The Role of the Val66Met Polymorphism of the Brain Derived Neurotrophic Factor Gene
in Coping Strategies Relevant to Depressive Symptoms.

By

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A thesis submitted to the Faculty of Graduate and Postdoctoral Affairs in partial
fulfillment of the requirements for the degree of

Master

in

Neuroscience

Carleton University

Ottawa, Canada

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ISBN: 978-0-494-93636-8

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ISBN: 978-0-494-93636-8

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Abstract

This study explored the possible relationship between the Val66Met brain-derived neurotrophic factor (BDNF) polymorphism, childhood maltreatment, and stress-coping styles relevant to depression and other mood disorders. Participants were a mixed sample of undergraduate students ranging in depressive symptoms ($N = 124$). Depressive symptoms were found to be equal across genotype groups. The results indicate that val/met and met/met individuals endorsed emotion-focused and avoidant coping strategies more than val/val individuals. Further, the val66met polymorphism moderates the relationship between childhood maltreatment and current depressive symptoms as well as endorsement of emotion-focused and avoidant coping. In both cases the met polymorphism was associated with greater depressive symptoms and emotion-focused and avoidant coping style than the val/val individuals when childhood maltreatment experiences were low but not as maltreatment increased.

Acknowledgements

First, I would like to thank my primary supervisor, Dr. Shawn Hayley, for providing me with an amazing opportunity and learning experience. His enthusiasm for research, openness to new ideas, and generosity of time and resources have made my education at Carleton truly excellent.

I would also like to thank Dr. Hymie Anisman for his magnanimous involvement in my studies - always being eager to share a his wealth of experience in research, analytical questioning, and statistical analyses. His guidance in my own project, as I'm sure is the case for many others, has been absolutely critical to any successes I have achieved as a master's student. Thank you also to Kelly Christie for her much needed and superb assistance with statistical analyses.

Thank you to Dr. John Stead for his patience, generosity of time and resources, and expertise in genetic analysis. Thank you also to Dr. Gele Lu for his aid in troubleshooting.

I would like to thank our technicians, Geoff Crowe and Cheri Bethune, for their advice in troubleshooting, constant willingness to help, and seemingly infinite patience for interruption. Also, thank you to Parnell MacNevin for her interest, time, and involvement in this research project.

On a personal note, much love and gratitude to my parents, family, and friends for their unwavering support, encouragement, and understanding. And to Véronique and Chris - whose brilliant insights, wicked sense of fun, and strong bonds of friendship have meant the world to me.

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Introduction

Background

The strategies we employ to cope with stressful life events are associated with a wide variety of psychological and health outcomes. Indeed, insufficient resources to cope in combination with chronic stressor exposure has been linked to pathologies ranging from mood disorders (Hammen, 2005; McEwen, 2002), to much less obvious physical conditions, like the progression of certain cancers (Sklar & Anisman, 1981).

Depression - which is a heterogeneous condition including symptoms such as low mood, anhedonia, sleep disturbance, fatigue, and cognitive deficits (APA, 2000) - is known to be adversely affected by stressors and has been well studied in the context of coping. Currently, the World Health Organization ranks depression as the fourth most common cause of disability (World Health Organization [WHO], 2011) and predicts that by 2020 it will have climbed to the number two position. In Canada, about 12.2% of individuals will experience a major depressive episode in their lives (Pattern et al., 2006). Accumulating evidence suggests that some coping strategies may mediate the stress-depression relationship (McEwan, 2006; Mello et al., 2003; Ravindran, Matheoson, Griffiths, Merali, & Anisman, 2002; Barnett & Gotlib, 1988; Coyne, Aldwin, & Lazarus, 1981). For instance, strong links have been established between rumination - a repetitive focus on negative past events - and the severity and recurrence of depressive episodes (Papageorgiou & Siegle, 2003; Nolen-Hoeksema, 2000). Rumination has also been found to adversely affect related conditions such as post-traumatic stress disorder (PTSD; Clohessy & Ehlers, 1999).

It is clear that depression is at least partially influenced by one's genetic background, given its heritability among family members and high frequency of co-occurrence in twins (McGue & Christensen, 2003). Genetic differences may also influence the development of effective or ineffective coping processes. While several genetic sites have been studied in this context, the specific loci involved in these processes remains obscure (Wray et al., 2012). Nevertheless, recent studies highlight the role of the val66met brain derived neurotrophic factor (BDNF) polymorphism (implicated in neuroplastic processes) in how individuals cope with stress. In fact, accumulating evidence suggests that BDNF, which normally provides trophic support for neurons, is reduced in response to stressors and such reductions could adversely affect emotional processes relevant for depression (Martinowich, Manji, & Lu, 2007).

Briefly, the aim of the current investigation is to characterize how the val66met polymorphism, and by extension BDNF, affects coping strategies and appraisal in response to psychosocial stressors. Specifically, we predict that a variant of the val66met polymorphism associated with abnormal trafficking and release of BDNF, will render individuals more vulnerable to using ineffective coping strategies and will be associated with a more inflexible coping style. Hence, it is hypothesized that individuals possessing the “high risk” val66met BDNF polymorphism, possibly in combination with a marked history of exposure to multiple and/or severe stressors, will display deficits in coping strategies.

The HPA Axis and Mood Disorders

One of the primary and immediate responses to stressful challenges involves the activation of the hypothalamic-pituitary-adrenal (HPA) axis. Briefly, in healthy

individuals, stressors trigger the release of corticotropin-releasing hormone (CRH) from the hypothalamus, which results in enhanced release of adrenocorticotrophic hormone (ACTH) from the pituitary gland, which in turn triggers the secretion of glucocorticoids from the adrenal glands. Importantly, glucocorticoids (e.g. cortisol) facilitate the mobilization of energy throughout the body in order to prepare the individual for the fight or flight response. Cortisol also controls the activation state of the HPA axis by acting directly on receptors in the hypothalamus, and indirectly via activation of extra-hypothalamic structures such as the hippocampus (Jacobson & Sapolsky, 1991).

At least in the short term, HPA activation is adaptive and prepares the organism to deal with stressors. By contrast, prolonged activation of this system may have deleterious health consequences (Tsigos & Chrousos, 2002; Selye, 1936). Chronic stressors like bereavement or the experience of a natural disaster have been shown to increase baseline levels of salivary cortisol in humans (Miller, Chen, Zou, 2007; Smyth et al., 1998; Nolen-Hoeksema & Morrow, 1991). Similarly, chronic stressors have been associated with prolonged glucocorticoid secretion in rodents (Checkley, 1996). Ultimately, such long-term effects could give rise to glucocorticoid insensitivity through the down-regulation of glucocorticoid receptors, and possibly even morphological impairments in stressor-sensitive brain regions, such as the hippocampus and prefrontal cortex (Checkley, 1996; Smith, Makino, Kvetnansky, & Post, 1995).

Abnormal HPA functioning is a hallmark for most mood disorders, although consistent up- or down-regulation of basal functioning and reactivity to stressors is not consistent across all mood disorders. For example, depression is associated with abnormally high baseline secretions of cortisol, while PTSD is associated with

hypocortisolism and an abnormally high reactivity to trauma-relevant stimuli (Carroll et al., 2007; Elzinga et al., 2003; Thaller et al., 1999). In addition, the etiology of mood disorders have been associated with a plethora of psychological and biological factors known to influence HPA activation including: early life stress (Caspi et al., 2003), appraisal styles (Billings & Moos, 1982), genetic makeup (Johnson, 2002), and structural brain abnormalities (Mello et al., 2003). Consistently, morphological differences from healthy controls are found in the amygdala, prefrontal cortex, and hippocampus (Sheline, Gado, & Kraemer, 2003; Bremner, 2000; Baxter, 1989) and activation in each of these structures has implications for HPA functioning. It is relevant to note that identical stressors can elicit disparate stress responses across individuals, which can in turn affect stress-related pathologies. Some of this variability can be attributed to idiosyncratic variables including: genetic factors, comorbid psychological disorders, stress history, level of social support, and importantly, coping style. Indeed, ineffective coping strategies have been associated with abnormally high stress sensitivity and have been shown to extend the physiological consequences of stressors (Alexander et al., 2010; Shalev et al., 2009; Zoccola, Dickerson, & Aldivar, 2008).

Effects of Maladaptive Coping

Coping can be defined as a process-oriented (focusing on thoughts and behaviours), context-dependent (focusing on situational demands and resources) response to a stressor, that aims to reduce distress via regulation of stressful emotions and/or by altering the person-environment interaction (Folkman et al., 1986; Folkman & Lazarus, 1985). It is typically studied in two ways - focusing on an individual's coping style, or by observing behaviour and physiological change in response to a specific stressor.

We define coping *style* as a preference for particular patterns of coping strategies that are stable across time. It has previously been shown that depressed individuals, when compared to controls, report a distinct pattern of coping behaviours (Matheson & Anisman, 2003). Typically, these individuals report higher levels of rumination, emotional expression, and emotional control alongside lower levels of cognitive restructuring, humour, and social support. Importantly, these differences in coping style are also evident at multiple levels of dysphoria in healthy individuals, indicating that the coping profile is associated with the symptoms of depression and not necessarily the disorder itself.

Situational coping can be divided into two main processes - appraisals and coping strategies. These processes are involved in both the anticipation of an upcoming stressor as well as in response to a recent stressor. During appraisal, an individual will assess how threatening they find the stressor and if adequate resources are available to cope. Following the initial appraisal, an individual may either re-appraise the situation or engage a coping strategy. Coping strategies have been divided into two large categories: emotion-focused and problem-focused coping (Folkman et al., 1986). It has been observed that using emotion-focused coping is optimal when a situation is appraised as uncontrollable, while using problem-focused coping optimal when a situation is appraised as controllable (Folkman & Lazarus, 1980).

On average, depressed individuals demonstrate excessive use of emotion-focused and avoidant styles of coping (Krackow & Rudolph, 2008; Tomaka, Blascovich, Kelsey, & Leitten, 1993). They also tend to appraise stressful events as being more threatening and personal. These behaviours are all associated with greater depressive symptoms in

this population (Nolen-Hoeksema, 1991; Folkman & Lazarus, 1986; Billings & Moos, 1984).

Rumination is an emotion-focused coping strategy and style which has been closely studied in relation to depressive symptoms and other mood disorders (Nolen-Hoeksema, 2000). It is defined as repetitive and passive self-focused thinking about negative emotions or past experiences (Nolen-Hoeksema, 2000). Importantly, rumination likely does not induce depressive symptoms, but rather appears to serve to exacerbate existing symptoms. For example, depressed individuals when asked to ruminate in the absence of a stressor, exhibit an increase in depressive symptoms, while healthy controls asked to ruminate did not display any depressive symptoms (Nolen-Hoeksema & Morrow, 1993). Further, when healthy undergraduate students were asked to ruminate following a negative mood induction, they displayed a significant increase in depression-related dysfunctional beliefs (for example, "If a person asks for help, it is a sign of weakness," or "If others dislike you, you cannot be happy") (Graaf, Roelofs, & Huibers, 2009, p. 350) as compared to groups that were instructed to use other coping strategies like distraction or mindful self-focus (Kuehner, Huffzinger & Liebsch, 2009). Additionally, participants who reported more depressive symptoms and were asked to ruminate showed a slower recovery to baseline cortisol levels after the termination of the stressor (in this case, a negative mood induction) (Kuehner et al., 2009).

Rumination has also been found to be a pathological coping style associated with PTSD. For example, in a study of ambulance workers (a group associated with an elevated incidence of PTSD) rumination was found to correlate with PTSD severity, along with two other coping styles - suppression and dissociation (both forms of avoidant

coping) (Clohessy & Ehlers, 1999). It was hypothesized that dwelling on intrusive memories may increase symptom severity, whereas suppression and dissociation forms of coping prevent the emotional processing necessary to move on from the trauma (Clohessy & Ehlers, 1999). From this we can conclude that rumination, while on its own pathological, may also act synergistically or additively as part of a collection of strategies to influence behavioural outcomes. It has further been suggested that rumination may inhibit the ability to engage more adaptive coping strategies (Fresco et al., 2002) thereby limiting the individual's means of minimizing the damaging impact of stressors.

Worry is another coping strategy which involves a repetitive focus on negative events. Although temporally different from rumination, as the focus is on future events instead of past ones, both strategies show a high rate of co-occurrence within individuals and both are implicated in negative mood induction (Segerstrom et al., 2000). Worry is typically studied in the context of anxiety and has been demonstrated to exacerbate anxious symptoms (Hong, 2007). In light of the relationship between worry and rumination, their shared characteristics (repetitive and shallow processing) (Fresco et al., 2002), and similar outcomes, the two strategies may share common etiological roots.

Repetitive thinking does not occur in a vacuum and the related pathological effects likely stem from an entire dysfunctional system of coping and appraisals. In line with this assertion, Watkins (2003) shows evidence that rumination and worry are associated with specific appraisal styles. Rumination is associated with more personal importance of the stressor and a greater need to understand the stressor, especially its causes and meanings. Adding to this work, Morrisson and O'Connor (2005) found that *ruminative coping style interacts with stress level to predict increased levels of social*

dysfunction. Their findings suggest that, individuals who tend to ruminate may be at a severe disadvantage in their abilities to cope with stressors - cognitively extending the experience of the stressor (by definition), while also interpreting the event as more personal, and lacking the skills to seek out social support under stress. With respect to more extreme behaviours, rumination has also been linked to increased self-harming behaviours (Borrill et al., 2009) and suicidality (Surrence et al., 2009)

A number of environmental factors can affect the behavioural and physiological consequences of stressors. Perhaps unsurprisingly, in the context of depression and other psychopathologies, such factors are associated with particular styles of coping. Two of the most frequently examined environmental factors with respect to mood disorders are childhood maltreatment and social support. Childhood maltreatment has been implicated in the etiology of mood disorders (Heim & Nemeroff, 2000), and has recently been shown to affect HPA reactivity (Carpenter et al., 2007). Further, the effect of childhood maltreatment on adult adjustment (measured as a combination of psychological distress and self-esteem) was found to be entirely mediated by social support and coping (Runtz & Shallow, 1997). In their model predicting adult psychological adjustment - childhood maltreatment, coping strategies, and social support were assessed. It was found that childhood physical (but not sexual) abuse decreased perceptions of social support of both family members and friends which lead to later adult maladjustment. However, childhood maltreatment was only predictive of 55% of the variance in later adult adjustment, and less than 10% of the variance in social support. This is consistent with other accounts of childhood maltreatment which show that the effect on later development is largely heterogeneous (Runtz & Schallow, 1997). It is likely then, that

the ultimate manifestation of pathological symptoms results from the interactions with additional factors including genetic differences. In addition, the study showed that maltreatment was associated with a constellation of coping styles which included self-defeating strategies, self-destructive behaviour, and avoidant coping. Rumination also contributes to negative outcomes in individuals who have experienced childhood maltreatment, as illustrated by Raes & Hermans (2007), who showed that ruminative coping style mediates the progression from childhood maltreatment to depression.

Thus far, we have focused on the influence of specific coping and appraisal styles (acting individually and in combination) on reactions to stressors. Adding another layer of complexity, coping flexibility may also play an integral role in mediating effective responses to stressors. Coping flexibility is a relatively new concept which is defined as an individual's ability to recognize the demands of a situation, select an appropriate strategy, and implement appropriate usage of such a strategy (Gan et al., 2006). Hence, such flexibility provides individuals with additional chances to optimize coping on a "situation-by-situation" basis. This concept is usually studied simultaneously with a related concept, cognitive flexibility, which includes an individual's ability to appraise situations on a continuum from controllable to uncontrollable - and not over-generalize. In a study performed by Gan et al. (2006), depressed individuals were asked to assess a number of stressful situations and how they thought they would cope with them. Coping and cognitive flexibility were shown to be significantly lower in depressed participants when compared to controls. Depressed individuals were also found to have poorer strategy-situation fit and coping effectiveness. While this data is correlational, these

findings open up the possibility that reduced coping effectiveness is, at least in part, due to lower flexibility.

In light of the detrimental consequences of certain coping strategies (specifically those involving highly repetitious thinking) and their relationship with stress-sensitive disorders, we will next briefly review the impact coping, childhood maltreatment, and social support have with respect to HPA activation.

Psychosocial Factors and HPA Functioning

As mentioned previously, dysregulation of the HPA axis is a hallmark of most mood disorders. While we have already shown that coping and other psychosocial factors play an important role in the development and maintenance of mood disorders, these etiological factors also have implications for HPA functioning. Particularly in the context of coping, it is hypothesized that these etiological factors exert their influence via changes to the HPA circuitry.

As we have previously described the relationship between psychosocial factors is complex, and often these factors act synergistically to affect pathology. The relationship between these factors and HPA reactivity is also likely complex; however the literature to date is largely preliminary - linking individual factors to changes in HPA activity.

Briefly, childhood maltreatment is typically associated with blunted cortisol response to acute stressors (Carpenter et al., 2007). When a good coping style-appraisal match is made (described previously) cortisol response to the stressor may be attenuated (Bohnen, Nicolson, Sulon, & Jolles, 1991), and increased social support has been robustly associated with an overall reduced HPA response to stressors in both human and animal models (e.g. Kirschbaum et al., 1995; Goldsmith, Brain, & Benton, 1978). Conversely, it

has also been suggested that social support may both promote mobilization of the glucocorticoids (i.e. promote higher peak-reactivity) in response to acute stressors, as well as prevent allostatic upregulation (change in the homeostatic set point and reactivity of the HPA axis) in the case of chronic stressful situations (Roy, Steptoe, & Clemens, 1998). It is important to note that, while interesting, these findings are all highly open to various interpretations. For example, a blunted cortisol response may mean two things: it could mean that the individual is experiencing very little stress because of appropriate coping measures or other factors, or alternatively, it may indicate that the HPA is not reacting in an appropriate and adaptive fashion in response to stressors.

With respect to ruminative coping, in a healthy population of undergraduates, it was found that ruminating on a recent personal transgression increases salivary cortisol (McCullough et al., 2007). Further, the use of ruminative coping style has been shown to extend elevated cortisol levels over prolonged intervals in response to real-life stressors, as well as laboratory stressors (Zoccola, Dickerson, & Zaldivar, 2008; Nolen-Hoeksema & Davis, 1999; Roger & Najarian, 1998; Nolen-Hoeksema & Morrow, 1991). Additionally, it has been found that high ruminators may express higher cortisol peak-reactivity when exposed to laboratory stressors (Zoccola, Quas, & Yim, 2010; Zoccola, Dickerson, & Zaldivar, 2008). Indeed, it has been hypothesized that such extended HPA activation is caused by the extended cognitive experience of the stressful event via rumination (Nolen-Hoeksema, 2000). Together, these data raise the possibility that the use of rumination as a coping style may foster a hyper-sensitive and slow-to-recover HPA response, which could render individuals vulnerable to depressive pathology. In fact, accumulating evidence has suggested that prolonged stressor induced corticoid

responses can promote atrophy in limbic regions critical for emotional processing, including the hippocampus and prefrontal cortex (Mizoguchi et al., 2003; Sapolsky et al., 1990). As will be discussed in the ensuing sections, BDNF and associated neurotrophic factors, are probable candidates mediating the impact of stress hormones upon brain morphology and plasticity; and ultimately, the long term structural changes that likely underlie depression.

BDNF As a Mediator of Coping and Depression

BDNF is a protein involved in the initial development and proliferation of neurons at early developmental stages and continues to influence the survival and functioning of neurons in adulthood (Huang & Reichardt, 2009; Acheson et al., 1995). The activity-dependent release of its mature form, mBDNF, has been implicated in neuronal dendritic branching as well as long-term potentiation (Kovalchuk et al., 2002). In animal models, hippocampal atrophy is associated with reductions in BDNF and higher levels of glucocorticoids (Murakami et al., 2005; Sapolsky et al., 1990). Such findings may tie into other reports that in monozygotic twins, smaller hippocampal size was associated with increased risk for the development of a stress-related pathology (Gilbertson et al., 2002).

Decreased hippocampal size and functioning has been observed in depressed patients, which supports the recently emerged neurotrophin hypothesis of depression (Sheline, Mokhtar, & Helena, 2003; Channon, 1996). This theory posits that failure in neurotrophic processes may be an important etiological factor for the development of depression (Duman, Heninger, & Nestler, 1997). Indeed, post-mortem findings of decreased trk B (the BDNF receptor) mRNA and BDNF protein expression have been

reported in depressed individuals (Ray, Weickert, Wyatt, & Webster, 2011; Karege et al., 2005). However, clearly this observation is not specific to depression, or even mood disorders in general, as decreased hippocampal and prefrontal volume are common to several stress-sensitive psychiatric conditions (Nelson et al., 1998; Bremner et al., 1995). Perhaps, these changes in morphology are related to a commonality between all these pathologies - a reduced ability to minimize the negative effects of stress.

BDNF has also been associated with the symptoms of depression as a bio-marker, where serum BDNF (sBDNF) is reduced in depressed individuals, and only recovers once the symptoms abate (Shimizu et al., 2003). In support of using sBDNF as a biomarker for central levels, some animal studies have shown a correlation between sBDNF and central BDNF protein (Sartorius et al., 2009; Karege, Schwalk, & Cisse, 2002). Importantly, recovery of sBDNF does not occur in conjunction with the onset of treatment with antidepressants but seems to respond only when depressive symptoms improve (Aydemir et al., 2006; Shimizu et al., 2003).

In animal models, BDNF has also been linked to the mechanism of action for most anti-depressants (Santarelli et al., 2003). It has been found that when mice are exposed to chronic mild stress - a model of depression - they exhibit reduced hippocampal BDNF, but that in groups treated with antidepressant medication (either as a prophylactic, or following stress exposure) this decrease is attenuated (Smith et al., 1995). These results parallel behavioural findings that demonstrate decreased time immobile in the forced swim test (currently the gold-standard for measuring antidepressant effects in an animal model) is associated with greater hippocampal BDNF (Russo-Neustadt et al., 2001; Nibuya, Morinobu, & Duman, 1995). Importantly, similar

antidepressant effects are evident when BDNF is infused directly into the hippocampus, which indicates that antidepressant drugs may be working through this brain region (Shirayama et al., 2002; Siuciak et al., 1997). Also, genetic or pharmacological suppression of BDNF has an anxiogenic effect - possibly indicating an increased susceptibility to stress (Hashimoto, 2007; MacQueen et al., 2001).

The release of BDNF is directly linked to morphological changes in the neurons of HPA-regulating structures in the brain including the hippocampus and prefrontal cortex, with reductions in BDNF associated with atrophy in these areas (Horch & Katz, 2002; Tongiorgi, Righi, & Cattaneo, 1997). As we shall see in the following section, the release and trafficking of BDNF may not be consistent across all individuals caused by polymorphisms in the gene, and this has implications for how individuals cope with stress, morphological changes of stress-regulating brain structures, as well as the release of hormonal correlates of the stress response.

Val66Met Polymorphism, Cortical Morphology, and Coping

A study performed by Egan et al. in 2003 suggests that abnormal secretion and trafficking of BDNF is associated with a valine to methionine substitution at codon 66, a single nucleotide polymorphism commonly referred to as the val66met polymorphism. This may adversely affect the development and function of the hippocampus and prefrontal cortex (Pezawas et al., 2004), and in turn may have implications for coping style and the development and outcome of stress-sensitive disorders.

At the codon 66 locus, three possible genotypes occur: val/val, val/met, and met/met. Both the val/met and met/met genotypes are associated with dysfunctional BDNF release in a gene dosing fashion (i.e. met/met causes the most drastic BDNF

reduction, whereas val/met shows an intermediate phenotype) (Egan et al., 2003). In populations of European descent, the frequencies for these genotypes are: .67 val/val, .28 val/met, .05 met/met (Egan et al., 2003).

The val/met and met/met genotypes are reported to be associated with impaired ability to extinguish anxiety and fear responses (Soliman et al., 2010). Specifically met carrying individuals showed resistance to extinction of a galvanic skin response following fear conditioning (pairings between one of three neutral geometric shapes and white noise with a 1000 Hz tone). This effect was further supported by fMRI evidence showing less ventromedial prefrontal activation and greater amygdalar activation occurred during extinction in the val/met and met/met genotypes (Soliman et al., 2010).

Differences between the val66met phenotypes have also been reported in terms of cortisol-reactivity in response to laboratory stressors (Alexander et al., 2010). Indeed, previous studies have shown that healthy individuals exposed to psychosocial stressors show differential cortisol responses between phenotypes - where the val/met and met/met genotypes are associated with attenuated reactivity, as well as slower recovery upon removal of the stressor.

In addition, recent evidence shows that the val/met and met/met genotypes (in females) are more frequently found in victims of violent suicide, and this frequency is increased in populations where individuals have been abused during childhood (Pregelj et al., 2011; Schenkel et al., 2010). While no differences from normal allele frequency were found in male victims, it is plausible that the already high rate of violent suicide in men masked any associations with the polymorphism. This evidence, while certainly not conclusive, suggests that val/met and met/met carriage may be associated with an

impaired ability to cope appropriately with stress, and this may augment the effect of other factors known to be associated with suicidality - such as childhood maltreatment.

Possibly as a result of abnormal BDNF trafficking, val/met and met/met carriage have been associated with smaller prefrontal and hippocampal volumes (Frodl et al., 2007; Pezawas et al., 2004). Consistent with reduced hippocampal volume, val/met and met/met individuals demonstrate poorer performance on hippocampal and prefrontal cortex-dependent neuropsychological tests, such as the Wisconsin Card Sorting Task (WCST) (Egan et al., 2003), and poorer episodic memory (Hashimoto et al., 2008). The WCST is conducted using a set of cards that can be matched according to the shape, colour or number of figures depicted. Subjects are asked to categorize the cards according to a specific matching rule (i.e. matching by shape, colour or number of figures), which they must deduce from the test administrator's feedback as to whether or not each categorization attempt is correct. The matching rule changes after a number of successful matches have been made. The subject is not notified when the rule changes and *becomes aware of the change only after they are told that the application a rule which was previously successful is no longer correct*. Performance on this task depends on the ability to properly assess all the features of the cards, see that the rules change, and importantly - not persevere on any one rule.

Focus of the Present Investigation

The inability to cope effectively with stressful events can have wide reaching negative effects that could contribute to numerous stress-sensitive disorders, most notably depression. Importantly, the val66met polymorphism of the BDNF gene has been linked to HPA abnormalities, ruminative coping and depressive behaviour. Hence, the present

investigation sought to better characterize the role of val66met in a range of coping styles and flexibility.

Although the literature associating the val66met polymorphism with coping factors is still in its infancy, some recent evidence suggests that val/met and met/met individuals are associated with increased use of rumination as a coping style in both adult females with a history of depression, as well as never-depressed healthy adults (Beevers, Wells, & McGeary, 2009, Hilt et al., 2007). Moreover, it is important to note that the deficits in WCST observed in the val/met and met/met genotypes, bear a striking resemblance to the processes involved in flexible coping (described earlier). In our current investigation, we are interested in differences in coping flexibility as a function of the BDNF polymorphisms. We hypothesize that dysfunction in stress-regulating structures of the brain (primarily the prefrontal cortex and the hippocampus) caused by dysfunctional BDNF secretion and trafficking may compromise effective coping behaviour in general, and that findings related to rumination specifically may not fully characterize the impact of the val66met polymorphism.

Little work has been reported that links the polymorphism to appraisals. To address this paucity of evidence, we aimed to have participants assess how stressful four thematically different hypothetical scenarios would be to them. Additionally, we asked participants to report what types of coping strategies they might employ in response to these tasks. Concurrently, we assessed cortisol before and after the appraisal of the four scenarios to determine if it is differentially related to variation on this polymorphism during this task. Finally, we aimed to expand the associative findings between the

polymorphism and rumination to a greater number of coping strategies - identifying a consistent constellation of coping strategies.

Methods

Participants

Participants were recruited online through Carleton University's SONA System (a web-based human subject pool management system) and consists of 124 students from introductory psychology classes. The current sample has 82 females and 42 males with ages ranging from 17- to 55-years (median was 20-years). The allele distribution of the val66met polymorphism was 90 val/val individuals (33 male, 57 female) and 31 val/met and met/met individuals (7 male, 24 female). The number of met/met individuals was very small ($n = 3$) and hence data from both the val/met and met/met genotypes were pooled. Three individuals were excluded from analysis because we were unable to determine a genotype from the sample they provided. All participants were compensated with course credit. Participants completed self-report inventories as well as provided saliva samples for cortisol analysis and genotyping. Subjects fully completed the study in a single 1.5 hour session.

Diagnosis of a current mental disorder was recorded (26 individuals reported a current diagnosis) however all individuals were included in the present analysis. No significant differences were found between the genotype groups based on age; $F(1, 119) = 0.006, p < 0.936$, sex; $\chi^2(1, 121) = 2.067, p < 0.15$, race; $F(1, 119) = 0.848, p < 0.359$, relationship status; $F(1, 119) = 0.009, p < 0.925$, past mental disorder; $F(1, 119) = 0.302, p < 0.583$, current mental disorder; $F(1, 119) = 0.111, p < 0.740$, or childhood maltreatment or any of its subscales: physical; $F(1, 119) = 0.407, p < 0.525$, psychological; $F(1, 119) = 0.746, p < 0.389$, neglect; $F(1, 119) = 0.009, p < 0.924$, or total; $F(1, 119) = 0.423, p < 0.517$.

Procedure

Upon arrival at the testing room, participants were invited to read and sign the informed consent. Special attention to the possible risks of participating in the study were discussed with the researcher in person, when going through the form, and the researcher reminded each participant that they may withdraw from the study at any time without penalty. Participants were then invited to fill out the demographic questionnaire and surveys. Each participant progressed through the surveys at their own pace and with minimal interaction with the researcher. Saliva samples were taken after the demographic questionnaire (DNA sample), as well as before and after their appraisal of the 4-stressful scenarios (cortisol samples).

Participants filled out questionnaires related to their current depressive symptoms, childhood maltreatment, social support, and coping-style. Participants were also asked to examine four stressful scenarios and to respond by revealing how stressful they would find each of the scenarios, as well as which coping strategies they thought they would use to cope with the stress.

Survey Measures

Demographic questionnaire. The demographic questionnaire (Appendix C, Item 1) used in this study assessed age, sex, racial heritage, relationship status, current and past mental health status, and if the individual was a smoker or non-smoker.

Depression. The Beck Depression inventory (BDI; Beck et al., 1961) (Appendix C, Item 10) is a widely used 21-item self-report measure of depressive symptoms used in both clinical and nonclinical populations. For each item the subject must respond by agreeing with one of a number of statements which represent a symptom of depression.

Each of the statements is associated with a number (0 to 3). The numbers accompanying each statement that the participant endorses are totalled to provide a measure of current depressive symptoms. Total scores can range from 0 to 63, 0 indicating no symptoms and 63 indicating very severe symptoms.

Social Support. Social support is assessed using the Consumption and Generation of Social Support Scale (CGSSS; Bertera, 1997) (Appendix C, Item 8). The CGSSS is a 24-item self-report measure designed to capture how much social support an individual receives (12-items) and how much they provide (12-items). Social support is rated on a scale from "not at all" to "about every day." Items are then coded from 0 to 5 and summed for a total score (maximum of 120), total consumption score (maximum of 60), and total generation score (maximum of 60).

Trait-Coping. Trait-like coping is assessed using the Survey of Coping Profiles Endorsed (SCOPE; Matheson, & Anisman, 2003) (Appendix C, Item 3). It is comprised of 50 questions representing 14 coping strategies. Participants are asked to indicate how frequently they use each item on a scale from 0 to 4. A score of 0 represents never using that item and a score of 4 represents a high frequency of use. Each of the 14 subscales can then be totalled and plotted on a graph to represent how each strategy is used in relation to the others.

Childhood maltreatment. Childhood maltreatment is assessed with the Childhood Maltreatment Questionnaire (short form) (Karlovic, Buljan-Flander, & Vranic, 2001) (Appendix C, Item 7). It is a self-report measure comprised of 31-items which span from neglect to psychological, physical, and sexual abuse. Each item can be rated

from 1 to 5 indicating the frequency each item was experienced (5 indicating the highest frequency). Scores range from 31 to 155.

Cognitive Flexibility. Cognitive flexibility is measured using the Cognitive Flexibility Inventory (Dennis & Vander Wal, 2010) (Appendix C, Item 9). The CFI is a 20-item self-report measure designed to assess flexibility in the face of stressful situations. Each of the 20 statements is rated by the participant from 1 to 7 (7 indicating the highest level of agreement). Two dimensions are assessed by the CFI - awareness of multiple alternative causes and solutions to stressful scenarios as well as perception of control over stressful scenarios. Higher scores represent greater flexibility and greater perception of control.

Appraisal and Coping. Four stressful scenarios were created for participants to respond to. The situations were designed to vary across multiple types of stressor content (economic stress, health-related stress, relocation stress, and academic stress) (Appendix C, Item 5). Stressor severity was measured using the Stress Appraisal Measure (SAM; Peacock & Wong, 1990) and the specific coping strategies that were appraised as being useful in that situation were assessed using the abbreviated 27-item version of the SCOPE.

Physiological Measures

Salivary Cortisol. Salivary cortisol fluctuations have been well established as a physiological indicator of a stress response. Samples were taken immediately before the first appraisal and immediately after the last appraisal of the aforementioned stressor scenario. Saliva samples were collected using Salivette collection devices (Starstedt Inc., Newton, NC) and were stored at -80 °C until analysis. Salivette tubes were centrifuged

(0-4°C) and were analyzed for cortisol using a ¹²⁵I immunoradiometric assay kit (Diagnostic Products Corporation, Los Angeles, CA).

Genotyping. Genotyping was conducted using a restriction fragment length polymorphism procedure. In general terms, this procedure makes use of a restriction enzyme that has a digestion site specific to only one of the polymorphisms. This allows the researcher to detect the presence of a polymorphism based on the action of the enzyme after it is visualized on agarose gel. Samples for genotyping were collected using Oragene OG-500 collection kits (DNA Genotek, Inc., Ottawa, Ontario, Canada). Genomic DNA was extracted from the sample collection kit according to the extraction procedure included with the kits. After extraction, samples were diluted to approximately equal concentration (50 ng/μL). Then, primers were designed and were used to replicate fragments for digestion after polymerase chain reaction (PCR). The PCR product is 297 base pairs long. Our PCR conditions were 94°C for 3 minutes, then 32 cycles of 94°C for 40 seconds, 68°C for 30 seconds, and 72°C for 45 seconds, and then 70°C for 5 minutes. Amplification reactions were performed in a total volume of 15 μL, containing approximately 1 μL (50 ng) of genomic template, 0.4 μL of each primer (concentration 10 μM), 1.2 μL of dNTP, 1.5 μL 10X Buffer, 0.6 μL of MgCl₂, 0.21 μL of Taq polymerase, and 10.69 μL of water.

Then, an aliquot of the PCR product was digested using the restriction enzyme Hsp92II and an aliquot of the PCR product was saved in its undigested state. The enzyme was selected based on a previous study demonstrating its ability to differentiate the val66met polymorphism (Sen et al., 2003). The digestion reaction was performed in a total volume of 20 μL containing 5 μL of PCR product, 2 μL of 10X Buffer, 0.2 μL of

BSA, 0.75 μ L of Hsp92II, and 12.05 μ L of water. Hsp92II digests the Val polymorphism into two fragment lengths (20 bp and 277bp) and the Met polymorphism into three fragment lengths (20 bp, 77 bp, and 200 bp). This enzyme was selected, in addition to having a discriminating site of digestion for the val66met polymorphism, because it has a secondary digestion site which is present in all individuals. This allowed researchers to determine if complete digestion was achieved in all cases.

Subsequently, digested and undigested PCR products were electrophoresed on 2% agarose gel for 80 minutes at 120 volts and then visualized using a transilluminator and ethidium bromide staining.

Statistical Analyses

After examining the data for outliers - histograms, Q-Q Plots, and the Shapiro-Wilk statistic were checked for each of the genotype groups separately. The data were judged to be approximately normal for consumption and generation of social support, wishful thinking, emotion-focused and avoidant coping factor, problem-focused coping factor, cognitive flexibility, and appraisals of stressfulness.

Notably this assumption was violated for measures of depressive symptoms (BDI) and childhood maltreatment (CMQ), where the data were positively skewed. This was not unexpected given the low frequency of occurrence for each of these measures in a normal student population. Logarithmic and square root transformations were attempted in order to normalize these measures. When verifying assumptions for ANOVA and hierarchical regression it was determined that a square root transformation should be used when the BDI was the measure of interest - normalizing both the distribution of responses as well as residuals. Additionally, as sexual abuse was only reported in 5 of 124 participants, this subscale of the CMQ was dropped from the analysis.

Levene's test for equality of variance was satisfied for all analyses performed indicating homogeneity of variance between groups and all data collected were determined to be independent between participants.

The resulting data were analyzed by one-way analysis of variance (ANOVA) where appropriate. As well, hierarchical regression analyses were used to evaluate the relationship between aspects of childhood maltreatment and BDI scores as well as coping methods used, and the contribution of genotype in moderating these relations.

Results

Depressive Symptoms

BDI scores were 8.32 ($S.E. = 0.84$) and 9.77 ($S.E. = 1.58$) for those individuals in the val/val and the combined val/met and met/met conditions. The ANOVA revealed that these groups did not differ from one another, $F(1,119) = 0.720, p < 0.40$).

Significant associations between current BDI scores and total amount of childhood maltreatment; $R^2 = 0.09, \beta = 0.314, t(122) = 3.655, p < 0.001$, neglect; $R^2 = 0.06, \beta = 0.245, t(122) = 2.795, p < 0.006$, and psychological abuse; $R^2 = 0.12, \beta = 0.352, t(122) = 4.152, p < 0.001$ were found. However there were no associations between current BDI scores and physical abuse; $\beta = 0.144, t(122) = 1.605, p < 0.111$.

The possible moderating effect of genotype was then explored regarding the relationship between total childhood maltreatment, neglect, and psychological abuse and current symptoms of depression. Significant interactions with genotype were found with the neglect subscale only, $\Delta R^2 = 0.01, F(1, 117) = 5.785, \beta = -0.118, t(117) = -2.405, p < 0.018$ (FIG 1). A simple slopes analysis was then conducted to determine if change in BDI scores differed from zero for each of the genotypes using Preacher's moderation calculator (Preacher, Curran, & Bauer, 2006). In this regard, no significant simple slope was found for the val/val group ($p < 0.262$) or val/met and met/met group ($p < 0.327$).

Social Support

Levels of reported *received* social support for the val/val and combined val/met and met/met group were 1.83 ($S.E. = 0.074$) and 1.67 ($S.E. = 0.12$), respectively. Levels of reported *generated* social support for the val/val and combined val/met and met/met group were 2.22 ($S.E. = 0.06$) and 2.02 ($S.E. = 0.10$), respectively. The ANOVAs

revealed that no differences in generated; $F(1, 119) = 2.595, p < 0.110$) or received; $F(1, 119) = 1.246, p < 0.267$ social support we apparent for the genotypes. Additionally, neither generated; $\beta = 0.059, t(122) = 0.650, p < 0.517$ nor received; $\beta = -1.140, t(122) = -1.061, p < 0.29$, social support were significantly associated with depression scores.

Coping

Based on previous use of the SCOPE (Matheson et al., 2007), we factor analyzed our results in order to examine broad differences in coping. The correlation matrix was examined to ensure correlations greater than 0.3 were present, and the determinant was greater than 0.00001 - indicating no problems with multicollinearity. Bartlett's test of sphericity was found to be significant, indicating that the data may be subjected to factor analysis. Given our concerns with small sample size, items loading lower than 0.50 (Guadagnoli & Velicer, 1988) on a factor were not used, and factors with fewer than 4 items were not interpreted. The results of the factor analysis accounted for 40.87% of the total variance with a 2 factor solution. It placed avoidance, rumination, emotional expression, other blame, passive resignation, and wishful thinking on factor 1 (Chronbach's $\alpha = 0.74$); and problem solving, cognitive restructuring, active distraction, humor, and social support on factor 2 (Chronbach's $\alpha = 0.69$). We re-labelled factor 1 as emotion-focused and avoidant coping style, and factor 2 as problem-focused coping style.

It was found that the val/val group endorsed a problem focused coping style an average of 47.47 ($S.E. = 1.23$) and the combined val/met and met/met group endorsed problem-focused coping style an average of 47.21 ($S.E. = 2.45$). The ANOVA revealed no significant differences in problem-focused coping between the genotype groups, $F(1,117) = 0.011, p < 0.919$. However, it was found that the val/val group endorsed

emotion-focused and avoidant coping style an average of 36.75 ($S.E. = 1.20$) while the combine val/met and met/met group these strategies an average of 41.68 ($S.E. = 1.67$). The ANOVA revealed that the combined val/met and met/met group endorsed a significantly more emotion-focused and avoidant coping style than the val/val group, $F(1,119) = 4.697, p < 0.032, d = 0.4735$ (FIG. 2).

As expected, it was found that emotion-focused and avoidant coping style is positively associated with depressive symptoms, $R^2 = 0.22, \beta = 0.43, t(122) = 5.265, p < 0.001$. However, there was no significant interaction with genotype to suggest moderation, $\beta = 0.093, t(117) = 0.288, p < 0.774$. Problem-focused coping style was negatively associated with depression scores, $R^2 = 0.07, \beta = -0.277, t(122) = -3.187, p < 0.002$. However, again there was no significant interaction with genotype to suggest moderation, $\beta = -0.140, t(117) = -1.333, p < 0.185$.

Possible moderation of the relationship between childhood maltreatment experiences and coping behaviour by genotype was also assessed. There were no significant associations between childhood maltreatment and problem-focused coping. However, significant associations were found between an emotion-focused and avoidant coping style and total amount of childhood maltreatment; $R^2 = 0.043, \beta = 0.207, t(122) = 2.338, p < 0.021$, as well as psychological abuse; $R^2 = 0.063, \beta = 0.251, t(122) = 2.866, p < 0.005$. There were no significant associations between an emotion-focused and avoidant coping style and neglect ($p < 0.219$) or physical abuse ($p < 0.537$).

Next, it was found that the relationship between emotion-focused and avoidant coping style and psychological abuse; $\Delta R^2 = 0.03, F(1, 117) = 4.143, \beta = -0.204, t(117) = -2.035, p < 0.044$, as well as the total amount of childhood maltreatment; $\Delta R^2 = 0.043,$

$F(1, 117) = 5.708, \beta = -0.247, t(117) = -2.389, p < 0.018$, were significantly moderated by genotype (FIG. 3 and FIG. 4). A simple slopes analysis was then conducted once again for both total childhood maltreatment and psychological abuse to determine if change in endorsement of emotion-focused and avoidant coping style differed from zero for each of the genotypes as psychological abuse and total maltreatment increased using Preacher's moderation calculator (Preacher, Curran, & Bauer, 2006). The simple slopes analysis indicated that the val/met and met/met group simple slope was not significant at different levels of total childhood maltreatment ($p < 0.99$) or psychological abuse ($p < 0.77$), however the val/val group's endorsement of emotion-focused and avoidant coping style was found to increase significantly as the total amount of childhood maltreatment increased ($p < 0.025$), as well as for psychological abuse specifically ($p < 0.02$).

Sex has also been shown to influence coping behaviour (Ptacek, Smith, & Dodge, 1994). In the current sample, the relative level of endorsement of emotion-focused and avoidant coping style was 32.50 ($S.E. = 1.56$) for males and 40.85 ($S.E. = 1.14$) for females. Endorsement of problem-focused coping was 47.91 ($S.E. = 1.46$) for males and 47.15 ($S.E. = 1.45$) for females. The ANOVAs revealed significantly different endorsement between the sexes for emotion-focused and avoidant coping style; $F(1, 122) = 18.290, p < 0.001, d = 0.8145$, however no differences were found for problem-focused coping style; $F(1, 122) = 0.114, p < 0.737$ (FIG. 5). When the effect of genotype on coping behaviour was reassessed considering sex as a second factor, sex and genotype were found not to interact to affect either problem focused coping; $F(1, 117) = 0.083, p = 0.774$, or emotion-focused and avoidant coping; $F(1, 117) = 0.310, p = 0.579$.

Cognitive Flexibility

The relative level of endorsement of awareness of multiple alternative causes and solutions for stressful scenarios was 5.41 ($S.E. = 0.10$) and 5.20 ($S.E. = 0.18$) for the val/val and combine val/met and met/met group respectively. Endorsement of control over stressful scenarios was 3.86 ($S.E. = 0.09$) and 4.06 ($S.E. = 0.17$) for the val/val and combined val/met and met/met group respectively. The ANOVAs revealed that there were no significant differences between genotypes on either the control, or alternatives subscales of the CFI.

Appraisal of Stressful Scenarios

Because of small sample size, it was decided that only the subscale for appraisal of stressfulness of the SAM would be analyzed. Table 1 presents ratings of stressfulness for the genotype groups across each of the scenarios. The appraisal of stressfulness was significantly higher for the val/met and met/met group than the val/val group in response to economic-stress situation, $F(1, 119) = 4.202, p < 0.043, d = 0.4498$. Additionally, a trend in the data indicated that the val/met and met/met appraisal of stressfulness for a health-related stressor was greater than the val/val group, $F(1, 119) = 3.571, p < 0.061, d = 0.4152$. No significant differences were found when scores were collapsed across scenarios.

A contrast analysis was performed to examine differences in stressfulness of the four scenarios for all participants (FIG. 6). Bonferroni correction was used to correct for inflated type I error caused by multiple comparisons. It was determined that an $\alpha = 0.004167$ should be used for six comparisons. Importantly, the economic and health-related situations were judged to be significantly more stressful than the other two situations. Table 2 summarizes the results of this analysis.

Appraisal of Coping for Stressful Scenarios

Factors representing emotion-focused and avoidant coping style and problem-focused coping style were constructed for each scenario using the results of the factor analysis described earlier. No significant differences between the genotypes on emotion-focused and avoidant coping or problem-focused coping when the four scenarios were collapsed, or analyzed individually.

Appraisal of Effectiveness of Coping for Stressful Scenarios

Participants were also asked to rate how effective their 'most often' used coping strategies would be in helping them cope with the four situations. The mean rating of effectiveness for their top three most highly endorsed coping strategies were used to represent coping effectiveness for each scenario. No significant differences were found in response to any of the four situations individually or when responses were collapsed across situations.

Cortisol Response to Appraising 4 Stressful Scenarios

There were no significant changes in cortisol in response to assessing the 4 stressful scenarios when all subjects were pooled, or when divided by genotype.

FIGURE 1 Simple effect of genotype and childhood neglect on depressive scores (BDI) at $M \pm 1$ SD. The val/met & met/met group had higher BDI scores than the val/val group under conditions of low neglect, however with higher neglect scores there was no difference between the genotypes.

FIGURE 2 Level of university students' endorsement of A) emotion-focused and avoidant coping style ($M \pm SEM$) and B) problem-focused coping style ($M \pm SEM$) as a function of genotype.

FIGURE 3 Simple effect of genotype and childhood psychological abuse on endorsement of emotion-focused and avoidant coping style at $M \pm 1$ SD. The val/met & met/met group endorsed more emotion-focused and avoidant coping style than the val/val group under conditions of low maltreatment, however with higher maltreatment scores there was no differences between the genotypes.

FIGURE 4 Simple effect of genotype and total childhood maltreatment on endorsement of emotion-focused and avoidant coping style at $M \pm 1$ SD. The val/met & met/met group endorsed more emotion-focused and avoidant coping style than the val/val group under conditions of low maltreatment, however with higher maltreatment scores there was no differences between the genotypes.

FIGURE 5 Level of university students endorsement of A) emotion-focused and avoidant coping style ($M \pm SEM$) and B) problem-focused coping style ($M \pm SEM$) as a function of sex.

FIGURE 6 Stress appraisal (scores range from 0 to 5) of each potentially stressful scenario ($M \pm SEM$).

Table 1

Ratings of Stressfulness of Four Stressful Scenarios According to Genotype

<i>Situation</i>	<i>Mean</i>	<i>SEM</i>
<i>Relocation</i>		
<i>val/val</i>	<i>2.78</i>	<i>0.09</i>
<i>val/met & met/met</i>	<i>2.91</i>	<i>0.18</i>
<i>Economic</i>		
<i>val/val</i>	<i>3.65</i>	<i>0.08</i>
<i>val/met & met/met</i>	<i>3.97</i>	<i>0.11</i>
<i>Academic</i>		
<i>val/val</i>	<i>2.67</i>	<i>0.11</i>
<i>val/met & met/met</i>	<i>2.65</i>	<i>0.17</i>
<i>Health</i>		
<i>val/val</i>	<i>3.99</i>	<i>0.09</i>
<i>val/met & met/met</i>	<i>4.30</i>	<i>0.12</i>

Table 2

Contrast of Appraisals of Stressfulness

<i>Contrast</i>	<i>Mean Difference (SEM)</i>	<i>t (df)</i>
Relocation - Economic	-0.92 (0.09)	-10.318 (123)*
Relocation - Academic	0.14 (0.10)	1.347 (123)
Relocation - Health	-1.25 (0.10)	-12.720 (123)*
Economic - Academic	1.06 (0.10)	10.653 (123)*
Economic - Health	-0.33 (0.07)	-4.454 (123)*
Academic - Health	-1.39 (0.10)	-13.803 (123)*

Note. * $p < 0.004167$

Discussion

The val66met polymorphism has previously been associated with differences in neurotrophic support in stress sensitive areas of the brain - primarily the hippocampus and prefrontal cortex (Egan et al., 2003; Pezawas et al., 2004). Further, the reduced neurotrophic support associated with the val/met and met/met polymorphisms have been linked to reduced size and function of these brain areas (Frodl et al., 2007; Pezawas et al., 2004) as well as an increased use of ruminative coping style (Beevers, Wells, & McGeary, 2009; Hilt et al., 2007). Depressive symptoms have also been associated with similar structural and behavioural changes as well as corresponding deficits in neurotrophic support in the hippocampus and prefrontal cortex (Ray, Weickert, Wyatt, & Webster, 2011; Karege et al., 2005). Thus, the current investigation sought to uncover the broad implications of reduced neurotrophic support on coping style, as well as potential gene-environment interactions with childhood maltreatment - which may bear particular relevance to the development of an emotion-focused and avoidant coping style (Raes & Hermans, 2008; Hyman & Sinha, 2007; Runtz & Schallow, 1997) and potentially mood disorders (Gibb et al., 2001).

Depressive Symptoms, Childhood Maltreatment, and Neurotrophic Support

Both depression and the val66met polymorphism have been associated with deficits in neurotrophic support (Ray, Weickert, Wyatt, & Webster, 2011; Karege et al., 2005; Egan et al., 2003), reduced size and function of the hippocampus and prefrontal cortex (Frodl et al., 2007; Pezawas et al., 2004; Sheline, Mokhtar, & Helena, 2003; Channon, 1996), as well as use of ruminative coping style (Beevers, Wells, & McGeary, 2009; Hilt et al., 2007; Nolen-Hoeksema, 2000). However, consistent with other studies

(Verhagen et al., 2010; Chen, et al., 2008; Gratacos et al., 2007; Surtees et al., 2007), our findings indicate that despite being associated with common factors - val/met and met/met individuals did not report more depressive symptoms than val/val individuals. Yet, others have reported mixed evidence that the val66met polymorphism *is* associated with differences in depressive symptoms. One study found that met/met and val/met individuals reported more depressive symptoms than the val/val genotype (Hilt et al., 2007), while another indicated that the val/val genotype may be associated with greater cognitive and affective symptoms of depression (Duncan et al., 2008). In both these cases, the sample sizes used were small, and it should be noted that the larger meta-analytic studies confirm our findings (Verhagen et al., 2010; Gratacos et al., 2007). However, with respect to specific populations, the link between the met polymorphism and depression has been better demonstrated in geriatric populations (Warren et al., 2007; Hwang et al., 2005). Hence, while our current findings are controversial, it is highly likely the discrepancies in the literature are due to small sample sizes. It is also possible that the relevance of the polymorphism to mood disorders may be more evident in vulnerable populations - like the elderly.

Recently it has been found that in a population of depressed women, the val/met and met/met genotypes are over-represented in those with more stressful childhood experiences than those with fewer stressful experiences (Lavebratt et al., 2010). Given that met carriers were not associated with greater depressive symptoms in the present study, we considered the possibility that BDNF genotype may act as a moderator, differentially changing the positive relationship between childhood maltreatment and current depressive symptoms (Agid, Kohn, & Lerer, 2000). In essence, we hypothesized

that reduced neurotrophic support (due to the met polymorphism) may act in combination with childhood maltreatment experiences to promote current depressive symptoms. To this end, our analysis did indicate that both psychological abuse and childhood neglect were associated with elevated BDI scores. This is consistent with some previous work indicating that emotional maltreatment is associated with current depressive symptoms but not necessarily physical or sexual abuse (Gibb et al., 2001). Further, hierarchical regression analyses indicated that the relationship between childhood neglect and current depressive symptoms was indeed significantly moderated by genotype. Our results suggest that at lower levels of neglect, val/met and met/met individuals report higher levels of depression than the val/val group. However, as childhood neglect increased, differences in BDI scores decreased between the polymorphisms. Given the positive skew of childhood neglect scores in the current sample, it would be inappropriate to interpret beyond a moderate level of childhood neglect. The result of our simple slope analysis indicated that while the change in depressive symptoms between the genotypes are different from each other at low levels of neglect - as reporting of neglect increased, change in depressive symptoms did not differ significantly from zero for either genotype group. Thus, no definite conclusion could be drawn as to which genotype interacted with childhood neglect.

These findings indicate that, under ideal conditions (i.e. those where no neglect is experienced in childhood), val/met and met/met individuals may have slightly elevated BDI scores as compared to val/val individuals. However, contrary to our hypothesis, this difference in reporting of depressive symptoms is decreased between the genotypes as childhood neglect increases. Therefore, while the val/met and met/met polymorphisms

may be associated with slightly elevated depressive symptoms under ideal conditions - the effect of even moderate childhood neglect seems to completely eliminate genotypic differences in depressive symptoms.

This provides partial support for the BDNF hypothesis of depression, showing that under ideal conditions - reduced neurotrophic support is associated with higher depressive symptoms. However, this reduction in neurotrophic support does not appear to represent a vulnerability to depression as a result of moderate levels of childhood neglect. This, at first, seems inconsistent with Lavebratt et al., 2010 - however, they considered all types of stressful childhood life events while the current investigation focused on caregiver-child interactions. It is probable that abnormal caregiver-child relationships, at least at the moderate levels recorded in the current investigation, are not a sufficient source of childhood stress to interact with the BDNF polymorphism. Indeed, another recent study examining potential interactions between the BDNF polymorphism and early life stress indicated that met carriers who experienced greater early life stress not only show reduced hippocampal volume compared to the val/val genotype, but this in turn predicted increased startle response (measured with heart rate) - indicating stress sensitivity, more neurotic personality traits, and increased depression and anxiety (Gatt et al., 2009).

Coping Style, Childhood Maltreatment, and Neurotrophic Support

Our main finding supports and expands upon previous reports that val/met and met/met individuals ruminate more than val/val individuals (Beevers, Wells, & McGeary, 2009). In general, the val/met and met/met group reported significantly greater endorsement of emotion-focused and avoidant coping strategies than the val/val group.

Additionally, we observed no differences between the genotypes on problem-focused strategies.

In the past, increased reporting of an emotion-focused and avoidant coping style has been associated with greater severity of mood disorders like depression (Nolen-Hoeksema, 1991; Folkman & Lazarus, 1986; Billings & Moos, 1984) and PTSD (Clohessy & Ehlers, 1999). In turn, depression has been associated with greater endorsement of emotion-focused coping (Matheson & Anisman, 2003) as well as reductions in hippocampal BDNF (Ray, Weickert, Wyatt, & Webster, 2011; Karege et al., 2005). The current findings indicate that reduced neurotrophic support may be associated with greater use of emotion-focused and avoidant coping strategies. Therefore, these findings support previous reports that neurotrophic disturbances may affect our interaction with stressors (Beevers, Wells, & McGeary, 2009) and may also develop into a stress-sensitive pathology (Gilbertson et al., 2002).

Previous reports indicate sex differences in coping style (Brougham et al., 2009), and so the current investigation also attempted to assess the potential interaction between the val66met polymorphism and sex on coping behaviour. First, it was determined that the genotypes were not significantly associated with gender, implying that the effect of genotype is not sex-linked, or simply a sampling error where one sex is over represented in a particular genotype-group. Next, the effect of sex on coping behaviour was assessed and it was found that while no sex differences were evident for problem-focused coping, emotion-focused and avoidant coping was used more in females than in males. Finally, both sex and genotype were assessed simultaneously in their ability to account for variability in problem-focused coping style and emotion-focused and avoidant coping

style. However, it was found that genotype and sex did not interact in the current sample to predict either coping style.

The effect size of the val66met polymorphism on emotion-focused and avoidant coping behaviours is small (Cohen, 1992), and thus the val66met polymorphism of the BDNF gene may not have a great impact on behaviour under all circumstances. Despite this, studying this site of genetic variation on coping behaviour does allow us some insight into the importance of neurotrophins as they relate to our interaction with stressors. It is likely that, while small differences exist when considering the polymorphism on its own, greater more dramatic changes in behavior may be observed under specific environmental conditions. Thus, we again considered childhood maltreatment in addition to the BDNF polymorphism - this time, as they related to coping style.

When examining associations between childhood maltreatment and coping strategies, the result of our initial analysis indicated that there were no associations between problem-focused coping and childhood maltreatment. However, it was found that both the total amount of childhood maltreatment (all types considered together), as well as psychological abuse specifically were significantly associated with emotion-focused and avoidant coping. This is consistent with previous reports that total childhood maltreatment is associated with avoidant stress-coping strategies (Hyman, Paliwal, & Sinha, 2007). In both cases this positive association was moderated by genotype. Under conditions where adverse childhood events were minimal we saw that an emotion-focused and avoidant coping style was more strongly endorsed by the val/met and met/met genotype group. However, as adverse childhood conditions increased the val/val

genotype increased endorsement of emotion-focused and avoidant coping style, rising to the level of the val/met and met/met genotypes, whereas the val/met and met/met genotypes were resilient - remaining at a higher, but constant level. Taken together, it is evident that while basal levels of emotion-focused and avoidant coping are higher in the val/met and met/met genotypes, it is the val/val genotype that increases use of emotion-focused and avoidant coping style in response to mild and moderate levels of childhood maltreatment and not the val/met and met/met genotypes - as one might expect if coping style is associated with poorer neurotrophic support.

One possible explanation for these results is that suppression of neurotrophic release in stress sensitive areas of the brain are limited to a minimum level of necessary neurotrophins, and by extension the behaviour associated with these changes may also be limited. Animal studies indicate that neurotrophic factor release in sensitive areas of the brain is downregulated by chronic stress (Murakami et al., 2005; Sapolsky et al., 1990) and that early life stress is associated with reductions in adult neurogenesis (Mirescu, Peters, & Gould, 2004). Additionally, these studies indicate a ceiling effect for the amount of possible suppression - demonstrating that normal reductions in neurogenesis as a result of early life stress were not made worse in response to a chronic stressor (Mirescu, Peters, & Gould, 2004). If this pattern is consistent in humans, it is possible that the early life stress of moderate childhood maltreatment may result in a reduction of neurotrophic factors for the val/val genotype in areas which are also affected by the *already* dysfunctional release of BDNF associated with the val/met and met/met genotypes. If the action of neurotrophins are indeed tied to coping behaviour, then our pattern of results is consistent with these findings - ultimately resulting in a similar

coping style across all variants of the val66met polymorphism at higher levels of childhood maltreatment.

It is also possible that the moderating effect of genotype is only observable under ideal and severe maltreatment conditions, and that genotypic differences are masked by the effect of moderate maltreatment. Future studies should examine the effect of more severe childhood maltreatment, or other types of early-life stressors, and endorsement of emotion-focused and avoidant coping to see if this pattern remains consistent or if the interaction between childhood environment and genotype change under conditions which have been more strongly associated with the development of mood disorders.

Taken together, these findings indicate that in general the val/met and met/met polymorphism may be associated with greater endorsement of an emotion-focused and avoidant coping style than the val/val polymorphism. In addition, the effect of childhood maltreatment does not seem to exaggerate these differences, which may indicate a ceiling effect for the action of neurotrophins on coping behaviour.

Cognitive Flexibility and Neurotrophic Support

Contrary to our hypothesis, no differences were found between the genotypes using the current measure of cognitive flexibility. This measure tapped into cognitive flexibility with self-report statements endorsing the appraisal of stressful situations as controllable, the generation of multiple hypothesizes about the causes of the stressors, and the generation of multiple alternative solutions to the stressful scenarios. Given previous studies linking findings between the val66met polymorphism, hippocampal function (Hashimoto et al., 2008), and cognitive flexibility (Egan et al., 2003) it is surprising that no differences were found for cognitive flexibility in the current sample.

However, from an examination of the items on this questionnaire, it is possible that it measured a related but separate concept from previous studies. The focus of the items on this questionnaire are largely about abstractly assessing stressful scenarios and weighing alternative responses with abstract reasoning and perspective taking. However, past associations with the val66met polymorphism are more closely related to response inhibition - which is also a necessary element of cognitive and coping flexibility (the suppression of automatic responding). Therefore, while both cognitive processes may be necessary for flexible coping, the val66met polymorphism may strictly be related to response inhibition and rather than abstract reasoning.

Appraisal of Stressfulness and Neurotrophic Support

No differences were found between the genotypes on either appraisal of stressfulness or appraisal of coping when the four scenarios were collapsed. Additionally, there was no change in salivary cortisol in response to the assessment activity. Initially, the situations were analyzed as a block because they were not randomized (therefore order effects were uncontrolled), and interactions between genotype and the content of each stressor individually would not be a meaningful analyses. Situation content was varied with the intent of allowing each participant to respond to a number of scenarios - allowing us to again assess general style of interaction with stressors.

However, while risking confounding order effects, it was decided that each situation was not likely to influence the assessment of the other situations and should also be analyzed separately. Primarily, differences between the genotypes were observed for only two of the four situations - economic stress and health-related stress. It was found

that in response to an economic stressor, the val/met and met/met group appraised this to be significantly more stressful than the val/val group and a second trend was identified in response to the health-related stressor demonstrating the same effect. However, no differences were found between the genotypes for appraisal of emotion-focused and avoidant coping, or problem-focused coping in response to any of the four scenarios.

A secondary set of contrasts were performed in order to attempt to explain why differences between the genotypes were found for some scenarios and not others. It was determined that the economic and health-related situations were judged to be significantly more stressful than the other two situations for the current sample.

Taken together, this set of analyses suggests that not all the situations used in the current study may have been sufficiently stressful to elicit a genuine response from our participants. This was confirmed by the lack of cortisol response before and after the activity. Despite this, these data do suggest that under conditions that are judged to be more stressful by both groups - val/met and met/met individuals judge the situation to be more stressful than the val/val genotypes. Additionally, differences between the genotypes were not observed for situations that were judged to be comparatively less stressful - suggesting that the differences in appraisals between the genotypes may be most evident under highly stressful conditions and not for less severe stressors. This indicates that differences in behaviour between the genotypes may be context dependent - where BDNF polymorphic differences may be most evident under significant stress. These findings are consistent with recent studies implicating the met polymorphism in higher anticipatory stress when faced with a physical challenge (Colzato et al., 2011).

Future studies should explore differences in coping behaviour between the genotypes in relation to significant personal stress, or under experimentally stressful conditions.

Conclusion

The results of the current exploratory investigation indicate that the val66met BDNF polymorphism, and by association neurotrophic support, is involved in our interactions with stressors. Specifically, we have observed that greater use of emotion-focused and avoidant coping style is associated with the met polymorphism. Additionally, the polymorphism preferentially affects endorsement of emotion-focused and avoidant coping and not problem-focused coping. The BDNF polymorphism also moderates mild to moderate childhood maltreatment, where the met polymorphism was associated with both greater current depressive symptoms and emotion-focused coping style than the val/val polymorphism under ideal conditions, but that these differences were reduced as maltreatment experiences increased in severity. Interestingly, the met polymorphism did not represent a vulnerability to moderate maltreatment as the met polymorphic individuals were unresponsive in both their current depressive symptoms as well as their use of emotion-focused and avoidant coping style. In this regard, the val/val polymorphism was most responsive to moderate maltreatment - increasing endorsement of emotion-focused and avoidant coping. Finally, while the current manipulation was probably not sufficiently potent to fully engage participants and elicit a genuine response, the polymorphism has been implicated in appraisal processes - where situations that are judged to be stressful show that met carrying individuals judge those situations to be more stressful than val/val individuals. Together, these findings indicate that reduced neurotrophic support may be associated with a coping style that has been associated with the development and exacerbation of mood disorders but that factors associated with the disruption of neurotrophic support may not act synergistically to affect behaviour.

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Appendices

Appendix A: SONA Recruitment Notice

Study Name "Genetic Variation and Coping with Stress"

Abstract The purpose of this study is to develop a greater understanding of the role our genes play with respect to the methods we use to cope with stress and the resultant risk of developing depression.

Description The purpose of this study is to develop a greater understanding of the role our genes play with respect to the methods we use to cope with stress and the resultant risk of developing depression. As you may know, depression is a very common illness in many countries including Canada. Life experience certainly plays a major role in the development of depression (for example, people who go through a divorce may be more likely to become depressed). However, previous research suggests that genetic differences also contribute to the likelihood of developing depression. We are particularly interested in investigating the contribution of one gene that plays a role in the brain's ability to change in response to one's experiences. Variation in the structure of this gene is also related to an increased risk for developing depression. By identifying genetic factors that contribute to the disease, we will develop a better understanding of the biology underlying this condition, which may help us to develop improved treatments for the illness. If you agree to take part in this study, you will be asked to respond to a number of questions about your mood and about how you tend to cope with stressful life events. You will also be asked to provide a DNA sample for genetic testing, which will involve you spitting into a tube. Of course, your responses will remain confidential, your genetic information will similarly remain confidential, and you will in no way be identified as a participant. Typically, collection of this information will require you to attend a private testing session at Carleton University which lasts approximately 90 minutes. In appreciation of your time, we will be awarding you 1.5% academic credit in Psychology 1001, 1002, 2001, or 2002. This study has received clearance by the Carleton University Psychology Research Ethics Board (11-030).

Eligibility Requirements We are looking for English speaking individuals with good or corrected vision.

Duration 90 minutes

Preparation Please do not eat, drink, smoke, brush your teeth, or chew gum in the 30 minutes prior to attending the session

Percentage 1.5 Percentage

Researcher Warren Caldwell
Email: wcaldwel@connect.carleton.ca

Participant Sign-Up Deadline 24 hours before the study is to occur

Participant Cancellation Deadline 24 hours before the study is to occur

Study Status Visible to participants (approved)
Active study (appears on list of available studies)

IRB Approval Code 11-030 (expires August 31, 2012)

Appendix B: Session Script

Intro:

- Welcome to the study
- Please sit down and read over the debrief - when you're done, and before you sign just let me know and I just want to highlight a few points.
 - there will be a question on suicidal ideation
 - there will be three saliva samples
- are you still okay to proceed?
 - Obtain signature

Data Linkage Form:

- This just insures that your data remains anonymous

Have you eaten or drank anything in the last 30 minutes? Smoked? Chewed gum?

Okay, so in the next hour and a half we're going to be doing a number of surveys - please fully read the instructions for each, and answer as honestly as you can.

And we're just going to start with a basic demographic questionnaire.

Demographic Questionnaire

Saliva Sample 1 (DNA)

- This is a tube for the first saliva sample
- here are the instruction on the inside of the lid - but what I want you to do is fill the test tube up to the line (point), so that the liquid part of the saliva - not the bubbles - comes up and meets the line. This should take 2 or 3 minutes so I'm going to leave the room, just come knock on the door when you've filled it up to the line and i'll come check. Don't close the tube before I've checked that you've filled the tube up to the line.
- <leave the room>
- <come back>
- Now just close the lid to release the fixing agent
- unscrew the cap
- put on the second cap
- and invert the tube 5 times

Survey of Coping Profiles Endorsed

- This is a questionnaire, just asking about how you normally cope with stressful situations. Please read the instructions carefully and then go ahead.

Saliva sample 2 (Cortisol)

- This sample is a bit different. We're going to have you do one saliva sample now, then fill out the next questionnaire, and then do another saliva sample.

- For this one, the test tube is in three parts. So just open them up. Now what you're going to do is place the cotton roll in your mouth until it becomes fully saturated. The cotton is sterile so don't worry. Now, this is a bit gross, but you'll know that the roll is fully saturated when you are unable to soak it with saliva anymore, and so you will be swallowing saliva again. This should take about 1 minute. I'm going to leave the room, just open the door after the cotton has become fully saturated and you have put it back in the tube.
- <leave room>
- <come back>
- Okay now place that test tube in the biohazards bag.

Appraisal Task

- For this next task what I want you to do is read each scenario and use the surveys to tell me how stressful you might find that scenario and what coping strategies you would use to deal with it. After that, for the strategies that you would use "almost always" - so a 4 - I want you to tell me what those are here <point>, and then rate how effective they would be in the situation.

Saliva Sample 3 (Cortisol)

- Okay, this will be the same as the saliva sample we just did - again, fully saturate the cotton roll, and then place it back in the test tube. Then open the door when you're done.

Childhood Maltreatment Questionnaire Consumption of General Social Support Cognitive Flexibility Inventory Beck Depression Inventory

- Okay, now we're done with the saliva samples.
- Just four more surveys to go. Again, please fully read the instructions for each one as you go along, and answer as honestly as you can.
- If you have any questions feel free to ask.

Let the person finish the last 4 surveys

CHECK the BDI - question 9

The following are the procedures adopted when suicidal ideation is identified in a research participant:

Item 9 (from 21-item version) on the Beck Depression Inventory is checked immediately.

If the Beck item #9 is 0 or 1, nothing is done except give credit and debriefing information. The debriefing includes a summary of the goals of the study as well as a list of contact numbers (e.g., Health and Counseling Services).

If the Beck item #9 is a 2a, the participant is reminded of counseling services available in the community, and of the ER at the hospital. Credit and debriefing are subsequently given. If there are many participants (group questionnaire

setting) and it is not feasible to remind the participant privately of services, then the credit and debriefing sheet are provided and the participant is called within 24 hours. During the phone call, the participant is informed that the call back is part of the study's protocol, and he or she is reminded of the information contained on the debriefing sheet.

If the Beck item #9 is 2b, c or 3, the participant is spoken to privately. If speaking privately is not feasible (group setting), then the participant is called as soon as possible within 24 hours. The researcher will state that they have noticed the Beck item, and are concerned about their welfare. The summarized 6-step protocol is listed below. The following will be assessed:

1. The length of time that the participant has had suicidal thoughts.
2. Whether the participant has talked to anyone regarding these thoughts.
3. Whether the participant is currently seeing a therapist.
4. Whether the participant has a plan and a means to carry out their plan.
5. Whether the thought to carry out their plan is imminent.
6. If plan is imminent then the protocol outlined below will be followed.

Note: A written record is kept documenting the assessment.

ADDITIONAL DETAILS:

The plan and means. The participant is questioned about the plan and the means to carry out this plan.

If there are no plans, or there are plans but no means (e.g., take painkillers but none around), the participant is reminded of counseling services available in the community and the ER at the hospital. If the participant is also seeing a therapist, it is suggested that the participant speak with the therapist about this. Then the credit and debriefing are given.

If there are both plans and means, the participant is asked whether thoughts to carry out this plan are imminent (that is, are they thinking of doing this very soon).

If not imminent, OR have plans and means but don't think they would carry them out, the participant is reminded of counseling services available in the community, and also the ER at the hospital. If also seeing a therapist, it is suggested that the participant speak with the therapist about this. Then the credit and debriefing are given.

If means are available and plan is imminent, and there is good reason to believe that the individual may in fact carry out the suicidal thoughts soon, then the participant is informed that the researcher will be calling 911. During the 911 call, the police are informed of the individual's imminent intent to commit suicide. The person's name and phone number are given to the police. We are aware that this step involves breaking confidentiality, but the welfare of the participant takes priority (APA and CPA and Tri-Council guideline 3.1). The situation is documented, and the supervisor and ethics chair are contacted.

Things NOT TO DO in both in-person and telephone situations.

Do not give out your lab number as a resource for somewhere to call for help.

Do not give out home phone numbers of research personnel.

Do not intervene directly with the participant. That is, do not escort the person to the hospital or health services. If a participant does call the lab for help, refer them again to the resources, such as Health Services or the Distress Centre or hospital. Assess for immediacy of suicidal intention, and follow the steps outlined above, such as finding out if there is someone else there, calling 911 directly if there is imminent suicidal intent, etc.

Do not engage in a helping relationship with the person. Provide the information about resources, but, for example, do not make follow-up calls to check up on the person and see how they are doing.

Do not do any of this assessment and suicidal screening if you do not feel confident about it. Refer it to your supervisor

Debrief

- This is a debriefing form, and it's just to let you know a bit about why we're conducting this study and what we hope to get out of it. Have a read through it - and then, if you don't have any questions, you're free to go!

Thank you for participating in our study! Have a good day!

Appendix C: Questionnaire Package

Linkage of Coded Data and Participant Name

This form is to allow researchers to link personally identifiable data (Name, address, etc) with the unique code that will be listed on all collected data. Information on this form will be treated as confidential, and kept in a locked filing cabinet in the office of the principal investigators. Data will also be entered on a computer, and stored in a password-protected document, with access restricted to the principal investigators. This document will be destroyed after two years.

Data code _____

Participant name _____

Participant date of birth _____

Participant Number: _____

1/23

Instructions:

Please complete the following in this order...

1. Demographic Questionnaire
- 2. DNA Saliva Sample**
3. Survey of Coping Profiles Endorsed
- 4. Saliva Sample**
5. Appraisal Task
- 6. Saliva Sample**
7. Childhood Maltreatment Questionnaire
8. Consumption of General Social Support
9. Cognitive Flexibility Inventory
10. Beck Depression Inventory

Participant Number: _____

2/23

Item 1
Demographic Questionnaire

The following is used for demographic purposes only, and will not be used to identify you.

1. How old are you? _____
2. What is your sex?
 - ☐ male
 - ☐ female
3. What is your ethnic/racial heritage (check all that apply up to 3)?
 - ☐ Asian (i.e. Chinese, Japanese, Korean)
 - ☐ South Asian (i.e. East Indian, Pakistani, Punjabi, Sri Lankan)
 - ☐ South East Asian (i.e. Cambodian, Indonesian, Laotian)
 - ☐ Arabic
 - ☐ Black
 - ☐ South/Latin American
 - ☐ Mexican
 - ☐ Aboriginal
 - ☐ Euro-Caucasian
 - ☐ Other *please specify*: _____
4. What is your current relationship status?
 - ☐ Single
 - ☐ In a serious dating relationship
 - ☐ Co-Habiting
 - ☐ Engaged
 - ☐ Married
 - ☐ Separated/Divorced
 - ☐ Widowed
5. What year of study are you in? _____
6. Do you smoke or use tobacco products?
 - ☐ Yes
 - ☐ No
7. Have you suffered from a diagnosed mental disorder in the past?
 - ☐ Yes
 - If yes, what disorder? _____
 - How many episodes? _____
 - ☐ No

Participant Number: _____

3/23

8. Are you currently suffering from: (Please check all that apply)

☐ a minor illness (e.g. a cold)?

If so, what? _____

☐ A major illness (e.g. chicken pox, Mono)?

If so, what? _____

☐ A chronic (e.g. cancer, diabetes) (3 months + without remittance) illness?

If so, what? _____

☐ Mild pain?

☐ Severe Pain?

☐ Chronic Pain (3+ months, more days than not without remittance)?

☐ A diagnosed mental disorder?

If yes, what disorder? _____

If yes, at what age was your first episode? _____

How many episodes have you had to date? _____

9. Please indicate any current regimens of psychoactive medications (i.e. anti-depressant, anti-anxiety, anti-psychotic medications etc.)

Item 2

Please provide a DNA saliva sample in the tube provided

Participant Number: _____

4/23

Item 3

Survey of Coping Profiles Endorsed (50-item SCOPE)

The purpose of this questionnaire is to find out how people deal with more general problems or stresses in their lives. The following are activities that you may have done. After each activity, please indicate the extent to which you would use this as a way of dealing with problems or stresses in recent weeks.

Ordinarily, in recent weeks have you:

Never Seldom Sometimes Often Almost
always

1. accepted that there was nothing you could do to change your situation?	0	1	2	3	4
2. tried to just take whatever came your way?	0	1	2	3	4
3. talked with friends or relatives about your problems?	0	1	2	3	4
4. tried to do things which you typically enjoy?	0	1	2	3	4
5. sought out information that would help you resolve your problems?	0	1	2	3	4
6. blamed others for creating your problems or making them worse?	0	1	2	3	4
7. sought the advice of others to resolve your problems?	0	1	2	3	4
8. blamed yourself for your problems?	0	1	2	3	4
9. exercised?	0	1	2	3	4
10. fantasized or thought about unreal things (eg., the perfect revenge, or winning a million dollars) to feel better?	0	1	2	3	4
11. been very emotional compared to your usual self?	0	1	2	3	4
12. gone over your problem in your mind over and over again?	0	1	2	3	4
13. asked others for help?	0	1	2	3	4
14. thought about your problem a lot?	0	1	2	3	4
15. became involved in recreation or pleasure activities?	0	1	2	3	4
16. worried about your problem a lot?	0	1	2	3	4
17. tried to keep your mind off things that are upsetting you?	0	1	2	3	4
18. tried to distract yourself from your troubles?	0	1	2	3	4
19. avoided thinking about your problems?	0	1	2	3	4
20. made plans to overcome your problems?	0	1	2	3	4
21. told jokes about your situation?	0	1	2	3	4
22. thought a lot about who is responsible for your problem (besides yourself)?	0	1	2	3	4
23. shared humorous stories etc. to cheer yourself and others up?	0	1	2	3	4

Participant Number: _____

5/23

Ordinarily, in recent weeks have you:

Never Seldom Sometimes Often Almost
Always

24. told yourself that other people have dealt with problems such as yours?	0	1	2	3	4
25. thought a lot about how you have brought your problem on yourself?	0	1	2	3	4
26. decided to wait and see how things turn out?	0	1	2	3	4
27. wished the situation would go away or be over with?	0	1	2	3	4
28. decided that your current problems are a result of your own past actions?	0	1	2	3	4
29. gone shopping?	0	1	2	3	4
30. asserted yourself and taken positive action on problems that are getting you down?	0	1	2	3	4
31. sought reassurance and moral support from others?	0	1	2	3	4
32. resigned yourself to your problem?	0	1	2	3	4
33. thought about how your problems have been caused by other people?	0	1	2	3	4
34. daydreamed about how things may turn out?	0	1	2	3	4
35. been very emotional in how you react, even to little things?	0	1	2	3	4
36. decided that you can grow and learn through your problem?	0	1	2	3	4
37. told yourself that other people have problems like your own?	0	1	2	3	4
38. wished you were a stronger person or better at dealing with problems?	0	1	2	3	4
39. looked for how you can learn something out of your bad situation?	0	1	2	3	4
40. asked for God's guidance?	0	1	2	3	4
41. kept your feelings bottled up inside?	0	1	2	3	4
42. found yourself crying more than usual?	0	1	2	3	4
43. tried to act as if you were not upset?	0	1	2	3	4
44. prayed for help?	0	1	2	3	4
45. gone out?	0	1	2	3	4
46. held in your feelings?	0	1	2	3	4
47. tried to act as if you weren't feeling bad?	0	1	2	3	4
48. taken steps to overcome your problems?	0	1	2	3	4
49. made humorous comments or wise cracks?	0	1	2	3	4
50. told others that you were depressed or emotionally upset?	0	1	2	3	4

Participant Number: _____

6/23

Item 4

Please provide a saliva sample using one of the cotton rolls and tubes provided.

Item 5**Appraisal Task**

Please examine each of the four situations below (A, B, C, and D). In response to each stressful situation, please fill out a SAM and a SCOPE-SF (which follow each description). In addition, for items you would use "almost always" - rate how effective that coping strategy is for helping you deal with the situation.

Situation A

You have recently been offered an amazing job opportunity in another city. You are excited about the job but it will mean leaving all of your friends and family behind.

Stress Appraisal Measure (SAM) - Situation A

This questionnaire is concerned with your thoughts about various aspects of the situation identified previously. There are no right or wrong answers. Please respond according to how you view this situation right NOW. Please answer ALL questions. Answer each question by CIRCLING the appropriate number corresponding to the following scale.

	1	2	3	4	5
	Not at all	Slightly	Moderately	Considerably	Extremely
1. Is this a totally hopeless situation?	1	2	3	4	5
2. Does this situation create tension in me?	1	2	3	4	5
3. Is the outcome of this situation uncontrollable by anyone?	1	2	3	4	5
4. Is there someone or some agency I can turn to for help if I need it?	1	2	3	4	5
5. Does this situation make me feel anxious?	1	2	3	4	5
6. Does this situation have important consequences for me?	1	2	3	4	5
7. Is this going to have a positive impact in me?	1	2	3	4	5
8. How eager am I to tackle this problem?	1	2	3	4	5
9. How much will I be affected by the outcome of this situation?	1	2	3	4	5
10. To what extent can I become a stronger person because of this problem?	1	2	3	4	5
11. Will the outcome of this situation be negative?	1	2	3	4	5
12. Do I have the ability to do well in this situation?	1	2	3	4	5
13. Does this situation have serious implications for me?	1	2	3	4	5
14. Do I have what it takes to do well in this situation?	1	2	3	4	5
15. Is there help available to me for dealing with this problem?	1	2	3	4	5
16. Does this situation tax or exceed my coping resources?	1	2	3	4	5
17. Are there sufficient resources available to help me in dealing?	1	2	3	4	5
18. Is this beyond anyone's power to do anything about this situation?	1	2	3	4	5
19. To what extent am I excited thinking about the outcome of this situation?	1	2	3	4	5

Participant Number: _____

7/23

20. How threatening is this situation?	1	2	3	4	5
21. Is the problem unresolvable by anyone?	1	2	3	4	5
22. Will I be able to overcome the problem?	1	2	3	4	5
23. Is there anyone who can help me manage the problem?	1	2	3	4	5
24. To what extent do I perceive this situation as stressful?	1	2	3	4	5
25. Do I have the skills necessary to achieve a successful outcome to this situation?	1	2	3	4	5
26. To what extent does this event require coping efforts on my part?	1	2	3	4	5
27. Does this situation have long-term consequences for me?	1	2	3	4	5
28. Is this going to have a negative impact on me?	1	2	3	4	5

Survey of Coping Profiles Endorsed (27-item SCOPE) - Situation A

Please re-read situation A. The purpose of this questionnaire is to find out how people deal with stresses in their lives. The following are activities that you may have done in response to situation A. After each activity, please indicate the extent to which you would use this as a way of dealing with the problem or stress.

In response to situation A, would you:

*Never Seldom Sometimes Often Almost
always*

1. accept that there is nothing I could do to change my situation.	0	1	2	3	4
2. blame myself for my problems.	0	1	2	3	4
3. tell others that I was really upset.	0	1	2	3	4
4. ask others for help or advice.	0	1	2	3	4
5. spend a lot of time thinking about my problem.	0	1	2	3	4
6. take time for recreation or pleasure activities.	0	1	2	3	4
7. make plans to overcome my concerns or problem.	0	1	2	3	4
8. avoid thinking about my problem.	0	1	2	3	4
9. tell jokes about my situation.	0	1	2	3	4
10. think a lot about who was responsible for my problem (besides me).	0	1	2	3	4
11. worry about my problem a lot.	0	1	2	3	4
12. make humorous comments or stories about my situation.	0	1	2	3	4
13. wish the situation would just go away or be over with	0	1	2	3	4
14. think a lot about how I brought my problem on myself.	0	1	2	3	4
15. decide to wait and see how things turned out.	0	1	2	3	4
16. try to keep my mind off things that were upsetting me.	0	1	2	3	4
17. seek reassurance and emotional support from others.	0	1	2	3	4
18. think about how my problem was caused by other people.	0	1	2	3	4
19. cry, even if someone else was around.	0	1	2	3	4
20. look for how I could grow and learn through my situation.	0	1	2	3	4
21. tell myself that other people have problems like mine.	0	1	2	3	4

Participant Number: _____

8/23

22. do things to keep busy or active (eg., exercised, went out).	0	1	2	3	4
23. hold in my feelings.	0	1	2	3	4
24. daydream about how things may turn out.	0	1	2	3	4
25. try to act as if I wasn't feeling bad.	0	1	2	3	4
26. take steps to overcome the problem.	0	1	2	3	4
27. turn to God or my faith.	0	1	2	3	4

Rating of Effectiveness
0 "not effective" to 4 "totally effective"
(Circle One)

SCOPE item number used almost always	0-----1-----2-----3-----4
	0-----1-----2-----3-----4
	0-----1-----2-----3-----4

Participant Number: _____

9/23

Situation #B

It is the last month of the semester and you have not been doing well in a course that you know is going to be important for your degree. It is too late to drop the course and the final is weighted at 60%.

Stress Appraisal Measure (SAM) - Situation B

This questionnaire is concerned with your thoughts about various aspects of the situation identified previously. There are no right or wrong answers. Please respond according to how you view this situation right NOW. Please answer ALL questions. Answer each question by CIRCLING the appropriate number corresponding to the following scale.

	1	2	3	4	5
	Not at all	Slightly	Moderately	Considerably	Extremely
1. Is this a totally hopeless situation?	1	2	3	4	5
2. Does this situation create tension in me?	1	2	3	4	5
3. Is the outcome of this situation uncontrollable by anyone?	1	2	3	4	5
4. Is there someone or some agency I can turn to for help if I need it?	1	2	3	4	5
5. Does this situation make me feel anxious?	1	2	3	4	5
6. Does this situation have important consequences for me?	1	2	3	4	5
7. Is this going to have a positive impact in me?	1	2	3	4	5
8. How eager am I to tackle this problem?	1	2	3	4	5
9. How much will I be affected by the outcome of this situation?	1	2	3	4	5
10. To what extent can I become a stronger person because of this problem?	1	2	3	4	5
11. Will the outcome of this situation be negative?	1	2	3	4	5
12. Do I have the ability to do well in this situation?	1	2	3	4	5
13. Does this situation have serious implications for me?	1	2	3	4	5
14. Do I have what it takes to do well in this situation?	1	2	3	4	5
15. Is there help available to me for dealing with this problem?	1	2	3	4	5
16. Does this situation tax or exceed my coping resources?	1	2	3	4	5
17. Are there sufficient resources available to help me in dealing?	1	2	3	4	5
18. Is this beyond anyone's power to do anything about this situation?	1	2	3	4	5
19. To what extent am I excited thinking about the outcome of this situation?	1	2	3	4	5
20. How threatening is this situation?	1	2	3	4	5
21. Is the problem unresolvable by anyone?	1	2	3	4	5
22. Will I be able to overcome the problem?	1	2	3	4	5
23. Is there anyone who can help me manage the problem?	1	2	3	4	5
24. To what extent do I perceive this situation as stressful?	1	2	3	4	5
25. Do I have the skills necessary to achieve a successful outcome to this situation?	1	2	3	4	5
26. To what extent does this event require coping efforts on my part?	1	2	3	4	5
27. Does this situation have long-term consequences for me?	1	2	3	4	5
28. Is this going to have a negative impact on me?	1	2	3	4	5

Participant Number: _____

10/23

Survey of Coping Profiles Endorsed (27-item SCOPE) - Situation B

Please re-read situation B. The purpose of this questionnaire is to find out how people deal with stresses in their lives. The following are activities that you may have done in response to situation B. After each activity, please indicate the extent to which you would use this as a way of dealing with the problem or stress.

In response to situation B, would you:

*Never Seldom Sometimes Often Almost
always*

1. accept that there is nothing I could do to change my situation.	0	1	2	3	4
2. blame myself for my problems.	0	1	2	3	4
3. tell others that I was really upset.	0	1	2	3	4
4. ask others for help or advice.	0	1	2	3	4
5. spend a lot of time thinking about my problem.	0	1	2	3	4
6. take time for recreation or pleasure activities.	0	1	2	3	4
7. make plans to overcome my concerns or problem.	0	1	2	3	4
8. avoid thinking about my problem.	0	1	2	3	4
9. tell jokes about my situation.	0	1	2	3	4
10. think a lot about who was responsible for my problem (besides me).	0	1	2	3	4
11. worry about my problem a lot.	0	1	2	3	4
12. make humorous comments or stories about my situation.	0	1	2	3	4
13. wish the situation would just go away or be over with	0	1	2	3	4
14. think a lot about how I brought my problem on myself.	0	1	2	3	4
15. decide to wait and see how things turned out.	0	1	2	3	4
16. try to keep my mind off things that were upsetting me.	0	1	2	3	4
17. seek reassurance and emotional support from others.	0	1	2	3	4
18. think about how my problem was caused by other people.	0	1	2	3	4
19. cry, even if someone else was around.	0	1	2	3	4
20. look for how I could grow and learn through my situation.	0	1	2	3	4
21. tell myself that other people have problems like mine.	0	1	2	3	4
22. do things to keep busy or active (eg., exercised, went out).	0	1	2	3	4
23. hold in my feelings.	0	1	2	3	4
24. daydream about how things may turn out.	0	1	2	3	4
25. try to act as if I wasn't feeling bad.	0	1	2	3	4
26. take steps to overcome the problem.	0	1	2	3	4
27. turn to God or my faith.	0	1	2	3	4

Participant Number: _____

11/23

Rating of Effectiveness 0 "not effective" to 4 "totally effective" (Circle One)	
SCOPE item number used almost always	0-----1-----2-----3-----4
	0-----1-----2-----3-----4
	0-----1-----2-----3-----4

Participant Number: _____

12/23

Situation C

You go to pay at a restaurant with a credit card and the card is declined.

Stress Appraisal Measure (SAM) - Situation C

This questionnaire is concerned with your thoughts about various aspects of the situation identified previously. There are no right or wrong answers. Please respond according to how you view this situation right NOW. Please answer ALL questions. Answer each question by CIRCLING the appropriate number corresponding to the following scale.

	1	2	3	4	5
	Not at all	Slightly	Moderately	Considerably	Extremely
1. Is this a totally hopeless situation?	1	2	3	4	5
2. Does this situation create tension in me?	1	2	3	4	5
3. Is the outcome of this situation uncontrollable by anyone?	1	2	3	4	5
4. Is there someone or some agency I can turn to for help if I need it?	1	2	3	4	5
5. Does this situation make me feel anxious?	1	2	3	4	5
6. Does this situation have important consequences for me?	1	2	3	4	5
7. Is this going to have a positive impact in me?	1	2	3	4	5
8. How eager am I to tackle this problem?	1	2	3	4	5
9. How much will I be affected by the outcome of this situation?	1	2	3	4	5
10. To what extent can I become a stronger person because of this problem?	1	2	3	4	5
11. Will the outcome of this situation be negative?	1	2	3	4	5
12. Do I have the ability to do well in this situation?	1	2	3	4	5
13. Does this situation have serious implications for me?	1	2	3	4	5
14. Do I have what it takes to do well in this situation?	1	2	3	4	5
15. Is there help available to me for dealing with this problem?	1	2	3	4	5
16. Does this situation tax or exceed my coping resources?	1	2	3	4	5
17. Are there sufficient resources available to help me in dealing?	1	2	3	4	5
18. Is this beyond anyone's power to do anything about this situation?	1	2	3	4	5
19. To what extent am I excited thinking about the outcome of this situation?	1	2	3	4	5
20. How threatening is this situation?	1	2	3	4	5
21. Is the problem unresolvable by anyone?	1	2	3	4	5
22. Will I be able to overcome the problem?	1	2	3	4	5
23. Is there anyone who can help me manage the problem?	1	2	3	4	5
24. To what extent do I perceive this situation as stressful?	1	2	3	4	5
25. Do I have the skills necessary to achieve a successful outcome to this situation?	1	2	3	4	5
26. To what extent does this event require coping efforts on my part?	1	2	3	4	5
27. Does this situation have long-term consequences for me?	1	2	3	4	5
28. Is this going to have a negative impact on me?	1	2	3	4	5

Participant Number: _____

13/23

Survey of Coping Profiles Endorsed (27-item SCOPE) - Situation C

Please re-read situation C. The purpose of this questionnaire is to find out how people deal with stresses in their lives. The following are activities that you may have done in response to situation C. After each activity, please indicate the extent to which you would use this as a way of dealing with the problem or stress.

<i>In response to <u>situation C</u>, would you:</i>	<i>Never</i>	<i>Seldom</i>	<i>Sometimes</i>	<i>Often</i>	<i>Almost always</i>
1. accept that there is nothing I could do to change my situation.	0	1	2	3	4
2. blame myself for my problems.	0	1	2	3	4
3. tell others that I was really upset.	0	1	2	3	4
4. ask others for help or advice.	0	1	2	3	4
5. spend a lot of time thinking about my problem.	0	1	2	3	4
6. take time for recreation or pleasure activities.	0	1	2	3	4
7. make plans to overcome my concerns or problem.	0	1	2	3	4
8. avoid thinking about my problem.	0	1	2	3	4
9. tell jokes about my situation.	0	1	2	3	4
10. think a lot about who was responsible for my problem (besides me).	0	1	2	3	4
11. worry about my problem a lot.	0	1	2	3	4
12. make humorous comments or stories about my situation.	0	1	2	3	4
13. wish the situation would just go away or be over with	0	1	2	3	4
14. think a lot about how I brought my problem on myself.	0	1	2	3	4
15. decide to wait and see how things turned out.	0	1	2	3	4
16. try to keep my mind off things that were upsetting me.	0	1	2	3	4
17. seek reassurance and emotional support from others.	0	1	2	3	4
18. think about how my problem was caused by other people.	0	1	2	3	4
19. cry, even if someone else was around.	0	1	2	3	4
20. look for how I could grow and learn through my situation.	0	1	2	3	4
21. tell myself that other people have problems like mine.	0	1	2	3	4
22. do things to keep busy or active (eg., exercised, went out).	0	1	2	3	4
23. hold in my feelings.	0	1	2	3	4
24. daydream about how things may turn out.	0	1	2	3	4
25. try to act as if I wasn't feeling bad.	0	1	2	3	4
26. take steps to overcome the problem.	0	1	2	3	4
27. turn to God or my faith.	0	1	2	3	4

Participant Number: _____

14/23

Rating of Effectiveness	
0 "not effective" to 4 "totally effective"	
(Circle One)	
SCOPE item number used almost always	0-----1-----2-----3-----4
	0-----1-----2-----3-----4
	0-----1-----2-----3-----4

Participant Number: _____

Situation D

On a holiday a few weeks ago you had unprotected sex with a stranger. Lately you have been experiencing flu-like symptoms and you tell your doctor about what happened. Your doctor says you probably just caught a bug on the plane home but takes some blood to check for possible HIV infection. However, the test results won't come back until next week.

Stress Appraisal Measure (SAM) - Situation D

This questionnaire is concerned with your thoughts about various aspects of the situation identified previously. There are no right or wrong answers. Please respond according to how you view this situation right NOW. Please answer ALL questions. Answer each question by CIRCLING the appropriate number corresponding to the following scale.

	1	2	3	4	5
	Not at all	Slightly	Moderately	Considerably	Extremely
1. Is this a totally hopeless situation?	1	2	3	4	5
2. Does this situation create tension in me?	1	2	3	4	5
3. Is the outcome of this situation uncontrollable by anyone?	1	2	3	4	5
4. Is there someone or some agency I can turn to for help if I need it?	1	2	3	4	5
5. Does this situation make me feel anxious?	1	2	3	4	5
6. Does this situation have important consequences for me?	1	2	3	4	5
7. Is this going to have a positive impact in me?	1	2	3	4	5
8. How eager am I to tackle this problem?	1	2	3	4	5
9. How much will I be affected by the outcome of this situation?	1	2	3	4	5
10. To what extent can I become a stronger person because of this problem?	1	2	3	4	5
11. Will the outcome of this situation be negative?	1	2	3	4	5
12. Do I have the ability to do well in this situation?	1	2	3	4	5
13. Does this situation have serious implications for me?	1	2	3	4	5
14. Do I have what it takes to do well in this situation?	1	2	3	4	5
15. Is there help available to me for dealing with this problem?	1	2	3	4	5
16. Does this situation tax or exceed my coping resources?	1	2	3	4	5
17. Are there sufficient resources available to help me in dealing?	1	2	3	4	5
18. Is this beyond anyone's power to do anything about this situation?	1	2	3	4	5
19. To what extent am I excited thinking about the outcome of this situation?	1	2	3	4	5
20. How threatening is this situation?	1	2	3	4	5
21. Is the problem unresolvable by anyone?	1	2	3	4	5
22. Will I be able to overcome the problem?	1	2	3	4	5
23. Is there anyone who can help me manage the problem?	1	2	3	4	5
24. To what extent do I perceive this situation as stressful?	1	2	3	4	5
25. Do I have the skills necessary to achieve a successful outcome to this situation?	1	2	3	4	5
26. To what extent does this event require coping efforts on my part?	1	2	3	4	5
27. Does this situation have long-term consequences for me?	1	2	3	4	5
28. Is this going to have a negative impact on me?	1	2	3	4	5

Participant Number: _____

16/23

Survey of Coping Profiles Endorsed (27-item SCOPE) - Situation D

Please re-read situation D. The purpose of this questionnaire is to find out how people deal with stresses in their lives. The following are activities that you may have done in response to situation D. After each activity, please indicate the extent to which you would use this as a way of dealing with the problem or stress.

<i>In response to <u>situation D</u>, would you:</i>	<i>Never</i>	<i>Seldom</i>	<i>Sometimes</i>	<i>Often</i>	<i>Almost always</i>
1. accept that there is nothing I could do to change my situation.	0	1	2	3	4
2. blame myself for my problems.	0	1	2	3	4
3. tell others that I was really upset.	0	1	2	3	4
4. ask others for help or advice.	0	1	2	3	4
5. spend a lot of time thinking about my problem.	0	1	2	3	4
6. take time for recreation or pleasure activities.	0	1	2	3	4
7. make plans to overcome my concerns or problem.	0	1	2	3	4
8. avoid thinking about my problem.	0	1	2	3	4
9. tell jokes about my situation.	0	1	2	3	4
10. think a lot about who was responsible for my problem (besides me).	0	1	2	3	4
11. worry about my problem a lot.	0	1	2	3	4
12. make humorous comments or stories about my situation.	0	1	2	3	4
13. wish the situation would just go away or be over with	0	1	2	3	4
14. think a lot about how I brought my problem on myself.	0	1	2	3	4
15. decide to wait and see how things turned out.	0	1	2	3	4
16. try to keep my mind off things that were upsetting me.	0	1	2	3	4
17. seek reassurance and emotional support from others.	0	1	2	3	4
18. think about how my problem was caused by other people.	0	1	2	3	4
19. cry, even if someone else was around.	0	1	2	3	4
20. look for how I could grow and learn through my situation.	0	1	2	3	4
21. tell myself that other people have problems like mine.	0	1	2	3	4
22. do things to keep busy or active (eg., exercised, went out).	0	1	2	3	4
23. hold in my feelings.	0	1	2	3	4
24. daydream about how things may turn out.	0	1	2	3	4
25. try to act as if I wasn't feeling bad.	0	1	2	3	4
26. take steps to overcome the problem.	0	1	2	3	4
27. turn to God or my faith.	0	1	2	3	4

Participant Number: _____

17/23

Rating of Effectiveness 0 "not effective" to 4 "totally effective" (Circle One)	
SCOPE item number used almost always	
	0-----1-----2-----3-----4
	0-----1-----2-----3-----4
	0-----1-----2-----3-----4

Item 6

Please provide a saliva sample using one of the cotton rolls and tubes provided.

Participant Number: _____

18/23

Item 7

Childhood Maltreatment Questionnaire (SF)

Children and adolescents growing up can experience a wide range of behaviours on the part of their parents, or other people who serve as parental figures for them. Please think back to your childhood and adolescence and indicate how often you experienced each of these behaviours by at least one of your "parental figures" before you were 18 years old.

Note that parental figures can include parents, step-parents, foster-parents, or other adults who routinely were in charge of you as a child or adolescent. An older sibling or other relative also may be considered a parental figure when this person routinely supervised or cared for you.

For each behaviour, please circle the appropriate number that corresponds to the following scale:

	1	2	3	4	5
	Never	Rarely	Sometimes	Often	Very Often
How often before you were 18 did one or more of your parental figures:					
1. Act emotionally "cold" toward you.	1	2	3	4	5
2. Fail to praise you when you deserved it.	1	2	3	4	5
3. Fail to listen to you or to comfort you when they knew you were sad and upset	1	2	3	4	5
4. Seem to be emotionally detached or unexpressive with you.	1	2	3	4	5
5. Appear to be disinterested in you and your life.	1	2	3	4	5
6. Ignore you.	1	2	3	4	5
7. Fail to take you to the doctor or give you medicine when you were ill and medical attention seemed to have been needed.	1	2	3	4	5
8. Leave you alone or unattended for periods of time when, looking back now, you believe it was unsafe or inappropriate for them to have done so.	1	2	3	4	5
9. Fail to provide adequate food or clothing for you even though they had the means to do so.	1	2	3	4	5
10. Fail to care for your injuries when you were physically hurt.	1	2	3	4	5
11. Have many unpredictable moods or frequently changing moods that affected their ability to provide reliable care for you.	1	2	3	4	5
12. Leave you with certain people (e.g., strangers, other children, casual acquaintances) for periods of time when, looking back now, you believe it was unsafe or inappropriate for them to have done so.	1	2	3	4	5
13. Speak to you in a way that frightened you.	1	2	3	4	5
14. Act in a way that implied they did not like or value you.	1	2	3	4	5
15. Totally disregard your input into decisions that affected you.	1	2	3	4	5
16. Put you down or treat you in a degrading manner.	1	2	3	4	5
17. Touch or handle you in a rough way that frightened you.	1	2	3	4	5
18. Make you cater to their desires or whims with little concern for your own comfort or welfare.	1	2	3	4	5
19. Spank you hard enough to cost you bruising, swelling or bleeding	1	2	3	4	5
20. Hit or punch you with a closed fist.	1	2	3	4	5
21. Kick you with their foot or strike you hard with a knee or elbow.	1	2	3	4	5
22. Hit you with an object such as belt, cord, kitchen utensil, board or stick.	1	2	3	4	5
23. Twist, yank or bend your leg, arm or finger in a painful manner.	1	2	3	4	5
24. Push, throw or knock you down or into an object such as a wall or a piece of furniture.	1	2	3	4	5
25. Make you show them a sexual part of your body (i.e., genitals, breasts, or buttocks).	1	2	3	4	5

Participant Number: _____

19/23

	1	2	3	4	5
	Never	Rarely	Sometimes	Often	Very Often
26. Get you to touch their genitals, breasts or anus with your mouth or tongue.	1	2	3	4	5
27. Rub or fondle a sexual part of your body (i.e., genitals, breasts, or buttocks).				1 2 3 4 5	
28. Engage in vaginal or anal intercourse with you.				1 2 3 4 5	
29. Get you to do something sexual with them				1 2 3 4 5	
30. Get you to touch them in a sexual way or fondle a sexual part of their or another person's body (i.e., genitals, breasts, or buttocks).				1 2 3 4 5	

31. Who were you thinking of when you answered the 30 questions above? Please list as many apply (e.g., mother stepfather, older sister etc.).

Participant Number: _____

20/23

Item 8

Consumption and Generation of Social Support (CGSS)

In the past few months, how often did you do these activities for other people and with other people? Please read each statement carefully and circle or underline the answer that best describes your experience.

1. You gave some information to help others understand a situation
 Not at all Once or twice About once a week Several times a week About every day
2. You checked back with people you have helped to see if they have followed your advice
 Not at all Once or twice About once a week Several times a week About every day
3. You gave information to others on how to do something
 Not at all Once or twice About once a week Several times a week About every day
4. You gave feedback on how others were doing without saying it was good or bad
 Not at all Once or twice About once a week Several times a week About every day
5. You told others that they are O.K. just the way they are
 Not at all Once or twice About once a week Several times a week About every day
6. You have expressed interest and concern in the well-being of others
 Not at all Once or twice About once a week Several times a week About every day
7. You have listened to others talk about their private feelings
 Not at all Once or twice About once a week Several times a week About every day
8. You have joked and kidded to try to cheer others up
 Not at all Once or twice About once a week Several times a week About every day
9. You have provided others with transportation
 Not at all Once or twice About once a week Several times a week About every day
10. You have pitched in to help others do something that needed to be done
 Not at all Once or twice About once a week Several times a week About every day
11. You have provided others with a place where they could get away for a while
 Not at all Once or twice About once a week Several times a week About every day
12. You have loaned or given others something (a physical object other than money) that they needed
 Not at all Once or twice About once a week Several times a week About every day

Participant Number: _____

21/23

In the past few months, how often have you been the recipient of these activities from other people? Please read each statement carefully and underline or circle the answer that best describes your experience.

1. You received some information from others which helped you understand a situation
 Not at all Once or twice About once a week Several times a week About every day
2. You were checked back from people who had helped you to see if you had followed their advice
 Not at all Once or twice About once a week Several times a week About every day
3. You received information from others on how to do something
 Not at all Once or twice About once a week Several times a week About every day
4. You received feedback from others on how you were doing without saying it was good or bad
 Not at all Once or twice About once a week Several times a week About every day
5. You were told from others that you are O.K. just the way you are
 Not at all Once or twice About once a week Several times a week About every day
6. You received interest and concern from others in your well-being
 Not at all Once or twice About once a week Several times a week About every day
7. You had someone who listened to you talking about your private feelings
 Not at all Once or twice About once a week Several times a week About every day
8. You had someone who joked and kidded to try cheering you up
 Not at all Once or twice About once a week Several times a week About every day
9. You were provided with transportation from others
 Not at all Once or twice About once a week Several times a week About every day
10. You were helped by others to do something that needed to be done
 Not at all Once or twice About once a week Several times a week About every day
11. You were provided by others with a place where you could get away for a while
 Not at all Once or twice About once a week Several times a week About every day
12. You were loaned or given something by others (a physical object other than money) that you needed
 Not at all Once or twice About once a week Several times a week About every day

Participant Number: _____

22/23

Item 9

20-Item Cognitive Flexibility Inventory (CFI)

Please use the scale below to indicate the extent to which you agree or disagree with the following statements.

Strongly Disagree Disagree Somewhat Disagree Neutral Somewhat Agree Agree Strongly Agree

	1	2	3	4	5	6	7
1. I am good at "sizing up" situations.	1	2	3	4	5	6	7
2. I have a hard time making decisions when faced with difficult situations.	1	2	3	4	5	6	7
3. I consider multiple options before making a decision	1	2	3	4	5	6	7
4. When I encounter difficult situations, I feel like I am losing control.	1	2	3	4	5	6	7
5. I like to look at difficult situations from many different angles.	1	2	3	4	5	6	7
6. I seek additional information not immediately available before attributing causes to behaviour.	1	2	3	4	5	6	7
7. When encountering difficult situations, I become so stressed that I can not think of a way to resolve the situation.	1	2	3	4	5	6	7
8. I try to think about things from another person's point of view.	1	2	3	4	5	6	7
9. I find it troublesome that there are so many different ways to deal with difficult situations.	1	2	3	4	5	6	7
10. I am good at putting myself in others' shoes.	1	2	3	4	5	6	7
11. When I encounter difficult situations, I just don't know what to do.	1	2	3	4	5	6	7
12. It is important to look at difficult situations from many angles.	1	2	3	4	5	6	7
13. When in difficult situations, I consider multiple options before deciding how to behave.	1	2	3	4	5	6	7
14. I often look at a situation from different view-points.	1	2	3	4	5	6	7
15. I am capable of overcoming the difficulties in life that I face.	1	2	3	4	5	6	7
16. I consider all the available facts and information when attributing causes to behaviour.	1	2	3	4	5	6	7
17. I feel I have no power to change things in difficult situations.	1	2	3	4	5	6	7
18. When I encounter difficult situations, I stop and try to think of several ways to resolve it.	1	2	3	4	5	6	7
19. I can think of more than one way to resolve a difficult situation I'm confronted with.	1	2	3	4	5	6	7
20. I consider multiple options before responding to difficult situations.	1	2	3	4	5	6	7

Participant Number: _____

23/23

Item 10

Beck Depression Inventory

On this questionnaire are groups of statements. Please read the entire group of statements of each category, then pick out ONE statement in that group which best describes the way you feel at the moment. Circle the shaded number beside the statement you have chosen.

1	0	I do not feel sad
	1	I feel sad or blue
	2a	I am blue or sad all of the time and I can't snap out of it
	2b	I am so sad or unhappy that it is very painful
	3	I am so sad or unhappy that I can't stand it

2	0	I am not particularly pessimistic or discouraged about the future
	1	I feel discouraged about the future
	2a	I feel I have nothing to look forward to
	2b	I feel I won't every get over my troubles
	3	I feel that the future is hopeless and things cannot improve

3	0	I do not feel like a failure
	1	I feel I have failed more than the average person
	2a	I feel I have accomplished very little that is worthwhile or that means anything
	2b	As I look back on my life, all I can see is a lot of failures
	3	I feel I am a complete failure as a person

4	0	I am not particularly dissatisfied
	1a	I feel bored most of the time
	1b	I don't enjoy things the way I used to
	2	I don't get satisfaction out of anything anymore
	3	I am dissatisfied with everything

5	0	I don't feel particularly guilty
	1	I feel bad or unworthy a good part of the time
	2a	I feel quite guilty
	2b	I feel bad or unworthy practically of the time now
	3	I feel as though I am very bad or worthless

6	0	I don't feel I am being punished
	1	I have a feeling that something bad may happen to me
	2	I feel I am being punished or will be punished
	3a	I feel I deserve to be punished
	3b	I want to be punished

7	0	I don't feel disappointed in myself
	1a	I am disappointed in myself
	1b	I don't like myself
	2	I am disgusted with myself
	3	I hate myself

8	0	I do not feel I am any worse than anybody else
	1	I am very critical of myself for my weaknesses or mistakes
	2a	I blame myself for everything that goes wrong
	2b	I feel I have many bad faults

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9	0	I don't have thoughts of harming myself
	1	I have thoughts of harming myself but I would not carry them out
	2a	<i>I feel I would be better off dead</i>
	2b	I have definite plans about committing suicide
	2c	I feel my family would be better off if I were dead
	3	I would kill myself if I could
10	0	I don't cry anymore than usual
	1	I cry more now than I used to
	2	I cry all the time now. I can't stop it
	3	I used to be able to cry but now I can't cry at all even though I want to
11	0	I am no more irritated now than I ever am
	1	I get annoyed or irritated more easily than I used to
	2	I get irritated all the time
	3	I don't get irritated at all the things that used to irritate me.
12	0	I have not lost interest in other people
	1	I am less interested in other people than I used to be
	2	<i>I have lost most of my interest in other people and I have little feeling for them</i>
	3	I have lost all my interest in other people and don't care about them at all
13	0	I make decisions about as well as I ever did
	1	I am less sure of myself now and try to put off making decisions
	2	I can't make decisions anymore without help
	3	I can't make decisions at all anymore
14	0	I don't feel I look any worse than I used to
	1	I am worried that I am looking old or unattractive
	2	I feel that there are permanent changes in my appearance and they make me look unattractive
	3	I feel that I am ugly or repulsive looking
15	0	I can work about as well as before
	1a	It takes extra effort to get started at doing something
	1b	I don't work as well as I used to
	2	I have to push myself very hard to do anything
	3	I can't do any work at all
16	0	I can sleep as well as usual
	1	I wake up more tired in the morning than I used to
	2	I wake up 1-2 hours earlier than usual and find it hard to get back to sleep
	3	I wake up early every day and can't get more than 5 hours sleep
17	0	I don't get any more tired than usual
	1	I get tired more easily than I used to
	2	I get tired from doing anything
	3	I get too tired to do anything

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- 18 0 My appetite is no worse than usual
 1 My appetite is not as good as it used to be
 2 My appetite is much worse now
 3 I have no appetite at all any more

- 19 0 I haven't lost much weight, if any, lately
 1 I have lost more than 5 pounds
 2 I have lost more than 10 pounds
 3 I have lost more than 15 pounds

- 20 0 I am no more concerned about my health than usual
 1 I am concerned about aches and pains or upset stomach or constipation or other unpleasant feelings in my body
 2 I am so concerned with how I feel or what I feel that it's hard to think of much else
 3 I am completely absorbed in what I feel

- 21 0 I have not noticed any recent change in my interest in sex
 1 I am less interested in sex than I used to be
 2 I am much less interested in sex now
 3 I have lost interest in sex completely

Thank you for participating in our study!
 Please wait for the researcher to collect your samples.

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