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Research Paper

Sustained engagement of attention is associated with increased negative self-referent processing in major depressive disorder

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ABSTRACT

This study investigated the link between self-reference and attentional engagement in adults with (n = 22) and without (HC; n = 24) Major Depressive Disorder (MDD). Event-related potentials (ERPs) were recorded while participants completed the Self-Referent Encoding Task (SRET). MDD participants endorsed significantly fewer positive words and more negative words as self-descriptive than HC participants. A whole-scalp data analysis technique revealed that the MDD participants had larger difference wave (negative words minus positive words) ERP amplitudes from 380 to 1000 ms across posterior sites, which positively correlated with number of negative words endorsed. No group differences were observed for earlier attentional components (P1, P2). The results suggest that among adults with MDD, negative stimuli capture attention during later information processing; this engagement is associated with greater self-referent endorsement of negative adjectives. Sustained cognitive engagement for self-referent negative stimuli may be an important target for neurocognitive depression interventions.

1. Introduction

The way that one views oneself, one's self-concept or self-schema, is intricately tied with mood. Beck's (1967) cognitive model of depression postulates that the schema – internal beliefs and knowledge about the self, the world, and the future – influences how life events are appraised and interpreted. Schemas also prioritize the processing of incoming information, such that environmental stimuli that are consistent with one's self-schema are attended to, processed, and subsequently recalled more readily (Segal, 1988). A negative self-schema may result in biased interpretation of ambiguous stimuli, or cause elaborative processing of over-attended stimuli (Everaert, Koster, & Derakshan, 2012). This in turn has been theorized to facilitate increased recall of negative stimuli, resulting in negatively biased memory. Although other mechanisms clearly also contribute to the maintenance of depression (e.g., emotional blunting), negative self-schema may be an important mechanism that fuels many of the negative cognitive biases thought to maintain depression.

Consistent with the cognitive model, individuals with Major Depressive Disorder (MDD) have been shown to display negatively biased attention, interpretation, and memory (Everaert et al., 2012). Further, depressed people often do not display protective positive cognitive biases that are observed in healthy individuals (Disner, Beevers, Haigh, & Beck, 2011; Walker, Skowronski, & Thompson, 2003). Major depression instead privileges negative processing and, as a result, individuals with MDD are likely to view themselves as having more negative and fewer positive characteristics than non-depressed individuals.

One method of measuring self-schema is the self-referent encoding task (SRET; Derry & Kuiper, 1981). The SRET is a binary-choice, affective decision-making task combined with incidental recall of SRET stimuli. The SRET is generally a computer-based task, where positive and negative adjectives are presented one at a time to participants who determine as quickly as possible whether each word is self-descriptive or not. Following presentation of the word stimuli, participants are then asked to recall as many of the SRET stimuli as possible. Studies have shown strong correlations between endorsement of negative (but not positive) words and depressive symptoms (e.g., Disner, Shumake, & Beevers, 2016); increased endorsement of negative words (and decreased endorsement of positive words) on the SRET is also predictive of depression symptom course (Connolly, Abramson, & Alloy, 2015; Disner et al., 2016). Responses on the SRET also appear to be consistent over time particularly when depression symptoms remain relatively stable (Auerbach et al., 2016; Goldstein, Hayden, & Klein, 2015).

These studies provide a clear link between negative self-referent

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cognition, as measured by the SRET, and depressive symptoms. Understanding the neural architecture of negative self-referent bias is important, as it could provide a more comprehensive understanding of this important cognitive bias and point to translational treatment targets for neurocognitive interventions.

In the current project, we used electroencephalography (EEG) to measure the temporal characteristics of cognitive processes involved in self-appraisal. Although the spatial resolution of EEG is not ideal, EEG is extremely effective at measuring information about the time course of cognitive phenomena (Kappenman & Luck, 2012). Thus, collecting event-related potentials (ERPs) during the SRET can provide information as to whether biased self-referent processing is occurring at an early processing level; whether it occurs at a later level of cognitive evaluation; or whether both processes contribute to this negative self-referent processing bias.

Early ERP processes include the P1 and P2, both positive deflections in an ERP waveform thought to reflect automatic processing of attentional information that may nonetheless be influenced by emotion (Delplanque, Lavoie, Hot, Silvert, & Sequeira, 2004; Hajcak, Weinberg, MacNamara, & Foti, 2012). These peaks occur between 100 and 300 ms following a stimulus. The P2 in particular may index post-perceptual selective attention, as it occurs late enough (peaking approximately 180 ms after stimulus onset) to be related to the association of new information with prior comprehension (Hajcak et al., 2012; Luck & Hillyard, 1994). As both occur early, they are understood to be related to early attentional engagement; both are typically increased when attending to emotional stimuli (Delplanque et al., 2004).

The late positive potential (LPP), conversely, is a component often considered an index of cognitive evaluation and engagement with stimuli. The LPP begins around 300 ms post-stimulus and continues up to 1500 ms (Cuthbert, Schupp, Bradley, Birbaumer, & Lang, 2000; Hajcak et al., 2012). The LPP is often either posterior or central in localization (Hajcak et al., 2012). The LPP increases in positive amplitude in response to prioritization of information, indicating increased engagement, especially to negative information. Schupp et al. (2004) demonstrated that the LPP is greater in response to unpleasant or negative images as compared to neutral or positive images, regardless of mood state; others have shown that attending to non-arousing images reduces the LPP (Hajcak, MacNamara, Foti, Ferri, & Keil, 2013). Moreover, some studies have shown a generally diminished LPP in participants with MDD (Blackburn, Roxborough, Muir, Glabus, & Blackwood, 1990; Proudfit, Bress, Foti, Kujawa, & Klein, 2015; Weinberg, Perlman, Kotov, & Hajcak, 2016).

Several studies have attempted to use EEG to identify the key ERP components that contribute to negative self-referent processing during the SRET. A prior study found that both current and remitted MDD groups had increased amplitudes for negative stimuli in an early component of attentional capture (the P2) in comparison to healthy controls (Shestyuk & Deldin, 2010). They also found that individuals who were currently depressed showed more positive amplitudes in the late positive potential (LPP) for negative stimuli than the other groups. This suggests that MDD participants selectively attended to negative information (due to the initial P2 amplitude difference from controls) and were engaging in increased cognitive evaluation of negative information (due to the increases in the LPP compared to healthy controls). Similarly, in a sample of depressed and healthy female adolescents, depressed girls were shown to exhibit greater early (P1) amplitudes in response to negative words, and greater later (LPP) amplitudes to negative words (Auerbach, Stanton, Proudfit, & Pizzagalli, 2015). These findings are consistent with the results of prior work, with the MDD group showing early attention to negative words that continues over the time-course of the ERP.

Further work with a large sample of younger female participants (N = 121) found indications that risk for depression (i.e., maternal history of MDD) was also associated with greater LPP amplitudes to negative words when compared to those at low risk for MDD (Speed, Nelson, Auerbach, Klein, & Hajcak, 2016). This study used a principle components analysis (PCA), which builds components from the EEG electrode channels that most strongly contribute to an outcome. With the LPP described by the PCA, there was no difference between positive and negative valence within groups; however, in response to negative words only, the at-risk participants showed increased LPP amplitudes and increased subsequent recall of negative stimuli compared to positive. This study did not find differences in the earlier waveforms (P1 or P2). An additional study investigated depressive response on the SRET from a semantic processing perspective (i.e., the N400 waveform), arguing that a diminished N400 suggests stronger self-reference (Kiang et al., 2017). This study demonstrated that participants with MDD had a diminished N400 in response to negative, but not positive, adjectives.

A recent SRET study using PCA techniques with ERPs in a large community sample of adults (N = 128) found that individuals with elevated depressive symptoms had enhanced negativity to both positive and negative words in early frontal regions (Waters & Tucker, 2016). A waveform that they believed to be an element of the late positive complex or P300, at a similar time frame to the LPP, was attenuated in response to all stimuli in parietal regions. Notably, these findings are in the opposite direction to the results reported above (e.g., the LPP measured at a similar point in time was increased in depressed female adolescents in Auerbach et al., 2015).

In summary, these studies reveal some conflicting results in terms of the waveforms associated with the SRET, raising a question of whether there is attenuation or augmentation of the early selective attention components (P1, P2) and later cognitive evaluation (LPP) in response to negative stimuli in depressed participants relative to healthy controls. Many of the above-reviewed studies were conducted in young, female participants; it is important to determine which of these findings, if any, extend to adult samples. Further, relatively few studies have been completed in a sample with a clinical diagnosis of MDD. Additionally, given the recent emphasis in psychology to replicate novel research (e.g., Munafò et al., 2017), this study's potential to independently replicate prior work in this area is important.

In the current study, we anticipated that behavioral results would follow in the same vein as previous work, with more endorsements of negative words as self-referent in participants diagnosed with MDD compared to healthy controls. Based on prior research and the cognitive model of depression, we predicted that adults with MDD, in comparison to healthy controls, would show early, differential attention between negative and positive words in the P1 and P2. We also predicted that MDD-diagnosed participants, as compared to healthy controls, would show increased cognitive evaluation in later components (similar to the LPP) for negative stimuli. Were this confirmed, it would imply that differential processing of self-referential information results from both the early components involved in perception and selective attention of negative stimuli, and also from the way that these stimuli are elaborated, processed, and encoded.

To better assess the full span of attentional processing in response to word presentations, we conducted analyses using a non-parametric technique often applied to functional neuroimaging analyses (Nichols & Holmes, 2002), which identified spatiotemporal areas that might be strongly differentiating between the MDD and HC groups during self-referential processing. This technique, discussed further below, uses randomized permutations of the data to conduct point-by-point t-tests, correcting for multiple comparisons, which allows spatiotemporal areas with strong differences to rise to the forefront. This data-driven method identifies the onset of differential between-group responses in a manner that is conservative compared to standard parametric approaches because, first, no assumptions of normality are required and, second, no *a priori* (and possibly biased) choices of time window or electrode region are necessary. This is in contrast to the traditional, parametric approach to ERP analysis, which examines activity within a limited number of electrode sites averaged across specified time windows. Nevertheless, we also conducted a limited number