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Pathways to Depression and Anxiety: Characterizing the Roles of Life Stress and Emotion Inhibition

A dissertation submitted in partial satisfaction of the

requirements for the degree Doctor of Philosophy

in Clinical Psychology

by

Morgan Elaine Bartholomew

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ABSTRACT OF THE DISSERTATION

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Professor Gregory Allen Miller, Co-Chair

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Individuals with depression and anxiety have difficulty inhibiting their response to emotional information. Depression has been related to more attentional bias to negative information as well as less attentional bias to positive information. Anxiety has been associated with more attentional bias to high arousal, negative (or threat-related) stimuli. Independent of depression and anxiety symptoms, stress across the lifespan has also been linked to alterations in emotion inhibition along with increased risk for the development of internalizing psychopathology in adulthood. Three studies were conducted in order to identify behavioral and neural correlates of a novel emotion inhibition task, and evaluate a potential mechanistic pathway linking stress exposure to psychopathology via alterations to emotion inhibition. To better characterize the role that distracting emotional contexts plays in disruption of inhibitory control, the Image-Color-Word Stroop (IMCWS) task was developed. Participants (N=133) completed the IMCWS as well as questionnaires assessing life stress, resilience, depression, and anxiety. EEG data were collected on a subset of participants (N = 72) during completion of the IMCWS task. The inclusion of emotionally valenced, high-arousal scenes resulted in longer reaction times during high-conflict conditions of the superimposed color-word Stroop, indicating that the IMCWS task successfully enhanced the automatic recruitment of emotion processing to be inhibited. Further, the IMCWS was found to alter event-related potential (ERP) components commonly associated with allocation of attention and emotion processing (e.g., N250, P300) and inhibitory control processes (N450), suggesting that emotion inhibition during the IMCWS involved increased early attentional allocation to emotional contexts followed by increased recruitment of inhibitory control mechanisms. Current life stress (CLS) was found to be predictive of anhedonic depression, and both were associated with alterations in emotion inhibition. Whereas CLS was associated with more biased attention and, therefore, reduced emotion inhibition during the presentation of negative-valence context images, anhedonic depression was found to be related to less biased attention (i.e., increased emotion inhibition) during the presentation of positive-valence context images. Emotion inhibition was not found to play a mechanistic role in the pathway from CLS to anhedonic depression. Rather, results suggest distinct, yet complementary impacts of CLS and anhedonic depression on emotion inhibition function. Given the comorbidity of CLS and depression, CLS should be considered in future studies of emotion regulation and cognitive control disruptions in depression.

The dissertation of Morgan Elaine Bartholomew is approved.

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General Introduction

Depression and anxiety are the most commonly diagnosed of all mental health conditions (GBD, 2017) and are associated with a diverse array of etiological hypotheses (e.g., Craske, 1999; Ehlers et al., 1988; Mineka & Zinbarg, 2006; Saveanu & Nemeroff, 2012). Prevalent among them is the diathesis-stress model, which posits that stressors across the lifespan interact with pre-existing vulnerabilities to influence the onset and severity of internalizing psychopathology (e.g., Eberhart et al., 2011; Hammen, 2005). Both depression and anxiety are associated with disruptions in inhibitory control of response to emotional information ("emotion inhibition") and are related to maladaptive attentional biases and altered neural activity (Auerbach et al., 2015; Benau et al., 2019; Gupta et al., 2019; Dai & Feng, 2001; Fox, Russo, & Dutton, 2002; Grunewald et al., 2018; Kujawa et al., 2015; Levin et al., 2007; Williams, Mathews, & MacLeod, 1996). Individuals who experience life stress demonstrate similar deficits, perhaps representing one mechanism by which early life stress (ELS) and current life stress (CLS) contribute to the development of depression and anxiety (Briggs et al., 2016; Iacono & Carola, 2017; Janess et al., 2016; Javanbakht et al., 2011; Kaiser et al., 2018). Despite a wealth of literature linking life stress exposure to internalizing psychopathology, and both to deficits in emotion inhibition and its correlates (e.g., effortful emotion regulation, attention, memory; McCabe et al., 2010; Joormann & Gotlib, 2010; Schweizer et al., 2013), gaps in our understanding of the mechanism(s) by which life stress contributes to adult internalizing psychopathology remain. Thus, the following set of studies were designed to characterize the behavioral and neural processes that support emotion inhibition and examine its role as a mechanism by which life stress exposure impacts severity of adult depression and anxiety symptoms.

A Role for Inhibitory Control

Inhibitory control involves the down-regulation of a response to distracting information in favor of the up-regulation of a response to goal-relevant information. Inhibitory control exists in coordination with a variety of psychological functions, such that it depends on memory and attention and supports the success of many other psychological processes (e.g., emotion regulation; Joormann & Gotlib, 2010; McCabe et al., 2010). Memory associated with a given stimulus is likely to impact the salience of a stimulus, the amount of attention that is immediately allocated to it, and the automatic response that it evokes, thus impacting the strength of the response to be inhibited during the process of inhibitory control (Ehrlich et al., 2009; Liu et al., 2020; Tudorache et al., 2019). Behaviorally, inhibitory control is typically assessed via reaction time (RT) and performance accuracy. Greater inhibitory control demand is typically associated with longer RTs and reduced accuracy (for a review, see Macleod, 1991).

At a neural level, inhibitory control is a dynamic process supported by the interaction of prefrontal and other brain regions relevant to the processing of content to be inhibited. For example, performance during high-conflict conditions of the color-word Stroop (CWS) task -- commonly used to assess inhibitory control success -- is related to increased activity in a prefrontal-cingulate network that is associated with allocation of attention to the goal-relevant response and decreased activity in a ventral visual processing network that is associated with the goal-irrelevant process of word-reading (Banich et al., 2009; Harrison et al., 2005; Ochsner & Gross, 2005; Song and Hakoda, 2015). Therefore, a hallmark of inhibitory control is an inverse relationship between activity in the top-down or goal-relevant cognitive control regions and the bottom-up or goal-irrelevant regions, reflecting a causal relationship (Anderson et al., 2004; Aron, 2007; Wager et al., 2005).

Inhibitory Control of Emotion and Everyday Emotion Regulation Function

When the response to be inhibited is emotional, the network of brain regions supporting inhibitory control change to encompass those brain regions involved in emotion processing, including the limbic system, amygdala, insula, hippocampus, and occipito-temporal regions (Banich et al., 2009; Compton et al., 2003; Garcia-Garcia et al., 2016). This is evidenced by fMRI and EEG studies of the emotion-word Stroop (EWS) task, which involves the presentation of emotion words in one of four colors. In this task, the goal-irrelevant response is the emotional response to the content of the words and the goal-relevant response is to the ink-color. Results demonstrate that the EWS successfully recruits inhibitory control processes, such that it prompts activation in prefrontal regions associated with inhibitory control as well as limbic regions associated with emotional response (Alvarez and Emory, 2006; Banich et al., 2009; Bartholomew et al., 2019; Compton et al., 2003; Mohanty et al., 2007; Sadeh et al., 2014; Spielberg et al., 2013).

Evidence suggests that emotion inhibition is an automatic process that supports the effortful emotion regulation strategies often studied in the clinical research literature, such as reappraisal (for a comprehensive review, see Bartholomew et al., 2021). Typically, reappraisal is conceptualized as the effortful re-evaluation of a negative automatic interpretation in a positive light. This process necessarily involves down-regulation of the automatic response (e.g., negative outlook) in favor of a response that is goal-relevant (e.g., positive outlook) and thus fits the definition of emotion inhibition.

Within this framework, many aspects of emotion regulation rely on emotion inhibition. If emotion regulation is defined as “how we try to influence which emotions we have, when we have them, and how we experience and express these emotions” (Gross, 1998), then emotion inhibition is one of the building blocks by which we accomplish this process. Specifically, the process involves orienting away from undesirable, automatic, emotional responses and towards the responses that fit our goals. Although often conceptualized as a distinct process or "category" of emotion regulation (Braunstein et al., 2017; Gyurak et al., 2011), emotion inhibition may be more accurately conceived of as part and parcel of effortful emotion regulation. Emotion inhibition has not been centered historically in the emotion regulation literature, however, as reflected by the limited presence that emotion inhibition has in publications on emotion regulation. Instead, the focus is most commonly on effortful strategies (e.g., reappraisal), leaving out other processes that are inherent to emotion regulation success such as emotion inhibition (see Bartholomew et al., 2021). Given that successful emotion inhibition is connected to functionality during moments of high intensity emotion as well as in the completion of daily tasks, and that deficits central to disorders such as depression and anxiety may be a result of maladaptive changes to these mechanisms, further characterization of the behavioral and neural processes supporting emotion inhibition is needed.

Exploring Potential Pathways to Depression and Anxiety

Exposure to ELS and CLS has been shown time and time again to alter the processes associated with attention and emotion inhibition, and increase risk for and severity of depression and anxiety. Recurrent exposure to ELS is associated with physiological changes that, over time, can result in alterations to hormone function (e.g., cortisol), inflammation, brain development (e.g., HPA axis), and emotion dysregulation (Gunnar & Vasquez, 2006; Nemeroff, 2004; Sanchez et al., 2001; Shalev et al., 2020; Tarullo & Gunnar, 2006). In adulthood, some individuals who have experienced high levels of ELS demonstrate blunting of resting cortisol levels paired with hyper-reactivity in response to acute stressors, and well as larger attentional biases to threatening information (Goldman-Mellor et al., 2012; Young et al., 2021). Evidence for attentional biases has been mixed, with some studies demonstrating that individuals high in CLS show less attentional bias to negative emotional stimuli (e.g., angry faces) which may signal a learned pattern of avoidance (Bodenschatz et al., 2019).

Repeated ELS exposure has been linked to more experiences of CLS, possibly due to ongoing, high-risk circumstances (e.g., low SES) or a transactional process whereby early stress exposure increases adult sensitization to acute stress (Raposa et al., 2014). Similar to ELS, CLS exposure is strongly linked to activation of the parasympathetic nervous system, which can impact hormone response, inflammation, and other basic functions such as sleep and appetite (for review see Gold, 2015). CLS is strongly linked to disruptions in cognitive function, including attention, memory, and emotion inhibition (Javanbakht et al., 2011; Kaiser et al., 2018). In many ways, such changes represent adaptive responses to threat. Specifically, heightened parasympathetic activity prepares the body for action in high stress situations where conflict may be imminent, and hyper-vigilance to threat cues increases the likelihood that one can react quickly, which may ensure survival in times of danger. When a stress response is chronic, however, negative behavioral and health outcomes can be observed (Juster et al., 2009; Lupien et al., 2009, 2019). Similarly, when the stress response does not adaptively match the situation -- perhaps due to maladaptive habits or inaccurate beliefs resulting from previous stress exposure, resultant changes to cognition and behavior may interfere with one's goals. Thus, emotion inhibition is a function that may be disrupted in the (mal)adaptive response to stress, as the automatic response overwhelms goal-directed intentions.

ELS and CLS have both been linked to increased incidence of depression and anxiety, with ELS typically linked to depression when CLS is present (Raposa et al., 2014). The mechanisms linking life stress exposure to psychopathology are a hotly researched area, and represent a wealth of opportunity for the development of effective interventions. A number of potential mechanisms explaining the relationship between ELS and depression have emerged in the research literature, such as inflammation, neuroendocrine function, brain function, diet, and sleep (Bauer & Teixeira, 2018). Several of these mechanisms have been linked to more negative attentional bias, a core feature of depression and a correlate of emotion inhibition function (Boyle et al., 2017; Maydych, 2019; Wen & Tsai, 2020). Further evaluation of emotion inhibition as a mechanism by which life stress impacts the development of internalizing psychopathology is therefore needed. Identification of such a mechanism could have implications for implementing treatments, such that interventions known to normalize negative attentional biases and increase the success of cognitive control processes (e.g., mindfulness) and novel interventions (e.g., attention bias modification) can be better understood and more effectively applied.

Study 1: Identification of Behavioral and Neural Correlates of Emotion Inhibition during the Novel Image-Color Word Stroop

Emotionally evocative stimuli are pervasive in our day-to-day lives and are well known to capture attentional resources, sometimes instantiating automatic bias or well-learned responses, which distract from and disrupt cognitive processes (Compton et al., 2003). Inhibitory control, or the down-regulation of a prepotent response in favor of the task-relevant response, is thought to reduce attentional interference during goal-directed tasks (Aron, 2007). Inhibitory control can be disrupted, however, likely accounting for the inefficiencies and lapses in performance that occur when an individual is confronted with an emotionally salient stimulus (Compton et al., 2003). Unsuccessful inhibitory control of an emotional response is characteristic of a diverse array of psychopathology, including depression and anxiety (Dai & Feng, 2011; Levin et al., 2007; Williams et al, 1996). In order to intervene effectively on such a pervasive phenomenon, it is valuable to understand the mechanism(s) by which emotional context disrupts inhibitory control as well as the mechanism(s) that support successful emotion inhibition.

Inhibitory control involves top-down direction of attentional resources towards goal-relevant aspects of a task and away from distracting, goal-irrelevant aspects. The CWS is a well-known task measuring inhibitory control success (Cohen et al., 1990). In the color-identification version of the task, participants are asked to identify the color that the ink is printed in while ignoring the often more salient lexical attribute of the word, which is processed automatically and may be challenging to suppress. Therefore, when the lexical content of the word is incongruent with the color of the ink the word is printed in, individuals are often slower to respond and make more frequent errors than when the lexical content and ink color of the word are congruent. Thus, faster RTs and fewer errors during the incongruent task condition represent greater inhibitory control success.

Despite wide reliance on the CWS task in the inhibitory control literature, studies of ERP correlates of inhibitory control success are surprisingly sparse and inconsistent. However, the available literature is largely consistent in the characterization of a fronto-central negativity peaking at a latency between 400 and 500 ms during CWS task (e.g., Silton et al., 2010). This N450 component is hypothesized to index dorsolateral anterior cingulate cortex (dACC) activity during the task and to be involved in attention selection at the time of task response (Liu et al., 2006). The N450 component is typically larger during incongruent CWS trials than congruent trials, due to the increase in inhibitory control demand during incongruent trials.

The processes supporting emotion inhibition likely differ as a function of the content to be inhibited, or the attentional demands of the task. Tasks such as the EWS require research participants to name the color of the ink a word is printed in, while varying the emotional content of the word, in an attempt to capture emotion inhibition and its associated neural processes. During the initial phase of information processing, emotional content is highly salient and has a profound and rapid impact on attention, an adaptation that serves to draw attention to potentially lifesaving cues under some circumstances. However, emotional information that is not goal-relevant can draw attention away from the task at hand, thereby impairing performance. Results reported in the EWS literature demonstrate such a relationship, showing that RT increases and percent correct (PC) decreases during high-arousal negative- and positive-valence word trials (Ben-Haim et al., 2014).

In addition to behavioral correlates, the emotional content of the EWS has effects on N450 and other ERP components associated with inhibitory control. Reflecting salience and ease of processing, N450 is smaller to negative than neutral words during EWS performance when emotion is primed, or when the object of the task is to determine emotionality of words (Schirmer & Kotz, 2003; Silton et al., 2010). In some studies, fronto-central N250 has been shown to be larger in response to high-arousal or threatening emotional stimuli (Duncan-Johnson & Donchin, 1982; Thomas et al., 2007). In others, N250 has been shown to be smaller to valenced than neutral stimuli, reflecting instantiation of cognitive control (Clayson & Larson, 2013). Similarly, posterior P300 has been demonstrated to be larger in response to emotionally valenced (high-arousal) images or words than to emotionally neutral stimuli (Fischler & Bradley, 2006; Schupp et al., 2004). More broadly, frontal N250 and parietal P300 are hypothesized to reflect increased deployment of attentional resources, instantiation of cognitive control, and higher-level processing (Clayson & Lawson, 2013; Duncan-Johnson & Donchin, 1982; Yee & Miller, 1994). The late positive potential (LPP) is thought to measure late, selective processing of emotional content (Brown et al., 2003). Likely reflecting down regulation of emotion processing in favor of goal-directed attention, previous work has demonstrated reduction or elimination of the late positive potential to emotional distractor images when they are shown in the periphery of simple cognitive tasks (Eimer, Homes, & McGlone, 2003; De Cesarei, Codispoti, & Schupp, 2009; Holmes, Vuilleumier, & Eimer, 2003; MacNamara & Hajcak, 2009).

During daily life, emotion inhibition processes are engaged when distracting emotions occur simultaneously with the performance of complex, goal-oriented tasks. To successfully complete the tasks of daily living, it may be necessary to direct attention towards the task at hand and down regulate a response to emotional content. These moments are brief, complex, and difficult to measure with ecological validity. Laboratory-based emotion inhibition tasks, such as the EWS, represent one way to examine these processes, and involve recruiting selective attention towards an emotionally neutral aspect of a stimulus and away from an emotionally valenced aspect.

Despite its significant role in disruptions to daily functioning, it remains to be established how an emotionally distracting context might further disrupt inhibitory control of non-emotional information. The closest approximation may be the limited research literature investigating the impact of affective context manipulation or "mood induction" on cognitive functioning, which has yielded inconsistent results. Whereas some studies show null or minimal effects of affective context manipulation on cognitive control function (Drueke et al., 2019; Guhn et al., 2018; Martin & Kerns, 2011), others demonstrate effects of affective context manipulation that varies as a function of the valence of the context. Some studies have reported that positive context manipulation increases the amplitude of N450 during incongruent (vs. congruent) CWS trials, indicating that positive affective context may improve inhibitory control function (Brand, Verspui, & Oving, 1997; Yuan et al., 2011). In contrast, other studies demonstrate that positive affective context manipulation results in reduced inhibitory control function (Rowe et al., 2007; Philips et al., 2002). Similarly, select studies suggest a deleterious effect of negative affective context manipulation on inhibitory control, such that negative (or depression congruent) context appears to be associated with longer RTs (Brand, Verspui, & Oving, 1997; Melcher et al., 2011; Nixon et al., 2013). These findings indicate that participants must use additional inhibitory control resources in order to resolve the attentional interference that negative affective states impose, over and above the interference posed by the CWS task itself. Several potential confounds, including small sample size, inappropriate or lack of a control condition, and insufficient attention to the impact of arousal and valence dimensions on cognition may be contributing to these mixed findings.

Consideration of arousal and valence of emotional stimuli is particularly important when interpreting the impact that an emotional context has on subsequent inhibitory control. Negative stimuli narrow attention to finer details of a scene, and positive stimuli broaden attention to the overall scene (Gasper & Clore, 2002). In much of the literature on the impact of valence on attention, consideration of the impact of the arousal level of stimuli has been neglected. Arousal has a significant impact on attention, such that low-arousal stimuli broaden and high-arousal stimuli narrow attentional scope (Gable & Harmon-Jones, 2010). Arousal is thought to modulate the impact that valence has on attention, such that positive- or negative-valence high-arousal stimuli can capture a narrow attentional focus at an equal rate (Lang et al., 1993). Consistent with these associations, the addition of task-irrelevant emotional contexts to an emotion-neutral cognitive task has demonstrated that low-arousal, negative-context images improve task performance, whereas high-arousal, negative-context images reduce task performance (Sussman et al., 2013). Given evidence that arousal and valence can have performance-enhancing and performance-diminishing effects depending on their level of intensity (i.e., low vs. high arousal), the ease with which emotion inhibition is employed may be impacted by the emotionality of the context in which processing takes place.

Thus, the arousal and valence of a distracting emotional context are likely to interact, such that low-arousal, highly valenced contexts enhance inhibitory control success. In contrast, high-arousal, highly valenced emotional contexts are likely to increase the demands on processes supporting inhibitory control and negatively impact cognitive performance. The addition of a task-irrelevant, emotionally distracting context to an emotion-neutral inhibitory control task is especially valuable, given the "distracting" role that highly emotional mood states can play in daily life, particularly for those suffering from depression and anxiety.

The present study builds on the existing literature by evaluating the behavioral and neural correlates of a novel emotion inhibition task, the Image-Color-Word Stroop (IMCWS). The IMCWS is a task designed to characterize the impact that the arousal and valence of a distracting emotional context image has on inhibitory control, as indexed by the CWS. Inclusion of high- and low-arousal, negative- and positive-valence images of human scenes in the newly developed IMCWS paradigm is intended to introduce a task-irrelevant contextual distractor that enhances the automatic recruitment of emotion salience processing to be inhibited by cognitive control regions, or to increase the coherence between these two processes. Successful inhibition of the emotion processing of these images is expected to manifest in shorter RTs and improved PC.

Using the EWS and International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 2008) literatures as a guide, high-arousal positive- and negative-valence context images were hypothesized to result in greater allocation of attentional resources than low-arousal images irrespective of valence, and thus result in smaller fronto-central N250 and larger P300 components relative to neutral context images. Previous CWS findings indicating a larger fronto-central N450 during incongruent word trials than during congruent and neutral word trials, due to greater inhibitory control demands, were expected to be replicated during the CWS portion of the trial. It was predicted that emotional context should disrupt CWS performance, such that high-arousal negative- and positive-valence context images would result in longer RTs and lower PC than low-arousal valenced and neutral context images. Similarly, high-arousal negative- and positive-valence context images should result in smaller N450 to task than neutral context image trails.

Method

Participants (N = 133, 60% female) were recruited through the UCLA undergraduate research subject pool and from the community. Participant ages ranged from 18 to 27 years (mean = 20.72). The full sample was used when evaluating behavioral outcomes associated with the task, such as RT and PC. A subsample of participants (N=72) participated in EEG data collection during completion of the IMCWS task. Participants received course credit for their involvement in all procedures.

Figure 1. Example of IMCWS combined IAPS and color-word Stroop stimulus.

IMAGE-CWS Task and Procedures. The IMCWS consisted of 300 trials of the CWS paired with image stimuli (see example slide in Figure 1). All images were of humans, featuring single individuals or interpersonal scenes, selected from the IAPS (Lang, Bradley, & Cuthbert, 2008), the Geneva Affective Picture Database (GAPED; Dan-Glauser & Sherer, 2011), and the Nencki Affective Picture System (NAPS; Marchewka et al, 2014). Normed arousal and valence ratings from each database were used to select images, and resulted in 100 each of positive, neutral, and negative context images. Image arousal was a continuous variable, matched across negative and positive context image categories (ranging from scores of 3 to 7.5 out of 1 to 9). Positive- and negative-valence context images were matched on valence ratings, which were scored on a 9-point scale (positive-valence mean = 7.00, SD = 0.58; negative-valence mean = 2.68, SD = 0.65). Neutral context images were selected if they had a neutral valence rating (mean = 5.12, SD = 0.39) and a low arousal rating (mean = 3.10, SD = 0.52). The task was developed with a 3-image context (positive, neutral, negative) by 3-word (congruent, neutral, incongruent) category design. Trials were blocked by image context with intermixed word trials rather than a fully intermixed design, to produce a larger inhibition effect (Compton et al., 2003).

During each trial, the context image was presented on-screen, with word onset in the center of the screen 500 ms later. Word and context image were then presented simultaneously for 1500 ms, followed by a fixation cross of 275-725 ms (onset to onset ITI 2000 ± 225 ms), based on procedures described in Silton et al. (2010). Images were presented full screen, behind each word, and words were presented in one of four colors (red, yellow, green, blue). During congruent word trials, lexical content of words matched their ink color (e.g., the word "RED" printed in red ink), and during incongruent word trials lexical content and ink color did not match. Word condition order was counter-balanced. Four neutral words were selected based on low-arousal and neutral valence ratings (Bradley & Lang, 1999) and were matched in length to color words. Blocked conditions were presented in pseudorandomized order and counterbalanced across participants. Participants were instructed to respond as quickly and accurately as possible to the color of the word on screen by pressing the appropriate button. Prior to completion of the primary IMCWS task, participants completed a 40-trial color-to-key-mapping and 18-trial IMCWS practice to ensure understanding of the task, mapping of colors to button box keys, and comfort with exposure to aversive images. The duration of the entire procedure was approximately 2 hours, inclusive of the EEG portion of the study.

EEG data collection, reduction, and analysis. Participants were seated comfortably in a chair in a sound-isolated, climate-controlled chamber with audio and video monitoring by researchers in the adjacent room. EEG was recorded on a Brain Products system from 96 scalp locations using actiCAP active electrodes referenced to the left mastoid and later re-referenced to average mastoids (Miller, Lutzenberger, & Elbert, 1991). At collection, sampling rate of EEG and EOG data was 2000hz. Electrodes were placed above, below, and near the canthus of each eye to record horizontal and vertical EOG, which was recorded for removal of blink and saccade artifact. All impedances were below 25kΩ.

The following procedure was completed for each individual subject's EEG data in BESA Research 7.1. Data were visually inspected for quality, and channels exhibiting high levels of noise (e.g., muscle movement, high impedance, poor contact) were excluded from analysis. A 20 s section of data demonstrating representative eye blinks and saccades was selected and subjected to BESA's extended infomax ICA procedure (Dimigen, 2020). ICA components representing blinks and saccades were selected, and variance associated with the components were removed from the dataset (Dimigen, 2020). This procedure was found to effectively remove blink and saccade artifact without distorting ERP components of interest.

Following ICA correction, trials were identified and excluded for artifact (e.g., large shifts in amplitude due to muscle movement). Stimulus-locked averages were then calculated for each of the nine experimental conditions (3 image context x 3 word). Only trials with correct responses were included. A minimum of 20 trials to a maximum of 33 trials was available for each condition.

Cross-trial average ERPs were computed for each condition and for each participant. Data were baseline-adjusted by subtracting the average amplitude for the 200 ms period prior to image onset. Choice of specific electrode sites and scoring windows for measurement was guided by prior research investigating the components using similar study designs (Sass et al., 2010; Silton et al., 2010; West & Alain, 1999, 2000), and based on examination of fit within the present dataset (e.g., visual confirmation of sites and time ranges at which components of interest were maximal). Exceptions were made for the average measurement of LPP, as the literature varies widely in choice of scoring window used for mean amplitude calculation. The present task included a complex stimulus presentation with a cognitive task occurring at 500 ms after picture presentation. Given that common scoring windows for LPP occur in the 400-1500 ms range, scores using methods typical in the literature would have been likely to capture components evoked by the present word stimulus. Therefore, in addition to mean amplitude scoring of LPP in two ranges (described below), peak amplitude scoring of P300 occurred between 250 and 400 ms after picture presentation. This method was intended to best characterize the P300/LPP of interest. Additionally, filter specifications were selected using the previous literature as a guide (Sass et al., 2010; Silton et al., 2010) and after ensuring that minimal spatial and temporal distortion of components of interest occurred. Prior to scoring P300, 6 db/octave .1 Hz (forward) high-pass and 24 db/octave 10 Hz (zero-phase) low-pass digital filters were applied to waveform averages. Latency and peak amplitude for P300 were scored from Pz. Mean amplitude scores were obtained for two windows to assess LPP at Pz, 400-600 ms and 600-900 ms. Prior to N250 and N450 scoring, 6 db/octave .1Hz (forward) high-pass and 24 db/octave 25 Hz (zero-phase) low-pass digital filters were applied to waveform averages. Latency and peak amplitude for N250 and N450 were scored at Cz and Fz, respectively. Peak amplitude and latency of N250 was scored between 150 and 300 ms after picture presentation. Peak amplitude and latency of N450 was scored between 850 and 1100 ms after picture presentation (350 and 600 ms after word presentation).

Results

Effects of task condition on RT and PC were assessed via Repeated Measures ANOVA (rmANOVA). rmANOVAs were used to test differences in latency, peak amplitude, and mean amplitude as a function of condition. Multilevel modeling (MLM) was conducted in R's LME4 package and was used to assess the relationship between component measures and task behavioral performance. Degrees of freedom reported for t-tests associated with MLM results were calculated in LME4 using Satterthwaite's method. Tests assessing the impact of task on individual component measures were treated as targeting distinct hypotheses and therefore corrections for multiple comparisons were not applied to results, as is common in the ERP literature.

Behavioral Performance

Analyses of the effect of task on RT and PC were performed in order to confirm expected Stroop effects of word condition and to characterize the novel IMCWS effects of image arousal x image context condition x word condition. rmANOVA was performed with image context condition (positive, neutral, negative) and word condition (congruent, neutral, incongruent). Orthogonal polynomial trend analysis was used to test contrasts, specifically the linear trend associated with word condition (i.e., incongruent condition – congruent condition) and the quadratic trend associated with image context condition to test effects of valence on performance (i.e., [positive + negative] – neutral).

The effect of the interaction of the dimensional measure of image arousal with image context condition and word condition on RT was assessed using a MLM in which image arousal, image context condition, and word condition were treated as fixed effects.

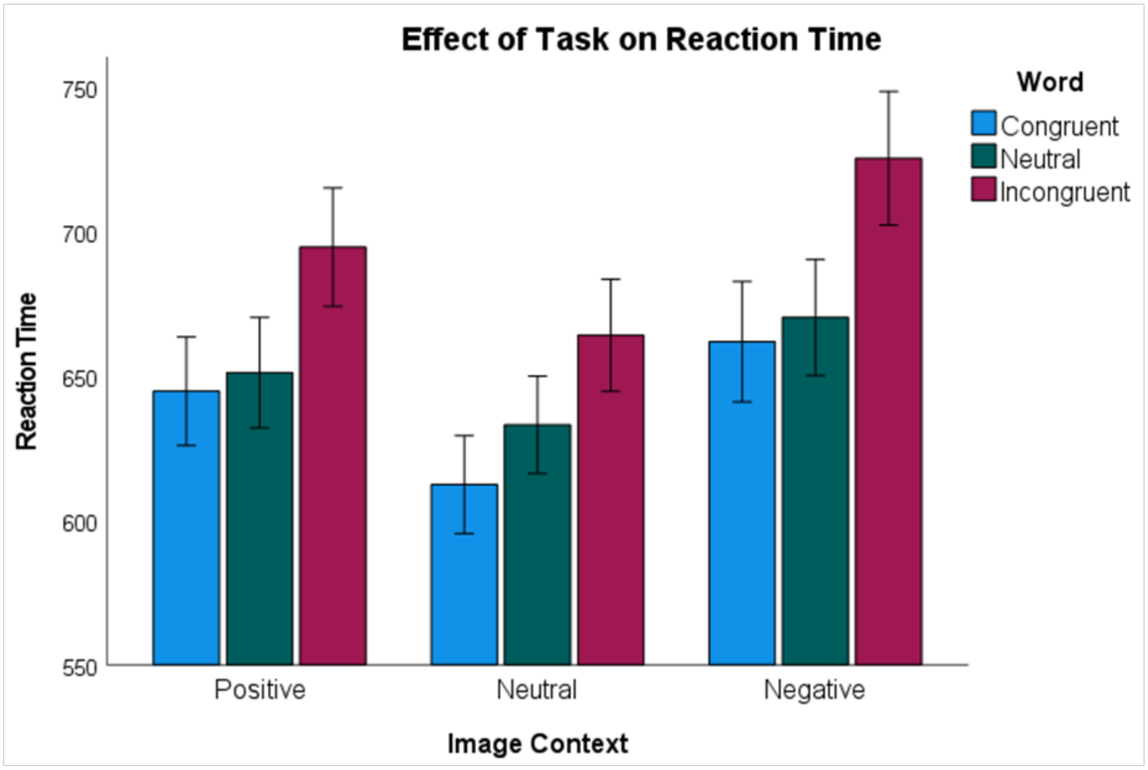

*Figure 2. Graphs depicting impact of task conditions (image context * word) on RT (in seconds) on the Y axis. Error bars represent +/- 2 standard errors around the mean.*

Reaction Time. Shown in Figure 2, rmANOVA confirmed a main effect of word condition on RT ($F(2, 264) = 201.26$, $p < 0.001$, Huynh-Feldt epsilon = 0.95). Orthogonal polynomial trend analysis showed that RT was slower during incongruent trials than during congruent trials (linear $F(1, 132) = 284.54$, $p < 0.001$). A main effect of image context condition was also detected ($F(2, 264) = 78.30$, $p < 0.001$, Huynh-Feldt epsilon = 0.95). Trend analysis showed that positive- and negative-valence images elicited slower RTs than did neutral images (quadratic $F(1, 132) = 128.30$, $p < 0.001$). Word moderated this effect ($F(4, 528) = 6.79$, $p < 0.001$, Huynh-Feldt epsilon = 0.95), with trend analysis showing that RTs to neutral words were less subject to the image arousal effect described above (quadratic image effect by quadratic word $F(1, 132) = 20.56$, $p < 0.001$).

The MLM assessing the impact of the dimensional measure of image arousal on IMCWS performance revealed a main effect of image arousal on RT (t(130) = 8.37, p < 0.001), such that higher levels of image arousal were associated with slower RTs. As shown in Figure 3, higher arousal positive and negative context trials resulted in slower RTs than did lower arousal positive and negative context trials, which were similar to RTs during neutral context trials (image arousal * image context condition * word condition *t* (138) = 2.23, p = 0.03).

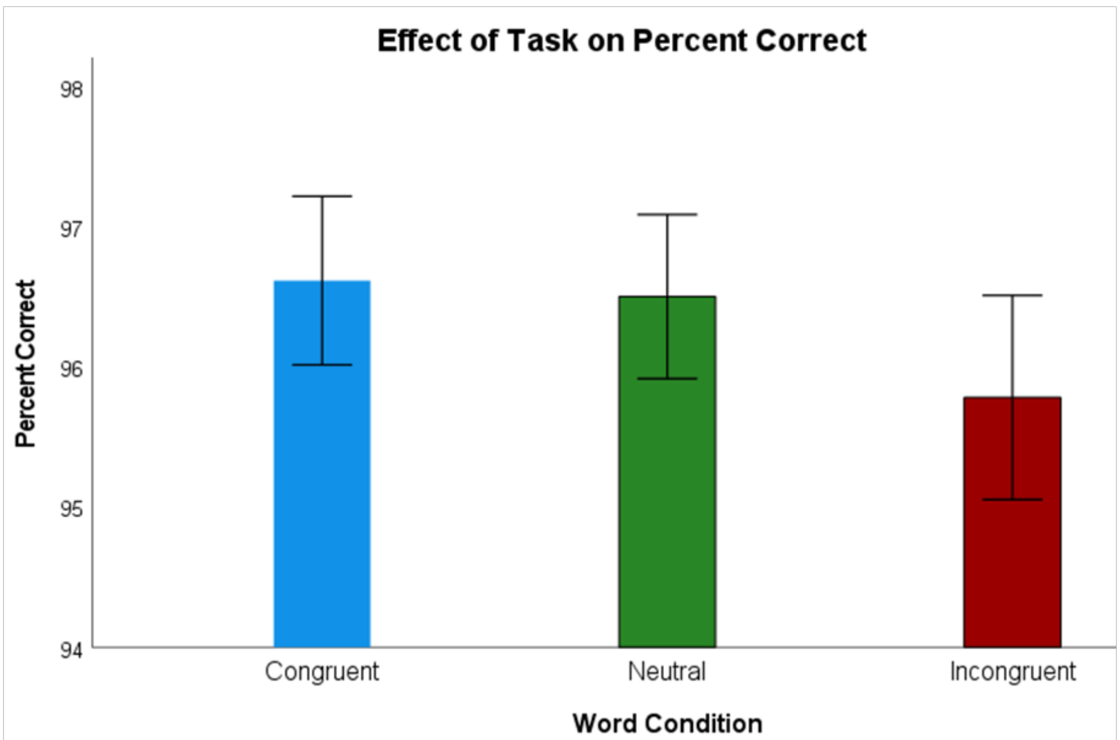

Figure 3. *Graph depicting impact of word condition on PC on the Y axis. Error bars represent +/- 2 standard errors around the mean.*

Percent Correct. Shown in Figure 3, rmANOVA with image context condition (positive, neutral, negative) and word condition (congruent, neutral, incongruent) effects did not reveal an effect of image context on PC (F(2, 264) = 1.216, p = 0.27, Huynh-Feldt epsilon = 0.95). A main effect of word condition on PC was detected (F(2, 264) = 4.98, p = 0.01, Huynh-Feldt epsilon =

0.95). Trend analysis showed that incongruent trials were associated with higher rates of incorrect color responses than congruent trials (linear $F(1, 132) = 6.11$, $p = 0.02$). Image context condition did not moderate the effect of word on PC ($F(4, 528) = 1.138$, $p = 0.34$, Huynh-Feldt epsilon = 0.95).

The interaction effect of the dimensional measure of image arousal with word condition on PC was assessed using MLM, in which the full dimension of image arousal and word condition were treated as fixed effects. The interaction was not found to have an effect on PC ($p = 0.93$).

Event-Related Potentials

Analyses of the effect of task on the latency and amplitude of N250 and P300 to image were performed in order to characterize the novel IMCWS effects on early attentional processing and subsequent CWS task performance. Analyses of the effect of task on the latency and amplitude of N450 to word were performed in order to confirm expected CWS effects of word condition on N450 and to characterize the novel IMCWS effects of image context on CWS performance.

N250. Shown in Figure 4, rmANOVA with image context condition (positive, neutral, negative) demonstrated an effect of image context condition on N250 latency ($F(2, 134) = 6.12$, $p = 0.02$, Huynh-Feldt epsilon = 0.95). Trend analysis showed that N250 occurred earlier for neutral image trials than positive or negative image trials, which did not differ from each other (quadratic $F(1, 67) = 9.94$, $p < 0.01$). An effect of image context condition on N250 amplitude was also found ($F(2, 134) = 6.02$, $p = 0.02$, Huynh-Feldt epsilon = 0.95). Trend analysis showed that positive and negative context image trials resulted in smaller N250 amplitudes than neutral context image trials (quadratic $F(1, 67) = 8.37$, $p < 0.01$).

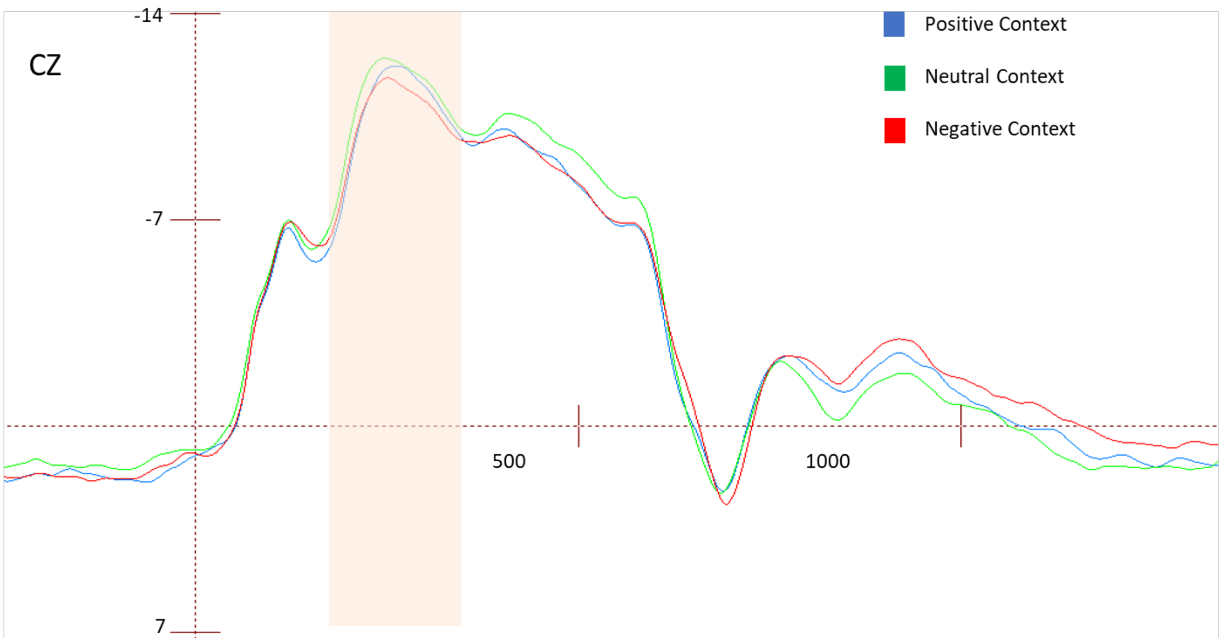

Figure 4. *Figure depicting ERP data collected at Cz. Three grand averages are shown depicting image context condition: positive context in blue, neutral context in green, and negative context in red. The scoring window overlaid on the data depicts the time period during which N250 was scored. Negative is up. Y axis is in microvolts. X axis depicts time in milliseconds.*

P300 and Late Positive Potential (LPP). Shown in Figure 5, rmANOVA revealed a main effect of image context condition (positive, neutral, negative) on P300 latency ($F(2, 134) = 6.28$, $p < 0.01$, Huynh-Feldt epsilon = 0.95). Trend showed that P300 occurred at an earlier latency for neutral image contexts than positive or negative image contexts, which did not differ (quadratic $F(1, 67) = 8.33$, $p < 0.01$). An effect of image context condition on P300 amplitude was also found ($F(2, 134) = 5.16$, $p = 0.03$, Huynh-Feldt epsilon = 0.95). Trend analysis showed that positive- and negative-valence context images resulted in larger P300 amplitudes than neutral context image (quadratic $F(1, 67) = 8.28$, $p < 0.01$).

The impact of image context condition on mean amplitude of the early (400-600) and late (600-900) phase of LPP were also assessed via rmANOVA. A main effect of image context

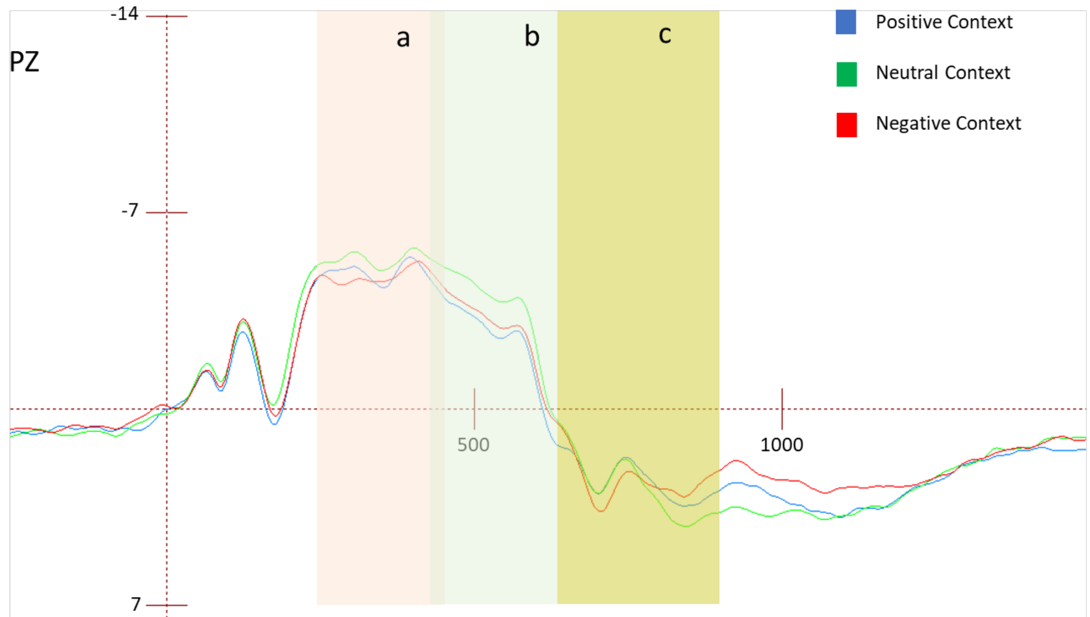

Figure 5. *Figure depicting ERP data collected at Pz. Three grand averages are shown depicting image context condition: positive context in blue, neutral context in green, and negative context in red. Three scoring windows are overlaid on the data to time periods in which a) P300, b) early phase of LPP, and c) late phase of LPP were scored. Negative is up. Y axis is in microvolts. X axis depicts time in milliseconds.*

condition (positive, neutral, negative) on the early phase of LPP was detected ($F(2, 134) = 10.74$, $p < 0.01$, Huynh-Feldt epsilon = 0.95). Trend analysis showed that mean amplitude LPP was lower during neutral context trials than positive or negative context trials, which did not differ (quadratic $F(1, 67) = 61.86$, $p < 0.001$). A main effect of image context condition (positive, neutral, negative) on the late phase of LPP was also detected ($F(2, 134) = 10.74$, $p < 0.01$, Huynh-Feldt epsilon = 0.95). In contrast to the early phase of LPP, trend analysis showed that mean amplitude LPP was higher during neutral context trials than positive or negative context trials, which did not differ (quadratic $F(1, 67) = 61.86$, $p < 0.001$).

N450. Shown in Figure 6, rmANOVA with image context condition (positive, neutral, negative) and word condition did not show effects of image context condition, word condition, or their interaction on N450 latency. An effect of image context condition on N450 amplitude was found ($F(2, 134) = 19.45$, $p < 0.001$, Huynh-Feldt epsilon = 0.95), such that neutral context image trials were associated with smaller N450 amplitudes than positive or negative image contexts (quadratic $F(1, 67) = 36.03$, $p < 0.001$). A main effect of word on N450 was not found in this model ($F(2, 134) = 0.24$, $p = 0.79$, Huynh-Feldt epsilon = 0.95). The interaction of image context condition and word condition was found to have an effect on N450 amplitude ($F(4, 528) = 9.10$, $p < 0.001$). Trend analysis showed that the effect of word on N450 amplitude reversed during neutral context image trials, such that N450 amplitude was larger during congruent trials than incongruent trials (quadratic image context by linear word $F(1, 67) = 25.64$, $p < 0.001$). A follow up analysis excluding neutral context image trials showed that incongruent word trials

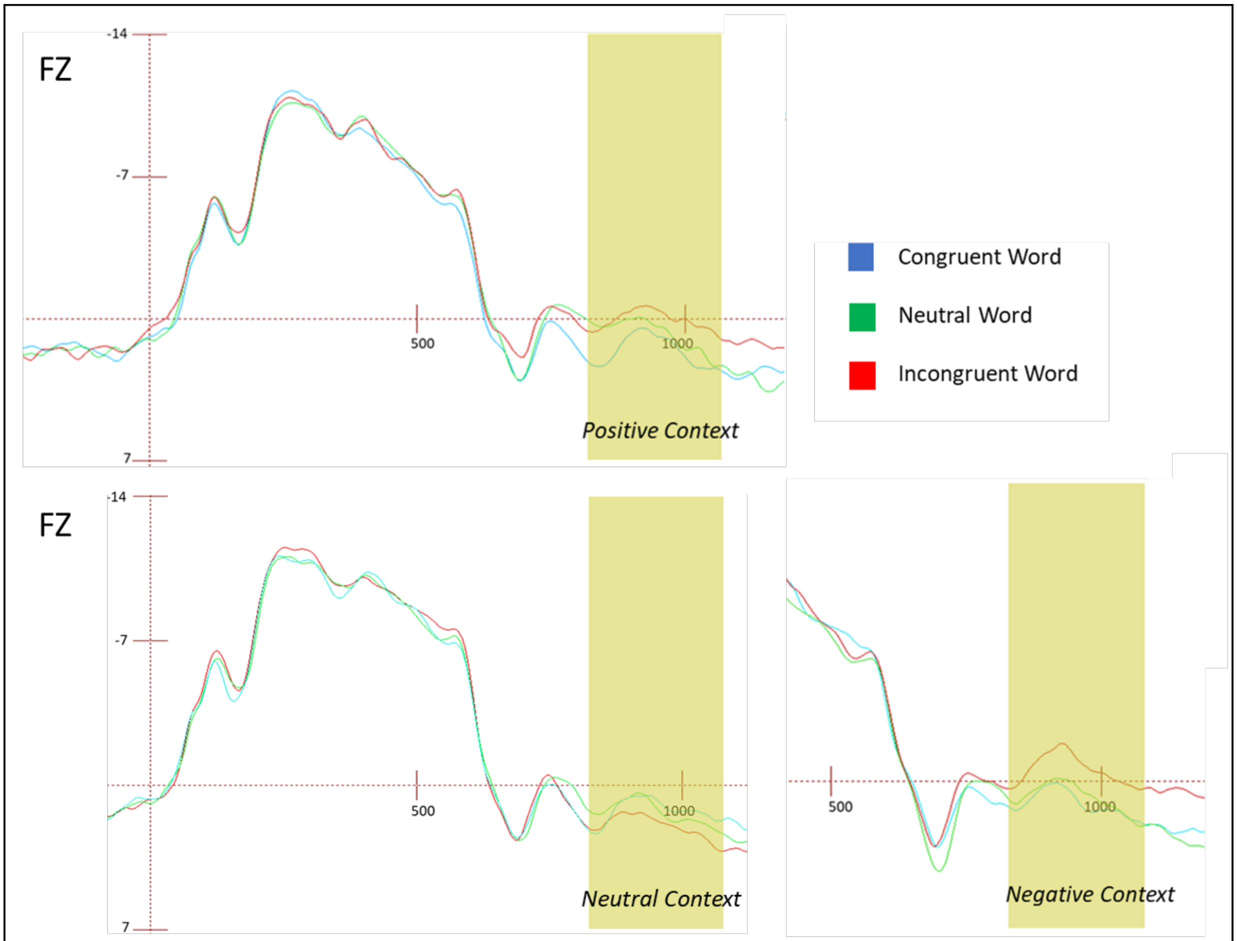

Figure 6. *Figure depicting 9 grand average waveforms of ERP data collected at Cz, lines are color-coded by word condition and grouped by image context condition. The scoring window overlaid on the data depicts the time periods in which N450 was scored. Effect of the interaction between image context condition and word condition on N450 amplitude is depicted. Negative is up. Y axis is in microvolts. X axis depicts time in milliseconds.*

resulted in larger N450 amplitudes than congruent word trials during positive and neutral context images (linear $F(1, 67) = 5.00$, $p = 0.03$).

Discussion

The novel IMCWS task was designed to characterize the role that distracting emotional contexts play in inhibitory control success, given the likely relationship between emotion inhibition success and symptom profiles associated with internalizing psychopathology. Additionally, the IMCWS was developed in an effort to create a more ecologically valid laboratory task of emotion inhibition, given that emotional scenes are hypothesized to be more emotionally stimulating than pictures of isolated emotional faces, the latter being more commonly used in emotion inhibition tasks (Thom et al., 2014). To that end, as variation in arousal and valence of emotional stimuli is known to impact attention and subsequent disruption of cognitive processes, context images varied along these dimensions. The present study sought to characterize the behavioral and ERP correlates of the novel IMCWS task.

The IMCWS task demonstrated the expected effects on participant behavior, such that the presence of an emotionally valenced context image resulted in slower RTs during presentation of incongruent words than congruent words during the CWS task. This result appears to be driven by higher arousal positive and negative-valence context image trials, such that low-arousal positive and negative-valence context images were associated with RTs comparable to those of neutral context image trials. Previous data characterizing the impact of arousal and valence of emotional content on inhibitory control suggested that arousal modulates the impact of valence on attention (Lang et al., 1993), and present findings provide evidence to support this claim. IMCWS task was also associated with alterations in latency and amplitude of select ERP components. Fronto-central N250 is thought to be related to increased attentional control due to conflicting information or a "gating" mechanism by which highly salient information is prioritized by cognitive control (Nieuwenhuis et al., 2003; van Veen & Carter, 2002). In the present data, N250 was impacted by image context condition such that the component occurred later for positive and negative context trials than for neutral context trials. Effects of emotion on N250 latency in the literature have varied, with some indicating earlier latency for threat stimuli than pleasant stimuli (Williams et al., 2006) and others showing no effect (Stockdale et al., 2019). One potential contributor to latency effects in the present data is image arousal, a factor often associated with higher visual complexity (Madan et al., 2018). In the present task, arousal levels were necessarily higher on average in the positive and negative image context conditions than the neutral condition. Future work will aim to characterize and control for variations in image complexity in order to evaluate this potential confound.

Amplitudes of fronto-central N250 were smaller to valenced contexts than neutral contexts and amplitudes of fronto-central P300 as well as mean amplitude of the early phase of LPP were larger to valenced contexts than neutral contexts, indicating greater cognitive control, higher-level processing of meaning and emotion processing. In combination with effects observed on RT, larger amplitudes during these conditions support the hypothesis that the emotional context images used during IMCWS task were successful in recruiting automatic, prepotent emotion responding in the form of attentional allocation.

Results for N450 during the CWS portion of the IMCWS task were somewhat contrary to hypotheses. In line with hypotheses and previous emotion inhibition tasks, larger N450 amplitudes were detected during CWS trials presented with negative and positive context images than during neutral context images. N450 was larger during incongruent trials than congruent trials during positive and negative emotional context images, which is also consistent with the literature examining effects of CWS tasks on N450 (West & Alain, 1999; West, 2003). However, this effect was altered during the presentation of neutral context images, such that N450 amplitude was largest during congruent CWS trials and smallest during incongruent CWS trials. One possible interpretation of this pattern of results is consistent with reduced allocation of resources during the lower-conflict neutral context trials in favor of enhanced resource allocation during the higher-conflict, valenced context trials. Alternatively, component overlap, specifically of later phases of LPP to images on word components, may be a potential explanation for this finding.

The design of the IMCWS paradigm reported in this study is such that overlap between later phases of components associated with image presentation such as LPP and components associated with word presentation are inevitable. The task was designed intentionally to maximize the distracting nature of emotional context images and their influence on inhibitory control performance. Early behavioral piloting of the task found that 500 ms maximized the impact of context image on CWS performance, as this latency appeared to be long enough for the context image to be meaningfully engaged with, but not too long that habituation to the image might occur. Future analyses of this dataset may seek to utilize principal components analysis in order to statistically isolate variability associated with particular task components. Further, future work with this paradigm may include continued refinement of the task itself. For example, further temporal separation of the emotional context from the cognitive task may facilitate more accurate characterization of the components of interest, and their interaction. Subsequent versions of this task might feature a separate affective context manipulation designed to facilitate passive viewing of emotionally valenced images immediately prior to beginning the CWS task. Evidence suggests that such designs are similarly effective at eliciting an emotional response to be inhibited, while creating sufficient temporal separation between ERP components of interest (Brand, Verspui, & Oving, 1997; Melcher et al., 2011; Nixon et al., 2013).

Measures of late LPP in the present data indicated that neutral context images were associated with greater positivity than were positive and negative image trials. Although surprising, these results might be interpreted in the following ways. First, given the larger amplitude associated with P300 and the early phase of LPP to negative and positive-valence context images, reduced later positivity to valenced contexts may represent an over-correction (or more effortful suppression) of emotion processing at the onset of the CWS portion of the task during emotionally valenced context images, as compared to an absence of such suppression during neutral context images. This interpretation is consistent with behavioral results, which do not suggest that neutral images impaired IMCWS performance more than valenced context images. Additionally, it is supported by previous studies that have demonstrated the LPP to emotional images shown in the periphery of a simple cognitive task was reduced or eliminated (De Cesarei, Codispoti, & Schupp, 2009; Eimer, Homes, & McGlone, 2003; Holmes, Vuilleumier, & Eimer, 2003; MacNamara & Hajcak, 2009). Therefore, LPP results suggest successful utilization of emotion inhibition processes.

Alternatively, there is a small literature indicating that human scenes (or faces) depicting "neutral" emotion may elicit anxiety similar to that of negative emotional scenes. IMCWS images were selected to include humans, as it was expected that these images would be the most representative of the emotional stimuli that participants encounter in their day-to-day social contexts. However, previous work has shown that neutral faces elicit LPPs similar to positive or negative-valence faces (Sharif et al, 2021). Other studies have reported that emotionally "neutral" faces are more similarly rated to their negative counterparts (Lee et al., 2008).

Finally, it is possible that neutral context images elicit a larger late LPP than valenced context because valenced contexts are more readily categorizable. Neutral contexts, on the other hand, may be more difficult to categorize and thus require later, sustained processing. This is in agreement with present findings that show larger P300 and early LPP amplitude to valenced contexts, perhaps indicating that the salience and categorical fluency associated with these contexts lends themselves to enhanced earlier engagement, but not enhanced later engagement as with the less readily categorizable neutral contexts. This interpretation is somewhat in line with a small literature demonstrating that when emotional stimuli are more salient or familiar, "neutral" stimuli can result in longer RTs than emotional stimuli (Andersson et al., 2005). Present results may call into question the utility, or the feasibility, of a truly "neutral" human scene. As the IMCWS task is novel in its structure, we were unable to locate literature to point definitively towards one explanation. Future work should aim to follow up on potential suppression effects associated with cognitive tasks and to identify appropriate control conditions for the study of emotional context scenes on cognitive processes such as inhibitory control.

In spite of limitations inherent in the first-round development of a novel task, evidence suggests that the IMCWS paradigm successfully manipulated processes supporting emotion inhibition and serves as a laboratory task that approximates the every-day, distracting emotional contexts that compound inhibitory control. Inclusion of emotionally valenced, high-and low-arousal context images successfully increased the emotion inhibition load associated with the CWS task, with emotionally valenced (high-arousal) contexts resulting in the largest emotion inhibition load as assessed by behavioral and ERP measures. Characterizing the processes that support successful emotion inhibition is an important first step in beginning to delineate how these processes are altered when emotion regulation is dysfunctional, such as in internalizing disorders. Depression and anxiety are associated with attentional biases that likely make them more susceptible to disruptions of inhibitory control associated with emotion inhibition. In pursuit of this, Study 2 will seek to characterize and differentiate the impacts of depression and anxiety on emotion inhibition processes during the IMCWS task.

Study 2: Differentiating the Role of Emotion Inhibition in Symptoms of Depression and Anxiety

Depression and anxiety are disorders characterized by maladaptive reductions in efficiency when inhibiting goal-irrelevant emotional processing in favor of goal-relevant responding, resulting in a greater attentional bias towards negative and high-arousal stimuli (Dai & Feng, 2001; Levin et al., 2007; Williams, Mathews, & MacLeod, 1996). Across depression and anxiety, attentional bias to negative information is associated with intensity of symptoms (Beevers et al., 2019; Macatee et al., 2017; Smith et al., 2018). Furthermore, there are likely differential deficits contributing to attention biases in depression and anxiety, as attentional biases are linked more consistently to the valence of stimuli in depression and to the arousal of stimuli in anxiety (Krompinger & Simons, 2009; Sass et al., 2010). Attentional biases also differentially predict treatment outcomes in depression and anxiety, depending on the goal of treatment and the mechanism of the intervention (Barry et al., 2015; Gollan et al., 2015). Therefore, characterizing and differentiating the role of inhibitory control in depression and anxiety may have significant impacts on the development of effective treatments.

Although the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) classifies depression and anxiety categorically, the overlap and considerable comorbidity between the two illnesses is widely recognized. In fact, many patients with depression exhibit episodes of anxiety at some point during their life. Therefore, a dimensional view of the common and differentiable components of what was traditionally characterized as two largely distinct illnesses, such as the tripartite model (Clark & Watson, 1991b), is likely more useful when one's goal is to characterize the mechanisms that support those differentiable components. The tripartite model asserts that the two disorders share a common factor of general distress and can be differentiated by two factors – hyper-arousal of the sympathetic nervous system, which is specific to anxiety, and anhedonic depression, which is specific to depression. These two symptom dimensions will be used in the present study to assess distinct patterns of emotion inhibition characterizing depression and anxiety.

The differences in the mechanisms supporting attentional bias in depression and anxiety are likely tied to the different roles that the emotion dimensions of arousal and valence play in attentional control. Although emotional content can be highly salient and may have profound and rapid impacts on attention, the nature of the impact is dependent on the arousal level and valence of the information. Specifically, low-arousal stimuli broaden and high-arousal stimuli narrow attentional scope (Gable & Harmon-Jones, 2010). Negative stimuli narrow attention to finer details of a scene, and positive stimuli broaden attention to the overall scene (Gasper & Clore, 2002). Consistent with these associations, Study 1 demonstrated that the impact of task-irrelevant emotional contexts to an emotion-neutral cognitive task is modulated by arousal and valence, such that high-arousal positive or negative-valence context images exacted deleterious effects on inhibitory control performance whereas low-arousal valenced context images did not.

Anhedonia, a core symptom of depression, is associated with a lack of sensitivity to reward, reduced motivation, and diminished response to common interventions for depression, such as behavioral activation (Clery-Melin et al., 2018; Gollan et al., 2015). Evidence suggests that depression that is high in anhedonia (or anhedonic depression, for simplicity) show attentional biases largely driven by the valence of information and its personal relevance. In some instances, depression has been associated with rapid-onset attentional biases to negative information (Krompinger & Simons, 2009) and reduced processing of positive information (Epstein et al., 2006; Green et al., 2019). In other cases, depression has been associated with overall reduction of engagement with valenced information, both negative and positive, perhaps reflecting a pattern of avoiding emotionally salient information (Cuthbert et al., 200; Proudfit et al., 2015). More consistently, anhedonic depression has been linked to unresponsiveness to any emotional content, unless it is mood-congruent (Gilboa, Roberts & Gotlib, 1997; Rottenberg, Gross, & Gotlib, 2005). Further, attentional biases to mood-congruent negative information are characterized by over-engagement and an inability to flexibly disengage (Nolen-Hoeksema, 1991).

In contrast, anxiety is associated with rapid-onset attentional biases to highly arousing emotional information (Sass et al., 2010) and to threat information in particular (MacLeod, Mathews, & Tata, 1986). These biases are associated with increased sympathetic hyper-arousal as well as increased frequency of worry (Rozenman et al., 2018; Wieser & Keil, 2020). There is evidence to suggest that attentional bias to threat is not only responsive to treatment but also that attentional bias to threat increases the efficacy of exposure therapy for anxiety disorder (Barry et al., 2015).

Although the mechanisms supporting bias toward negative stimuli are likely to differ in depression and anxiety (e.g., Levin et al., 2007; Sass et al., 2014), over-attending and reacting to negative-valence information can result in functional impairment in both conditions. Such a tendency is reflected in decreased performance on EWS tasks in individuals with heightened depression and anxiety (Dai & Feng, 2011; Williams, Mathews, & MacLeod, 1996). Whereas both conditions are related to more biased attention to negative-valence stimuli, only depression is consistently related to less biased attention to positive-valence stimuli in favor of negative-valence stimuli (Armstrong & Olatunji, 2012; Girz et al., 2017). This pattern is reflected in longer RTs during the presentation of negative-valence stimuli than during positive-valence and neutral stimuli, and increased engagement of amygdala and ventro-rostral ACC and decreased activation of dACC – brain regions frequently shown to be involved in processing emotional information and salience (Mohanty et al., 2007; Jaworska et al., 2015).

The ERP literature provides some helpful insights into these patterns, although inconsistencies remain. Individuals high in depression demonstrate smaller amplitude of early ERP components (e.g., N250) in response to positive stimuli than negative stimuli in some cases, and no modulation of early components by emotional stimuli in other cases (Deldin et al., 2000; Kayser et al., 2000; Sass et al., 2014; Mingtian et al., 2010). Similarly, some studies demonstrate that depression is related to larger ERP components associated with inhibitory control (e.g., N450) during positive and negative-valence trials of the EWS, perhaps indicating that valenced trials evoke a larger response to be inhibited than neutral trials in depressed individuals (McNeely et al., 2008) and others have not (Fisher et al., 2010). Further, depression has been associated with reduced modulation of later components (e.g., P300, LPP) by positive-valence or reward-salient stimuli (Sandre et al., 2019; Weinberg et al., 2016). The late positive potential (LPP) is a broad component that begins 200-400 ms following the onset of emotional stimuli, continuing for the duration of the presentation up to several seconds, and peaking at centro-parietal sites (Hajcak & Olvet, 2008; Hajcak & Dennis, 2009). The LPP is larger for positive and negative-valence emotional content than neutral content and is therefore thought to be reflective of emotion processing (Schupp et al., 2004). The literature indicates that depression is generally associated with smaller LPP to positive emotional information and larger LPP to mood-congruent, self-referential or personally significant negative emotional information – perhaps reflecting processes such as rumination (Auerbach et al., 2015; Grunewald et al., 2018, Benau et al., 2019).

Individuals high in anxiety demonstrate larger amplitude of early ERP components (e.g., N250) in response to high-arousal emotional stimuli, reflecting early attentional biases driven by arousal (Sass et al., 2010; Kujawa et al., 2015). Further, anxiety is associated with shorter latency and continued modulation of later components (e.g., P300, LPP), perhaps indicating increased evaluation of threat and difficulty flexibly disengaging from arousing emotional content (Gupta et al., 2019; Fox, Russo, & Dutton, 2002). There is some evidence that reduced engagement with high-arousal, threatening stimuli follows an initial period of increased involvement, known as the vigilance-avoidance hypothesis (Mogg et al., 2010).

Many studies examining the differential impact of emotional arousal and valence on attention in psychopathology have collapsed dimensions of arousal within positive- and negative-valence categories (e.g., Sass et al., 2010; Silton et al., 2010, 2011). Although this allows for examination of simple arousal and valence effects, it prevents the characterization of the impact that arousal has on the intensity of valence effects for a given individual. For example, at low levels of arousal, individuals high in anxiety may find that increased narrowing of attention provides an adaptive advantage in completing cognitive tasks. However, at higher levels of arousal, that increased sensitivity to threat information may prove more disruptive than beneficial. Therefore, simultaneously and orthogonally varying the arousal and valence dimensions of emotional distractors during emotion inhibition tasks may allow for more accurate characterization and differentiation of the impact of arousal and valence on inhibitory control in depression and anxiety.

As previously described in Study 1, the IMCWS task was developed to characterize the impact that the arousal and valence of a distracting emotional context has on inhibitory control, as indexed by the CWS. Inclusion of images of human scenes that vary along a continuum of arousal as well as valence introduces a task-irrelevant contextual distractor that will enhance the automatic recruitment of emotion salience processing to be inhibited by cognitive control regions.

Performance-disrupting effects associated with positive stimuli and low-arousal negative stimuli are likely attenuated in individuals high in depression, due to documented reductions in attention to positive stimuli and lack of sensitivity to arousal level in this population (Armstrong & Olatunji, 2012; Girz et al., 2017). Consequently, anhedonic depression are expected to be associated with increased success of emotion inhibition during presentation of positive and low-arousal negative context images as reflected by smaller ERP component scores associated with image context valence (e.g., N250, P300, LPP) and faster RT and larger ERP component scores associated with inhibitory control performance (e.g., N450). Greater severity of anhedonic depression should also be associated with increased biased attention during higher-arousal, negative context images and therefore less emotion inhibition, resulting in larger ERP component scores associated with image context valence and slower RT and smaller ERP component scores associated with inhibitory control performance.

In contrast to depression, anxiety is associated with heightened early attention to high-arousal stimuli, and particularly high-arousal negative-valence stimuli (Fisher et al., 2014). Consequently, anxious arousal are predicted to be associated with decreased success of emotion inhibition during presentation of high arousal context images (positive- and negative-valence) as reflected by larger ERP component scores associated with image context valence (e.g., N250, P300, and LPP) and longer RTs and smaller ERP component scores associated with inhibitory control performance (e.g., N450), indicating a larger response to high-arousal contexts and reduced success of inhibitory control. The emotion inhibition enhancing effects (and associated modulations of ERP components) associated with low-arousal negative contexts are expected to be attenuated in individuals high in anxious arousal, due to attentional biases to negative stimuli (Fisher et al., 2014).

Method

Participants (N = 133) were recruited through the UCLA undergraduate research subject pool and from the community. UCLA undergraduate participants were recruited through the research subject pool using an online survey to assess depression and anxiety (see self-report measures below). In line with the NIMH RDoC approach, participants were over-sampled from the top quartile of responders to assure substantial representation of depression and anxiety phenomena, but the full range of scores was represented. The full sample was used when evaluating the impact of depression and anxiety measures on behavioral outcomes associated with the task, such as RT and PC. A subsample of participants (N=72) participated in EEG data collection during completion of the IMCWS task and were utilized in analyses of ERP components (e.g., N250, P300/LPP, N450). Participants received course credit for participation in all procedures.

Psychopathology Measures. The Patient Health Questionnaire-9 (PHQ-9; Kroenke & Spitzer, 2002) and the Generalized Anxiety Disorder-7 (GAD-7; Spitzer et al., 2006) are brief clinical tools that assess the severity of primary symptoms associated with depression and anxiety, respectively. The PHQ-8, rather than the PHQ-8, was used to screen participants and over-select for individuals in the top quartile of responders. Question 9 of the PHQ concerns suicidality and was omitted from online screening for safety reasons, as adequate follow-up was not possible.

To assess and evaluate symptoms of depression and anxiety that are likely to affect emotion inhibition, participants completed the Penn State Worry Questionnaire (PSWQ; Meyer et al., 1990) and the Mood and Anxiety Symptom Questionnaire (MASQ; Watson et al., 1995a), which provide dimensional measures of worry, anhedonic depression, and anxious arousal. The PSWQ is a 16-item questionnaire used to measure trait worry. It was developed and validated in a sample of undergraduate students and has been found to discriminate those who do not meet criteria for generalized anxiety disorder from those who meet full criteria or demonstrate subthreshold symptoms (Meyer et al., 1990). The MASQ consists of three subscales that map onto the tripartite model of depression and anxiety. The present study relied on the 39-item version, which consists of anxious arousal and anhedonic depression subscales. These subscales were selected for use as predictors due to their demonstrated utility in discriminating depression and anxiety disorders (Watson et al., 1995b).

IMAGE-CWS Task and Procedures. IMCWS consists of 300 trials of CWS paired with image stimuli. See Methods section of Study 1 for a more detailed discussion of this task and the procedures used during the study visit.

EEG data collection, reduction, and analysis. The Methods section of Study 1 provides a detailed description of equipment, EEG and EOG data collection procedures, and preprocessing procedures for EEG data, including methods used for data quality control, EEG data reduction (filtering, channel selection), and scoring procedures for select ERP component measures.

Results

MLM was conducted using R's LME4 package to evaluate how symptoms of depression and anxiety (i.e., worry, anxious arousal, anhedonic depression) moderate task effects on RT, PC, and ERP components. In the MLM, the full dimensions of each task variable (i.e., image arousal, image context, word condition) and psychopathology variable (i.e., worry, anhedonic depression, anxious arousal) were fixed effects, and the participant was a random effect predicting RT.

Table 1. Descriptive Statistics Associated with Study 2 Psychopathology Variables

Variable	***Mean***	***SD***	***Skewness***	***Kurtosis***
Anxious Arousal	25.18	6.54	1.35	1.35
Anhedonic Depression	61.45	11.90	0.07	0.48
PSWQ	43.73	7.99	0.22	-0.76

Summary of descriptive statistics associated with psychopathology variables is provided in Table 1. Anxious arousal scores were low and positively skewed, indicating a lack of representation at the high end of scores. On other metrics, however, the present sample demonstrated expected variability. For example, when using a cutoff of 23 on the 8 item AD subscale of the MASQ -- a cutoff that has been previously shown to predict clinical depression symptoms (Bredemeier et al., 2010) -- the present sample demonstrated equal representation of high and low scorers in anhedonic depression (64 high scorers, 69 low scorers). Additionally, PSWQ scores in the present sample were comparable to those observed in other samples (Fresco et al., 2003). Log-transformed versions of variables displaying skewness and kurtosis (anxious arousal) were used in subsequent analyses.

Behavioral Performance

Previously reported ANOVA analyses of IMCWS data (see Results section of Study 1 for details) revealed main effects of image context and word conditions, such that longer RT was observed for positive and negative context images and longer RT was observed for incongruent trials than neutral trials and congruent trials. Further, MLM analysis revealed that higher levels of image arousal were associated with longer RTs. The interaction of image arousal, image context, and word conditions affected RT, such that higher-arousal positive- and negative-context image trials resulted in longer RTs than low-arousal positive- and negative context image trials, which did not differ from neutral trials. Study 1 did not detect effect of image arousal and image context on PC; therefore, PC was not included in Study 2 analyses.

In subsequent analyses, psychopathology variables (worry, anhedonic depression, anxious arousal) were added to the MLM as moderators of the interaction between image arousal, image context, and word condition with task performance (RT) and related ERPs (i.e., N250, P300, LPP, N450) as the dependent measures.

Worry. PSWQ was not found to moderate the effect of image arousal ($t(129) = -1.418$, $p = 0.16$), image context ($t(129) = 0.27$, $p = 0.79$), word condition ($t(133) = 1.11$, $p = 0.27$), or their interaction ($t(130) = -0.15$, $p = 0.89$) on RT.

Anhedonic depression. Anhedonic depression did not moderate the effect of image arousal ($t(128) = 0.74$, $p = 0.46$) or word condition ($t(132) = 0.93$, $p = 0.35$) on RT. However, anhedonic depression moderated the interaction effect of image context on RT (See Figure 7, $t\ (134) = 2.23$,

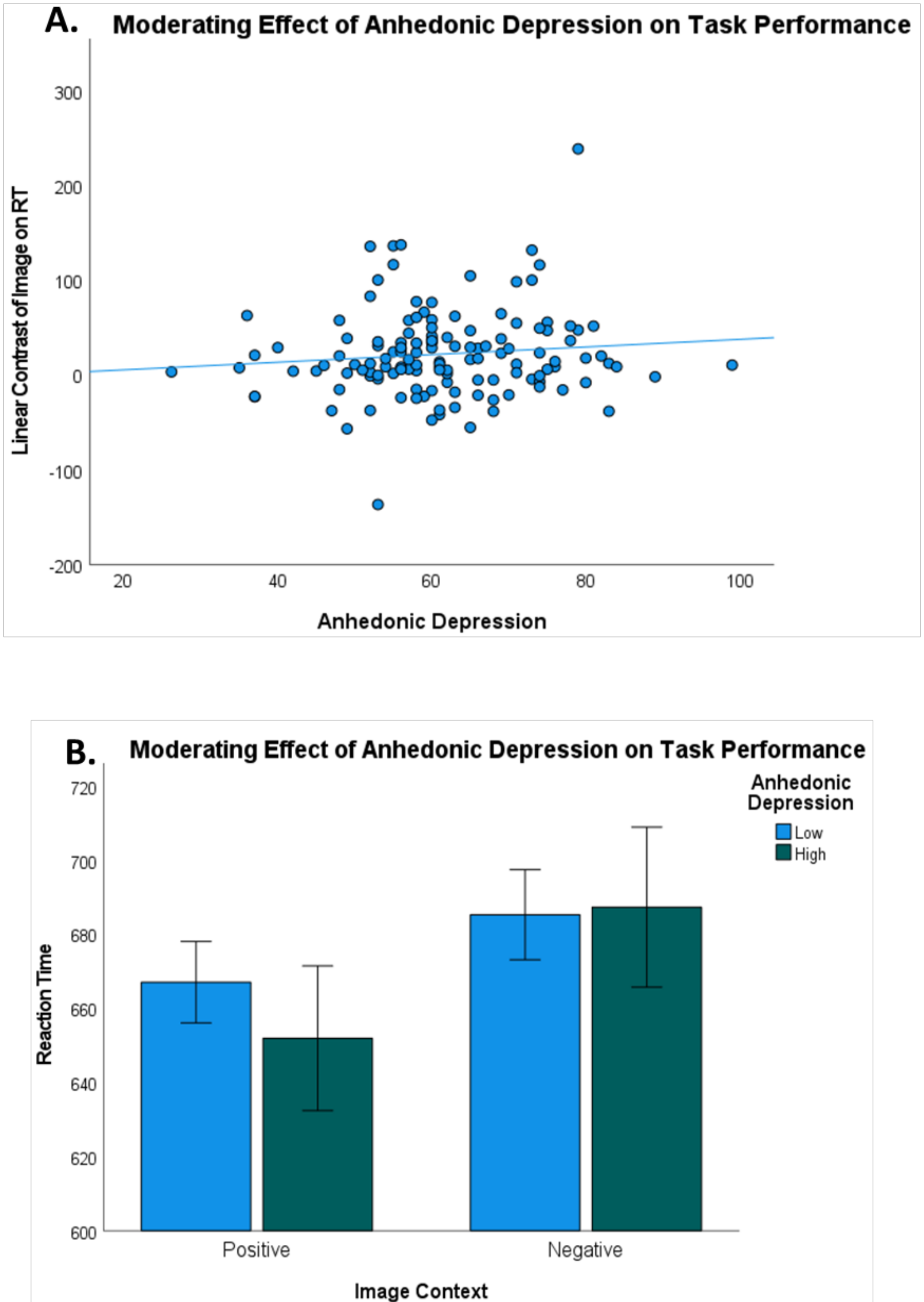

Figure 7. A. *Graph depicting the moderating effect of anhedonic depression scores on task performance. Task performance is represented as the linear contrast of image context condition (Negative context RT – positive context RT) on the Y axis. Anhedonic depression scores are represented on the X Axis.* **B.** *To further illustrate effect, second graph shows the difference in response times between low and high anhedonic depression scorers during positive and negative context images. Scores are dichotomized according to cutoffs specified in Bredemier et al., 2010. Reaction time is in ms on Y axis. Error bars represent +/- 2 standard errors around the mean.*

p = 0.03), such that individuals higher in anhedonic depression demonstrated shorter RT during the presentation of positive and neutral images, but not negative images, than did individuals low in anhedonic depression.

Anxious arousal. Anxious arousal was not found to moderate the effect of image arousal (t(127) = 1.62, p = 0.11), image context (t(128) = 0.98, p = 0.33), word condition (t(132) = 1.10, p = 0.27), or their interaction (t(129) = 1.12 , p = 0.26) on RT.

Event-Related Potentials

Worry, anhedonic depression, and anxious arousal were entered as moderators into a MLM assessing the effect of task condition on ERP latency and amplitude measures associated with the task, including N250 to context image, P300/LPP to context image, and N450 to word condition. Significant moderation effects of psychopathology variables on the relationship between task condition and ERP measures were not detected. A marginal effect of the interaction of anhedonic depression and word condition on RT (t(499) = -1.66, p = 0.09) was observed, such that higher anhedonic depression scores were associated with a smaller difference in N450 amplitude between incongruent and congruent word condition, due to larger N450 on congruent trials.

Discussion

In order to better understand the role of emotion inhibition in depression and anxiety, the present study sought to characterize and differentiate alterations in behavioral and electrophysiological performance on the novel IMCWS task. Symptoms of depression were expected to relate to more emotion inhibition during positive-valence trials, due to evidence that depression is associated with less responsivity to reward-based or appetitive stimuli, and to reduced emotion inhibition to high-arousal negative-valence stimuli. Anxiety symptoms were expected to relate to decreased emotion inhibition success during the presentation of high-arousal stimuli irrespective of valence. Differentiation of the attentional processes that support the severity of depression and anxiety symptoms may have important implications for clinical interventions.

Behavioral findings from Study 2 support the hypothesis that depression, specifically the symptom dimension of anhedonia, is associated with emotion inhibition success. Anhedonic depression was associated with shorter RT during positive context trials, indicating less bias in attention to positive-valence images. Contrary to hypotheses, present data did not indicate an effect of image arousal or a difference in performance during the presentation of negative-valence images. Rather, results suggested that anhedonic depression is characterized by a distinct lack of responsivity to positive-valence images. Anhedonia is a symptom dimension of depression characterized by a failure to experience pleasure. Therefore, decreased RT to positive images implies that inhibitory control processes were more efficient given less reactivity to positive-valence content.

Higher anhedonic depression scores were marginally associated with larger N450 amplitudes during congruent and neutral trials. This pattern of effects is consistent with previous findings indicating that individuals with depression have longer RTs than healthy individuals during the neutral and congruent conditions of the CWS (Kertzman et al., 2010). Depression was not associated with alterations in ERP components associated with early attentional processes. This is in agreement with previous work suggesting that depression is not associated with changes in early attentional processes but rather later attentional processes (e.g., rumination). Work by Gotlib and colleagues suggests that negative attentional bias in depression is dependent on length of exposure to the emotional stimuli, such that longer (e.g., 1000 ms) exposure to negative stimuli best captures negative attentional bias and associated neural activity (Gotlib et al., 2004;

Gotlib & Joorman, 2007). Given that the IMCWS task involves a cognitive process beginning at 500 ms after image presentation, which likely results in disruption of attention and suppression of LPP to the image, an ERP component associated with late processing of emotional content (see Study 1), it is unsurprising that changes in LPP associated with anhedonic depression were not detected in this study. Further development of the IMCWS task may pursue delaying the onset of word stimulus to 1000 ms, in order to determine if length of exposure increases the ability to capture emotion effects associated with depression.

These findings fit into a wealth of research that indicates that depression is characterized by a lack of reactivity to positive-valence stimuli (Epstein et al., 2006; Green et al., 2019). The literature is largely inconclusive about whether depressed individuals are overly reactive to negative-valence stimuli, with some studies indicating this is not the case (Epstein et al., 2006; Green et al., 2019), some indicating depressed individuals are only reactive to "self-referential" or mood-congruent stimuli (Gilboa, Roberts, & Gotlib, 1997; Rottenberg, Gross, & Gotlib, 2005), and still others providing evidence that depressed individuals do show a negative attentional bias (Armstrong & Olatunji, 2012; Girz et al., 2017; Krompinger & Simons, 2009). While the anhedonic depression subscale of the MASQ was selected for assessment of depression symptoms due to its discriminant validity (i.e., strong association with depression over anxiety), it is possible that more robust sampling of depression symptomatology would have enabled this study to capture variance associated with reactivity to negative images as well. Alternatively, individual-difference factors in exposure to stressors or resilience to stress exposure may interact with anhedonic depression to affect emotion inhibition success.

Contrary to hypotheses, present analyses did not provide evidence that symptom variables associated with anxiety (e.g., PSQW and anxious arousal subscale of MASQ) moderated

IMCWS performance or associated ERP measures. Whereas depression symptoms and trait worry as measured by the PSWQ were well represented in the data, sampling methods did not result in the full range of anxious arousal scores. Although the PSWQ has been shown to relate strongly to diagnosis of GAD (Fresco et al., 2003), it is not surprising that a trait variable would be unrelated to state-dependent cognitive performance. Previous work has demonstrated that cognitive performance is not well predicted by trait anxiety variables and that state variables may be more predictive of the processes that interfere with cognitive performance, such as sympathetic hyper-arousal and rumination (Wetherell et al., 2002). Anxious arousal was selected as the primary symptom scale to capture state anxiety variability, due to its strong discriminant validity (i.e., association with anxiety over depression; Watson et al., 1995). However, lack of representation of the upper end of the anxious arousal spectrum certainly limits the ability to capture the effect of anxious arousal on IMCWS task performance, should it exist.

Depression is strongly related to both ELS (Mandelli, Petrelli, & Seretti, 2015) and CLS (Kendler et al., 2003; Vrshek-Shallhorn et al., 2015). Further, both ELS and CLS are associated with increased reactivity to high-arousal, negative-valence stimuli, suggesting potential deficits of emotion inhibition. Study 3 explored the relationship between individual-difference factors (i.e., ELS, CLS, resilience), anhedonic depression, and emotion inhibition.

Study 3: Characterizing the Relationship Between Stress Across the Lifespan, Emotion Inhibition, and Psychopathology

Stress across the lifespan has been linked to incidence and severity of adult psychopathology, including depression (Mandelli, Petrelli, & Serretti, 2015). Alterations to attentional biases and emotion processing are highly implicated in the pathway linking life stress exposure to adult depression. Exposure to ELS is believed to alter brain regions or functions important in emotion processing and cognitive control, such that individuals exposed to more severe ELS (e.g., higher chronicity, frequency of events, or impact) are more likely to attend to stress-relevant threat in their environment (e.g., Iacono & Carola, 2017; Javanbakht et al., 2011; Kaiser et al., 2018). ELS has also been shown to increase risk for current life stress (CLS; Raposa et al., 2014) which, in turn, may contribute independently to negative sequela associated with cognitive dysfunction and risk for psychopathology. Given that current understanding of emotion inhibition involves interactions between brain regions that contribute to a goal-driven, cognitive-control network and a stimulus-driven, salience network, aberrant emotion inhibition may represent one mechanism by which stress increases negative attentional bias, degrading emotion regulation in adulthood and increasing psychopathology risk. Determining the contribution of factors that foster or undermine the success of emotion inhibition and risk for the development depression is an important step in the development of targeted interventions for this disorder

Depression has been characterized by alterations to processes supporting emotion inhibition, or the goal-directed allocation of attention away from goal-irrelevant emotional processing in favor of goal-relevant responding. However, inconsistencies in the literature prevent a consensus on the role of emotion inhibition in depression. In tasks of emotion inhibition, lack of sensitivity to positive-valence emotional stimuli would present as increased success of emotion inhibition during the presentation of positive-valence emotional distractors, due to a reduction of the emotional response to be inhibited. Increased reactivity to negative-valence or mood-congruent stimuli would present as decreased success of emotion inhibition (e.g., longer RTs and reduced PC). In Study 2, arousal was not determined to impact emotion inhibition success for individuals high in depression. Rather, anhedonic depression was related to decreased reactivity (increased emotion inhibition success) during the presentation of positive-valence images.

Additional factors are known to contribute at the individual level to an individual's reactivity to emotional stimuli. Environmental contexts (e.g., stress, trauma) can influence how one takes notice of and processes emotional content. For example, individuals exposed to ELS are more likely to attend to threat in their environments, with such patterns persisting into adulthood (Javanbakht et al., 2011; Kaiser et al., 2018) and serving as a risk factor for depression (Mandelli, Petrelli, & Seretti, 2015). ELS may be particularly detrimental when the stress is endured during a sensitive period of development and brain plasticity (Iocono & Carola, 2017). The principal mechanism is hypothesized to be the HPA axis, disruption of which is associated with alterations in the function of brain regions that are linked to cognitive control and emotion processing, including amygdala, hippocampus, and prefrontal cortex (McEwen, 2017; Van Bodegom et al., 2017). These changes are of particular interest when considering the effects of ELS and how they contribute to risk for psychopathology. Brain regions implicated in emotion salience and inhibitory control may be detrimentally affected by ELS, contributing to dysfunction in emotion regulation, sustained attention, and cognitive control, and increased depression severity (Baker et al., 2013; Ganzel et al., 2013; Harms et al, 2016).

Although associated with exposure to ELS (Raposa et al., 2014), CLS is independently and consistently linked to alterations in emotion inhibition and risk for psychopathology. Individuals experiencing recent increases in CLS show biased attention to negative-valence or threat-related stimuli (Briggs-Gowan, et al., 2016; Janness et al., 2016). During emotion inhibition tasks such as the EWS, recent exposure to traumatic stress has been linked with lower performance accuracy to negative-valence words relative to those that are positive-valenced, and an overall slowing of RT during the task (Sadeh et al., 2014). Perhaps due in part to increased attentional bias to negative emotional stimuli, CLS has been shown to increase risk for current depression (Kendler et al., 2003; Vrshek-Shallhorn et al., 2015).

Some individuals possess qualities that increase their resilience to life stress and do not report significant psychopathology following exposure. Resilience is a construct that can be operationalized in terms of both individual and environmental qualities. Factors such as peer and familial social support, adaptive coping strategies, beliefs, and certain personality traits are known to confer resilience to psychopathology in the face of stress (Ozbay et al., 2007; Southwick et al., 2005). Higher levels of resilience are associated with more frequent use of “adaptive” emotion regulation strategies such as reappraisal and less frequent use of “maladaptive” emotion regulation strategies such as suppression, as well as lower risk for the development of internalizing psychopathology (Min et al., 2013; Lindsey, 2021). Effortful emotion regulation strategies, such as reappraisal, are likely supported by emotion inhibition processes, as the direction of attention during reappraisal requires successful inhibitory control (for a review see Bartholomew et al., 2021). Disengagement from negative content by stopping the process of rumination is also likely supported by inhibitory control. Both require the allocation of attentional resources away from an automatic, maladaptive process and towards one that is goal relevant.

Evidence suggests that psychopathology and life stress exposure (ELS and CLS) are both related to a disruption of emotion inhibition processes (Dai & Feng, 2011; Javanbakht et al, 2011; Kaiser et al., 2018; Levin et al., 2007). Previously established relationships between life stress and depression suggest that emotion inhibition may mediate the pathway between stress exposure and adult depression. Further, resilience may moderate the relationship between life stress exposure and emotion inhibition success. Accordingly, Study 3 utilized data from the

IMCWS paradigm to characterize relationships involving moderated mediation as shown in

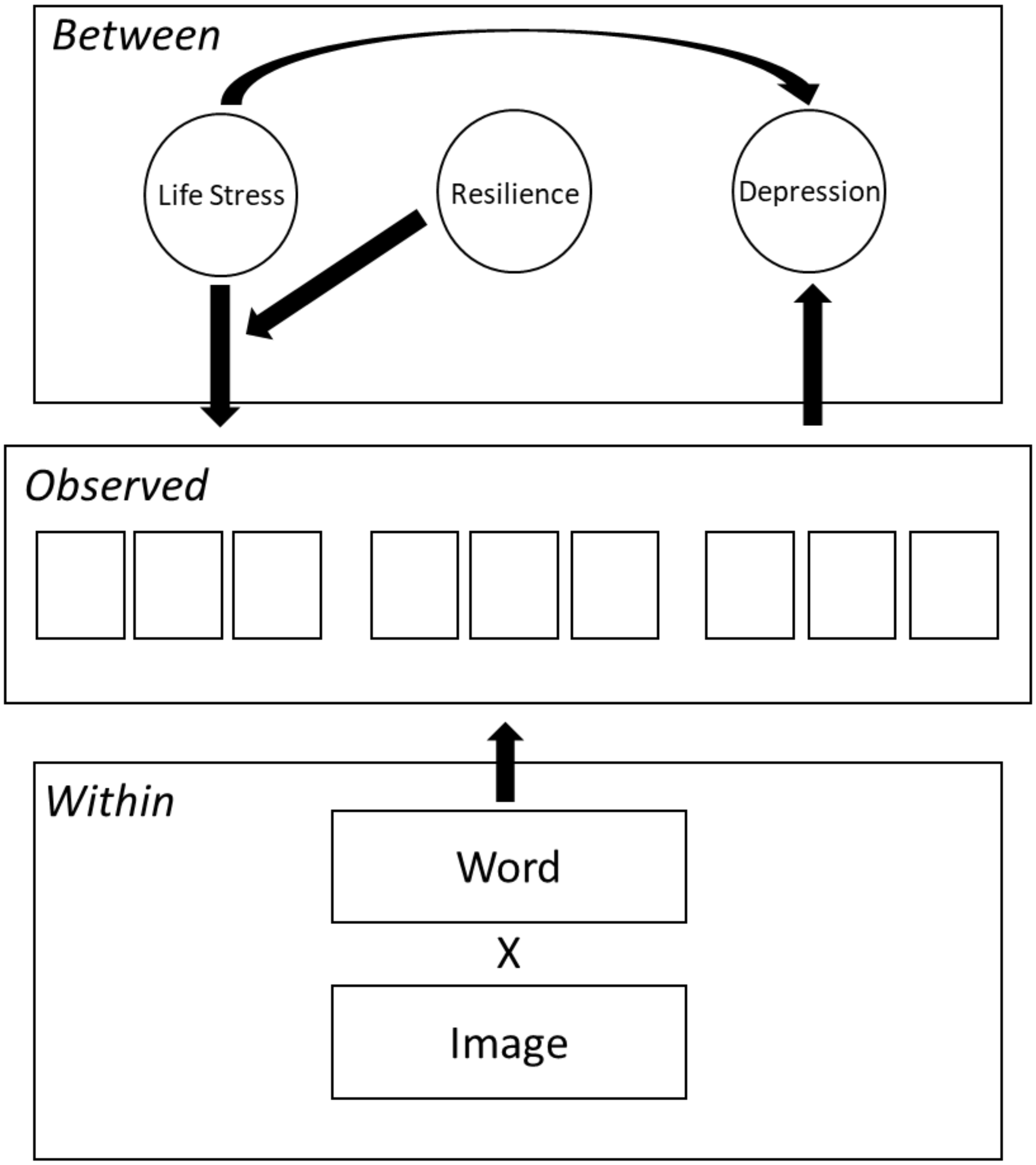

Figure 8. Graphic representation of 2-1-2 mediation model to be assessed in Study 3.

Figure 8. In the proposed model, individuals reporting ELS or CLS were expected to demonstrate less emotion inhibition success during the IMCWS task, such that higher levels of life stress would be related to more biased attention (e.g., longer RTs) to negative-valence context images than positive-valence context images, mediating a positive relationship between

life stress and anhedonic depression. Given the hypothesized positive relationship between resilience and emotion inhibition success, resilience was expected to moderate the relationship between life stress and IMCWS performance. Specifically, individuals high in resilience and high in life stress exposure were predicted to demonstrate more emotion inhibition success than their low-resilience counterparts.

Method

See Methods section of Study 2 for a description of participant population (N=133), including recruitment, sampling strategies, and participant compensation. Contrary to Studies 1 and 2, analyses focused on behavioral data associated with IMCWS task, rather than ERP data, in order to maximize power to detect effects of interest given smaller sample size associated with ERP data.

Self-Report Measures. The Patient Health Questionnaire-9 (PHQ-9; Kroenke & Spitzer, 2002) is a brief clinical tool that assesses the severity of primary symptoms of depression. The PHQ-8 was used to screen participants and over-select for individuals in the top quartile of responders. Question 9 of the PHQ concerns suicidality and was omitted for safety reasons from online screening, as adequate follow-up was not possible.

To assess and evaluate symptoms of depression that are likely to affect emotion inhibition, the Mood and Anxiety Symptom Questionnaire was utilized (MASQ; Watson et al., 1995a; Watson et al., 1995b). As in Study 2, subscales of the MASQ were scored in order to obtain the dimensional measure of anhedonic depression .

To assess current life stress, participants completed the Life Events Scale for Students (LESS), a 45-item questionnaire assessing exposure to episodic life stress over the previous 12 months (Clements & Turpin, 1996). The LESS was developed to include events appropriate for an undergraduate population. The scale was adapted to elicit the participant's subjective rating of the impact of the event, using a scale from 1(minor impact) to 4 (severe impact; Niklova et al., 2012). A summary score of total stressful life events experienced was calculated and used in subsequent analyses.

The Childhood Trauma Questionnaire was used to assess ELS (CTQ; Bernstein et al., 2003). The CTQ is a 28-item questionnaire designed to assess five domains of ELS, including emotional abuse, physical abuse, sexual abuse, emotional neglect, and physical neglect. Validity of reporting is evaluated by assessing the degree to which participants minimize their negative experiences. The CTQ has been shown to be valid and reliable in a college sample (Gerke et al, 2006; Welsh et al., 2017) and was selected due to its comparatively broad inclusion of adverse childhood experiences.

Resilience to stress was assessed the Connor-Davidson Resilience Scale (CD-RISC; Connor & Davidson, 2003). The CD-RISC is a 25-item questionnaire that broadly assesses resilience to stress including factors such as one's notion of personal competence, trust in instincts, distress tolerance skills, security in relationships, sense of control, and spirituality. It has been validated and normed in a variety of samples, including undergraduate populations (Connor & Davidson, 2003).

IMAGE-CWS Task and Procedures. See methods section of Study 1 for detailed description of equipment used, IMCWS task, and study session procedures.

Results

MLM was conducted using R's LME4 package to evaluate how experience of ELS and CLS moderated IMCWS task effects on RT. As Study 1 did not find a relationship between image context condition and PC, PC was not included as a DV in subsequent analyses. In the MLM, the full dimensions of each task variable (image context, word condition) and life stress variable (CTQ, LESS) are fixed effects, and the participant is a random effect predicting RT.

Linear regression was performed to confirm previously demonstrated associations between ELS, CLS, and depression (Raposa et al., 2014). The mediation model was specified first utilizing multilevel structural equation modeling (mSEM) in Mplus. Subsequent moderated mediation analysis was performed using the SPSS macro, PROCESS (Hayes & Montoya, 2017), to test the proposed model shown in Figure 8. Bootstrap confidence intervals were used to test the significance of the indirect effect, as this allows for estimation of the sampling distribution of the indirect effect rather than relying upon assumptions of normality central to other tests (Hayes & Montoya, 2017).

Table 2. Descriptive Statistics Associated with Study 3 Self-Report Variables

Variable	***Mean***	***SD***	***Skewness***	***Kurtosis***
LESS events	5.41	4.5	1.06	1.49
CTQ	38.66	13.66	1.46	2.28
CD-risc	70.65	13.24	-0.28	0.04

Table 3. Correlations between psychopathology and life stress variables

Variable	Anxious Arousal	Worry	***ELS***	***CLS***
Anhedonic Depression	0.33**	0.39**	0.19*	0.20*
Anxious Arousal	-	0.30**	0.02	0.28**
Worry		-	0.20**	0.20*
ELS			-	0.40**
CLS				-

* Correlation is significant at the 0.05 level (two-tailed), ** Correlation is significant at the 0.01 level (two tailed).

Table 2 lists descriptive statistics relevant to the psychology data collected in the present sample. The overall reported frequency of childhood trauma experiences as assessed by the CTQ was lower in the present sample than previously reported psychiatric populations (mean = 136.5, SD = 47.0; Bernstein et al., 1997). On other metrics, however, the present sample demonstrated expected variability. For example, high anhedonic depression scorers and low anhedonic depression scorers (see results section of Study 2) in the present sample reported comparative resilience scores on the CD-RISC (mean = 66.34, SD = 14.12 and mean = 74.47, SD = 11.13, respectively) to psychiatric outpatient populations and non-clinical samples reported elsewhere (mean = 68, SD = 15.3 and mean = 80.4, SD = 12.8 respectively; Connor & Davidson, 2003). The present sample was also similar to previously reported samples in number of recent stressful life events (mean = 4.56, SD = 2.96; Niklova et al., 2012). Log-transformed versions of variables showing skewness and kurtosis (LESS, CTQ) were used in subsequent analyses.

Table 3 lists correlations between psychopathology variables (anhedonic depression, anxious arousal, and worry) and life stress variables (ELS, CLS). Results indicate association amongst psychopathology variables, as well as life stress variables.

Associations Between Life Stress Variables and IMCWS Task

The moderation of IMCWS task performance (image context condition, word condition, and their interaction with RT) by ELS and CLS was assessed using MLM. CTQ scores were not found to moderate the IMCWS task effects on RT ($p = 0.428$). LESS scores were found to moderate the relationship between image context condition and RT ($t\,(130) = 2.10$, $p = 0.03$), such that experience of current life stress was related to slower performance during presentation of negative context images than positive or neutral context images.

Associations Between Life Stress Variables And Anhedonic Depression

As in previous work, individuals reporting increased frequency of ELS experienced more frequent CLS ($F(1,125) = 22.73$, $p < 0.001$). Although CTQ scores predicted anhedonic depression scores ($F(1,125) = 4.57$, $p = 0.03$), this relationship was not significant after controlling for variance associated with CLS ($p = 0.25$). CLS predicted anhedonic depression, when controlling for ELS ($p = 0.02$, 95% CI 0.11 1.60). indicating that individuals experiencing more current life stressors also reported higher rates of anhedonic depression.

Given that ELS was not found to be uniquely related to anhedonic depression or to IMCWS performance, CTQ was not included as an independent variable in the subsequent mediation model predicting anhedonic depression.

Modeling Individual Factors In The Pathway From CLS To Anhedonic Depression

The proposed model of IMCWS performance as a mechanism by which CLS affects anhedonic depression, with moderation of the effect of CLS on IMCWS performance by individual resilience factors (see Figure 8) was evaluated with two approaches. Initially, mSEM was used to estimate the model. First, the individual variability associated with the interaction between image context condition and word condition was modelled as a random slope predicting RT. This random effects coefficient was then used as a mediator in the relationship between CLS and anhedonic depression. In standard MLM procedures, it is not possible to model a level 1 predictor as a mediator in the pathway between two level 2 predictors. Therefore, this approach represented an exploratory analytical strategy. The model did not detect evidence that the random effects coefficients associated with IMCWS task performance mediated the relationship between CLS and anhedonic depression, as IMCWS task performance did not predict anhedonic depression when controlling for the effect of LESS ($p = 0.96$). Individual variability associated with the interaction slope used in this model was low and likely not sufficient to reject the null hypothesis. As even standard MLM tends to shrink coefficients towards the mean, making coefficients more similar than they are and underestimating real variability, this model may have been underpowered in the present sample to find real effects.

In order to better represent individual effects, a follow-up mediation model was estimated utilizing the participant-level beta coefficients associated with the regression of image context condition on RT during the IMCWS task. These coefficients were estimated per subject by performing a linear regression estimating the relationship between image context condition, word condition, and their interaction on RT during individual trials of the IMCWS task (N = 300 trials). The beta coefficient associated with the main effect of image context condition was entered into PROCESS as the mediator representing emotion inhibition success. This contrast was selected as analyses conducted in Study 2 revealed that anhedonic depression scores had the largest impact on CWS performance during the positive context image condition, such that individuals higher in anhedonic depression demonstrated less reactivity to positive contexts, and thus better CWS performance than individuals with lower anhedonic depression scores.

Resilience was found to moderate the relationship between life stress and emotion inhibition success, such that higher levels of resilience were related to longer RTs to negative context images than positive context images when rates of CLS were high, and lower levels of resilience related to longer RTs to negative context images when rates of recent life stress were low (See Figure 9, p = 0.05, 95% CI 0.00 0.01).

Results did not support the hypothesis that IMCWS performance mediates the relationship between CLS and anhedonic depression. In this sample, IMCWS performance also did not predict adult anhedonic depression, when holding LESS scores constant (p = 0.29, 95% CI -28.65   93.83). No conditional indirect effect of LESS scores on anhedonic depression through IMCWS performance was found as a function of CD-risc scores, indicating that level of resilience did not change the indirect effect of CLS exposure on anhedonic depression through IMCWS performance in this sample (index of the moderated mediation = 0.001, 95% CI -0.001 0.004).

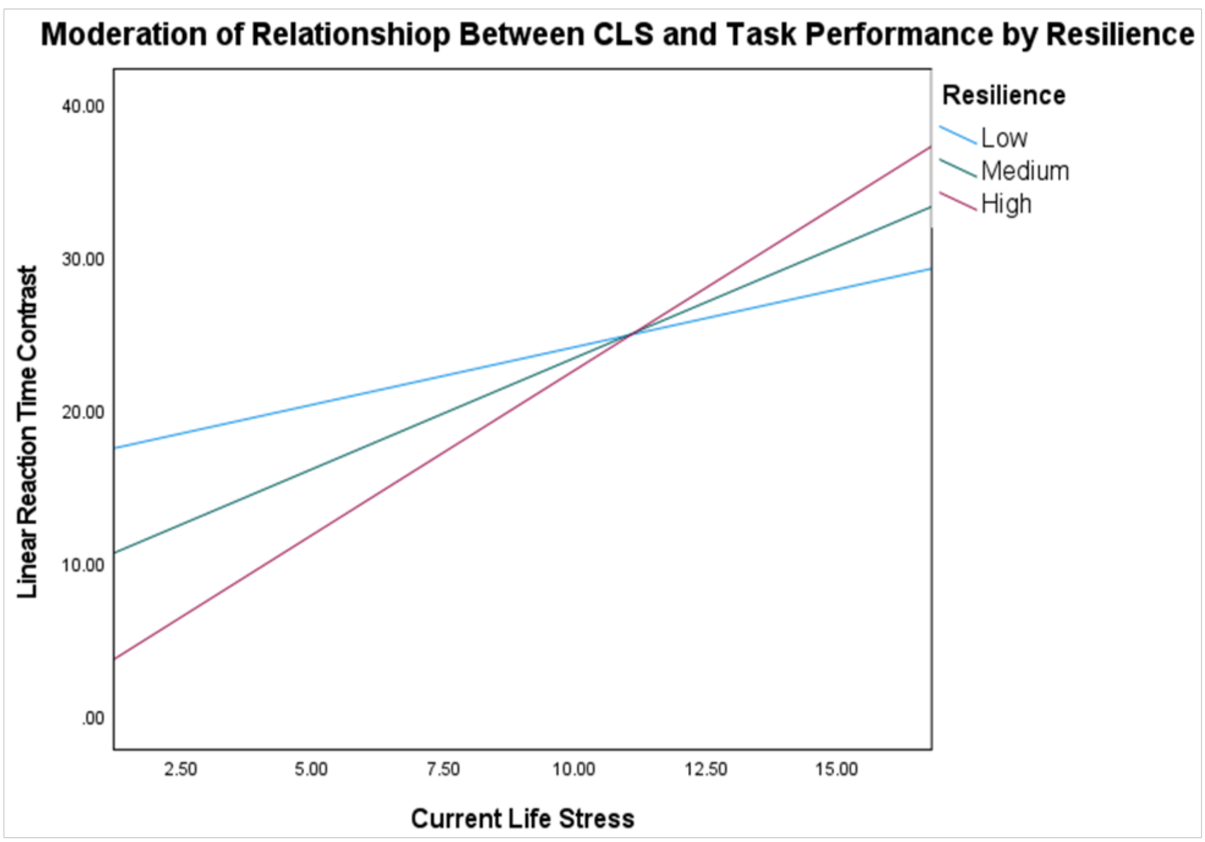

Figure 9. *Graph depicting the effect of CLS on IMCWS performance (the linear contrast of image context on RT, i.e., RT to negative contexts – RT to positive contexts) at different levels of the moderating factor, resilience (CD-risc). RT in milliseconds.*

Discussion

Emotion inhibition is known to be impacted by stress across the lifespan, and to be dysfunctional in adult depression. There is evidence to suggest that life stress impacts adult depression severity via alterations to emotion inhibition. However, few studies have modelled this pathway. Although it was predicted that emotion inhibition (as assessed by IMCWS performance) would mediate the pathway from CLS to adult anhedonic depression severity, evidence obtained in Study 3 did not support this hypothesis. Considerations regarding the null results are explored below, as well as implications stemming from the hypotheses that were supported by the present data.

Many studies have demonstrated that ELS predicts adult depression and that ELS impacts emotion inhibition success, attention biases, and cognitive control. In the present sample, however, ELS did not predict emotion inhibition function or adult depression severity. One limitation is the sample was largely (85%) UCLA undergraduates, a population with limited generalizability due to limited age range and relatively low racial/ethnic diversity as compared to the general population. The overall reported frequency of childhood trauma experiences as assessed by the CTQ was also low in the present sample as compared to psychiatric populations (Bernstein et al., 1997). Thus, it is likely that the sampling techniques used were not successful in capturing the variability in ELS necessary to characterize the impact of ELS on the outcomes of interest (e.g., emotion inhibition, anhedonic depression). On other metrics, such as resilience (CD-RISC) and CLS (LESS), the present sample demonstrated expected variability.

In contrast to ELS, results obtained in the present study support the hypothesis that CLS predicts alterations in emotion inhibition success and severity of adult anhedonic depression. CLS was related to longer RTs during negative context images than positive context images, indicating increased emotion inhibition load during negative context trials. Further, this relationship was found to be moderated by resilience such that individuals higher in resilience demonstrated more attentional bias to negative-valence stimuli than those lower in resilience. Although contrary to hypotheses, these patterns can be understood when one accounts for an evolutionary perspective on the role of attentional bias in the stress response. Acute stress is thought to predict increased attentional bias to threat stimuli as an adaptive function (Anderson & Britton, 2020). When in a high stress context, it is protective to attend to potential threat cues as it increases one's likelihood of responding quickly and effectively, keeping oneself safe from further harm when in an already vulnerable state.

Results of present analyses did not support the hypothesized role of IMCWS performance as a mediator in the relationship between CLS and depression, as IMCWS performance did not predict depression when controlling for CLS. Given limited variability associated with IMCWS task performance in the present sample, it is possible that Study 3 was underpowered to detect a real mediation effect using either model. Indeed, the sample size was limited by restrictions associated with the COVID-19 pandemic as the actual N of 133 fell short of the projected N of 200, originally estimated in preliminary power analyses to be required to detect a real effect. Alternatively, it is possible that emotion inhibition does not have a mechanistic role in the pathway from CLS to anhedonic depression. Results obtained in Study 2 demonstrated attention biases associated with depression that could be conceptualized as functionally distinct from those related to CLS. Whereas CLS was associated with more attentional bias to negative context images than positive context images, depression was associated with reduced attentional bias to positive context images. This pattern of results suggests distinct, though complimentary, contributions of CLS and depression to attentional biases. Given the strong relationship between

CLS and depression in the present sample and in the wider literature (Kendler et al., 2003; Vrshek-Shallhorn et al., 2015), it is likely that these patterns of emotion inhibition disruption frequently co-occur in the population. Variable co-occurrence of these epiphenomena in the depression literature is one possible explanation for the variation seen in emotion inhibition deficits associated with depression (e.g., reduced attention to positive-valence stimuli vs. increased reactivity to mood-congruent stimuli).

In summary, CLS increases risk for depression and alters processes supporting emotion inhibition, such that high-arousal, negative-valence stimuli increase RTs during a task of inhibitory control. Resilience moderates this relationship, with individuals reporting higher levels of CLS and higher levels of resilience exhibiting more attentional bias towards negative-valence stimuli than those lower in resilience. This is in line with research suggesting that CLS adaptively increases attention to threatening stimuli and suggests that suppressing or ignoring a response to emotional stimuli during periods of stress is maladaptive. While these changes may be adaptive in the short term, inflexible negative attentional bias and reduced engagement with positive stimuli over the long term are associated with increased incidence and severity of depression, as well as increased resistance to commonly effective depression interventions (Nolen-Hoeksema, 1991; Clery-Melin et al., 2018; Gollan et al., 2015). Understanding how to intervene effectively, in order to prevent such habits from persisting to the point of becoming maladaptive remains an area for future research.

General Discussion

Although the data presented do not support emotion inhibition as an explanatory mechanism for the relationship between CLS and anhedonic depression, several important findings were revealed across the three studies. Results indicated that the IMCWS task, a novel emotion inhibition paradigm, successfully manipulated behavior and ERP components consistent with increased emotion inhibition load during the presentation of high-arousal, emotionally valenced context images. While measures of anxiety were not related to task performance, anhedonic depression was found to be related to reduced reactivity during the presentation of positive images (i.e., increased emotion inhibition success). Examination of the impact of life stress variables on CWS performance and anhedonic depression severity provided evidence for a role of CLS, but not ELS, in anhedonic depression. Specifically, CLS was related to more biased attention (i.e., less emotion inhibition success) during the presentation of negative images, and this relationship was moderated by resilience.

These results have implications for future work in several domains. Although evidence for emotion inhibition as a mediator was not found, Study 3 explored a relatively novel method for modeling a repeated measures interaction between level 1 variables as a mediator in a pathway between two level 2 variables. There is little guidance in the extant literature on the best practices associated with mSEM models utilizing random slopes for interactions in a mediation analysis (e.g., the necessity of specifying random effects for lower order coefficients). Future work in this dataset will follow up on evaluating the mediation methods presented, as they represent a potentially helpful way of modelling mediation using repeated measures data to characterize a mechanism of interest. Given the onslaught of longitudinal research examining potential mechanisms by which stress exposure impacts the course of psychopathology, it is likely such modeling techniques would be powerful tools that are heavily utilized.

Depression has been inconsistently associated with emotion inhibition function, such that some studies demonstrate that individuals with depression show more emotion inhibition success during the presentation of positive-valence stimuli and less emotion inhibition success during the presentation of mood-congruent, negative stimuli (Cuthbert et al., 2000; Epstein et al., 2006; Gilboa, Roberts & Gotlib, 1997; Green et al., 2019; Krompinger & Simons, 2009; Proudfit et al., 2015; Rottenberg, Gross, & Gotlib, 2005). Studies 2 and 3 indicated distinct patterns of emotion inhibition associated with anhedonic depression and CLS, and a strong predictive relationship between CLS and anhedonic depression. Study 3 examined a mediation model that assumed a causal relationship between CLS and depression, which was ultimately not supported. The stress generation hypothesis (Hammen, 1991) offers an explanation for the relationship between these two variables that is not unidirectionally causal, but rather transactional, such that depression increases stress and stress increases depression. Therefore, a moderation model may be more appropriate to account for some of the above-described variability in the emotion inhibition literature. Future work with this dataset will explore a potential moderation model, whereby life stress and resilience moderate the impact of depression on emotion inhibition success.

Data presented here provides insights concerning the impact of depression, life stress, and resilience on emotion inhibition and may have implications for the application of interventions to at-risk populations. As such, subsequent work might focus on translation of findings concerning emotion inhibition mechanisms elucidated here and elsewhere into the development of effective interventions for depression. Of particular interest, are interventions that a) foster flexible awareness of automatic responses to emotion as well as goals in the present moment, b) facilitate effective stress management, and c) target and modify attentional biases. Mindfulness skills are a likely candidate for the first set of interventions. Mindfulness is typically defined in the western clinical literature as "the awareness that arises from paying attention, on purpose, in the present moment and non-judgmentally" (Kabat-Zinn, 2003). These skills have been growing steadily in popularity in clinical practice (e.g., acceptance and commitment therapy [ACT], dialectical behavioral therapy [DBT], mindfulness-based stress reduction [MBSR]) due to their success in fostering awareness of and flexibility in response to automatic thoughts, urges, and emotions (for a review, see Kashdan & Rottenburg, 2010; Lee & Orsillo, 2014; Zhang et al., 2018). Mindfulness is associated with increased ability to hold goals in mind and resist acting on an ineffective behavioral urge when a more effective, goal-congruent behavior is available (Zhang et al., 2018). The similarity between this process and emotion inhibition is quite clear. However, the link between mindfulness skills training and measures of emotion inhibition success has not been examined. The available research strongly suggests that mindfulness skills training would be an effective intervention to increase emotion inhibition success, insofar as training in mindfulness has been shown to increase effortful emotion regulation success (Crosswell et al., 2017; Elices et al., 2017) and reduce symptoms of internalizing psychopathology (Hofmann & Gomez, 2017), but the likely intervening mechanism, emotion inhibition, has not been evaluated. Brown and colleagues (2013) illustrated that dispositional mindfulness was related to reductions in later emotion processing in favor of goal-relevant activation. Thus, mindfulness may bolster the neural mechanisms supporting successful emotion inhibition, given that Study 1 found emotion inhibition to be associated with reductions in neural correlates of later emotion processing (LPP) during emotionally valenced images in favor of activation associated with inhibitory control (N450). Interventions that bolster top-down processes are likely to increase the individual's ability to remain flexible, present-centered, and goal-focused in their attention and, thus more likely to successfully enact emotion inhibition processes in order to apply more effortful emotion regulation interventions, such as those subsumed by stress-management.

It is likely that CLS impacts how emotion inhibition deficits manifest in depression, by increasing attentional bias to high arousal, negative stimuli. Stress management interventions are largely built on training in effortful emotion regulation (e.g., reappraisal, distraction) and relaxation skills training (e.g., deep breathing, progressive muscle relaxation; Ertekin-Pinar et al., 2018; Jones et al., 2008). Previous work investigating the impact of stress management skills training indicates that skills training reduces self-reported depression symptom severity as well as severity of negative attentional biases (Ertekin-Pinar et al., 2018; Jones et al., 2008). As described above, it is likely that more successful emotion inhibition would result in more successful application of such skills in the moment, such that the redirection of attention away from automatic urges prompted by negative stimuli and towards effective regulatory skills would be more efficient. Therefore, future work may examine the relationship between effective stress management skill use and emotion inhibition.

Another relevant area of interest is a relatively novel set of interventions involving attention bias modification (ABM) training. ABM involves tasks commonly used for the assessment of attentional bias (e.g., dot-probe, visual-search), that have been adapted to include emotionally valenced stimuli (Leeman et al., 2014; Zhang et al, 2018). In ABM treatment studies of depression, these tasks are used to train individuals to direct their attention towards positive-valence or reward stimuli and away from negative-valence or mood-congruent stimuli (Woolridge et al., 2021; Zhang et al., 2018). Results indicate that ABM may be successful in increasing automatic processing of pleasant/appetitive stimuli and reducing attention towards negative stimuli in individuals with depression (Dai et al., 2019; Woolridge et al., 2021; Yang et al., 2016). ABM training has also been associated with reduction in severity of depression symptoms (Bø et al, 2021; Yang et al., 2016). Further, some work indicates that a pre-treatment course of ABM increases the later efficacy of a variety of interventions, including group-based cognitive behavioral therapy (CBT) for anxiety disorders and ACT (Bø et al, 2021; Lazarov et al., 2018). However, replication studies, follow-up studies, and meta-analyses of ABM indicate small or inconclusive effects of the intervention (Everaert et al., 2014; Fodor et al., 2020; Østergaard et al., 2019; Zhang et al., 2018). Pending careful evaluation and validation of the methods being used for ABM training, the approach might be adapted to provide an effective intervention that increases emotion inhibition success.

Conclusions

Results presented here demonstrate successful manipulation of emotion inhibition processes by the IMCWS task, as well as important relationships between CLS, anhedonic depression, resilience, and emotion inhibition. However, the current project is only the first step in a much larger program of research, evaluating the role of emotion inhibition in the network of cognitive constructs that support emotion regulation, and characterizing mechanisms in the path from life stress to psychopathology with an eye towards effective intervention development. Future work is needed to continue to evaluate and refine the IMCWS task, develop statistical methods of mediation analysis, and characterize the impact of common and novel interventions on emotion inhibition and its correlates.

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