activated the precuneus and elicited a negative polarity ERP maximal over posterior electrodes that is referred to as the late posterior negativity, or LPN (Cycowicz, Friedman, & Snodgrass, 2001; Johansson & Mecklinger, 2003; Mecklinger, Johansson, Parra, & Hanslmayr, 2007). Intriguingly, the LPN extended over left frontal scalp during conceptual but not perceptual retrieval, and this was mirrored by fMRI activation in left dorsolateral PFC (DLPFC). Related fMRI studies confirmed that left and medial PFC regions were more strongly activated during conceptual vs. perceptual source retrieval (Simons, Gilbert et al., 2005; Simons, Owen, Fletcher, & Burgess, 2005).

In light of the prior literature linking depression to poor performance on cognitively demanding retrieval tasks, we expected reduced source memory accuracy in MDD. In particular, because depression has been consistently linked to DLPFC hypofunction (Koenigs & Grafman, 2009) and diminished left PFC activation at rest (Davidson, Pizzagalli, Nitschke, & Putnam, 2002), and because brooding rumination — a common problem in depression (Treynor, Gonzalez, & Nolen-Hoeksema, 2003) — can recruit DLPFC neurons that would otherwise support conceptual memory (Cooney, Joormann, Eugène, Dennis, & Gotlib, 2010), we predicted that MDD would have an especially strong negative impact on conceptual source memory. To test these hypotheses, we computed between-group contrasts of ERPs elicited during conceptual and perceptual source retrieval, collapsed over the encoding tasks. In a second analysis intended to more closely track the behavioral results described below, we examined group differences in conceptual and perceptual retrieval for words from each encoding task considered separately. This analysis provided an opportunity to determine whether the different degrees of support provided at encoding and retrieval affected memory in a manner consistent with the cognitive initiative framework (Hertel, 1997).

Finally, we computed correlations that related behavior and ERP amplitudes to individual differences in depressive severity, brooding rumination, and sleep disturbance in the MDD group. Our decision to investigate relationships with depressive severity and brooding rumination was based on the literature reviewed above—we expected that more severe depression and a greater tendency to ruminate would be associated with poorer memory. We examined sleep disturbance because it affects processes relevant to episodic retrieval, including executive function and the activation of parietal regions implicated in recollection (Chee et al., 2006; Durmer & Dinges, 2005; McEwen, 2006), and because of substantial evidence of disrupted sleep in MDD and other psychiatric disorders (Deldin, Phillips, & Thomas, 2006; Tsuno, Besset, & Ritchie, 2005; Wulff, Gatti, Wettstein, & Foster, 2010). We anticipated that negative relationships between memory, left parietal ERPs associated with recollection, and depression would be strongest in those individuals who reported the worst sleep.

2. Materials and methods

2.1. Participants and self-report

Adults (18–62 years old, right-handed, no neurological or unstable medical conditions) were recruited from the community and compensated $25/hour, following a protocol approved by the Partners HealthCare Human Research Committee. They were screened by phone or online, at which time the Beck Depression Inventory II (BDI-II; Beck, Steer, & Brown, 1996) was administered. Individuals were invited to participate in the MDD group if they endorsed symptoms consistent with a current Major Depressive Episode, had a BDI-II score ≥ 14 (the cut-off for mild depression; Beck et al., 1996), and reported no other Axis I psychopathology with the exception of generalized anxiety, social anxiety, and/or specific phobia. Controls had to report no current or past Axis I psychopathology. On the day of the ERP session, we assessed psychiatric status with the MINI International Neuropsychiatric Interview, version 6.0 (Sheehan et al., 1998). Depressed adults had to again report current depression, no history of other DSM-IV Axis I diagnosis (except generalized anxiety, social anxiety, or specific phobia), and no medication use in the past two weeks (six weeks for fluoxetine, six months for neuroleptics). Thirty-four controls and 26 depressed adults completed the session. Data from 10 controls and 2 depressed adults were excluded due to excessive artifacts (see below), leaving 24 individuals per group.

Following the EEG session, we administered the BDI-II again, along with the Mood and Anxiety Symptom Questionnaire (MASQ; Watson et al., 1995), the Ruminative Responses Scale (RRS; Treynor et al., 2003), and the Pittsburgh Sleep Quality Index (PSQI; Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). These probe symptoms of depression and anxiety, trait rumination, and sleep quality over the last month, respectively. Finally, the Wechsler Test of Adult Reading (WTAR; Holdnack, 2001) was used to estimate IQ. One control did not complete the MASQ and one depressed participant did not complete the PSQI. WTAR data from non-native English speakers (2 controls, 2 MDD) were not analyzed, as WTAR results may be invalid in this population. The entire protocol took between 2.5 and 3.0 h to complete.

As shown in Table 1, there were no group differences in gender, age, education, or WTAR scores. Relative to controls, the MDD group endorsed poorer sleep, more rumination, and greater depression and anxiety. The mean BDI-II score indicated moderate depression. Regarding comorbid anxiety, two depressed participants met criteria for generalized anxiety disorder in the past six months, several reported subthreshold symptoms in the past month (social anxiety, $n = 2$; panic attacks, $n = 2$; agoraphobia, $n = 2$), and seven reported at least one lifetime panic attack.