11-25-2019 10:30 AM

Baseline and Stress-Induced Cognitive Control Deficits and Pro-Inflammatory Cytokines in Currently, Remitted, and Never Depressed Individuals

Katerina Rnic, *The University of Western Ontario*

Supervisor: Dozois, David JA, *The University of Western Ontario*

A thesis submitted in partial fulfillment of the requirements for the Doctor of Philosophy degree in Psychology

Abstract

Background: Cognitive theories posit that cognitive control deficits promote depression by reducing ability to self-regulate under stress. When activated by stress and accessible to working memory, negative cognitive content and structure (i.e., schemas), may interfere with cognitive control abilities, resulting in even greater declines in executive functioning. Moreover, burgeoning evidence indicates that social stress upregulates inflammation, resulting in a pro-inflammatory phenotype that drives depression pathogenesis. However, cognitive mechanisms underlying this process are not well understood. An objective of this study was to examine depression-related deficits in cognitive control and their association with poor self-regulation. Another purpose was to evaluate the role of cognitive vulnerability in determining stress-induced declines in cognitive control. This study was the first to investigate the role of cognitive control and cognitive vulnerability (content, structure, and rumination) in shaping both resting-state and stress-induced upregulation of pro-inflammatory cytokines. **Method:** A clinical sample of currently depressed (n=40), remitted depressed (n=69), and healthy control (n=57) participants completed measures of cognitive content (core beliefs, dysfunctional attitudes), self-schema structure, rumination, depressive symptoms, and a battery of affective cognitive control tasks assessing inhibition, updating, and shifting. Salivary levels of four pro-inflammatory cytokines (IL-8, IL-6, IL-1β, and TNF-α) and updating abilities were assessed before and after a laboratory social stress induction. Depressive symptoms were evaluated at 2-week and 6-month follow-up. **Results:** Depressed individuals evinced deficits in inhibition and updating, which were associated with rumination, but not in shifting. As hypothesized, core beliefs and self-schema structure predicted declines in updating abilities following stress, and several cognitive control and vulnerability variables were related to baseline and stress-induced changes in cytokines. A

fairly consistent pattern of findings emerged whereby deficits in cognitive control were associated with greater resting-state and stress-induced inflammation among individuals with low, and not high, cognitive vulnerability. Moreover, greater inflammatory reactivity to the stressor predicted decreases in depressive symptoms at follow-up. **Conclusion:** Cognitive content and structure are important in determining stress-induced declines in cognitive control, and inflammation represents a biological pathway through which cognitive vulnerability and cognitive control may influence depression. Theoretical and clinical implications of findings and directions for future research are discussed.

Keywords: Cognitive Control, Cognitive Vulnerability, Depression, Social Stress, Cytokines, Inflammation, Inhibition, Shifting, Updating

Summary for Lay Audience

Background: Cognitive control refers to the ability to control the contents of current awareness. Theories of depression suggest that poor cognitive control interferes with emotion regulation during stress and that this promotes low mood. During stressful experiences, negative memories and thoughts may enter current awareness, further reducing cognitive control and resulting in poorer self-regulation, including ruminative thinking. Moreover, evidence indicates that social stress upregulates inflammation, which may promote depression. However, cognitive mechanisms underlying this process are not well understood. The current study examined cognitive control and rumination in individuals with current and past diagnoses of depression, as well as never-depressed individuals. Another goal was to examine the role of negative thinking in shaping declines in cognitive control under stress, and the role of cognitive control and negative thinking in influencing both resting-state and stress-induced upregulation of inflammation. **Method:** A total of 166 participants completed measures of negative thinking, rumination, depressive symptoms, and a battery of cognitive control tasks. Salivary levels of four inflammatory markers and cognitive control abilities were assessed before and after a laboratory social stress induction. Depressive symptoms were evaluated at 2-week and 6-month follow-up. **Results:** Depressed individuals showed deficits across several facets of cognitive control, and these were associated with rumination. Negative thinking predicted declines in cognitive control abilities following stress, and several cognitive control and negative thinking variables were related to baseline and stress-induced changes in inflammation. A fairly consistent pattern of findings emerged whereby deficits in cognitive control were associated with greater resting-state and stress-induced inflammation among individuals with low, and not high, negative thinking. Moreover, greater inflammatory reactivity to the stressor predicted decreases in depressive

symptoms at follow-up. **Conclusion:** Negative thinking is important in determining stress-induced declines in cognitive control, and inflammation represents a biological pathway through which negative thinking and cognitive control may influence depression. Theoretical and clinical implications of findings and directions for future research are discussed.

Acknowledgments

I would like to express my gratitude to my supervisor, Dr. David Dozois, for his guidance and support over the years. He has shaped my development as an academic, clinician, and professional, and I feel incredibly fortunate to have had the opportunity to train under his supervision. Dr. Dozois inspires me to work hard and to enjoy the process, and I could not have asked for a better role model and mentor.

I would also like to thank my supervisory and examination committee members, Dr. Paul Tremblay, Dr. Nick Kuiper, Dr. Leora Swartzman, Dr. Saad Chahine, and Dr. Naomi Koerner, for their insightful comments and feedback on my manuscript. I would also like to thank Dr. Gregory Dekaban, Christy Barreira, and the team at Salimetrics for their help in the collection and analysis of my salivary cytokine data. Special thanks to Dr. Rod Martin for creating the online program for my measures, and to Dr. Elizabeth Hampson for her expert consultation on the design of this study.

I would like to express my gratitude to my research team: Callista, Rohin, Alice, Ethan, Frasia, Vanessa, Ivana, Christine, Jasmine, Sarena, Veselina, Kavita, Christine, Sally, Adam, Ola, Matthew, Sarah, Erin, Kimberley, Jesse, and Monica. This project would not have been possible without your hard work and dedication, and I feel privileged to have worked with all of you. I would also like to thank the Social Sciences and Humanities Research Council and the University of Western Ontario for funding my doctoral research.

Heartfelt thanks to my friends, cohort, and lab mates Daniel, Monica, Jesse, Lindsay, Jennifer, Nadia, Christian, and Martin, as well as my residency cohort in Calgary, Carlos, Megan, Chantal, Leah, and Camille, for making my PhD a wonderful experience. Thank you for your support, laughs, and friendship.

Finally, I would also like to thank my family for their love and support in everything I do. Thank you Mom, Dad, Amanda, and Vicki for always being in my corner. To my loving partner Justin: thank you for being there every step of the way. I can't wait for our next adventure on the west coast.

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Introduction

Depression is a common and debilitating disorder, with over 3.5 million Canadians experiencing an episode at some point in their lifetime (Statistics Canada, 2013). Not only is the disorder chronic, with the average episode of Major Depressive Disorder (MDD) lasting 20-30 weeks on average (Keller et al., 2013; Rohde, Lewinsohn, Klein, Seeley, & Gau, 2013), but rates of recurrence are high, such that 50% of individuals with a first onset of depression go on to experience a further episode (Rohde et al., 2013), ultimately experiencing an average of 5-9 episodes over their lifetime (Kessler & Walters, 1998; Kessler, Zhao, Blazer, & Swartz, 1997). Despite numerous evidence-based treatments for depression, effect sizes for pharmacological and psychotherapy treatment outcomes are only moderate (Cuijpers, 2017), and relapse and recurrence are common (Kupfer, Frank, & Wamhoff, 1996). Better understanding the predictors and maintaining factors of depression has therefore become a key concern.

Diathesis-stress models of psychopathology have long underscored the importance of life stress as a causal mechanism for the onset and recurrence of depression. Indeed, the best proximal predictor of depression is a severe life event, and those major life events involving social threat result in the shortest time to onset (Slavich, Thornton, Torres, Monroe, & Gotlib, 2009). However, many individuals experience severe interpersonal life events and do not go on to become depressed. After experiencing a stressful life event, individuals with depression are thought to be more reactive to stress than others due to a poor ability to effectively regulate emotional responses, thereby leading to persistent negative mood. In fact, given that the cardinal symptoms of depression are sustained negative affect or loss of pleasure, depression has been characterized as primarily a disorder of emotion dysregulation (Gotlib & Joormann, 2010).

Fundamental to emotion regulation are cognitive control abilities. Cognitive control abilities are comprised of executive functions (e.g., inhibition) that gate information in and out of working memory, permitting the individual to focus on information relevant to the current task at hand (Joormann & Arditte, 2014). However, under conditions of stress, negative cognitive vulnerabilities, including dysfunctional attitudes, core beliefs, and schemas, are activated in depression-prone individuals (Dozois & Beck, 2008), making them accessible to working memory. This may increase the load on cognitive control functions for individuals with depression, potentially impacting on their ability to regulate affective and biological responses. Consistent with this novel idea, depression is associated with deficits in cognitive control, and evidence is strongest for deficits in cognitive control of negative affective stimuli (e.g., sad words or images; Joormann & Tanovic, 2015). In turn, these deficits are related to poor emotion regulation. This includes use of rumination (i.e., passive and repetitive negative thinking about the causes, consequences, and meaning of low mood) as a maladaptive and misguided attempt to improve mood (Joormann & Tanovic, 2015).

A striking finding is that the very stressors that are most predictive of depression (i.e., interpersonal events involving social threat or loss), also provoke immune system responding, with emerging evidence suggesting that chronic activation of the immune system is highly depressogenic (Slavich & Irwin, 2014; Slavich & Sacher, 2019). Psychoneuroimmunology research and theory suggest that when social stressors are interpreted as threatening, the immune system upregulates and redistributes cytokines, protein molecules that are the key mediators of the immune response, in order to protect the body from potential wounding. However, cognitive mechanisms underlying this process are not well understood. An intriguing possibility is that cognitive control and cognitive vulnerability may be implicated in shaping immunological

activity. Cognitive control abilities are critical for self-regulation during stress and, when activated by stress and accessible to working memory, negative cognitive content (e.g., dysfunctional attitudes, core beliefs), structures (i.e., schemas), and processes (e.g., rumination) may interfere with cognitive control abilities, resulting in even greater declines in executive functioning. As such, cognitive control and cognitive vulnerability appear to be likely moderators of the stress-cytokine link.

Despite compelling theory and evidence to support these dynamics, very little research has examined how various forms of cognitive control, cognitive vulnerability, and inflammation interrelate under conditions of social stress or in the context of depression. A goal of the present dissertation was to replicate and extend prior research by comprehensively examining depression-related deficits in cognitive control of negative stimuli, both at baseline and following a social-evaluative laboratory stressor, in a clinical sample of currently depressed, remitted depressed, and healthy control participants. The association of these deficits with poor emotion regulation, in terms of greater trait rumination, was also investigated. Another purpose was to evaluate the role of cognitive content and structure in determining declines in cognitive control following stress, when these executive functions are most needed for self-regulation. Additionally, a further key objective was to investigate the role of cognitive control and cognitive vulnerability (i.e., cognitive content, structure, and process) in shaping both resting-state and stress-induced upregulation of pro-inflammatory cytokines. Given that inflammation is posited to be a risk factor for the onset and course of depression, the link between resting-state and post-stress changes in cytokines with depressive diagnoses at baseline and with depressive symptoms at baseline, two-week, and six-month follow-up was also investigated.

The literature on cognitive control is first reviewed, including types of cognitive control, their association with emotion regulation (particularly rumination), and how abilities vary in the context of depression and stress. Preliminary evidence for a link between cognitive control, depressive cognitive content, and inflammatory activity is discussed. The role of inflammatory responses to social threat in the context of depression is then reviewed, as is the relatively unexplored role that cognition (both content and process) may play in determining immunological reactivity to stress.

Cognitive Control

Cognitive control determines an individual's moment-to-moment experience by gating information in and out of working memory, and therefore influences how events are experienced and responded to (Joormann & Tanovic, 2015). Working memory is a limited capacity system that reflects the contents of awareness, including the current focus of attention and temporary access to select representations, in order to facilitate current cognitive processes (Joormann & Arditte, 2013). Given the restricted capacity of working memory, continuous and efficient updating of contents is essential. Cognitive control encompasses executive functions that enable individuals to control contents of working memory by directing attention, overriding dominant cognitive responses, and inhibiting the processing of irrelevant information. These abilities allow for goal-directed behaviour, such as carrying out complex tasks, making decisions, and implementing cognitive and behavioural strategies to effectively adjust emotional and behavioural responses as situations unfold (Banich, 2009). Cognitive control is therefore critical for effective functioning and self-regulation during changing, novel, or stressful situations.

Cognitive control subsumes the executive control processes of working memory, including inhibition, shifting, and updating. These functions selectively gate access of

information into working memory, prevent intrusion of goal-irrelevant information, and discard no longer relevant content (Joormann & Tanovic, 2015). Deficits in any of these functions results in the experience and poor resolution of interference and are linked with poor emotion regulation and depression (Joormann, 2010; Whitmer & Gotlib, 2012). A key distinction is between cognitive control deficits, or broad impairments in cognitive control across a range of stimuli, and cognitive control biases, which are impairments specific to affective stimuli and that result from prioritizing the processing of emotional (typically negative) information. Impairment in inhibiting activations of mood-congruent negative content from working memory (e.g., representations of depressive symptoms; Baddeley, 2013) likely plays an important role in the amplification of the experience of aversive symptoms and events, development of prolonged negative self-focused or goal-irrelevant thoughts, sustained negative affect, and poor recovery from negative mood, all of which are indicators of poor emotion regulation. Furthermore, impairments likely make it difficult to focus on current tasks, as individuals cannot inhibit or disengage from prepotent responses, resulting in issues with concentration and decision-making commonly reported in individuals with MDD.

To conduct a comprehensive investigation of the relation of cognitive control with cognitive vulnerability and inflammation, the current thesis examined depression-related deficits across the three major facets of cognitive control: inhibition, shifting, and updating. Accordingly, the literature on depression-related impairments for each of these types of cognitive control are reviewed next. Tasks commonly used to assess each type of cognitive control, as well as findings for biases among individuals with dysphoria or with current or remitted depression, are described. Given that rumination is thought to constitute a maladaptive emotion regulation strategy, associations of cognitive control with rumination are believed to be indicative of

emotion regulation problems (Joormann & Stanton, 2016). Therefore, relations of rumination, as well as other forms of emotion regulation, with each type of cognitive control are discussed.

Inhibition. Inhibition, the ability prevent the processing of irrelevant information in working memory and to override prepotent or dominant responses (Joormann & Tanovic, 2015), can be assessed using a variety of methods, including the Emotional Stroop Task, the Cued Emotional Conflict Task, the Negative Affect Priming Task, and the Emotional Flanker Task (Joormann, 2004). To better illustrate how inhibition is conceptualized and assessed, and to provide important background context for findings on depression-related inhibitory deficits, the design of key inhibitory tasks is described.

The Emotional Stroop asks participants to identify the colour of a word when a negative emotion word or neutral word is presented (e.g., Compton et al., 2011), such that longer response latencies on negative word trials are an indicator of deficits in inhibition. The task has also been adapted using faces, whereby an emotional word is presented alongside an emotional or blurred face, and participants are required to either inhibit the facial expression in order to report the emotion represented by the word, or to inhibit the word to report the emotion expressed by the face. The Cued Emotional Conflict Task requires participants to respond to an upcoming presentation of a face by identifying the emotion it is displaying, identifying the opposite emotion, or by pressing an unrelated button. Performance on trials asking individuals to label the emotion opposite to what the face is displaying is indicative of inhibitory ability. In contrast, the Negative Affect Priming Task presents participants with a target and distractor word during each trial, and measures response times to positive and negative targets that were distractors or were closely related to distractors (e.g., same valence) on the last trial, and therefore had previously been deemed irrelevant. Shorter reaction times responding to targets that were previously

distractors (and therefore should be inhibited) are indicative of weak inhibitory abilities. Finally, the Emotional Flanker Task asks participants to indicate whether a given word is positive or negative while ignoring flanking distractor stimuli presented simultaneously and of varying valence. Interference is measured as the difference in response time on trials where distractors are congruent versus incongruent with the target stimulus in valence, with longer response times for incongruent compared to congruent trials denoting poor inhibition.

There is good evidence for inhibitory biases in depression. For example, individuals with dysphoria and depression exhibit deficits inhibiting negative, not positive, words on the Negative Affect Priming Task. This bias is associated with trait rumination, even after controlling for depressive symptoms (Joormann, 2004, 2006; Joormann & Gotlib, 2010). Findings have also been replicated in a study that used a Negative Affect Priming Task with faces as stimuli, which found evidence for poor inhibition for sad faces and intact inhibition for happy faces in depressed individuals (Goeleven, DeRaedt, Baert, & Koster, 2006). Similarly, Saunders and Jentzsch (2014) found that participants with depression exhibited deficits on an Emotional face Stroop, but not on an unemotional version of the task. A meta-analysis of studies using the Emotional word Stroop found that depressed individuals show significant slowing on trials with negative words compared to neutral or positive words, whereas control participants did not show this difference (Epp, Dobson, Dozois, & Frewen, 2012). Furthermore, using the Emotional Flanker Task, Zetsche, D'Avanzato, and Joormann (2012) found that currently depressed individuals evince marginally greater interference for negative distractor words as compared to controls, although interference was not associated with depressive symptoms in a nonclinical sample (Zetsche & Joormann, 2011). Moreover, compared to healthy controls, individuals with depression also demonstrate slower reaction times and attenuated N450 event related potentials

(which are thought to be involved in detecting discrepancies that require inhibitory control; Munakata et al., 2011) when inhibiting negative images in the Cued Emotional Conflict Task (Vanderhasselt et al., 2012). Finally, neuroimaging research provides converging evidence, with findings suggesting that individuals with depression and those who ruminate need to recruit greater cognitive resources in order to inhibit negative material (Vanderhasselt et al., 2013).

Evidence for inhibitory impairments in individuals with remitted depression is more mixed. Whereas Ardal and Hammar (2011) found that individuals with MDD demonstrate inhibitory deficits on the original Stroop even at 10-year follow-up (Ardal & Hammar, 2011), their analyses did not account for whether participants were acutely depressed at follow-up. A number of studies using the Emotional Stroop have not found evidence for inhibitory biases among individuals with remitted depression (Gotlib & Cane, 1987; Hedlund & Rude, 1995; Merens, Booij, & Van Der Does, 2008; Wekking, Bockting, Koeter, & Schene, 2012). However, Vanderhasselt and De Raedt (2009) found that, although performance on the original Stroop did not differ among individuals with past depression and nondepressed controls, reduced N450 event related potentials during the original Stroop persisted during remission and were associated with number of past episodes. Furthermore, Joormann (2004) found that remitted depressed individuals showed a marginally significant difference in inhibitory ability on the Negative Affect Priming Task relative to controls, whereas Joormann and Gotlib (2010) found no negative affect prime effect amongst remitted depressed individuals.

Inhibitory biases appear to be a risk factor for the development of depression. Biases are observed in healthy first-degree relatives of individuals with MDD (Lisiecka et al., 2012) and prospectively predict depressive symptoms (Kertz, Belden, Tillman, & Luby, 2016; Zetsche & Joormann, 2011). Compton et al. (2011) examined potential mechanisms that may explain the

link between poor inhibition and subsequent depression, and found that longer reaction times after an error on the Emotional Stroop predicted negative affect and reduced task-focused coping in response to daily stress, whereas greater executive control was associated with a tendency to use problem-focused coping to manage daily stressors. Importantly, this finding speaks to the critical role cognitive control has in determining self-regulation under stress.

Inhibitory biases are evident in depression across a range of tasks, indicating that individuals with depression have difficulty keeping irrelevant affective material, (particularly negative irrelevant material), out of their working memory. Impairments in inhibition may lead to depression as a result of poor self-regulation following stress. Along these lines, inhibition has also been linked to a tendency to ruminate, as inhibitory biases make it difficult to prevent intrusions of irrelevant, mood-congruent negative material in working memory. Additionally, rumination may interfere with the ability to recruit the cognitive resources needed to engage inhibitory abilities.

Updating. Whereas inhibition comprises the ability to prevent irrelevant information from entering working memory, updating is the continuous monitoring and manipulation of the contents of working memory, whereby information is added or removed. The ability to flexibly and efficiently remove information that is not or is no longer relevant to goals optimizes task-focused attention and self-regulation, and prevents perseverative thinking following negative events or mood states. There are a number of measures used to assess updating, including the Working Memory Manipulation Task, a modified Sternberg task, a variety of directed forgetting tasks, and the Emotional N-back Task.

The Working Memory Manipulation Task (Joormann, Levens, & Gotlib, 2011) presents participants with lists of three positive, negative, or neutral words, and participants are required

to memorize words in the order presented on some trials, and in reverse order on other trials. Participants are then shown a probe word that was presented in the list and asked to indicate whether the word was first, second, or third, counting in the order they were instructed to memorize. Updating is assessed as differences in response times between forward and backward trials. Individuals with depression show more difficulty manipulating information in working memory on this task as compared to controls, particularly when content is negative. Of note, this effect was associated with rumination (Joormann et al., 2011).

Joormann and Gotlib (2008) used a modified Sternberg task that simultaneously presents participants with two lists of emotional words that they are instructed to memorize. Participants are then cued as to which list is relevant for an upcoming recognition memory task. On each trial of this task, participants indicate if a probe word came from the relevant list. The authors found that individuals with MDD have difficulty removing negative (not positive) emotional words from working memory, as indicated by longer latencies in rejecting intrusion probes from a previously relevant list relative to novel probes. Response latencies reflect the strength of residual activation of the contents of working memory declared no longer relevant and the ability to remove irrelevant information from working memory. Importantly, longer response latencies were associated with trait rumination, even after controlling for depressive symptoms. Impairment on this task appears to be specific to emotional content, as differences between depressed participants and controls were not found in a version that uses neutral stimuli (Joormann, Nee, Berman, Jonides, & Gotlib, 2010). Further research using this task has found that individuals with MDD have more difficulty removing emotional words from working memory than do those with social anxiety disorder or healthy controls, suggesting that updating impairments may have some specificity to depression (Yoon, LeMoult, & Joormann, 2014).

Similarly, Joormann and colleagues (2010) asked participants to complete an 'ignore' task where they were instructed to memorize a series of words and ignore other words, and a 'suppress' task in which they were told to forget previously memorized words. Participants were then presented with words and asked to indicate if a word was one that they were instructed to remember. Compared to nondepressed participants, individuals with depression demonstrated longer latencies for negative words they were instructed to suppress, indicating that individuals with depression have difficulty removing negative material from working memory. This effect was not found for words they were instructed to ignore. Notably, longer latencies in the suppression condition were associated with trait rumination. Similarly, Joormann and Tran (2009) found that individuals high in rumination exhibited reduced forgetting of negative words, even after controlling for depressive symptoms.

An intentional forgetting task asks participants to learn a series of word pairs consisting of a neutral noun (target) and emotional adjective (cue), which imbues the targets with an emotional valence. Participants are then presented with the cue words and practice recalling or suppressing the associated targets. Recall for targets is then assessed. Studies have found that individuals with dysphoria and depression show greater recall of suppressed words (particularly those that are negative), compared to control participants, indicating difficulty with updating (Joormann, Hertel, Brozovich, & Gotlib, 2005; Joormann, Hertel, LeMoult, & Gotlib, 2009). Again, this impairment is associated with self-reported rumination (Hertel & Gerstle, 2003). Neuroimaging data also provide converging evidence for updating difficulties in depression, as indicated by greater recruitment of cognitive resources in a directed forgetting and modified Sternberg task (Berman et al., 2011; Foland-Ross et al., 2013).

In the Emotional N-back task (Chatham et al., 2011; Levens & Gotlib, 2010), participants are shown a series of emotional and neutral words one at a time and are asked during each trial to indicate whether or not the word matches the word that appeared a specified number of trials previously. This task assesses participants' ability to continuously update working memory with emotional information and requires participants to not only remove information from working memory (similar to the tasks reviewed above), but to also add new information. Using this task, Pe, Raes, and Kuppens (2013) found that among healthy individuals, rumination increases high arousal negative emotions only in those with poor updating ability. This finding suggests that it is the combination of both poor updating and a tendency to ruminate that results in negative affect. There are also versions of the N-back task that use emotional faces and ask participants to indicate if the emotional expression of a face matches the expression of the face presented two trials earlier. Individuals with MDD are slower to discard sad faces and faster to discard happy faces in this version of the task (Levens & Gotlib, 2010).

A paucity of research has examined updating biases in individuals with remitted depression. Using the Working Memory Manipulation Task, Liu, Zhou, Wang, Jiang, and Liu (2017) found that individuals with remitted depression evinced impaired updating abilities for negative material, compared to controls, and unimpaired ability to manipulate positive material. Furthermore, individuals with remitted depression showed greater event related potential amplitudes in response to negative pictures, suggesting that they needed to allocate more cognitive resources to updating and that depression may leave a "scar" (Lewinsohn, Steinmetz, Larson, & Franklin, 1981) on updating abilities. Similarly, Levens and Gotlib (2015) found that remitted depressed individuals were slower to disengage from sad faces than happy faces using the faces version of the Emotional N-back task.

In summary, there is evidence that individuals with dysphoria, depression, and remitted depression demonstrate biases in updating ability across various tasks. These findings indicate that depression is associated with difficulty monitoring information in working memory and efficiently adding or removing content, particularly negative content, in order to achieve task goals. In turn, updating biases are associated with perseverative negative thinking (i.e., rumination), likely due to poor ability to discard negative content from working memory.

Shifting. Shifting is the ability to flexibly switch between tasks or mental sets (Joormann & Tanovic, 2015; Miyake et al., 2000), and is commonly measured using the Affective Flexibility Task (Genet, Malooly, & Siemer, 2013) or Internal Shift Task (De Lissnyder, Koster, Everaert, et al., 2012). The Affective Flexibility Task requires participants to categorize pictures based on an affective or a non-affective rule. Each trial includes a picture and indicates which kind of rule to apply. Difference in reaction times between trials preceded by a trial using the same rule versus trials preceded by those using the other rule are indicative of shifting ability. This task allows for the assessment of continuous switching between discrete tasks. In contrast, the Internal Shift Task involves counting the number of angry and neutral faces presented in a block of trials, and participants press a button to indicate they have updated their count after each trial. Shifting is assessed as the change in reaction time for the button press between trials where the preceding trial featured a different stimuli valence, versus trials preceded by faces of the same category.

Shifting biases for emotional stimuli have been documented in depression. Individuals with depression demonstrated poor shifting compared to individuals without depression in a go/no-go task using emotional stimuli, but did not evince deficits when stimuli were neutral (Murphy, Michael, & Sahakian, 2012). Research using the Internal Shift Task found that

adolescents with dysphoria exhibited shifting impairments for emotional stimuli, particularly when shifting from negative to neutral stimuli. There were no impairments for non-emotional information (Wante, Mueller, Demeyer, Naets, & Braet, 2017). Similarly, Ravizza and Delgado (2014) found that dysphoric individuals are less able to improve task switching speed based on performance feedback on a task using neutral stimuli. Furthermore, compared to healthy controls, individuals with MDD showed impaired shifting on the Internal Shift Task. Of particular interest, shifting biases were associated with rumination regardless of neutral or angry stimuli valence (De Lissnyder, Koster, Everaert, et al., 2012), a finding that has also been observed in nonclinical samples using the Internal Shift Task (Beckwé, Deroost, Koster, De Lissnyder, De Raedt, 2014) and a task switching paradigm that involves switches between variations of the same task (Owens & Derakshan, 2013). De Lissnyder, Koster, Derakshan, and De Raedt (2010) similarly found shifting impairments in individuals with moderate to severe depressive symptoms as well as individuals with high trait rumination using an affective shift task. Neuroimaging findings also provide complementary evidence for shifting dysfunction in depression (Beevers, Clasen, Stice, & Schnyer, 2010), as indicated by deficits in recruiting cortical regions needed for shifting. Very little research has examined shifting biases in remitted depressed individuals. However, there is some evidence to suggest that shifting deficits are stable outside of depressive episodes, with general shifting impairments found in a sample of remitted depressed individuals (Preiss et al., 2009).

Evidence suggests that shifting impairments may be a risk factor for depression (Kertz et al., 2016). This relation appears to be driven by emotion regulation problems, including rumination, that arise from shifting biases (De Lissnyder, Koster, Goubert, et al. 2012; Demeyer, De Lissnyder, Koster, & De Raedt, 2012; Rochat, Billieux, & Van der Linden, 2012). Shifting is

relevant to emotion regulation because it allows individuals to better allocate attention by switching attention away from negative emotional material, and toward positive or goal-relevant material. When individuals have poor shifting ability, they may perseverate on negative information. For example, using the Affective Flexibility Task, Genet and colleagues (2013) found that difficulties task-switching away from the affective aspects of negative affective stimuli was related to increased rumination as assessed using a daily diary measure, whereas difficulties task switching away from the affective aspects of positive stimuli was related to decreased rumination. This finding indicates that flexibility is adaptive for negative, and not necessarily for positive, stimuli. In a related study, Malooly, Genet, and Siemer (2013) found that better performance switching to the neutral aspects of negative images or the positive aspects of positive images was related to greater effectiveness of reappraisal in reducing negative affect during a sad film clip.

Extant research indicates that individuals with dysphoria and depression evince biases in switching between tasks or mental sets. Preliminary research also suggests that individuals with remitted depression may show shifting impairments. Furthermore, the literature on shifting reports robust relations with rumination, likely resulting from inflexibility switching processing away from or toward affective aspects of stimuli.

Cognitive Control in Demanding Contexts

Demanding and stressful contexts may lead to state reductions in cognitive control as individuals with depression become cognitively overloaded, thereby leading to greater difficulty with effortful self-regulation, such as the selection of nondominant responses (e.g., reappraisal), and resulting in prolonged processing of negative, goal-irrelevant content (i.e., rumination). Consistent with this idea, burgeoning evidence indicates that, while there is evidence that it is

trait-like and remains fairly stable over time (Miyake & Friedman, 2012), executive control can become impaired in demanding or stressful contexts. A number of studies using laboratory stressors have found temporary declines in executive control (Plessow, Kiesel, & Kirschbaum, 2012; Schoofs, Preuss, & Wolf, 2008; Schoofs, Wolf, & Smeets, 2009; see Shields, Sazma, & Yonelinas, 2016 for a meta-analytic review). For example, Levens, Muhtadie, and Gotlib (2009) found that individuals with depression performed as well as nondepressed participants in a low-interference condition of the Recency Probes Task. In this task, participants are shown three words, and are then presented with a word and asked to indicate if it has just been shown, therefore requiring updating from trial to trial. However, in a high interference condition whereby participants were asked to complete another task simultaneously (i.e., counting the number of words that fit a category across trials in a block), therefore also requiring shifting between tasks, participants with depression performed significantly more poorly than nondepressed individuals. Similarly, Doumas, Smolders, Brunfaut, Bouckaert, and Krampe (2012) found that individuals with depression performed more poorly than did nondepressed individuals on a working memory task, and performance progressively decreased as difficulty increased during a concurrent task of postural control. Furthermore, Schoofs, Preuß, and Wolf, (2008) found that individuals who were exposed to a social-evaluative laboratory stressor (the Trier Social Stress Task, or TSST; Kirschbaum, Pirke, & Hellhammer, 1993) evinced deficits in updating on the N-back task compared to those in a control condition.

Stress-induced changes in cognitive control may be especially informative for predicting stress reactivity and depression. Quinn and Joormann (2015a) found that poor performance on the N-back task after undergoing the TSST was correlated with current depressive symptoms in an undergraduate sample. This relation was moderated by trait rumination, such that only

individuals with a tendency to brood showed a relation between reduced executive control under stress and depression. Interestingly, change in N-back task performance from pre- to post-stress induction was unrelated to changes in self-reported affect, and pre-stress updating was unrelated to depressive symptoms. In a subsequent study of undergraduates, Quinn and Joormann (2015b) found that a decrease in cognitive control following the TSST predicted an increase in depressive symptoms during final exams, suggesting that a decline in executive functioning during times of stress, when these functions are most needed for self-regulation, may make some individuals more vulnerable to depression. Given that trait executive control was not a predictor of subsequent depressive symptoms, the authors suggested that the degree to which executive control is influenced by stress is a better predictor of mood during stress than is trait executive control. However, the generalizability of this finding is limited by the nonclinical nature of the sample. Quinn and Joormann (2015b) also found that change in N-back task performance was not related to change in affect.

Given evidence that stress-induced changes in cognitive control may represent a separate construct from trait cognitive control, and that declines in cognitive control under stress may be particularly important for understanding stress reactivity, the current thesis examined stress-induced changes in cognitive control in addition to baseline measures.

Cognitive Control and Cognitive Content/Structure

Cognitive control deficits result in difficulty gating and manipulating the contents of working memory such that, in the context of depression, working memory becomes overrun with mood-congruent, goal-irrelevant thoughts. As such, it would be expected that individuals with greater negative thought content that could be activated by low mood would demonstrate the

largest deficits in cognitive control after experiencing stress, and that this would result in even more difficulty with self-regulation and stress reactivity.

Beck proposed a hierarchical organization of cognition, with self-schemas, or cognitive structures comprised of organized self-representations, representing the deepest level of thinking (Beck & Dozois, 2011, 2014). Schemas allow individuals to efficiently interpret and organize incoming information and consist of content elements, such as core beliefs, as well as organizational properties. Core beliefs and their organization develop over time through life experience and become increasingly consolidated as they act to filter information and guide the appraisal of life events (Dozois & Rnic, 2015). Negative experiences, such as maltreatment, can result in a depressotypic schema structure characterized by tightly interconnected negative beliefs about self (e.g., worthlessness, unlovability). When activated by stress, the negative belief structure may impact more surface-level, accessible cognitions, such as negative automatic thoughts and dysfunctional attitudes, (i.e., beliefs in contingencies for achieving happiness, approval from others, and success).

Only one study has examined the relation of cognitive control and cognitive content. Vergara-Lopez, Lopez-Vergara, & Roberts (2016) found a marginally significant effect, such that individuals with a tendency to make negative attributions, and who showed poor shifting of emotional content on the emotional Wisconsin Card Sorting Task, reported a greater tendency to ruminate. Additionally, attenuated resting state connectivity in the cognitive control neural network mediates the relation of remitted depression status with cognitive risk factors, including brooding, negative attributional style, and negative automatic thoughts (Stange et al., 2017). This finding also points to a link between cognitive control and negative cognitive content in depression. Cognitive content that is implicated in depression (Gotlib & Joormann, 2010), and

may be made more accessible in working memory as a result of control deficits, include core beliefs and dysfunctional attitudes. The organization of this content may also be important, such that more tightly interconnected negative material may be more likely to interfere with executive control processes.

Cognitive Control and Biological Reactivity

Impairments in executive control following stress are associated with sympathetic nervous system (SNS) and hypothalamic-pituitary-adrenal (HPA) activation (e.g., Qin, Hermans, van Marle, Luo, & Fernández, 2009). Furthermore, altered activation of the dorsal anterior cingulate cortex (dACC) has been implicated in difficulties with updating in individuals with depression (Foland-Ross et al., 2013). Strikingly, SNS, HPA axis and dACC activation are implicated in immunological reactivity to social stress, which has been posited as a major contributor to the onset and course of depression, at least in some individuals.

Very little research has examined the relation of cognitive control with immune responses. Shields, Kuchenbecker, Pressman, Sumida, and Slavich (2016) randomly assigned participants to an emotional stressor (watching an upsetting video) or a control condition (watching an unemotional video). Salivary levels of pro-inflammatory biomarkers (i.e., interleukin-1β [IL-1β], interleukin-6 [IL-6], and interleukin-8 [IL-8], described below) were measured before and after participants watched the video. Cognitive control was then assessed using the faces version of the Emotional Stroop. Participants who viewed the emotional video exhibited increases in IL-1β, IL-6, and IL-8, and better cognitive control predicted less pronounced inflammatory responses for individuals in the emotional stress, and not control, condition. This study is limited in that it examined only one facet of cognitive control (inhibition), and only assessed it post-stress. Furthermore, a recent study reported preliminary

evidence that stress-induced declines in updating are associated with increases in IL-6, and marginally associated with increases in IL-1β, following a variation of the TSST in a small nonclinical sample of 16 adults (Quinn, Stanton, Slavich, & Joormann, 2019). The nature of the relation of various facets of cognitive control with inflammatory responding, particularly in the context of depression and cognitive vulnerability, remain important questions. Moreover, although cognition is thought to determine immunological reactivity to social stress (Slavich & Irwin, 2014), very little research has examined this association, and the current thesis therefore aims to fill some of these gaps in the literature. As a key and under-researched component of stress reactivity, inflammatory processes in depression are discussed next.

Inflammatory Processes in Depression

The Social Signal Transduction Theory of Depression (Slavich & Irwin, 2014; Slavich & Sacher, 2019) posits that social adversity upregulates inflammation, resulting in a pro-inflammatory phenotype that drives depression pathogenesis. Slavich and Irwin (2014) argue that humans have a conserved transcriptional response to adversity (CTRA) that is evolutionarily adaptive and is represented by skewing of the basal gene expression profile, involving activation of pro-inflammatory immune response genes and the downstream production of pro-inflammatory cytokines (i.e., small protein molecules that are the main effectors of the immune response; see Slavich & Cole, 2013). The CTRA serves to enhance wound healing and to combat bacterial infections in the event of a physical altercation, but at the cost of reciprocal downregulation of antiviral immune response genes involved in antibody production, thereby resulting in heightened risk for viral infection and inflammation-related disease. Moreover, pro-inflammatory cytokines elicit profound changes in behaviour and affect, including anhedonia, sad mood, fatigue, psychomotor retardation, and social-behavioural withdrawal (Slavich &

Irwin, 2014; Slavich & Sacher, 2019), all core symptoms of depression. A model of physiological pathways involved in the CTRA is presented in Figure 1.

The immune system has evolved to respond not only to existing wounds and infections, but to proactively respond in advance of these to prepare the body for wounding in advance of assault, which could result in a pathogen-related infection. This speaks to the importance of cognition in eliciting the CTRA response. The neuro-inflammatory link means that CTRA can be activated by perceived threats, including social conflict, evaluation, rejection, isolation, and exclusion. When the CTRA is chronically activated, a pro-inflammatory phenotype results, which may drive the initial pathogenesis and recurrence of depression, and may result in somatic conditions commonly comorbid with depression, such as asthma, rheumatoid arthritis, chronic pain, metabolic syndrome, cardiovascular disease, obesity, and neurodegeneration (e.g., Barton, 2008; Calder, 2006).

The CTRA involves the innate immune system, which is comprised of immune cells that circulate to detect pathogens (Medzhitov, 2007). The acute phase of innate immunity involves local and systemic increases in inflammatory activity occurring over minutes or hours. When the innate immune system is activated, a signaling cascade is triggered that results in production of cytokines. Cytokines coordinate communication among cells and alter neurochemical and neuroendocrine processes that affect physiology and behaviour, and in this sense function similarly to hormones and neurotransmitters (Jain & Mills, 2007). Some cytokines, such as IL-8, IL-6, IL-1β, and tumor necrosis factor-α (TNF-α) are pro-inflammatory, whereas others are anti-inflammatory. Cytokines cause local redness, heat, swelling, and pain. In addition, IL-6 induces the production of C-reactive protein (CRP), which also increases body temperature, heart rate,

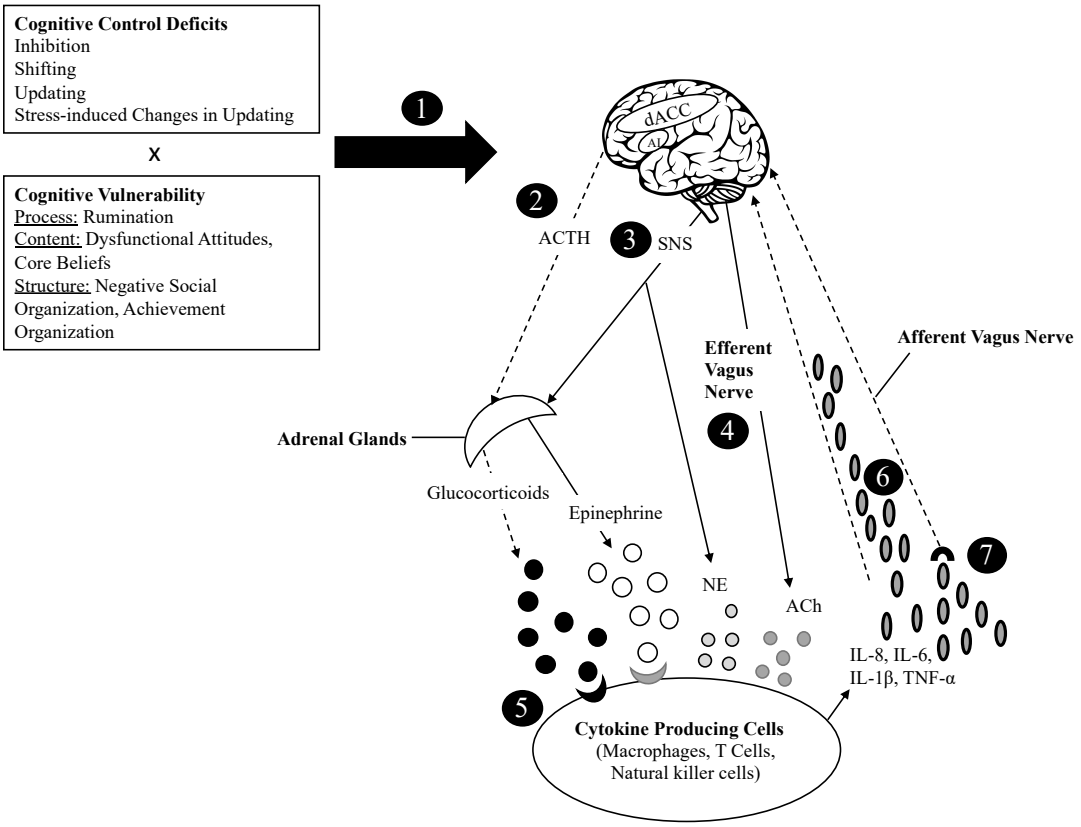

Figure 1. Physiological pathways underlying the CTRA, and hypothesized associations of cognitive control deficits and cognitive vulnerability. (1) Cognitive control deficits (inhibition, shifting, updating, stress-induced changes in updating) and cognitive vulnerability (process, content, and structure) may interfere with self-regulation ability during interpersonal experiences, resulting in social stressors being perceived as threatening. Threatening social stressors are represented in neural pathways that process pain, which include the anterior insula and dorsal anterior cingulate cortex (dACC). These brain regions project to lower areas that initiate and modulate inflammation via the (2) hypothalamic-pituitary-adrenal axis, (3) sympathetic nervous system (SNS), and (4) efferent vagus nerve. (5) Activation of these pathways results in production of glucocorticoids (e.g., cortisol), epinephrine, norepinephrine (NE), and acetylcholine (Ach). Glucocorticoids and acetylcholine interact with receptors on cytokine producing cells to result in anti-inflammatory effects. In contrast, epinephrine and norepinephrine up-regulate inflammatory gene expression in cytokine producing cells, resulting in the production of pro-inflammatory cytokines, such as interleukin-8 (IL-8), interleukin-6 (IL-6), interleukin-1β (IL-1β), and tumor necrosis factor-α (TNF-α). Pro-inflammatory cytokines signal the brain to promote behavioural, cognitive, and emotional changes that comprise symptoms of depression (e.g., anhedonia, sad mood, fatigue, altered appetite and sleep). Cytokines communicate with the brain by (6) passing through permeable or incomplete regions of the blood-brain barrier and by (7) stimulating the afferent vagus nerve, which conveys information to brain areas that regulate motivation, mood, activity, and arousal. Activation of these pathways is self-promoting and can result in neuro-inflammatory sensitization and persistent activation of the CTRA. ACTH = adrenocorticotropic hormone. (Figure adapted from Slavich & Irwin, 2014).

and respiratory rate, and causes fever to accelerate wound healing (Poon, Ho, Chiu, & Chang, 2013). As noted above, cytokines also promote social-behavioural withdrawal, as this allows the organism to recuperate and reduces likelihood of an infection being spread to conspecifics (Murphy, 2011).

Converging evidence highlights the role stress plays in elevating inflammation. Early life stress (e.g., maltreatment) and stressful life events occurring in adulthood (evidence is strongest for those involving conflict, threat, isolation, and rejection; see Kiecolt-Glaser, Gouin, & Hantsoo, 2010) are both associated with elevated concentrations of inflammatory biomarkers, and this has been replicated in individuals with depression (see Slavich & Irwin, 2014, for review). Moreover, laboratory-based social stressors, which provide the greatest internal validity and allow for careful monitoring of immune responses, have been found to trigger inflammatory responses.

The most popular paradigm for assessing stress reactivity in the laboratory is the TSST, which asks participants to prepare and present a speech and perform difficult mental arithmetic in front of a panel of socially rejecting raters. Studies using the TSST and modified versions of it have found greater production of TNF-α in individuals who had performed in front of raters versus those who had not. Importantly, those who reported feeling evaluated in either condition evinced greater increases in TNF-α production, even when controlling for perceptions of challenge, control, and difficulty, indicating that cognitions regarding the social component of the task (i.e., evaluation by others) play an important role in immune system reactivity (Dickerson, Gable, Irwin, Aziz, & Kemeny, 2009). Research has also found that self-reported fear during the TSST resulted in greater levels of the pro-inflammatory marker sTNF-R11 (Moons, Eisenberger, & Taylor, 2010), greater perceived stress during the TSST predicted

greater increases in IL-1β (Yamakawa et al., 2009), and increases in anxiety and anger during a public speaking task similar to the TSST resulted in increases in circulating IL-6 (Carroll et al., 2011). Furthermore, studies that have examined moderators of inflammatory responses to acute laboratory stressors have found effects for early life stress (Carpenter et al., 2010), trait loneliness (Jaremka et al., 2013), and depression status (Miller, Rohleder, Stetler, & Kirschbaum, 2005), such that history of early stress, greater loneliness, and current depression are all associated with greater stress-induced production of inflammatory biomarkers. Difficulty maintaining a positive cognitive-affective state during the TSST was similarly associated with greater circulating IL-1β, which in turn predicted increasing depressive symptoms over the following year and mediated the link between cognitive-affective response to the TSST and subsequent depression (Aschbacher et al., 2012). Notably, emotion regulation abilities needed to maintain a positive cognitive-affective state are determined in part by executive control processes, suggesting that these may play an important role in the degree of biological reactivity to stress. Finally, Giletta and colleagues (2018) found that adolescents with a history of peer victimization and with greater levels of hopelessness evinced greater increases in IL-6, IL-1β, and TNF-α following the TSST, highlighting the role of negative cognitive content in determining cytokine reactivity to stress. In sum, feeling evaluated during the TSST, greater fear or negative affect during the TSST, trait loneliness, early life stress, depression, difficulty maintaining a positive cognitive-affective state, and greater hopelessness combined with a history of victimization all predict a greater pro-inflammatory response to the TSST. All of these moderators may be driven by underlying cognitive vulnerability (see Dobson & Dozois, 2008). However schemas, core beliefs, and dysfunctional attitudes have not been examined in relation with inflammation, highlighting a key gap in the field.

All humans have adapted to be sensitive to detecting social threats, and the experience of social stress appears to 'piggyback' on the neural pathways involved in the experience of pain (Kross, Berman, Mischel, Smith, & Wager, 2011). Slavich, Way, Eisenberger, & Taylor (2010) found that salivary cytokine concentrations in response to the TSST were associated with neural responses to ostracism elicited by a computer game (Cyberball) as assessed using fMRI. More specifically, greater activity in the bilateral anterior insula and dACC was related to greater sTNF-RII responses, suggesting that individuals who are more neurologically sensitive to rejection also have greater inflammatory responses to social stress. Moreover, these brain regions are known to be engaged during experiences of physical pain, suggesting that rejection is experienced as 'social pain.' An inflammatory challenge study that involved administering randomly assigned participants with a bacterial endotoxin found that increases in IL-6 resulting from injection of the endotoxin were associated with greater activity in the anterior insula and dACC when playing Cyberball, and brain activity in these regions mediated the relation of increases in IL-6 with endotoxin-induced depressive mood (Eisenberger, Inagaki, Rameson, Mashal, & Irwin, 2009). This study suggests that inflammatory activity leads to a greater neural social pain response. Together, the findings of these two studies suggest a bidirectional, self-promoting link between inflammation and pain-related brain regions, such that individuals with greater baseline inflammation may be more sensitive to social threats, and this sensitivity may result in greater inflammatory reactivity during social stress. Slavich and Irwin (2014) refer to this process as neuro-inflammatory sensitization.

Whereas the brain communicates to the immune system via the SNS and HPA axis, research has also found that cytokines communicate with the brain via cellular, molecular, and neural mechanisms (see Slavich & Irwin, 2014). For example, cytokines can pass through

permeable or incomplete regions of the blood–brain barrier, and can stimulate primary afferent nerve fibers in the vagus nerve (see Figure 1), which in turn relays information to brain systems that regulate mood, motor activity, motivation, sensitivity to social threat, and arousal and lead to neurochemical cascades, including release of norepinephrine, dopamine, and serotonin (Anisman & Merali, 2002; Camacho-Arroyo, López-Griego, & Morales-Montor, 2009). Inflammatory challenge studies using rodent models have found that these communication pathways with the central nervous system allow cytokines to induce cognitive, emotional, and behavioural alterations that are collectively referred to as sickness behaviours (Hart, 1988), and that include several hallmark somatic and vegetative symptoms of depression (sad mood, anhedonia, fatigue, psychomotor retardation, altered appetite and sleep, impaired cognition, and social-behavioural withdrawal; Anisman & Mathieson, 2005; De La Garza, 2005; Pecchi, Dallaporta, Jean, Thirion, & Troadec, 2009).

Given that stress upregulates cytokines, and cytokines signal the brain to induce a depressive state, it is unsurprising that converging research indicates that inflammation is associated with the pathogenesis of depression. Not only does depression frequently co-occur with numerous inflammatory diseases (Barton, 2008; Calder, 2006), but it is also associated with higher circulating levels of IL-1, IL-6, TNF-α, CRP (Dowlati et al., 2010; Hiles, Baker, de Malmanche, & Attia, 2012; Howren, Lamkin, & Suls, 2009; Kuo et al., 2005; Zorrilla et al., 2001), and reduced IL-10, an anti-inflammatory cytokine (Dhabhar et al., 2009). Longitudinal studies have found that increases in IL-6 and CRP prospectively predict depressive symptoms (Gimeno et al., 2009; van den Biggelaar et al., 2007), and depressive symptoms predict inflammation (Stewart, Rand, Muldoon, & Kamarck, 2009). Some evidence exists suggesting that antidepressant medications reduce concentrations of IL-1β, IL-2, and IL-6 (e.g., Hernández

et al., 2008), and conversely, cytokines reduce levels of serotonin by decreasing availability of the serotonin precursor tryptophan (e.g., Schwarcz, Bruno, Muchowski, & Wu, 2012). Depression is also associated with decreases in antiviral immunity (Irwin et al., 2013), consistent with persistent activation of the CTRA. Moreover, research examining depressogenic effects of typhoid vaccination and immunotherapy (e.g., IFN-α for hepatitis C or cancer) indicate that these naturalistic inflammatory challenges elicit depressive symptoms in humans, and there is evidence that the effects are mediated by increases in cytokines such as IL-6 and TNF-α (e.g., Brydon et al., 2008; Raison & Miller, 2011). Administration of bacterial endotoxin similarly causes depressive symptoms, including feelings of social disconnection (Eisenberger, Inagaki, Mashal, & Irwin, 2010), which are associated with changes in IL-6 and TNF-α (Hannestad, DellaGioia, Ortiz, Pittman, & Bhagwagar, 2011). Moreover, immune challenges are associated with activation in brain regions implicated in modulating mood, motivation, motor control, and reward processing, and that are associated with depression (see Slavich & Irwin, 2014; Slavich & Sacher, 2019). Other evidence for the role inflammatory processes play in causing depression comes from double-blind, placebo controlled studies demonstrating that anti-inflammatory agents are effective in reducing depressive symptoms (Müller et al., 2006; Raison et al., 2013; Tyring et al., 2006). Altogether, these disparate lines of research provide strong evidence for the important role immune functioning plays in depression.

Slavich and Irwin's (2014; Slavich & Sacher, 2019) Social Signal Transduction Theory of Depression explains how perceptions of social threat are transduced to inflammation and ultimately, depression. Social threat is represented in brain regions including the anterior insula and dACC as painful experiences, and project to the lower level brain regions of the hypothalamus and brainstem, which modulate HPA axis and SNS activity. SNS activity in turn

leads to cytokine production and resulting affective, cognitive, and behavioural changes, a process that is adaptive when occurring intermittently, but when activated too frequently, can become self-promoting as a result of neuro-inflammatory sensitization. Slavich and Irwin (2014) posit that neuro-inflammatory sensitization leads not only to heightened inflammation following stress, but also exaggerated perceptions of social threat. When this neuro-inflammatory response to threat becomes entrenched, it increases risk for depression and likely other physical diseases associated with inflammation. One component of this theory that has received relatively sparse attention is how individual differences in cognition may influence perceptions and experiences of social stressors (which include not only true threats, but also those that are symbolic, anticipated, or imagined), and therefore, the strength of the immune response.

The Current Study

A growing body of research indicates that inflammation plays an important role in the pathogenesis of depression; however, very few studies have examined cognition (content or process) as a predictor of stress-related cytokine upregulation. Given that cognitive control determines individuals' moment-to-moment experience of the world in terms of what they are thinking, and not thinking, about, as well as their ability to respond flexibly, it is a particularly intriguing construct to investigate in the context of stress and depression. The experience of negative affect following stress activates negative schemas, thereby allowing mood-congruent cognitions to enter working memory, such that individuals with greater negative cognitive content that is highly interconnected are those likely to have the most content active and accessible to working memory. This may overload cognitive control resources, particularly for those with greater cognitive vulnerability, such that the interaction of cognitive content and poor cognitive control likely results in greater resting-state cytokines (likely indicative of a

persistently activated CTRA or neuro-inflammatory sensitization) and immune reactivity to a social stressor. Cognitive control may also interact with a tendency to ruminate, as once the process of rumination begins, it may introduce greater cognitive content into working memory, further interfering with executive functioning and self-regulation. The current study is the first to examine predictors of stress-induced cognitive control deficits. It is also the first to examine how cognitive control and cognitive vulnerability influence baseline inflammation and acute inflammatory responses to social stress. It is among the first to investigate whether immunological stress reactivity predicts depression over time using a longitudinal design.

The current study examines how various diatheses (cognitive content, structure, and control) predict cognitive (stress-induced cognitive control impairment) and immunological responses to a laboratory social-evaluative stressor. The study included participants with a range of depressive symptoms by recruiting individuals with current and remitted depression as well as never-depressed controls. Participants completed measures of cognitive content and structure (dysfunctional attitudes, core beliefs, schemas) and a battery of cognitive control measures using affective stimuli to assess inhibitory (Emotional Stroop), updating (Emotional N-back task), and shifting (Affective Flexibility task) impairments. The Emotional Stroop task was used in the current study given the large body of research demonstrating its effectiveness in capturing depression-related inhibitory biases (Epp et al., 2012). The N-back was selected as it is the only task to assess continuous monitoring, addition, *and* removal of contents of working memory (Schoofs et al., 2008; Quinn & Joormann, 2015a, 2015b). Further, the Affective Flexibility Task was used to assess shifting given that it measures continuous switching across discrete tasks rather than shifts in focus, and is thereby most consistent with conceptualizations of shifting (Miyake et al., 2000). Participants also provided a saliva sample after a period of relaxation.

Following exposure to the TSST, participants completed the N-back task a second time to assess stress-induced cognitive control biases. Updating was selected as the facet of cognitive control to examine stress-induced changes given past research documenting meaningful post-stress changes using the N-back (e.g., Schoofs et al., 2008, Quinn & Joormann, 2015a, 2015b). Participants provided a second post-stressor saliva sample, and also returned to the lab two weeks and six-months later to complete a measure of depressive symptoms, as well as other measures as part of the larger study.

Mounting evidence supports the validity of salivary cytokines in psychoneuroimmunology research. Research has found that salivary cytokines are responsive to acute emotional and physiological stress, and that they increase on a faster time scale and are more detectable than cytokines in serum and plasma (see Slavish, Graham-Engeland, Smyth, & Engeland, 2015). Like cytokines in serum, salivary cytokines can influence neural activity via afferent nerves (Dantzer, O'Connor, Freund, Johnson, & Kelley, 2008), and are associated with activation of the anterior cingulate cortex, which is involved in emotional processing (O'Connor, Irwin, & Wellisch, 2009). Importantly, salivary cytokines are associated with psychopathology (Keller, El-Sheikh, Vaughn, & Granger 2010). The cytokines that were assessed were IL-8, IL-6, IL-1β, and TNF-α. These are all pro-inflammatory cytokines that are involved in the acute phase of innate immunity and that have been found to increase in saliva following stress. These cytokines are mediators of systemic inflammation and are associated with the pathophysiology of several health conditions as well as depression (Mikova, Yakimova, Bosmans, Kenis, & Maes, 2001; Slavich & Irwin, 2014; Slavich & Sacher, 2019).

A number of diverse and novel hypotheses were tested:

1. Deficits in cognitive control for affective stimuli will be evident in both the depressed and remitted depressed groups compared to the control group.
2. Deficits in cognitive control will be associated with a greater tendency to ruminate.
3. The TSST will result in decreased updating abilities across all groups.
4. Depressotypic cognitive content (dysfunctional attitudes and core beliefs) and structure (self-schema organization) will predict stress-induced changes in updating abilities, as negative content would be activated by the lab stressor, thereby causing greater impairment in cognitive control as tightly interconnected negative representations are activated. This is expected to result in more information to inhibit and control as compared to those without tightly interconnected negative schemas.
5. The TSST will result in increases in cytokines.
6. Greater baseline and post-stressor cytokines are anticipated in individuals with depression and remitted depression.
7. Deficits in inhibition, shifting, and updating, as well as stress-induced deficits in updating (all of which are anticipated in individuals with current or past depression), will predict greater baseline inflammation (which may be indicative of neuro-inflammatory sensitivity), as well as greater cytokine reactivity, in terms of higher pro-inflammatory cytokine concentrations both pre- and post-stressor. Given that difficulty shifting away from positive affective information has been associated with greater adaptive emotion regulation ability and decreased rumination, deficits in this facet of shifting are expected to be associated with *lower* inflammation. Responding to social threat with rapid updating or shifting toward goal-relevant information, and with inhibition of distracting, negative thoughts or information as the event unfolds, allows the individual to select

adaptive behaviours rather than getting "stuck" on thoughts and feelings about the interaction, and may result in less cytokine reactivity. Any differences in findings across types of cognitive control for predicting baseline inflammation or the immune response to stress will be examined in an exploratory manner. See Figure 1 for a visual model of Hypotheses 7-10.

8. Depressotypic cognitive content and structure and rumination will predict baseline inflammation and inflammatory reactivity, as individuals with negative schemas are likely to make negative automatic appraisals about the threatening nature of stressors, thereby triggering an immune response.
9. Cognitive content (dysfunctional attitudes, core beliefs) and rumination will interact with cognitive control deficits to predict greater baseline inflammation and stress reactivity as indicated by increased inflammatory biomarkers. Individuals with greater negative cognitive content *and* poorer cognitive control are expected to show the greatest cytokines.
10. Cognitive control and cognitive organization will interact to predict baseline and stress-induced inflammation. Specifically, individuals with more tightly interconnected negative cognitive content *and* poorer cognitive control will evince the greatest cytokines.
11. Finally, inflammatory indices of stress reactivity are expected to predict greater depressive symptoms at follow-up.

Methods

Participants

A sample of 177 individuals were recruited through public advertisements. These included posters (see Appendix A) distributed around campus and in the community, including

physician's offices, health clinics, private therapy practices, hospitals, bus stops, grocery stores, community centres, gyms, places of worship, libraries, and coffee shops. Participants were also recruited from posts on social media (i.e., Facebook) and referrals from local mental health clinicians. The sample was comprised of three groups: individuals with current depression, individuals with remitted depression, and healthy, non-clinical controls. To be eligible to participate, individuals were required to meet *Diagnostic and Statistical Manual of Mental Disorders – 5* (DSM-5; American Psychiatric Association, 2013) criteria for current or remitted MDD or Persistent Depressive Disorder (PDD), or to have never met criteria for any depressive diagnosis, including premenstrual dysphoric disorder. Additional inclusion criteria were that participants were 18 years or older, fluent in English, and had a smartphone with a data plan or regular access to internet in order to complete measures as part of the larger study. Exclusionary criteria involved having any current or remitted psychosis, bipolar disorder, or cyclothymic disorder, or having cardinal symptoms of MDD (i.e., clinically significant low mood or anhedonia for two weeks) without ever meeting full criteria for MDD or PDD. Exclusionary criteria also included having a medical condition or regularly taking medications known to influence inflammation locally in the mouth or systemically. Use of antidepressant medication was not an exclusionary criterion. Individuals were excluded if they reported bleeding gums, gum disease (i.e., periodontal disease, gingivitis), a chronic inflammatory disease (e.g., arthritis, thyroid problems, chronic active hepatitis, chronic peptic ulcer, asthma, tuberculosis, ulcerative colitis, Crohn's disease, chronic sinusitis), cancer or other neoplastic disease, a sleep disorder diagnosis (i.e., insomnia, hypersomnolence disorder, sleep apnea, narcolepsy), were pregnant, trying to become pregnant, or breastfeeding, or had undergone an organ transplant. Participants were also excluded if they reported undergoing chemotherapy or radiation therapy, or taking

immunosuppressant or immunomodulator medication (e.g., tacrolimus, interferon), or any Non-Steroidal Anti-Inflammatory drugs (NSAIDs) on a daily basis (e.g., naproxen, aspirin, ibuprofen).

Individuals interested in participating were asked to complete an online form for initial eligibility screening (see Appendix B). This form included questions about participants' age and medical exclusionary criteria. A total of 1,164 individuals completed the online form, and 704 were eligible based on initial screening. These individuals were then contacted by telephone for further screening. Telephone screening included a detailed review of all medical and health-related exclusionary criteria with individuals in order to further screen for any conditions or medications they may not have accurately endorsed on the online form. In cases where it was unclear whether a participant met exclusion criteria, the principal investigator (KR) consulted with a collaborating researcher who is a professor of biochemistry at the Robarts Research Institute in London, Ontario.

Participants were also administered modules of the *Structured Clinical Interview for DSM-5* (SCID-5; First, Williams, Karg, & Spitzer, 2015) to establish diagnoses and diagnostic eligibility for the study. A total of 211 individuals were eligible after completing phone screening and invited to participate in the study. The remaining 493 individuals who passed online screening either completed telephone screening but were not eligible for the study, were not reached after multiple attempts, or indicated they were no longer interested or available to participate. The study was completed in one online battery of measures (Phase 1) and three laboratory sessions (Phases 2-4). Of the 211 participants who passed phone screening, 177 completed the baseline battery of measures and attended the first laboratory session (Phases 1 and 2). A total of 172 participants returned to the lab two weeks after the first laboratory visit

(Phase 3), and 144 participants returned 6 months after the first visit (Phase 4) to complete the Beck Depression and Inventory (BDI-II; Beck, Steer, & Brown, 1996b) as well as other measures as part of the larger study (see Appendix C for a description of the larger study). Of the full sample of 177 individuals who completed Phases 1 and 2, 11 had no current or remitted depressive diagnoses, but did have other current or remitted mental disorder diagnoses. These individuals were excluded from the analyses as they did not represent healthy, non-clinical controls. This resulted in a final sample of 166 participants (119 women, 47 men). See Figure 2 for a flow diagram of participants through each phase of the study. An a priori power analysis indicated that with $\alpha = .05$, and power = 0.80, this sample size was adequate to detect moderate effects ($d = 0.5$), which were anticipated across hypotheses based on effect sizes reported in past research (e.g., Epp et al., 2012; Giletta et al., 2017; Shields et al., 2016; Quinn & Joormann, 2015a, 2015b).

The final sample consisted of 40 currently depressed, 69 remitted depressed, and 57 non-clinical controls. Among the currently depressed individuals, 34 had a diagnosis of current MDD (among these, 11 also had current PDD and 9 had remitted PDD) and 6 had current PDD (all 6 also had remitted MDD). All 69 individuals in the remitted depressed group had remitted MDD, and 12 participants in the remitted depressed group also had remitted PDD. Participants were 18-65 years old, with a mean age of 26.09 ($SD = 8.96$).

Measures

Baseline measures. ***Structured Clinical Interview for DSM-5 (SCID-5; First, Williams, Karg, & Spitzer, 2015).*** Individuals were administered the Mood, Anxiety, Obsessive-Compulsive and Related Disorders, Trauma- and Stressor-Related Disorders, and Psychotic Screening modules of the SCID-5 to determine diagnostic status and eligibility, as well as to

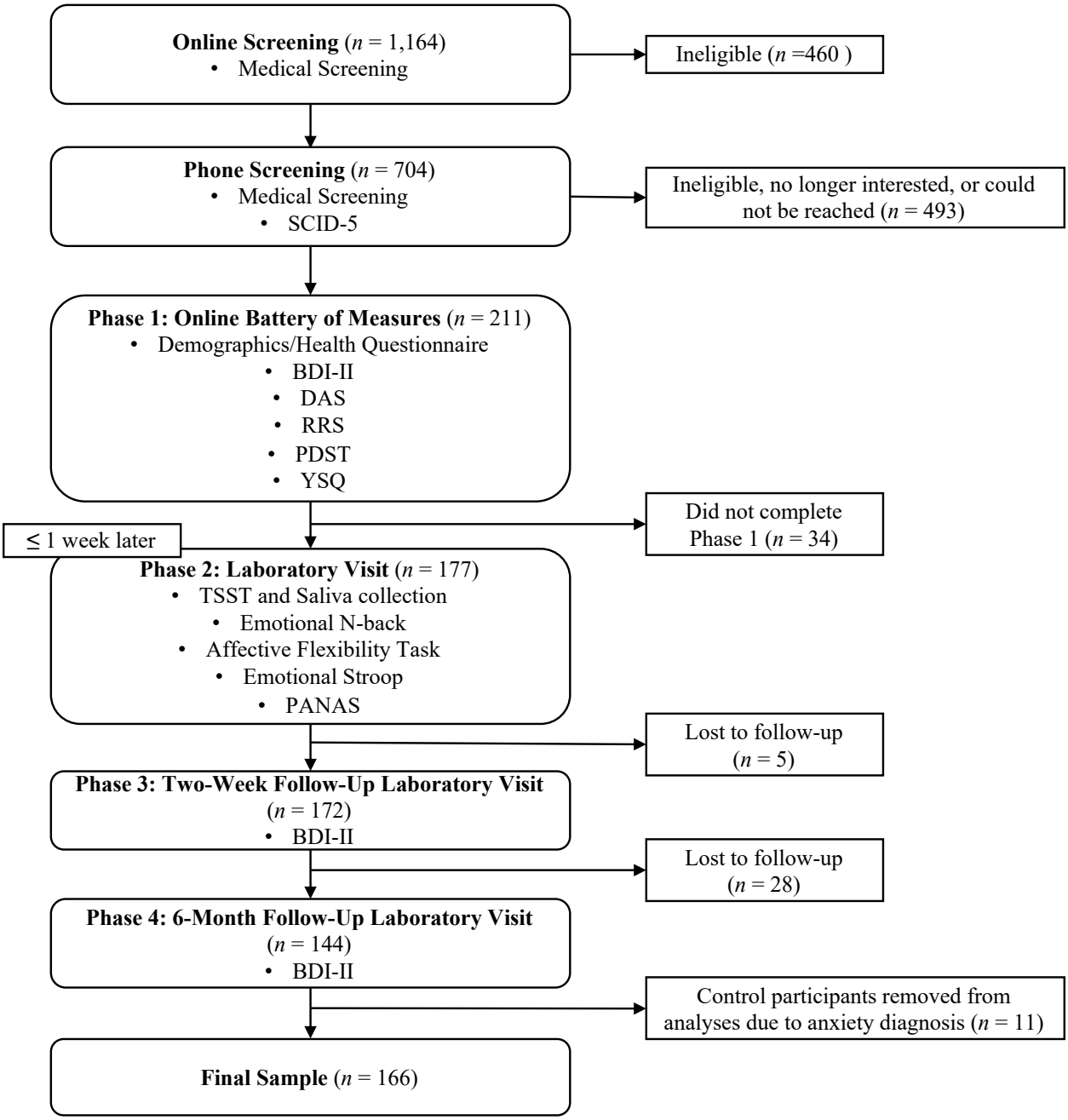

Figure 2. Flow diagram of participants through each phase of the study. SCID-5 = Structured Clinical Interview for DSM-5. BDI-II = Beck Depression Inventory-II. DAS = Dysfunctional Attitude Scale. RRS = Ruminative Response Styles Questionnaire. PDST = Psychological Distance Scaling Task. YSQ = Young Schema Questionnaire. TSST = Trier Social Stress Test. PANAS = Positive and Negative Affect Scale.

gather relevant clinical information such as number of past depressive episodes, age of depression onset, and comorbid diagnoses. The SCID-5 is a semi-structured interview that is widely considered to be the gold standard for diagnostic assessment, and its reliability and validity in detecting psychopathology has been well-documented (e.g., Lobbestael, Leurgans, & Arntz, 2011; Williams et al., 1992). Inter-rater reliability (Kappa coefficients) range from .61 to .80 for MDD diagnoses, .59 to .83 for social anxiety disorder, .44 to .75 for generalized anxiety disorder, .65 to .67 for panic disorder, .60 to .65 for obsessive compulsive disorder, and .77 to .88 for posttraumatic stress disorder (Lobbestael et al., 2011; Zanarini et al., 2000). Studies examining 'best-estimate diagnoses' (Spitzer, 1983) performed by experts and based on longitudinal assessment of all data available (e.g., family informants, medical records, observations) have found superior validity of the SCID compared to standard clinical diagnoses made at intake (Basco et al., 2000; Fennig, Craig, Tanenberg-Karant, & Bromet, 1994; Fennig, Naisberg-Fennig, Craig, Tanenberg-Karant, & Bromet, 1996; Kranzler, Kadden, Babor, Tennen, & Rounsaville, 1996; Kranzler et al. 1995).

SCID-5 interviews were conducted by the principal investigator and PhD-level clinical psychology students. Training consisted of reviewing the SCID-5 Users Guide, viewing the training videos, and completing a SCID-5 interview while being observed by an experienced SCID-5 interviewer. Supervision on the SCID-5 was provided by a licensed clinical psychologist.

Beck Depression Inventory-II (BDI-II; Beck, Steer, & Brown, 1996). The BDI-II is a 21-item instrument that assesses the presence and severity of unipolar depressive symptoms in the past two weeks. Individuals rate each item on a 4-point scale from 0 (lack of symptomatology) to 3 (high symptomatology), with summary scores ranging from 0 to 63. The

BDI-II has been widely used with adult and clinical samples and is recognized for its strong psychometric properties. Past research reports internal reliability (Cronbach's alpha) estimates of .91-.92 (e.g., Beck et al., 1996; Dozois, Dobson, & Ahnberg, 1998) and good convergent and discriminant validity, as indicated by high associations with other measures of depression (i.e., the Hamilton Rating Scale for Depression, the depression subscale of the SCL-90-R) and lower associations with measures of anxiety (i.e., the Hamilton Rating Scale for Anxiety, anxiety subscale of the SCL-90-R; Beck et al., 1996; Steer, Ball, Ranieri, & Beck, 1996). The internal consistency (Cronbach's alpha) of the BDI-II in the current sample was $\alpha = .95$ at baseline, .95 at Phase 3, and .96 at Phase 4.

Dysfunctional Attitude Scale - Form A (DAS-A; Weissman, 1979; Weissman & Beck, 1978). This 40-item self-report questionnaire measures the presence and intensity of dysfunctional attitudes. The DAS-A asks participants to rate their agreement on a 7-point Likert scale (1 = *fully disagree*; 7 = *fully agree*) with statements concerning approval from others (e.g., "What other people think of me is very important"), prerequisites for happiness ("It is difficult to be happy unless one is good looking, intelligent, rich and creative"), and perfectionistic standards ("If I am to be a worthwhile person, I must be truly outstanding in at least one major respect"). Scores range from 40-280. The DAS-A has good psychometric properties, including high internal consistency (Cronbach's alpha = .86 - .91), split-half reliability of .90-.95 and test-retest reliability of $r = .73$ over six weeks (Oliver & Baumgart, 1985; Weissman, 1979). Past research also supports the concurrent validity of the DAS, as indicated by its association with measures of depressive severity, cognitive distortions, and negative automatic thoughts (Dobson & Shaw, 1986; Hamilton & Abramson, 1983; Hollon, Kendall, & Lumry, 1986). Coefficient alpha in the present sample was $\alpha = .94$.

The Psychological Distance Scaling Task (PDST; Dozois & Dobson, 2001). The PDST is a computer-administrated cognitive task that assesses cognitive organization (i.e., self-schema structure). Participants simultaneously rate the self-descriptiveness and valence of adjectives by placing them on a grid, such that the x-axis measures self-relevance (*very much like me* at the far right of the axis to *not at all like me* at the far left of the axis) and the y-axis measures valence (*positive* at the top of the axis, *negative* at the bottom). Each adjective appears one at a time at the center of the grid. Participants are asked to consider both axes as they place each adjective on the grid, using the computer mouse and visually presented pointer. Participants complete 4 practice trials, followed by 80 trials. The 80 adjectives consist of 20 words from each of the following categories: achievement positive (e.g., *successful, capable*); achievement negative (e.g., *incompetent, deficient*); interpersonal positive (e.g., *encouraged, comforted*); and interpersonal negative (e.g., *unwanted, rejected*). Words were presented in random order and have been matched for emotional intensity, imaginability, word length, and word frequency (Dozois 2007; Dozois & Frewen, 2006). Coordinate points for each adjective are used to calculate interstimulus distances among positive and negative self-referent adjectives. Smaller distances among adjectives are indicative of greater consolidation and interconnectedness of self-referent content, whereas large distances are indicative of less consolidation. Past research supports the psychometric properties of this task, including high convergent and discriminant validity (Dozois, 2002; Dozois & Dobson, 2001, 2003).

Young Schema Questionnaire-Short Form 3rd Edition (YSQ-S3; Young, 2005). The YSQ-SF is a 90-item self-report questionnaire that assesses 18 core beliefs: Emotional Inhibition, Emotional Deprivation, Mistrust/Abuse, Social Isolation/Alienation, Defectiveness/Shame, Abandonment/Instability, Failure, Dependence/Incompetence,

Vulnerability to Harm or Illness, Enmeshment/Undeveloped Self, Subjugation/Invalidation, Entitlement/Grandiosity, Insufficient Self-Control/Self-Discipline, Self-Sacrifice, and Unrelenting Standards/Hypercriticalness, Approval-Seeking/Recognition-Seeking, Negativity/Pessimism, and Punitiveness. Participants rate the self-descriptiveness of each statement on a 6-point scale from 1 (*completely untrue of me*) to 6 (*describes me perfectly*), with total scores ranging from 90-540. Subscale scores can also be computed for each schema. This instrument has strong psychometric properties in both clinical and nonclinical samples, including high internal consistency for the total score (Cronbach's alpha = .91) and 6-month test-retest reliability across schemas, as well as convergent validity with a measure of schema modes (Calvete, Orue, & González-Diez, 2013; Phillips, Brockman, Bailey, & Kneebone, 2019). Internal consistency (Cronbach's alpha) for the total score in the current sample was α = .97.

Ruminative Response Styles Questionnaire (RRS; Nolen-Hoeksema & Morrow, 1991). The RRS is a 22-item self-report questionnaire that assesses the tendency to respond to low mood by ruminating about its causes, consequences, and symptoms. Items are rated on a 4-point scale from 1 (*almost never*) to 4 (*almost always*), with possible summary scores ranging from 22-88, and higher scores indicating a greater tendency to ruminate. The RRS has been used extensively in community and clinical samples, and has good internal reliability (α = .89-.90) and test-retest reliability (*r* = .80 over five months and .67 over one year; Nolen-Hoeksema, 2000; Nolen-Hoeksema & Morrow, 1991; Nolen-Hoeksema, Parker, & Larson, 1994). There is evidence that the RRS has convergent validity, as it is associated with daily diary measures of rumination (Nolen-Hoeksema, Morrow, & Fredrickson, 1990), and predictive validity, as evinced by its relation with subsequent depressive symptoms and episodes (Nolen-Hoeksema,

2000; Nolen-Hoeksema, Parker, & Larson, 1994; Treynor et al., 2003). Internal consistency was $\alpha = .93$ in the present sample.

Demographic and health questionnaire. Participants completed a demographic questionnaire (see Appendix D) that queried about their age, sex, ethnicity, educational attainment, and marital status. Information was also collected on health-relevant behaviours (i.e., smoking, alcohol consumption), use of hormonal contraceptives, menstrual cycle, current medications, and whether participants were receiving therapy or have in the past. This information was collected for sample description and to assess for potential covariates.

Laboratory measures. ***Saliva collection and cytokine assays.*** Salivary cytokines are ideal for examining immunological stress reactivity because they are clinically relevant and increase on a faster time scale than do cytokines in serum or plasma. Moreover, cytokine levels tend to be higher in saliva than in blood and are therefore more detectable (Slavish et al., 2015). The cytokines IL-1β, IL-6, IL-8, and TNF-α were assessed as these are known to be responsive to emotional or social stressors.

Saliva was collected using the passive drool method and SalivaBio Collection Aids (Salimetrics, Carlsbad, CA). Participants were asked to provide 2ml of saliva at each collection. Immediately after collection, 20 microliters of protease inhibitor (Thermo Scientific Halt Protease Inhibitor Cocktail, Rockford, IL) were aliquoted into each sample, which was then vortexed. Cryovials of saliva were stored in cryostorage boxes in a -20 degree Celsius freezer. At the end of each day, samples were transported on ice to a -80 degree Celsius freezer at Robarts Research Institute for long-term storage. Following the completion of data collection, samples were shipped on dry ice to Salimetrics (Carlsbad, CA) where they were assayed using the Salimetrics multiplex salivary cytokine electrochemiluminescence assay on the Meso Scale

Discovery platform (MSD; Rockville, MD). The manufacturer reports an assay detectability range of 0.0314 – 380.000 pg/mL for TNF- α, 0.0195-589.000 pg/mL for IL-1β, 0.0491-736.000 pg/mL for IL-6, and 0.0201-574 pg/mL for IL-8. All samples were tested in duplicate for greater reliability.

The Salimetrics multiplex assay is specifically optimized and validated for use with saliva, which represents a significant advantage over multiplex assays or enzyme-linked immunosorbent assays (ELISAs) developed and validated for use with serum or plasma. Given limited options available for multiplex assays optimized for saliva, the majority of past research on salivary cytokines has used assays designed for serum or plasma, which can lead to problems with matrix interference (i.e., the effect that other substances in the sample have on the assay's ability to detect the target protein) and missing or invalid data. Cytokine values were logarithmic transformed to correct for skewness before analysis. Only one saliva sample (collected post-stressor) had undetectable levels of cytokines.

Emotional N-back Task (Chatham et al., 2011). This task assesses updating abilities for affective stimuli. In each trial, participants are shown an emotionally-valenced word on a screen for 500ms followed by a blank screen shown for 2,500ms. A sample of trials is presented in Figure 3. During each trial, participants are asked to indicate as quickly and accurately as possible whether or not each word matches (i.e., target trial) or does not match (i.e., nontarget trial) the word presented two trials earlier by pressing a corresponding computer key labelled "yes" or "no." A total of 120 trials are completed, and the total number of errors is indicative of updating ability (Kopf, Dresler, Reicherts, Herrmann, & Reif, 2013). Words used in this task were selected from the Affective Norms of English Words list (Bradley & Lang, 1999). Negative and positive words are matched on arousal ratings and word length, and significantly differ in

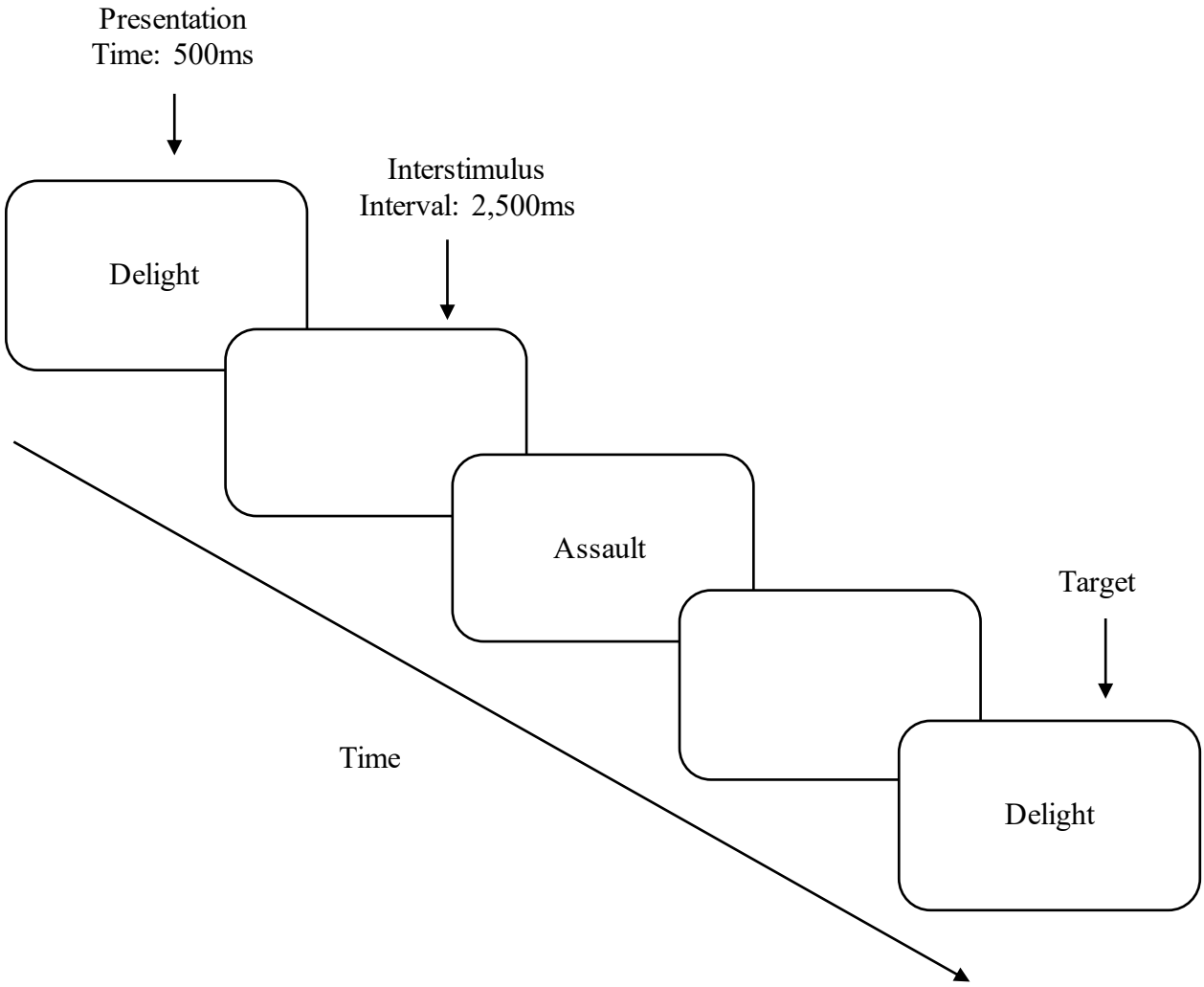

Figure 3. Example series of trials in the N-Back task. Words are presented one at a time, and participants are asked to identify whether or not each word is a target (i.e., matches the word presented two trials previously). The third trial is a target in this example. (Figure adapted from Quinn & Joormann, 2015a, 2015b).

valence ratings (Quinn & Joormann, 2015a, 2015b). This task has good construct validity and reliability (Jaeggi et al., 2010; Miyake & Friedman, 2012).

Affective Flexibility Task (Genet, Malooly, & Siemer, 2013). This task assesses the ability to shift between processing affective and neutral components of emotionally evocative stimuli. Participants are asked to sort a series of 160 affective pictures by valence or by the number of people in the picture. Pictures were drawn from the International Affective Picture Set (IAPS; Lang, Bradley, & Cuthbert, 2008). Genet et al. (2013) selected 40 pictures from each of four categories based on reliability of categorization and valence ratings on a 9-point scale (*1 = negative, 9 = positive*) according to pilot data. Categories include negative pictures with one or no people (mean valence = 2.79), negative pictures with two or more people (mean valence = 2.65), positive pictures with one or no people (mean valence = 7.38), and positive pictures with two or more people (mean valence = 7.39). All negative pictures had a mean valence between 2 and 4, and positive pictures had a mean valence between 6 and 8.

During task administration, pictures are presented one at a time surrounded by a coloured frame. In each trial, participants are asked to sort the picture according to valence or number of people depicted. These correspond to affective and nonaffective categorization rules, respectively. Cues for how to sort each picture are provided on the left and right side of the frame ("+" and "-" for positive and negative, "≤1" and "≥2" for one or no people and two or more people), and participants indicate their response by pressing one of two adjacent computer keys. Participants are instructed to place their index and middle fingers of their right hand on the two computer keys and to respond as quickly and accurately as possible. The cues for how to sort the stimuli were shown on a white or gray frame, and each frame colour corresponded to one of the sorting rules. Participants were randomized into one of eight versions of the task which

counterbalances which frame colour corresponds to which cue, as well as the mapping of the cue categories onto the two response keys, across participants. In each trial, a fixation cross is shown in the center of the screen for 250ms before the stimulus is presented. Stimuli remain on the screen until the participant makes a response, with no time limit imposed. The screen is then blank for 250ms until the next trial begins (see Figure 4 for a sample trial sequence). Participants completed two 24-trial practice blocks with the experimenter present to answer any questions. One practice trial asked the participants to sort the image based on the affective rule, and the other asked them to sort based on the nonaffective rule. This was followed by two blocks of 160 trials each. Cue and picture category change from trial to trial based on a pseudorandom sequence, with an equal number of switch (from one categorization rule to the other) and no-switch trials.

The cost of switching is calculated as the difference in reaction times between switch and repetition trials. Four outcome variables are computed, including negative and positive nonaffective switch costs, and negative and positive affective switch costs. Nonaffective switch costs represent the cost associated with switching from the affective and toward the nonaffective rule when the image is negative (Negative Nonaffective Switch Cost) or positive (Positive Nonaffective Switch Cost). Specifically, Negative Nonaffective Switch Costs are computed by subtracting reaction times on trials in which the nonaffective rule was repeated and the picture is negative from reaction times on trials in which the cue switches to the nonaffective rule and the picture is negative. Positive Nonaffective Switch Costs are computed the same way for trials in which the picture is positive.

Negative Affective Switch Costs and Positive Affective Switch Costs were calculated as the costs of switching from the nonaffective to the affective rule when the picture was negative

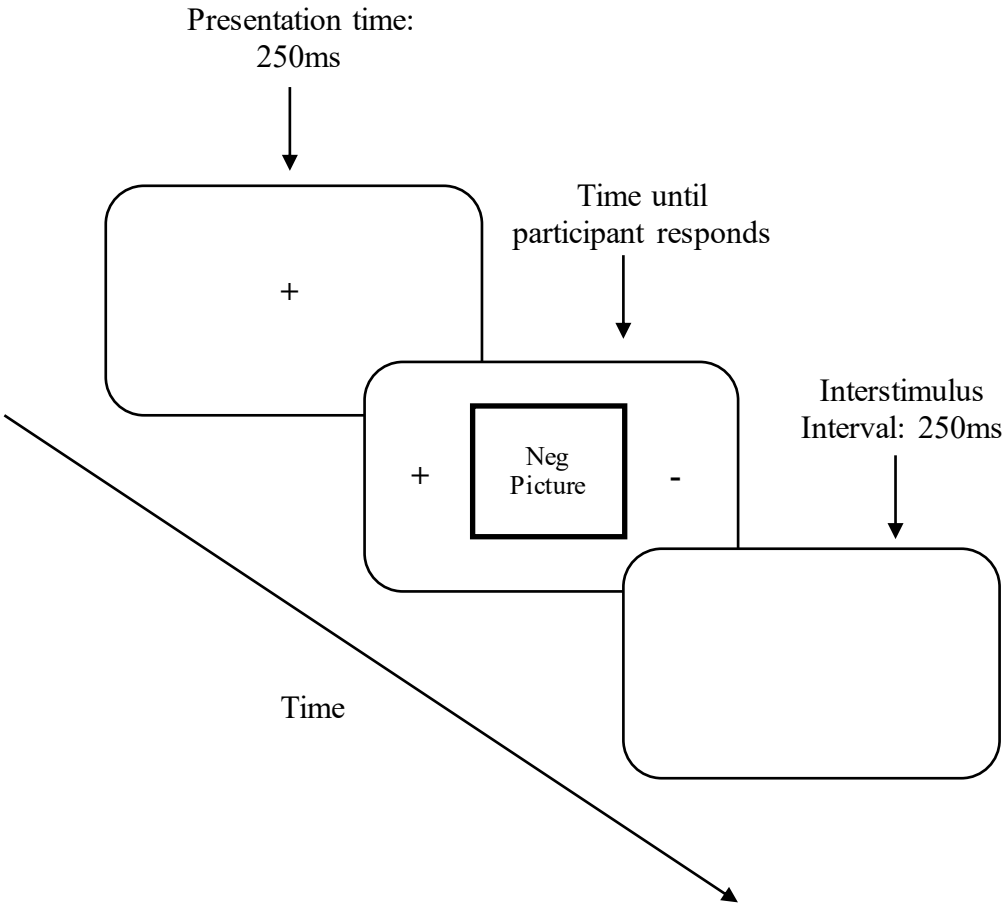

Figure 4. Example series of trials in the Affective Flexibility Task. Pictures are presented one at a time, and participants are asked to categorize them according to an affective (valence) or nonaffective (number of people depicted) rule.

or positive, respectively. In particular, Negative Affective Switch Costs were computed by subtracting reaction times on trials in which the affective rule was repeated and the picture was negative from reaction times on trials in which the cue switches to the affective rule and the image is negative. Positive Affective Switch Costs were computed the same way with trials in which pictures were positive. For all four outcome variables, lower switch costs are associated with greater switching ability. Examples of negative nonaffective, positive nonaffective, negative affective, and positive affective switch trials and positive and negative repetition trials are presented in Figure 5.

Emotional Stroop (see Mitterschiffthaler et al., 2008). This task assesses the ability to inhibit neutral and affective information irrelevant to task goals. A lowercase word in coloured font is presented in the center of the screen with a black background. Participants are asked to indicate the colour of the font (red, green, blue, yellow) as quickly and accurately as possible by pressing a corresponding computer key, with response options mapped onto the first two fingers of each hand. A fixation cross is shown in the center of the screen for 500ms before the stimulus is presented. The stimulus is shown until the participant responds, and then a blank screen is shown for 500ms until the next trial begins (see Figure 6 for a sample trial sequence). Mitterschiffthaler and colleagues (2008) selected sad and neutral words from two lists of emotional and neutral words (Bradley & Lang, 1999; John, 1988), and words were matched for frequency, pronounceability, and word length. Neutral and sad words differed significantly in valence.

Participants first complete a 40-trial training session in order to learn the mapping of each colour with its corresponding computer key. Stimuli for the training trials were ‘XXXXXX,’ and participants were instructed to indicate the colour of the font by pressing the correct computer

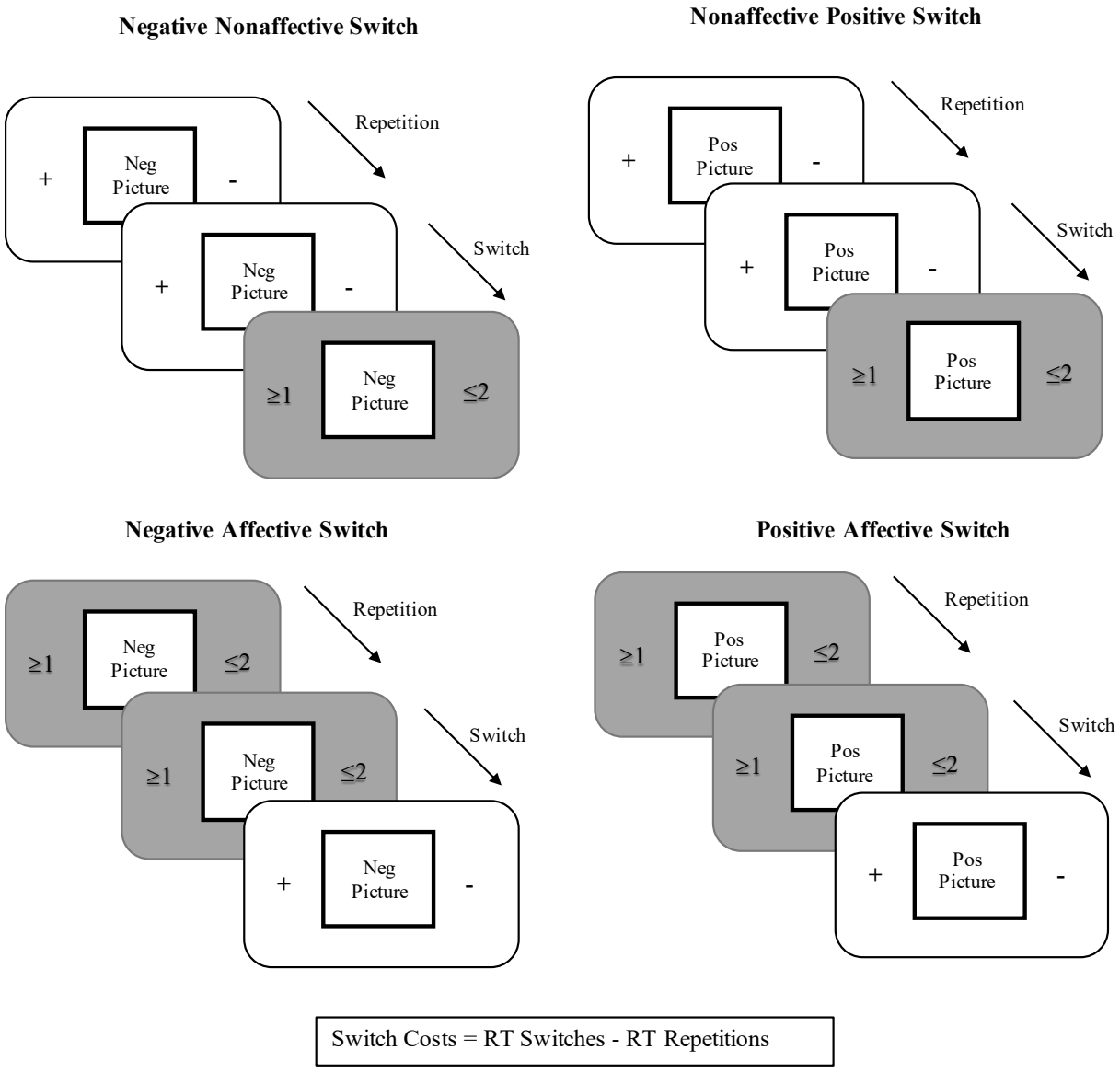

Figure 5. Examples of trial types in the Affective Flexibility Task. Note that for a negative affective or nonaffective switch, the preceding trial did not need to also be a negative image. The same is true for positive affective and nonaffective switches. Figure is adapted from Genet, Malooly, & Siemer, 2013.

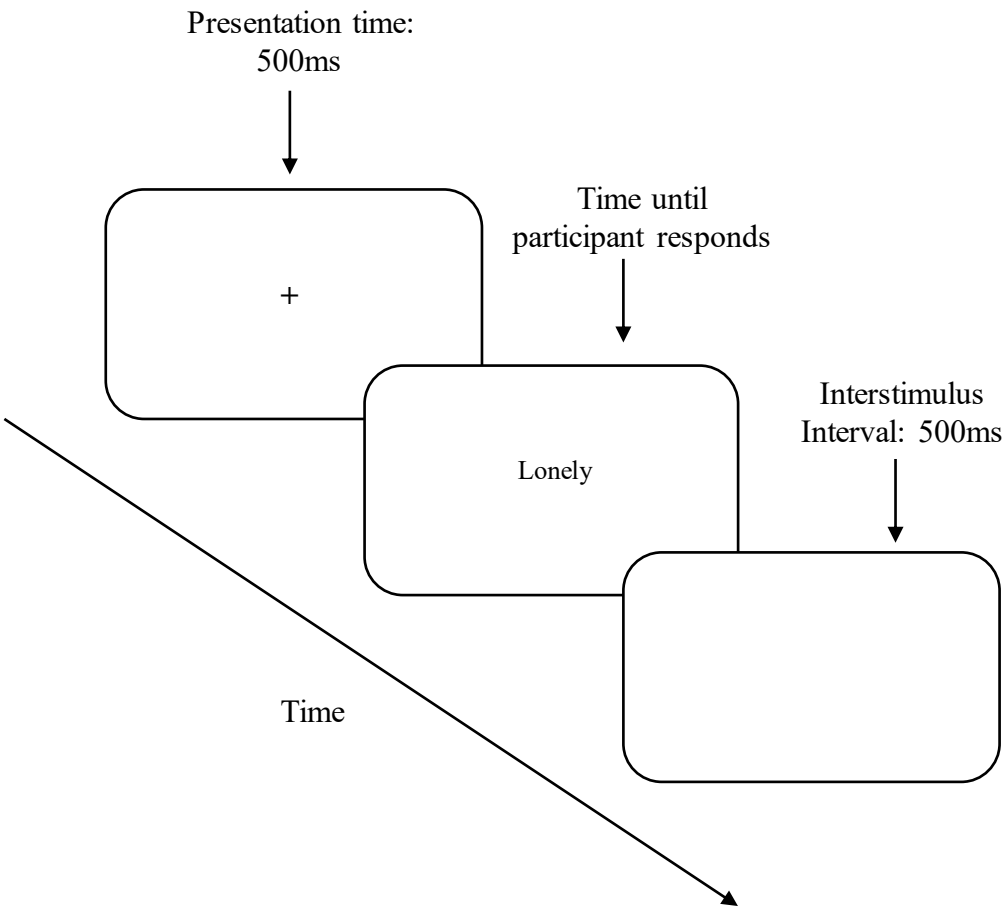

Figure 6. Example series of trials in the Emotional Stroop Task. Words are presented one at a time, and participants are asked to indicate the colour of the font the word is presented in.

key. Participants were provided with accuracy feedback after each trial. Participants had a 30 second break after completing the training session. They then completed a 40-trial block of neutral words, followed by another 30 second break. Finally, participants completed a 40-trial block of negative emotional words. Font colours were shown in a pseudo-random order, such that the same colour was never repeated over two consecutive trials. Each word was only shown once, and was presented in a random order within its block. Longer latencies for neutral or sad words are indicative of poor inhibition.

Trier Social Stress Test (TSST; Kirschbaum et al., 1993). The TSST is a commonly used laboratory social-evaluative stress induction. Participants are brought into an interview room with two individuals (who are research assistants) seated across from them at table. Participants are informed that these are members of a selection committee from the human resources department at the local hospital. A selection committee member informs participants that they are to deliver a 5-minute speech that serves as a mock job interview, and that they have ten minutes to prepare for it. Participants are told that the speech will be videotaped for video analysis of their performance, and informed that they are not permitted to use notes or cue cards during the speech. Participants are then led to another room and given 10 minutes to prepare. Afterward, participants are led back to the interview room to deliver their speech. Participants who complete their speech in less than five minutes are encouraged to continue. Those who still have difficulty filling the time are asked a series of interview questions. After the 5-minute speech portion of the TSST, the participant is asked to perform mental arithmetic in front of the committee members by subtracting the number 13 from 2,083 as quickly as possible and without making mistakes. If the participant makes an error, a research committee member asks the participant to restart the task. Participants who do not make errors are also periodically asked to

restart the task. The mental arithmetic portion of the task is five minutes long. Research assistants who are acting as selection committee members are trained to maintain a neutral expression throughout the TSST and to refrain from providing minimal encouragers to participants (e.g., nodding, smiling). Past research has found that the TSST reliably elicits a subjective and physiological stress response (e.g., Kirchbaum et al., 1993; Vors, Marqueste, & Mascret, 2018).

Positive and Negative Affect Scale (PANAS; Watson, Clark, & Tellegen, 1988). This 20-item self-report measure assesses negative and positive affect states. Participants indicate the extent to which they are currently experiencing emotional states (e.g., hostile, excited) ranging from 1 (*very slightly or not at all*) to 5 (*extremely*), with possible summary scores ranging from 10-50. The PANAS has good reliability (Cronbach's alpha = .85-.89) and construct validity, as indicated by associations with measures of depression and anxiety (Crawford & Henry, 2004). Cronbach's alpha in the present sample was $\alpha = .88$ for positive affect and $\alpha = .86$ for negative affect at pre-stress, and $\alpha = .91$ for positive affect and $\alpha = .92$ for negative affect at post-stress.

Procedure

The study included initial online eligibility screening, followed by a more detailed telephone screen. The study was comprised of an online battery of measures (Phase 1), followed by three laboratory sessions (Phases 2-4) that occurred over a 6-month time frame. Participants were presented with a letter of information at each phase of the study (see Appendix E) and provided written consent to participate at each phase (see Appendix F). At the end of each phase, participants were provided with a debriefing form (see Appendix G), which included local and online mental health resources. At the end of Phases 2-4, participants were also debriefed

verbally and had an opportunity to ask questions about the study. Participants received $20 as compensation for participation in each phase of the study.

Screening. Individuals interested in participating in the study were asked to complete initial online screening to assess age and health-related exclusionary criteria (see Appendix B), followed by a telephone screen which included further assessment of health-related exclusionary criteria, and the SCID-5 interview to establish diagnostic status and eligibility. Telephone screens were conducted by the principal investigator (KR) and PhD-level clinical psychology students trained on the SCID-5.

During online screening, individuals were asked if they had a current sore or lesion in their mouth, if they had dental work in the past two weeks, or if they currently had an acute condition (e.g., cold, flu, tonsillitis, bronchitis, sinus infection), or symptoms consistent with a cold or infection. Individuals who endorsed these items were contacted for telephone screening, but their first laboratory session was scheduled for later in time to ensure at least two weeks had elapsed since dental work and/or that they had fully recovered from their acute condition or oral lesion before coming in for the first laboratory session.

After phone screening was complete, eligible individuals were provided with instructions for preparing for saliva collection. Instructions were presented verbally at the end of the phone screen, and in written format over email. Specifically, participants were asked to refrain from physical exercise during the day of the appointment and to avoid taking antihistamines or anti-inflammatory medications (e.g., ibuprofen) for 24 hours before their appointment, as these can influence cytokine levels. Participants were also asked not to drink anything besides plain water and not to eat, smoke, chew gum, or brush their teeth for one hour before their appointment, as these could affect the quality and purity of saliva samples. Moreover, participants were

encouraged to drink a full glass of plain water within an hour of coming to the lab to increase hydration levels and make saliva collection quicker and easier for them. Finally, participants were also encouraged to try to have a full night's sleep the night before the study to limit the impact of sleep deprivation on cytokine levels or cognitive control abilities.

Phase 1. One week before their first scheduled laboratory appointment, participants were emailed a link to the online battery of baseline questionnaires, including the demographic questionnaire and measures related to depressive symptoms (BDI-II), cognitive content (DAS-A, YSQ-S3), cognitive organization (PDST) and rumination (RRS), as well as other measures as part of the larger study.

Phase 2. Participants were run one at a time for Phase 2. Upon arrival at the laboratory, participants were taken to a testing room. After obtaining informed consent, participants were asked whether or not they had exercised that day, taken an antihistamine or anti-inflammatory medication in the past 24 hours, or had drunk fluids besides plain water, eaten, smoked, chewed gum, or brushed their teeth within the past hour. Participants (n = 3) who had eaten, drank, smoked, chewed gum, or brushed their teeth within the past hour were asked to wait until an hour had elapsed since they had broken the protocol before commencing the study. No participants reported same-day exercise or having recently taken antihistamines or anti-inflammatory medications in the past 24 hours.

Participants then completed a mouth rinse with water to remove any food particles. Next, they completed a 10-minute quiet relaxation period in which they were invited to sit quietly or to read books and magazines that were provided. The intention of the relaxation period was to allow participants to adjust to the laboratory setting in order to obtain a valid baseline measurement of salivary cytokines. Following the relaxation period, participants were provided

with makeup wipes to remove any lip products and were given instructions for saliva collection. The experimenter waited outside the testing room during saliva collection and recorded the salivary flow rate (i.e., the time it took for participants to provide 2ml of saliva) using a stopwatch. After processing the saliva sample for storage, the experimenter then measured the participant's height and weight.

Participants then completed the battery of cognitive control tasks. Tasks were displayed on an ASUS ® 22" monitor with 1920 × 1080 resolution and widescreen (16:9) aspect ratio. They first completed the N-back, followed by the Affective Flexibility Task and the Emotional Stroop task. The N-back was administered first as it is requires sustained attention for a prolonged duration and is therefore most sensitive to fatigue effects. The Emotional Stroop was administered last as it is more robust to fatigue effects (E. Hampson, personal communication, December 3, 2017). Next, the PANAS was administered to obtain information on baseline affect. The experimenter then led the participant to an interview room in the laboratory where instructions for the speech component of the TSST were provided by two research assistants, who were introduced to the participant as members of the human resources department at the hospital. The experimenter then led the participant back to the testing room for the 10-minute preparation period for the speech component of the TSST. At the end of the preparation period, the experimenter brought the participant back into the interview room, where he or she completed the speech and arithmetic tasks. At this point, participants were not permitted to have any water to ensure that post-stressor saliva samples would not be diluted. After completion of the TSST, participants were led back to the testing room, where they were asked to complete the N-back a second time, followed by the second administration of the PANAS to obtain information on post-stressor affect. Participants were then asked to provide a second saliva

sample, and the experimenter recorded salivary flow rate. Four participants refused to complete the TSST. Although these participants were invited to continue in the study, they were not asked to complete the post-stressor N-back or PANAS, or to provide a second saliva sample. The order of post-stressor tasks was chosen such that participants would complete the N-back directly after the stressor, when negative cognitive content is most likely to be highly activated. Saliva was collected last to allow sufficient time (approximately 40 minutes since the beginning of the stressor) for cytokine reactivity to be captured (Giletta et al. 2017; Newton et al. 2017). Participants were then debriefed, and a risk assessment was conducted if the participant had scored a 2 or 3 on item 9 of the BDI-II (endorsing suicidal ideation). Participants were then debriefed about this portion of the study.

Phase 2 sessions were run by research assistants trained by the principal investigator (KR). Each research assistant was shadowed by the principal investigator for a minimum of two participant sessions before running participants independently. All Phase 2 sessions were run between 12:00 – 7:30pm in order to experimentally control for diurnal variations in cytokines (e.g., Ghazali, Steele, Koh, & Idris, 2017; Izawa, Miki, Liu, & Ogawa, 2013).

Phase 3. Two weeks after Phase 2, participants returned to the laboratory and completed a second administration of the BDI-II, as well as a brief interview as part of the larger study. All Phase 3 study sessions were conducted by the principal investigator (KR).

Phase 4. Participants returned to the laboratory 6 months after their Phase 2 appointments and completed the BDI-II, as well as interviews as part of the larger study. Phase 4 study sessions were run by the principal investigator (KR) or PhD-level clinical psychology students.

Results

A priori study hypotheses were tested at a significance level of $p < .05$, and marginally significant findings were identified at a significance level of $p < .10$. As appropriate, follow-up tests were conducted for both significant and marginally significant findings. Analyses were conducted in IBM SPSS Statistics Version 25 and Mplus Version 8.3. See Appendix H for a glossary summarizing terms, acronyms, and variables used in the study.

Preliminary Analyses

Demographic, health, and clinical information. The sample consisted of 40 currently depressed, 69 remitted depressed, and 57 non-clinical controls. Demographic information for participant groups and the full sample is presented in Table 1. A univariate analysis of variance (ANOVA) or chi-square test was conducted, as appropriate, to test for differences across diagnostic groups on each demographic variable. Currently depressed, remitted depressed, and control participants did not significantly differ in age, ethnicity, years of education, level of educational attainment, or marital status, all ps > .05. However, age and ethnicity approached significance. Follow-up Tukey tests for age indicated that individuals in the currently depressed group were marginally older than those in the control group (mean difference = 4.22, SE = 1.83, p = .058). Furthermore, an inspection of standardized residuals for ethnicity indicated that there were marginally more Asian participants in the control group (z = 1.6) and fewer in the currently depressed group (z = -1.4). The chi-square test comparing groups in terms of the proportion of individuals of each sex was significant, $\chi^2(2) = 8.61$, p = .014. Inspection of standardized residuals indicated that a greater proportion of control participants were male (z = 2.0) than would be expected under the null hypothesis of independence between diagnostic group and sex.

Table 1

Demographic Characteristics of Currently Depressed, Remitted Depressed, and Control Participants

Variable	Currently Depressed (*n* = 40)	Remitted Depressed (*n* = 69)	Control (*n* = 57)	Full Sample (*n* = 166)	F/ χ^2
Sex					
Male *n* (%)	10 (25.0)	13 (18.8)	24 (42.1)	47 (28.3)	8.61*
Female *n* (%)	30 (75.0)	56 (81.2)	33 (57.9)	119 (71.7)	
Age *M* (*SD*)	28.63 (10.05)	26.01 (9.60)	24.40 (6.85)	26.09 (8.96)	2.66†
Ethnicity					
White *n* (%)	26 (65.0)	38 (55.1)	21 (36.8)	85 (51.2)	9.00†
Asian *n* (%)	9 (22.5)	23(33.3)	28 (49.1)	60 (36.1)	
Other *n* (%)	5 (12.5)	8 (11.6)	8 (14.0)	21 (12.7)	
Years of Education *M* (*SD*)	15.14 (2.78)	15.55 (2.41)	15.64 (2.32)	15.49 (2.46)	.46
Educational Attainment					
Partial high school, 10th or 11th grade *n* (%)	1 (2.5)	1 (1.4)	0 (0.0)	2 (1.2)	7.82
High school graduate *n* (%)	9 (22.5)	18 (26.1)	19 (33.3)	46 (27.7)	
Partial college, at least one year of specialized training *n* (%)	14 (35.0)	17 (24.6)	9 (15.8)	40 (24.1)	
College or university graduate *n* (%)	14 (35.0)	24 (34.8)	22 (38.6)	60 (36.1)	
Graduate or professional training *n* (%)	2 (5.0)	9 (13.0)	7 (12.3)	18 (10.8)	
Marital Status[a]					
Single and Never married *n* (%)	28 (70.0)	51 (73.9)	46 (80.7)	125 (75.3)	13.29
Living with partner *n* (%)	8 (20.0)	5 (7.2)	2 (3.5)	15 (9.0)	
Common-law *n* (%)	1 (2.5)	3 (4.3)	1 (1.8)	5 (3.0)	
Married *n* (%)	1 (2.5)	8 (11.6)	6 (10.5)	15 (9.0)	
Separated *n* (%)	2 (5.0)	1 (1.4)	1 (1.8)	4 (2.4)	
Divorced *n* (%)	0 (0.0)	1(1.4)	1 (1.8)	2 (1.2)	

[a]No participants reported being widowed.

†$p < .10$; *$p < 0.05$.

Biological and health characteristics of the full sample and separate participant groups are presented in Table 2. Participant groups did not differ in number of alcoholic drinks consumed per week, or the number of hours participants slept the night before Phase 2, all *p*s > .05. Among female participants, there was no significant difference across groups in use of hormonal contraceptives or length of time since last menstrual cycle, *p*s > .05. There were significant differences in body mass index index (BMI) across participant groups, $F(2, 163) = 4.79$, $p = .010$, $\eta_p^2 = .056$. Follow-up Tukey tests indicated that control participants had significantly lower BMI scores than did remitted depressed participants (mean difference = -2.57, $SE = 1.06$, $p = .043$), and currently depressed participants (mean difference = -3.48, $SE = 1.22$, $p = .014$). The difference between currently depressed and remitted depressed participants was nonsignificant (mean difference = 0.90, $SE = 1.18$, $p = .723$). A chi-square test also indicated a significant difference in smoking status, $\chi^2(2) = 19.89$, $p < .001$. Examination of the standardized residuals indicated that a greater number of currently depressed individuals were current smokers ($z = 3.6$) than would be expected under the null hypothesis of independence between participant group and smoking status.

Clinical characteristics across participant groups are presented in Table 3. The currently depressed group had a mean BDI-II score in the 'severe' range, whereas remitted depressed and control groups had mean BDI-II scores in the 'minimal' range (Beck et al., 1996). As anticipated, BDI-II scores significantly differed across diagnostic groups, $F(2, 163) = 78.54$, $p < .001$, $\eta_p^2 = .491$. Follow-up Tukey tests confirmed that currently depressed participants had greater depressive symptoms than remitted depressed (mean difference = 14.36, $SE = 1.75$, $p < .001$) and control participants (mean difference = 22.67, $SE = 1.81$, $p < .001$). Remitted

Table 2

Biological and Health Characteristics of Currently Depressed, Remitted Depressed, and Control Participants

	Currently Depressed (n = 40)	Remitted Depressed (n = 69)	Control (n = 57)	Full Sample (n = 166)	F/ χ^2
Body Mass Index (BMI) *M* (*SD*)	27.54 (5.87)	26.64 (6.68)	24.06 (4.89)	25.97 (6.06)	4.79*
Using hormonal contraceptives:[a]					1.04
Yes *n* (%)	9 (30.0)	23 (41.1)	12 (36.4)	44 (37.0)	
No *n* (%)	21 (70.0)	33 (58.9)	21 (63.6)	75 (63.0)	
Menstrual Cycle:[a]					7.60
Having period now	3 (10.0)	6 (10.7)	5 (15.2)	14 (11.8)	
< 2 months ago	19 (63.3)	35 (62.5)	25 (75.8)	79 (66.4)	
2-12 months ago	4 (13.3)	4 (7.1)	1 (3.0)	9 (7.6)	
More than 12 months ago	4 (13.3)	11 (19.6)	1 (3.0)	16 (13.4)	
Unknown	0 (0.0)	0 (0.0)	1 (3.0)	1 (0.01)	
Smoking:					19.89***
Current Smoker *n* (%)	11 (27.5)	4 (5.8)	1 (1.8)	16 (9.6)	
Nonsmoker *n* (%)	29 (72.5)	65 (94.2)	56 (98.2)	150 (90.4)	
Number of alcoholic drinks consumed per week *M* (*SD*)	2.53 (5.29)	1.86 (2.40)	1.79 (2.58)	1.97 (3.36)	.66
Number of Hours Slept Before Phase 2 *M* (*SD*)	7.80 (1.76)	7.80 (1.23)	7.42 (1.22)	7.68 (1.37)	1.47

[a]Percentages are calculated based on proportion of total female participants in each group (current depressed: n = 30, remitted depressed: n = 56; controls: n = 33).
*$p < 0.05$; **$p < .01$, ***$p < 0.001$.

Table 3

Clinical Characteristics of Currently Depressed, Remitted Depressed, and Control Participants

	Currently Depressed (n = 40)	Remitted Depressed (n = 69)	Control (n = 57)
BDI-II at Phase 1 *M (SD*)	27.12 (10.91)	12.76 (9.73)	4.46 (5.18)
Core Beliefs *M (SD*)	302.76 (59.97)	242.77 (51.65)	190.64 (44.65)
Dysfunctional Attitudes *M (SD*)	151.00 (34.66)	129.82 (33.40)	110.84 (28.32)
Rumination *M (SD*)	63.78 (10.66)	56.93 (11.61)	41.03 (12.11)
Negative Social Organization	0.87 (0.31)	1.10 (0.42)	1.33 (0.50)
Negative Achievement Organization	0.81 (0.39)	1.23 (0.55)	1.47 (0.52)
Age of first depression onset *M (SD*)	16.39 (6.77)	17.49 (5.99)	
Depression history:			
First episode *n* (%)	3 (7.5)	21 (30.4)	
Recurrence *n* (%)	37 (92.5)	46 (66.7)	
Unknown *n* (%)	0 (0.0)	2 (2.9)	
Number of Depressive Episodes *M* (*SD*)	5.60 (4.60)	2.94 (3.03)	
Comorbid diagnosis:			
Yes (1 comorbidity) *n* (%)	7 (17.5)	17 (24.6)	
Yes (2+ comorbidities) *n* (%)	29 (72.5)	26 (37.7)	
No *n* (%)	4 (10.0)	26 (37.7)	
Comorbid diagnosis:[a]			
Premenstrual Dysphoric Disorder *n* (%)	4 (1.0)	11 (15.9)	
Agoraphobia *n* (%)	9 (2.3)	5 (7.2)	
Generalized Anxiety Disorder *n* (%)	23 (57.5)	15 (21.7)	
Panic Disorder *n* (%)	8 (2.0)	8 (11.6)	
Social Anxiety *n* (%)	21 (52.5)	21 (30.4)	
Specific Phobia *n* (%)	8 (20.0)	10 (14.5)	
Other Specified Anxiety Disorder *n* (%)	4 (10.0)	4 (5.8)	
Obsessive Compulsive Disorder *n* (%)	9 (22.5)	12 (17.4)	
Other Specified Obsessive Compulsive Disorder *n* (%)	0 (0.0)	1 (1.4)	
Posttraumatic Stress Disorder *n* (%)	13 (32.5)	10 (14.5)	
Other Specified Trauma-related Disorder *n* (%)	7 (17.5)	2 (2.9)	
Currently using antidepressant medication *n* (%):[b]			
Yes *n* (%)	19 (47.5)	16 (23.2)	0 (0.0)
No *n* (%)	21 (52.5)	53 (76.8)	57 (100.0)
Currently receiving therapy:			
Yes *n* (%)	12 (30.0)	10 (14.5)	0 (0.0)
No *n* (%)	28 (70.0)	58 (84.1)	57 (100.0)
Unknown *n* (%)	0 (0.0)	1 (1.4)	0 (0.0)
Ever received therapy:			
Yes *n* (%)	31 (77.5)	40 (58.8)	3 (5.3)
No *n* (%)	9 (22.5)	28 (41.2)	54 (94.7)

[a]Percentages total more than 100% as some individuals had multiple comorbidities.
[b]Antidepressant medications in the sample included buproprion (*n* = 5), citalopram (*n* = 1), desvenlafaxine (*n* = 2), duloxetine (*n* = 1), escitalopram (*n* = 10), fluoxetine (*n* = 3), paroxetine (*n* =1), quetiapine (*n* = 3), sertraline (*n* = 7), trazodone (*n* = 4), venlafaxine (*n* = 4), and vortioxetine (*n* = 2).

depressed participants also had a greater number of symptoms than control participants (mean difference = 14.36, *SE* = 1.57, $p < .001$).

There were also significant group differences in core beliefs, $F(2, 162) = 55.20$, $p < .001$, $\eta_p^2 = .405$. Post hoc Tukey tests revealed that currently depressed individuals reported greater maladaptive core beliefs than remitted depressed (mean difference = 59.99, *SE* = 10.32, $p < .001$) and control participants (mean difference = 112.13, *SE* = 10.70, $p < .001$). The remitted depressed group reported greater core beliefs than the control group (mean difference = 52.13, *SE* = 9.22, $p < .001$). Similarly, dysfunctional attitudes also differed across diagnostic groups, $F(2, 163) = 18.55$, $p < .001$, $\eta_p^2 = .185$, and currently depressed individuals reported greater dysfunctional attitudes than remitted depressed (mean difference = 21.18, *SE* = 6.37, $p = .003$) and control participants (mean difference = 40.17, *SE* = 6.61, $p < .001$). Remitted depressed and control groups also differed, with the remitted depressed group reporting greater dysfunctional attitudes (mean difference =18.99, *SE* = 5.74, $p = .003$). Additionally, there were significant group difference in trait rumination, $F(2, 162) = 51.36$, $p < .001$, $\eta_p^2 = .388$, with post hoc Tukey tests indicating that currently depressed participants reported a significantly greater tendency to ruminate than both remitted depressed (mean difference = 6.85, *SE* = 2.32, $p = .010$) and control participants (mean difference = 22.74, *SE* = 2.40, $p < .001$). Remitted depressed participants also reported greater rumination than control participants (mean difference = 15.89, *SE* = 2.07, $p < .001$).

Significant group differences emerged on measures of the PDST, as expected. The ANOVA for negative social organization revealed group differences, $F(2, 140) = 12.51$, $p < .001$, $\eta_p^2 = .152$. Tukey tests confirmed that currently depressed participants demonstrated more tightly connected negative social schemas than both remitted depressed (mean difference = -0.23,

SE = 0.09, *p* = .026) and control participants (mean difference = -0.46, *SE* = 0.09, *p* < .001). Remitted depressed participants also showed more tightly interconnected negative social organization than controls (mean difference = -0.23, *SE* = 0.08, *p* = .015). Similarly, there were diagnostic group differences in negative achievement organization, $F(2, 136) = 18.24$, $p < .001$, $\eta_p^2 = .212$. Again, depressed participants evinced more tightly interwoven schemas than both remitted depressed (mean difference = -0.42, *SE* = 0.10, *p* < .001) and control individuals (mean difference = -0.67, *SE* = 0.11, *p* < .001), and remitted depressed individuals demonstrated more tightly interconnected schemas than did control participants (mean difference = -0.25, *SE* = 0.10, *p* = .043).

The majority of current and remitted depressed participants had experienced recurrent depressive episodes and met criteria for at least one comorbid psychiatric diagnosis. The most commonly reported comorbid diagnoses across both groups were generalized anxiety disorder and social anxiety disorder. Based on selection criteria, the non-clinical control group did not meet criteria for any current or remitted psychiatric diagnoses.

Data preparation and screening. Descriptive statistics for study variables are reported in Table 4, and bivariate correlations among cognitive content, cognitive organization, and cognitive control variables are presented in Table 5. Data were screened for non-normality and, with the exception of cytokines (see Cytokine Screening below), all study variables were normally distributed.

Self-report data. For all self-report questionnaires (i.e., BDI-II, YSQ, DAS, RRS) missing item data were imputed with the participant's mean score when at least 80% of items for that scale were completed. If more than 20% of items for a scale were missing, participant data for that scale were coded as missing. Very few data (0.50% of items) were missing. No extreme

Table 4

Descriptive Statistics of Cytokines, Depressive Symptoms, and Cognitive Measures

	N	Mean (*SD*)
IL-6		
Pre-stress	166	4.36 (8.93)
Post-stress	161	5.34 (12.50)
IL-8		
Pre-stress	166	540.99 (608.07)
Post-stress	161	852.65 (891.50)
IL-1β		
Pre-stress	166	61.51 (78.48)
Post-stress	161	96.84 (132.40)
TNF-α		
Pre-stress	166	1.65 (1.37)
Post-stress	161	2.17 (2.00)
Depressive Symptoms at Phase 1	166	13.37 (12.23)
Depressive Symptoms at Phase 3	161	12.79 (12.09)
Depressive Symptoms at Phase 4	134	11.42 (12.25)
Core Beliefs	165	238.94 (66.38)
Dysfunctional Attitudes	166	128.41 (35.32)
Rumination	165	53.06 (14.70)
Negative Social Organization	143	1.11 (0.45)
Negative Achievement Organization	139	1.19 (0.56)
Neutral Stroop RT (ms)	165	615.70 (135.54)
Emotional Stroop RT (ms)	165	595.80 (132.88)
P/A Switch Costs (ms)	166	161.63 (187.41)
N/A Switch Costs (ms)	165	261.16 (187.26)
P/NA Switch Costs (ms)	166	158.04 (204.59)
N/NA Switch Costs (ms)	166	75.82 (195.28)
Pre-stress N-back Errors	160	23.94 (11.74)
Post-stress N-back Errors	150	21.63 (11.28)

Note. Raw values are presented, however cytokines values were log transformed before analysis. IL-6 = interleukin-6; IL-8 = interleukin-8; IL-1β = interleukin -1β, TNF-α = tumor necrosis factor- α; RT = reaction time; NS Organization = Negative Social Organization; NA Organization = Negative Achievement Organization; P/A Switch Costs = Positive Affective Switch Costs; N/A Switch Costs = Negative Affective Switch Costs; P/NA Switch Costs = Positive Nonaffective Switch Costs; N/NA Switch Costs = Negative Nonaffective Switch Costs.

Table 5

Bivariate Correlations among Cognitive Content, Organization, and Control Variables

	1	2	3	4	5	6	7	8	9	10	11	12	13
1. Core Beliefs	-												
2. Dysfunctional Attitudes	.73***	-											
3. Rumination	.70***	.48***	-										
4. NS Organization	-.51**	-.47***	-.39***	-									
5. NA Organization	.60***	-.56***	-.45***	.56***	-								
6. Neutral Stroop RT	.10	.03	.19*	-.08	-.10	-							
7. Emotional Stroop RT	.10	.01	.20*	-.06	-.07	.89***	-						
8. Pre-stress N-back	.17*	.11	.17*	-.06	.004	.31***	.33***	-					
9. Post-stress N-back	.19*	.06	.23**	.07	.12	.28**	.30***	.66***	-				
10. P/A Switch Costs	.06	.06	.05	-.002	-.08	.16*	.08	.11	.03	-			
11. N/A Switch Costs	.02	.13†	.10	-.05	-.07	.04	.06	-.03	.01	.13	-		
12. P/NA Switch Costs	.15†	.23**	.14†	-.06	-.12	.06	.01	.05	.00	.20*	.26**	-	
13. N/NA Switch Costs	.04	.04	.04	.05	.07	.16*	.19*	.04	.08	.27***	.15†	.33***	-

Note. NS Organization = Negative Social Organization; NA Organization = Negative Achievement Organization; RT = reaction time; P/A Switch Costs = Positive Affective Switch Costs; N/A Switch Costs = Negative Affective Switch Costs; P/NA Switch Costs = Positive Nonaffective Switch Costs; N/NA Switch Costs = Negative Nonaffective Switch Costs.

†$p < .10$; *$p < .05$; **$p < .01$; ***$p < .001$

outliers (i.e., cases with values three times greater or less than the interquartile range) were identified on the PDST, BDI-II, YSQ, DAS, or RRS.

Emotional Stroop screening. Mean accuracy was 96.4% (*SD* = 4.1%) on the neutral block and 96.2% (*SD* = 4.2%) on the emotional block of the Stroop. Trials with inaccurate responses (3.6% of trials) were removed from further analysis. The influence of outliers was handled by replacing all trials with anticipatory responses (i.e., operationalized as a reaction time less than 250ms, given the time needed for stimulus perception and motor response) with a value of 250ms. Trials with slow reaction times that were at least 2.5 standard deviations above the mean were replaced with the value corresponding to 2.5 standard deviations above the mean. Altogether, 2.29% of trials were winsorized in this manner. This winsorizing procedure is consistent with other studies using reaction time data (e.g., Greenwald, Nosek, & Banaji, 2003) and retains the rank order of outliers while reducing their impact on mean performance. Average response time for neutral and emotional trials were then computed. Practice effects, as indicated by faster reaction times on the emotional block compared with the neutral block ($t(164) = 4.06$, $p < .001$) of the Stroop, were observed. Practice effects precluded a direct comparison of performance on the emotional block to the neutral block. As a result, interference scores, which demark interference resulting from inhibiting affective stimuli by taking performance when stimuli are not affective into account, could not be computed. Therefore, neutral and emotional block reaction times were examined separately in subsequent analyses. As the focus of the current study was on cognitive control abilities for affective stimuli, analyses of the emotional block of the Stroop are reported below. Analyses of the neutral block are reported in Appendix I. As noted in the appendix, there were not significant group differences in general inhibitory abilities as assessed by the neutral Stroop. Poor general inhibition was associated with greater

trait rumination and predicted greater resting-state inflammation. Interactions of cognitive vulnerability with neutral Stroop performance followed a pattern similar to other interactions, as described under the Summary of Moderating Effects in the Discussion.

Affective Flexibility Task screening. Trials with inaccurate responses (8.4% of trials) were removed from analysis. Using the same procedure as for the Stroop, trials with reaction times less than 250ms were replaced with a value of 250ms, and trials with reaction times 2.5 standard deviations above the mean were replaced with the value corresponding to 2.5 standard deviations above the mean. Altogether, 2.74% of trials were winsorized in this manner. This procedure is consistent with other studies using the Affective Flexibility Task (Genet, Malooly, & Siemer, 2013) and reaction time data more broadly (e.g., Greenwald, Nosek, & Banaji, 2003). Specific switch costs for various trial types were then calculated.

Emotional N-Back screening. In order to reduce the influence of participants who did not understand the task, expended low effort, or responded randomly, all outliers (defined as cases with values one and a half times greater or less than the interquartile range for their diagnostic group) were removed from analyses. Six individuals (3.61% of the sample) were classified as outliers on the first administration of the N-back, and 12 (7.23%) were classified as outliers on the second administration. This cutoff for removal of outliers was used in order to capture individuals performing significantly worse than chance based on a binomial distribution.

Cytokine screening. Due to the characteristic skewness and kurtosis of cytokine data, all pre- and post-stress cytokine variables were logarithmically transformed before analysis. This resolved issues with skew, although IL-6 remained somewhat leptokurtic (pre-stress kurtosis = 2.50, *SE* = .38, post-stress kurtosis = 2.52, *SE* = .38). Correlations among cytokines are reported

in Table 6, and correlations of cytokines with other main study variables are presented in Table 7.

Hypothesis 1: Group differences in Cognitive Control

Given group differences in the proportion of participants of each sex, a series of analysis of covariance (ANCOVA) tests were run to assess group differences in cognitive control while controlling for sex. As the same pattern of findings emerged without controlling for sex, the more parsimonious models excluding sex as a covariate are presented.

Emotional Stroop. Consistent with hypotheses, a one-way ANOVA assessing the relation of depression to reaction time for the emotional word block of the Stroop indicated that reaction times significantly differed across groups, $F(2, 162) = 3.13$, $p = .046$, $\eta_p^2 = .037$. An inspection of group means indicated that currently depressed individuals had the slowest reaction times ($M = 638.27$; $SD = 149.94$), followed by remitted depressed individuals ($M = 591.35$; $SD = 129.99$). Control participants had the fastest reaction times ($M = 571.31$; $SE = 117.94$). Follow-up Tukey tests indicated that depressed participants had significantly longer reaction times than control participants (mean difference = 66.96, $SE = 27.06$, $p = .038$). Remitted depressed participants did not differ significant from currently depressed (mean difference = -46.92, $SE = 26.14$, $p = .175$) or control participants (mean difference = 20.05, $SE = 23.56$, $p = .672$).

Affective Flexibility Task. A one-way multivariate ANOVA was conducted to examine group differences in performance on the Affective Flexibility Task, as indicated by negative affective switch costs, positive affective switch costs, positive nonaffective switch costs, and negative nonaffective switch costs. Contrary to hypotheses, there was no effect of diagnostic group on task performance, Wilk's $\lambda = .96$, $F(8, 318) = 0.55$, $p = .549$, $\eta_p^2 = .021$.

Table 6

Correlations among Cytokines

	1	2	3	4	5	6	7	8
1. Pre-stress IL-6	-							
2. Post-stress IL-6	.90***	-						
3. Pre-stress IL-8	.51***	.51***	-					
4. Post-stress IL-8	.45***	.57***	.91***	-				
5. Pre-stress IL-1β	.60***	.63***	.58***	.53***	-			
6. Post-stress IL-1β	.59***	.69***	.53***	.62***	.90***	-		
7. Pre-stress TNF-α	.73***	.65***	.57***	.48***	.63***	.57***	-	
8. Post-stress TNF-α	.68***	.81***	.57***	.66***	.68***	.75***	.75***	-

Note. IL-6 = interleukin-6; IL-8 = interleukin-8; IL-1β = interleukin -1β, TNF-α = tumor necrosis factor- α.

***$p < .001$.

Table 7

Bivariate Correlations Between Cytokines and Cognitive Content, Organization, and Control Variables

	Pre-stress IL-6	Post-stress IL-6	Pre-stress IL-8	Post-stress IL-8	Pre-stress IL-1β	Post-stress IL-1β	Pre-stress TNF-α	Post-stress TNF-α
Core Beliefs	.03	-.01	.01	.04	-.09	-.09	-.10	-.11
Dysfunctional Attitudes	-.05	-.12	.06	-.20	-.08	-.10	-.08	-.15†
Rumination	-.04	-.09	.15†	.06	-.06	-.11	-.06	-.12
NS Organization	-.15†	-.10	-.15†	-.05	-.05	-.01	-.07	-.02
NA Organization	-.11	-.09	-.27**	-.20*	-.10	-.03	-.05	-.05
Neutral Stroop RT	.16*	.24**	.22**	.28***	.27***	.34***	.18*	.28***
Emotional Stroop RT	.11	.18*	.19*	.24**	.23**	.31***	.11	.22**
P/A Switch Costs	.11	.22**	.13	.21**	.11	.15†	.03	.21**
N/A Switch Costs	-.12	-.09	-.02	-.02	-.08	-.05	-.05	-.04
P/NA Switch Costs	.04	.01	.08	.03	-.09	-.09	.08	.002
N/NA Switch Costs	.16*	.14†	.08	.10	.05	.09	.13†	.09
Pre-stress N-Back Errors	.05	.09	.17*	.19*	.15†	.19*	.04	.15†
Post-stress N-Back Errors	-.02	.00	.06	.07	.08	.12	-.03	.08

Note. IL-6 = interleukin-6; IL-8 = interleukin-8; IL-1β = interleukin -1β, TNF-α = tumor necrosis factor- α; NS Organization = Negative Social Organization; NA Organization = Negative Achievement Organization; P/A Switch Costs = Positive Affective Switch Costs; N/A Switch Costs = Negative Affective Switch Costs; P/NA Switch Costs = Positive Nonaffective Switch Costs; N/NA Switch Costs = Negative Nonaffective Switch Costs.

$^{\dagger}p < .10$; $^{*}p < .05$; $^{**}p < .01$; $^{***}p < .001$

Emotional N-back. A one-way ANOVA was conducted to assess group differences in number of errors on the N-back at baseline. As predicted, number of errors differed significantly across groups, $F(2, 157) = 6.11$, $p = .003$, $\eta_p^2 = .072$. Post-hoc pairwise comparisons using Tukey tests indicated that the control group made significantly fewer errors ($M = 21.40$; $SD = 10.61$) than did the currently depressed group ($M = 29.36$; $SD = 13.66$; mean difference = -7.96, $SE = 2.36$, $p = .003$). The number of errors the remitted depressed group made was intermediate between the current depressed and control groups ($M = 22.91$; $SD = 10.49$), and differed significantly from currently depressed participants (mean difference = -6.45, $SE = 2.31$, $p = .016$), but not from control participants (mean difference = 1.50, $SE = 2.07$, $p = .749$).

Similarly, a one-way ANOVA was conducted to examine group differences in number of errors on the N-back after the TSST. Again, number of errors differed significantly across groups, $F(2, 147) = 7.23$, $p = .001$, $\eta_p^2 = .090$. Tukey tests indicated that currently depressed individuals made more errors ($M = 27.44$; $SD = 13.46$) than both remitted depressed participants ($M = 20.64$; $SD = 9.65$; mean difference = 6.81, $SE = 2.28$, $p = .009$) and controls ($M = 18.81$; $SD = 10.13$; mean difference = 8.63, $SE = 2.34$, $p = .001$). Remitted depressed participants did not differ significantly from the control group (mean difference = 1.83, $SE = 2.04$, $p = .642$).

Hypothesis 2: Association of Deficits in Cognitive Control with Rumination

A series of bivariate correlations were conducted to examine the relation of cognitive control deficits with rumination (see Table 5). Consistent with hypotheses, greater rumination was associated with longer reaction times on the emotional block of the Stroop, ($r[164] = .20$, $p = .010$). Furthermore, greater pre-stressor ($r[159] = .17$, $p = .030$) and post-stressor ($r[149] = .23$ $p = .005$) N-back errors were associated with higher rumination. Positive nonaffective switch

costs were marginally associated with rumination (r[165] = .14, p = .068), whereas negative nonaffective, positive affective, and positive affective switch costs were not, all ps > .05.

Hypothesis 3: Decreased Updating Abilities Following the Stressor

Stress induction manipulation check. The validity of the stress induction was evaluated by assessing whether participants reported greater levels of negative affect and lower positive affect after the TSST. Participants reported significantly greater negative affect after the TSST (M = 22.38, SD = 9.61) compared with before the TSST (M = 16.10, SD = 6.10), t(161) = -10.54, p < .001, d = -0.83. Participants also reported significantly lower positive affect following the TSST (M = 22.93, SD = 8.84) compared with before the TSST (M = 25.08, SD =7.54), t(161) = 3.77, p < .001, d = 0.30. Together, these results indicate that the TSST elicited a subjective stress response.

Two 3(group) x 2(pre-stress vs. post-stress) repeated measures ANOVAs were conducted to examine diagnostic group differences in affective response to the stressor. For changes in negative affect, there was a significant main effect of group F(2, 159) = 14.89, p < .001, η_p^2 = .158. This was qualified by a significant interaction of stress with group, Wilk's λ = .95, F(2, 159) = 4.04, p = .019, η_p^2 = .048. To facilitate interpretation of this significant interaction, follow-up univariate ANOVAs were run separately with group as the independent variable for pre- and post-stress negative affect. Groups differed significantly in negative affect before the TSST, F(2, 163) = 10.78, p < .001, η_p^2 = .117. Follow up Tukey tests indicated that currently depressed participants reported greater negative affect (M = 19.25; SD = 7.03) than remitted depressed (M = 16.42; SD = 5.86; mean difference = 2.83, SE = 1.15, p = .039) or control participants (M = 13.74; SD = 4.61; mean difference = 5.51, SE = 1.19, p < .001) at baseline. Furthermore, remitted depressed individuals reported greater negative affect than controls (mean

difference = 2.68, *SE* = 1.04, *p* = .028). There were also significant group differences in negative affect after the TSST, $F(2, 159) = 13.16$, $p < .001$, $\eta_p^2 = .142$. Follow-up Tukey tests revealed that control participants (*M* = 17.77; *SD* = 7.33) reported significantly lower negative affect than currently depressed (*M* = 26.95; *SD* = 10.03; mean difference = -9.17, *SE* = 1.89, *p* = .009) or remitted depressed individuals (*M* = 23.76; *SD* = 9.56; mean difference = -5.99, *SE* = 1.61, *p* = .001) following the stressor. In contrast to baseline negative affect, remitted depressed individuals did not differ from currently depressed participants in negative affect following the TSST (mean difference = -3.18, *SE* = 1.83, *p* = .194).

The 3(group) x 2(pre-stress vs. post-stress) repeated measures ANOVA for positive affect indicated a significant main effect of group $F(2, 159) = 8.40$, $p < .001$, $\eta_p^2 = .096$. This was qualified by a significant interaction of stress with group, Wilk's $\lambda = .90$, $F(2, 159) = 8.99$, $p < .001$, $\eta_p^2 = .102$. Separate follow-up univariate ANOVAs were conducted with group as the independent variable for pre- and post-stress positive affect. In the first ANOVA examining pre-stress positive affect, there were no significant group differences in positive affect, $F(2, 163) = 2.26$, $p = .108$, $\eta_p^2 = .027$. However, group means for positive affect fell in the expected direction, with control participants reporting high positive affect (*M* = 26.61; *SD* = 7.05), followed by remitted depressed (*M* = 24.59; *SD* = 8.15) and currently depressed participants (*M* = 23.45; *SD* = 7.08). Significant group differences did emerge on positive affect following the TSST, $F(2, 159) = 13.75$, $p < .001$, $\eta_p^2 = .147$. Control participants had significantly higher positive affect (*M* = 27.53; *SD* = 9.31) than currently depressed (*M* = 20.39; *SD* = 7.56; mean difference = 7.14, *SE* = 1.73, *p* < .001) and remitted depressed (*M* = 20.47; *SD* = 7.54; mean difference = 7.06, *SE* = 1.47, *p* < .001) individuals. However, similar to findings for negative

affect, currently depressed and remitted depressed individuals did not differ with regard to positive affect following the stressor (mean difference = -0.08, *SE* = 1.68, *p* = .999).

Changes in updating following stress. A 3(group) × 2(pre-stress vs. post-stress) repeated measures ANOVA was conducted to examine whether there were increases in N-back errors after the stressor. Contrary to hypotheses, there was no main effect of stress on N-back errors, Wilk's $\lambda = .99$, $F(1, 145) = 1.56$, $p = .214$, $\eta_p^2 = .011$, nor was there an interaction on stress with diagnostic group, Wilk's $\lambda = .99$, $F(2, 145) = .62$, $p = .541$, $\eta_p^2 = .008$.

Hypothesis 4: Cognitive Content and Structure Predicting Stress-Induced Change in N-Back Performance

Associations of changes in N-back performance with changes in negative and positive affect were examined using partial correlations. Controlling for baseline N-back errors and baseline negative affect, greater post-stress N-back errors were significantly associated with increased post-stress negative affect, $r(144) = .20$, $n = 148$, $p = .016$. However, controlling for both baseline N-back errors and baseline positive affect, stress-induced changes in N-back errors were not related to positive affect following the stressor, $r(144) = .02$, $n = 148$, $p = .792$.

A hierarchical linear regression was conducted to examine the role of negative cognitive content and structure in predicting stress-induced changes in performance on the N-back (Table 8). Because a goal was to assess how N-back performance changed following stress, pre-stressor N-back errors were entered in Step 1 to control for baseline performance. Diagnostic group was also entered as a covariate in Step 1 since it is associated with updating abilities. Negative affect at pre-stress and at post-stress were entered in Step 2 to control for the influence of changes in affect on N-back task performance. Negative affect was entered separately from diagnostic status so that group effects could be examined independently given that diagnostic group was

Table 8

Hierarchical Linear Regression with N-Back Errors Before Stress Induction, Negative Cognitive Content and Negative Cognitive Organization Predicting Post-Stressor N-Back Errors

Variable	*B*	*SE*	95% CI	β	*t*	*p*
Step 1						
Pre-stress N-back Errors	.60	.08	[.45, .75]	.58	7.77	<.001
Diagnostic Group						
Currently Depressed vs. Controls	4.23	2.07	[.12, 8.33]	.18	2.04	.044
Remitted Depressed vs. Controls	-1.52	1.87	[-5.22, 2.19]	-.07	-0.81	.419
Step 2						
Pre-stress N-back Errors	.56	.08	[.41, .72]	.55	7.28	<.001
Diagnostic Group						
Currently Depressed vs. Controls	2.87	2.20	[-1.48, 7.23]	.12	1.31	.194
Remitted Depressed vs. Controls	-2.34	1.89	[-6.08, 1.40]	-.11	-1.24	.217
Pre-stress Negative Affect	-.11	.15	[-.41, .18]	-.07	-0.76	.449
Post-stress Negative Affect	.23	.11	[.02, .44]	.20	2.19	.031
Step 3						
Pre-stress N-back Errors	.50	.07	[.36, .65]	.49	6.79	<.001
Diagnostic Group						
Currently Depressed vs. Controls	3.52	2.47	[-1.38, 8.43]	.15	1.42	.158
Remitted Depressed vs. Controls	-2.21	1.92	[-6.00, 1.59]	-.10	-1.15	.252
Pre-stress Negative Affect	-.15	.14	[-.43, .14]	-.09	-1.01	.317
Post-stress Negative Affect	.27	.10	[.06, .47]	.23	2.61	.011
Core Beliefs	.04	.02	[.002, .09]	.26	2.08	.040
Dysfunctional Attitudes	-.01	.03	[-.07, .05]	-.04	-0.42	.679
Negative Social Organization	5.23	2.14	[.98, 9.48]	.21	2.44	.016
Negative Achievement Organization	4.47	1.86	[.77, 8.16]	.22	2.40	.018

Model	R^2	ΔR^2	ΔF	*p*
Step 1	.44	.44	28.03	<.001
Step 2	.46	.03	2.51	.086
Step 3	.55	.09	5.00	.001

Note. 95% CI = 95% confidence intervals for unstandardized coefficients (*B*s). Diagnostic Group was dummy coded as Controls = 0, Currently Depressed = 1, and Remitted Depressed = 1.

associated with affective responses to the stressor. In Step 3, cognitive content (core beliefs, dysfunctional attitudes) and structure (negative social organization, negative achievement organization) variables were added.

Findings in Step 1 indicate that pre-stress N-back errors significantly predicted post-stress errors. Diagnostic status was associated with updating errors, such that currently depressed participants showed greater declines in cognitive control than controls. There were no differences between participants in the remitted depressed and control groups.

Greater post-stress negative affect was related to increases in post-stress N-back errors in Step 2. As pre-stress negative affect was also entered in Step 2, this finding indicates that post-stress *increases* in negative affect were related to stress-induced increases in N-back errors. Diagnostic status was no longer associated with post-stressor changes in N-back performance in Step 2, indicating that increases in negative affect better account for declines in updating following the stressor, although the inclusion of negative affect did not significantly improve the model, $\Delta R^2 = .03$, $\Delta F(2, 106) = 2.51$, $p = .086$.

As anticipated, the addition of cognitive content and organization variables in Step 3 significantly improved the model, $\Delta R^2 = .09$, $\Delta F(4, 102) = 5.00$, $p = .001$. The final model indicates that, as hypothesized, greater maladaptive core beliefs were associated with decreases in updating abilities following stress (i.e., greater N-back errors). Dysfunctional attitudes did not predict changes in updating. Unexpectedly, more diffuse negative social cognitive structure and more diffuse negative achievement structure predicted greater post-stress N-back errors. This suggests that less negative schema consolidation results in greater stress-induced declines in updating. Collinearity was assessed, and in the final model all tolerance values were .28 or higher, and VIF values were 3.61 or lower.

Hypotheses 5-10: Predicting Baseline Inflammation and Stress-Induced Changes in Inflammation

Analytic strategy. In order to examine cytokine reactivity to the TSST, a series of latent change score models were conducted using structural equation modeling (SEM; Burt & Obradović, 2013; McArdle, 2009, see Giletta et al., 2017). In these models, a latent factor of inflammation was constructed at pre-stress and at post-stress and was comprised of the four inflammatory cytokines at each time point as indicators. A latent factor of inflammation represents a more reliable phenotype compared to examining each cytokine independently, and also has the advantage of accounting for measurement error (Burt & Obradović, 2013). To construct the latent inflammation factor, a series of measurement models were estimated using confirmatory factor analysis (CFA) in order to assess whether the four cytokines loaded on a common factor at both pre- and post-stress. CFA models were also used to test whether parameter estimates of this latent factor were equivalent (i.e., measurement invariant) across both time points (see Appendix J for details). Evidence was found for configural and metric invariance, and partial scalar invariance. Partial scalar invariance indicates that the intercepts (i.e., means) of some of the indicators (cytokines) changed at different rates from pre-stress to post-stress. Although there was a reduction in model fit statistics when constraining the intercepts to full scalar invariance, this approach was used due to the greater reliability of parameter estimates in fully constrained models. The same models constrained only to partial scalar invariance are presented in Appendix K and show the same general pattern of findings.

Within-person changes in cytokines from pre- to post-stress were examined by defining a second-order latent change score variable. This latent change factor was defined by regressing the inflammation latent variable at post-stress on the pre-stress inflammation latent variable and

on the second-order latent change factor, with both of these paths fixed to 1. In the first unconditional model, pre-stressor inflammation and the latent change factor were covaried. This unconditional model was estimated first to assess mean changes and individual differences in cytokine reactivity (Figure 7).

Next, a series of conditional models were computed to examine whether cognitive control, cognitive content, cognitive organization, or rumination account for individual differences in pre-stress cytokine levels and stress-induced changes in inflammation. In these models, the path from pre-stress to post-stress inflammation factors was freely estimated, whereas the covariance between the latent change factor and the pre-stress inflammation factor were set to zero (Figure 8). Constraining parameters in this manner renders the second-order latent change factor a 'baseline-free' latent change variable. Therefore, in the conditional models, latent change scores were predicted while taking individual differences in baseline levels of cytokines (which may influence the extent of reactivity to the stressor) into account.

For each type of cognitive control, two sets of models were run. The first set of models assessed the role of cognitive content (i.e., core beliefs and dysfunctional attitudes) and rumination, cognitive control, and the interaction of cognitive content and rumination with cognitive control on both pre-stress inflammation and post-stress changes in inflammation. The second set of models assessed the role of negative cognitive structure and cognitive control and the interaction of negative cognitive organization with cognitive control on pre-stress cytokines and stress-induced changes in cytokines. Models including cognitive content and rumination variables assessed impacts of more surface level cognitions that represent cognitive processes (i.e., rumination) and cognitive *products* of schemas (i.e., dysfunctional attitudes, core beliefs; Beck & Dozois, 2014; Dozois & Beck, 2008) that were measured via item endorsement. In

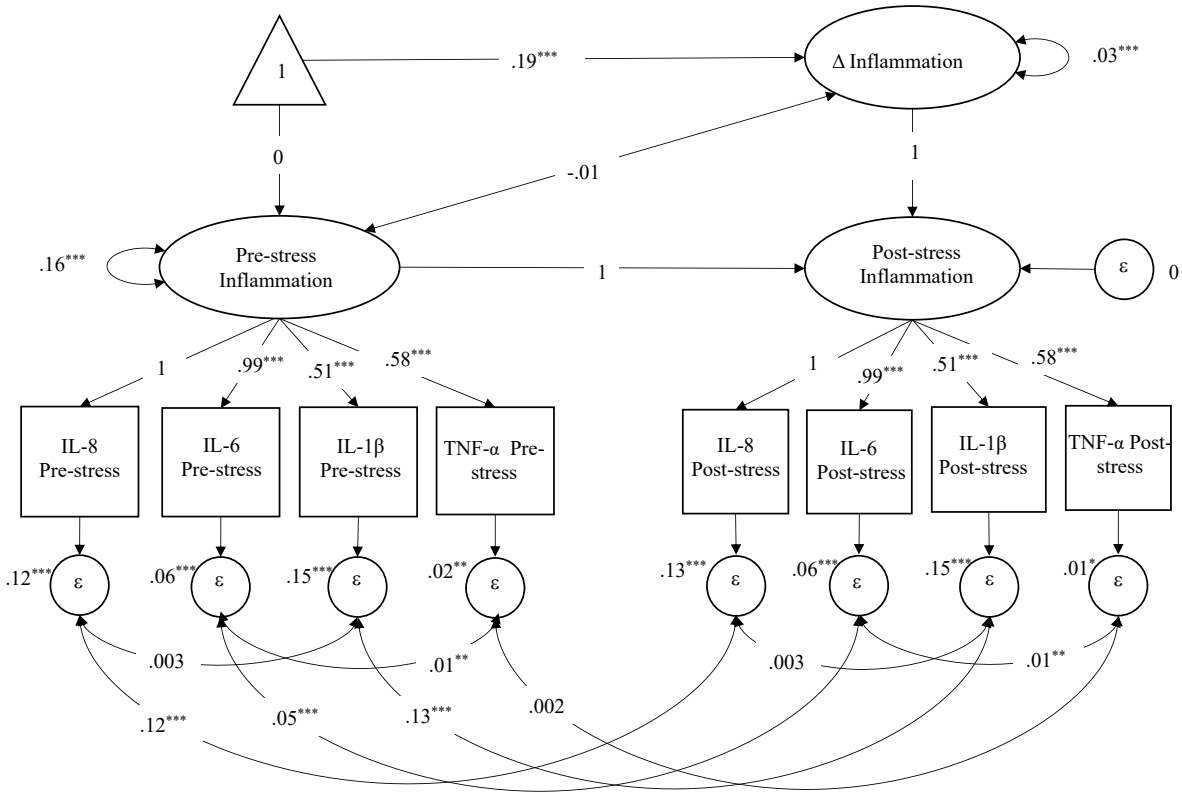

Figure 7. Unconditional second-order latent change score model with first-order latent change factor of inflammation. Unstandardized estimates are reported. Model fit: $\chi^2(19, N = 166) = 81.44$, $p < .001$, CFI = .955, TLI = .934 and RMSEA = .141, SRMR = .170.
$^{*}p < .05$; $^{**}p < .01$; $^{***}p < .001$.

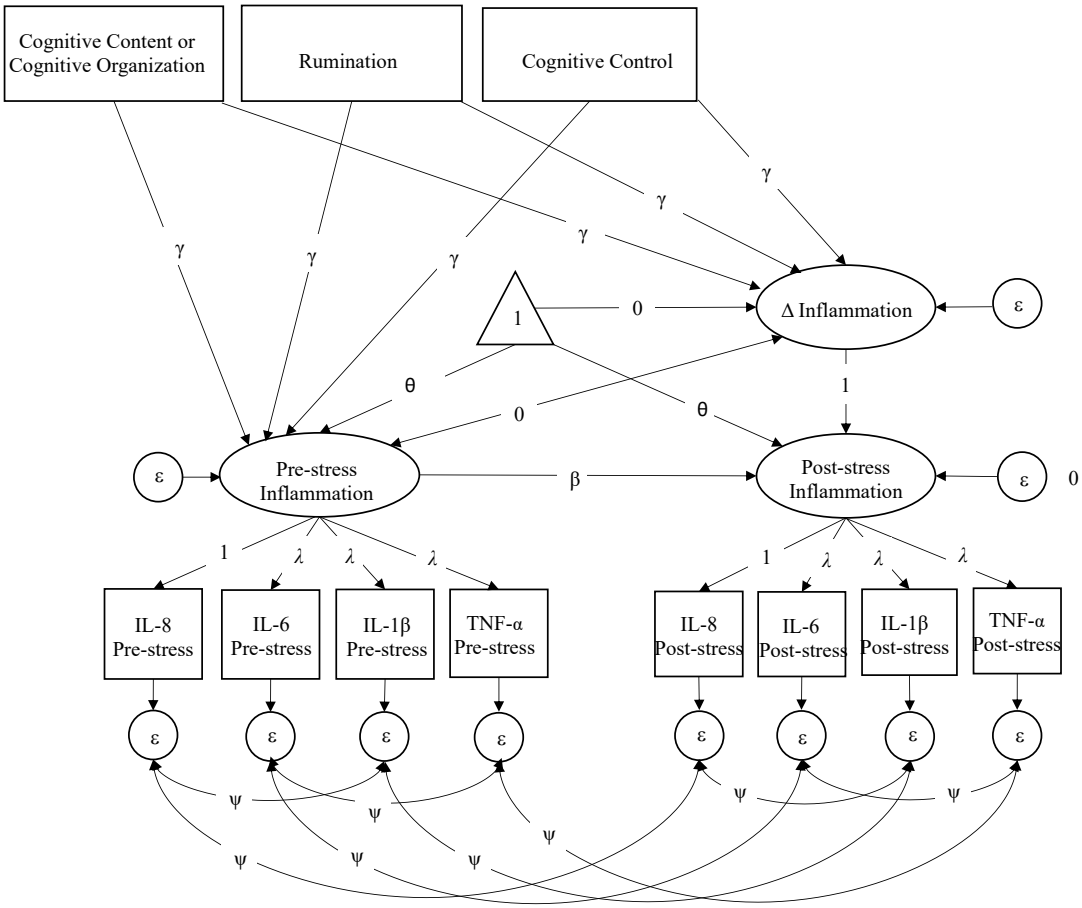

Figure 8. Conditional second-order latent change score model with first-order latent change factor of inflammation. Note that models examined either cognitive content or cognitive organization variables. Rumination was only included in models that also examined cognitive content.

contrast, models including cognitive organization variables assessed the *structure* of schemas, which represent deeper cognitions that individuals are not able to explicitly report on. Separate models were also run in order to avoid potential problems with multicollinearity or suppression on parameter estimates of interactions and due to the number of individuals with missing data on the PDST (i.e., individuals that did not obtain a score on a scale of the PDST). In order to obtain a score for negative achievement or negative social organization on the PDST, participants must endorse at least two negative adjectives as being self-descriptive. Therefore, individuals who do not endorse negative schematic information, which would likely include some of the less vulnerable participants in the sample, would be excluded from analyses. A total of 23 (13.96% of the sample) did not obtain a score for negative social organization, and 27 (16.27% of the sample) did not obtain a score for negative achievement organization. In part to minimize the influence of missing data, cognitive organization was analyzed independently of the cognitive content and rumination variables.

Maximum likelihood estimation with robust standard errors was used, which is optimal for nonnormal data (e.g., cytokines), and handles missing data in the endogenous variables. Listwise deletion was used for exogenous variables. A series of conditional models were conducted to examine which demographic, biological, and health characteristics relevant to inflammation were associated with pre-stress inflammation or change in inflammation by regressing the latent factor of baseline inflammation and latent change in inflammation on each variable (Table 9). Salivary flow rate, or the total time taken to collect the desired volume of saliva, was not assessed as a potential covariate as a number of participants had difficulty providing the requested 2ml of saliva at one or both of the collection points. Salivary flow rate therefore was not a valid variable for comparison across participants.

Table 9

Relation of Demographic, Clinical, and Health Characteristics with Latent Pre-Stressor Inflammation and Latent Change in Inflammation.

	Pre-stress inflammation			Δ inflammation		
	β	95% CI	*b*	β	95% CI	*b*
Age	.26**	[0.10, .41]	.01	.21*	[.02, .39]	.004
BMI	.40***	[.25, .54]	.03	.02	[-.15, .18]	.00
Ethnicity						
White vs. Other	-.12	[-.28, .04]	-.15	.09	[-.10, .27]	.05
White vs. Asian	-.33***	[-.48, -.17]	-.28	-.14	[-.33, .05]	-.06
Sex	.04	[-.13, .20]	.03	.22*	[.05, .39]	.09
Depressive Symptoms	.04	[-.12, .21]	.001	-.10	[-.28, .08]	-.001
Diagnostic Group						
Currently Depressed vs. Controls	.11	[-.08, .30]	.10	-.12	[-.32, .09]	-.05
Remitted Depressed vs. Controls	.11	[-.06, .28]	.09	-.10	[-.28, .09]	-.04
Use of contraceptives	-.06	[-.20, .09]	-.05	-.16†	[-.33, .02]	-.07
Time since last menstrual period	.13	[-.09, .35]	.06	.38**	[.26, .61]	.08
Smoking Status	.002	[-.19, .20]	.03	.07	[-.09, .23]	.04
Number of alcoholic drinks consumed per week	.07	[-.15, .29]	.01	.21†	[-.004, .43]	.01
Number of Hours Slept Before Phase 2	.10	[-.09, .30]	.03	-.06	[-.28, .16]	.58
Using ADM[a]	.18†	[-.01, .21]	.18	.03	[-.14, .21]	.02

Note. Each variable was entered in a separate model. 95% CI = 95% confidence intervals for standardized coefficients (βs). Values of .00 are < .001. Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1; Sex was coded as 0 = female and 1 = male; Diagnostic Group was coded as Controls = 0, Currently Depressed = 1, and Remitted Depressed = 1; Smoking status was coded as 0 = nonsmoker and 1 = current smoker; Using ADM was coded as 0 = not using ADM and 1 = currently taking ADM.

[a]Antidepressant medication.

†$p < .10$; *$p < .05$; **$p < .01$; ***$p < .001$

Consistent with past research (e.g., Giletta et al., 2017; Shields et al. 2016; Slavish et al., 2015), age, BMI, and ethnicity emerged as key covariates of inflammation. To a lesser extent, sex was associated with post-stress changes in inflammation. However, inclusion of sex as a covariate did not result in a different pattern of findings across models. Therefore, the more parsimonious models that exclude sex are presented. Furthermore, menstrual cycle was associated with stress-induced changes in cytokines among female participants. However, given that analyses controlling for this covariate would exclude male participants, this variable was not entered as a covariate in subsequent analyses. Analyses for conditional models therefore adjusted for age, ethnicity, and BMI. Continuous predictor variables were centred before analyses, and significant and marginally significant interactions (identified at a significance level of $p < .10$) were examined by assessing simple slopes. Regions of significance were examined for significant interactions using the Johnson-Neyman technique (see Hayes & Rockwood, 2017). This analytic procedure derives values of the moderator that indicate the range, or ranges, where the independent variable is significantly related to the dependent variable, as well as ranges of the moderator where it is not. Confidence intervals are reported in both tables and figures, which provide an indication of the degree of precision of the parameter estimates within the current sample. Structural equation modeling analyses were conducted in Mplus version 8.3.

Hypothesis 5: Increases in Inflammatory Cytokines in Response to the Stressor

An unconditional latent change score model was constructed to examine mean changes and individual differences in overall cytokine reactivity to the social stressor (see Figure 7). As anticipated, the mean of the latent change factor of inflammation was significant ($b = .19$, 95% CI = [.16, .23], $p < .001$), indicating significant mean increases in the inflammatory phenotype following the social stressor. In addition, there was significant individual variability around the

latent change factor mean, (σ^2 = .03, 95% CI = [.02, .05], p < .001), indicating inter-individual differences in within-person cytokine reactivity to the stressor.

Furthermore, a series of paired sample t-tests were conducted for each cytokine to examine whether an increase in cytokines following the stressor was also evident when examining raw change as compared to latent change. There were significant stress-induced increases for all four cytokines (see Table 4 for descriptive statistics), and effect sizes were medium to large: IL-6: $t(160) = -4.40$, $p < .001$, $d = .35$; IL-8: $t(160) = -12.25$, $p < .001$, $d = .97$; IL-1β: $t(160) = -7.98$, $p < .001$, $d = .63$; TNF-α: $t(160) = -7.88$, $p < .001$, $d = .62$.

Hypothesis 6: Association of Diagnostic Group with Baseline Cytokines and Post-Stress Changes in Cytokines

As shown in Table 9, a conditional model regressing pre-stress cytokines and changes in cytokines on diagnostic group indicated, contrary to hypotheses, that there were no significant group differences in baseline inflammation or on inflammatory stress reactivity. There was also no association of depressive symptoms with baseline or stress-induced changes in inflammation.

Hypotheses 7-10: Prediction of Baseline Cytokines and Changes in Cytokines by Cognitive Control, Cognitive Content, Rumination, and Cognitive Organization

In models assessing the role of cognitive content and rumination, it was expected that there would be main effects of cognitive content and rumination on changes in inflammation, such that greater vulnerability (i.e., greater core beliefs, dysfunctional attitudes, and rumination) would be associated with greater resting-state and post-stress increases in cytokines. It was also anticipated that poorer cognitive control would be associated with greater pre-stress and post-stress increases in inflammation. An exception to this was for positive nonaffective switch costs, where greater switch costs were expected to predict lower levels of inflammation. Finally, it was

hypothesized that cognitive vulnerability would interact with cognitive control on inflammation, such that greater cognitive vulnerability in combination with poor cognitive control was expected to result in the highest levels of baseline or post-stress increases in cytokines.

Similarly, in models assessing the role of negative cognitive structure, it was anticipated that there would be main effects of negative social and achievement schemas on inflammation, such that more tightly interconnected schemas would be related to greater baseline and stress-induced changes in cytokines. Again, it was hypothesized that poor cognitive control (or in the case of positive nonaffective switch costs, lower switch costs) would predict greater resting-state and post-stress increases in cytokines. Cognitive organization was expected to interact with cognitive control on inflammation, such that more tightly connected schemas and poorer cognitive control were expected to result in the highest resting-state and post-stress increases in inflammation.

Emotional Stroop. ***Cognitive content and rumination.*** Table 10 presents estimates from the conditional models predicting baseline and stress-induced changes in cytokines by negative cognitive content, rumination, and reaction times on the Emotional Stroop. Consistent with hypotheses, in Model 1 reaction times on the Emotional Stroop marginally predicted baseline inflammation, such that longer reaction times were associated with greater inflammation. Maladaptive core beliefs marginally predicted increases in inflammation after the stressor. Unexpectedly, greater rumination was associated with post-stress *decreases* in inflammation.

There was no evidence of moderation between core beliefs or dysfunctional attitudes and Emotional Stroop performance on pre-stress inflammation or changes in inflammation in Models 2 and 3. However, rumination marginally moderated the relation of inhibition of emotional stimuli with pre-stress inflammation. There was a trend for simple slopes to indicate that poor

Table 10

Prediction of Latent Pre-stress Cytokines and Latent Change in Cytokines by Emotional Stroop, Negative Cognitive Content, and Rumination

	Pre-stress inflammation			Δ inflammation		
Model and predictor	β	95% CI	*b*	β	95% CI	*b*
Model 1: Main effects		R^2 = .22, p < .001			R^2 = .14, p = .013	
Age	-.002	[-.16, .15]	.00	.16	[-.05, .37]	.003
BMI	.34***	[.18, .49]	.02	-.03	[-.22, .16]	-.001
Ethnicity						
White vs. Other	-.09	[-.25, .07]	-.11	.10	[-.08, .27]	.05
White vs. Asian	-.19*	[-.36, -.03]	-.17	-.06	[-.27, .15]	-.02
Core Beliefs	-.14	[-.40, .13]	-.001	.26†	[-.03, .56]	.001
Dysfunctional Attitudes	.05	[-.17, .26]	.001	-.16	[-.41, .09]	-.001
Rumination	.03	[-.18, .23]	.001	-.33**	[-.54, -.12]	-.004
Emotional Stroop RT	.16†	[-.01, .33]	.05	.13	[-.06, .31]	.02
Model 2: Interaction effect		R^2 = .23, p < .001			R^2 = .14, p = .010	
Core Beliefs × Emotional Stroop RT	-.10	[-.22, .03]	.00	.09	[-.06, .24]	.00
Model 3: Interaction effect		R^2 = .23, p < .001			R^2 = .14, p = .012	
Dysfunctional Attitudes × Emotional Stroop RT	-.08	[-.20, .04]	-.001	-.03	[-.17, .10]	.00
Model 4: Interaction effect		R^2 = .24, p < .001			R^2 = .14, p = .013	
Rumination × Emotional Stroop RT	-.13†	[-.27, .01]	-.002	-.01	[-.15, .14]	.00

Note. 95% CI = 95% confidence intervals for standardized coefficients (βs). Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1. Values of .00 are < .001. Model fit: Model 1, $\chi^2(67, N = 164) = 170.01$, $p < .001$, CFI = .937, TLI = .913 and RMSEA = .097, SRMR = .118; Model 2, $\chi^2(73, N = 164) = 181.19$, $p < .001$, CFI = .936, TLI = .912 and RMSEA = .095, SRMR = .112; Model 3, $\chi^2(73, N = 164) = 175.23$, $p < .001$, CFI = .939, TLI = .916 and RMSEA = .092, SRMR = .114; Model 4, $\chi^2(73, N = 164) = 175.59$, $p < .001$, CFI = .938, TLI = .915 and RMSEA = .093, SRMR = .114.
†$p < .10$; *$p < .05$; **$p < .01$; ***$p < .001$.

inhibition of emotional information was associated with greater cytokine levels at baseline for individuals with low (b = .09, 95% CI = [.02, .16], p = .008), and not high (b = .02, 95% CI = [-.04, .08], p = .532) tendencies to ruminate (Figure 9). Rumination did not interact with the Emotional Stroop on changes in inflammation.

Cognitive organization. Results from the conditional models predicting baseline and stress-induced changes in cytokines by cognitive organization and Emotional Stroop reaction times are presented in Table 11. The first model (Model 1) examining main effects indicated that, consistent with hypotheses, both Negative Achievement Organization and Emotional Stroop reaction times predicted baseline cytokines, such that more tightly connected negative achievement schemas and longer reaction times on the Emotional Stroop were associated with greater pre-stress inflammation. Contrary to hypotheses, more dispersed negative social schemas marginally predicted greater increases in cytokines following stress.

The potential moderating role of cognitive organization was explored in Models 2 and 3. Across both models, no significant interactions were found between reaction time on the Emotional Stroop and negative social cognitive structure or negative achievement structure on pre-stress cytokines or post-stress changes in cytokines.

Positive Affective Switch Costs. ***Cognitive content and rumination.*** Findings from the conditional models predicting baseline and stress-induced changes in cytokines by negative cognitive content, rumination, and positive affective switch costs are presented in Table 12. In Model 1, main effects emerged for maladaptive core beliefs, rumination, and positive affective switch costs on changes in inflammation. Greater core beliefs and lower rumination predicted increases in inflammation. Consistent with hypotheses, positive affective switch costs predicted changes in cytokines, such that individuals who took longer switching to the affective

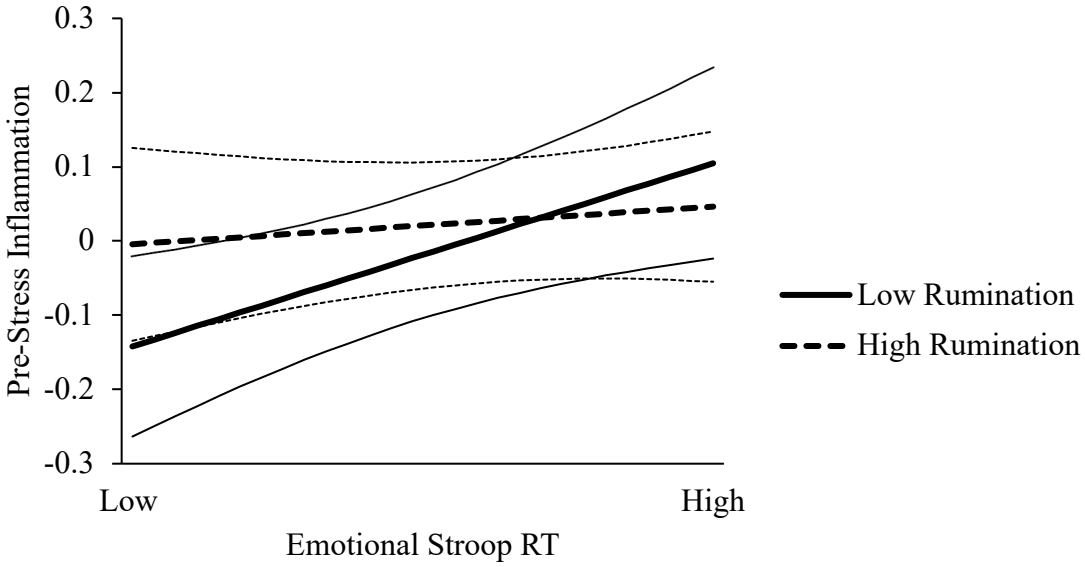

Figure 9. Marginally significant interaction effect between Emotional Stroop reaction time and rumination on pre-stress cytokines. Prestress Inflammation = latent factor of baseline inflammation. RT = reaction time. 'Low' and 'High' Emotional Stroop reaction time and rumination indicate scores one standard deviation below and above the mean, respectively. The thinner lines represent 95% confidence intervals.

Table 11

Prediction of Latent Pre-stress Cytokines and Latent Change in Cytokines by Emotional Stroop and Cognitive Organization

	Pre-stress inflammation			Δ inflammation		
Model and predictor	β	95% CI	*b*	β	95% CI	*b*
Model 1: Main effects		$R^2 = .27$, $p < .001$			$R^2 = .10$, $p = .060$	
Age	.05	[-.13, .24]	.002	.09	[-.15, .32]	.002
BMI	.25**	[.09, .41]	.02	-.02	[-.20, .15]	-.001
Ethnicity						
White vs. Other	-.16†	[-.33, .002]	-.22	.07	[-.18, .31]	.04
White vs. Asian	-.19*	[-.38, -.002]	-.17	-.12	[-.35, .11]	-.05
Negative Social Organization	.12	[-.09, .31]	.12	.19†	[-.01, .40]	.09
Negative Achievement Organization	-.25*	[-.44, -.06]	-.20	.07	[-.14, .29]	.03
Emotional Stroop RT	.19*	[.02, .36]	.06	-.01	[-.21, .19]	-.001
Model 2: Interaction effect		$R^2 = .28$, $p < .001$			$R^2 = .10$, $p = .043$	
Negative Social Organization × Emotional Stroop RT	-.09	[-.23, .05]	-.08	-.08	[-.23, .08]	-.03
Model 3: Interaction effect		$R^2 = .27$, $p < .001$			$R^2 = .10$, $p = .061$	
Negative Achievement Organization × Emotional Stroop RT	-.04	[-.19, .11]	-.02	.00	[-.17, .17]	.00

Note. 95% CI = 95% confidence intervals for standardized coefficients (βs). Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1. Values of .00 are < .001. Model fit: Model 1, $\chi^2(61, N = 127) = 140.57$, $p < .001$, CFI = .938, TLI = .914 and RMSEA = .101, SRMR = .134; Model 2, $\chi^2(67, N = 127) = 143.25$, $p < .001$, CFI = .941, TLI = .919 and RMSEA = .095, SRMR = .130; Model 3, $\chi^2(67, N = 127) = 143.57$, $p < .001$, CFI = .940, TLI = .918 and RMSEA = .095, SRMR = .129.
†$p < .10$; *$p < .05$; **$p < .01$; ***$p < .001$.

Table 12

Prediction of Latent Pre-stress Cytokines and Latent Change in Cytokines by Positive Affective Switch Costs, Negative Cognitive Content, and Rumination

	Pre-stress inflammation			Δ inflammation		
Model and predictor	β	95% CI	*b*	β	95% CI	*b*
Model 1: Main effects		R^2 = .21, *p* = .001			R^2 = .19, *p* = .007	
Age	.06	[-.10, .22]	.003	.17†	[-.03, .37]	.004
BMI	.33***	[.18, .48]	.02	-.05	[-.22, .12]	-.002
Ethnicity						
White vs. Other	-.05	[-.21, .10]	-.07	.15†	[-.01, .32]	.08
White vs. Asian	-.19*	[-.36, -.02]	-.16	-.02	[-.22, .19]	-.01
Core Beliefs	-.11	[-.39, .16]	-.001	.28*	[.00, .57]	.001
Dysfunctional Attitudes	.02	[-.20, .23]	.00	-.21†	[-.45, .03]	-.001
Rumination	.04	[-.16, .24]	.001	-.31**	[-.52, -.11]	-.004
Positive Affective Switch Costs	.04	[-.12, .20]	.01	.25**	[.07, .44]	.03
Model 2: Interaction effect		R^2 = .22, *p* = .001			R^2 = .20, *p* = .003	
Core Beliefs × Positive Affective Switch Costs	.10	[-.07, .26]	.00	-.11	[-.30, .08]	.00
Model 3: Interaction effect		R^2 = .21, *p* = .001			R^2 = .19, *p* = .008	
Dysfunctional Attitudes × Positive Affective Switch Costs	-.04	[-.17, .09]	.00	.03	[-.10, .16]	.00
Model 4: Interaction effect		R^2 = .26, *p* < .001			R^2 = .27, *p* < .001	
Rumination × Positive Affective Switch Costs	.25**	[.10, .40]	.004	-.32***	[-.49, -.15]	-.002

Note. 95% CI = 95% confidence intervals for standardized coefficients (βs). Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1. Values of .00 are < .001. Model fit: Model 1, $\chi^2(67, N = 165) = 170.14$, $p < .001$, CFI = .937, TLI = .914 and RMSEA = .097, SRMR = .115; Model 2, $\chi^2(73, N = 165) = 184.62$, $p < .001$, CFI = .933, TLI = .908 and RMSEA = .096, SRMR = .111; Model 3, $\chi^2(73, N = 165) = 178.33$, $p < .001$, CFI = .937, TLI = .914 and RMSEA = .094, SRMR = .112; Model 4, $\chi^2(73, N = 165) = 179.69$, $p < .001$, CFI = .937, TLI = .913 and RMSEA = .094, SRMR = .111.

$^{\dagger}p < .10$; $^{*}p < .05$; $^{**}p < .01$; $^{***}p < .001$.

categorization rule for positive images demonstrated greater increases in cytokines following stress. Furthermore, and contrary to hypotheses, there was a trend whereby lower levels of dysfunctional attitudes were associated with decreases in inflammation after the stressor.

There was no evidence of moderation by core beliefs or dysfunctional attitudes on the relation of positive affective switch costs with pre-stress or post-stress changes in inflammation in Model 2. However, in Model 3 significant interactions of rumination with positive affective switch costs on both baseline and post-stress changes in cytokines emerged. Further examination of the interaction on pre-stress inflammation revealed that rumination moderated the relation of positive affective switch costs on baseline inflammation for individuals with both high and low rumination. As anticipated, greater positive affective switch costs were associated with greater baseline inflammation in individuals high in rumination (b = .05, 95% CI = [.01, .09], p = .009), and, unexpectedly, greater switch costs were associated with lower baseline cytokines in individuals with low rumination (b = -.06, 95% CI = [-.12, -.01], p = .031; Figure 10). In contrast, examination of the simple slopes for the significant interaction of rumination and positive affective switch costs on acute inflammatory responses to stress indicated that positive affective switch costs were associated with greater increases in inflammation only in individuals with low (b = .07, 95% CI = [.04, .09], p < .001), and not high (b = -.001, 95% CI = [-.02, .02], p = .924) rumination (Figure 11).

Cognitive organization. Table 13 presents estimates from the conditional models predicting baseline and stress-induced changes in cytokines by negative cognitive organization and positive affective switch costs. Consistent with findings reported above, in Model 1 there was a main effect of negative achievement organization on baseline inflammation such that more tightly connected structure was associated with greater pre-stress cytokines. There was also a

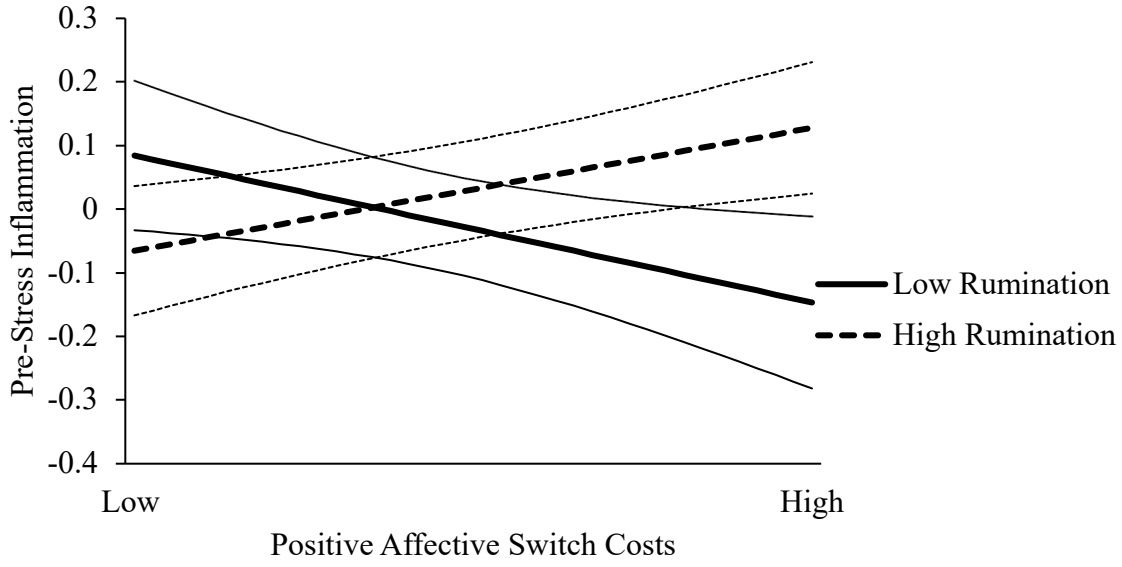

Figure 10. Interaction effect between Positive Affective Switch Costs and rumination on pre-stress cytokines. Prestress Inflammation = latent factor of baseline inflammation. 'Low' and 'High' Positive Affective Switch Costs and rumination indicate scores one standard deviation below and above the mean, respectively. The thinner lines represent 95% confidence intervals. The lower and upper bounds of the regions of significance on rumination were -0.74 *SD* and 0.63 *SD* from the mean. These values indicate that Positive Affective Switch Costs were associated with greater inflammation among individuals with rumination >0.63 *SD* from the mean, but with lower inflammation among individuals with Positive Affective Switch Costs lower than 0.74 *SD* below the mean.

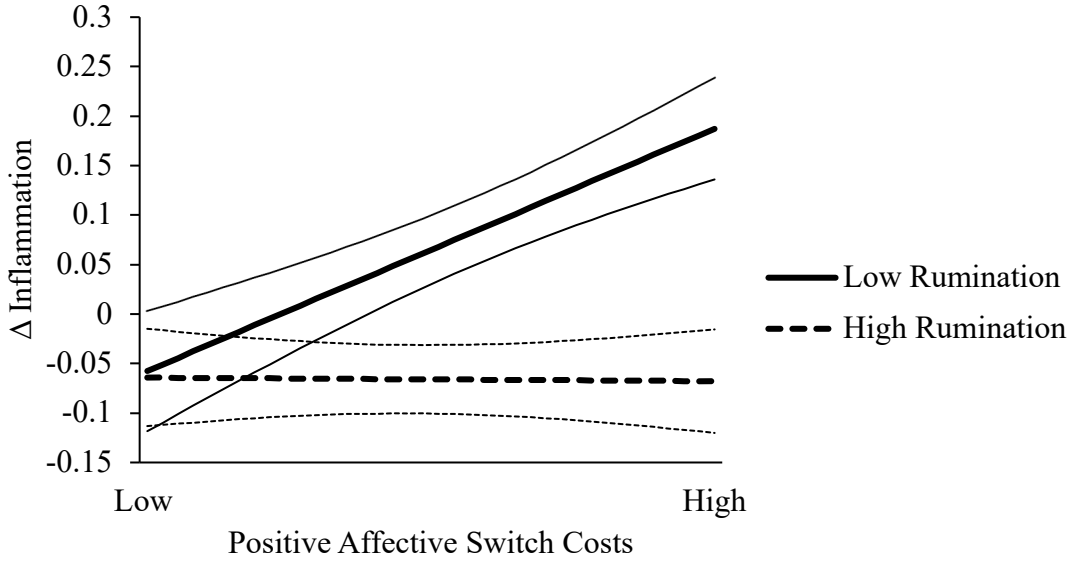

Figure 11. Interaction effect between Positive Affective Switch Costs and rumination on acute responses to the laboratory stressor. Change in Inflammation = latent change score for inflammation. 'Low' and 'High' Positive Affective Switch Costs and rumination indicate scores one standard deviation below and above the mean, respectively. The thinner lines represent 95% confidence intervals. The region of significance on rumination was 0.50 *SD* above the mean. This value indicates that Positive Affective Switch Costs were associated with increases in inflammation among individuals with rumination <0.50 *SD* above the mean, but was not associated with inflammation for individuals with rumination >0.50 *SD* above the mean.

Table 13

Prediction of Latent Pre-stress Cytokines and Latent Change in Cytokines by Positive Affective Switch Costs and Cognitive Organization

	Pre-stress inflammation			Δ inflammation		
Model and predictor	β	95% CI	*b*	β	95% CI	*b*
Model 1: Main effects		R^2 = .25, p < .001			R^2 = .15, p = .049	
Age	.10	[-.08, .29]	.004	.05	[-.16, .25]	.001
BMI	.25**	[.09, .41]	.02	-.03	[-.20, .15]	-.001
Ethnicity						
White vs. Other	-.12†	[-.27, .02]	-.17	.09	[-.14, .32]	.05
White vs. Asian	-.19†	[-.38, .01]	-.16	-.10	[-.32, .13]	-.04
Negative Social Organization	.11	[-.10, .31]	.11	.19*	[.00, .38]	.08
Negative Achievement Organization	-.24*	[-.43, -.06]	-.19	.09	[-.12, .29]	.03
Positive Affective Switch Costs	.09	[-.08, .26]	.02	.23*	[.02, .44]	.02
Model 2: Interaction effect		R^2 = .25, p < .001			R^2 = .21, p = .011	
Negative Social × Positive Affective Switch Costs	-.06	[-.23, .11]	-.03	.27**	[.08, .45]	.06
Model 3: Interaction effect		R^2 = .25, p = .001			R^2 = .19, p = .01	
Negative Achievement × Positive Affective Switch Costs	-.03	[-.16, .10]	-.01	.20*	[.03, .38]	.04

Note. 95% CI = 95% confidence intervals for standardized coefficients (βs). Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1. Values of .00 are < .001. Model fit: Model 1, $\chi^2(61, N = 127) = 141.17$, $p < .001$, CFI = .937, TLI = .914 and RMSEA = .102, SRMR = .133; Model 2, $\chi^2(67, N = 127) = 145.55$, $p < .001$, CFI = .940, TLI = .917 and RMSEA = .096, SRMR = .125; Model 3, $\chi^2(67, N = 127) = 148.22$, $p < .001$, CFI = .937, TLI = .914 and RMSEA = .098, SRMR = .126.
$^{\dagger}p < .10$; $^{*}p < .05$; $^{**}p < .01$; $^{***}p < .001$.

main effect of negative social organization on changes in inflammation, such that more dispersed structure was related to greater increases in inflammation. Positive affective switch costs predicted changes in inflammation following stress, such that individuals who took longer switching away from using the nonaffective categorization rule to using the affective rule for positive images demonstrated greater increases in cytokines following stress.

In Model 2, there was a significant interaction of negative social organization with positive affective switch costs on changes in inflammation. An examination of the simple slopes of the interaction indicated that greater positive affective switch costs were associated with greater increases in cytokines in response to the laboratory stressor for individuals with loosely interconnected (b = .04, 95% CI = [.02, .06], p < .001), and not tightly interconnected (b = -.01, 95% CI = [-.04, .02], p = .487), schemas (Figure 12). There was no interaction of negative social schemas with positive affective switch costs on pre-stress inflammation.

Similarly, in Model 3 there was an interaction of negative achievement organization on changes in inflammation, but not on pre-stress inflammation. Probing the interaction revealed a similar pattern of findings as for negative social organization, such that positive affective switch costs were associated with greater increases in inflammation following stress in individuals with loosely connected (b = .05, 95% CI = [.03, .07], p < .001), and not tightly interconnected (b = -.02, 95% CI = [-.05, .02], p = .307), schema structure (Figure 13).

Negative Affective Switch Costs. ***Cognitive content and rumination.*** Parameter estimates from the conditional models predicting baseline and stress-induced changes in cytokines by negative cognitive content, rumination, and negative affective switch costs are presented in Table 14. There were no main effects of cognitive content, rumination, or negative affective switch costs on pre-stress inflammation in Model 1. However, greater maladaptive core

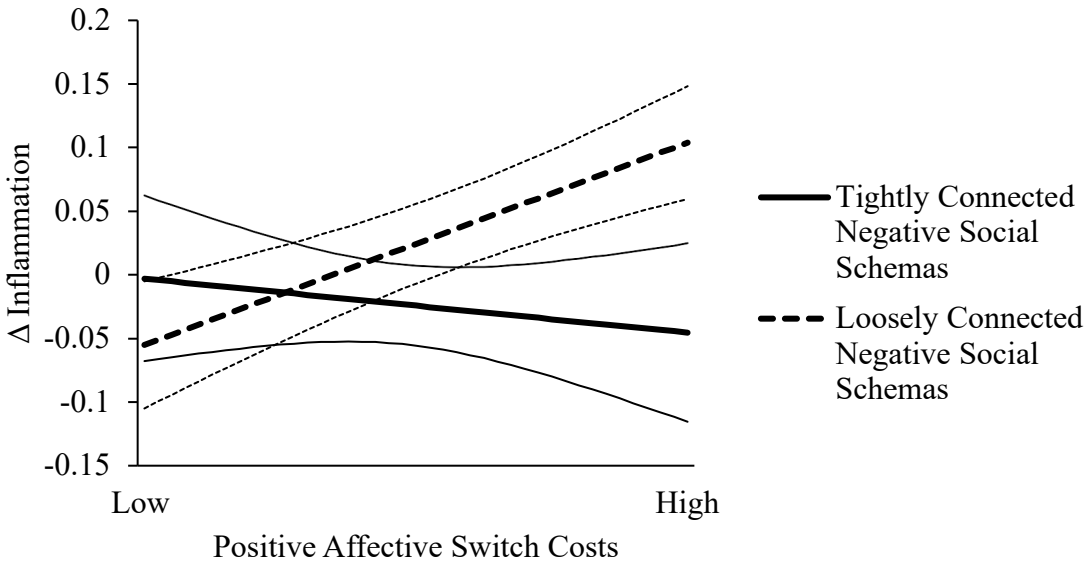

Figure 12. Interaction effect between Positive Affective Switch Costs and Negative Social Organization on acute responses to the laboratory stressor. Change in Inflammation = latent change score for inflammation. 'Low' and 'High' Positive Affective Switch Costs and Negative Social Organization indicate scores one standard deviation below and above the mean, respectively. The thinner lines represent 95% confidence intervals. The region of significance on negative social organization was 0.16 *SD* above the mean. This value indicates that Positive Affective Switch Costs were associated with increases in inflammation among individuals with negative social schemas >0.15 *SD* above the mean (i.e., more dispersed schemas), but was not associated with inflammation for individuals with social schemas <0.15 *SD* above the mean.

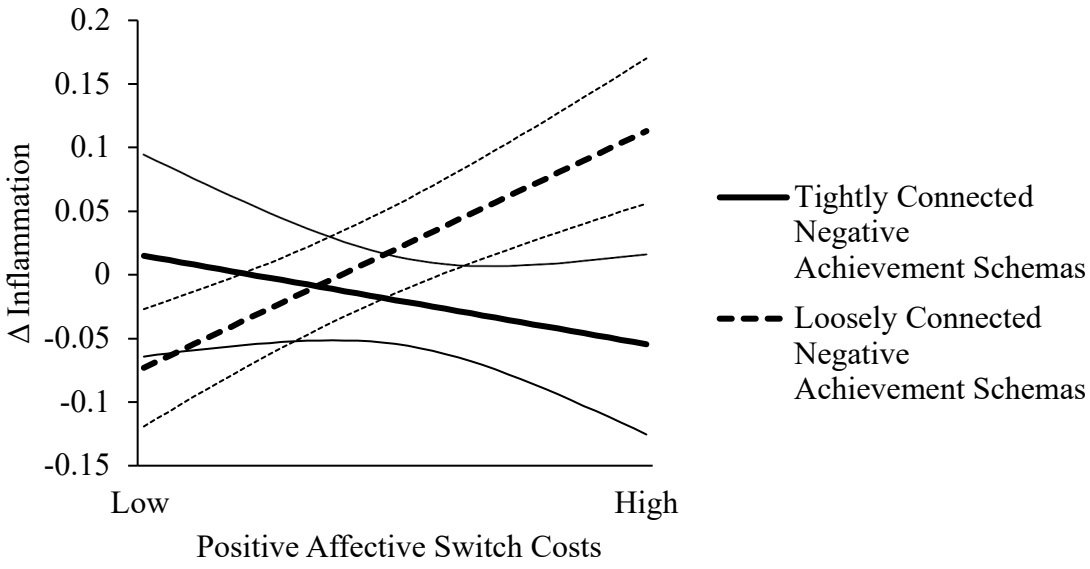

Figure 13. Interaction effect between Positive Affective Switch Costs and Negative Achievement Organization on acute responses to the laboratory stressor. Change in Inflammation = latent change score for inflammation. 'Low' and 'High' Positive Affective Switch Costs and Negative Achievement Organization indicate scores one standard deviation below and above the mean, respectively. The thinner lines represent 95% confidence intervals. The region of significance on negative achievement organization was -0.08 *SD* from the mean. This value indicates that Positive Affective Switch Costs were associated with increases in inflammation among individuals with negative social schemas >0.08 *SD* below the mean (i.e., more dispersed schemas), but was not associated with inflammation for individuals with social schemas <0.08 *SD* below the mean.

Table 14

Prediction of Latent Pre-stress Cytokines and Latent Change in Cytokines by Negative Affective Switch Costs, Negative Cognitive Content, and Rumination

	Pre-stress inflammation			Δ inflammation		
Model and predictor	β	95% CI	*b*	β	95% CI	*b*
Model 1: Main effects		R^2 = .22, p < .001			R^2 = .14, p = .011	
Age	.09	[-.07, .25]	.004	.19†	[-.01, .40]	.004
BMI	.33***	[.18, .48]	.02	-.06	[-.24, .12]	-.002
Ethnicity						
White vs. Other	-.05	[-.20, .11]	-.06	.12	[-.05, .29]	.07
White vs. Asian	-.19*	[-.35, -.02]	-.16	-.05	[-.26, .16]	-.02
Core Beliefs	-.15	[-.42, .13]	-.001	.33*	[.03, .63]	.001
Dysfunctional Attitudes	.05	[-.16, .26]	.001	-.22†	[-.47, .04]	-.001
Rumination	.06	[-.14, .26]	.002	-.34**	[-.55, -.14]	-.004
Negative Affective Switch Costs	-.12	[-.27, .03]	-.03	.13†	[-.02, .27]	.01
Model 2: Interaction effect		R^2 = .22, p < .001			R^2 = .14, p = .012	
Core Beliefs × Negative Affective Switch Costs	.03	[-.15, .21]	.00	.02	[-.15, .19]	.00
Model 3: Interaction effect		R^2 = .23, p < .001			R^2 = .15, p = .011	
Dysfunctional Attitudes × Negative Affective Switch Costs	.05	[-.11, .22]	.00	.05	[-.10, .21]	.00
Model 4: Interaction effect		R^2 = .23, p < .001			R^2 = .14, p = .011	
Rumination × Negative Affective Switch Costs	.07	[-.08, .21]	.001	-.03	[-.16, .11]	.00

Note. 95% CI = 95% confidence intervals for standardized coefficients (βs). Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1. Values of .00 are < .001. Model fit: Model 1, $\chi^2(67, N = 165) = 163.81$, $p < .001$, CFI = .940, TLI = .918 and RMSEA = .094, SRMR = .115; Model 2, $\chi^2(73, N = 165) = 167.75$, $p < .001$, CFI = .941, TLI = .920 and RMSEA = .089, SRMR = .111; Model 3, $\chi^2(73, N = 165) = 174.54$, $p < .001$, CFI = .938, TLI = .915 and RMSEA = .092, SRMR = .111; Model 4, $\chi^2(73, N = 165) = 167.47$, $p < .001$, CFI = .942, TLI = .921 and RMSEA = .089, SRMR = .111.

$^{\dagger}p < .10$; $^{*}p < .05$; $^{**}p < .01$; $^{***}p < .001$.

beliefs predicted increases in inflammation following stress and greater rumination predicted decreases in cytokines post-stress. Trends also emerged whereby greater dysfunctional attitudes marginally predicted decreases in inflammation and, consistent with hypotheses, greater negative affective switch costs marginally predicted increases in cytokines. This indicates that taking longer to switch away from using the nonaffective categorization rule to using the affective rule for negative images was marginally associated with greater increases in cytokines following stress. In Models 2, 3, and 4, there were no significant interactions between core beliefs, dysfunctional attitudes, or rumination and negative affective switch costs on inflammation, either before or after the stressor.

Cognitive organization. Table 15 presents estimates from the conditional models predicting baseline and stress-induced changes in cytokines by negative cognitive organization and negative affective switch costs. In Model 1 negative achievement cognitive structure predicted baseline inflammation, such that a more tightly interconnected organization was associated with greater cytokines pre-stress. More dispersed negative social organization predicted increases in inflammation following the stressor, and, as anticipated, greater negative affective switch costs marginally predicted greater stress-induced increases in inflammation.

In Model 2, there was a significant interaction of negative social structure with negative affective switch costs on changes in inflammation, but not on pre-stress inflammation. Probing this interaction indicated that greater negative affective switch costs were associated with greater increases in inflammation following the stressor in individuals with more loosely connected negative social cognitive structure (b = .04, 95% CI = [.02, .06], p = .001), and not in those with more tightly connected organization (b = -.01, 95% CI = [-.04, .02], p = .378; Figure 14).

Table 15

Prediction of Latent Pre-stress Cytokines and Latent Change in Cytokines by Negative Affective Switch Costs and Cognitive Organization

	Pre-stress inflammation			Δ inflammation		
Model and predictor	β	95% CI	*b*	β	95% CI	*b*
Model 1: Main effects		$R^2 = .26$, $p < .001$			$R^2 = .11$, $p = .051$	
Age	.15	[-.04, .34]	.01	.04	[-.18, .26]	.001
BMI	.25**	[.09, .41]	.02	-.03	[-.21, .14]	-.001
Ethnicity						
White vs. Other	-.13	[-.28, .03]	-.17	.06	[-.16, .28]	.04
White vs. Asian	-.18†	[-.38, .01]	-.16	-.13	[-.36, .11]	-.05
Negative Social Organization	.09	[-.12, .31]	.09	.21*	[.004, .42]	.09
Negative Achievement Organization	-.25*	[-.44, -.05]	-.20	.06	[-.14, .27]	.02
Negative Affective Switch Costs	-.13	[-.31, .05]	-.03	.16†	[-.02, .33]	.02
Model 2: Interaction effect		$R^2 = .26$, $p < .001$			$R^2 = .15$, $p = .019$	
Negative Social × Negative Affective Switch Costs	-.03	[-.20, .13]	-.02	.22**	[.06, .39]	.06
Model 3: Interaction effect		$R^2 = .26$, $p < .001$			$R^2 = .13$, $p = .023$	
Negative Achievement × Negative Affective Switch Costs	-.01	[-.19, .17]	-.004	.17†	[-.01, .34]	.02

Note. 95% CI = 95% confidence intervals for standardized coefficients (βs). Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1. Model fit: Model 1, $\chi^2(61, N = 126) = 138.19$, $p < .001$, CFI = .939, TLI = .916 and RMSEA = .100, SRMR = .129; Model 2, $\chi^2(67, N = 126) = 142.40$, $p < .001$, CFI = .941, TLI = .918 and RMSEA = .095, SRMR = .128; Model 3, $\chi^2(67, N = 126) = 142.89$, $p < .001$, CFI = .941, TLI = .919 and RMSEA = .095, SRMR = .124.
†$p < .10$; *$p < .05$; **$p < .01$; ***$p < .001$.

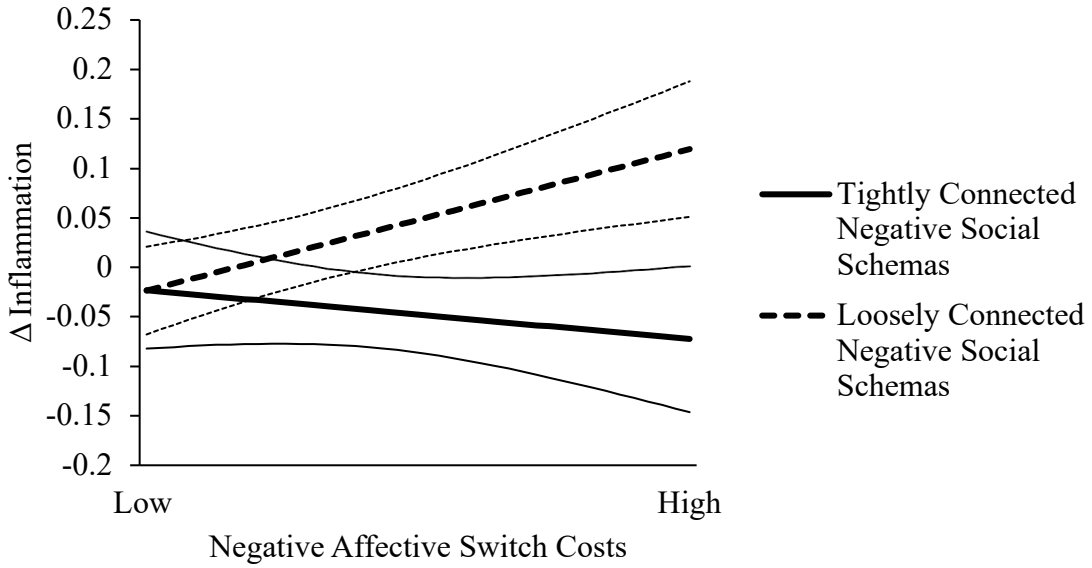

Figure 14. Interaction effect between Negative Affective Switch Costs and Negative Social Organization on acute responses to the laboratory stressor. Change in Inflammation = latent change score for inflammation. 'Low' and 'High' Negative Affective Switch Costs and Negative Social Organization indicate scores one standard deviation below and above the mean, respectively. The thinner lines represent 95% confidence intervals. The region of significance on negative social organization was 0.16 *SD* from the mean. This value indicates that Negative Affective Switch Costs were associated with increases in inflammation among individuals with negative social schemas >0.16 *SD* above the mean (i.e., more dispersed schemas), but was not associated with inflammation for individuals with social schemas <0.16 *SD* above the mean.

Negative achievement organization was also found to marginally interact with negative affective switch costs on changes in inflammation in Model 3. Similar to the findings for negative social structure, negative affective switch costs were related to greater increases in inflammation in individuals with more dispersed negative achievement organization (b = .02, 95% CI = [.01, .04], p = .003), and not those with highly interconnected schemas (b = -.002, 95% CI = [-.03, .02], p = .884; Figure 15). Negative achievement organization did not interact with negative affective switch costs on pre-stress cytokines.

Positive Nonaffective Switch Costs. ***Cognitive content and rumination.*** Table 16 presents estimates from the conditional models predicting baseline and stress-induced changes in cytokines by negative cognitive content, rumination, and positive nonaffective switch costs. There were no significant main effects of cognitive content, rumination, or positive nonaffective switch costs on baseline inflammation, contrary to hypotheses. However, lower rumination predicted greater post-stress increases in cytokines, and greater maladaptive core beliefs marginally predicted post-stress increases in cytokines.

There was no interaction of core beliefs with positive nonaffective switch costs in Model 2. In Model 3, there was a marginally significant interaction of dysfunctional attitudes with positive nonaffective switch costs on pre-stress inflammation. The simple slopes were not significant, but the direction of findings was such that as positive nonaffective switch costs increased, baseline inflammation tended to increase in individuals with high dysfunctional attitudes (b = .03, 95% CI = [-.01, .08], p = .132). The reverse was true for those with low dysfunctional attitudes (b = -.03, 95% CI = [-.07, .02], p = .311; Figure 16). A significant interaction of dysfunctional attitudes with positive nonaffective switch costs on changes in inflammation also emerged in Model 3. Neither simple slope was significant (b = .01, 95% CI =

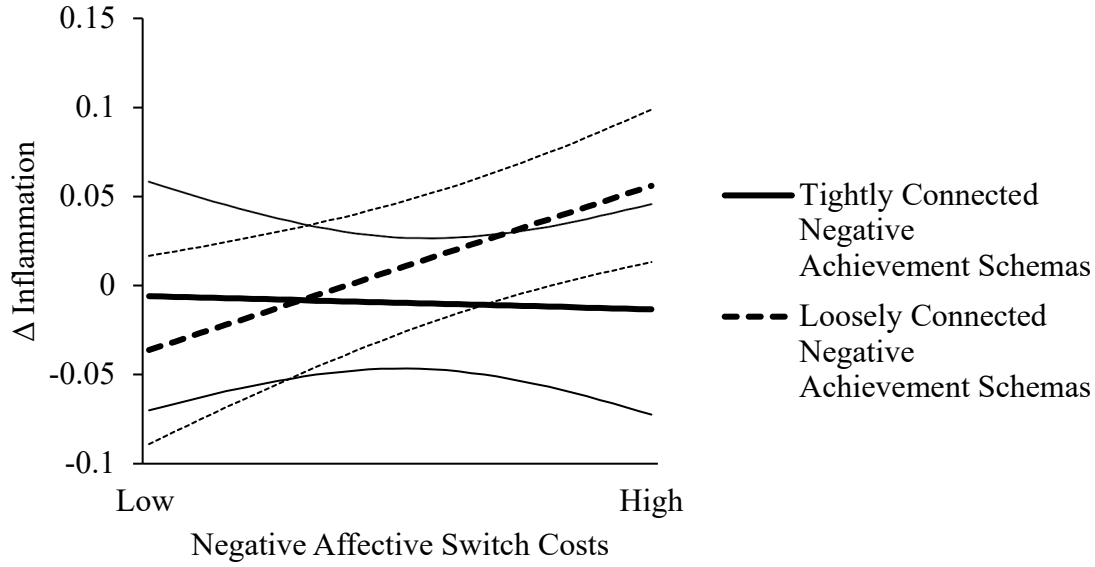

Figure 15. Marginally significant interaction effect between Negative Affective Switch Costs and Negative Achievement Organization on acute responses to the laboratory stressor. Change in Inflammation = latent change score for inflammation. 'Low' and 'High' Negative Affective Switch Costs and Negative Achievement Organization indicate scores one standard deviation below and above the mean, respectively. The thinner lines represent 95% confidence intervals.

Table 16

Prediction of Latent Pre-stress Cytokines and Latent Change in Cytokines by Positive Nonaffective Switch Costs, Negative Cognitive Content, and Rumination

	Pre-stress inflammation			Δ inflammation		
Model and predictor	β	95% CI	*b*	β	95% CI	*b*
Model 1: Main effects		R^2 = .21, *p* = .001			R^2 = .13, *p* = .013	
Age	.06	[-.10, .23]	.003	.21*	[.01, .41]	.004
BMI	.33***	[.17, .48]	.02	-.04	[-.23, .14]	-.001
Ethnicity						
White vs. Other	-.06	[-.22, .10]	-.07	.13	[-.04, .30]	.07
White vs. Asian	-.20*	[-.36, -.03]	-.17	-.05	[-.27, .16]	-.02
Core Beliefs	-.10	[-.38, .17]	-.001	.29†	[-.01, .59]	.001
Dysfunctional Attitudes	.003	[-.21, .22]	.00	-.19	[-.44, .06]	-.001
Rumination	.04	[-.17, .24]	.001	-.32**	[-.52, -.11]	-.004
Positive Nonaffective Switch Costs	.06	[-.11, .22]	.01	.02	[-.15, .18]	.002
Model 2: Interaction effect		R^2 = .21, *p* = .001			R^2 = .14, *p* = .011	
Core Beliefs × Positive Nonaffective Switch Costs	-.003	[-.18, .18]	.00	.10	[-.06, .26]	.00
Model 3: Interaction effect		R^2 = .23, *p* = .001			R^2 = .15, *p* = .005	
Dysfunctional Attitudes × Positive Nonaffective Switch Costs	.14†	[-.02, .30]	.001	.17*	[.01, .32]	.00
Model 4: Interaction effect		R^2 = .21, *p* = .001			R^2 = .13, *p* = .014	
Rumination × Positive Nonaffective Switch Costs	.03	[-.14, .19]	.00	.01	[-.20, .22]	.00

Note. 95% CI = 95% confidence intervals for standardized coefficients (βs). Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1. Model fit: Model 1, $\chi^2(67, N = 165) = 171.64$, $p < .001$, CFI = .936, TLI = .912 and RMSEA = .097, SRMR = .117; Model 2, $\chi^2(73, N = 165) = 178.18$, $p < .001$, CFI = .936, TLI = .913 and RMSEA = .093, SRMR = .113; Model 3, $\chi^2(73, N = 165) = 174.12$, $p < .001$, CFI = .938, TLI = .916 and RMSEA = .092, SRMR = .112; Model 4, $\chi^2(73, N = 165) = 174.11$, $p < .001$, CFI = .938, TLI = .915 and RMSEA = .092, SRMR = .113.

†$p < .10$; *$p < .05$; **$p < .01$; ***$p < .001$.

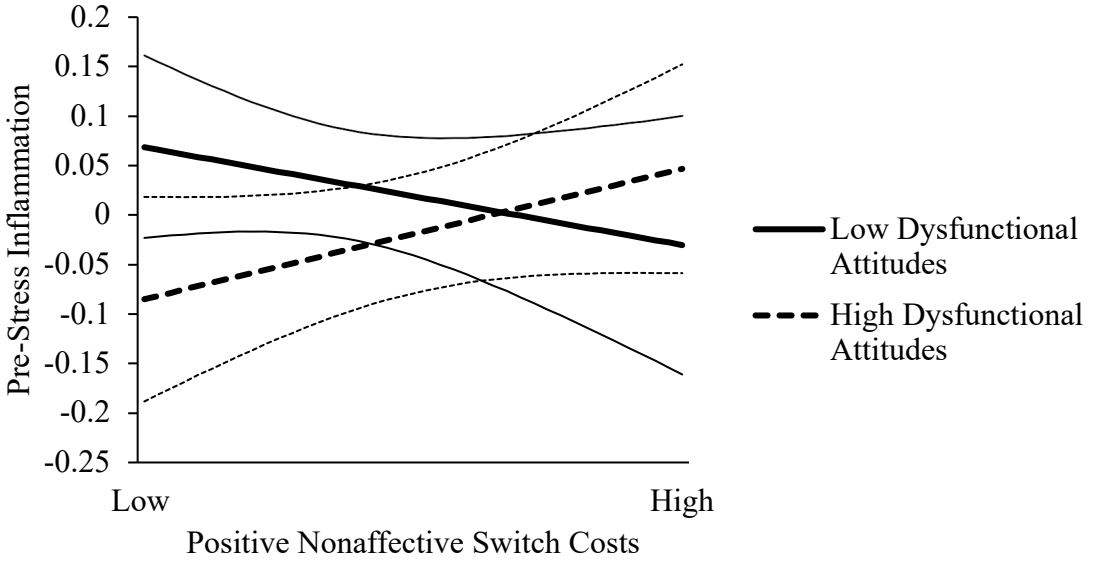

Figure 16. Marginally significant interaction effect between Positive Nonaffective Switch Costs and dysfunctional attitudes on pre-stress cytokines.Prestress Inflammation = latent factor of baseline inflammation. 'Low' and 'High' Positive Nonaffective Switch Costs and dysfunctional attitudes indicate scores one standard deviation below and above the mean, respectively. The thinner lines represent 95% confidence intervals.

[-.003, .03], p = .106 for those with high dysfunctional attitudes, b = -.02, 95% CI = [-.05, .01], p = .158 for those with low dysfunctional attitudes; Figure 17). However, the direction of slopes indicates that as positive nonaffective switch costs increased, inflammatory responses to stress tended to increase in those with high dysfunctional attitudes. Conversely, as switch costs increased, inflammatory responses to stress tended to decrease in those with low dysfunctional attitudes. Finally, in Model 4 there were no significant interactions of rumination with positive nonaffective switch costs on pre- or post-stress changes in cytokines.

Cognitive organization. Table 17 presents estimates from the conditional models predicting baseline and stress-induced changes in cytokines by negative cognitive organization and positive nonaffective switch costs. In Model 1, there were no main effects of positive nonaffective switch costs on baseline or stress-induced inflammation. Consistent with the results presented above, tightly interconnected negative achievement cognitive organization was associated with lower inflammation at baseline, and loosely connected negative social organization was marginally associated with increases in cytokines following stress.

In Model 2 there was no interaction of negative social organization with positive nonaffective switch costs on baseline or stress-induced changes in inflammation. However, in Model 3 there was a trend whereby negative achievement schemas marginally interacted with positive nonaffective switch costs on pre-stress inflammation. The simple slopes were not significant, however there was a trend for simple slopes to indicate that as positive nonaffective switch costs increased, baseline inflammation tended to increase for individuals with tightly connected negative achievement schemas (b = .03, 95% CI = [-.02, .07], p = .199). For those with loosely interconnected negative achievement schemas, as positive nonaffective switch costs

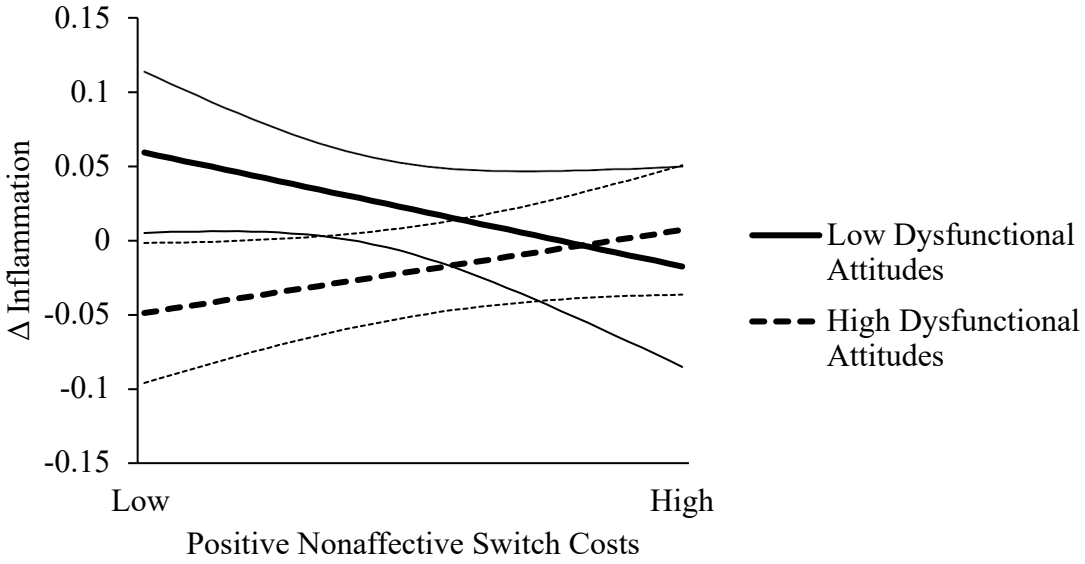

Figure 17. Interaction effect between Positive Nonaffective Switch Costs and dysfunctional attitudes on acute responses to the laboratory stressor. Change in Inflammation = latent change score for inflammation. 'Low' and 'High' Positive Nonaffective Switch Costs and dysfunctional attitudes indicate scores one standard deviation below and above the mean, respectively. The thinner lines represent 95% confidence intervals. As neither simple slope was significant, regions of significance could not be examined.

Table 17

Prediction of Latent Pre-stress Cytokines and Latent Change in Cytokines by Positive Nonaffective Switch Costs and Cognitive Organization

	Pre-stress inflammation			Δ inflammation		
Model and predictor	β	95% CI	*b*	β	95% CI	*b*
Model 1: Main effects		$R^2 = .24$, $p < .001$			$R^2 = .10$, $p = .057$	
Age	.12	[-.06, .30]	.01	.08	[-.13, .30]	.002
BMI	.25**	[.09, .41]	.02	-.02	[-.20, .15]	-.001
Ethnicity						
White vs. Other	-.13	[-.29, .03]	-.18	.06	[-.17, .30]	.04
White vs. Asian	-.20*	[-.39, -.002]	-.17	-.12	[-.36, .11]	-.05
Negative Social Organization	.11	[-.09, .31]	.11	.19†	[-.02, .40]	.08
Negative Achievement Organization	-.25**	[-.43, -.07]	-.20	.08	[-.13, .29]	.03
Positive Nonaffective Switch Costs	.05	[-.13, .22]	.01	.05	[-.12, .22]	.01
Model 2: Interaction effect		$R^2 = .24$, $p < .001$			$R^2 = .10$, $p = .041$	
Negative Social × Positive Nonaffective Switch Costs	-.01	[-.16, .14]	-.01	-.07	[-.24, .09]	-.02
Model 3: Interaction effect		$R^2 = .25$, $p < .001$			$R^2 = .10$, $p = .058$	
Negative Achievement × Positive Nonaffective Switch Costs	-.12†	[-.25, .02]	-.04	.01	[-.15, .18]	.002

Note. 95% CI = 95% confidence intervals for standardized coefficients (βs). Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1. Model fit: Model 1, $\chi^2(61, N = 127) = 149.73$, $p < .001$, CFI = .931, TLI = .905 and RMSEA = .107, SRMR = .133; Model 2, $\chi^2(67, N = 127) = 157.75$, $p < .001$, CFI = .930, TLI = .904 and RMSEA = .103, SRMR = .128; Model 3, $\chi^2(67, N = 127) = 157.07$, $p < .001$, CFI = .931, TLI = .905 and RMSEA = .103, SRMR = .129.
†$p < .10$; *$p < .05$; **$p < .01$; ***$p < .001$.

increased, baseline inflammation tended to decrease (b = -.02, 95% CI = [-.06, .02], p = .349; Figure 18).

Negative Nonaffective Switch Costs. ***Cognitive content and rumination.*** Results from the conditional models predicting baseline and stress-induced changes in cytokines by negative cognitive content, rumination, and negative nonaffective switch costs are presented in Table 18. Contrary to hypotheses, there were no main effects of negative nonaffective switch costs on pre-stress or post-stress changes in cytokines in Model 1. Higher rumination was associated with decreases in inflammation following stress, and there was a trend whereby greater maladaptive core beliefs marginally predicted increases in stress.

In Models 2 and 3, there was no evidence of interaction effects between core beliefs or dysfunctional attitudes and negative nonaffective switch costs on inflammation. However, in Model 4 there was a marginally significant interaction of rumination with negative nonaffective switch costs on pre-stress cytokines. The simple slopes for this marginal interaction were nonsignificant, although the direction of effects suggest that among individuals high in rumination, as negative nonaffective switch costs increase, baseline inflammation also tends to increase (b = .02, 95% CI = [-.01, .06], p = .240). The opposite trend emerged for those with low rumination (b = -.04, 95% CI = [-.09, .02], p = .180; Figure 19).

Cognitive organization. Table 19 presents estimates from the conditional models predicting baseline and stress-induced changes in cytokines by negative cognitive organization and negative nonaffective switch costs. In Model 1 there was no main effect of negative nonaffective switch costs on inflammation. Tightly connected negative achievement organization predicted lower baseline cytokines, and loosely connected negative social organization marginally predicted increases in cytokines after stress. There was no evidence of interaction

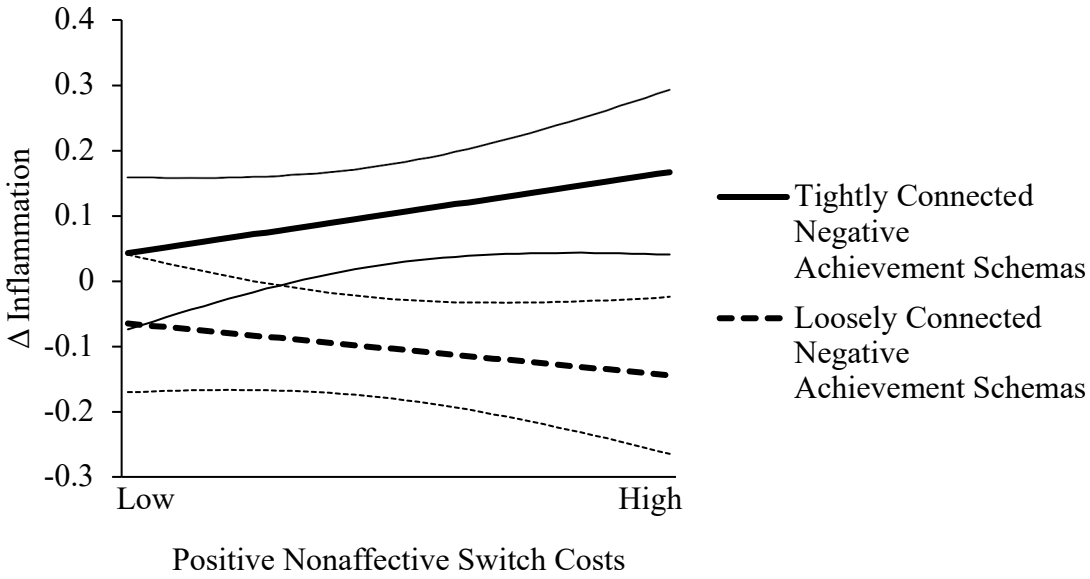

Figure 18. Marginally significant interaction effect between Positive Nonaffective Switch Costs and Negative Achievement Organization on pre-stress cytokines. Prestress Inflammation = latent factor of baseline inflammation. 'Low' and 'High' Positive Nonaffective Switch Costs and Negative Achievement Organization indicate scores one standard deviation below and above the mean, respectively. The thinner lines represent 95% confidence intervals.

Table 18

Prediction of Latent Pre-stress Cytokines and Latent Change in Cytokines by Negative Nonaffective Switch Costs, Negative Cognitive Content, and Rumination

	Pre-stress inflammation			Δ inflammation		
Model and predictor	β	95% CI	*b*	β	95% CI	*b*
Model 1: Main effects		R^2 = .21, *p* = .001			R^2 = .14, *p* = .011	
Age	.07	[-.09, .23]	.003	.20†	[.00, .39]	.004
BMI	.33***	[.17, .48]	.02	-.06	[-.25, .13]	-.002
Ethnicity						
White vs. Other	-.06	[-.21, .10]	-.07	.12	[-.05, .28]	.07
White vs. Asian	-.19*	[-.36, -.02]	-.16	-.06	[-.27, .15]	-.02
Core Beliefs	-.11	[-.38, .16]	-.001	.28†	[-.02, .58]	.001
Dysfunctional Attitudes	.02	[-.20, .23]	.00	-.18	[-.43, .06]	-.001
Rumination	.04	[-.16, .24]	.001	-.31**	[-.52, -.11]	-.004
Negative Nonaffective Switch Costs	.01	[-.15, .16]	.002	.09	[-.06, .24]	.01
Model 2: Interaction effect		R^2 = .21, *p* = .001			R^2 = .14, *p* = .010	
Core Beliefs × Negative Nonaffective Switch Costs	.08	[-.09, .25]	.00	-.04	[-.21, .13]	.00
Model 3: Interaction effect		R^2 = .21, *p* = .001			R^2 = .14, *p* = .008	
Dysfunctional Attitudes × Negative Nonaffective Switch Costs	.05	[-.10, .20]	.00	.10	[-.04, .24]	.00
Model 4: Interaction effect		R^2 = .22, *p* < .001			R^2 = .14, *p* = .010	
Rumination × Negative Nonaffective Switch Costs	.14†	[-.01, .29]	.002	-.02	[-.20, .16]	.00

Note. 95% CI = 95% confidence intervals for standardized coefficients (βs). Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1. Values of .00 are < .001. Model fit: Model 1, $\chi^2(67, N = 165) = 170.59$, $p < .001$, CFI = .937, TLI = .914 and RMSEA = .097, SRMR = .117; Model 2, $\chi^2(73, N = 165) = 178.14$, $p < .001$, CFI = .937, TLI = .914 and RMSEA = .093, SRMR = .113; Model 3, $\chi^2(73, N = 165) = 175.69$, $p < .001$, CFI = .939, TLI = .916 and RMSEA = .092, SRMR = .113; Model 4, $\chi^2(73, N = 165) = 188.47$, $p < .001$, CFI = .932, TLI = .907 and RMSEA = .098, SRMR = .115.

$^{\dagger}p < .10$; $^{*}p < .05$; $^{**}p < .01$; $^{***}p < .001$.

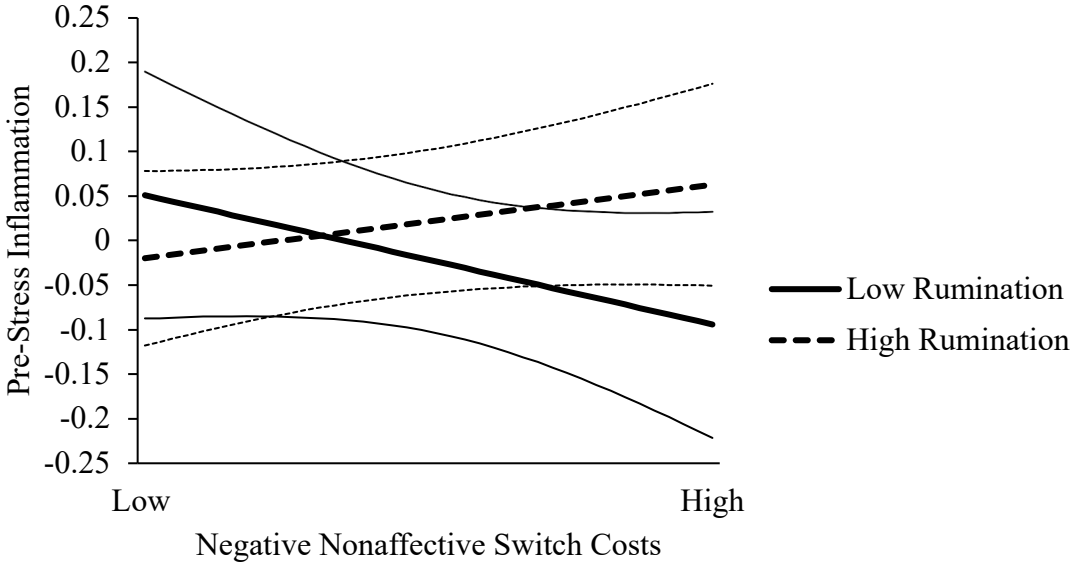

Figure 19 Marginally significant interaction effect between Negative Nonaffective Switch Costs and rumination on pre-stress cytokines. Prestress Inflammation = latent factor of baseline inflammation. 'Low' and 'High' Negative Nonaffective Switch Costs and rumination indicate scores one standard deviation below and above the mean, respectively. The thinner lines represent 95% confidence intervals.

Table 19

Prediction of Latent Pre-stress Cytokines and Latent Change in Cytokines by Negative Nonaffective Switch Costs and Cognitive Organization

	Pre-stress inflammation			Δ inflammation		
Model and predictor	β	95% CI	*b*	β	95% CI	*b*
Model 1: Main effects		R^2 = .24, *p* = .001			R^2 = .10, *p* = .063	
Age	.12	[-.06, .30]	.01	.08	[-.13, .29]	.001
BMI	.25**	[.08, .41]	.02	-.03	[-.21, .14]	-.001
Ethnicity						
White vs. Other	-.13	[-.29, .03]	-.18	.07	[-.16, .29]	.04
White vs. Asian	-.19†	[-.39, .001]	-.17	-.12	[-.36, .11]	-.05
Negative Social Organization	.11	[-.09, .31]	.11	.19†	[-.02, .39]	.08
Negative Achievement Organization	-.25**	[-.44, -.07]	-.20	.07	[-.14, .28]	.02
Negative Nonaffective Switch Costs	.01	[-.17, .18]	.002	.05	[-.13, .23]	.004
Model 2: Interaction effect		R^2 = .24, *p* = .001			R^2 = .10, *p* = .066	
Negative Social × Negative Nonaffective Switch Costs	-.02	[-.17, .14]	-.01	.04	[-.14, .22]	.01
Model 3: Interaction effect		R^2 = .24, *p* < .001			R^2 = .10, *p* = .062	
Negative Achievement × Negative Nonaffective Switch Costs	-.001	[-.13, .13]	.00	.01	[-.18, .20]	.002

Note. 95% CI = 95% confidence intervals for standardized coefficients (βs). Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1. Values of .00 are < .001. Model fit: Model 1, $\chi^2(61, N = 127) = 140.04$, $p < .001$, CFI = .939, TLI = .916 and RMSEA = .101, SRMR = .133; Model 2, $\chi^2(67, N = 127) = 150.00$, $p < .001$, CFI = .937, TLI = .913 and RMSEA = .099, SRMR = .129; Model 3, $\chi^2(67, N = 127) = 149.25$, $p < .001$, CFI = .938, TLI = .914 and RMSEA = .098, SRMR = .128.
†$p < .10$; *$p < .05$; **$p < .01$; ***$p < .001$.

effects of negative nonaffective switch costs with negative social organization (Model 2) or with negative achievement organization (Model 3) on pre- or post-stress changes in cytokines.

Pre-stress N-back. ***Cognitive content and rumination.*** Estimates from the conditional models predicting baseline and stress-induced changes in cytokines by negative cognitive content, rumination, and pre-stress N-back errors are presented in Table 20. In Model 1, pre-stress updating did not predict pre-stress or post-stress changes in cytokines, contrary to expectations. Greater maladaptive core beliefs and lower rumination predicted stress-induced increases in cytokines, and greater dysfunctional attitudes marginally predicted decreases in cytokines following stress. In Models 2, 3, and 4, there was no evidence of interaction effects of core beliefs, dysfunctional attitudes, or rumination with pre-stress N-back errors on inflammation.

Cognitive organization. Table 21 presents findings from the conditional models predicting baseline and stress-induced changes in cytokines by negative cognitive organization and pre-stress cytokines. There was no main effect of pre-stress N-back errors on baseline cytokines or on acute inflammatory responses to the stressor in Model 1. Tightly connected negative achievement organization predicted greater baseline inflammation, and more dispersed negative social schemas predicted greater increases in inflammation following the stressor.

In Model 2, a significant interaction between negative social organization and pre-stress cytokines on changes in inflammation was revealed. Examination of the simple slopes indicated that there was a trend whereby more errors on the N-back at baseline were related to greater increases in inflammation among individuals with tightly interconnected negative social schemas (b = .003, 95% CI = [-.001, .01], p = .095), but not those with loosely connected negative social organization (b = -.002, 95% CI = [-.01, .002], p = .285; Figure 20). There was no moderating

Table 20

Prediction of Latent Pre-stress Cytokines and Latent Change in Cytokines by Pre-stress N-back Errors, Negative Cognitive Content, and Rumination

	Pre-stress inflammation			Δ inflammation		
Model and predictor	β	95% CI	*b*	β	95% CI	*b*
Model 1: Main effects		R^2 = .21, *p* = .001			R^2 = .16, *p* = .006	
Age	.04	[-.13, .21]	.002	.22*	[.01, .43]	.01
BMI	.33***	[.18, .49]	.02	-.04	[-.23, .15]	-.001
Ethnicity						
White vs. Other	-.04	[-.21, .12]	-.05	.10	[-.08, .27]	.06
White vs. Asian	-.18*	[-.34, -.01]	-.15	-.05	[-.26, .17]	-.02
Core Beliefs	-.14	[-.43, .15]	-.001	.31*	[.003, .61]	.001
Dysfunctional Attitudes	.02	[-.21, .24]	.00	-.21†	[-.46, .04]	-.001
Rumination	.05	[-.16, .27]	.001	-.33**	[-.55, -.12]	-.004
Pre-stress N-Back Errors	.09	[-.05, .24]	.003	.11	[-.06, .28]	.002
Model 2: Interaction effect		R^2 = .21, *p* = .001			R^2 = .16, *p* = .004	
Core Beliefs × Pre-stress N-Back Errors	.05	[-.08, .18]	.00	.08	[-.05, .22]	.00
Model 3: Interaction effect		R^2 = .21, *p* = .001			R^2 = .16, *p* = .006	
Dysfunctional Attitudes × Pre-stress N-Back Errors	.07	[-.06, .20]	.00	.06	[-.09, .21]	.00
Model 4: Interaction effect		R^2 = .21, *p* = .001			R^2 = .16, *p* = .006	
Rumination × Pre-stress N-Back Errors	.04	[-.07, .16]	.00	.003	[-.14, .15]	.00

Note. 95% CI = 95% confidence intervals for standardized coefficients (βs). Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1. Values of .00 are < .001. Model fit: Model 1, $\chi^2(67, N = 159) = 175.34$, $p < .001$, CFI = .932, TLI = .907 and RMSEA = .101, SRMR = .117; Model 2, $\chi^2(73, N = 159) = 180.78$, $p < .001$, CFI = .933, TLI = .909 and RMSEA = .096, SRMR = .114; Model 3, $\chi^2(73, N = 159) = 181.42$, $p < .001$, CFI = .933, TLI = .908 and RMSEA = .097, SRMR = .114; Model 4, $\chi^2(73, N = 159) = 178.85$, $p < .001$, CFI = .934, TLI = .910 and RMSEA = .095, SRMR = .113.

†$p < .10$; *$p < .05$; **$p < .01$; ***$p < .001$.

Table 21

Prediction of Latent Pre-stress Cytokines and Latent Change in Cytokines by Pre-stress N-back Errors and Cognitive Organization

	Pre-stress inflammation			Δ inflammation		
Model and predictor	β	95% CI	*b*	β	95% CI	*b*
Model 1: Main effects		R^2 = .23, *p* = .002			R^2 = .12, *p* = .036	
Age	.10	[-.10, .30]	.01	.09	[-.15, .33]	.002
BMI	.24**	[.08, .41]	.02	-.01	[-.20, .18]	.00
Ethnicity						
White vs. Other	-.11	[-.27, .04]	-.15	.05	[-.19, .30]	.03
White vs. Asian	-.17†	[-.37, .03]	-.14	-.13	[-.37, .10]	-.05
Negative Social Organization	.10	[-.11, .31]	.10	.22*	[.01, .42]	.10
Negative Achievement Organization	-.23*	[-.42, -.04]	-.18	.08	[-.13, .30]	.03
Pre-stress N-Back Errors	.12	[-.04, .29]	.004	.03	[-.15, .21]	.00
Model 2: Interaction effect		R^2 = .23, *p* = .002			R^2 = .14, *p* = .021	
Negative Social Organization × Pre-stress N-Back Errors	.04	[-.13, .21]	.003	-.17*	[-.31, -.02]	-.01
Model 3: Interaction effect		R^2 = .27, *p* = .002			R^2 = .13, *p* = .023	
Negative Achievement Organization × Pre-stress N-Back Errors	-.02	[-.20, .15]	-.002	-.10	[-.25, .05]	-.003

Note. 95% CI = 95% confidence intervals for standardized coefficients (βs). Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1. Values of .00 are < .001. Model fit: Model 1, $\chi^2(61, N = 121) = 143.32$, $p < .001$, CFI = .933, TLI = .908 and RMSEA = .106, SRMR = .138; Model 2, $\chi^2(67, N = 121) = 149.46$, $p < .001$, CFI = .935, TLI = .910 and RMSEA = .101, SRMR = .135; Model 3, $\chi^2(67, N = 121) = 155.59$, $p < .001$, CFI = .930, TLI = .903 and RMSEA = .105, SRMR = .135.
†$p < .10$; *$p < .05$; **$p < .01$; ***$p < .001$.

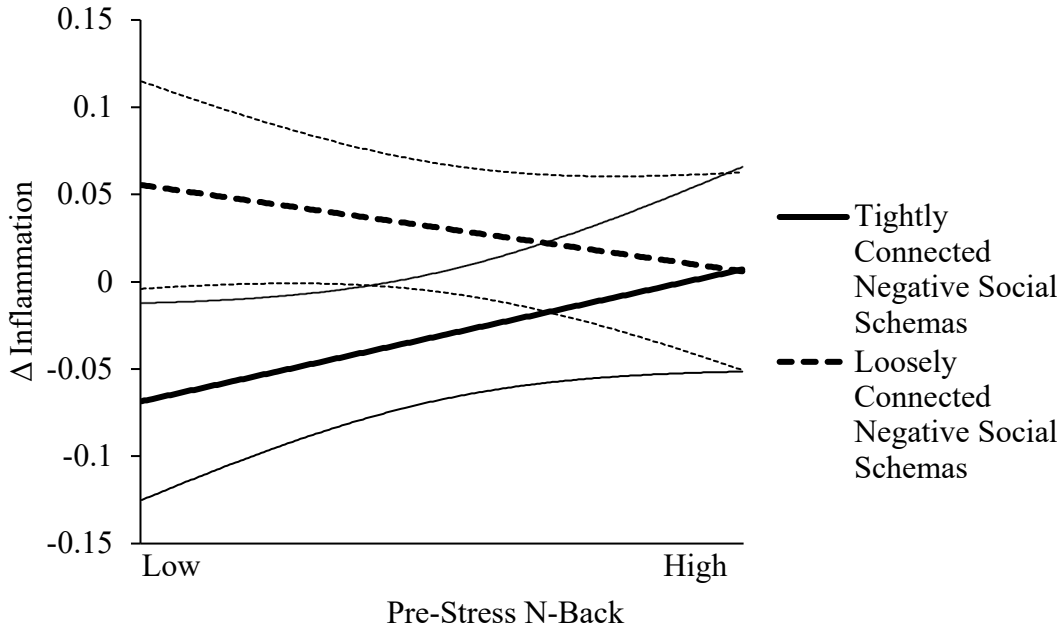

Figure 20. Interaction effect between Pre-stress N-back errors and Negative Social Organization on acute responses to the laboratory stressor. Change in Inflammation = latent change score for inflammation. 'Low' and 'High' Negative Nonaffective Switch Costs and rumination indicate scores one standard deviation below and above the mean, respectively. The thinner lines represent 95% confidence intervals. As neither simple slope was significant, regions of significance could not be examined.

effect of negative social organization on baseline inflammation. Further, there was no interaction effect of negative achievement organization with pre-stress N-back errors on inflammation in Model 3.

Post-stress N-Back. ***Cognitive content and rumination.*** Table 22 presents findings from the conditional models predicting baseline and stress-induced changes in cytokines by negative cognitive content, rumination, and post-stress N-back errors. In order to examine the influence of stress on updating abilities, baseline N-back errors were entered in the model as a covariate. In Model 1, greater maladaptive core beliefs and lower dysfunctional attitudes marginally predicted stress-induced increases in inflammation. Higher rumination was associated with decreases in inflammation following the TSST. Contrary to hypotheses, there was no main effect of post-stress N-back errors on pre-stress or post-stress changes in cytokines.

In Model 2, there was a marginally significant interaction of core beliefs with post-stress N-back errors on baseline inflammation. Examination of the simple slopes revealed a trend whereby increases in post-stress N-back errors was marginally associated with greater baseline inflammation in individuals with low (b = .01, 95% CI = [-.001, .02], p = .076), but not high (b = .001, 95% CI = [-.01, .01], p = .906), maladaptive core beliefs (Figure 21). Post-stress N-back errors did not interact with core beliefs on changes in inflammation.

There was a significant interaction of post-stress N-back errors with dysfunctional attitudes on baseline cytokines in Model 3. Probing this interaction indicated that greater post-stress N-back errors were associated with greater baseline inflammation in individuals with low (b = .01, 95% CI = [.00, .02], p = .044), but not high (b = -.002, 95% CI = [-.01, .01], p = .671), dysfunctional attitudes (Figure 22). Furthermore, there was also a marginally significant interaction of post-stress N-back errors with dysfunctional attitudes on post-stress changes in

Table 22

Prediction of Latent Pre-stress Cytokines and Latent Change in Cytokines by Post-stress N-back Errors, Negative Cognitive Content, and Rumination

	Pre-stress inflammation			Δ inflammation		
Model and predictor	β	95% CI	*b*	β	95% CI	*b*
Model 1: Main effects		R^2 = .22, *p* = .001			R^2 = .19, *p* = .003	
Age	.04	[-.14, .22]	.002	.21†	[-.004, .43]	.01
BMI	.37***	[.21, .53]	.02	-.002	[-.20, .20]	.00
Ethnicity						
White vs. Other	-.04	[-.20, .13]	-.05	.10	[-.07, .27]	.06
White vs. Asian	-.16†	[-.33, .01]	-.13	-.07	[-.28, .15]	-.03
Pre-stress N-Back Errors	.004	[-.21, .22]	.00	.06	[-.18, .31]	.001
Core Beliefs	-.07	[-.37, .23]	.00	.28†	[-.03, .59]	.001
Dysfunctional Attitudes	-.08	[-.31, .15]	-.001	-.21†	[-.45, .04]	-.001
Rumination	.03	[-.20, .25]	.001	-.35**	[-.58, -.12]	-.01
Post-stress N-Back Errors	.10	[-.11, .31]	.004	.10	[-.20, .39]	.002
Model 2: Interaction effect		R^2 = .24, *p* = .001			R^2 = .19, *p* = .002	
Core Beliefs × Post-stress N-Back Errors	-.12†	[-.25, .01]	.00	-.04	[-.25, .17]	.00
Model 3: Interaction effect		R^2 = .24, *p* = .001			R^2 = .21, *p* = .001	
Dysfunctional Attitudes × Post-stress N-Back Errors	-.14*	[-.27, -.01]	.00	-.15†	[-.32, .02]	.00
Model 4: Interaction effect		R^2 = .24, *p* = .001			R^2 = .19, *p* = .003	
Rumination × Post-stress N-Back Errors	-.13*	[-.26, -.001]	.00	.06	[-.11, .23]	.00

Note. 95% CI = 95% confidence intervals for standardized coefficients (βs). Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1. Values of .00 are < .001. Model fit: Model 1, $\chi^2(73, N = 147) = 179.42$, $p < .001$, CFI = .929, TLI = .903 and RMSEA = .100, SRMR = .122; Model 2, $\chi^2(79, N = 147) = 190.37$, $p < .001$, CFI = .927, TLI = .900 and RMSEA = .098, SRMR = .118; Model 3, $\chi^2(79, N = 147) = 189.69$, $p < .001$, CFI = .928, TLI =.902 and RMSEA =.098, SRMR =.116; Model 4, $\chi^2(79, N = 147) = 185.77$, $p < .001$, CFI = .930, TLI = .904 and RMSEA = .096, SRMR = .119.

$^{\dagger}p < .10$; $^{*}p < .05$; $^{**}p < .01$; $^{***}p < .001$.

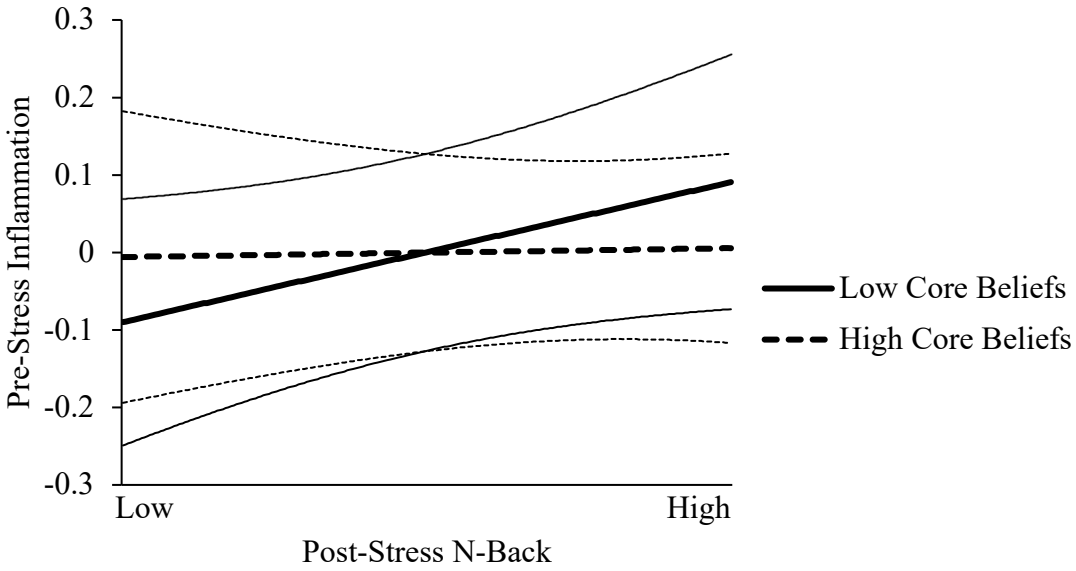

Figure 21. Marginally significant interaction effect between Post-stress N-back errors and maladaptive core beliefs on pre-stress cytokines. Prestress Inflammation = latent factor of baseline inflammation. 'Low' and 'High' Post-stress N-back errors and core beliefs indicate scores one standard deviation below and above the mean, respectively. The thinner lines represent 95% confidence intervals.

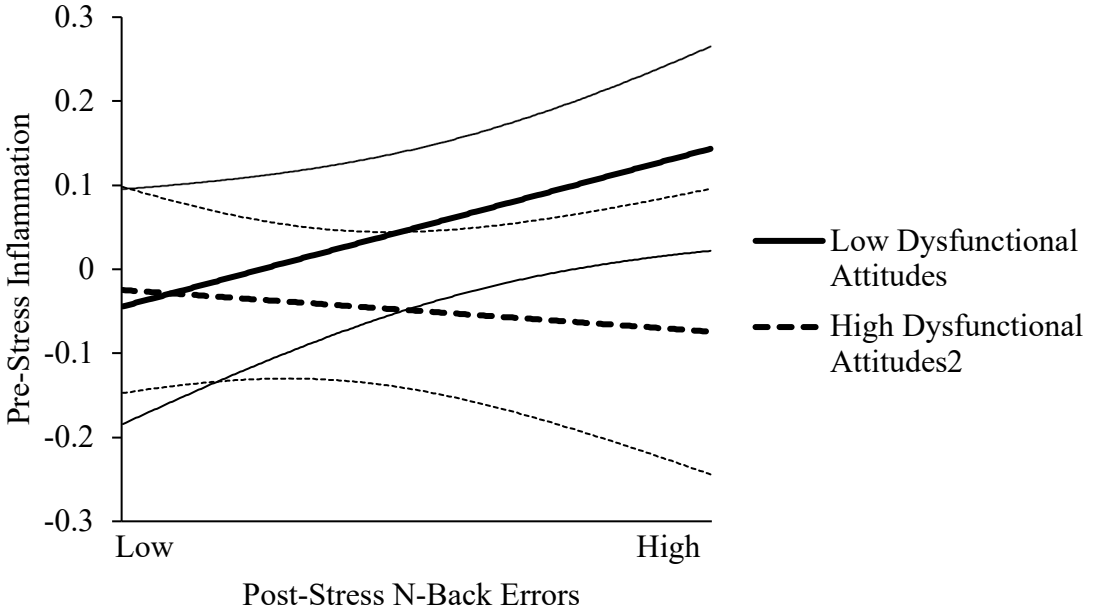

Figure 22. Interaction effect between Post-stress N-back errors and dysfunctional attitudes on pre-stress cytokines. Prestress Inflammation = latent factor of baseline inflammation. 'Low' and 'High' Post-stress N-back errors and dysfunctional attitudes indicate scores one standard deviation below and above the mean, respectively. The thinner lines represent 95% confidence intervals. The region of significance on dysfunctional attitudes was -0.98 *SD* from the mean. This value indicates that Post-stress N-back errors were associated with increases in inflammation among individuals with dysfunctional attitudes <0.98 *SD* below the mean, but was not associated with inflammation for individuals with dysfunctional attitudes >0.98 *SD* below the mean.

cytokines. Similar to the findings for baseline inflammation, there was a trend for simple slopes to indicate that greater post-stress N-back errors were associated with greater acute inflammatory responses to the stressor in individuals with low (b = .004, 95% CI = [.00, .01], p = .048), but not high (b = -.001, 95% CI = [-.01, .01], p = .700), dysfunctional attitudes (Figure 23).

In Model 3, a significant interaction of post-stress N-back errors with rumination on baseline cytokines emerged. Examination of the simple slopes revealed a trend whereby increases in post-stress N-back errors were marginally associated with greater baseline inflammation in individuals with a low (b = .01, 95% CI = [-.001, .02], p = .070), but not high (b = .00,[1] 95% CI = [-.01, .01], p = .973), tendency to ruminate (Figure 24). Rumination did not interact with post-stress N-back errors on stress-induced changes in inflammation.

Cognitive organization. Findings from the conditional models predicting baseline and stress-induced changes in cytokines by negative cognitive organization and post-stress N-back errors are presented in Table 23. Analyses controlled for baseline N-back errors in order to examine stress-induced changes in N-back performance. Tightly interconnected negative achievement organization was related to greater baseline inflammation, and more loosely interconnected negative social organization was associated with greater acute inflammatory responses to stress. There were no main effects of post-stress N-back errors on pre-stress or post-stress changes in cytokines.

In Model 2, there was a significant moderating effect of negative social organization with post-stress N-back errors on baseline inflammation. Further assessment of this interaction revealed that, whereas the simple slopes were not significant, the direction of association of post-

[1] b value is < .001.

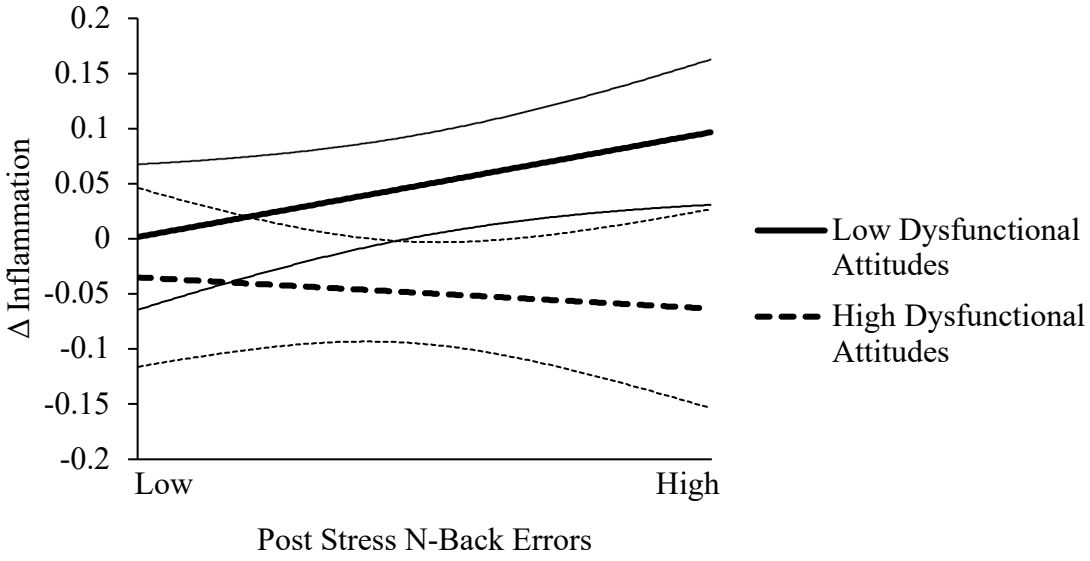

Figure 23. Marginally significant interaction effect between Post-stress N-back errors and dysfunctional attitudes on acute responses to the laboratory stressor. Change in Inflammation = latent change score for inflammation. 'Low' and 'High' Post-stress N-back errors and dysfunctional attitudes indicate scores one standard deviation below and above the mean, respectively. The thinner lines represent 95% confidence intervals.

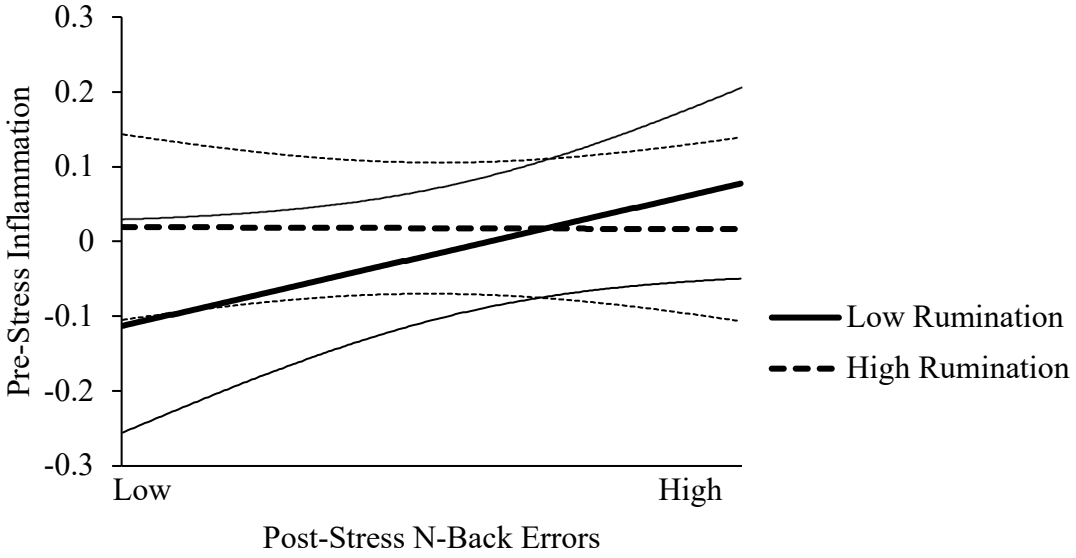

Figure 24. Interaction effect between Post-stress N-back errors and rumination on pre-stress cytokines. Prestress Inflammation = latent factor of baseline inflammation. 'Low' and 'High' Post-stress N-back errors and rumination indicate scores one standard deviation below and above the mean, respectively. The thinner lines represent 95% confidence intervals. The region of significance on rumination was 0.50 *SD* above the mean. This value indicates that Post-stress N-back errors were associated with increases in inflammation among individuals with rumination <0.50 *SD* above the mean, but was not associated with inflammation for individuals with rumination >0.50 *SD* above the mean.

Table 23

Prediction of Latent Pre-stress Cytokines and Latent Change in Cytokines by Post-stress N-back Errors and Cognitive Organization

	Pre-stress inflammation			Δ inflammation		
Model and predictor	β	95% CI	*b*	β	95% CI	*b*
Model 1: Main effects		R^2 = .22, *p* = .003			R^2 = .16, *p* = .026	
Age	.10	[-.10, .31]	.01	.08	[-.16, .32]	.002
BMI	.27**	[.09, .44]	.02	.01	[-.18, .19]	.00
Ethnicity						
White vs. Other	-.10	[-.27, .07]	-.14	.11	[-.12, .34]	.07
White vs. Asian	-.16	[-.36, .05]	-.14	-.14	[-.37, .09]	-.06
Pre-stress N-Back Errors	.11	[-.14, .36]	.004	-.04	[-.32, .23]	-.001
Negative Social Organization	.05	[-.16, .26]	.05	.20*	[.002, .40]	.09
Negative Achievement Organization	-.19*	[-.37, -.003]	-.14	.10	[-.10, .30]	.04
Post-stress N-Back Errors	.01	[-.23, .24]	.00	.16	[-.19, .51]	.003
Model 2: Interaction effect		R^2 = .25, *p* = .001			R^2 = .17, *p* = .015	
Negative Social Organization × Post-stress N-Back Errors	.18*	[.01, .36]	.02	-.13	[-.31, .05]	-.01
Model 3: Interaction effect		R^2 = .26, *p* = .001			R^2 = .17, *p* = .021	
Negative Achievement Organization × Post-stress N-Back Errors	.21**	[.05, .37]	.01	-.12	[-.29, .05]	-.004

Note. 95% CI = 95% confidence intervals for standardized coefficients (βs). Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1. Values of .00 are < .001. Model fit: Model 1, $\chi^2(67, N = 113) = 144.51$, $p < .001$, CFI = .933, TLI = .908 and RMSEA = .101, SRMR = .145; Model 2, $\chi^2(73, N = 113) = 151.09$, $p < .001$, CFI = .934, TLI = .910 and RMSEA = .097, SRMR = .141; Model 3, $\chi^2(73, N = 113) = 151.98$, $p < .001$, CFI = .933, TLI = .909 and RMSEA = .098, SRMR = .139.
$^{\dagger}p < .10$; $^{*}p < .05$; $^{**}p < .01$; $^{***}p < .001$.

stress N-back errors with baseline inflammation was positive in individuals with loosely connected schemas (b = .01, 95% CI = [-.003, .02], p = .167) and negative for those with tightly connected schemas (b = .-01, 95% CI = [-.02, .004], p = .178; Figure 25). Negative social organization did not moderate the relation of post-stress N-back errors on changes in inflammation.

Similarly, in Model 3 there was a significant interaction of negative achievement organization with post-stress N-back errors on baseline inflammation. The simple slopes were not significant, however the same pattern of findings emerged as with the interaction of negative social organization, in that the direction of association of post-stress N-back errors with baseline inflammation was positive in individuals with loosely connected schemas (b = .01, 95% CI = [-.003, .02], p = .169) and negative for those with tightly connected schemas (b = .-01, 95% CI = [-.02, .002], p = .119; Figure 26). There was no interaction of negative achievement organization with updating on change in cytokines in Model 3.

Hypothesis 11: Predicting Depressive Symptoms at Follow-up by Pre-stress and Stress-Induced Changes in Inflammation

Two conditional latent change score models were constructed to assess whether pre-stress inflammation or post-stress changes in inflammation predict subsequent depression at Phases 3 (two weeks after saliva collection) and 4 (six months after saliva collection). Analyses controlled for baseline depressive symptoms at Phase 1. In the first model, Phase 3 depressive symptoms were regressed on both pre-stress cytokines and stress-induced changes in cytokines. Baseline depressive symptoms were significantly associated with Phase 3 depressive symptoms (b = .81; β = .83, 95% CI = [.76, .90], p < .001). However, neither pre-stress inflammation (b = -.08;

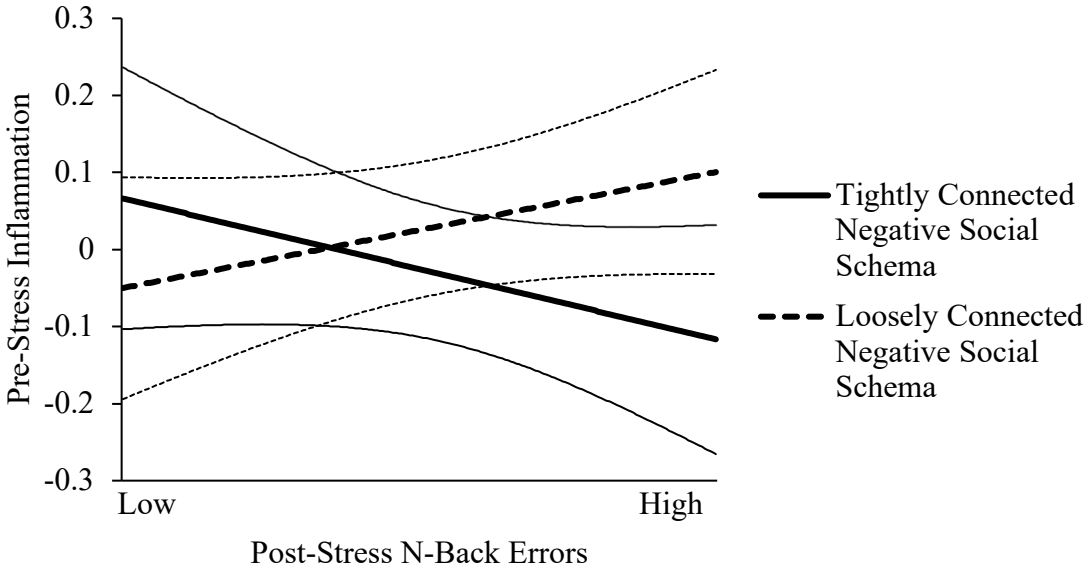

Figure 25. Interaction effect between Post-stress N-back errors and Negative Social Organization on pre-stress cytokines. Prestress Inflammation = latent factor of baseline inflammation. 'Low' and 'High' Post-stress N-back errors and Negative Social Organization indicate scores one standard deviation below and above the mean, respectively. The thinner lines represent 95% confidence intervals. As neither simple slope was significant, regions of significance could not be examined.

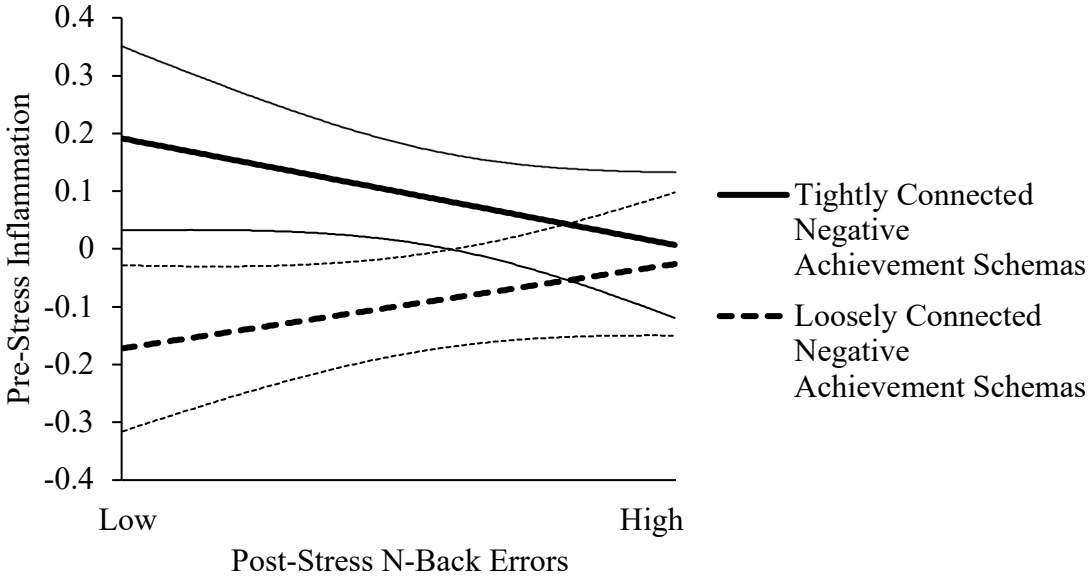

Figure 26. Interaction effect between Post-stress N-back errors and Negative Achievement Organization on pre-stress cytokines. Prestress Inflammation = latent factor of baseline inflammation. 'Low' and 'High' Post-stress N-back errors and Negative Achievement Organization indicate scores one standard deviation below and above the mean, respectively. The thinner lines represent 95% confidence intervals. As neither simple slope was significant, regions of significance could not be examined.

β = -.003, 95% CI = [-.08, .07], p = .947), nor post-stress changes in inflammation (b = -.27; β = -.004, 95% CI = [-.10, .09], p = .933) predicted depressive symptoms at Phase 3.[2]

The second model examined whether inflammation predicts depressive symptoms at Phase 4. Again, baseline depressive symptoms were significantly associated with follow-up depressive symptoms (b = .76; β = .75, 95% CI = [.66, .85], p < .001). Baseline inflammation did not predict Phase 4 depressive symptoms (b = .68; β = .02, 95% CI = [-.06, .10], p = .583). However, lower inflammatory reactivity to the laboratory stressor unexpectedly predicted increases in depressive symptoms at 6-month follow-up (b = -7.81; β = -.12, 95% CI = [-.22, -.02], p = .024).[3]

Discussion

Cognitive control, a key factor in determining individuals' experience of and response to life events, has emerged as a critical construct for better understanding emotion regulation processes in depression (Joormann & Vanderlind, 2014). Individuals with current or remitted depression tend to exhibit poorer cognitive control abilities, particularly for affective content (Joormann & Tanovic, 2015). Difficulty inhibiting negative stimuli, shifting away from processing negative material, or updating the contents of current awareness to discard negative goal-irrelevant information, is thought to result in prolonged accessibility and processing of negative material. Increased processing of negative information is theorized to result in rumination and other emotion regulation problems. In turn, this leads to persistent negative mood

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[2]Model fit: $\chi^2(33, N = 166) = 108.41$, $p < .001$, CFI = .953, TLI = .936 and RMSEA = .117, SRMR = .149.

[3]Model fit: $\chi^2(33, N = 166) = 104.31$, $p < .001$, CFI = .954, TLI = .938 and RMSEA = .114, SRMR = .150.

and eventually, a depressed state (Joormann & Stanton, 2016). Cognitive control abilities are required most for effective self-regulation following stressful experiences (Quinn & Joormann, 2015b). As such, they are particularly important for determining an individual's ability to respond adaptively to stress. The current study replicated and extended past research by examining diagnostic group differences across a battery of tasks assessing various cognitive control abilities, including cognitive control changes following a laboratory stressor, and the relation of these tasks with rumination. This study also bridged the extensive body of literature on cognitive vulnerability in depression with cognitive control research. As such, it was the first to examine the role that schemas, in the form of maladaptive cognitive content and structure, play in determining stress-induced changes in cognitive control abilities.

Cognitive control may influence depression not only via rumination, but through other facets of stress reactivity. An emerging body of research has found that inflammation is associated with depression and stress (e.g., Osimo, Baxter, Lewis, Jones, & Khandaker, 2019; Rohleder, 2019), and that greater levels of inflammation may explain a number of the physical (e.g., changes in sleep and appetite, low energy) and affective (e.g., anhedonia) symptoms of depression (Dantzer et al., 2008). Moreover, the Social Signal Transduction Theory of Depression (Slavich & Irwin, 2014; Slavich & Sacher, 2019) posits that when interpersonal life events are perceived as stressful or threatening, they are transduced into greater inflammation, eventually resulting in a pro-inflammatory state that may drive the pathogenesis of depression. For a social situation to be experienced as threatening and transduced to greater inflammation, cognition must be implicated. However, cognitive mechanisms underlying this process are not well understood and a paucity of research has examined the role that cognition plays in determining resting-state inflammation or acute inflammatory responses to stress. The current

study filled an important gap in the field of psychoneuroimmunology by examining how cognitive control, rumination, and depressotypic negative cognitive content and structure interact with each other and predict individuals' baseline and laboratory stress-induced changes in inflammation. The association of inflammation with subsequent depressive symptoms at 2-week and 6-month follow-up was also examined.

Hypothesis 1: Group differences in Cognitive Control

The first objective of this study was to replicate past research findings that depressed individuals demonstrate cognitive control deficits on tasks involving affective stimuli. Less research has examined cognitive control in remitted depressed individuals, and findings are somewhat less consistent (e.g., Joormann and Gotlib, 2010; Liu et al., 2017). Therefore, another goal was to examine depression-related cognitive control abilities following the active phase of the disorder. The current study replicated past research using cognitive control tasks that have been previously studied in clinical samples (i.e., the N-back and Emotional Stroop) and was the first to test diagnostic group differences using the Affective Flexibility Task. Significant group differences in inhibitory abilities were found, as indicated by reaction times on the Emotional Stroop. Currently depressed individuals evinced the slowest reaction times, followed by the remitted depressed group. The control group showed the fastest reaction times, and therefore the greatest inhibitory ability for negative affective stimuli. Given that the remitted depressed group did not differ significantly from either of the other groups, it is unclear whether or not they demonstrated inhibitory impairment. The intermediate inhibitory abilities found in the remitted depressed group could be more difficult to detect without sufficient power, and therefore may explain inconsistencies in past research.

There was also evidence of updating deficits among the currently depressed group for both the pre- and post-stress administrations of the N-back. On both occasions, depressed individuals made more errors on the task than did both remitted depressed and control participants. There was no evidence of updating deficits among remitted depressed individuals, as they performed similarly to the control group. This finding suggests that updating deficits, both under normal conditions and following a stressor, are specific to the symptomatic phase of depression. Given that impairments did not emerge in the remitted depressed group after the stress induction, this finding also implies that updating difficulties do not constitute a latent vulnerability that surfaces following priming by stress or low mood in the aftermath of a depressive episode.

Contrary to hypotheses, diagnostic group differences did not emerge on the Affective Flexibility Task. Although switch costs on this task have been found to relate to emotion regulation abilities highly relevant to depression, including rumination (Genet et al., 2013) and reappraisal (Malooly et al., 2013), this study was the first to use this task in a clinical sample. No group differences were detected across the four types of switch costs (i.e., positive affective, negative affective, positive nonaffective, and negative nonaffective switch costs). One possible explanation for this finding is that task switching abilities may not be strongly associated with depression. Although a number of past studies have found an association of shifting biases with depressive symptoms or diagnoses, the majority of these have used tasks that require a shift in focus among varying categories of stimuli (e.g., Internal Shift Task, De Lissnyder, Koster, Everaert, et al., 2012; an affective switch task; De Lissnyder et al., 2010), but not a shift in task sets or operations, which is how shifting has been defined (Miyake et al., 2000). Another study examined task switching, but switches were among variations of the same task rather than

discrete tasks (Owens & Derakshan, 2013). Moreover, switches occurred infrequently, from one block of trials to the next, rather than continuously within a block. The only other study to examine the relation of continuous shifting between discrete tasks within a block of trials did find evidence of shifting deficits; currently depressed individuals were slower than remitted depressed or healthy controls at switching away from a task that required processing emotional stimuli (Quigley, 2017). However, this task differed from the Affective Flexibility Task in that trials alternated between switch and non-switch trials in a predictable order. In contrast, group differences may not be evident when switch trials occur in a pseudorandom sequence and individuals cannot prepare for an expected switch in tasks, as in the Affective Flexibility Task. This suggests that depressed individuals may have more difficulty than those who are currently nondepressed in mustering cognitive resources to prepare for an expected switch in tasks, but do not have more difficulty making unexpected switches. As such, the present findings are preliminary and need replication, and the nature and specificity of deficits across various forms and components of shifting are an important empirical question for future research to explore in greater detail.

Hypothesis 2: Association of Deficits in Cognitive Control with Rumination

Consistent with hypotheses, rumination was associated with a number of cognitive control impairments. Inhibitory deficits (as indicated by longer reaction times on the Emotional Stroop), updating deficits (as assessed by greater errors on the Emotional N-back), and stress-induced declines in updating, were each correlated with a tendency to ruminate. These findings are consistent with prior research that has reported associations of inhibition and updating with rumination (e.g., Joormann & Gotlib, 2010; Joormann et al., 2011). Difficulty inhibiting irrelevant information and manipulating the contents of working memory in order to discard

previously-relevant content are therefore tied to a greater tendency to passively and repetitively think about the causes, consequences, and meaning of low mood. Individuals with these deficits may ruminate more because they are less able to filter negative content out of working memory, leading to prolonged processing of negative material. It is important to note that it is also possible that greater trait rumination may interfere with inhibition and updating, as the process of negative repetitive thought may consume cognitive resources, thereby overwhelming the ability to effectively control the contents of working memory. However, as the current findings are cross-sectional, the direction of this link is unclear. Whereas cognitive theories have focused on the role of cognitive control on rumination (e.g., Joormann & Tanovic, 2015), a bidirectional link is possible, and should be considered in future studies.

Positive nonaffective switch costs were marginally associated with greater rumination. However, contrary to hypotheses, positive affective, negative affective, and negative nonaffective switch costs were not associated with rumination. The current findings for negative affective and positive nonaffective switch costs are in contrast to those of Genet and colleagues (2013), who found that greater negative nonaffective switch costs were associated with greater daily rumination, and greater positive nonaffective switch costs were related to *decreased* daily rumination. Rather than assessing a general tendency to ruminate about the causes, consequences, and meaning of low mood as was done in the current study, Genet and colleagues assessed daily stress-reactive rumination in response to the worst event of the day over the course of six days. If replicable, these findings indicate that negative nonaffective switch costs are predictive of stress-reactive rumination about specific life events, and not of a more general tendency to respond to low mood with ruminative thinking. This may be because individuals are confronted with explicit negative stimuli during a negative life event that they need to switch

focus away from in order to prevent stress-reactive rumination. This is not necessarily the case for trait rumination, where the focus of ruminative thoughts may be less concrete.

The current finding of a positive association between positive nonaffective switch costs and rumination is more surprising. Although only marginally significant, the effect was in the opposite direction of what Genet et al. (2013) reported. Positive nonaffective switch costs may be protective in reducing stress-reactive rumination because difficulty disengaging from the affective features of positive stimuli may prevent individuals from allocating cognitive resources to the negative elements of an event. This may result in less negative material for stress-reactive rumination to center on. Conversely, cognitive inflexibility, even when it involves difficulty disengaging from positive affective information, may reinforce general ruminative thinking, particularly in a clinical sample. After all, difficulty switching from processing the positive elements of stimuli does not necessarily indicate that the individual is engaging in adaptive thinking about that stimuli. In contrast, it is possible that the individual may be engaging in negative ruminative thinking (e.g., making upward social comparisons). Again, this finding was only marginally significant, and should be interpreted with caution prior to replication in future research.

The current findings were consistent with Genet et al. (2013) in that positive and negative affective switch costs were not associated with rumination. In other words, an ability to flexibly switch to processing the affective elements of stimuli does not seem to be relevant to rumination. As rumination primarily involves difficulty disengaging from negative information for protracted periods of time (Joormann & Gotlib, 2010), rather than initial engagement with affective material, the lack of association of affective switch costs with rumination corresponds with theory.

Hypothesis 3: Decreased Updating Abilities Following the Stressor

The Trier Social Stress Test (TSST) was effective in producing an affective stress response, in that participants with current and remitted depression showed the lowest positive affect and highest negative affect after the stress induction as compared to controls. However, as pre- and post-stress N-back errors did not significantly differ from each other, there was not evidence for a stress-induced decline in updating abilities following the stressor. This finding is consistent with two previous studies (Quinn & Joormann, 2015a, 2015b) that also asked participants to complete the emotional N-back before and after the TSST. Despite experiencing an affective response to the TSST, participants may, on average, perform similarly on the post-stress administration of the N-back as a result of practice effects or habituation to the emotional words presented in the task, thereby obscuring stress-induced decreases in updating. One way for future research to mitigate against the issue of habituation would be to use different words on the second administration of the N-back that are matched to words used in the first administration for word length, frequency, and emotional intensity. Although an overall decrease in updating abilities was not observed, there was still meaningful individual variability in post-stress changes in updating ability as reported in the findings discussed directly below.

Hypothesis 4: Cognitive Content and Structure Predicting Stress-Induced Changes in N-Back Performance

Cognitive control abilities immediately following a stressor, when they are most needed for self-regulation, are critical for understanding differences in stress reactivity. For example, stress-induced declines in cognitive control determine the degree to which individuals develop depressive symptoms following stressful life events (Quinn & Joormann, 2015b). However, mechanisms underlying stress-induced changes in cognitive control have not been examined.

The current study was the first to elucidate predictors of post-stress changes in updating abilities by investigating whether greater maladaptive cognitive content and structure interfere with cognitive control abilities following a stressful experience.

Controlling for baseline updating, individuals with current depression demonstrated greater post-stress errors than did control participants. Furthermore, the current findings revealed that individuals who experienced greater negative affect following the laboratory stressor also evinced greater stress-induced decreases in updating, as indicated by greater errors on the N-back. As anticipated, maladaptive core beliefs were associated with a decline in updating following the stressor. During a stressful experience such as the TSST, negative cognitive content is primed and becomes accessible to working memory. Individuals with maladaptive core beliefs about themselves and others have greater negative cognitive content, including thoughts and memories, that can be activated by stress (Dozois & Beck, 2008). This activation results in more information becoming accessible to, and active in, the contents of current awareness following a stressor (e.g., Loeffler, Myrtek, & Peper, 2013). Greater accessibility and processing of this information adds an additional load of material to be monitored and manipulated by executive functions, likely overwhelming cognitive resources, and thereby leading to greater errors on the updating task. It is important to note that, although individuals with greater maladaptive core beliefs may be more likely to experience the TSST as upsetting, a stronger emotional response to the stressor does not fully explain the relation of core beliefs with decreases in updating, as increases in negative affect were controlled statistically. In other words, maladaptive core beliefs result in stress-induced declines in updating *over and above* the impact that post-stress increases in negative affect have on updating changes.

Dysfunctional attitudes did not predict changes in updating. This finding suggests that it may be *deeper* negative beliefs about oneself and others that are primed by the TSST, activate a network of congruent thoughts that become accessible to working memory, overload cognitive resources, and ultimately, interfere with efficient updating. While the Dysfunctional Attitudes Scale (DAS) assesses negative cognitive content, it is a measure of conditional assumptions, and therefore is an index of more intermediate cognitions than the Young Schema Questionnaire (YSQ), which was used to assess core beliefs (Dozois & Beck, 2008). Moreover, although conditional assumptions may have been primed by the TSST, they may not activate as large a network of negative information, thoughts, and memories as do deeper core beliefs. This may be particularly true given the more restricted content areas that the DAS assesses (i.e., importance of social approval, perfectionistic standards, conditions for happiness) as compared to the YSQ, which examines more nuanced beliefs about self, others, and interpersonal relationships.

Negative social and negative achievement cognitive organization both predicted stress-induced changes in updating above and beyond the impact of diagnostic status and negative emotional reactivity to the TSST. This underscores the importance of deeper cognitive structures in determining cognitive control following stress. Unexpectedly, more *loosely* connected social and achievement self-schemas were associated with greater increases in errors on the N-back task. In contrast, individuals with more *tightly* interconnected schemas were hypothesized to show the greatest post-stress reduction in updating abilities. These individuals were expected to have more consolidated negative cognitions that would be primed by the stressor and would in turn facilitate retrieval of other, closely interconnected negative content. The activation of this network of negative thoughts and memories was anticipated to result in greater information entering working memory and overloading cognitive control abilities. However, it is important to

note that, in order to obtain a score for either negative social or achievement cognitive organization, participants had to endorse at least two negative adjectives as self-relevant on that scale. Therefore, individuals who did not obtain a score on a scale of the Psychological Distance Scaling Task (PDST) were the least vulnerable in the sample in terms of cognitive organization. Those individuals with more loosely connected negative schema structures, who did endorse negative adjectives as self-relevant, reported a degree, albeit relatively small, of cognitive vulnerability. Given their more dispersed negative cognitive structure, these individuals may have experienced the TSST as more dissonant with their expectations, experiences, and sense of self than those individuals with tightly interconnected negative self-schemas. Expectancy violations can increase the salience of a stimulus (Craske, Treanor, Conway, Zbozinek, Vervliet, 2014). Therefore, a violation of expectations may have rendered the TSST a more potent prime for these individuals, effectively activating their less consolidated negative schema structure, and resulting in greater interference on the post-stress N-back.

Diagnostic group was no longer associated with stress-induced changes in updating after negative affect and cognitive vulnerability were accounted for. The current findings suggest that it is affective reactivity and negative cognitive content and how it is structured, rather than diagnostic status in and of itself, that account for stress-induced changes in cognitive control.

Hypothesis 5: Increases in Inflammatory Cytokines in Response to the Stressor

As hypothesized, the TSST elicited an immune response, as indicated by increases in a pro-inflammatory phenotype comprised of the salivary cytokines IL-8, IL-6, IL-1β, and TNF-α. This replicates past findings that individuals react to social-evaluative stressors with an immune system response (e.g., Carroll et al., 2011; Dickerson et al., 2009; Moons et al., 2010). Slavich and Irwin (2014)'s Social Signal Transduction Theory of Depression posits that when individuals

interpret a social interaction as threatening, the sympathetic nervous system upregulates the production and distribution of cytokines in order to prepare for potential wounding and infection should a physical altercation occur. This evolutionarily adaptive process is referred to as the CTRA (conserved transcriptional response to adversity). Importantly, there was also significant inter-individual variability in the degree of post-stress change in cytokines. In the current study, cognitive control and cognitive vulnerability (i.e., dysfunctional attitudes, core beliefs, rumination, and cognitive structure) were expected to be important in determining an individual's experience of the stressor and to predict differences in inflammatory reactivity.

Hypothesis 6: Greater Baseline and Post-Stressor Cytokines in Individuals with Depression and Remitted Depression

In contrast to Hypothesis 6, there were no differences in baseline cytokines across currently depressed, remitted depressed, and control participants. Depressive symptoms also were not associated with resting-state inflammation. This is in contrast to a number of meta-analyses that have documented greater baseline IL-6 and/or TNF-α in individuals with MDD as compared to healthy controls (Dowlati et al., 2010; Haapakoski, Mathieu, Ebmeier, Alenius, & Kivimäki, 2015; Hiles et al., 2012; Howren et al., 2009; Köhler et al., 2017). Notably, meta-analyses have reported no differences in resting-state IL-1β and IL-8 among individuals with MDD and healthy controls (Dowlati et al., 2010; Eyre et al., 2016; Köhler et al., 2017), consistent with the current findings. However, it is important to note that existing meta-analyses examined cytokine levels in peripheral blood and not in saliva, which could account for differences in the current findings. Studies have yielded inconsistent findings in terms of whether cytokines in blood and saliva correlate (Byrne et al. 2013; Minetto et al., 2007; Rahnama, Jastrzebska, Jamrogiewicz, & Kocki, 2013; Riis et al., 2014; Williamson, Munro, Grap, &

Elswick, 2012). Furthermore, while salivary cytokines are a valid marker of inflammation (Slavish et al., 2015), the processes that underlie the relation of salivary cytokines with cytokines in plasma or serum are still not fully understood. It is noteworthy that the current study is among the first to examine differences in salivary cytokines in a clinical sample of individuals with depression. One other study examined differences in adolescents with and without a depressive diagnosis, and similarly found no diagnostic group differences in cytokines (Byrne et al. 2013). Taken together, extant findings suggest that depression may be more closely associated with specific immune markers (e.g., IL-6, TNF-α) of peripheral systemic inflammation, for which blood is the gold standard for assessment, than more localized oral inflammation as assessed with saliva.

Similarly, there were no diagnostic group differences in stress-induced changes in cytokines. Depressive symptoms also were not related to post-stress changes in inflammation. This is in contrast to past research that found greater increases in plasma TNF-α and/or IL-6 in individuals with MDD compared to healthy controls following the TSST or a variant of it (Pace et al., 2006; Weinstein et al., 2010). However, in direct contrast, Niemegeers and colleagues (2016) found reductions in serum IFN-γ (a pro-inflammatory cytokine) and TNF-α, and no changes in IL-6, after the TSST in both remitted depressed and healthy control participants. No group differences in post-stress changes in cytokines were evident, and the authors attributed reductions in inflammation to increases in the glucocorticoid cortisol (which has anti-inflammatory properties) following the stressor. Similarly, Miller et al. (2005) did not find differences in circulating serum TNF-α and IL-6, or endotoxin-stimulated production of TNF-α and IL-6, between women with and without depression following a variant of the TSST. These investigators note this may have been due to the relatively shorter post-stress time period in

which they collected blood samples. However, differences did emerge in white blood cell sensitivity to the anti-inflammatory properties of glucocorticoids following the stressor, in that sensitivity declined among individuals with depression (which would allow for greater downstream expression of cytokines), and increased in nondepressed individuals, following the stressor. This indicates a pathway through which stress may lead to dysregulation of immune mediators. In sum, findings for group differences in post-stressor changes in inflammation are inconsistent, and differences may arise from type of biological sample assessed (serum/plasma vs. saliva), timing of post-stressor sample collection, and sample characteristics (e.g., currently vs. remitted depressed). Miller et al. (2005)'s findings highlight that even in the absence of changes in circulating cytokine levels, other differences in immune response may be present, which could result in increased expression and dysregulation in cytokines over time. In this vein, it is possible that greater post-stress cytokines may only be evident in individuals with depression who have developed glucocorticoid resistance following periods of chronic or recurring stress, rather than in individuals with less extensive histories of life stress.

Another reason for the lack of diagnostic group differences in salivary cytokines may be related to the extensive medical exclusionary criteria that were used in the current study. Depression is associated with a number of commonly comorbid medical conditions (e.g., Barton, 2008; Calder, 2006), and this is thought to result from the third variable of underlying pro-inflammatory processes. As a result of intensive pre-screening, one of the current study's strengths may have also been a limitation due to the exclusion of individuals with medical conditions who are likely to have a chronically activated CTRA and to be characterized by a systemic pro-inflammatory state. Pre-screening for medication and conditions that influence inflammation may have therefore led to a restriction of range in cytokines. Consistent with this

idea, high levels of statistical heterogeneity reported in meta-analyses among studies examining group differences in cytokines is thought to result in part from sample differences in participants' health status (Köhler et al., 2017). Although careful screening for inflammatory conditions reduced the number of confounds in this study, future research is needed to examine diagnostic differences in cytokines in a more generalizable sample that includes individuals with pro-inflammatory medical conditions or who are taking medications that influence inflammation.

Slavich and Irwin (2014) note that inflammation may not be necessary or sufficient in all cases of depression, and this may further explain the lack of diagnostic group differences in cytokines in the present study. Given the heterogeneity in symptoms and causes of the disorder, they suggest that a pro-inflammatory phenotype may only characterize a subset of patients with depression. Consistent with this idea, there was evidence in the current study that, amongst individuals with current or remitted depression, a greater number of past episodes was associated with greater reactivity to the stressor (b = .01; β = .24, 95% CI = [0.02, 0.46], p = .031) but not with baseline inflammation (b = .02; β = .20, 95% CI = [-0.09, 0.49], p = .179). This indicates that elevated inflammation, at least in terms of acute inflammatory responses, may be more relevant to highly recurrent cases than to depression more generally. Moreover, this finding suggests that a kindling effect (Monroe & Harkness, 2005, 2011; Post, 1992) may occur as the process of neuro-inflammatory sensitization unfolds over time. That is, as the neuro-inflammatory link becomes reinforced following the experience of numerous stressors, a self-promoting cycle of exaggerated perceptions of social threat and greater inflammatory responses to stress occur, and less stress is therefore needed to promote inflammation and ultimately, depressive episodes. It is important to note that number of episodes was assessed using the SCID-5. Given that this variable is sensitive to memory biases, however, its reliability and

validity are limited. Further research is therefore needed to examine whether neuro-inflammatory sensitization represents an endophenotype of depression and whether highly recurrent depression corresponds to a pro-inflammatory subtype of the disorder.

Hypothesis 7: Main Effects of Deficits in Inhibition, Shifting, and Updating on Baseline and Stress-Induced Inflammation

This study was the first to examine whether deficits in shifting predict cytokines, and was among the first to investigate whether inhibitory and updating impairments are associated with inflammation. Indices of cognitive control were hypothesized to predict both baseline and stress-induced inflammation. Differences in findings across types of cognitive control for predicting resting-state inflammation versus acute inflammatory response to stress were examined in an exploratory manner.

Poor inhibition, as indicated by longer reaction times on the Emotional Stroop, predicted greater baseline inflammation. Resting state-inflammation may reflect the degree to which an individual is in a chronically activated inflammatory state, possibly as a result of a persistently activated CTRA. Inhibition of negative emotional stimuli may reduce the degree to which an individual experiences social stressors as threatening, potentially limiting opportunities for the CTRA to become persistently activated over time. In contrast, inhibition was not associated with changes in cytokines following the stressor. This finding suggests that inhibition may influence inflammatory activity to stress over longer time periods, thereby shaping resting-state inflammation as opposed to inflammatory reactivity to acute stress. Consistent with this idea, it is also possible that inhibition may be more influential in shaping reactivity to chronic or ongoing stressors and difficult circumstances as compared to acute stressors, although this has not been tested.

In contrast to the current findings, Shields and colleagues (2016) found that poor performance on a faces version of the Emotional Stroop predicted greater salivary IL-1β, IL-6, and IL-8 reactivity among participants exposed to a stressor compared to those who completed a control task. It is possible that differences in findings emerged as a result of the tasks used to assess inhibition. By requiring participants to inhibit emotional faces, the version of the Stroop that Shields and colleagues used was more socially relevant, and therefore may have tapped into inhibitory abilities particularly important for regulating reactivity to social stress. Another key difference was that Shields et al. measured inhibitory abilities *after* the stressor, and therefore their measure of inhibition may have captured stress-induced declines in inhibition rather than trait inhibitory ability, which may be more relevant to acute inflammatory reactivity. Finally, the current study employed a social-evaluative stressor, whereas Shields et al. used an emotional stressor that involved viewing a film-clip of a crying infant being circumcised. It is possible that inhibition is more significant for acute reactivity to stressors relating to physical threat or harm, or in which there is very specific stimuli to inhibit, than to a more involved and immersive interpersonal stressor such as the TSST. Future research will need to examine precisely what components (e.g., immersive versus film clip) of various stressors (e.g., uncontrollable, evaluative, emotional) moderate the relation of cognitive control with cytokine reactivity.

As hypothesized, greater positive affective switch costs were associated with greater increases in inflammation following the stressor. Similarly, greater negative affective switch costs marginally predicted greater post-stress increases in cytokines. These findings indicate that individuals who took longer to switch from categorizing stimuli by a nonaffective categorization rule to an affective categorization rule were more reactive to the stressor. The cost of switching to categorizing an image by its affective rule is thought to be indicative of how effective that

individual is at switching from processing the nonaffective aspects to the affective aspects of stimuli (Genet et al., 2013; Malooly et al., 2013). Flexibility in shifting the focus of one's current attention and awareness to positive affective information in the environment is posited to facilitate emotion regulation and, along this vein, has been found to relate to greater reappraisal ability (Malooly et al., 2013). Individuals who have difficulty switching to processing positive affective information also likely had difficulty shifting their attention to positive information during or after the TSST. As a result, they may have been less able to integrate positive content in order to self-regulate, resulting in greater inflammatory reactivity. The marginal finding for negative affective switch costs indicates that flexibility in shifting to processing *negative* affective information may also be problematic for regulating responses to stress. Although past research has not found an association of negative affective switch costs with emotion regulation (Genet et al., 2013; Malooly et al., 2013), poor flexibility in shifting to negative affective information may result in it being processed less efficiently, which could contribute to greater stress reactivity. Given that this finding was only at trend-level, this interpretation is tentative.

Contrary to hypotheses, positive and negative nonaffective switch costs were not associated with either resting-state or stress-induced changes in inflammation. As such, the cost of switching away from processing affective information to processing nonaffective information does not appear to be associated with levels of salivary cytokines. In contrast, difficulty disengaging from negative affective information was expected to result in prolonged processing of the negative features of stressors, thereby resulting in greater resting-state or stress-induced inflammation. Further, given that past research has found that greater positive nonaffective switch costs are related to better reappraisal ability, and to a reduced tendency to ruminate (Genet et al., 2013; Malooly et al., 2013), positive nonaffective switch costs were anticipated to

predict *less* inflammation at baseline or following stress. However, the current findings suggest that switching *away* from processing affective information (and therefore engaging in potentially prolonged processing of affective information) is not as important for acute immune reactivity as is flexibility in *initiating* the processing of affective information (i.e., affective switch costs). Reasons for this difference need to be explored further.

Finally, there was no main effect of updating on resting state or stress-induced changes in cytokines either before or after the TSST. This finding suggests that updating did not have a marked and invariant impact on inflammation across the sample. Recent research (Quinn et al., 2019) similarly reported no associations of baseline updating with cytokines. However, Quinn and colleagues found that declines in updating were associated with increases in IL-6 following a variant of the TSST. It is important to note that this previous study used a small sample of 16 individuals and that key covariates, including ethnicity and BMI, were not controlled for, thereby increasing the probability of Type II error. However, it is also possible that differences in findings were due to the clinical composition of the current sample, and that the association of stress-induced declines in updating are only evident in less vulnerable individuals. This is discussed further under Hypotheses 9 and 10 below.

While this study conceptualizes cognitive control as influencing the process of social signal transduction by reducing ability to regulate under stress, thereby resulting in greater resting-state and stress-induced changes in cytokines, other interpretations are possible. Inflammation is associated with SNS and HPA axis activation and the release of norepinephrine and glucocorticoids, which can impair cognitive control when concentrations are high in the prefrontal cortex. Therefore, it is also possible that greater baseline or stress-reactive inflammation results in lower inhibitory abilities. Giollabhui and colleagues (2019), for example,

assessed adolescents' depressive symptoms, measures of executive functioning (selective attention and selective shifting), and IL-6 annually over three years. Results indicated that depression was associated with subsequent executive functioning via increases in IL-6, although there was no direct association of IL-6 with prospective executive functioning. Additional longitudinal research is needed to continue to elucidate the direction, or bidirectional nature, of effects of cognitive control with inflammation.

It is also noteworthy that a number of main effects were qualified by interactions with cognitive content, structure, or rumination. These interactions suggest that some forms of cognitive control were important in determining stress reactivity only among subgroups of participants, even in cases where main effects were not evident. These findings are described under Hypothesis 9 and 10.

Hypothesis 8: Main Effects of Cognitive Vulnerability on Baseline and Stress-Induced Cytokines

This study was the first to examine depressotypic cognitive content (core beliefs and dysfunctional attitudes) and structure as predictors of baseline and stress-induced cytokines, and was among the first to examine the relation of rumination with inflammation. As predicted, greater maladaptive core beliefs were associated with post-stress increases in inflammation. Individuals' negative core beliefs were likely activated by the stressor, and those with greater negative beliefs about themselves and others may have interpreted and experienced the TSST as more threatening and self-relevant, leading to a greater inflammatory response. This finding is similar to Giletta et al.'s (2017), who found that greater hopelessness predicted increases in IL-1β following the TSST in a high risk sample of adolescents. Before the stressor, core beliefs were not necessarily primed, and this may explain why they did not have an impact on resting

state inflammation. Furthermore, a trend emerged in some analyses whereby dysfunctional attitudes were marginally associated with decreases in inflammation following the stressor, possibly indicating habituation. This was unexpected, given that greater negative content was hypothesized to predict greater inflammation. Again, Giletta and colleagues similarly found that negative cognitive style was marginally associated with decreases in IL-1β after the TSST. Future research is needed to examine whether some types of negative cognitive content result in faster habituation to the TSST.

Tightly connected negative social and achievement cognitive organization were hypothesized to predict inflammation. Consistent with predictions, findings indicated that individuals with tightly connected negative achievement organization demonstrated greater baseline inflammation. Individuals with highly consolidated negative achievement schemas view themselves in terms of being incompetent, lazy, stupid, or a failure, and these beliefs are closely intertwined as a network. Given that the majority of participants were employed or were students, achievement schemas may have been particularly relevant to a large proportion of the sample. Negative achievement schemas also may be primed more regularly than negative social schemas in the context of daily life as a student or in the workforce. Regular priming and activation of these schemas may have resulted in the CTRA being activated more readily and regularly, leading to a chronic pro-inflammatory phenotype.

Conversely, and in contrast to hypotheses, more *loosely* interconnected negative social organization was associated with increases in acute inflammation following the stressor. In order to obtain a negative social organization score, participants had to endorse at least two negative adjectives as self-descriptive on that scale of the PDST. As noted above, individuals who did not obtain a score on a scale of the PDST were the least vulnerable in the sample in terms of

cognitive organization. Conversely, those with more loosely connected negative schema structure did endorse negative adjectives as self-relevant, indicating some degree of cognitive vulnerability. Similar to the findings reported under Hypothesis 4, individuals with more loosely connected schemas may have experienced expectancy violations during the TSST, whereas those with more tightly interconnected social schemas may have been more likely to expect the evaluators in the TSST to be aloof. Incongruity between interpersonal feedback on the TSST and expectancies based on a more dispersed negative social self-schema organization may also have resulted in a sense of cognitive dissonance. This violation of expectations and dissonance was likely accompanied by priming of their existing negative schema structure. Together, this may have resulted in the TSST being perceived as more threatening, (making it more immunologically activating), than it was for individuals with consolidated social schemas, who are more likely to expect social contexts to be unpleasant and challenging. As well, the finding that social schemas were more relevant than achievement schemas for acute immunological responding conceptually fits with Social Signal Transduction Theory (Slavich & Irwin, 2014; Slavich & Sacher, 2019) in that social schemas are more pertinent to judging the degree of threat posed by a social encounter (such as the TSST).

Finally, a lower tendency to ruminate was associated with greater stress-induced increases in cytokines. This is in direct contrast to the hypothesis that individuals who engage in prolonged negative thinking would be more likely to have a chronically activated inflammatory state and greater reactivity to the stressor. There are a number of viable explanations for this finding. Trait rumination is associated with greater cortisol reactivity or delayed cortisol recovery from social-evaluative stress (Zoccola & Dickerson, 2012). Given that cortisol has anti-inflammatory effects, it is possible that heightened cortisol acted as a third variable in

downregulating cytokines following the stressor. Alternatively, it is possible that individuals who tend to engage in repetitive negative thinking may have anticipated the difficulty of the TSST and the unresponsive demeanor of the evaluators, resulting in greater habituation. Another possibility is that individuals may ruminate in an attempt to suppress more intense emotional responses (Liverant, Kamholz, Sloan, & Brown, 2010) which could potentially result in dampened biological responses to stress. For example, worry has been characterized as a cognitive strategy for suppressing negative affect, aversive imagery, and somatic arousal (Borkovec, Ray, & Stöber, 1998), and is similar to rumination in that they both involve repetitive negative thinking. Given that trait rumination was assessed rather than individuals' engagement in state rumination during and after the TSST, it is unclear to what degree stress-reactive, state rumination influenced immune responding. Future research should examine this by experimentally manipulating use of rumination, as well as other emotion regulation strategies, following stress.

Hypothesis 9 and 10: Moderation of Cognitive Content, Cognitive Structure, and Rumination with Cognitive Control on Inflammation

This study was the first to examine the novel hypothesis that cognitive content, structure, and rumination would interact with cognitive control to predict inflammation. See Table 24 for a summary of findings. A fairly consistent pattern emerged whereby greater baseline or stress-induced changes in inflammation were associated with poor cognitive control among individuals with low cognitive vulnerability, whereas those with high cognitive vulnerability tended to evince high pre-stress inflammation and dampened immunological reactivity to stress regardless of their cognitive control abilities. This is in contrast to the hypothesis that poor cognitive control abilities combined with greater cognitive vulnerability would result in the greatest inflammation.

Table 24

Summary of Findings for Significant and Marginally Significant Interactions of Cognitive Vulnerability with Cognitive Control on Baseline or Stress-Induced Inflammation

Cognitive Control Task	Cognitive Vulnerability Mediator	Outcome Variable	Level of Significance	Interpretation
Emotional Stroop	Rumination	Pre-stress Inflammation	<.10	Greater reaction times were associated with greater baseline inflammation for individuals with low, and not high, trait rumination.
Positive Affective Switch Costs	Rumination	Pre-stress Inflammation	<.05	Positive affective switch costs were associated with greater baseline inflammation for individuals with high trait rumination, and with lower baseline inflammation for individuals with low trait rumination.
Positive Affective Switch Costs	Rumination	Change in Inflammation	<.05	Positive affective switch costs were associated with greater increases in inflammation for individuals with low, and not high, trait rumination.
Positive Affective Switch Costs	Negative Social Organization	Change in Inflammation	<.05	Positive affective switch costs were associated with greater increases in inflammation for individuals with loosely interconnected, and not tightly interconnected, schemas.
Positive Affective Switch Costs	Negative Achievement Organization	Change in Inflammation	<.05	Positive affective switch costs were associated with greater increases in inflammation for individuals with loosely interconnected, and not tightly interconnected, schemas.
Negative Affective Switch Costs	Negative Social Organization	Change in Inflammation	<.05	Negative affective switch costs were associated with greater increases in inflammation for individuals with loosely interconnected, and not tightly interconnected, schemas.
Negative Affective Switch Costs	Negative Achievement Organization	Change in Inflammation	<.10	Negative affective switch costs were associated with greater increases in inflammation for individuals with loosely interconnected, and not tightly interconnected, schemas.
Positive Nonaffective Switch Costs	Dysfunctional Attitudes	Pre-stress Inflammation	<.10	Positive nonaffective switch costs were associated with greater baseline inflammation for individuals with high

				dysfunctional attitudes, and with lower baseline inflammation for individuals with low dysfunctional attitudes.
Positive Nonaffective Switch Costs	Dysfunctional Attitudes	Change in Inflammation	<.05	Positive nonaffective switch costs were associated with greater increases in inflammation for individuals with high dysfunctional attitudes, and with decreases in inflammation for individuals with low dysfunctional attitudes.
Positive Nonaffective Switch Costs	Negative Achievement Organization	Pre-stress Inflammation	<.10	Positive nonaffective switch costs were associated with greater baseline inflammation for individuals with tightly interconnected schemas, and with lower baseline inflammation for individuals with loosely interconnected schemas.
Negative Nonaffective Switch Costs	Rumination	Pre-stress Inflammation	<.10	Negative nonaffective switch costs were associated with greater baseline inflammation in individuals with high trait rumination, and with lower baseline inflammation for individuals with low trait rumination.
Pre-stress N-back	Negative Social Organization	Change in Inflammation	<.05	Baseline N-back errors were related to greater increases in inflammation for individuals with tightly interconnected, and not loosely interconnected, schemas.
Post-stress N-back	Core beliefs	Pre-stress Inflammation	<.10	Post-stress N-back errors were associated with greater baseline inflammation in individuals with low, and not high, maladaptive core beliefs
Post-stress N-back	Dysfunctional Attitudes	Pre-stress Inflammation	<.05	Post-stress N-back errors were associated with greater baseline inflammation in individuals with low, and not high, dysfunctional attitudes.
Post-stress N-back	Dysfunctional Attitudes	Change in Inflammation	<.10	Post-stress N-back errors were associated with increases in inflammation for individuals with low, but not high, dysfunctional attitudes.
Post-stress N-back	Rumination	Pre-stress Inflammation	<.05	Post-stress N-back errors were associated with greater baseline inflammation in individuals with low, but not high, trait rumination.
Post-stress N-back	Negative Social Organization	Pre-stress Inflammation	<.05	Post-stress N-back errors were associated with greater baseline inflammation for individuals with loosely

				interconnected schemas, and lower baseline inflammation for those with tightly interconnected schemas.
Post-stress N-back	Negative Achievement Organization	Pre-stress Inflammation	<.05	Post-stress N-back errors were associated with greater baseline inflammation for individuals with loosely interconnected schemas, and lower inflammation for those with tightly interconnected schemas.

Greater negative content, more consolidated negative cognitive structure, or a greater tendency to ruminate were expected to render more cognitive content accessible to working memory, thereby overwhelming already poor cognitive control abilities.

Inhibition. A marginal interaction of rumination with reaction times on the Emotional Stroop was observed. Among individuals with low trait rumination, resting-state inflammation increased alongside longer reaction times (i.e., poorer inhibitory abilities) on the Stroop. These individuals appeared to benefit the most from high inhibitory abilities in terms of lower baseline inflammation. In contrast, inhibitory abilities did not appear to influence baseline cytokines among individuals with high rumination. This finding suggests that individuals with low rumination may have greater capacity to benefit from inhibitory abilities, at least in terms of immune system activation. In contrast, those who ruminate may continue to repetitively brood about negative information regardless of their ability to inhibit it, thereby counteracting any benefits of greater cognitive control ability on cytokine levels.

Shifting. ***Positive Affective Switch Costs.*** The association of positive affective switch costs with inflammation was moderated by a number of forms of cognitive vulnerability. First, positive affective switch costs interacted with rumination in the prediction of pre-stress inflammation. As hypothesized, among those with high levels of rumination, greater positive affective switch costs were associated with higher baseline cytokines. That is, individuals with greater difficulty switching away from nonaffective information to process positive affective information showed greater resting-state inflammation when they also had a tendency to ruminate. This suggests that the focus these individuals place on negative information (resulting from the combination of poor shifting and rumination) may contribute to the development of a pro-inflammatory baseline state. In direct contrast, greater positive affective switch costs were

associated with *lower* inflammation amongst individuals with a low tendency to ruminate. This finding was unexpected, and it is difficult to explain why individuals with low trait rumination would benefit from inflexibility in shifting to positive affective information. Future work is needed to disentangle the differential impacts of positive affective switch costs on emotion regulation and daily functioning amongst individuals with varying levels of vulnerability.

Rumination, negative social schema organization, and negative achievement organization all interacted with positive affective switch costs to predict acute immune responses to the laboratory stressor. A consistent pattern of findings emerged whereby individuals with high vulnerability evinced no changes or small decreases in cytokines after the stressor, suggesting habituation, regardless of their shifting ability. This indicates that more vulnerable individuals evince dampened reactivity regardless of their positive affective switching ability. These individuals may have anticipated a socially difficult interaction given their prior experiences or expectations, leading to faster habituation. Other possible reasons for this finding are discussed in the Summary of Moderating Effects below. Individuals low in vulnerability (i.e., low rumination, loosely connected negative social schemas, loosely connected negative achievement schemas) demonstrated the hypothesized relation of cognitive control with inflammation, such that as positive affective switch costs increased (indicating worse cognitive control), so did post-stress cytokines. For these less vulnerable individuals, poor switching appears to have resulted in greater cytokine reactivity, likely due to poor self-regulation resulting from limited cognitive control ability.

Negative Affective Switch Costs. Negative social and achievement cognitive organization interacted with negative affective switch costs on post-stress changes in cytokines. Similar to findings for positive affective switch costs, individuals with tightly interconnected negative

social organization evinced slight decreases in cytokines after the stressor, indicating habituation to the TSST, regardless of their negative affective switch abilities. In contrast, among those with loosely interconnected negative social schemas, greater negative affective switch costs were associated with greater post-stress increases in cytokines. Furthermore, although the interaction only approached significance for negative achievement schemas, the same pattern was found again in that individuals with tightly connected negative achievement organization showed dampened reactivity to the TSST, and greater negative affective switch costs were associated with greater stress-induced increases in inflammation among individuals with dispersed achievement schemas.

Positive Nonaffective Switch Costs. Dysfunctional attitudes marginally interacted with positive nonaffective switch costs on baseline inflammation, and significantly interacted with positive nonaffective switch costs on post-stress changes in inflammation. For both interactions, the opposite trend was found in individuals with high versus low dysfunctional attitudes. Individuals with low dysfunctional attitudes tended to show greater inflammation (including both pre-stress and post-stress changes in cytokines) as switch costs decreased. Past research has found benefits for positive nonaffective switch costs in terms of greater appraisal abilities and reduced state rumination (Genet et al., 2013; Malooly et al., 2013). Therefore, this finding is consistent with those reported above in terms of individuals with lower vulnerability tending to show greater inflammation when their cognitive control abilities are poor, or in this case, when cognitive control abilities are potentially disadvantageous to emotion regulation. Individuals with high dysfunctional attitudes showed the opposite pattern. It is possible that any cognitive inflexibility may be problematic for people with high vulnerability, including inflexibility in switching away from positive affective information. This may be particularly true for individuals

with high dysfunctional attitudes, as positive information may be connected to their rigid assumptions about social approval, achievement, and happiness.

Negative achievement cognitive organization also marginally interacted with positive nonaffective switch costs on baseline inflammation. Similar to the findings for dysfunctional attitudes, individuals with more tightly connected negative achievement schemas tended to show greater resting-state inflammation alongside greater switching abilities, likely due to any inflexibility being maladaptive for them. In contrast, those with loosely connected negative achievement schemas showed a trend whereby greater positive nonaffective switch costs (which may support emotion regulation) tended to be associated with lower inflammation.

Negative Nonaffective Switch Costs. Only rumination marginally interacted with negative nonaffective switch costs on baseline inflammation. There was a trend whereby greater switch costs were associated with greater pre-stress inflammation among individuals with high trait rumination. However, individuals with low levels of rumination showed lower inflammation alongside greater negative nonaffective switch costs. This pattern is similar to the findings for the interaction of rumination with positive switch costs on baseline inflammation. Again, it appears that poor switching combined with greater rumination is associated with a pro-inflammatory state in those with high rumination, consistent with hypotheses. In contrast, those with low rumination showed lower resting-state inflammation when they also demonstrated poor switch costs. It is possible that among those with low trait rumination, difficulty switching from negative affective information allows them to better process negative stimuli that may be important for adaptive functioning, allowing them to maintain lower levels of inflammation. This interpretation is speculative, however, and further research is necessary to explore the differential impacts of switching ability.

Updating. ***Pre-stress N-back Errors.*** Only negative social organization interacted with pre-stress N-back errors to predict changes in inflammation. Although those individuals with more loosely connected negative social organization showed greater inflammatory reactivity overall, baseline updating did not have an impact on their immune responses to the TSST. There was a trend indicating that, among those more tightly connected negative social organization, poorer updating ability at baseline (i.e., pre-stress N-back errors) was related to greater acute inflammatory responses. This result is consistent with hypotheses that poor cognitive control, particularly in combination with greater vulnerability, would predict greater inflammatory reactivity.

Post-stress N-back Errors. A number of cognitive vulnerability factors interacted with stress-induced changes in updating abilities on baseline inflammation. The same pattern of findings was evident for core beliefs, dysfunctional attitudes, and rumination. In each case, individuals with high vulnerability showed low to average baseline inflammation, regardless of updating ability. In contrast, among individuals with low vulnerability (i.e., low maladaptive core beliefs, low dysfunctional attitudes, low tendency to ruminate), declines in post-stress updating ability were associated with higher baseline inflammation, and enhanced post-stress updating ability was associated with lower resting-state inflammation. This was found at trend level for core beliefs and rumination, and was significant for dysfunctional attitudes. Altogether, these findings suggest that individuals low in maladaptive core beliefs, dysfunctional attitudes, and rumination benefit from good updating abilities under stress in terms of maintaining lower resting-state inflammation. This may indicate that their CTRA is activated less often. However, declines in updating ability under stress were related to a pro-inflammatory state, possibly due to difficulty responding to stressors over time gradually leading to overall upregulation in

cytokines. In contrast, individuals with higher cognitive vulnerability (i.e., greater maladaptive core beliefs, dysfunctional attitudes, and tendency to ruminate) showed average to low baseline inflammation regardless of their updating abilities. This finding suggests that, in contrast to hypotheses, updating abilities under stress may have limited influence on baseline inflammation in those with higher vulnerability. For these individuals, updating abilities under stress may not have an impact on their resting-state inflammation in part because their habitual patterns of negative thinking may overshadow any potential benefits of cognitive control.

A similar finding was revealed for the marginal moderating effect of dysfunctional attitudes with post-stress updating on changes in inflammation. Individuals with high dysfunctional attitudes showed no post-stress changes in cytokines, denoting habituation to the TSST, regardless of updating abilities. In contrast, greater post-stress updating errors were associated with increases in cytokines after stress among those with low dysfunctional attitudes.

Negative social and negative achievement organization also interacted with post-stress updating abilities on baseline inflammation. In both cases, greater post-stress updating errors tended to be associated with more cytokines at baseline among individuals with lower vulnerability (those with more loosely connected cognitive structure), consistent with other findings. In contrast, those with more tightly connected negative social and achievement schemas showed the opposite pattern. One possible interpretation is that individuals with tightly interconnected negative cognitive structure may benefit from declines in updating abilities under stress. Poor updating may result in less negative information from their current stressful context entering working memory, which, given how negative their thinking is, may be beneficial in terms of how frequently their CTRA is activated over time.

It is interesting that stress-induced changes in updating appear to be more relevant to resting-state inflammation than to acute inflammatory reactivity. Findings suggest that updating abilities following acute stress may not have a major influence on acute reactivity to that particular stressor, except in the case of individuals with low dysfunctional attitudes. Conversely, changes in updating abilities following stress appear to be more influential in shaping resting state cytokines among those with lower cognitive vulnerability. Habitual patterns of cognitive control under stress may therefore influence an inflammatory phenotype more gradually over time.

Summary of moderating effects. Altogether, there was evidence for moderating effects of cognitive vulnerability on the association of cognitive control with inflammation. A fairly consistent pattern of findings indicated that cytokine levels are influenced by cognitive control abilities among individuals with lower vulnerability, whereby resting state cytokines or stress-induced changes in cytokines increased with poorer cognitive control. In the case of positive nonaffective switch costs, greater switch costs were associated with decreased inflammation, which was unsurprising given evidence that positive nonaffective switch costs facilitate emotion regulation. This set of findings suggests that poor cognitive control results in greater immunological reactivity to a stressor or to greater resting state inflammation, likely characterized by a more chronically activated pro-inflammatory state, among those with lower cognitive vulnerability. Poor cognitive control may result in greater inflammation as a result of reduced capacity for emotion regulation, leading to enhanced stress reactivity. As noted above, it is also possible that inflammation may contribute to lower cognitive control abilities as a result of SNS and HPA axis activation.

In contrast, cognitive control was not associated with differences in baseline or stress-induced changes in inflammation among individuals with higher vulnerability, who tended to have average to high baseline inflammation and dampened reactivity to stress. There are a number of potential reasons for reduced influence of cognitive control on cytokines and dampened acute immune responding in these more vulnerable individuals. Given that these cognitively vulnerable individuals already exhibited negative thinking, for example, they may have anticipated the interpersonally aversive nature of the TSST, resulting in faster habituation regardless of cognitive control ability. The TSST may have been less discrepant with their views of themselves and others as compared to less vulnerable individuals, leading to lower cognitive dissonance. Moreover, the TSST may have validated these individuals' maladaptive self-relevant cognitions, resulting in greater comfort with the experience compared to those with more adaptive thinking. This explanation is consistent with Self-verification Theory (Swann, 1983; Swann, Stein-Seroussie, & Giesler, 1992), which posits that individuals prefer to receive feedback that is consistent with their self-concept. Another possibility is that the immune states of vulnerable individuals were less influenced by cognitive control due to learned helplessness (Seligman, 1972). Learned helplessness, or an unwillingness to attempt to avoid aversive stimuli resulting from repeated exposure to uncontrollable stressors, may reduce engagement of cognitive control abilities under duress, resulting in reduced impact of cognitive control on inflammation. Learned helplessness may have also dampened individuals' immunological reactivity to the stressor. A similar interpretation is based on Selye's (1936) general adaptation syndrome, whereby after an initial stressor, organisms first enter an alarm phase (activation of the autonomic nervous system), followed by a resistance phase (activation of the parasympathetic nervous system while the organism remains alert), and after chronic or recurrent

stress, the exhaustion stage (depletion of resources). It is possible that individuals with low vulnerability may have exhibited immune activation consistent with the alarm and resistance phases, whereas those with higher vulnerability exhibited exhaustion. Finally, another possibility is that individuals with greater vulnerability may have exhibited excessive cortisol responses, which, given the anti-inflammatory effects of glucocorticoids, could have downregulated cytokines. Slavich and Irwin (2014) suggested that over time, a chronically activated immune state may result in glucocorticoid desensitization, thereby allowing glucocorticoids and cytokines to be upregulated simultaneously. However, as noted above, exclusion of individuals with medical conditions in the current study may have precluded assessment of those most likely to be characterized by significant problems with a pro-inflammatory phenotype and concomitant glucocorticoid desensitization, in whom upregulation of both cytokines and cortisol may be expected. As cortisol was not assessed in the current study, it is unclear to what extent it may have influenced the observed pattern of interactions, and future research is needed to explore its role.

There were some exceptions to the general pattern of moderating effects. These emerged for the interaction of rumination with positive affective and negative nonaffective shifting on baseline inflammation, the interaction of pre-stress updating with negative social schemas on changes in inflammation, and the interaction of post-stress updating with negative social and achievement schemas on baseline inflammation. It is unclear why the general pattern of findings differed for the interactions of rumination with some types of shifting, and for negative schemas with updating. Furthermore, it is uncertain why particular cognitive vulnerabilities interacted with some types of cognitive control and not others. It is possible that some vulnerabilities are

more or less disruptive to specific types of cognitive control, although this is an empirical question that requires further investigation.

Hypothesis 11: Predicting Depressive Symptoms at Follow-up by Pre-stress and Stress-Induced Changes in Inflammation

Surprisingly, dampened reactivity to the laboratory stressor was associated with increases in depression six months later. The CTRA is an evolutionarily adaptive response, and it is frequent or persistent activation of the CTRA rather than a single acute response that is depressogenic. It is possible that in the current sample, reactivity to a single acute stressor represented an adaptive response that may have been somewhat exaggerated in a subset of participants with poor cognitive control and/or particular cognitive vulnerabilities. On the other hand, dampened reactivity may have belied greater cortisol responses, or some of the deleterious processes described above (e.g., habituation, learned helplessness, exhaustion). Studies examining other indices of immunological responding, including endotoxin-stimulated production of cytokines and white blood cell sensitivity to glucocorticoids, as well as longitudinal studies examining the relation of acute inflammatory responses to stress with depression over time, would further inform processes underlying this finding.

Strengths and Limitations

This study has a number of notable strengths and methodological features that bolster conclusions drawn from these findings. First, a clinical sample was recruited from the community, and diagnoses were made using the SCID-5, the gold-standard semi-structured diagnostic interview. This procedure allowed for comparisons to be made among diagnostic groups, and for differences in cognitive control abilities and inflammation in the symptomatic versus remitted phases of depression to be explored. Use of a clinical sample also allowed for

extensions of past research that have examined cognitive control and/or inflammation in nonclinical populations, thereby increasing the clinical relevance and generalizability of findings to those with diagnosed depression. Second, the sample size was determined using an a priori power analysis and was considerably larger than most studies of cognitive control or psychoneuroimmunology, particularly amongst those using clinical samples. A large sample enhances reliability and increases the likelihood that findings are replicable as compared to past research using smaller samples.

Furthermore, the current study used a comprehensive strategy to evaluate cognition. To assess cognitive vulnerability, a multi-method, multi-trait approach was used to assess both cognitive content, using two self-report questionnaires, and cognitive structure, using a task-based measure of both achievement and social schemas. Examining moderating effects of various measures of cognitive vulnerability with cognitive control on inflammation revealed similar patterns of findings using both measurement approaches, further supporting the replicability and validity of findings. In a similar vein, this study was among the first to use a comprehensive battery of cognitive control measures to assess inhibition, shifting, and updating abilities among a single sample of clinically depressed and remitted depressed individuals. Updating was assessed both at baseline and after the stressor, which was manipulated using a highly controlled, well-validated social-evaluative stressor. This methodology allowed for an examination of both trait updating and stress-induced changes. Together, this comprehensive assessment of multiple facets of cognitive control facilitated a more nuanced investigation of depression-related cognitive control deficits. This procedure also allowed for an investigation of the specificity of various types of cognitive control in shaping baseline and/or stress-induced changes in cytokines.

Optimal methods for saliva collection, storage, and assays were used in the present study, effectively reducing the impact of potential confounds and enhancing the quality of cytokine data. Participants, who were screened for medical conditions or medications that could influence their inflammation, received detailed instructions on preparation for saliva collection in order to reduce the impact of behaviours known to influence cytokine levels or sample quality (e.g., eating or drinking before the appointment). Saliva was collected using the passive drool method. Passive drool is the gold standard method for saliva collection as it avoids collecting only localized secretions from specific salivary glands, resulting in a more consistent specimen. It also avoids compromising samples with the use of absorbent materials, as with other collection methods. Protease inhibitor was added to samples before freezing to minimize breakdown of cytokines, and saliva was assayed in duplicate to ensure reliability using the highest sensitivity multiplex assay optimized for saliva available.

The present study also used sophisticated statistical methods for assessing and analyzing both baseline and stress-induced changes in cytokines using latent change score models. These structural equation models reduce the influence of measurement error, which is particularly important when multiple time points are used to assess change. By creating latent factors to represent an inflammatory phenotype, models are more robust and reliable than an independent analysis of each cytokine. Moreover, and in contrast to more traditional statistical methods (e.g., repeated measures ANOVA), latent change score models allowed for 'baseline-free' change to be assessed. This means that changes in cytokines take participants' initial cytokine levels into account (which likely have an impact on the degree of stress-induced change observed; Giletta et al., 2017). Given that baseline inflammation and stress-induced inflammation showed different relations with cognitive vulnerability, cognitive control, and subsequent depression, they likely

represent different constructs that are regulated by different cognitive (and very likely biological) processes. It is important that future research attends to both of these indices of inflammation using appropriate analytic techniques. Finally, the study also included a longitudinal component as two-week and six-month follow-up data were collected on depressive symptoms, allowing for the longer-term impact of inflammation on depressive symptoms to be assessed.

The current findings should also be interpreted, however, in the context of this study's limitations. First, the large number of interactions tested may have increased the Type I error rate. After a family-wise Bonferroni correction was conducted for each type of cognitive control, only 45% of previously statistically significant interactions remained significant. However, it is important to note that although a large number of tests were conducted, these were based on a priori hypotheses. Moreover, a number of the moderation effects evinced the same or similar pattern, resulting in replication within the same sample. Additionally, it is possible that some of the interactions, particularly those that were marginally significant, were underpowered. However, marginally significant findings were still interpreted given that categorical rejection of the alternative hypothesis when the effect is consistent with other findings could lead to Type II errors, and introduce confusion to the literature. Importantly, confidence intervals are reported in both tables and figures, which provide an indication of the degree of precision of the parameter estimates within the current sample.

As noted above, participants were thoroughly screened for medical eligibility, and while this reduced the number of potential confounding factors, it also limits the generalizability of findings to relatively physically healthy individuals. Moreover, this study assessed inflammation using saliva, and while salivary cytokines are a valid indicator of inflammation that allow for assessment of rapid responses to stress (Slavish et al., 2015), blood is the gold standard measure

of peripheral inflammation. Furthermore, saliva was collected at only one time point post-stressor, which precluded an examination of recovery from the stressor.

Several limitations related to the assessment of cognitive variables are noted. Individuals did not receive a mood prime before assessment of cognitive vulnerability variables (i.e., core beliefs, dysfunctional attitudes, cognitive organization). Although research has found these measures to be valid without the use of mood primes (see Rnic & Dozois, 2017, for review), it is possible that some individuals, particularly those in the remitted depressed group, may have underreported dormant cognitive vulnerabilities. Furthermore, this study did not examine updating and shifting abilities using neutral stimuli, which precluded determining whether individuals with poor cognitive control demonstrated biases for affective stimuli as opposed to more general deficits. Although the Emotional Stroop did include a neutral block, interference scores could not be calculated. Interference scores are computed by subtracting reaction times for neutral stimuli from reaction times for emotional stimuli. This produces an outcome score that is indicative of interference on the task specifically resulting from difficulty inhibiting the affective aspects of stimuli, as general performance when stimuli are not emotional is accounted for in the score. However, in the current study, practice effects were evident on the emotional block, which precluded a direct comparison of performance on the emotional block to the neutral block. Future research should employ a multi-block version of the Stroop task that alternates emotional and neutral blocks so that both are equally impacted by practice effects, which would better allow for interference scores to be computed. Additionally, since the study employed emotional stimuli in cognitive control tasks, it is possible that these may have elicited a stress response in some individuals (e.g., cognitive activation). Although the timing and ordering of tasks was kept constant across participants, it is possible that some individuals may have begun to upregulate

cytokines before the TSST as a result of viewing emotional stimuli. This may be another explanation for habituation to the TSST that was observed in more cognitively vulnerable individuals.

Finally, the groups of individuals with current or remitted depression were comprised of a greater proportion of women than the control group. To an extent, this difference likely reflects higher base rates of depression among females (e.g., Kessler et al., 2003). Group differences in the proportion of males and females was mitigated against by statistically controlling for sex in analyses. Where including sex as a covariate did not alter the pattern of findings, more parsimonious models were presented. Additionally, while not significant, there appeared to be a greater proportion of Asian participants in the control group and relatively fewer in the currently depressed group. There is a possibility that this difference may have arisen in part due to cultural differences in depression self-stigma (Shamblaw, Botha, & Dozois, 2015). As there was no prior theoretical or empirical basis to expect ethnicity to relate to cognitive control, it was not included as a covariate in analyses examining cognitive control as an outcome variable. However, given that ethnicity is an important covariate of inflammation, all models examining cytokines included ethnicity. Differences in proportions of female or Asian participants across diagnostic groups may also reflect bias in scope and response to recruitment methods, and further research is needed that better stratifies diagnostic groups by major demographic differences.

Theoretical and Clinical Implications

The current results have key implications for cognitive and psychoneuroimmunological theories of depression. This study was among the first to comprehensively examine inhibition, updating, and shifting in a single clinical sample, and was the first to examine stress-induced updating deficits in currently and remitted depressed individuals. Deficits in inhibition and

updating of affective stimuli were found in the currently depressed group, corroborating findings of a number of past studies (e.g., Epp et al., 2012; Joormann & Gotlib, 2010; Levens & Gotlib, 2010). This study also made a novel contribution to the literature by finding evidence for stress-induced updating deficits in depressed individuals.

Limited prior research has examined whether cognitive control deficits are apparent among remitted depressed individuals, and findings have been somewhat mixed. Evidence for inhibitory deficits in remitted depressed individuals was equivocal in the present study. Although their performance fell between the control and currently depressed groups, it was not significantly different from either group. This may indicate that more minor difficulties with inhibition may occur outside of the symptomatic phase of depression, which could explain why diagnostic group differences are not always detected. This study also contributes to the small body of research on updating in remitted individuals. Results suggest that individuals with remitted depression do not have difficulty with the continuous updating of negative information. While it is possible that cognitive control biases become latent vulnerabilities that need to be primed to be observed among individuals with remitted depression, the current study does not support this hypothesis as no evidence for post-stress updating deficits was found. Although dormant cognitive control biases cannot be ruled out for other forms of cognitive control, the current results indicate that updating deficits improve along with the remission of other symptoms following an active episode of depression.

The current findings suggest that there are no diagnostic group differences in shifting, at least for task switches that are unpredictable. In contrast, past research has found evidence for deficits in mental set shifting or predictable task switching (e.g., De Lissnyder, Koster, Everaert, et al., 2012; Quigley, 2017). This study was the first to assess continuous and unpredictable task

switching, and, although requiring replication, suggests that shifting biases in depression may be more specific to particular types of shifting than previously thought.

One pathway through which cognitive control biases are thought to increase risk for depression is by increasing the accessibility and processing of negative information. Difficulty inhibiting negative stimuli, discarding it from working memory, and shifting away from it allows negative material to enter and remain in working memory for prolonged periods, which is thought to lead to greater rumination. The process of rumination results in greater negative mood and eventually, a depressed state. The current study further supports theory and past research on the cognitive control deficit-rumination link as it found associations of trait rumination with deficits in inhibition, trait updating, and stress-induced updating deficits. Contrary to prior research, only one aspect of shifting was marginally associated with trait rumination, further underscoring key differences among different forms of shifting.

Cognitive control deficits are thought to be particularly important during times of stress, when abilities are most needed to facilitate self-regulation. This study bridged research on cognitive control with the literature on cognitive vulnerability. This was accomplished by testing how core beliefs, dysfunctional attitudes, and cognitive organization influence an individuals' updating abilities after stress, above and beyond the impact of diagnostic status or change in affect. Findings support cognitive theories that posit that stress activates networks of negative thoughts, memories, and beliefs, and that their increased accessibility in working memory impair cognitive control abilities when they are most needed.

Findings from this study are among the first to demonstrate that cognitive control and cognitive vulnerability influence inflammatory processes. Results underscore the role that cognitive vulnerability, cognitive control, and the interaction of the two have on both resting-

state inflammation and acute inflammatory responses to stress. Cognitive risk factors appear to represent a mechanism through which depression-prone individuals may develop a pro-inflammatory phenotype and associated physical symptoms although, as noted above, inflammation may also influence cognitive control. It is possible that cognitive control and cognitive vulnerability may be implicated in neuroinflammatory sensitization. Longitudinal research is needed to examine bidirectional, possibly self-promoting, relations of cognition and inflammation. Results also highlight the need to investigate not only the relation of depression with inflammation, but also the relation of inflammation with underlying vulnerabilities to and endophenotypes of depression.

Given evidence for specificity of effects of cognitive control and vulnerability on indices of inflammation, as well as different associations of inflammatory indices with later depression, baseline and stress-induced changes in inflammation appear to demark different immune processes. Furthermore, findings suggest that individuals with lower vulnerability may be most influenced by the pernicious effects of poor cognitive control abilities (or in the case of positive nonaffective switch costs, cognitive control abilities that are disadvantageous to self-regulation) on inflammation. This study also highlights that individuals with greater vulnerability are less influenced by cognitive control in terms of immune functioning and that, in some cases, may actually show greater habituation or reduced responses to a stressor. This pattern of findings underscore the need for further research to investigate the cognitive-immune system link and differences amongst individuals of greater or lesser cognitive vulnerability. The importance of assessing both resting-state cytokines and stress-induced changes in cytokines for dysregulation, rather than simply upregulation, is apparent.

Results from this study have important clinical implications. Findings indicate the key role cognitive vulnerability plays in shaping stress-induced declines in cognitive control, which is critical in shaping an individual's immediate experience as well as their ability to engage emotion regulation skills. In turn, findings indicate that both cognitive control and vulnerability (including content, process, and structure) shape inflammation. Given increasing evidence that inflammation may be involved in depression pathogenesis, interventions that disrupt the mechanisms underlying dysregulated inflammation may be important for some cases of depression. Although not all cases of depression may be characterized by a pro-inflammatory phenotype, results of the current study documented influences of cognitive vulnerability and cognitive control on inflammation across a sample of non-clinical healthy controls, and in individuals with remitted and current depression, suggesting that treatments that disrupt the mechanisms underlying inflammation could potentially have mental or physical health benefits for a range of individuals.

A variety of treatments may be beneficial in altering depressogenic cognitive and immunological processes highlighted by the current findings. These include both top-down and bottom-up treatments. Cognitive-behavioural therapy, a top-down treatment, targets negatively biased thinking, including content, rumination, and ultimately, schemas (Beck & Dozois, 2011). It is highly effective in treating symptoms, promoting remission, and reducing relapse (e.g., Beck & Dozois, 2014; Cuijpers et al., 2013). More realistic and adaptive thinking may reduce interference on cognitive control abilities, particularly during times of stress. Cognitive control training, which is a bottom-up intervention that trains individuals to better inhibit, update, or shift from negative goal-irrelevant information, may enable individuals to better self-regulate and to disengage from rumination. Few effectiveness or efficacy studies have been conducted on

cognitive control training, and, while some have reported promising findings, effects are only small to moderate (see Motter et al., 2015 and Koster, Hoorelbeke, Onraedt, Owens, & Derakshan, 2017, for reviews). This may be explained by the reduced impact that cognitive control appears to have on stress reactivity among cognitively vulnerable individuals (at least in terms of immune responding) found in the current study. As such, cognitive control training may be more beneficial for individuals with relatively lower cognitive vulnerability. More adaptive schemas and/or enhanced cognitive control may both have an impact on immune responding by altering perceptions of social threat and the individual's appraisal of their ability to manage social threat, as well as their actual ability to self-regulate. Consistent with this idea, a few studies have begun to document promising effects of psychological treatments on immune functioning (e.g., Moreira et al., 2015; Zabihiyeganeh et al., 2019). Future research examining the role of top-down or bottom-up interventions on resting-state and stress-induced inflammation would provide robust tests of the cognition-inflammation link and the role inflammation plays in the course of depression. Given the role inflammation has on a number of medical conditions, this also represents an exciting area for future research examining the role of psychological treatment on physical health.

Conclusion

Cognitive theories posit that cognitive control deficits promote depression by reducing ability to self-regulate under stress (Joormann & Tanovic, 2015). In particular, poor ability to inhibit negative information, discard negative material, and shift away from negative content may result in rumination. In addition to extending past research findings on depression-related cognitive control deficits and their association with rumination, this study was the first to investigate the effect of cognitive content and structure on cognitive control following social-

evaluative stress. When activated by stress and accessible to working memory, negative cognitive content and structure were found to interfere with cognitive control abilities, resulting in even greater declines in executive functioning when it is most needed.

Burgeoning evidence indicates that social stress upregulates inflammation, resulting in a pro-inflammatory phenotype that drives depression pathogenesis. However, cognitive mechanisms underlying this process are not well understood. This study filled an important gap in the psychoneuroimmunology literature by demonstrating that cognitive vulnerability and cognitive control influence baseline inflammation and reactivity to a laboratory stressor. This thesis also contributed novel findings to the literature by providing evidence that individuals with low vulnerability combined with poor cognitive control tend to show higher resting-state and stress-induced increases in inflammatory reactivity. Individuals with greater vulnerability were less influenced by cognitive control and, in some cases, appeared to show less reactivity to the stressor. Lower reactivity to the stressor in turn predicted greater depressive symptoms six months later. Altogether, these results suggest complex relations between cognition and inflammation that are not uniform across individuals of varying vulnerability to depression. Given that cognitive vulnerability and cognitive control are amenable to intervention and modification, these findings have key implications for treatment and for possible alteration of immunological mechanisms underlying the pathogenesis of depression. The current study reveals inflammation as a pathway through which both cognitive vulnerability and cognitive control may shape mental and physical health among individuals both with and without depression over time.

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Appendix A

Advertisement for Participant Recruitment

Appendix B

Online Form for Initial Eligibility Screening

Welcome the Western Mood Study!

The Western Mood Study is exploring how mood is related to thoughts, emotions, inflammation, and behaviour before and after life events in individuals who have, and have not, experienced depression. Because we are interested in inflammation, we need to ask individuals about medical conditions and medications that may influence levels of inflammation.

Participating in this study involves 3 lab visits and two online components, and participants will be asked to complete questionnaires and interviews about thoughts, emotions, behaviours, life events, and mood, and to engage in cognitive tasks and a task designed to induce mild stress in the lab. Participants will also be asked to provide two saliva samples during one of the lab visits to assess inflammation. Participants will be compensated $20 for each component of the study they participate in. For individuals who participate in all the components, the total compensation will be $100. Participants will also be entered in a draw to win one of four iPads.

Please complete this form to let us know that you are interested in participating in the study. Please note you must be 18 years or older and willing to be audio- and video-recorded to participate. After completing the form, you will be notified whether or not you are eligible. If you are, one of our research assistants will call you shortly for further eligibility screening and, if applicable, to arrange for you to begin the study. Completion of this screening survey is indication of your consent to complete screening and to be contacted by us by telephone for further screening for the study, and does not provide consent for study participation.

Please indicate your age:

Do you have a smartphone with a data plan or regular access to wifi? _____Yes _____No

Please indicate below if any of the following apply to you.

you have a current injury, cut, wound, sore, or lesion in your mouth _____Yes _____No
you have bleeding gums _____Yes _____No
you have gum disease (i.e., periodontal disease, gingivitis) _____Yes _____No
you have had dental work in the past two weeks _____Yes _____No
you have a chronic inflammatory disease such as, but not restricted to, arthritis, thyroid problems, chronic active hepatitis, chronic peptic ulcer, asthma, tuberculosis, ulcerative colitis, Crohn's disease, or chronic sinusitis _____Yes _____No
you have cancer or any other neoplastic disease _____Yes _____No
you are currently undergoing chemotherapy or radiation therapy _____Yes _____No
you have undergone an organ transplant _____Yes _____No

you are taking immunosuppressant or immunomodulator medication (such as but not restricted to, tacrolimus, azathioprine, mercaptopurine, methotrexate, cyclosporine, interferon _____Yes _____No
you are taking any Non-Steroidal Anti-Inflammatory drugs on a daily basis (NSAIDS such as, but not restricted to, naproxen, aspirin, or ibuprofen) _____Yes _____No
you are taking any oral steroid medication (such as, but not restricted to, prednisone, dexamethasone, hydrocortisone) _____Yes _____No
you are currently pregnant, trying to become pregnant, or breastfeeding _____Yes _____No
you have been diagnosed with a sleep disorder, such as, but not restricted to, insomnia, hypersomnia or hypersomnolence disorder, sleep apnea, narcolepsy _____Yes _____No
you have an acute condition such as a cold, flu, tonsillitis, bronchitis, or sinus infection, or you have symptoms consistent with a cold or infection (e.g., sore throat, runny nose, sweating, coughing) _____Yes _____No

Comments:

If participants are over 18, indicate they have a smartphone, and select NO for all medical items, excluding the fourth or last item

Thank you for completing the form. Please provide your contact information below and one of our research assistants will call you shortly for further eligibility screening and, if applicable, to arrange for you to begin the study.

Name:
Email:
Phone Number:
Can we leave a voicemail? _____Yes _____No
Comments: E.g., preferred time of day to be called

If you have any questions or concerns, please do not hesitate to contact us by email at XXXXX@uwo.ca or at XXX-XXX-XXXX ext. XXXXX. Please note, the Principal Investigator for this study is Dr. David Dozois and the Co-Investigator is Katerina Rnic. Thank you.

If participants are under 18, do not have a smartphone, or select YES for any medical item, excluding the fourth or last item'

We are sorry, but based on your responses, you are not eligible to participate in the Western Mood Study. The Western Mood Study will be examining the role of inflammation in depression, so unfortunately we cannot include individuals who are taking medications or who have medical conditions that could affect our measurement of markers of inflammation. If you have any questions or concerns, please do not hesitate to contact us by email at XXXXX@uwo.ca or at XXX-XXX-XXXX ext. XXXXX. Please note, the Principal Investigator for this study is Dr. David Dozois and the Co-Investigator is Katerina Rnic. Thank you for your time, and we hope you will consider participating in future studies in the Mood Lab.

Appendix C

Description of Larger Study

The current study was part of a larger study conducted with the additional goals of assessing the relation of emotion regulation and stress generation with cognitive control and inflammation. At Phase 1, participants completed a number of additional measures not included in the present study. These were the negative urgency scale of the UPPS-P Impulsivity Scale (Whiteside & Lynam, 2001), the Stress Reactive Rumination Scale (SRRS; Robinson & Alloy, 2003), the Cognitive-Behavioral Avoidance Scale (CBAS; Ottenbreit & Dobson, 2004), the Depressive Interpersonal Relationships Inventory-Reassurance Seeking Subscale (DIRI-RS; Joiner, Alfano, & Metalsky, 1992), and the Emotion Regulation Questionnaire (ERQ; Gross & John, 2003).

Following the Phase 2 laboratory visit, participants completed one week of ecological momentary assessment. Participants received 4 texts per day on their smartphone. The text provided them with a link to an online form, which asked them to report on any negative life events that occurred since the last form they completed, and to report on their affect, use of emotion regulation strategies and maladaptive behaviours. This portion of the study used the modified Stress Reactive Rumination Scale as well as items from other ecological momentary assessment studies (Moberly & Watkins, 2008; Ruscio et al., 2015) or adapted from standard instruments.

At Phase 3 (two weeks after Phase 2), participants completed an interview with the principal investigator (KR) in addition to completing the BDI-II. In the interview, participants were queried in order to obtain contextual detail on negative life events, hassles, and difficulties they had reported over the previous week, in order for these to be rated using the Life Events Scale criteria (Alloy & Clements, 1992; Safford, Alloy, Abramson, & Crossfield, 2007), which provides criteria and ratings for a broad range of negative events, including minor, daily hassles.

Finally, at Phase 4 (6 months after Phase 2), participants completed the mood module of the SCID-5 to ascertain patterns of relapse and recurrence, and the Life Events and Difficulties Schedule (LEDS-II Bifulco et al., 1989) interview in order to assess stress generation, in addition to completing the BDI-II again.

Appendix D

Demographic and Health Questionnaire

Age: _____

Biological Sex: _____ Male
_____ Female
_____Intersex

Ethnicity:
_____ African Canadian or Black
_____ First Nations or Native Canadian
_____ East Asian
_____ South Asian
_____ Hispanic or Latino
_____ Native Hawaiian or other Pacific Islander
_____ White or Caucasian
_____Mixed. Please specify:_____
_____Other. Please specify: _____

What is your current marital status? Please select the item that best describes your current
a) single and never married
b) living with partner
c) common-law
d) married
e) separated
f) widowed
g) divorced

How many years of education have you completed? Please count beginning at grade 1
_____

What level of education have you completed?
1= less than 7th grade
2= junior high school, 8th or 9th grade
3=partial high school, 10th or 11th grade
4= high school graduate
5=partial college, at least one year of specialized training
6= college or university graduation
7=graduate/professional training

What kind of work do you do? _____

Approximate total household income (from all sources) before taxes last year:
-Less than $10,000
-$10,000 - $24,999

-$25,000 - $49,999
-$50,000 - $74,999
-$75,000 - $99,999
-$100,000 - $149,000
-$150,000 - $199,999
-$200,000 or more
-Don't know
-Prefer not to answer

Are you taking any hormonal contraceptives ? (Such as, but not restricted to, oral birth control pills, hormonal intrauterine device or IUD, birth control patch)

_____Yes. What kind? Please list the type of contraceptive (e.g., patch, pill, IUD, ring) and brand name _____
_____No

Are you receiving hormone replacement treatment or therapy? ____Yes _____No

About how long ago was your last menstrual period?
a) having it now
b) less than 2 months ago
c) 2-12 months ago
d) more than 12 months ago

Please list all medications you are taking, including dosage and dosing frequency_____

Do you smoke cigarettes? _____Yes (about how many cigarettes did you smoke per day?_____)
_____No
If no: Did you used to smoke cigarettes? ____Yes _____No
If yes: When did you quit? _____(MM/YYYY). About how many cigarettes did you smoke per day?_____

Approximately how many ounces of alcohol (equivalent to 1 beer, 1 glass of wine, or 1 shot of liquor) do you drink per week? _____

Are you receiving any therapy or counseling for a psychological problem? ____Yes _____No

Have you ever received any therapy or counseling for a psychological problem? ____Yes _____No

Appendix E

Letter of Information

Project Title: Western Mood Study
Document Title: Letter of Information and Consent - Time 1
Principal Investigator:
David Dozois, PhD, Psychology
Western University
Co-Investigator:
Katerina, MSc, Psychology
Western University

1. Invitation to Participate

You are invited to participate in a research study exploring how mood is related to thoughts, emotions, inflammation, and behaviour before and after life events, and because you met eligibility criteria for this study. This means that you are age 18 and older, own a smartphone (smartphones are needed to complete part of the study), and are currently depressed, have been depressed in the past, or have never been depressed. Individuals with any of the health issues or conditions listed below are not eligible, as the presence of certain conditions or use of particular medications may affect the validity of our measurements of markers of inflammation. If any of the below apply to you, please click the 'I am not eligible' button below. If an item applies to you only temporarily, please inform us and we will arrange for you to begin the study once you are eligible.
You are not eligible to participate at this time if you:

- have bipolar disorder (manic-depression)
- have ever experienced psychosis (severe impairment or distortion in the experience of reality)
- have a current injury, cut, wound, sore, or lesion in your mouth
- have bleeding gums
- have gum disease (i.e., periodontal disease, gingivitis)
- have had dental work in the past two weeks
- have a chronic inflammatory disease such as, but not restricted to, arthritis, thyroid problems, chronic active hepatitis, chronic peptic ulcer, asthma, tuberculosis, ulcerative colitis, Crohn's disease, or chronic sinusitis
- have cancer or any other neoplastic disease
- are currently undergoing chemotherapy or radiation therapy
- have undergone an organ transplant
- are taking immunosuppressant or immunomodulator medication (such as but not restricted to, tacrolimus, azathioprine, mercaptopurine, methotrexate, cyclosporine, interferon)
- are taking any Non-Steroidal Anti-Inflammatory drugs(NSAIDS such as, but not restricted to, naproxen, ibuprofen, aspirin) on a regular basis or 24 hours before the first laboratory appointment

- are taking any oral steroid medication (such as, but not restricted to, Prednisone, dexamethasone, hydrocortisone)
- are currently pregnant, trying to become pregnant, or breastfeeding
- have an acute condition such as a cold, flu, tonsillitis, bronchitis, or sinus infection, or you have symptoms consistent with a cold or infection (sore throat, runny nose, sweating, coughing)

2. Why is this study being done?

The purpose of this study is to learn how thinking, emotions, inflammation and behaviours relate to each other before and after life events. This will help us to better understand the factors that are involved in the onset, recurrence and maintenance of depression, which is an area in need of further research.

3. How long will you be in the study?

It is expected that you will be in the study for 6 months, there will be two online components and 3 laboratory visits during your participation in this study.

4. What are the study procedures?

If you agree to participate you will be asked to complete a number of questionnaires about your mood, the types of thoughts you have, and your tendency to engage in different types of behaviours. This portion of the study will be completed online. It is anticipated that this portion of the study will involve a time commitment of two hours, after which you will be debriefed on this portion of the study. In the next part of the study, you will be asked to complete a number of tasks in the laboratory that assess different cognitive functions. You will also be asked to complete a task that will cause some temporary stress, which will be video-recorded and will allow us to examine how you react to stress and to measure markers of inflammation that are secreted during stress. You cannot participate if you do not agree to be video-recorded. Furthermore, over the course of this session, you will be asked to provide saliva samples and we will measure your height and weight. The laboratory portion of the study will take approximately 2 hours. We will then ask you to report on your daily experiences, including daily hassles, what you are feeling, thinking and doing, 4 times per day for a one week period. This is the experience sampling component of the study. Altogether, we expect participants will spend up to 2 hours and 20 minutes over the entire week answering questions. A week later, you will be asked to return to the laboratory to answer questions in an interview about the life events you experienced over the week and to report on your mood in a questionnaire, which will take approximately 40 minutes. Finally, you will be asked to return to the laboratory in 6 months to report (in a questionnaire and an interview) on your mood and the life events you experienced since you started the study, and this visit will be approximately one hour long. Altogether, we anticipate the study to involve a total of 8 hours of your time. Please note that all interviews will be audio-recorded, and you cannot participate if you do not agree to be audio-recorded.

5. **What are the risks and harms of participating in this study?**

   Although you may experience some mild discomfort when completing the questionnaires and/or tasks, this should be temporary. We recognize that you may be experiencing symptoms of depression; however, the tasks in this study have been previously used with individuals with varying levels of depression and have not been found to result in negative effects. Further, you will be provided with a debriefing form at the end of the session today that provides resources online, on campus, and in the community that you can use if you are distressed.

6. **What are the benefits?**

   You may not directly benefit from participating in this study, but information gathered may provide benefits to society as a whole which includes learning more about the course of depression and associated risk factors.

7. **Can participants choose to leave the study?**

   Participation in this study is voluntary. You may refuse to participate, refuse to answer any questions, or withdraw from the study at any time with no effect on your academic status or relationship to the university or to your referral source if you were referred to the study. If you decide to withdraw from the study, you have the right to request withdrawal of information collected about you. If you wish to have your information removed please let the researcher know.

8. **How will participants' information be kept confidential?**

   All data collected will remain confidential. All identifiable information will be deleted from the dataset collected so that individual participants' anonymity will be protected. The de-identified data will be accessible by the study investigators as well as the broader scientific community. More specifically, the data may be posted on a specific database or made available to other researchers upon publication so that data may be inspected and analyzed by other researchers. The data that may be shared will not contain any information that can identify you. Data are stored by Western University Psychology Department's secure server and all forms are stored in locked filing cabinets. If the results are published, your name will not be used. The researcher will keep any personal information about you in a secure and confidential location for a minimum of 5 years. A list linking your study number with your name will be kept by the researcher in a secure place, separate from your study file. While we do our best to protect your information there is no guarantee that we will be able to do so. If data is collected during the project which may be required to report by law we have a duty to report. Representatives of The University of Western Ontario Non-Medical Research Ethics Board may require access to your study-related records to monitor the conduct of the research.

9. **Are participants compensated to be in this study?**

   You will be compensated $20 for each component of the study you participate in.

   - Time 1: Online survey: $20 + 1 entry in iPad draw

- Time 2: First laboratory visit: $20 + 1 entry in iPad draw
- Time 3: Experience Sampling: $20 + 1 entry in iPad draw
- Time 4: Second laboratory visit: $20 + 1 entry in iPad draw
- Time 5: Third laboratory visit: $20 + 1 entry in iPad draw
- Bonus: If you completed 80% of the smartphone alerts within 30 minutes of receiving them for the Experience Sampling, or Time 3, component of the study: $20 + 1 entry in iPad draw

Participants who participate in every component of the study will therefore receive a total of $100 over the course of the study and 5 entries in a draw to win one of 4 iPads, and those who participate in every component of the study **and** complete 80% of their smartphone alerts on time for the experience sampling component of the study will receive a total of $120 and 6 entries in the iPad draw over the course of the study. If you do not complete the entire study you will still be compensated for every portion of the study you completed or began. Please note that you will receive your compensation for Time 1 when you come to the lab for your first laboratory appointment.

10. What are the rights of participants?

Your participation in this study is voluntary. You may decide not to be in this study. Even if you consent to participate you have the right to not answer individual questions or to withdraw from the study at any time. If you choose not to participate or to leave the study at any time it will have no effect on your academic standing if you are a student at Western, your employment status if you work at Western, or your care if you were referred to the study by a care provider. We will give you new information that is learned during the study that might affect your decision to stay in the study.
You do not waive any legal right by signing this consent form.

11. Whom do participants contact for questions?

If you have any questions about this research study please contact the Principal Investigator: Dr. David Dozois (XXX) XXX-XXXX ext. XXXXX, email: XXXXXXX@uwo.ca, or Katerina Rnic (XXX) XXX-XXXX ext. XXXXX, email: XXXXX@uwo.ca.

If you have any questions about your rights as a research participant or the conduct of this study, you may contact The Office of Human Research Ethics (519) 661-3036, email: ethics@uwo.ca.

12. Consent

Completion of the survey is indication of your consent to participate in this portion of the study.

Please print or save a copy of this letter for future reference

Note: Participants were presented with a letter of information at the start of each phase of the study. Other letters of information used in the study are available from the primary investigator: Katerina Rnic.

Appendix F

Consent Form

Project Title: Western Mood Study
Document Title: Letter of Information and Consent
Principal Investigator:
David Dozois, PhD, Psychology
Western University
Co-Investigator:
Katerina, MSc, Psychology
Western University

I have read the Letter of Information, have had the nature of the study explained to me and I agree to participate. All questions have been answered to my satisfaction.

_____	_____	_____
Print Name of Participant	Signature	*Date (DD-MM- YYYY)*

My signature means that I have explained the study to the participant named above. I have answered all questions.

_____	_____	_____
Print Name of Person Obtaining Consent	Signature	*Date (DD-MM- YYYY)*

Appendix G

Debriefing Form

Phase 2

Project Title: Western Mood Study
Principal Investigator:
David Dozois, PhD, Psychology
Western University
Co-Investigator:
Katerina, MSc, Psychology
Western University

Thank you for participating in this study. Research has shown that depression is associated with difficulty controlling what information an individual is attending to at a given moment (i.e., "cognitive control"; see Joorman & Tanovic, 2015). Furthermore, difficulty with cognitive control is associated with a greater inflammatory response following stress (Shields et al., 2016), such that the body releases small protein molecules called cytokines. People with poor cognitive control may therefore show biological responses to stress that are similar to responses to infections. Cognitive control is also known to decrease after stress (Quinn & Joormann, 2015), when this ability is needed most. Furthermore, emerging evidence indicates that inflammation may cause or maintain some forms of depression (Slavich & Irwin, 2013), making inflammation a very important topic to study. However, it is unclear what types of cognitive control are most closely associated with increases in inflammation after stress, or whether inflammation after stress is also tied to changes in cognitive control after stress. It is also unclear if a combination of negative thoughts and difficulty with cognitive control lead to greater inflammation and even greater difficulty with cognitive control under conditions of stress. The tasks you completed on the computer assessed your cognitive control abilities, and you were asked to complete one task twice to assess how your abilities changed following stress. We elicited stress by asking you to complete a mock job interview and to perform mental arithmetic in front of a panel of "evaluators." You were asked to indicate how you were feeling before and after the stress task to ensure that the task resulted in changes in how you felt.

Please note that this study involved deception. You were led to believe that you would complete a mock job interview and mental arithmetic so that a committee of individuals from a human resources department could analyze your ability to maintain a professional demeanor under stress. **In reality, these individuals were not evaluating you, and are not members of a human resources department. They are actually research assistants in the lab.** Deception was necessary in order for you feel like you were being evaluated by other people in order to elicit feelings of stress. This allows us to examine how stress leads to changes in inflammation and cognitive control ability, which is important for helping us to understand why some people are more vulnerable to life stress than others, particularly in the context of depression. The recording of your speech will be deleted immediately. If you wish to withdraw your consent at this time, please notify us and we will delete all of your data from the dataset.

Your results are confidential to the experimenters and all results are published anonymously as group data. If you have any questions or concerns, please contact the Principal Investigator: Dr. David Dozois (XXX) XXX-XXXX ext. XXXXX, email: XXXXX@uwo.ca, or Katerina Rnic XXX) XXX-XXXX ext. XXXXX, email: XXXXX@uwo.ca.
Finally, we ask that you do not leave this form out in the open and that you do not tell others about the true nature of this study, as others will be participating in this study, and if they are aware of the deception involved the validity of the study will be compromised.

Thanks again!

Katerina, MSc, Psychology
Western University

Below is a list of some readings if you would like to learn more about research on cognitive and behavioural vulnerability and depression.

Dobson, K. S., & Dozois, D. J. (Eds.). (2011). *Risk factors in depression*. San Diego, CA: Academic Press.

Gotlib, I. H., & Hammen, C. L. (Eds.). (2014). Handbook of depression (3rd ed.). New York: Guilford Press.

Joormann, J., & Tanovic, E. (2015). Cognitive vulnerability to depression: Examining cognitive control and emotion regulation. *Current Opinion in Psychology*, *4*, 86-92.

Quinn, M. E., & Joormann, J. (2015a). Control when it counts: Change in executive control under stress predicts depression symptoms. *Emotion*, *15*, 522-530.

Slavich, G. M., & Irwin, M. R. (2014). From stress to inflammation and major depressive disorder: A social signal transduction theory of depression. *Psychological bulletin*, *140*, 774.

Shields, G. S., Kuchenbecker, S. Y., Pressman, S. D., Sumida, K. D., & Slavich, G. M. (2016). Better cognitive control of emotional information is associated with reduced pro-inflammatory cytokine reactivity to emotional stress. *Stress*, *19*, 63-68.

Should you have any questions or concerns about this study, please contact:

Katerina Rnic or Dr. David Dozois. If you have any questions about your rights as a research participant, you should contact the Director of the Office of Research Ethics at 519 661-3036.

Below are a variety of resources if you are interested in learning more about depression, how you can help yourself, or how you can arrange for professional help.

Self-Help References:

If you would like to look up some good self-help books on changing negative thinking, please see:

- Burns, D. D. (1980). *Feeling good.* New York: Penguin.
- Burns, D. D. (1989). *The feeling good handbook*. New York: Penguin.
- Greenberger, D., & Padesky, C. A. (2015). *Mind over mood: Change how you feel by changing the way you think.* Guilford Press.
- Wright, J. H., & McCray, L. W. (2011). *Breaking free from depression: Pathways to wellness.* Guilford Press

Available Services

There are several ways in which individuals can access psychological or psychiatric help both on campus and within the City of London, Ontario. If you are feeling depressed or anxious or feel that you could benefit from some individual assistance, the following information may be of use to you.

The Student Development Centre at the University of Western Ontario

- Individual appointments are available for students. To make an appointment you can call **661-3031**, or you can make an appointment in person at the Reception Desk, Room 4100 of the Western Student Services Building.
- Psychological Services Staff will make every effort to respond as quickly as possible when an individual student requires an emergency appointment.
- Psychological Services Staff can help you deal with a variety of issues including those related to Traumatic Events, Sexual or Physical Assault, Date rape, Interpersonal Violence, and Gay, Lesbian, Bisexual, or Transgendered situations.
- More information about the services offered at SDC can be found on the World Wide Web at **http://www.sdc.uwo.ca/**

London Crisis Centres

Psychological Services Staff will make every effort to respond as quickly as possible when an individual requires an emergency appointment. If you are in crisis when the office is closed please call one of the numbers listed below.

- **Reach Out**: Crisis line: 519-433-2023
  - Web chat crisis support: http://reachout247.ca/
- **Good2Talk**: Crisis line: 1-866-925-5454
- **Mental Health and Addictions Crisis Centre**
  - Walk-in support for individuals who do not require hospital or emergency services. Located at 648 Huron St. open 24 hours a day, 7 days a week.
- **Sexual Assault Centre London Crisis Line**: 519-438-2272
  - Also 24 hour support line for sex trade workers: 519-438-2272
- **Women's Community House Help Line**: 519-642-3000
  - Out-of-Town calls: 1-800-265-1576
- **Zhaawanong (Atenlos) Shelter**: 519-432-2270
  - Outside of the London area code: 1-800-605-7477
  - 24 hour crisis line: 519-432-0122

- **St. Joseph's Sexual Assault and Domestic Violence Centre**: 519-646-6100 ext 64224

Student Health Services Counselling Centre

- SHS is located in **Room 11, (Lower Level) University Community Centre**, U.W.O. Main telephone line: (519) 661-3030.
- The Student Health Services Counselling Centre provides individual counselling for students. The Counselling Centre can be reached at (519) **661-3771**.
- The Counselling Centre's Hours of Operation are as follows: Monday to Friday 8:30 a.m.- 4:30 p.m. (Please note the Counselling Centre will be closed when the university is closed.)

Addiction Services of Thames Valley

- Alcohol & Drug Services of Thames Valley is located at **200 Queens Ave., Suite 260, London, Ontario N6A 1J3**
- A community service, funded by the Provincial Ministry of Health, Ontario Substance Abuse Bureau. There are currently no charges for clinical services, although fees may be charged for training or seminars.
- Service is available to any resident of Middlesex, Elgin or Oxford County. There are no admission restrictions.
- Provide early intervention to persons who are concerned about substance use and/or problem gambling.
- ADSTV is a gay, lesbian, bisexual, transsexual, and transgender positive environment
- Services include assessment of individuals who have an alcohol and/or drug related problem. Assessments are also available for problem gambling. Based on these assessments the ADS will develop treatment plans for clients and assist with referrals to provide outpatient counselling and aftercare.
- Hours of operation in London are as follows: Monday and Tuesday - 8:30 a.m. to 8:00 p.m.; Wednesday 8:30 a.m. to 12:00 p.m. and 1:00 p.m. to 4:30 p.m; Thursday and Friday 8:30 a.m. to 4:30 p.m.
- Self-referrals are welcome, call **519-673-3242** (extension 222 for substance abuse services, extension 234 for problem gambling services).

Emergencies After Hours

- If you are in distress during an after-hours time, please go to the **nearest hospital emergency room**.
- **On Campus:** University Hospital: 519-663-3197, 339 Windermere Rd.
- **South London:** Victoria Hospital:519-685-8141, 800 Commissioners Rd. East
- **North London:** St. Joseph's Hospital: 519-646-6100, 268 Grosvenor Rd.

Referrals to Other Resources

- Family physicians can provide you with counselling services, and can make referrals to other community resources as needed.
- Specialized services for emotional and interpersonal problems are available, however, a referral from a physician is often necessary.

We hope that this information is helpful to those who need it.
If you are suffering from distress, we encourage you to seek help from an appropriately qualified individual or service centre. Please contact a University or Community Agency that can help you, or to speak with a physician who can refer you to the appropriate resource.

Note: Participants were presented with a debriefing form at the end of each phase of the study. Other debriefing forms used in the study are available from the primary investigator: Katerina Rnic.

Appendix H

Glossary

Baseline/ resting-state/ pre-stress inflammation or cytokines: latent factor of the four cytokines IL-8, IL-6, IL-1β, and TNF-α after a relaxation period, and before the laboratory stressor.

Cognitive organization/ Cognitive structure: The degree of interconnectedness of social or achievement self-schemas; assessed using the PDST.

DAS (Dysfunctional Attitudes Scale): A self-report questionnaire assessing conditional assumptions of approval from others, prerequisites for happiness, and perfectionistic standards.

Negative affective switch costs: The average cost of switching from the nonaffective to the affective categorization rule when an image is negative. This is thought to reflect difficulty switching to processing the negative aspects of stimuli.

Negative nonaffective switch costs: The average cost of switching from the affective to the nonaffective categorization rule when an image is negative. This is thought to reflect difficulty switching away from processing the negative aspects of stimuli.

PDST (Psychological Distance Scaling Task): A cognitive task that assesses self-schema organization/structure.

Positive affective switch costs: The average cost of switching from the nonaffective to the affective categorization rule when an image is positive. This is thought to reflect difficulty switching to processing the positive aspects of stimuli.

Positive nonaffective switch costs: The average cost of switching from the affective to the nonaffective categorization rule when an image is positive. This is thought to reflect difficulty switching away from processing the negative aspects of stimuli.

Stress-induced/ post-stress changes in inflammation or cytokines: second order latent change factor of the four cytokines IL-8, IL-6, IL-1β, and TNF-α from pre- to post- laboratory stressor. This factor is ‘baseline-free’ in that it takes baseline levels of cytokines into account.

TSST (Trier Social Stress Test): A social-evaluative laboratory stress paradigm.

Young Schema Questionnaire (YSQ): A self-report questionnaire that assesses maladaptive core beliefs.

Appendix I

Analyses of the Neutral Stroop

Group differences in General Inhibition

A one-way ANOVA was run for reaction time for the neutral word block of the Stroop. Reaction times did not differ significantly across groups, $F(2, 162) = 1.92$, $p = .149$, partial $\eta_p^2 = .023$. Although differences were not significant, currently depressed participants evinced the slowest reaction times ($M = 651.66$; $SD = 156.18$), followed by remitted depressed individuals ($M = 607.47$; $SD = 130.16$), and finally, controls ($M = 600.28$; $SD = 123.69$).

Association of Deficits in Cognitive Control with Rumination

Consistent with hypotheses, greater trait rumination was associated with longer reaction times on the neutral ($r[164] = .19$, $p = .015$) block of the Stroop.

Predicting Baseline Inflammation and Stress-Induced Changes in Inflammation

Cognitive Content and Rumination. Table 1 presents estimates from the conditional models predicting baseline and stress-induced changes in cytokines by negative cognitive content, rumination, and Neutral Stroop reaction time. The first model (Model 1) examined main effects. Longer reaction times on the Neutral Stroop predicted greater inflammation at baseline. Rumination predicted changes in inflammation after the stressor, such that a greater tendency to ruminate was associated with decreased inflammation. Further, there was a trend whereby greater maladaptive core beliefs marginally predicted greater increases in inflammation following stress.

In Model 2, core beliefs marginally moderated the effects of inhibition on pre-stress inflammation. An examination of the simple slopes revealed that poorer inhibitory ability (i.e., longer Neutral Stroop reaction times) was associated with greater baseline inflammation in

Table 1

Prediction of Latent Pre-stress Cytokines and Latent Change in Cytokines by Neutral Stroop, Negative Cognitive Content, and Rumination

	Pre-stress inflammation			Δ inflammation		
Model and predictor	β	95% CI	*b*	β	95% CI	*b*
Model 1: Main effects		R^2 = .25, p < .001			R^2 = .13, p = .013	
Age	-.07	[-.24, .10]	-.003	.15	[-.08, .38]	.003
BMI	.35***	[.20, .50]	.02	-.02	[-.21, .16]	-.001
Ethnicity						
White vs. Other	-.10	[-.25, .06]	-.12	.11	[-.07, .28]	.06
White vs. Asian	-.21*	[-.37, -.05]	-.18	-.07	[-.28, .15]	-.03
Core Beliefs	-.14	[-.40, .12]	-.001	.26†	[-.04, .56]	.001
Dysfunctional Attitudes	.05	[-.16, .25]	.001	-.17	[-.42, .08]	-.001
Rumination	.02	[-.18, .21]	.00	-.32**	[-.53, -.11]	-.004
Neutral Stroop RT	.26**	[.08, .44]	.08	.12	[-.08, .32]	.02
Model 2: Interaction effect		R^2 = .27, p < .001			R^2 = .15, p = .009	
Core Beliefs × Neutral Stroop RT	-.13†	[-.26, .01]	-.001	.11	[-.04, .26]	.00
Model 3: Interaction effect		R^2 = .26, p < .001			R^2 = .14, p = .014	
Dysfunctional Attitudes × Neutral Stroop RT	-.10	[-.24, .03]	-.001	-.01	[-.15, .13]	.00
Model 4: Interaction effect		R^2 = .27, p < .001			R^2 = .14, p = .013	
Rumination × Neutral Stroop RT	-.13†	[-.27, .01]	-.003	.02	[-.13, .17]	.00

Note. 95% CI = 95% confidence intervals for standardized coefficients (βs). Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1. Values of .00 are < .001. Model fit: Model 1, $\chi^2(67, N = 164) = 166.65$, $p < .001$, CFI = .939, TLI = .916 and RMSEA = .095, SRMR = .118; Model 2, $\chi^2(73, N = 164) = 174.95$, $p < .001$, CFI = .939, TLI = .916 and RMSEA = .092, SRMR = .112; Model 3, $\chi^2(73, N = 164) = 173.77$, $p < .001$, CFI = .939, TLI = .917 and RMSEA = .092, SRMR = .114; Model 4, $\chi^2(73, N = 164) = 171.78$, $p < .001$, CFI = .940, TLI =.918 and RMSEA =.091, SRMR =.114.

†$p < .10$; * $p < .05$; ** $p < .01$; *** $p < .001$.

individuals reporting low (b = .12, 95% CI = [.05, .18], p < .001), but not high, (b = .05, 95% CI = [-.02, 0.11], p = .175), maladaptive core beliefs (Figure 1). Core beliefs did not moderate effects of inhibition on changes in inflammation.

In Model 3, dysfunctional attitudes did not moderate effects of inhibition on pre-stress inflammation or on changes in inflammation. Finally, rumination marginally moderated the relation of inhibition on pre-stress inflammation in Model 4, but did not moderate the effect of inhibition on changes in cytokines. Simple slopes were examined for this marginally significant interaction. Similar to the findings for core beliefs, poor inhibition was associated with greater baseline inflammation in individuals with low (b = .12, 95% CI = [.06, .18], p < .001), but not high (b = .04, 95% CI = [-.03, 0.11], p = .253), rumination (Figure 2).

Cognitive organization. Estimates from the conditional models predicting baseline and stress-induced changes in cytokines by cognitive organization and Neutral Stroop reaction time are presented in Table 2. In the first conditional model (Model 1), negative achievement organization and Neutral Stroop reaction time both predicted pre-stress inflammation. Results indicated that, as hypothesized, individuals with more tightly interconnected negative achievement-related schemas and those with longer reaction times on the Neutral Stroop (indicating poorer inhibitory abilities) demonstrated greater inflammation at baseline. There was also a trend whereby negative social organization was marginally associated with post-stress changes in inflammation, such that having more loosely connected negative social schemas was associated with greater increases in cytokines.

In Model 2, a marginally significant interaction of negative social achievement organization with Neutral Stroop reaction time on pre-stress cytokines emerged. Probing this marginal interaction revealed that poorer inhibitory abilities for neutral stimuli were associated

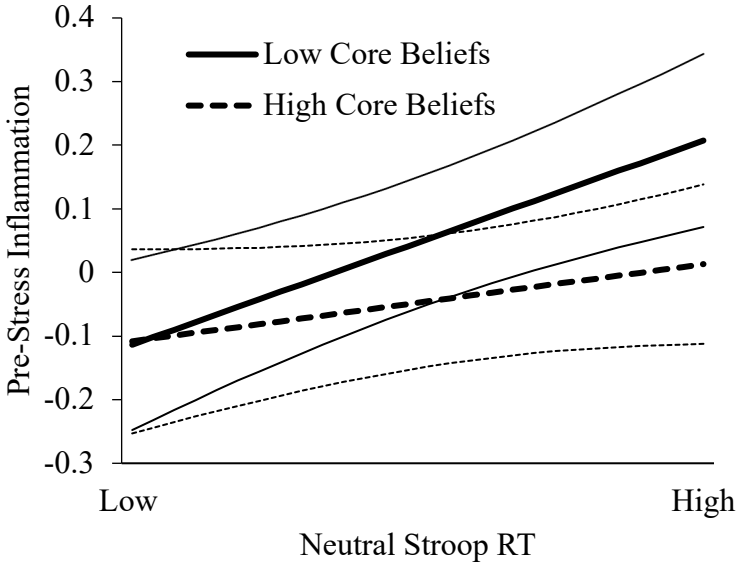

Figure 1. Marginally significant interaction effect between Neutral Stroop reaction time and maladaptive core beliefs on pre-stress cytokines. Prestress Inflammation = latent factor of baseline inflammation. RT= reaction time. 'Low' and 'High' Neutral Stroop reaction time and core beliefs indicate scores one standard deviation below and above the mean, respectively. The thinner lines represent 95% confidence intervals.

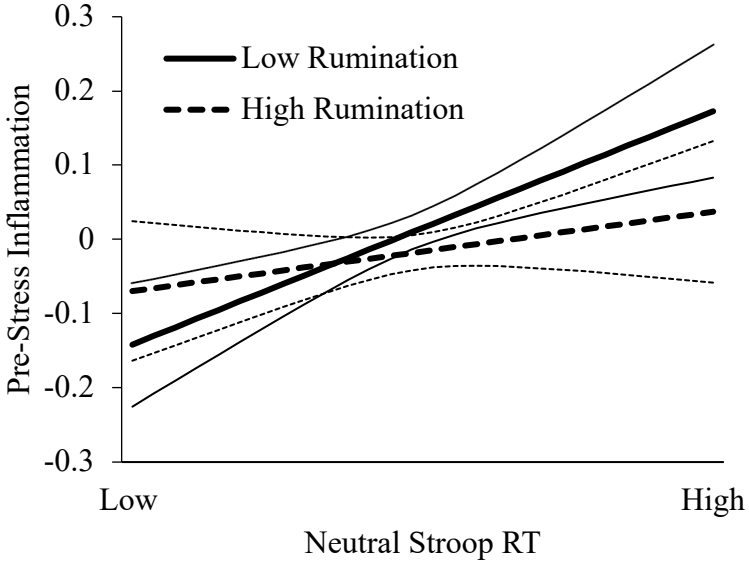

Figure 2. Marginally significant interaction effect between Neutral Stroop reaction time and rumination on pre-stress cytokines. Prestress Inflammation = latent factor of baseline inflammation. RT= reaction time. 'Low' and 'High' Neutral Stroop reaction time and rumination indicate scores one standard deviation below and above the mean, respectively. The thinner lines represent 95% confidence intervals.

Table 2

Prediction of Latent Pre-stress Cytokines and Latent Change in Cytokines by Neutral Stroop and Cognitive Organization

	Pre-stress inflammation			Δ inflammation		
Model and predictor	β	95% CI	*b*	β	95% CI	*b*
Model 1: Main effects		R^2 = .31, p < .001			R^2 = .10, p = .061	
Age	-.04	[-.25, .18]	-.002	.10	[-.15, .35]	.002
BMI	.26**	[.11, .42]	.02	-.03	[-.20, .15]	-.001
Ethnicity						
White vs. Other	-.17†	[-.33, .001]	-.22	.07	[-.17, .31]	.04
White vs. Asian	-.23*	[-.41, -.04]	-.20	-.11	[-.35, .13]	-.05
Negative Social Organization	.12	[-.08, .31]	.12	.19†	[-.01, .39]	.09
Negative Achievement Organization	-.25*	[-.45, -.06]	-.20	.08	[-.14, .29]	.03
Neutral Stroop RT	.30**	[.10, .49]	.09	-.03	[-.26, .20]	-.004
Model 2: Interaction effect		R^2 = .32, p < .001			R^2 = .10, p =.045	
Negative Social Organization × Neutral Stroop RT	-.13†	[-.28, .01]	-.12	-.07	[-.24, .10]	-.03
Model 3: Interaction effect		R^2 = .31, p < .001			R^2 = .10, p =.06	
Negative Achievement Organization × Neutral Stroop RT	-.04	[-.19, .12]	-.02	.03	[-.14, .21]	.01

Note. 95% CI = 95% confidence intervals for standardized coefficients (βs). Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1. Model fit: Model 1, $\chi^2(61, N = 127) = 138.55$, $p < .001$, CFI = .939, TLI = .916 and RMSEA = .100, SRMR = .135; Model 2, $\chi^2(67, N = 127) = 143.34$, $p < .001$, CFI = .941, TLI = .919 and RMSEA = .095, SRMR = .130; Model 3, $\chi^2(67, N = 127) = 139.85$, $p < .001$, CFI = .943, TLI = .922 and RMSEA = .093, SRMR = .129.

$^{\dagger}p < .10$; $^{*}p < .05$; $^{**}p < .01$; $^{***}p < .001$.

with greater baseline cytokines in individuals with tightly interconnected (b = .14, 95% CI = [.07, .21], p < .001), and not loosely connected (b = .04, 95% CI = [-.05, .13], p = .419), negative social schemas (Figure 3). Finally, there was no interaction between Negative Achievement Organization and Neutral Stroop reaction time on either baseline inflammation or stress-induced changes in inflammation in Model 3.

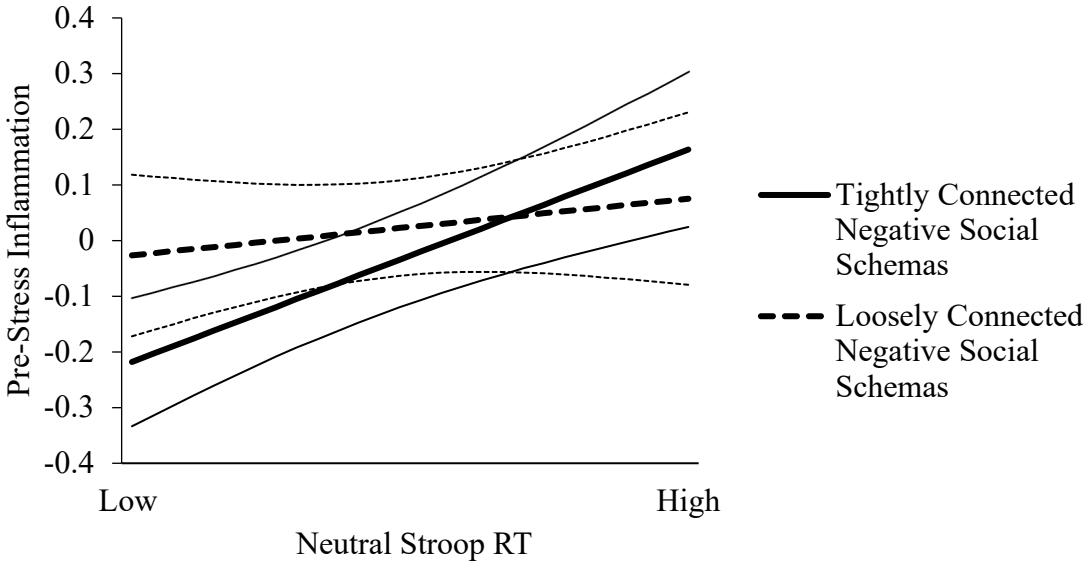

Figure 3. Marginally significant interaction effect between Neutral Stroop reaction time and Negative Social Organization on pre-stress cytokines. Prestress Inflammation = latent factor of baseline inflammation. RT = reaction time. 'Low' and 'High' Neutral Stroop reaction time and Negative Social Organization indicate scores one standard deviation below and above the mean, respectively. The thinner lines represent 95% confidence intervals.

Appendix J

Description of Tests of Measurement Invariance

A series of measurement models were estimated in order to assess whether the four cytokines loaded on a common factor at both pre- and post-stress and, in turn, whether this latent factor was equivalent across both time points (i.e., measurement invariant). Five measurement models were evaluated using confirmatory factor analysis (CFA) with the four cytokines (IL-6, IL-8, IL-1β, and TNF-α) as observed indicators, and models were compared using chi-square difference tests. A nonsignificant $\Delta\chi^2$ indicates that the model constraints do not worsen the model fit and is therefore indicative of measurement invariance. Model fit indices and chi-square difference tests for the five models are shown in Table 1.

The first model did not impose any equality constraints across the two assessments in order to test for configural invariance. Pre- and post-stressor measures of each cytokine were allowed to correlate. Next, to account for the correlation of inflammatory cytokines with each other and to improve model fit, IL-8 and IL-1β, as well as TNF-α and IL-6, were allowed to correlate with each other at each time point. The fit for the configural invariance model was good, and constraining the correlations to be equal across time points did not result in worse model fit (nonsignificant $\Delta\chi^2$). To test for metric invariance, the model with correlations constrained to be equal was compared to a model where the factor loadings were constrained to be equal at pre- and post-stress. Otherwise, the model was constructed the same way. There was support for metric invariance, as constraining the factor loadings to be equal across pre- and post-stress assessments did not result in significantly worse fit (nonsignificant $\Delta\chi^2$). Finally, to test scalar invariance, the metric invariance model was compared to a model in which the intercepts of the indicators were also constrained to be equal across the two assessments. There

was not support for scalar invariance, as constraining the intercepts of the indicators to be equal across time points significantly worsened model fit (significant $\Delta\chi^2$). Based on modification indices, IL-8 and IL-6 were unconstrained in order to test partial invariance of intercepts. A comparison of the partial scalar invariance model with the metric invariance model indicated that the model fit did not change significantly (nonsignificant $\Delta\chi^2$), indicating partial scalar invariance.

Table 1

Model Fit Indices and Model Fit Comparisons of Measurement Models of Latent Factor of Inflammation

	Model fit indices							Difference test		
Model	χ^2	*df*	*p*	CFI	TLI	RMSEA	SRMR	$\Delta\chi^2$	Δdf	*p*
Configural invariance	24.60	11	.010	.990	.975	.086	.065			
Invariance of correlations	26.39	13	.015	.990	.979	.079	.066	2.81	2	ns
Metric invariance	28.66	16	.026	.991	.984	.069	.054	2.98	3	ns
Scalar invariance	81.44	19	<.001	.955	.934	.141	.170	42.84	3	<.001
Partial Scalar invariance	30.49	17	.023	.990	.984	.069	.059	1.83	1	ns

Note. Maximum-likelihood estimation with robust standard errors (MLR) was used; therefore, the chi-square difference tests ($\Delta\chi^2$) were Satorra-Bentler adjusted (Satorra & Bentler, 2001)

Appendix K

Predicting Baseline and Stress-Induced Changes in Inflammation Using Models Constrained to Partial Invariance

Table 1

Prediction of Latent Pre-stress Cytokines and Latent Change in Cytokines by Emotional Stroop, Negative Cognitive Content, and Rumination

	Pre-stress inflammation			Δ inflammation		
Model and predictor	β	95% CI	*b*	β	95% CI	*b*
Model 1: Main effects		R^2 = .22, p < .001			R^2 = .15, p = .018	
Age	-.01	[-.16, .15]	.00	.20†	[-.02, .41]	.003
BMI	.32***	[.17, .48]	.02	-.01	[-.22, .20]	.00
Ethnicity						
White vs. Other	-.09	[-.26, .08]	-.09	.09	[-.08, .27]	.04
White vs. Asian	-.22*	[-.38, -.05]	-.16	-.01	[-.25, .22]	-.004
Core Beliefs	-.11	[-.39, .17]	-.001	.31†	[-.01, .63]	.001
Dysfunctional Attitudes	.04	[-.18, .25]	.00	-.19	[-.46, .07]	-.001
Rumination	.003	[-.21, .21]	.00	-.33**	[-.56, -.10]	-.003
Emotional Stroop RT	.15†	[-.02, .32]	.04	.15	[-.05, .34]	.02
Model 2: Interaction effect		R^2 = .23, p < .001			R^2 = .16, p = .012	
Core Beliefs × Emotional Stroop RT	-.11	[-.24, .03]	.00	.11	[-.04, .27]	.00
Model 3: Interaction effect		R^2 = .23, p < .001			R^2 = .15, p = .017	
Dysfunctional Attitudes × Emotional Stroop RT	-.09	[-.21, .04]	-.001	-.02	[-.17, .13]	.00
Model 4: Interaction effect		R^2 = .24, p < .001			R^2 = .15, p = .019	
Rumination × Emotional Stroop RT	-.13†	[-.26, .01]	-.002	-.03	[-.19, .13]	.00

Note. 95% CI = 95% confidence intervals for standardized coefficients (βs). Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1. Values of .00 are < .001. Model fit: Model 1, $\chi^2(65, N = 164) = 120.47$, $p < .001$, CFI = .966, TLI = .952 and RMSEA = .072, SRMR = .062; Model 2, $\chi^2(71, N = 164) = 129.49$, $p < .001$, CFI = .965, TLI = .951 and RMSEA = .071, SRMR = .060; Model

3, $\chi^2(71, N = 164) = 124.67$, $p < .001$, CFI = .968, TLI = .955 and RMSEA = .068, SRMR = .060; Model 4, $\chi^2(71, N = 164) = 125.42$, $p < .001$, CFI = .967, TLI = .954 and RMSEA = .068, SRMR = .060.
$^{\dagger}p < .10$; $^{*}p < .05$; $^{**}p < .01$; $^{***}p < .001$.

Table 2

Prediction of Latent Pre-stress Cytokines and Latent Change in Cytokines by Emotional Stroop and Cognitive Organization

	Pre-stress inflammation			Δ inflammation		
Model and predictor	β	95% CI	*b*	β	95% CI	*b*
Model 1: Main effects		$R^2 = .26$, $p < .001$			$R^2 = .11$, $p = .083$	
Age	.04	[-.15, .23]	.002	.13	[-.15, .41]	.002
BMI	.24**	[.08, .40]	.01	.01	[-.22, .24]	.00
Ethnicity						
White vs. Other	-.17†	[-.33, .01]	-.18	.06	[-.20, .31]	.03
White vs. Asian	-.22*	[-.41, -.03]	-.16	-.10	[-.38, .17]	-.03
Negative Social Organization	.11	[-.09, .32]	.10	.23†	[-.03, .48]	.08
Negative Achievement Organization	-.24*	[-.44, -.05]	-.16	.05	[-.20, .30]	.01
Emotional Stroop RT	.18*	[.01, .35]	.05	.03	[-.19, .26]	.004
Model 2: Interaction effect		$R^2 = .27$, $p < .001$			$R^2 = .11$, $p = .082$	
Negative Social Organization × Emotional Stroop RT	-.11	[-.24, .03]	-.08	-.03	[-.24, .18]	-.01
Model 3: Interaction effect		$R^2 = .27$, $p < .001$			$R^2 = .11$, $p = .084$	
Negative Achievement Organization × Emotional Stroop RT	-.05	[-.19, .10]	-.02	.03	[-.18, .24]	.01

Note. 95% CI = 95% confidence intervals for standardized coefficients (βs). Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1. Values of .00 are < .001. Model fit: Model 1, $\chi^2(59, N = 127) = 97.09$, $p = .001$, CFI = .970, TLI = .958 and RMSEA = .071, SRMR = .063; Model 2, $\chi^2(65, N = 127) = 99.91$, $p = .004$, CFI = .973, TLI = .962 and RMSEA = .065, SRMR = .061; Model 3, $\chi^2(65, N = 127) = 100.02$, $p = .003$, CFI = .973, TLI = .961 and RMSEA = .065, SRMR = .060.
†$p < .10$; *$p < .05$; **$p < .01$; ***$p < .001$.

Table 3

Prediction of Latent Pre-stress Cytokines and Latent Change in Cytokines by Positive Affective Switch Costs, Negative Cognitive Content, and Rumination

	Pre-stress inflammation			Δ inflammation		
Model and predictor	β	95% CI	*b*	β	95% CI	*b*
Model 1: Main effects		R^2 = .21, *p* = .001			R^2 = .22, *p* = .007	
Age	.06	[-.10, .22]	.002	.20*	[.002, .40]	.003
BMI	.31***	[.16, .47]	.02	-.01	[-.21, .18]	.00
Ethnicity						
White vs. Other	-.05	[-.21, .11]	-.06	.15†	[-.02, .32]	.07
White vs. Asian	-.21*	[-.38, -.04]	-.15	.03	[-.18, .25]	.01
Core Beliefs	-.09	[-.37, .20]	.00	.31*	[.01, .62]	.001
Dysfunctional Attitudes	.01	[-.21, .22]	.00	-.24†	[-.49, .01]	-.001
Rumination	.02	[-.19, .22]	.00	-.30**	[-.51, -.08]	-.003
Positive Affective Switch Costs	.03	[-.13, .19]	.01	.29**	[.10, .49]	.02
Model 2: Interaction effect		R^2 = .21, *p* = .001			R^2 = .23, *p* = .003	
Core Beliefs × Positive Affective Switch Costs	.08	[-.08, .25]	.00	-.12	[-.33, .09]	.00
Model 3: Interaction effect		R^2 = .21, *p* = .001			R^2 = .22, *p* = .007	
Dysfunctional Attitudes × Positive Affective Switch Costs	-.05	[-.18, .09]	.00	.03	[-.12, .18]	.00
Model 4: Interaction effect		R^2 = .26, *p* < .001			R^2 = .33, *p* < .001	
Rumination × Positive Affective Switch Costs	.25**	[.10, .40]	.003	-.37***	[-.57, -.17]	-.002

Note. 95% CI = 95% confidence intervals for standardized coefficients (βs). Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1. Values of .00 are < .001. Model fit: Model 1, $\chi^2(65, N = 165) = 117.30$, $p < .001$, CFI = .968, TLI = .955 and RMSEA = .070, SRMR = .060; Model 2, $\chi^2(71, N = 165) = 131.64$, $p < .001$, CFI = .964, TLI = .949 and RMSEA = .072, SRMR = .059; Model 3, $\chi^2(71, N = 165) = 124.54$, $p < .001$, CFI = .968, TLI = .955 and RMSEA = .068, SRMR = .059; Model 4, $\chi^2(71, N = 165) = 126.39$, $p <. 001$, CFI = .967, TLI = .954 and RMSEA = .069, SRMR = .059.

$^{\dagger}p < .10$; $^{*}p < .05$; $^{**}p < .01$; $^{***}p < .001$.

Table 4

Prediction of Latent Pre-stress Cytokines and Latent Change in Cytokines by Positive Affective Switch Costs and Cognitive Organization

	Pre-stress inflammation			Δ inflammation		
Model and predictor	β	95% CI	*b*	β	95% CI	*b*
Model 1: Main effects		R^2 = .24, p < .001			R^2 = .18, p = .063	
Age	.09	[-.09, .27]	.003	.09	[-.15, .33]	.001
BMI	.23**	[.07, .39]	.01	.01	[-.21, .24]	.00
Ethnicity						
White vs. Other	-.13†	[-.28, .02]	-.14	.09	[-.15, .33]	.04
White vs. Asian	-.21*	[-.41, -.02]	-.15	-.07	[-.33, .19]	-.02
Negative Social Organization	.11	[-.10, .31]	.09	.22†	[-.004, .45]	.08
Negative Achievement Organization	-.24*	[-.43, -.05]	-.16	.06	[-.18, .30]	.02
Positive Affective Switch Costs	.09	[-.08, .26]	.02	.27*	[.04, .50]	.02
Model 2: Interaction effect		R^2 = .25, p < .001			R^2 = .25, p < .001	
Negative Social × Positive Affective Switch Costs	-.06	[-.23, .11]	-.03	.32**	[.12, .53]	.06
Model 3: Interaction effect		R^2 = .24, p = .001			R^2 = .24, p = .009	
Negative Achievement × Positive Affective Switch Costs	-.02	[-.15, .12]	-.01	.25*	[.05, .45]	.04

Note. 95% CI = 95% confidence intervals for standardized coefficients (βs). Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1. Values of .00 are < .001. Model fit: Model 1, $\chi^2(59, N = 127) = 96.00$, p = .002, CFI = .971, TLI = .959 and RMSEA = .070, SRMR = .064; Model 2, $\chi^2(65, N = 127) = 98.28$, p = .005, CFI = .974, TLI = .964 and RMSEA = .063, SRMR = .059; Model 3, $\chi^2(65, N = 127) = 102.17$, p = .002, CFI = .971, TLI = .959 and RMSEA = .067, SRMR = .061.
†p < .10; *p < .05; **p < .01; ***p < .001.

Table 5

Prediction of Latent Pre-stress Cytokines and Latent Change in Cytokines by Negative Affective Switch Costs, Negative Cognitive Content, and Rumination

	Pre-stress inflammation			Δ inflammation		
Model and predictor	β	95% CI	*b*	β	95% CI	*b*
Model 1: Main effects		$R^2 = .22$, $p < .001$			$R^2 = .16$, $p = .016$	
Age	.09	[-.07, .24]	.003	.22*	[.01, .43]	.004
BMI	.32***	[.17, .47]	.02	-.03	[-.24, .17]	-.001
Ethnicity						
White vs. Other	-.05	[-.21, .12]	-.05	.12	[-.05, .28]	.05
White vs. Asian	-.21*	[-.38, -.04]	-.15	-.01	[-.24, .23]	-.002
Core Beliefs	-.12	[-.40, .16]	-.001	.38*	[.06, .70]	.001
Dysfunctional Attitudes	.04	[-.17, .25]	.00	-.26†	[-.53, .003]	-.001
Rumination	.04	[-.17, .24]	.001	-.34**	[-.56, -.12]	-.004
Negative Affective Switch Costs	-.13†	[-.28, .02]	-.02	.17*	[.01, .33]	.01
Model 2: Interaction effect		$R^2 = .23$, $p < .001$			$R^2 = .16$, $p = .017$	
Core Beliefs × Negative Affective Switch Costs	.03	[-.15, .22]	.00	.01	[-.17, .19]	.00
Model 3: Interaction effect		$R^2 = .23$, $p < .001$			$R^2 = .16$, $p = .017$	
Dysfunctional Attitudes × Negative Affective Switch Costs	.06	[-.11, .23]	.00	.00	[-.17, .17]	.00
Model 4: Interaction effect		$R^2 = .23$, $p < .001$			$R^2 = .16$, $p = .015$	
Rumination × Negative Affective Switch Costs	.07	[-.08, .22]	.001	-.05	[-.19, .09]	.00

Note. 95% CI = 95% confidence intervals for standardized coefficients (βs). Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1. Values of .00 are < .001. Model fit: Model 1, $\chi^2(65, N = 165) = 112.96$, $p < .001$, CFI = .970, TLI = .958 and RMSEA = .067, SRMR = .058; Model 2, $\chi^2(71, N = 165) = 116.98$, $p = .001$, CFI = .971, TLI = .960 and RMSEA = .063, SRMR = .057; Model 3, $\chi^2(71, N = 165) = 123.89$, $p < .001$, CFI = .968, TLI = .954 and RMSEA = .067, SRMR = .058; Model 4, $\chi^2(71, N = 165) = 115.94$, $p = .001$, CFI = .973, TLI = .961 and RMSEA = .062, SRMR = .057.

†$p < .10$; *$p < .05$; **$p < .01$; ***$p < .001$.

Table 6

Prediction of Latent Pre-stress Cytokines and Latent Change in Cytokines by Negative Affective Switch Costs and Cognitive Organization

	Pre-stress inflammation			Δ inflammation		
Model and predictor	β	95% CI	*b*	β	95% CI	*b*
Model 1: Main effects		$R^2 = .25$, $p < .001$			$R^2 = .15$, $p = .056$	
Age	.15	[-.05, .33]	.01	.07	[-.19, .33]	.001
BMI	.23**	[.07, .39]	.01	.001	[-.23, .23]	.00
Ethnicity						
White vs. Other	-.13	[-.29, .03]	-.15	.06	[-.18, .29]	.03
White vs. Asian	-.21*	[-.40, -.01]	-.15	-.11	[-.38, .16]	-.03
Negative Social Organization	.09	[-.13, .31]	.08	.25†	[-.001, .51]	.09
Negative Achievement Organization	-.24*	[-.44, -.04]	-.16	.03	[-.20, .27]	.01
Negative Affective Switch Costs	-.14	[-.32, .05]	-.02	.22*	[.03, .41]	.02
Model 2: Interaction effect		$R^2 = .25$, $p < .001$			$R^2 = .18$, $p = .021$	
Negative Social × Negative Affective Switch Costs	-.01	[-.18, .16]	-.01	.20*	[.01, .40]	.04
Model 3: Interaction effect		$R^2 = .25$, $p < .001$			$R^2 = .17$, $p = .016$	
Negative Achievement × Negative Affective Switch Costs	-.003	[-.19, .18]	-.001	.20*	[.01, .38]	.02

Note. 95% CI = 95% confidence intervals for standardized coefficients (βs). Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1. Model fit: Model 1, $\chi^2(59, N = 126) = 94.50$, $p = .002$, CFI = .972, TLI = .960 and RMSEA = .069, SRMR = .061; Model 2, $\chi^2(65, N = 126) = 101.90$, $p = .002$, CFI = .971, TLI = .959 and RMSEA = .067, SRMR = .063; Model 3, $\chi^2(65, N = 126) = 98.84$, $p = .004$, CFI = .974, TLI = .963 and RMSEA = .064, SRMR = .060.

†$p < .10$; *$p < .05$; **$p < .01$; ***$p < .001$.

Table 7

Prediction of Latent Pre-stress Cytokines and Latent Change in Cytokines by Positive Nonaffective Switch Costs, Negative Cognitive Content, and Rumination

	Pre-stress inflammation			Δ inflammation		
Model and predictor	β	95% CI	*b*	β	95% CI	*b*
Model 1: Main effects		R^2 = .21, *p* = .001			R^2 = .14, *p* = .022	
Age	.06	[-.10, .22]	.002	.26*	[.05, .46]	.004
BMI	.31***	[.16, .47]	.02	-.02	[-.23, .19]	.00
Ethnicity						
White vs. Other	-.06	[-.22, .11]	-.06	.12	[-.05, .30]	.06
White vs. Asian	-.22*	[-.39, -.05]	-.16	-.01	[-.24, .23]	-.002
Core Beliefs	-.08	[-.36, .20]	.00	.33*	[.01, .65]	.001
Dysfunctional Attitudes	-.01	[-.22, .21]	.00	-.22†	[-.49, .04]	-.001
Rumination	.01	[-.19, .22]	.00	-.31**	[-.53, -.09]	-.003
Positive Nonaffective Switch Costs	.06	[-.11, .22]	.01	.03	[-.15, .21]	.002
Model 2: Interaction effect		R^2 = .21, *p* = .001			R^2 = .15, *p* = .018	
Core Beliefs × Positive Nonaffective Switch Costs	.004	[-.18, .19]	.00	.12	[-.05, .30]	.00
Model 3: Interaction effect		R^2 = .23, *p* < .001			R^2 = .16, *p* = .008	
Dysfunctional Attitudes × Positive Nonaffective Switch Costs	.14†	[-.02, .30]	.001	.17*	[.01, .33]	.00
Model 4: Interaction effect		R^2 = .21, *p* = .001			R^2 = .14, *p* = .025	
Rumination × Positive Nonaffective Switch Costs	.02	[-.14, .18]	.00	.05	[-.16, .27]	.00

Note. 95% CI = 95% confidence intervals for standardized coefficients (βs). Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1. Model fit: Model 1, $\chi^2(65, N = 165) = 121.29$, $p < .001$, CFI = .966, TLI = .951 and RMSEA = .072, SRMR = .061; Model 2, $\chi^2(71, N = 165) = 126.64$, $p < .001$, CFI = .966, TLI = .952 and RMSEA = .069, SRMR = .059; Model 3, $\chi^2(71, N = 165) = 123.64$, $p < .001$, CFI = .968, TLI = .955 and RMSEA = .067, SRMR = .060; Model 4, $\chi^2(71, N = 165) = 123.12$, $p < .001$, CFI = .968, TLI = .955 and RMSEA = .067, SRMR = .059.

†$p < .10$; *$p < .05$; **$p < .01$; ***$p < .001$.

Table 8

Prediction of Latent Pre-stress Cytokines and Latent Change in Cytokines by Positive Nonaffective Switch Costs and Cognitive Organization

	Pre-stress inflammation			Δ inflammation		
Model and predictor	β	95% CI	*b*	β	95% CI	*b*
Model 1: Main effects		R^2 = .24, *p* = .001			R^2 = .12, *p* = .076	
Age	.11	[-.07, .29]	.004	.13	[-.13, .39]	.002
BMI	.23**	[.07, .39]	.01	.01	[-.22, .24]	.00
Ethnicity						
White vs. Other	-.14†	[-.30, .02]	-.15	.06	[-.19, .31]	.03
White vs. Asian	-.22*	[-.42, -.03]	-.16	-.11	[-.39, .17]	-.03
Negative Social Organization	.11	[-.10, .31]	.09	.22†	[-.03, .48]	.08
Negative Achievement Organization	-.24*	[-.43, -.06]	-.16	.05	[-.20, .30]	.01
Positive Nonaffective Switch Costs	.04	[-.13, .21]	.01	.10	[-.10, .30]	.01
Model 2: Interaction effect		R^2 = .24, *p* = .001			R^2 = .13, *p* = .053	
Negative Social × Positive Nonaffective Switch Costs	.01	[-.15, .16]	.003	-.10	[-.30, .09]	-.02
Model 3: Interaction effect		R^2 = .25, *p* < .001			R^2 = .12, *p* = .075	
Negative Achievement × Positive Nonaffective Switch Costs	-.10	[-.24, .04]	-.03	.02	[-.17, .21]	.003

Note. 95% CI = 95% confidence intervals for standardized coefficients (βs). Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1. Model fit: Model 1, $\chi^2(59, N = 127) = 105.37$, $p < .001$, CFI = .964, TLI = .949 and RMSEA = .079, SRMR = .063; Model 2, $\chi^2(65, N = 127) = 112.65$, $p < .001$, CFI = .963, TLI = .948 and RMSEA = .076, SRMR = .062; Model 3, $\chi^2(65, N = 127) = 112.79$, $p < .001$, CFI = .963, TLI = .948 and RMSEA = .076, SRMR = .063.
†$p < .10$; *$p < .05$; **$p < .01$; ***$p < .001$.

Table 9

Prediction of Latent Pre-stress Cytokines and Latent Change in Cytokines by Negative Nonaffective Switch Costs, Negative Cognitive Content, and Rumination

	Pre-stress inflammation			Δ inflammation		
Model and predictor	β	95% CI	*b*	β	95% CI	*b*
Model 1: Main effects		R^2 = .21, *p* = .001			R^2 = .14, *p* = .021	
Age	.06	[-.10, .22]	.002	.25*	[.04, .45]	.004
BMI	.31***	[.15, .47]	.02	-.03	[-.25, .19]	-.001
Ethnicity						
White vs. Other	-.06	[-.22, .10]	-.06	.12	[-.05, .29]	.06
White vs. Asian	-.21*	[-.38, -.05]	-.16	-.01	[-.24, .22]	-.003
Core Beliefs	-.09	[-.37, .20]	.00	.33*	[.01, .65]	.001
Dysfunctional Attitudes	.01	[-.21, .22]	.00	-.22	[-.47, .04]	-.001
Rumination	.02	[-.19, .22]	.00	-.31**	[-.53, -.09]	-.003
Negative Nonaffective Switch Costs	.03	[-.13, .18]	.01	.06	[-.10, .22]	.01
Model 2: Interaction effect		R^2 = .21, *p* = .001			R^2 = .14, *p* = .020	
Core Beliefs × Negative Nonaffective Switch Costs	.07	[-.10, .24]	.00	-.03	[-.21, .14]	.00
Model 3: Interaction effect		R^2 = .21, *p* = .001			R^2 = .15, *p* = .019	
Dysfunctional Attitudes × Negative Nonaffective Switch Costs	.04	[-.11, .20]	.00	.09	[-.05, .23]	.00
Model 4: Interaction effect		R^2 = .22, *p* < .001			R^2 = .14, *p* = .021	
Rumination × Negative Nonaffective Switch Costs	.13†	[-.01, .28]	.002	-.02	[-.21, .18]	.00

Note. 95% CI = 95% confidence intervals for standardized coefficients (βs). Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1. Values of .00 are < .001. Model fit: Model 1, $\chi^2(65, N = 165) = 120.46$, $p < .001$, CFI = .966, TLI = .952 and RMSEA = .072, SRMR = .059; Model 2, $\chi^2(71, N = 165) = 127.35$, $p < .001$, CFI = .966, TLI = .953 and RMSEA = .069, SRMR = .058; Model 3, $\chi^2(71, N = 165) = 125.38$, $p < .001$, CFI = .967, TLI = .954 and RMSEA = .068, SRMR = .058; Model 4, $\chi^2(71, N = 165) = 137.44$, $p < .001$, CFI = .961, TLI = .945 and RMSEA = .075, SRMR = .060.

†$p < .10$; *$p < .05$; **$p < .01$; ***$p < .001$.

Table 10

Prediction of Latent Pre-stress Cytokines and Latent Change in Cytokines by Negative Nonaffective Switch Costs and Cognitive Organization

	Pre-stress inflammation			Δ inflammation		
Model and predictor	β	95% CI	*b*	β	95% CI	*b*
Model 1: Main effects		R^2 = .24, *p* = .001			R^2 = .11, *p* = .089	
Age	.11	[-.07, .29]	.004	.13	[-.13, .40]	.002
BMI	.23**	[.06, .39]	.01	.001	[-.24, .24]	.00
Ethnicity						
White vs. Other	-.13†	[-.29, .03]	-.15	.07	[-.18, .31]	.03
White vs. Asian	-.22*	[-.42, -.03]	-.16	-.10	[-.38, .18]	-.03
Negative Social Organization	.11	[-.09, .31]	.09	.22†	[-.03, .48]	.08
Negative Achievement Organization	-.25*	[-.44, -.06]	-.16	.05	[-.20, .30]	.01
Negative Nonaffective Switch Costs	.02	[-.16, .20]	.004	.03	[-.19, .24]	.002
Model 2: Interaction effect		R^2 = .24, *p* = .001			R^2 = .11, *p* = .091	
Negative Social × Negative Nonaffective Switch Costs	.01	[-.16, .17]	.002	.01	[-.21, .23]	.002
Model 3: Interaction effect		R^2 = .24, *p* = .001			R^2 = .11, *p* = .087	
Negative Achievement × Negative Nonaffective Switch Costs	.02	[-.12, .15]	.01	-.04	[-.26, .17]	-.01

Note. 95% CI = 95% confidence intervals for standardized coefficients (βs). Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1. Values of .00 are < .001. Model fit: Model 1, $\chi^2(59, N = 127) = 95.62$, $p = .002$, CFI = .972, TLI = .960 and RMSEA = .070, SRMR = .062; Model 2, $\chi^2(65, N = 127) = 105.47$, $p = .001$, CFI = .969, TLI = .956 and RMSEA = .070, SRMR = .061; Model 3, $\chi^2(65, N = 127) = 103.70$, $p = .002$, CFI = .971, TLI = .958 and RMSEA = .068, SRMR = .060.
†$p < .10$; *$p < .05$; **$p < .01$; ***$p < .001$.

Table 11

Prediction of Latent Pre-stress Cytokines and Latent Change in Cytokines by Pre-stress N-back Errors, Negative Cognitive Content, and Rumination

	Pre-stress inflammation			Δ inflammation		
Model and predictor	β	95% CI	*b*	β	95% CI	*b*
Model 1: Main effects		R^2 = .20, *p* = .001			R^2 = .16, *p* = .011	
Age	.03	[-.13, .20]	.001	.25*	[.03, .47]	.01
BMI	.32***	[.16, .48]	.02	-.02	[-.23, .20]	.00
Ethnicity						
White vs. Other	-.04	[-.21, .13]	-.04	.09	[-.09, .26]	.04
White vs. Asian	-.20*	[-.37, -.03]	-.14	-.01	[-.24, .22]	-.003
Core Beliefs	-.11	[-.41, .19]	-.001	.33*	[.01, .66]	.001
Dysfunctional Attitudes	.01	[-.22, .23]	.00	-.23†	[-.49, .02]	-.001
Rumination	.02	[-.20, .25]	.001	-.32*	[-.56, -.07]	-.003
Pre-stress N-Back Errors	.08	[-.06, .22]	.002	.14	[-.04, .31]	.002
Model 2: Interaction effect		R^2 = .21, *p* = .001			R^2 = .17, *p* = .010	
Core Beliefs × Pre-stress N-Back Errors	.06	[-.08, .19]	.00	.05	[-.10, .21]	.00
Model 3: Interaction effect		R^2 = .21, *p* = .001			R^2 = .16, *p* = .011	
Dysfunctional Attitudes × Pre-stress N-Back Errors	.07	[-.06, .20]	.00	.03	[-.13, .20]	.00
Model 4: Interaction effect		R^2 = .21, *p* = .001			R^2 = .16, *p* = .011	
Rumination × Pre-stress N-Back Errors	.05	[-.06, .16]	.00	-.03	[-.18, .13]	.00

Note. 95% CI = 95% confidence intervals for standardized coefficients (βs). Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1. Values of .00 are < .001. Model fit: Model 1, $\chi^2(65, N = 159) = 121.56$, $p < .001$, CFI = .965, TLI = .950 and RMSEA = .074, SRMR = .062; Model 2, $\chi^2(71, N = 159) = 127.23$, $p < .001$, CFI = .965, TLI = .951 and RMSEA = .071, SRMR = .061; Model 3, $\chi^2(71, N = 159) = 127.58$, $p < .001$, CFI = .965, TLI = .951 and RMSEA = .071, SRMR = .062; Model 4, $\chi^2(71, N = 159) = 124.37$, $p < .001$, CFI = .967, TLI = .953 and RMSEA = .069, SRMR = .060.
†$p < .10$; *$p < .05$; **$p < .01$; ***$p < .001$.

Table 12

Prediction of Latent Pre-stress Cytokines and Latent Change in Cytokines by Pre-stress N-back Errors and Cognitive Organization

	Pre-stress inflammation			Δ inflammation		
Model and predictor	β	95% CI	*b*	β	95% CI	*b*
Model 1: Main effects		R^2 = .21, *p* = .003			R^2 = .13, *p* = .056	
Age	.08	[-.11, .28]	.003	.14	[-.15, .42]	.002
BMI	.23**	[.06, .40]	.01	.02	[-.21, .25]	.00
Ethnicity						
White vs. Other	-.12	[-.28, .05]	-.13	.04	[-.22, .28]	.02
White vs. Asian	-.20†	[-.39, .003]	-.14	-.12	[-.39, .16]	-.04
Negative Social Organization	.10	[-.12, .32]	.08	.24†	[-.01, .49]	.08
Negative Achievement Organization	-.23*	[-.42, -.03]	-.15	.05	[-.19, .30]	.02
Pre-stress N-Back Errors	.11	[-.05, .27]	.003	.08	[-.12, .27]	.001
Model 2: Interaction effect		R^2 = .22, *p* = .003			R^2 = .15, *p* = .043	
Negative Social Organization × Pre-stress N-Back Errors	.02	[-.15, .19]	.002	-.14	[-.32, .04]	-.004
Model 3: Interaction effect		R^2 = .22, *p* = .002			R^2 = .14, *p* = .049	
Negative Achievement Organization × Pre-stress N-Back Errors	-.04	[-.21, .12]	-.002	-.07	[-.25, .11]	-.002

Note. 95% CI = 95% confidence intervals for standardized coefficients (βs). Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1. Values of .00 are < .001. Model fit: Model 1, $\chi^2(59, N = 121) = 94.06$, $p = .003$, CFI = .972, TLI = .960 and RMSEA = .070, SRMR = .066; Model 2, $\chi^2(65, N = 121) = 100.70$, $p = .003$, CFI = .972, TLI = .960 and RMSEA = .067, SRMR = .066; Model 3, $\chi^2(65, N = 121) = 106.17$, $p = .001$, CFI = .967, TLI = .954 and RMSEA = .072, SRMR = .067.
†$p < .10$; *$p < .05$; **$p < .01$; ***$p < .001$.

Table 13

Prediction of Latent Pre-stress Cytokines and Latent Change in Cytokines by Post-stress N-back Errors, Negative Cognitive Content, and Rumination

	Pre-stress inflammation			Δ inflammation		
Model and predictor	β	95% CI	*b*	β	95% CI	*b*
Model 1: Main effects		R^2 = .22, *p* = .001			R^2 = .19, *p* = .010	
Age	.03	[-.14, .21]	.001	.25*	[.02, .48]	.01
BMI	.35***	[.19, .52]	.02	.03	[-.20, .25]	.001
Ethnicity						
White vs. Other	-.03	[-.20, .15]	-.03	.08	[-.09, .24]	.04
White vs. Asian	-.18*	[-.35, -.01]	-.13	-.02	[-.25, .22]	-.01
Pre-stress N-Back Errors	.002	[-.21, .21]	.00	.08	[-.19, .35]	.001
Core Beliefs	-.05	[-.36, .27]	.00	.31†	[-.01, .63]	.001
Dysfunctional Attitudes	-.08	[-.32, .15]	-.001	-.23†	[-.48, .02]	-.001
Rumination	-.003	[-.23, .22]	.00	-.33*	[-.59, -.07]	-.003
Post-stress N-Back Errors	.09	[-.12, .30]	.003	.10	[-.24, .43]	.001
Model 2: Interaction effect		R^2 = .23, *p* = .001			R^2 = .20, *p* = .005	
Core Beliefs × Post-stress N-Back Errors	-.11	[-.24, .03]	.00	-.10	[-.33, .14]	.00
Model 3: Interaction effect		R^2 = .23, *p* = .001			R^2 = .23, *p* = .001	
Dysfunctional Attitudes × Post-stress N-Back Errors	-.12†	[-.26, .01]	.00	-.20*	[-.39, -.02]	.00
Model 4: Interaction effect		R^2 = .23, *p* = .001			R^2 = .19, *p* = .009	
Rumination × Post-stress N-Back Errors	-.12†	[-.25, .01]	.00	.03	[-.15, .21]	.00

Note. 95% CI = 95% confidence intervals for standardized coefficients (βs). Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1. Values of .00 are < .001. Model fit: Model 1, $\chi^2(71, N = 147) = 126.56$, $p < .001$, CFI = .963, TLI = .948 and RMSEA = .073, SRMR = .064; Model 2, $\chi^2(77, N = 147) = 136.69$, $p < .001$, CFI = .961, TLI = .945 and RMSEA = .073, SRMR = .062; Model 3, $\chi^2(77, N = 147) = 134.86$, $p < .001$, CFI = .962, TLI = .947 and RMSEA = .071, SRMR = .062; Model 4, $\chi^2(77, N = 147) = 133.01$, $p < .001$, CFI = .963, TLI = .949 and RMSEA = .070, SRMR = .063.

†$p < .10$; *$p < .05$; **$p < .01$; ***$p < .001$.

Table 14

Prediction of Latent Pre-stress Cytokines and Latent Change in Cytokines by Post-stress N-back Errors and Cognitive Organization

	Pre-stress inflammation			Δ inflammation		
Model and predictor	β	95% CI	*b*	β	95% CI	*b*
Model 1: Main effects		R^2 = .21, *p* = .005			R^2 = .17, *p* = .047	
Age	.09	[-.11, .29]	.003	.13	[-.15, .41]	.002
BMI	.25**	[.07, .43]	.01	.03	[-.20, .26]	.001
Ethnicity						
White vs. Other	-.10	[-.27, .08]	-.11	.09	[-.15, .33]	.05
White vs. Asian	-.18†	[-.39, .02]	-.13	-.12	[-.39, .15]	-.04
Pre-stress N-Back Errors	.10	[-.15, .35]	.003	-.003	[-.32, .32]	.00
Negative Social Organization	.05	[-.17, .26]	.04	.23†	[-.01, .47]	.08
Negative Achievement Organization	-.18†	[-.36, .01]	-.11	.06	[-.19, .30]	.02
Post-stress N-Back Errors	.004	[-.23, .24]	.00	.18	[-.25, .60]	.002
Model 2: Interaction effect		R^2 = .24, *p* = .002			R^2 = .18, *p* = .030	
Negative Social Organization × Post-stress N-Back Errors	.17†	[-.01, .34]	.01	-.12	[-.34, .10]	-.004
Model 3: Interaction effect		R^2 = .25, *p* = .001			R^2 = .18, *p* = .039	
Negative Achievement Organization × Post-stress N-Back Errors	.20*	[.04, .36]	.01	-.13	[-.34, .08]	-.003

Note. 95% CI = 95% confidence intervals for standardized coefficients (βs). Ethnicity was dummy coded as White = 0, Asian = 1, and Other = 1. Values of .00 are < .001. Model fit: Model 1, $\chi^2(65, N = 113) = 99.00$, *p* = .004, CFI = .971, TLI = .959 and RMSEA = .068, SRMR = .071; Model 2, $\chi^2(71, N = 113) = 107.03$, *p* = .004, CFI = .970, TLI = .957 and RMSEA = .067, SRMR = .071; Model 3, $\chi^2(71, N = 113) = 107.66$, *p* = .003, CFI = .969, TLI = .956 and RMSEA = .068, SRMR = .069.
†*p* < .10; **p* < .05; ***p* < .01; ****p* < .001.

Appendix L

Ethics Approval

Western Research

Research Ethics

Western University Non-Medical Research Ethics Board
NMREB Delegated Initial Approval Notice

Principal Investigator: Prof. David Dozois
Department & Institution: Social Science/Psychology,Western University

NMREB File Number: 109666
Study Title: Stress reactivity and stress generation in depression

NMREB Initial Approval Date: October 23, 2017
NMREB Expiry Date: October 23, 2018

Documents Approved and/or Received for Information:

Document Name	Comments	Version Date
Western University Protocol	Received October 4, 2017	
Advertisement	Facebook or Kijiji	2017/09/12
Advertisement	Study Poster	2017/09/12
Letter of Information & Consent	T1 - Online	2017/10/01
Letter of Information & Consent	T2 - Lab	2017/10/01
Letter of Information & Consent	T3 - EMA	2017/10/01
Letter of Information & Consent	T4 - Lab	2017/10/01
Letter of Information & Consent	T5 - Lab	2017/10/01
Instruments	Interest in Participation Web Form	2017/09/12
Other	Telephone Script for Eligibility - Received September 14, 2017	
Other	Telephone Script for T1 Reminder - Received August 8, 2017	
Other	T1 Reminder Email - Received August 8, 2017	
Other	T1 Questionnaires Email - Received August 8, 2017	
Other	Reminder Email for T2 Appointment - Received August 8, 2017	
Other	Confirmation Email for T2 Lab Appointment (if in over a week) - Received August 8, 2017	
Other	Confirmation Email for T2 Lab Appointment (if in a week or less) - Received August 8, 2017	
Other	T3 Text Message Script	2017/09/13
Other	Reminder Email for T4 or T5 - Received October 4, 2017	
Other	Confirmation Email for T4 of T5 lab appointments - Received October 4, 2017	
Other	Telephone Script for Booking T5 Appointment - Received August 8, 2017	
Instruments	TSST Script - Received August 8, 2017	
Instruments	Measures - Received October 4, 2017	
Instruments	SCID (DSM-IV) - Received for Information Only October 4, 2017	
Instruments	SCID (DSM-V) - Received October 23, 2017	
Other	Debriefing T1 Online	2017/09/12
Other	Debriefing T2 Lab	2017/09/12
Other	Debriefing T3 and T4	2017/10/01
Other	Debriefing T5	2017/10/01

The Western University Non-Medical Research Ethics Board (NMREB) has reviewed and approved the above named study, as of the NMREB Initial Approval Date noted above.

NMREB approval for this study remains valid until the NMREB Expiry Date noted above, conditional to timely submission and acceptance of NMREB Continuing Ethics Review.

The Western University NMREB operates in compliance with the Tri-Council Policy Statement Ethical Conduct for Research Involving Humans (TCPS2), the Ontario Personal Health Information Protection Act (PHIPA, 2004), and the applicable laws and regulations of Ontario.

Members of the NMREB who are named as Investigators in research studies do not participate in discussions related to, nor vote on such studies when they are presented to the REB.

The NMREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000941.

EO: Erika Basile __ Grace Kelly __ Katelyn Harris ✓ Nicola Morphet __ Karen Gopaul __ Patricia Sargeant __ Kelly Patterson __

Western University, Research, Support Services Bldg., Rm. 5150
London, ON, Canada N6G 1G9 t. 519.661.3036 f. 519.850.2466 www.uwo.ca/research/ethics

KATERINA RNIC, M.Sc., Ph.D. Candidate

Curriculum Vitae

EDUCATION

In Progress	**Doctorate of Philosophy (Ph.D), Clinical Psychology** The University of Western Ontario, London, Ontario, Canada *Advisor:* David Dozois, Ph.D., C. Psych. *Doctoral Dissertation:* Baseline and Stress-Induced Cognitive Control Deficits and Pro-Inflammatory Cytokines in Currently, Remitted, and Never Depressed Individuals *Residency:* Calgary Clinical Psychology Residency, Alberta Health Services (September 2018 – August 2019)
2014	**Master of Science, Clinical Psychology** The University of Western Ontario, London, Ontario *Advisor:* David Dozois, Ph.D., C. Psych. *Master's Thesis:* Cognitive Predictors and Behavioural Mediators of Vulnerability-Specific Stress Generation in Depressed Adults
2011	**Bachelor of Arts, Honours Psychology with Distinction** Queen's University, Kingston, Ontario, Canada *Advisor:* Kate Harkness, Ph.D., C. Psych *Undergraduate Honours Thesis:* Theory of Mind Decoding Abilities in Depressed Young Adults with a History of Childhood Maltreatment
2010	**Undergraduate Exchange** University of Sydney, Sydney, Australia

PUBLICATIONS

Peer-Reviewed Journal Articles

1. Vodermaier, A., **Rnic, K.,** Linden, W., & Olson, R. A. (Revise and Resubmit). Social support and survival in patients with stage III lung cancer: A population-based cohort study. *European Journal of Cancer Care.*

2. **Rnic, K.,** Sabbagh, M. A., Washburn, D., Bagby, R. M., & Harkness, K. L. (2018). Childhood emotional abuse, physical abuse, and neglect are associated with theory of mind decoding accuracy in young adults with depression. *Psychiatry Research, 268*, 501-507.

3. Fazakas-DeHoog, L. L., **Rnic, K.,** & Dozois, D. J. A. (2017). A cognitive distortions and deficits model of suicide ideation. *Europe's Journal of Psychology, 13,* 178-193.

4. **Rnic, K.,** Dozois, D. J. A., & Martin, R. A. (2016). Cognitive distortions, humor styles, and depression. *Europe's Journal of Psychology, 12, 348-362.*

5. Smith, M. M., Sherry, S. B., **Rnic, K.,** Saklofske, D. H., Enns, M. W., & Gralnick, T.M. (2016). Are perfectionism dimensions vulnerability factors for depressive symptoms after controlling for neuroticism? A meta-analysis of 10 longitudinal studies. *European Journal of Personality. 230, 201-212.*

6. Washburn, D., Wilson, G., Roes, M., **Rnic, K.,** & Harkness, K. L. (2016). Theory of mind in social anxiety disorder, depression, and comorbid conditions*. Journal of Anxiety Disorders, 37*, 71-77.

7. Dozois, D. J. A., & **Rnic, K.** (2015). Core beliefs and self-schematic structure in depression. *Current Opinion in Psychology, 4,* 98-103.

8. Linden, W., MacKenzie, R., **Rnic, K.,** Marshall, C., & Vodermaier, A. (2014). Emotional adjustment over 1 year post-diagnosis in patients with cancer: Understanding and predicting adjustment trajectories. *Supportive Care in Cancer, 23*, 1-9.

9. Pullmer, R., Linden, W., **Rnic, K.,** & Vodermaier, A. (2014). Measuring symptoms in gastrointestinal cancer: A systematic review of assessment instruments. *Supportive Care in Cancer, 22*, 2941-2955.

10. Vodermaier, A., Linden, W., **Rnic, K.,** Ng, A., Wang, C., Ditsch, N., Olson, R. (2014). Prospective associations of depression with survival: A population-based cohort study in patients with newly diagnosed breast cancer. *Breast Cancer Research and Treatment, 143*, 373-384.

11. **Rnic, K.,** Linden, W., Tudor, I., Pullmer, R., & Vodermaier, A. (2013). Measuring symptoms in prostate cancer: A systematic review of assessment instruments. *Prostate Cancer and Prostatic Diseases, 16*, 111-122.

Invited Book and Encyclopedia Chapters

12. Dozois, D. J. A., Dobson, K. S., & **Rnic, K.** (2019). Historical and philosophical bases of the cognitive–behavioral therapies. In K. S. Dobson & D. J. A. Dozois (Eds.), *Handbook of Cognitive-Behavioral Therapies* (4th ed.). New York: Guilford Press.

13. **Rnic, K.,** & Dozois, D. J. A. (In press). Depression. In B. J. Carducci (Editor-in-Chief) & A. Di Fabio, D. H. Saklofske, & C. Stough (Vol. Eds.), *Wiley-Blackwell encyclopedia of personality and individual differences: Vol. III. Personality processes and individual differences*. Hoboken, NJ: John Wiley & Sons.

14. Dozois, D. J. A., & **Rnic, K.** (2018). Classification and diagnosis. In D. J. A. Dozois (Ed.). *Abnormal Psychology: Perspectives* (6th ed.). Toronto, ON: Prentice Hall.

15. **Rnic, K.,** & Dozois, D. J. A. (2017). Treatment-relevant assessments in cognitive-behavioural therapy. In S. G. Hofmann & G. Asmundson (Eds.), *The science of cognitive-behavioral therapy: From theory to therapy.* Philadelphia: Elsevier/Academic Press.

16. Rehman, U. S., Dozois, D. J. A., & **Rnic, K.** (2015). Classification and Diagnosis. In D. J. A. Dozois (Ed.). *Abnormal Psychology:* Perspectives (5th ed., DSM-5 Update Edition). Toronto, ON: Prentice Hall.

17. Linden, W., & **Rnic, K.** (2013). Psycho-Oncology. In L. Grossman & S. Walfish (Eds.), *Translating Research into Practice.* Springer Publishing, NY.

TREATMENT MANUALS

- Developed a session on stress generation for the Depression Group Cognitive Behavioural Therapy manual for the Student Development Center at the University of Western Ontario. The group is comprised of eight 2-hour sessions. This work was completed under the supervision of Dr. Naomi Wiesenthal

RESEARCH GRANTS

Date	Grant	Value
2016-19	Social Science and Humanities Research Council (SSHRC) Insight Grant: "Interpersonal and Cognitive Dynamics of Stress Generation" (co-wrote grant with Dr. David Dozois)	$188,285
2016-17	Social Science and Humanities Research Board (SSHRB), Bridge Research Grant: "Interpersonal and Cognitive Dynamics of Stress Generation" (co-wrote grant with Dr. David Dozois):	$25,000
2014-17	Research Western Grant	$10,000

AWARDS AND HONOURS

Date	Award	Value
2019-20	University of British Columbia Institute of Mental Health Marshall Postdoctoral Fellowship	$75,000
2019	Dr. Sam Paunonen Award in Psychology	$1,000
2017	Beck Institute Student Workshop Scholarship	$500
2017-18	Western Graduate Research Scholarship	$4,405
2017	Canadian Association of Cognitive and Behavioural Therapies (CACBT) Student Travel Award	$500
2017-18	Ontario Graduate Scholarship (OGS) - Doctoral	$15,000
2017	University of Western Ontario 3 Minute Thesis (3MT) Finalist	-
2016	Elsie Ramos Memorial Student Poster Award from the Association for Behavioral and Cognitive Therapy (ABCT)	-
2016-17	Western Doctoral Excellence Research Award	$10,000
2016-17	Western Graduate Research Scholarship	$10,899

2016	London Regional Psychological Association: Student of the Year Award	-
2016	The University of Western Ontario, Student Experience: Innovation Award	-
2015-16	Western Graduate Research Scholarship	$7,998
2015	Poster Award Winner from the Division 12 Society of Clinical Psychology, American Psychological Association (APA)	-
2014-17	Social Sciences and Humanities Research Council of Canada Vanier Canada Graduate Scholarship (Vanier-CGS)	$150,000
2014-17	Joseph-Armand Bombardier Social Sciences and Humanities Research Council of Canada Graduate Scholarship (SSHRC-CGS) – Doctoral (Declined)	$105,000
2014-15	Ontario Graduate Scholarship (OGS) – Doctoral (Declined)	$15,000
2014-15	Western Graduate Research Scholarship	$1,433
2013-14	Ontario Graduate Scholarship (OGS) – Master's	$15,000
2013-14	Western Graduate Research Scholarship	$1,900
2012-13	Frederick Banting and Charles Best Canadian Institute of Health Research Canada Graduate Scholarship (CIHR-CGS) – Master's	$17,500
2012-13	Western Graduate Research Scholarship	$1,500
2011	Queen's University Medal in Psychology (Highest Academic Standing in graduating class)	-
2010	The University of Sydney, School of Psychology, Best Student in Learning and Behaviour (PSYC3011)	-
2010	Ann Adamson Scholarship in Psychology	$1,960
2009	Kathleen Ryan International Exchange Bursary	$500
2009	Ann Adamson Scholarship in Psychology	$2,060
2009	Gordon and Myrtle Adams Scholarship	$1,310
2008	Carl Reinhardt Scholarship	$450
2008	William Mitchell Silliman Scholarship	$1,735
2007-11	Dean's Honour List with Distinction (Top 3% of program), Queen's University	-
2007	Queen's University Excellence Scholarship	$2,500
2007	Vancouver Foundation Scholarship	$500

CONFERENCE PRESENTATIONS

1. **Rnic, K.** & Dozois, D. J. A. (2017). *Early maladaptive schemas and social rejection moderate theory of mind.* Poster, 2017 meeting of the Association for Behavioral and Cognitive Therapies, San Diego, CA.

2. **Rnic, K.,** & Dozois, D. J. A. (2017). *Self-referent information processing biases and rejection enhance theory of mind in dysphoric women: Evidence of valence specificity.* Poster, 2017 meeting of the Society for Research in Psychopathology, Denver, CO.

3. Dozois, D. J. A. & **Rnic, K.** (2017). The generation of interpersonal stress and responses to rejection in depression. In *Interpersonal stress and depression*. Symposium, 2017 meeting of the European Congress of Psychology, Amsterdam, Netherlands.

4. **Rnic, K.,** Dozois, & Dozois, D. J. A. (2017). *Cognitive behavioural therapy in cancer patients: A meta-analysis of treatment outcomes*. Poster, 2017 meeting of the Canadian Association of Cognitive and Behavioural Therapies, Ottawa, ON.

5. **Rnic, K.,** & Dozois, D. J. A. (2016). *Social rejection influences theory of mind abilities in women with anxious attachment or depressive symptoms.* Poster, 2016 meeting of the Society for Research in Psychopathology, Baltimore, MD.

6. **Rnic, K.,** & Dozois, D. J. A. (2016). *Early maladaptive schemas and persistence of effects of social rejection.* Poster, 2016 meeting of the Association for Behavioral and Cognitive Therapies, New York, NY.

7. **Rnic, K.,** Squires, S. D., & Dozois, D. J. A. (2016). *Cognitive behavioral therapy in cancer patients: A meta-analysis of treatment outcomes.* Talk, 2016 meeting of the International Congress of Psychology, Yokohama, Japan.

8. Machado, D., Dozois, D. J. A., Shumlich, E., **Rnic, K., &** Maiolino, N. (2016). *Cognitive schemas as longitudinal predictors of depressive relapse*. Talk, 2016 meeting of the International Congress of Psychology, Yokohama, Japan.

9. **Rnic, K.,** Hanna, J., Cunningham, S., & Dozois, D. J. A. (2016). Social rejection influences theory of mind abilities in women with depressive symptoms. In *A multi-modal examination of interpersonal factors in the development and maintenance of depression.* Symposium, 2016 meeting of the Canadian Psychological Association, Victoria, BC.

10. Wilde, J. L., **Rnic, K.,** Dozois, D. J. A., & Martin, R. A. (2016). Early maladaptive schemas and depression: The mediating role of interpersonal competence. In *A multi-modal examination of interpersonal factors in the development and maintenance of depression.* Symposium, 2016 meeting of the Canadian Psychological Association, Victoria, BC.

11. Smith, M. M., Sherry, S. B., **Rnic, K.,** Saklofske, D. H., Enns, M. W., & Gralnick,T. M. (2016). Are perfectionism dimensions vulnerability factors for depressive symptoms after controlling for neuroticism? A meta-analysis of 10 longitudinal studies. In *Perfectionism in Personal and Interpersonal Dysfunction.* Symposium, 2016 meeting of the Canadian Psychological Association, Victoria, BC.

12. **Rnic, K.,** Dozois, D. J. A., & Martin, R. A. (2016). *Cognitive distortions, humor styles, and depression*. Poster, 2016 meeting of the Canadian Association of Cognitive and Behavioural Therapies, Hamilton, ON.

13. **Rnic, K.,** Cunningham, S., Hanna, J., & Dozois, D. J. A. (November, 2015). *Persistence of effects of social rejection in depressed individuals.* Poster, 2015 meeting of the Association for Behavioral and Cognitive Therapies, Chicago, IL.

14. **Rnic, K.,** Dozois, D. J. A., & Machado, D. A. (October, 2015). *A meta-analytic review of stress generation in unipolar depression.* Poster, 2015 meeting of the Society for Research in Psychopathology, New Orleans, LA.

15. Maheu, C., Vodermaier, A., **Rnic, K.,** Linden, W., Singh, M., & Filion, L. (October, 2015). *Return to work questionnaire for cancer survivors*. Talk, 2015 meeting of Canadian Association of Nurses in Oncology, Toronto, ON.

16. **Rnic, K.** & Dozois, D. J. A. (August, 2015). *Behavioural, not cognitive, avoidance predicts interpersonal stress generation in depressed adults.* Poster, 2015 meeting of the American Psychological Association, Toronto, ON.

17. **Rnic, K.** & Dozois, D. J. A. (June, 2015). Cognitive and Behavioral Predictors Of Stress Generation In Depressed Adults. In *A multi-modal examination of cognitive vulnerability in the development and maintenance of depression.* Symposium, 2015 meeting of the Canadian Psychological Association, Ottawa, ON.

18. **Rnic, K.** & Dozois, D. J. A. (June, 2015). *Negative urgency predicts interpersonal stress generation in depressed adults.* Poster, 2015 meeting of the Canadian Psychological Association, Ottawa, ON.

19. **Rnic, K.,** Harkness, K. L., Washburn, D., & Roes, M. (July, 2014). *Theory of mind decoding abilities in depressed young adults with a history of childhood maltreatment.* Talk, 2014 meeting of the International Congress of Applied Psychology, Paris, France.

20. **Rnic, K.,** Dozois, D. J. A., & Szota, L. (July, 2014). *Avoidance, excessive reassurance seeking and rumination mediate the relation between cognitive organization of social schemas and depression*. Talk, 2014 meeting of the International Congress of Applied Psychology, Paris, France.

21. **Rnic, K.,** & Dozois, D. J. A. (June, 2014). *The relation of negative urgency and depression.* Poster, 2014 meeting of the Canadian Psychological Association, Vancouver, BC.

22. **Rnic, K.,** Dozois, D. J. A. & Szota, L. (June, 2014). *Avoidance and rumination mediate the relation between early maladaptive schemas and depression.* Poster, 2014 meeting of the Canadian Psychological Association, Vancouver, BC.

23. Szota, L., **Rnic, K.,** & Dozois, D. J. A. (June, 2014). *Early maladaptive schemas and depression: The mediating role of rumination and reassurance seeking.* Poster, 2014 meeting of the Canadian Psychological Association, Vancouver, BC.

24. Vodermaier, A., Linden, W., **Rnic, K.,** Ng, A., Wang, C., Ditsch, N., & Olson, R. (June, 2013). *Prospective associations of depression with survival: Population-based cohort study in patients with newly diagnosed breast cancer.* Poster, 2012 meeting of Senologie, Munich, Germany.

25. **Rnic, K.,** McDermott, R. Dozois, D. (June, 2013). *The relationship between excessive reassurance seeking and cognitive organization.* Poster, 2013 meeting of the Canadian Psychological Association, Quebec City, QC.

26. Pullmer, R., Linden, W., **Rnic, K.,** Vodermaier, A. (June, 2013). *Symptom assessment in patients with gastrointestinal cancers: A systematic review.* Poster, 2013 meeting of the Canadian Psychological Association, Quebec City, QC.

27. Tudor, I., Linden, W., & **Rnic, K**. *Symptom assessment in breast cancer patients: A systematic review*. (June, 2013). Poster, 2013 meeting of the Canadian Psychological Association, Quebec City, QC.

28. Linden, W., Vodermaier, A., Mackenzie, G., & **Rnic, K.** (April, 2012). *A comparison of four paths of emotional adjustment in cancer patients: From diagnosis to 6-month follow-up.* Talk, 2012 meeting of the Canadian Association of Psychosocial Oncology, Vancouver, BC.

29. Roes, M., Washburn, D. S., **Rnic, K.,** & Harkness, K. L. (September, 2011). *Role of theory of mind decoding abilities in the generation of interpersonal life events*. Poster, 2011 meeting of the Society for Research in Psychopathology, Boston, MA.

INVITED TALKS AND OTHER PROFESSIONAL PRESENTATIONS

Rnic, K. (February, 2018). *Understanding and Coping with Depression after a Spinal Cord Injury.* Presented to inpatients at the Spinal Cord Regional Rehabilitation Service on behalf of Spinal Cord Injury Ontario, London, ON.

Rnic, K. (November, 2017). *Understanding and Coping with Depression after a Spinal Cord Injury.* Presented to inpatients at the Spinal Cord Regional Rehabilitation Service on behalf of Spinal Cord Injury Ontario, London, ON.

Rnic, K. (February, 2017). *Core Beliefs: Our Mind's Unwritten Rules.* Community lecture presented at the London Public Library as a member of Advocacy through Action, London, ON.

Rnic, K. (April, 2016). *Assertiveness Skills for Healthy Relationships.* Community lecture presented at the London Public Library as a member of Advocacy through Action, London, ON.

Rnic, K. (March, 2016). *Assertiveness Skills for Healthy Relationships.* Community lecture presented at the London Public Library as a member of Advocacy through Action, London, ON.

Rnic, K. (February, 2016). *Assertiveness Skills for Healthy Relationships.* Community lecture presented at the London Public Library as a member of Advocacy through Action, London, ON.

Rnic, K. (November, 2015). *Effects of Bullying on Mental Health.* Talk presented to students at Sir Frederick Banting Secondary School, London, ON.

Rnic, K. (March, 2015). *Self-Assertion.* Public lecture presented at The University of Western Ontario as part of the Laura Evans Lecture Series, London, ON.

Rnic, K. (February, 2015). *Core Beliefs: The Filters Through Which We Experience the World.* Community lecture presented at the London Public Library as a member of Advocacy through Action, London, ON.

Rnic, K. (October, 2014). *Self-Assertion.* Public lecture presented at The University of Western Ontario as part of the Laura Evans Lecture Series, London, ON.

Rnic, K. (February, 2014). *Emotion Regulation: Keeping Emotions in Check.* Community lecture presented at the London Public Library as a member of Advocacy through Action, London, ON.

Rnic, K. (March, 2014). *Emotion Regulation: Keeping Emotions in Check.* Lecture presented at London Life Insurance Company, London, ON.

Rnic, K., Maiolino, N., and Otchet, F. (May-June 2013). *What can I do when people come to me for help?* Workshops presented at Western University for undergraduate orientation leaders, London, ON.

Rnic, K. (February, 2013). *Emotion Regulation: Keeping Emotions in Check.* Community lecture presented at the London Public Library as a member of Advocacy through Action, London, ON.

TEACHING EXPERIENCE

Course Instructor

- Abnormal Psychology (September 2016 – December 2016)
- Abnormal Psychology (January 2016 – April 2016)

Teaching Assistant

- Honours Thesis (September 2017 – April 2018)
- Adult Psychopathology (September 2015 – December 2015)
- Child Psychopathology (September 2013 – December 2015)
- Forensic Psychology (January 2014 – April 2014)
- Applications of Psychology (September 2013 – December 2013)
- Research Methods – Lab Instructor (September 2012 – April 2013)

Guest Lectures

- *Mood Disorders*. Presented to Abnormal Psychopathology Course at the University of Western Ontario – King's College (September 2017)
- *Introduction to Child Psychopathology*. Presented to Child Psychopathology Course at the University of Western Ontario – King's College (January 2015)
- *Biological and Environmental Contexts.* Presented to Child Psychopathology Course at the University of Western Ontario – King's College (September 2014)

Research Supervision Experience

Honours Thesis Research Advisor, The University of Western Ontario (2017-2018)

- Project title: The influence of cognitive structure on stress-induced cognitive control deficits in depression

Honours Thesis Research Advisor, The University of Western Ontario (2014-2015) for two honours students

- Project title: Rumination Mediates the Relationship Between Anxious Attachment and Immediate Response to Ostracism
- Project title: Ostracism Increases Positive-Valence Theory of Mind Decoding Accuracy

Honours Thesis Research Advisor, The University of Western Ontario (2013-2014)

- Project title: Cognitive and Interpersonal Vulnerabilities to Depression
- Winner of the W. J. McClelland Award (best Honors thesis in the Department)

SUPERVISED CLINICAL EXPERIENCE

Calgary Clinical Psychology Residency (September 2018 – August 2019)

- Psychosocial Oncology
  - *Supervisors:* Dr. Andrea Feldstain and Dr. Guy Pelletier
- Cognitive Behavioural Therapy Service
  - *Supervisors:* Dr. Barb Backs-Dermott, Dr. Gayle Belsher, and Dr. Michael Enman
- Regional Psychological Assessment Service
  - *Supervisor:* Dr. Kerry Mothersill

Western Mood Study Diagnostician and Clinical Interviewer (January 2018 – September 2018)

- *Supervisor:* Dr. David Dozois

Private Practice, London Ontario (March 2018 – August 2018)

- *Supervisor:* Dr. Charles Nelson

Behavioural Medicine Service, London Health Sciences Centre, London, Ontario (September 2016 – June 2018)

- *Supervisor:* Dr. Tony Iezzi

Spinal Cord Regional Rehabilitation Service and Acquired Brain Injury Rehabilitation Program, Parkwood Institute, St. Joseph's Health Care, London, Ontario (September 2017 – February 2018)

- *Supervisor:* Dr. Steven Orenczuk

Private Practice, London, Ontario (May, 2017)

- *Supervisor:* Dr. Lindsey Forbes

Clinical Neurological Services and Epilepsy Monitoring Unit, London Health Sciences Centre (*September 2016 – March 2017)*

- *Supervisor:* Dr. Sarah Vernon-Scott

Concurrent Disorders Services, Regional Mental Health – London, London, Ontario (March 2016 – August 2016)
- *Supervisor:* Dr. David LeMarquand

Psychological Services, Student Development Centre, University of Western Ontario, London, Ontario (September 2014 – April 2016)
- *Supervisor:* Dr. Naomi Wiesenthal

Private Practice, London, Ontario (July 2015 – December 2015)
- *Supervisor:* Dr. David Dozois

Child and Adolescent Mental Health Care Program, London Health Sciences Centre, London, Ontario (September 2015 – February 2016)
- *Supervisor:* Dr. Kerry Collins

Mood Disorder Unit, Regional Mental Health – London, London, Ontario (April 2015 – August 2015)
- *Supervisor:* Dr. Mustaq Khan

Southwest Centre for Forensic Mental Health, Regional Mental Health Care, St. Thomas, Ontario (June 2014 – August 2014)
- *Supervisor:* Dr. Laura Fazakas-DeHoog

Madame Vanier Children's Services (June 2014 – August 2014)
- *Supervisor:* Dr. Carla Smith

Mood and Thinking Study (February 2014-April 2014)
- *Supervisor:* Dr. David Dozois

Psychological Services, Student Development Centre, University of Western Ontario, London, Ontario (May 2013 – August 2013)
- *Supervisor:* Dr. Beverley Ulak and Dana Menard

London Waitlist Clinic, Canadian Mental Health Association, London Ontario
(January 2013 – August 2013)
- *Supervisor:* Dr. Felicia Otchet

CLINICAL SUPERVISION EXPERIENCE

London Waitlist Clinic, Canadian Mental Health Association, London Ontario (September 2016 – June 2017)
- *Supervisor:* Dr. William Newby
- *Activities:*
    - Co-supervised 8 novice therapists

Psychological Services, Student Development Centre, University of Western Ontario, London, Ontario (September 2014 – April 2016)

- *Supervisor:* Dr. Naomi Wiesenthal
- *Activities:*
    - Co-supervised a clinical psychology student (first-year MSc) with whom I co-facilitated a Stress and Anxiety Management Group

CLINICALLY RELEVANT EMPLOYMENT AND RESEARCH EXPERIENCE

Diagnostician and Clinical Interviewer, The University of Western Ontario, London, Ontario (2016-2017) *March 2016 – November 2017*

- *Supervisor:* Dr. Elizabeth Hayden

Research Coordinator/ Lab Manager, The University of British Columbia, Vancouver, British Columbia (*2011 –2012):*

- *Supervisor:* Dr. Wolfgang Linden

Research Assistant, Queen's University, Kingston, Ontario (2010-2011)

- *Supervisor:* Dr. Kate Harkness

Research Assistant, Queen's University, Kingston, Ontario (2010 – 2011)

- *Supervisor:* Dr. Leandre Fabrigar

Research Assistant, Queen's University, Kingston, Ontario (2011)

- *Supervisor:* Dr. Tara MacDonald

Research Assistant, Queen's University, Kingston, Ontario (2008 – 2009)

- *Supervisor:* Dr. Mark Sabbagh

SERVICE ACTIVITIES

Journal Reviewer

- *Journal of Abnormal Psychology* – Co-reviewer with Dr. David Dozois
- *Clinical Psychological Science* – Co-reviewer with Dr. David Dozois
- *Clinical Psychology: Science and Practice* – Co-reviewer with Dr. David Dozois
- *Canadian Journal of Behavioural Science* – Co-reviewer with Dr. David Dozois
- *Europe's Journal of Psychology*

Psychology Department Colloquium Committee, University of Western Ontario (2014 – 2018)

- Invited professors from other institutions to UWO to present a colloquium talk; coordinated with speakers and UWO staff to organize travel and lodging arrangements;

organized itineraries for speakers' visits, including events and meetings; hosted speakers during the day of their colloquium

Society for Research in Psychopathology (SRP)

- **Contributor for Publication Committee** (2017): conducted an interview with the Early Career Award winner, wrote an article about the interview for publication in the SRP newsletter

Advocacy through Action (2012 – 2017)

- Advocacy through Action is a graduate student organization that provides public education to the community of London, Ontario, through an annual series of public talks related to the psychology of mental health and well-being. Along with being an active member of this group and presenting at each series, I have also held the following roles and leadership positions:
    - **Chair of Advocacy Committee** (2016-2017): I developed and led a campaign for members of the public and the psychology community to send letters to their Members of Provincial Parliament asking for greater resources for and access to psychologists
    - **Co-President** (2013-2015): responsible for liaising with the library regarding scheduling of the series; monitoring and overseeing the duties of the various committees; coordinating members and running meetings
    - **Member of the Marketing Committee** (2012-2013): advertising for the annual series of talks through social media and by distributing posters and flyers

London Regional Psychological Association (LRPA)

- **Secretary** (2013-2016): recorded minutes at all executive meetings; helped to plan and organize continuing education talks for psychologists and psychological associates in the community; managed the LRPA listserv

PROFESSIONAL AFFILIATIONS

- Society for Research in Psychopathology (SRP; associate member)
- Association for Cognitive and Behavioral Therapies (ABCT; student member)
- Canadian Psychological Association (CPA; student member)
- Canadian Association of Cognitive Behavioural Therapies (CACBT; student member)