Archival Report

Competition Effects in Visual Cortex Between Emotional Distractors and a Primary Task in Remitted Depression

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ABSTRACT

BACKGROUND: Attentional biases, particularly difficulty inhibiting attention to negative stimuli, are implicated in risk for major depressive disorder (MDD). The current study examined a neural measure of attentional bias using a continuous index of visuocortical engagement (steady-state visual evoked potentials) before and after a negative mood induction in a population at high risk for MDD recurrence because of a recently remitted MDD (rMDD) episode. Additionally, we examined working-memory (WM) capacity as a potential moderator of the link between rMDD and visuocortical responses.

METHODS: Our sample consisted of 27 women with rMDD and 28 never-depressed women. To assess attentional inhibition to emotional stimuli, we measured frequency-tagged steady-state visual evoked potentials created from spatially superimposed task-relevant stimuli and emotional distractors (facial displays of emotion) oscillating at distinct frequencies. WM capacity was assessed during a visuospatial memory task.

RESULTS: Women with rMDD, relative to never-depressed women, displayed difficulty inhibiting attention to all emotional distractors before a negative mood induction, with the strongest effect for negative distractors (sad faces). Following the mood induction, rMDD women's attention to emotional distractors remained largely unchanged. Among women with rMDD, lower WM capacity predicted greater difficulty inhibiting attention to negative and neutral distractors.

CONCLUSIONS: By exploiting the phenomenon of oscillatory resonance in the visual cortex, we tracked competition in neural responses for spatially superimposed stimuli differing in valence. Results demonstrated that women with rMDD display impaired attentional inhibition of emotional distractors independent of state mood and that this bias is strongest among those with lower WM capacity.

Keywords: Attentional bias, Major depressive disorder, Risk and resilience, Steady-state visual evoked potentials, Visuocortical competition, Working memory

http://dx.doi.org/10.1016/j.bpsc.2016.12.007

The human visual system is exposed to more information than it can process given constraints on bandwidth and representational capacity (1). To enable adaptive behavior in complex environments, individuals display selective attention to information relevant to a certain task while inhibiting attention to task-irrelevant information (2). However, even while engrossed in a primary task (e.g., reading in a subway car), our attention can be readily captured by salient emotional distractors (e.g., the loud argument of a copassenger) (3). The neural circuitry involved in this involuntary (bottom-up) capture of attention consists of several corticolimbic regions that send projections into sensory systems. Under some circumstances, the extent of bottom-up capture of attention, particularly for negative emotional content, can become excessive, outcompeting top-down regulatory inputs from frontoparietal systems that maintain task-focused attention (2). Chronic biases in attention to distracting emotional information are central to theories of emotional disorders such as major depressive disorder (MDD) (4).

There is considerable evidence that individuals with MDD display attentional biases to depression-relevant information (5). This trait persists following remission as individuals with remitted MDD (rMDD) exhibit selective attention to negative stimuli (6–10), which predicts prospective increases in depressive symptoms (11–13) and MDD recurrence (10). Despite the strengths of previous research in this area, the majority of these studies have relied on behavioral protocols such as the dot-probe task, which uses reaction time indices to examine static "snapshots" of attentional deployment. Recent research has highlighted problems with the reliability of reaction time–based measures of attention (14–16), leading to the use of eye-tracking indices with greater reliability and precision (14). Despite the utility of having a continuous index of visual processing, eye tracking still relies on overt behavior and

396
Biological Psychiatry: Cognitive Neuroscience and Neuroimaging July 2017; 2:396–403 www.sobp.org/BPCNNI   ISSN: 2451-9022

cannot capture covert shifts of attention (17). Additionally, neither reaction time nor eye-tracking indices can discriminate the focus of attention when stimuli overlap in space and time, which precludes a direct examination of attention under conditions of maximal competition (18). Depending on the amount of spatial separation between stimuli, the actual competition for neural responses may be considerably weakened or, in some situations, eliminated altogether if the visual receptive fields are nonoverlapping (1,19). Therefore, although behavioral measures have provided evidence of attentional biases (5–10) and inhibition deficits in MDD (20), there is scant evidence to specifically link difficulty inhibiting attention to emotionally salient distractors relative to concurrent task-relevant stimuli in MDD. This is concerning as attentional biases in MDD are thought to be specific to difficulties inhibiting attention to distracting depression-relevant information relative to goal-relevant information (4). To address these limitations, we used an electrophysiological measure—steady-state visual evoked potentials (SSVEPs)—that provides a continuous index of the degree to which attention is allocated to irrelevant versus goal-relevant stimuli.

In brief, SSVEPs are large-scale oscillatory field responses of the visual cortex evoked in response to rhythmic luminance modulation of a visual stimulus at a fixed frequency. The SSVEP has the same temporal frequency as the driving stimulus and its amplitude tracks fluctuations in attention to the driving stimulus (21,22). Of particular interest here is the possibility of "frequency-tagging" SSVEPs to discriminate neural responses to items that are spatiotemporally superimposed in the visual field by assigning a distinct frequency to each stimulus (23). This is particularly advantageous because competition effects are maximal in situations that involve overlap of visual receptive fields as happens with spatiotemporal superposition of stimuli (3,24,25).

The primary aim of the current study, therefore, was to use SSVEPs to evaluate how the visual system resolves the trade-off between task-relevant neutral stimuli and emotional distractors in women known to be at high risk for MDD recurrence compared to women who were never depressed. This high-risk population (i.e., women who had a fully remitted episode of MDD within the past 5 years) is at risk for two key reasons: 1) women have twice the rate of MDD than men (26–28) and 2) over 60% of individuals who develop MDD will experience at least one recurrent episode within 5 years of remission (29). Based on previous research using behavioral measures of attention (6–10), we hypothesized that rMDD women, compared with their never-depressed counterparts, would display difficulty inhibiting attention to negative distractors. Given some evidence that attentional biases in individuals with rMDD may remain latent until primed by a negative mood induction [(30,31); but see (32)], our secondary aim was to determine whether women's attention to emotional distractors changed from before to after a sad mood induction.

Finally, although there is a clear link between attention and depression, there is also a well-known heterogeneity of cognitive profiles in MDD (33). Therefore, when seeking to identify moderators of attentional bias, it is helpful to focus on neuropsychological factors known to affect the visual system. With regard to attentional inhibition, visuospatial working memory (WM) may be important because of its role in an

individual's ability to filter relevant from irrelevant visual information. Research has demonstrated that WM capacity predicts activity in the visual cortex when suppressing distracting information and that individuals with lower WM capacity have difficulty inhibiting attention to task-irrelevant information (34), an effect exacerbated by dysphoria (35). Additionally, there is a well-established link between MDD and WM deficits (36) and evidence that WM training can improve dysphoric individuals' ability to filter irrelevant information from visual attention (37). Notably, WM deficits in MDD are not typically resolved with intervention or remission (38), so the identification of cognitive biases linked to WM deficits may provide novel avenues for intervention. In the current study, we predicted that rMDD women with lower WM capacity would have the greatest difficulty inhibiting attention to task-irrelevant negative distractors.

METHODS AND MATERIALS

Participants

Participants were 55 women recruited from the community. Twenty-seven women had a history of MDD currently in full remission (rMDD) and 28 women had no lifetime history of any depressive disorder. Women in the never-depressed group had no history of any Axis I DSM-IV disorder (39). The rMDD women could not have any current Axis I diagnosis, history of alcohol or substance dependence or abuse within the last 6 months, or a lifetime history of schizophrenia or bipolar disorder, and their MDD must have fully remitted within the last 5 years. Women with a lifetime history of seizures were excluded from the study given concerns that the luminance modulation used during the change-detection task could induce a seizure in these women. Similar to previous research (32), we excluded participants who experienced no change or decreases in sadness from before to after the negative mood induction ($n = 4$) to ensure that the mood induction was successful. The mean age of women in the sample was 31.80 ± 6.23 years, 76% were Caucasian, and the median annual family income was $45,001 to $50,000.

Measures

The Structured Clinical Interview for DSM-IV Disorders (40) was used to assess for lifetime histories of psychiatric disorders. Women's current depression symptoms in the past 2 weeks were assessed using the Beck Depression Inventory-II (41).

Women's attentional inhibition to emotional distractors relative to task-relevant stimuli was assessed both before and after the negative mood induction using a simple change-detection paradigm [adapted from (25); see Figure 1]. Participants sat 65 cm away from a 27-inch ASUS LCD monitor (AsusTek Computer Inc., Taipei, Taiwan) with a refresh rate of 60 Hz. On each trial, a facial stimulus was presented at the center of the screen for 5000 ms. Faces were flickered on and off (40% active duty cycle) at a frequency of 12 Hz (f^1) to evoke SSVEPs frequency-tagged to the face. A semitransparent 90°-oriented Gabor patch was superimposed over the face, flickering on and off (50% active duty cycle) at 15 Hz (f^2) to evoke SSVEPs frequency-tagged to the Gabor. Trials ended
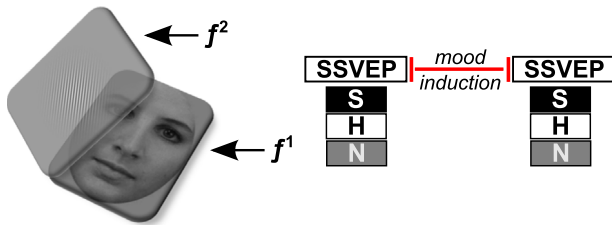
Figure 1. A schematic layout of the change-detection task, employing the frequency-tagging technique. Faces (distractors) were luminance modulated (i.e., flickered on and off) at a constant rate of 12 Hz (f^1). The Gabor patch was fully spatially superimposed over the face as a second, translucent layer, flickering at a distinct rate of 15 Hz (f^2); individuals were tasked with monitoring the Gabor patch layer for changes in orientation. Subjectively, participants perceived a fused percept of face plus Gabor; however, the frequency-tagging approach allowed us to analyze visuocortical responses separately. The distractor faces contained sad (S), happy (H), or neutral (N) expressions on any given trial. The same steady-state visual evoked potential (SSVEP) task was administered twice: once before and once following a negative mood induction procedure.

with a variable (2000–4000 ms) intertrial interval. On a random 25% of trials, the Gabor orientation was rotated clockwise 25° during the trial, and participants indicated whether the Gabor shifted orientation by clicking the mouse button (task instructions are presented in the Supplement). Stimuli for the task were randomly selected without replacement for each trial and consisted of 90 pictures of 30 actors (15 male and 15 female) selected from the Karolinska Directed Emotional Faces stimulus set (42). Each actor was shown with a happy, neutral, or sad expression gazing directly at the camera. Pictures were converted to grayscale, trimmed of all nonfacial features (i.e., hair and neck), cropped into an oval, and displayed against a gray background. The compound Gabor–face stimuli subtended of 10.5° visual angle vertically and 10.9° horizontally.

Continuous electroencephalogram (EEG) was recorded during both change-detection tasks using a BioSemi Active-Two system (Biosemi B.V., Amsterdam, Netherlands), and recordings were taken from 34 scalp electrodes based on the 10/20 system (see Supplement for additional information). Off-line EEG analysis was performed using EEGLAB software and in-house scripts in MATLAB (The Mathworks, Inc., Natick, MA) (43). Data were band-pass filtered with cutoffs of 0.01 Hz and 40 Hz and rereferenced to the average of the left and right mastoid electrodes. Large and stereotypical ocular components were identified and removed using independent component analysis scalp maps (44). Epochs were then extracted from raw EEG and included 1000-ms prestimulus onset and 5000-ms poststimulus onset. Epochs with large artifacts (>200 μV) were excluded from analysis. Participants' trial rejection did not exceed 30%. The artifact-free EEG trials were then averaged in the time domain, separately for the various viewing conditions and groups, and subjected to linear detrending (removing the straight-line fit) prior to calculation of frequency spectra. Finally, the separate time domain averages were transformed into the frequency domain using a fast Fourier transform at the Oz electrode site for segments extracted from 1000 ms to 5000 ms poststimulus onset, resulting in a frequency resolution of 0.25 Hz. This epoch was chosen to exclude the initial nonstationary components of

steady-state entrainment from calculation of the power spectrum. Mean SSVEP amplitudes were extracted as the magnitude of complex Fourier coefficients, normalized by the number of sample points submitted for the fast Fourier transform analysis. The split-half reliabilities of the SSVEP indices to the Gabor and faces were excellent (Guttman split-half coefficients ranged from 0.92 to 0.99; see Supplemental Table S1).

To directly examine neural competition between the overlapping stimuli, a standardized SSVEP competition score was created to reflect the relative visual cortical activity evoked by each facial expression relative to the concurrent Gabor. Consistent with previous research (25), SSVEP amplitudes were T-transformed for the entire sample across the two time and three emotion conditions by first Z-transforming individual SSVEP amplitudes in response to faces and the Gabor separately and then multiplying values by 10 and adding a constant of 50. Competition scores were calculated by dividing T-transformed SSVEP amplitudes in response to the face by the sum of the T-transformed amplitudes to both the face and the concurrent Gabor: $TSSVEP_{face}/(TSSVEP_{face} + TSSVEP_{Gabor})$. Scores >0.50 reflect greater attention to the emotional face relative to the Gabor, whereas scores <0.50 indicate greater attention to the Gabor relative to the emotional face.[1]

During the visuospatial WM task [adapted from (45)], a series of blue circles was presented at different locations on a computer screen, one at a time, and participants were asked to remember their locations. The different locations were selected randomly from a 16 × 16 grid. Each circle was displayed for 500 ms with no delay between circle presentations. Trials included an array of either four or six circles, and array size was selected randomly for each trial. The memory probe was a blue circle presented at one location on the grid, and participants were asked to indicate whether the probe matched one of the locations of the array. Individual estimates of visuospatial WM capacity were calculated using Cowan's K estimate (46,47) separately for the four- and six-item arrays.

Procedure

Potential participants were screened over the telephone to determine eligibility. On arrival in the laboratory, participants completed informed consent forms and were administered questionnaires and the change-detection and visuospatial WM tasks. Next, they completed a standardized negative mood induction by watching a 3-minute scene from *The Champ* [(48); see the Supplement for additional information]. Then, the change-detection task was readministered. Finally, diagnoses were confirmed using diagnostic interviews. Participants were compensated $50 for their time. All study procedures were approved by Binghamton University's institutional review board.

RESULTS

Demographic and clinical characteristics of the sample are provided in Supplemental Tables S3 and S4. SSVEP frequency

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[1]Results based on raw steady-state visual evoked potentials amplitudes can be found in the Supplement.
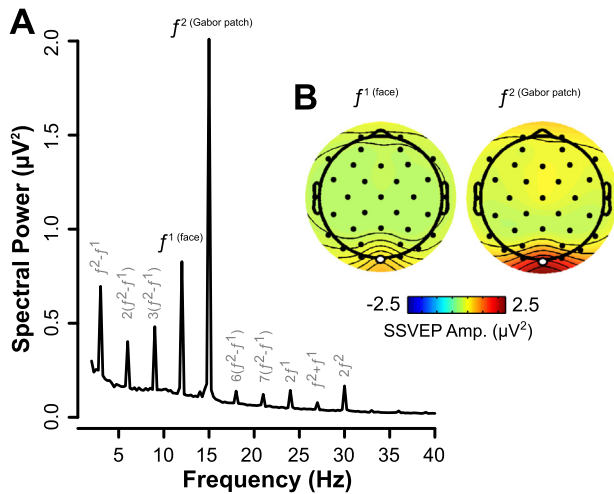
Figure 2. The average power spectrum from the Oz electrode is depicted in **(A)**, collapsing across all emotional expressions and preassessments and postassessments. Note that in addition to the discrete peaks matching the input frequency of the face (f^1: 12 Hz) and the Gabor patch (f^2: 15 Hz) there are also various intermodulation frequencies and higher harmonics. Both subtractive ($f^2 - f^1$) and additive ($f^1 + f^2$) intermodulation frequencies are evoked. The spatial topography corresponding to the frequency of the face and Gabor patch, collapsing across experimental groups, is depicted in **(B)** with electrode Oz highlighted in white. Note that steady-state visual evoked potential (SSVEP) amplitudes (Amp) were overall considerably stronger for the task-relevant Gabor patch compared with the face distractors. Note also that this figure provides an average of the spatial topography to both the face and Gabor patch separately (collapsed across all emotion conditions and time points). Information regarding changes in the power spectrum across emotion, time, and group conditions can be found in the Results and the Supplement.

power spectrum and corresponding scalp topographies are illustrated in Figure 2.

Do rMDD Women Exhibit Difficulty Inhibiting Attention to Emotional Distractors Relative to Never-Depressed Women in the Absence of a Mood Manipulation?

To examine the impact of rMDD history on attentional inhibition to emotional distractors before the negative mood induction, we conducted a 2 (group: rMDD, no MDD) × 3 (emotion: sad, happy, neutral) mixed-model analysis of variance with SSVEP competition scores serving as the dependent variable (as noted above, scores >0.50 reflect greater attention to the emotional distractor relative to the Gabor). Mauchly's test indicated that the assumption of sphericity had been violated ($\chi^2_2 = 7.11$, $p = .03$) for the emotion condition; therefore, degrees of freedom and p values for emotion effects and interactions were corrected using Greenhouse-Geisser corrections. Results revealed a group × emotion interaction, $F_{1.77,53} = 3.55$, $p = .04$, $\eta_p^2 = .06$, shown in Figure 3A. To determine the form of this interaction, we examined the group difference for each emotion separately. Women with rMDD displayed more difficulty inhibiting attention to sad, $F_{1,53} = 16.68$, $p < .001$, $\eta_p^2 = .24$; happy, $F_{1,53} = 7.19$, $p = .01$, $\eta_p^2 = .12$; and neutral faces, $F_{1,53} = 8.79$, $p = .01$, $\eta_p^2 = .14$, than never-depressed women. Notably, although
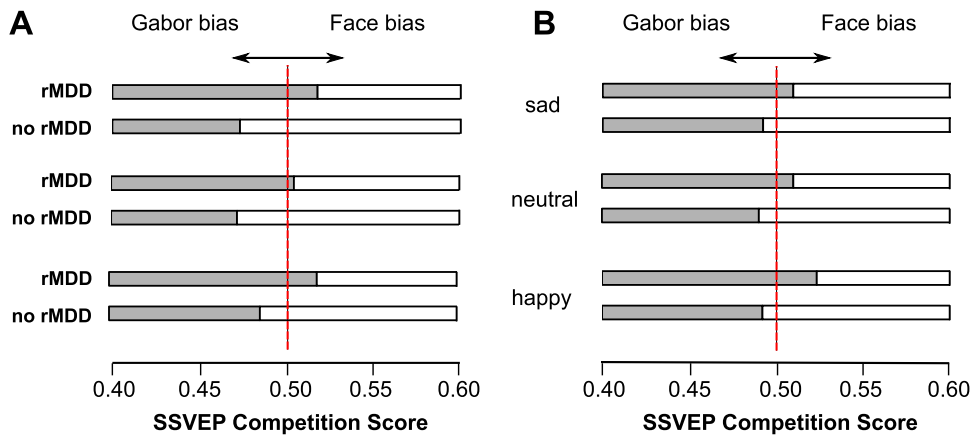
there were group differences for each emotion, the group difference was stronger for sad faces than for happy ($z = 2.53$, $p = .006$) or neutral ($z = 2.52$, $p = .006$) faces, with the latter two not differing significantly ($z = 0.55$, $p = .29$). To examine the robustness of these group differences, we repeated the analyses statistically controlling for women's current levels of depressive symptoms, state sadness, and history of anxiety disorders, and each of the findings was maintained ($p < .05$ for all).

Next, we conducted one-sample t tests to determine whether either group's competition scores differed significantly from 0.50, thereby indicating the presence of a true attentional bias to emotional distractors. For the rMDD group, the SSVEP competition bias scores were significantly > 0.50 for both sad, $t_{26} = 3.30$, $p = .003$, Cohen's $d_z = 0.65$, and happy, $t_{26} = 3.32$, $p = .003$, Cohen's $d_z = 0.65$, faces but not for neutral faces, $t_{26} = 0.95$, $p = .35$, Cohen's $d_z = 0.19$, suggesting that rMDD women display difficulty inhibiting attention to distracting sad and happy faces relative to the Gabor. In contrast, for the never-depressed group, the competition scores were significantly <0.50 for sad, $t_{27} = -2.85$, $p = .01$, Cohen's $d_z = 0.55$, and neutral, $t_{27} = -2.93$, $p = .01$, Cohen's $d_z = 0.56$, faces but not for happy faces, $t_{27} = -1.25$, $p = .22$, Cohen's $d_z = 0.24$, indicating that never-depressed women were allocating attention to the task-relevant information (i.e., the Gabor) relative to distracting sad and neutral faces.

Does Attentional Inhibition to Emotional Distractors Change From Before to After a Negative Mood Induction and Is This Moderated by MDD History?

To examine changes in attentional inhibition to emotional distractors from before to after the negative mood induction, we conducted a 2 (group) × 2 (time: pre, post) × 3 (emotion) mixed-model analysis of variance with SSVEP competition scores serving as the dependent variable, shown in Figure 3. Mauchly's test indicated that the assumption of sphericity had been violated, $\chi^2_2 = 22.59$, $p < .001$, for the emotion condition; therefore, degrees of freedom and p values for emotion effects and interactions were corrected using Greenhouse-Geisser corrections.

Importantly, there was a significant group × time × emotion interaction, $F_{1.93,53} = 6.78$, $p = .002$, $\eta_p^2 = .11$. To examine the form of this interaction, we examined the group × time interaction separately for each of the three emotion conditions (see Table 1). For sad faces, although the main effect of time was nonsignificant, there was a significant group × time interaction. Examining the two groups separately, there was an effect of time for never-depressed women, $F_{1,27} = 11.41$, $p = .002$, $\eta_p^2 = .30$, where difficulty inhibiting attention to sad faces increased from before (0.47 ± 0.05) to after (0.49 ± 0.04) the negative mood induction. In contrast, for rMDD women, the main effect of tme was not significant for sad faces, $F_{1,26} = 3.43$, $p = .08$, $\eta_p^2 = .12$. For happy faces, the main effects of time and the group × time interaction were both nonsignificant. For neutral faces, there was a significant main effect of time, indicating that attention to neutral faces increased for all women from before (0.48 ± 0.04) to after

A

Gabor bias   Face bias

rMDD
no rMDD

rMDD
no rMDD   neutral

rMDD
no rMDD   happy

0.40   0.45   0.50   0.55   0.60
SSVEP Competition Score

B

Gabor bias   Face bias

sad

neutral

happy

0.40   0.45   0.50   0.55   0.60
SSVEP Competition Score

Figure 3. Steady-state visual evoked potential (SSVEP) competition scores as a function of emotion condition (sad, neutral, happy) and group (remitted major depressive disorder [rMDD], no rMDD) before the negative mood induction are depicted in panel **(A)**. SSVEP competition scores following the negative mood induction are depicted in panel **(B)**. Competition scores above >0.50 reflect greater selective attention toward the emotional face relative to the Gabor, whereas scores <0.50 indicate greater selective attention toward the Gabor relative to the emotional face.

(0.51 ± 0.04) the negative mood induction. In contrast, the group × time interaction was nonsignificant.[2]

Does WM Capacity Moderate the Link Between MDD History and Attentional Inhibition to Emotional Distractors?

To determine whether WM capacity moderated the above analyses, we conducted two separate 2 (group) × 2 (time) × 3 (emotion) general linear models with the four- and six-item K scores added as a continuous predictor variable, respectively. The four-item K score did not moderate any of the previous analyses (lowest $p = .22$). However, for the six-item K score, there was a three-way group × memory × emotion interaction, $F_{1.51,51} = 4.17$, $p = .03$, $\eta_p^2 = .08$. To examine the form of this interaction, we examined the memory × emotion interaction separately for each group. For rMDD women, there was a significant memory × emotion interaction, $F_{1.49,25} = 4.02$, $p = .04$, $\eta_p^2 = .14$, such that lower WM capacity during six-item trials was associated with greater difficulty inhibiting attention to sad, $r = -.51$, $p = .01$, and neutral, $r = -.58$, $p = .001$, but not happy, $r = -.33$, $p = .10$, faces. In contrast, for never-depressed women, the memory × emotion interaction was not significant, $F_{1.54,26} = 0.99$, $p = .36$, $\eta_p^2 = .04$. Notably, the group × memory × emotion × time interaction was also nonsignificant, $F_{1.93, 51} = 0.46$, $p = .63$, $\eta_p^2 = .01$, suggesting that the above effects were not moderated by the mood induction.

DISCUSSION

The primary aim of this study was to test the hypothesis that women with rMDD versus those with no depression history would

exhibit difficulty inhibiting attention to negative emotional distractors relative to a task-relevant neutral stimulus using a direct neural measure of visuocortical competition (SSVEPs). Women with rMDD, compared with never-depressed women, displayed difficulty inhibiting attention to all distracting facial expressions of emotion before a negative mood induction, and this effect was strongest for negative distractors (i.e., sad facial expressions). Notably, following the negative mood induction, rMDD women's attentional inhibition to emotional distractors remained largely unchanged. Finally, results indicated that WM moderated the link between MDD history and attentional inhibition to distractors, such that rMDD women with lower WM capacity displayed even greater difficulty inhibiting attention to negative and neutral distractors.

The current findings demonstrate that individuals with rMDD, compared with those with no lifetime history of depression, display greater preferential processing in the visual cortex for emotional distractors, which suggests that emotional facial expressions confer a bottom-up competitive advantage in rMDD, especially for sad faces. This is consistent with research demonstrating that biased processing of facial expressions is a vulnerability for MDD (49), though a meta-analysis suggested that attentional biases in MDD are not different for facial expressions versus other emotional stimuli (5). The results of the current study are also noteworthy as the majority of past behavioral research has shown an attentional bias only for negative stimuli (6–10). This discrepancy could be due to the reduced reliability of behavioral measures of attention bias (14–16) and/or the inability of behavioral

[2]Of note, the exclusion of participants who experienced no change or decreases in sadness from before to after the negative mood induction did not impact the analyses examining changes in attentional inhibition to emotional faces; the significant three-way group × time × emotion interaction from the 2 (group) × 2 (time) × 3 (emotion) mixed-model analysis of variance was maintained when including the excluded participants ($p = .002$). In addition, all subsequent significant follow-up analyses from this interaction were maintained when these participants were included ($p < .05$ for all).

Table 1. Mixed-Model Analysis of Variance Results Examining Group Differences in Changes in Attentional Inhibition to Emotional Distractors From Before to After the Negative Mood Induction for Each Emotion Condition Separately

	Group F (η_p^2)	Time F (η_p^2)	Group × Time F (η_p^2)
Sad	9.53 (.15)[a]	2.17 (.04)	14.27 (.21)[b]
Happy	7.78 (.13)[c]	2.15 (.04)	0.07 (< .001)
Neutral	7.01 (.12)[c]	8.48 (.14)[a]	2.83 (.05)

[a]$p \leq .01$.
[b]$p \leq .001$.
[c]$p \leq .05$.

measures to directly examine competition between spatiotemporally imposed stimuli. Notably, studies examining attentional bias in MDD using other neurophysiological measures have also shown a bias toward emotional stimuli in general (50), though these previous studies also did not test attention toward competing stimuli. Taken together, the current study and others suggest that individuals susceptible to MDD display biased visuocortical processing of emotional stimuli and that this bias may be strongest for negative stimuli and enhanced in the context of competition.

Importantly, the findings also suggest that attentional biases in rMDD are exacerbated by deficits in WM, such that rMDD women with lower WM capacity exhibit the greatest difficulty inhibiting attention to emotional distractors. These findings have important clinical implications. First, they could aid in the identification of subgroups most likely to display attentional biases. Identification of high-risk subgroups may be essential for reliably assessing and manipulating attentional biases in psychiatric disorders as it reduces the noise associated with the heterogeneity of disorders (33). Second, given that WM training improves dysphoric individuals' ability to filter irrelevant information (37), WM training may be an important component of translational research to ameliorate attentional biases in MDD.

In a similar vein, because an attentional bias for negative stimuli is a risk factor for MDD recurrence (10), there is considerable interest in modifying attentional biases to treat or prevent MDD (51). However, large-scale reviews examining the efficacy of attention-bias modifications (ABM) for emotional disorders such as depression and anxiety have provided mixed results (52,53), with researchers suggesting that the unreliability of the measures used to assess the biases may be to blame (54). Because the vast majority of ABM programs use behavioral measures of attentional bias, future studies of ABM may be better served by SSVEP indices, which exhibit excellent reliability (55). Furthermore, behavioral ABM programs seek to "retrain" attention by diverting attention away from negative and toward positive information, assuming that MDD is only characterized by a bias toward negative stimuli, whereas SSVEP paradigms would instead provide opportunities to retrain attention more generally by training attention away from "task-irrelevant" emotional distractors and toward more neutral "task-relevant" stimuli. Finally, SSVEPs might be used to implement a brain-based version of attention training incorporating targeted neurofeedback similar to interventions using real-time functional magnetic resonance imaging neurofeedback to retrain attentional biases in depression (56). Importantly, SSVEPs could improve neurofeedback paradigms by providing almost instantaneous brain-based feedback to participants and drastically reducing the cost of neurofeedback implementation for clinicians and researchers.

In conclusion, the current study provides evidence that women with rMDD are more likely than their never-depressed counterparts to exhibit difficulties inhibiting attention to emotional distractors, compared with task-relevant neutral stimuli, both before and after a negative mood induction. By recording frequency-tagged SSVEPs, we were able to evaluate this perceptual competition at the level of neuronal populations in the visual cortex. This approach may be particularly helpful

in the examination of attentional biases in MDD and other emotional disorders because it permits the examination of attention to concurrent, competing stimuli involving full overlap of visual receptive fields. Furthermore, our findings and others suggest that attentional biases for emotional stimuli in rMDD are not mood-state dependent and can be detected even in the absence of a sad mood induction (32). However, care must be taken in the interpretation of this finding, given research suggesting the limited effectiveness of mood inductions on affective and physiological responses (57). Finally, these findings complement and extend the findings of prior studies showing attentional biases in rMDD via behavioral measures (6–10), while also supporting the role of WM in attentional biases in MDD. However, the sample size of the current study was fairly modest and consisted of predominately white women; thus, future studies are needed to determine whether the findings would replicate and extend to a more representative population. A nuanced understanding of how attentional bias to emotional stimuli plays a role in MDD recurrence and for whom is key for individualized models of risk essential for intervention efforts.

ARTICLE INFORMATION

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