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Increased parasympathetic activity and ability to generate positive emotion: The influence of the BDNF Val66Met polymorphism on emotion flexibility

Karin Maria Nylocks[1] · T. Lee Gilman[2] · Maeson S. Latsko[1] · Aaron M. Jasnow[1] · Karin G. Coifman[1]

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Abstract
Cross-species behavioral research suggests that a single nucleotide polymorphism (SNP) in the brain-derived neurotrophic factor (BDNF) gene (rs6265, Val66Met), influences behavioral inflexibility. This SNP has not yet been linked to variability in emotion-related behaviors, despite broader evidence suggesting an association may be present. This investigation explored the role of the BDNF Val66Met polymorphism in emotion response behaviors measured during a lab-based emotional provocation. Specifically, the influence of BDNF Val66Met in emotion flexibility was explored in a sample of healthy adults ($N = 120$), emotion responses were recorded during the emotional provocation on multiple dimensions, in response to emotionally-evocative videos of negative then positive valence. These results suggest that Met carriers exhibit decreased parasympathetic responding, and reduced ability to generate positive emotion, relative to Val homozygotes. These findings are the first to suggest an association between the Met allele and a pattern of responding indicative of emotion inflexibility that might afford greater risk for psychopathology.

Keywords Brain-derived neurotrophic factor · BDNF Val66Met · Parasympathetic activity · Emotion flexibility · Positive emotions

Introduction

BDNF and plasticity

Flexible responding to environmental changes, a function of synaptic plasticity, is a highly adaptive process for which brain-derived neurotrophic factor (BDNF) is essential. Synaptic plasticity specifically refers to the strengthening and weakening of neural synapses in an experience-driven way, leading to changes in neural circuits and sometimes to changes in behavior (Holtmaat and Svoboda 2009). For example, BDNF is central to learning and the ability to override previously learned information with newly acquired information (e.g. fear extinction) (Chhatwal et al. 2006; Johnson and Casey 2015; Rattiner et al. 2004). Importantly, decreased synaptic plasticity has been identified as a risk factor for development of emotion-linked disorders, such as depression and anxiety (Colzato et al. 2011; Duman et al. 2016).

A single nucleotide polymorphism (SNP) (Val66Met, rs6265) in the pro-region of the BDNF gene has been studied extensively in both human and rodent models due to its influence on levels of available BDNF protein (Notaras et al. 2015). The Val66Met polymorphism leads to a substitution of methionine for valine at position 66 of the prodomain region of the precursor proBDNF protein (leading to the following potential genotypes in humans: ValVal, ValMet, MetMet). An individual who carries two Val alleles (genotype ValVal) is often referred to as Val homozygote, and an individual who carries at least one Met allele (ValMet or MetMet) is often referred to as a Met carrier. The substitution of methionine for valine reduces available BDNF (Liebl et al. 1997) and impairs BDNF secretion in primary hippocampal neurons (Anastasia et al. 2013; Egan et al. 2003). There has been extensive research aimed at clarifying the complex relationships between variation in the

✉ Karin Maria Nylocks
knylocks@kent.edu

[1] Department of Psychological Sciences, Kent State University, 276 Kent Hall, Kent, OH 44242-0001, USA

[2] Department of Cellular and Integrative Physiology, University of Texas Health Science Center at San Antonio, San Antonio, TX, USA

Val66Met polymorphism and emotion-related psychopathology or symptoms (e.g. depression and anxiety). However, the current literature is mixed (Notaras et al. 2015), likely due to some methodological limitations and lack of objective measurement of emotion responses. Notably, there are currently no studies directly testing how Val66Met might influence specific emotion-related, clinically relevant behaviors (including emotion flexibility).

Emotions have evolved across species for the purpose of survival and adaptation to the environment (Ekman 1992; LeDoux 1995). Specific emotions serve discrete functions, and are adaptive when flexibly limited or matched to the appropriate context, but can be maladaptive when they occur outside of the evolutionarily appropriate environment, or in conflict with individual needs. For example, fear is adaptive in the presence of threat (Öhman and Mineka 2001). However, outside the context of threat, increased fear reactivity or generalized fear is typically maladaptive and a hallmark of anxiety disorders (Graham and Milad 2011). Emotion flexibility can be defined as the ability to respond to shifting emotional contexts, including environmental contexts as well as internally elicited emotion (c.f. Ochsner et al. 2009), with appropriate flexibility of emotional responses, encompassing automatic, implicit as well as deliberate processing. This includes the ability to generate or up-regulate emotions in response to contextual factors as well as the ability to shift or down-regulate emotions as contextual parameters or features change (Aldao et al. 2015; Bonanno and Burton 2013; Coifman and Almahmoud 2016; Hollenstein 2015; Kashdan and Rottenberg 2010; Waugh et al. 2011). Emotion flexibility likely depends upon a range of resources and systems including executive cognitive resources and autonomic nervous system activity which may contribute to an individuals' ability to notice contextual changes, and then respond to such changes in an efficient manner via one or several regulatory strategies (for a more comprehensive review see, Stange et al. 2017). For example, adults with decreased autonomic flexibility (i.e. decreased parasympathetic activity) have been hypothesized to show a diminished capacity for emotion flexibility (Porges 1995; Thayer et al. 2009). Emotion inflexibility broadly serves as a risk factor for psychopathology, such that individuals with decreased capacity to both generate and modulate emotion responses, might be more likely to develop emotion linked psychological illness (Coifman and Bonanno 2010; Coifman and Almahmoud 2016; Kashdan and Rottenberg 2010; Rottenberg et al. 2005).

BDNF reduction and emotion-linked behaviors across species

Across species, associations have emerged between reduced available BDNF and emotion-related behaviors that suggest decreased flexibility, and would suggest risk for psychological illness in humans (da Silveira da Luz et al. 2013; Soliman et al. 2010). Much of the current understanding about the Val66Met polymorphism in humans has been derived through candidate gene studies, a scientific approach that has lately received criticism due to instances of insufficient replication (Koenen et al. 2015; Tabor et al. 2001). However, evidence from this research suggests consistent relationships between the Val66Met polymorphism and psychiatric risk. For example, research conducted over the past decade has found that carriers of the Met allele at the BDNF Val66Met polymorphism (leading to reduced BDNF) generally report more symptoms of emotion-linked psychological disorders (e.g. depression) (Beevers et al. 2009; Lotrich et al. 2013). However, evidence of a significant association between the Met allele and psychiatric symptoms has also been debated (Notaras et al. 2015; Chen et al. 2008; Lopez-Leon et al. 2008; Verhagen et al. 2010). These mixed findings might stem from the emphasis in most candidate gene studies on measuring distal outcomes (e.g. retrospective self-report of symptoms), rather than specific and objective behavioral response patterns, more likely to be under influence of genetic variation (Insel and Cuthbert 2009). Indeed, despite the recent criticism of candidate gene studies, translational research suggests largely consistent findings across species (Caspi et al. 2010). For example, research has shown that BDNF-deficient mice exhibit greater anxiety-like behaviors (e.g. less exploration of novel environments in open-field and elevated plus maze paradigms) (Chen et al. 2006; Chourbaji et al. 2008) and more helplessness-like behaviors (e.g. less mobility in a forced swim test) (Bath et al. 2012). In addition, human Met carriers are more likely than Val homozygotes to generalize cued fear to novel contexts and show weaker fear extinction in fear conditioning paradigms, consistent with emotional inflexibility (Asthana et al. 2016; Mühlberger et al. 2014; Soliman et al. 2010), and a hallmark of anxiety disorders (e.g. panic disorder) (Lissek et al. 2010). Importantly, a translational study by Soliman et al. (2010) replicated these human findings and presented a parallel link between impaired fear extinction (but not fear acquisition) and the Met allele in a rodent model of the BDNF Val66Met (knock-in mice that have been genetically modified to express the human Val66Met polymorphism). Such cross-species evidence suggests that reduced BDNF might decrease the ability to override previously learned associations, resulting in inflexible and potentially maladaptive behavioral responses.

Although ample cross-species research has identified reduced BDNF as a risk factor for psychopathology, the Met allele might also afford some benefits. For example, human Met carriers have shown decreased hypothalamic–pituitary–adrenal axis (HPA-axis) response in a laboratory stress test (Alexander et al. 2010) and fewer

symptoms of anxiety in response to early life stress (Gatt et al. 2009). However, evidence of potential benefits afforded by the Met allele is complex and nuanced. Indeed, following stress, mice with the Met allele show elevated stress hormone levels (i.e. increased HPA axis activity), increased depressive-like and anxiety-like behaviors, and decreased BDNF mRNA levels in the prefrontal cortex, as compared to wild-type mice (Yu et al. 2012). Moreover, research in mice has found that Met carriers with a history of chronic stress might show increased potentiation of the fear circuitry, as compared to Val homozygotes (Notaras et al. 2016).

Negative and positive emotion inflexibility as hallmarks of psychopathology

Inability to flexibly shift negative emotional responses is broadly associated with poor psychological and social functioning and is present in both depression and anxiety (c.f., Gotlib and Joorman 2010; Mathews and MacLeod 2005). For example, depressed adults show a diminished ability to recall positive memories, for the purpose of reducing the intensity of sadness, a strategy which often reduces sadness in healthy controls (Joorman et al. 2007). Moreover, toddlers (two years of age) who demonstrate a contextually-insensitive fear behavior (e.g., freezing responses in low threat environments) are more likely to develop symptoms of anxiety by age 5 years (Buss 2011; Buss et al. 2004). Importantly, however, low *positive* emotion responsivity to positive emotion contexts is also key and a hallmark of psychopathology (Bylsma et al. 2008; Kashdan and Steger 2006). Indeed, increasingly it is evident that a central feature of depression and anxiety disorders is a decreased capacity to generate positive emotion (e.g. joy, contentment) in situations where such emotional responses are appropriate (e.g., Kendall et al. 2015; Kovacs et al. 2015). Notably, positive emotion responsivity may be a hallmark feature of emotion flexibility, as positive emotions are thought to broaden coping responses and cognitive resources, facilitating greater adaptation and greater psychological health (Fredrickson et al. 2003; Tugade and Fredrickson 2007). In fact, positive emotion expression (smiling) has been found to help down-regulate negative emotion while discussing negative personal experiences (e.g. adjustment to college) (Papa and Bonanno 2008) and to down-regulate cardiovascular arousal (Fredrickson and Levenson 1998). In addition, an association has emerged between greater capacity to generate positive emotion in daily life and increased autonomic flexibility, suggesting a link between positive emotion generation and increased capacity for the parasympathetic nervous system to modulate physiological arousal in response to contextual demands (Porges 1995; Kok and Fredrickson 2010).

Methodological approaches within the emotion flexibility literature

Given the complex nature of emotion flexibility, multiple approaches to measuring and quantifying this construct have emerged within the emotion literature. First, emotion flexibility can be operationalized as occurring on different time-scales including momentary fluctuations in affect as well as contextual shifts in affect (Hollenstein et al. 2013). An individual who shows more moment-to-moment fluctuations in positive and negative affect, within one emotion eliciting event (i.e. dynamic flexibility) could be considered more flexible. This model of flexibility has inspired excellent research on real-time changes in emotion, in particular, utilizing parent–child interactions (Sravish et al. 2013; Hollenstein and Lewis 2006). Additionally, emotion flexibility has been measured as responsiveness to regulatory directions in lab paradigms or naturally occurring variability in reports of regulation during experience sampling (e.g., Sheppes et al. 2014). For example, Bonanno et al. developed a within-subject paradigm in which individuals are directed to either visibly suppress or express emotional responses to evocative pictures. A higher combined score capturing both behaviors (scored via coded facial emotion behavior) is conceptualized as emotion flexibility (2004). This paradigm has been influential, demonstrating the association between emotion flexibility and psychological health and resilience (Westphal et al. 2010). The current study follows conventions established in research where emotion flexibility is indexed as emotion output that is responsive to a series of shifting, emotionally-evocative contexts. The primary benefit of this method is inclusion of both automatic and implicit regulatory responses, as participants are given no specific instructions other than to engage with the material as it is presented. For example, in the current investigation as in prior research, film clips (validated to elicit specific emotions) are employed in a specific sequence. Emotion responses are measured on multiple dimensions by film context (e.g. Rottenberg et al. 2002, 2005) and individual differences in emotion generation (or up-regulation) that are responsive to the context (i.e., negative emotions generated in response to a disturbing film) as well as shifts (or down-regulation) that occurs across contexts (i.e., reduction in negative emotions when an amusing film begins) constitute emotion flexibility (c.f., Coifman and Almahmoud 2016).

Parasympathetic activity as a transdiagnostic indicator of health and flexibility

Finally, increasing evidence suggests a key role of the autonomic nervous system in emotion flexibility. Specifically, parasympathetic activity (often referred to as *vagal tone*: influence of the vagus nerve on the heart) has been theorized

to function as a mediator for individual differences in emotion responsivity (Porges et al. 1994). Vagal tone is often indexed by respiratory sinus arrhythmia (RSA: Porges 2007), reflecting the respiratory rhythm in heart rate (greater RSA produces slower heart rate) (Porges 2007). Notably, vagal tone might be directly linked to emotional facial expressions given the proximity of brain stem structures controlling facial expressions and those controlling autonomic responses (Porges et al. 1994; Stifter et al. 1989). Indeed, adults with decreased RSA (low vagal tone) have been hypothesized to show a diminished capacity for emotion flexibility (Porges et al. 1994; Thayer et al. 2009), and decreased RSA has been associated with emotion-linked disorders (e.g. panic disorder, posttraumatic stress disorder, depression) (Friedman 2007). Accordingly, greater RSA serves as a broad indicator of health and regulatory resources (Porges 2009; Thayer et al. 2012). Lastly, individual differences in parasympathetic activation might be partly heritable (Singh et al. 1999). Indeed, Met carriers at the BDNF Val66Met polymorphism have been found to show decreased parasympathetic activity at rest, as compared to Val homozygotes (Yang et al. 2010), suggesting a link between the Met allele and a less flexible or responsive autonomic nervous system.

Current investigation

To examine emotion flexibility, we administered a lab-based emotion provocation that consisted of evaluating spontaneous emotional responses to two emotionally-evocative film clips; one of positive, and one of negative, valence. This type of design has been consistently employed in research examining the context-sensitivity of naturally occurring emotion (e.g., Rottenberg et al. 2005) and is sensitive to brain-related genetic polymorphisms (Gilman et al. 2015; Latsko et al. 2016). Flexibility was operationalized as the ability to generate emotion in response to the eliciting context, and the ability to shift emotion as contextual demands changed, according to contemporary models of flexibility (Coifman and Almahmoud 2016). Emotion responses were assessed across multiple dimensions, including self-reported emotion experience, coded facial behavior, and autonomic activity. Specifically, RSA (Porges 2007) was employed as an index of autonomic flexibility and skin conductance was used as an indicator of emotional engagement and sympathetic activity (Dawson et al. 2007). Increased skin conductance is broadly considered an index of emotional activation and has been associated with both negative and positive emotions that are characterized by high arousal (e.g. fear; amusement; c.f. Kreibig 2010). For the purpose of the current study, where high arousal stimuli were utilized (see below for more detail), it was particularly important to measure the up-regulation of emotion. Indeed, since emotion up-regulation is a part of emotion flexibility, skin conductance response (SCR) was included as one dimension of emotional response.

Consistent with this theoretical framework and methods, as well as extensive cross-species literature, we identified two dimensions of emotion flexibility that could be tested in relation to variation in the BDNF Val66Met polymorphism. First, we considered the ability for individuals to respond to the primary emotion eliciting context, in this case a negative emotion eliciting film, with up-generation of negative emotion. Next we considered the ability for individuals to shift emotion responses, down-regulating negative emotions and up-regulating positive emotions in response to the film that followed, a positive-emotion eliciting film. Both indices are considered core components of emotion flexibility (c.f., Coifman and Almahmoud 2016). Hence, we hypothesized that Val homozygotes would generate greater negative emotion responses to negative emotion contexts (or greater negative emotion reactivity), as compared to individuals with at least one copy of the Met allele given that prior research has suggested increased reactivity in Val homozygotes (Alexander et al. 2010; Gatt et al. 2009). However, we also anticipated that Val homozygotes, relative to Met allele carriers, would demonstrate an increased ability to down-regulate negative emotion responses, as contextual parameters shifted to positive. This is based on evidence suggesting greater behavioral inflexibility in human Met allele carriers but most convincingly in comparable rodent models (e.g. Soliman et al. 2010). Although, we could not establish a priori hypotheses regarding positive emotion responses due to limited evidence on potential effects of BDNF reduction and ability to generate or shift positive emotions (Van Winkel et al. 2014; Wichers et al. 2008), we did consider that positive emotions might be particularly important to understand as a component of emotion flexibility in association with BDNF. Indeed, positive emotion generation has been clearly established as a broad indicator of emotion flexibility (Bonanno et al. 2004; Papa and Bonanno 2008). Specifically, ability to generate positive emotion has been linked to psychological resilience up to 18 months following a stressful event (e.g. loss of spouse: Coifman and Bonanno 2010). Similarly, no a priori hypothesis was established regarding RSA due to limited evidence of potential effects of BDNF reduction on autonomic nervous system activity (Yang et al. 2010). However, given previous research indicating that increased RSA and positive emotions increases capacity for emotion flexibility, we found these dimensions of emotion to be important to include in the current investigation.

Table 1 Demographic variables

Demographic variables	A Full sample (n = 120)	B ValVal	C ValMet/MetMet	ValVal versus met carrier
Hardy–Weinberg: $\chi^2 = 1.04$, p = .30		75 (62.5%)	45 (37.5%)	
Age	M = 20.87, SD = 6.43	M = 20.7, SD = 6.4	M = 21.1, SD = 6.5	*t(118)*= -2.7, p = .80
Sex	74 (62.2%) Female	50 (66.7%) Female	24 (54.5%) Female	$\chi^2(1,N = 120) = 1.73$, p = .13
Race				$\chi^2(1,N = 120) = 3.31$,
Caucasian	94 (79%)	57 (76%)	37 (84.1%)	p = .35
African American	14 (11.8%)	11 (14.7%)	3 (6.8%)	
Asian	3 (2.5%)	1 (1.3%)	2 (4.5%)	
Other	8 (6.7%)	6 (8%)	2 (4.5%)	
Ethnicity				$\chi^2(1,N = 116) = .13$,
Not Hispanic or Latino	108 (90.8%)	69 (92%)	39 (88.6%)	p = .50
Hispanic or Latino	7 (5.9%)	4 (5.3%)	3 (6.8%)	
Depression symptoms (CES-D)	M = 11.1, SD = 7.2	M = 11.2, SD = 7.6	M = 10.9, SD = 6.4	$t(118) = -.12$, p = .91

Method

Participants

One hundred and twenty adult participants (79% Caucasian, 62.2% female, mean age = 20.87 years) were recruited from the subject pool within the Psychology department at a large public university in the Midwest in the United States (see Table 1 for summary of demographic information of this sample). Participants needed to be 18 years of age of older to be eligible for the study. No other exclusion criteria were established for this study.

Measures

All participants completed questionnaires that included factors known to influence emotion responses including age, gender, race, ethnicity, and depressive symptoms (Bradley et al. 2001; Gotlib and Joorman 2010; Kring and Gordon 1998; Vrana and Rollock 2002; Zimmerman and Iwanski 2014), in order to isolate the effect of genotype as much as possible. To index depressive symptoms, participants completed the Center for Epidemiologic Studies Depression Scale (CES-D), a well-validated scale of depressive symptoms (Radloff 1977). A CES-D mean of M = 11.1 SD = 7.2 ($\alpha = .85$) was found in this sample. Based on the mean, this sample demonstrates comparable levels of depressive symptoms to other healthy, college-age, samples (Shean and Baldwin 2008).

Collection of saliva, and subsequent DNA extraction, were completed according to procedures specified in Gilman et al. (2015). The frequency of the BDNF Val66Met alleles in this sample [ValVal = 75 (62.5%); ValMet = 42 (35%); MetMet = 3 (2.5%)] did not differ from the Hardy–Weinberg equilibrium (Gaunt et al. 2007), $\chi^2 = 1.04$, p = .30. Based on prior research on the BDNF Val66Met polymorphism (e.g. Beevers et al. 2009; Egan et al. 2003; Lotrich et al. 2013; Soliman et al. 2010), participants in this sample were grouped into two groups (ValVal genotype versus Met allele carriers). Pearson's Chi square tests were utilized to examine group differences in demographic variables (gender, ethnicity, race), and *t* tests were utilized to examine group differences in age and symptoms of depression (CES-D). No significant group differences across the genotype groups were found on any key study variables (see Table 1).

To complete the emotion response assessment, participants were comfortably seated in a private study room, in front of a computer, and were instructed to engage with the content of a sequence of two validated (Gilman et al. 2017), emotionally evocative video clips. Each clip was 5-min long and was followed by a 2-min long break before the next video started. This task design is based on established conventions in emotion research (Bonanno et al. 2004; Coifman et al. 2007) and the break between film clips was included so that participants' emotional responses were given adequate time to recover, and so that participants were able to rate their emotions (detailed below). Moreover, by including this break, emotion responses that were present beyond the break, during the subsequent elicitation context, likely present stronger evidence of inflexible responding (i.e., in this study negative emotions present during the next explicitly positive film).

The video sequence started with a neutral content clip (*Big Cat Diary*, BBC Earth) in order for the participant to acclimate to the study conditions. For the purpose of explicitly examining shifts in emotion responses between a high arousal negative context and a low arousal positive context, participants were next shown a high arousal negative

emotion (e.g. disgust, anger) video (*The Road to Guantanamo*, Revolution Films, 2006) followed by a low arousal positive emotion video (*Alive*, Paramount Pictures, 1993). Specifically, this video sequence (*The Road to Guantanamo* to *Alive*) allowed for examination of spontaneous down-regulation of high arousal negative emotion in response to a low arousal positive emotion context, in addition to examination of contextually appropriate negative and positive emotion generation, abilities that are central to emotion flexibility. The two video clips were part of a larger investigation (Gilman et al. 2015; Latsko et al. 2016) which contained two additional, well-validated films (Gilman et al. 2017), known to elicit low arousal negative emotion (*The Champ*, Metro-Goldwyn Mayer 1979) and high arousal positive emotion (*Between Two Ferns*, http://www.comedyordie.com, 2010). This assessment was administered using E*Prime* 2.0 (Psychology Software Tools, Sharpsburg, PA). During the entire assessment, emotional responses were measured on multiple dimensions including: coded facial expressions, and sympathetic and parasympathetic arousal (autonomic activity). Participants were also asked to provide self-report of their emotional experience following each film clip, during the 2-min break.

In vivo assessment of emotion during flexibility assessment

Recording of physiological signals: respiratory sinus arrhythmia and skin conductance Electrocardiogram (ECG) was recorded during the entire assessment, in order to calculate a value to represent RSA (Porges 2007) for each participant. Electrodermal activity (EDA) was also recorded during the entire assessment, in order to calculate a value to represent skin conductance (SC) for each participant. This procedure was conducted as follows. The study room was kept at a steady temperature of 74.3° Fahrenheit and participants were encouraged to drink one 8-ounce bottle of water before the assessment began. These procedures were followed in order to minimize interference with EDA recording. To record the ECG signal, three disposable Ag/AgCl ECG spot electrodes were placed on the participant. One electrode was placed underneath the right collarbone, and two electrodes were placed on either side of the ribcage. To record the EDA signal, an electrolyte gel of sodium chloride was applied to two Beckman electrodes that were attached to the palmar surface of the participant's middle phalanges of the first and second fingers of the non-dominant hand. The ECG signal was acquired using a 2-slot BioNex bioamplifier (Mindware Technologies, Gahanna, OH) and sampled at a rate of 1000 Hz. ECG data was amplified with a gain of 500 μS/VS. To filter out noise, a high pass filter was set at 0.5 Hz and a low pass filter was set at 45 Hz. A bandpass filter (0.25–0.40 Hz) and notch filter (60 Hz) were used to filter out frequencies in the ECG not relevant to RSA. The EDA signal was acquired through a 31-channel A/D converter operating at a resolution of 12 bits and with an input range of −2.5 to +2.5 V. The EDA signal was sampled at a rate of 500 Hz and was amplified with a gain of 5 μS/VS. A high pass filter for the EDA signal was set at 1 Hz, and a low pass filter was set at 45 Hz.

Physiological data were cleaned and artifacts removed using customized *Bio-Lab*™ Software (MindWare Technologies, Gahanna, OH) and visual inspection of artifacts. Missed or mislabeled parts of the ECG wave were deleted and problematic beats were interpolated, and problematic segments of the EDA wave were excluded following visual inspection. RSA was derived by spectral analysis of the interbeat interval (RR) series derived from the ECG. High frequency spectral power was then integrated over the respiratory frequency band (0.12–0.4 Hz) and averaged for each video resulting in one average value of RSA for each video. Mean skin conductance data was averaged across each film and a SCR value (in μSiemens) was calculated for each film, for each individual.

Coded emotion expression and reported experience To measure behavioral expression of emotion during the emotion response assessment, participant's emotional facial behavior was recorded with a high-resolution camera. Emotional facial behaviors were later coded by five independent coders, naïve to any study details.[1] Coders viewed participant videos individually, on a 23″ computer monitor without sound. After viewing each video from beginning to end, coders rated degree of positive and degree of negative emotional facial behaviors to each video on a 7-point Likert scale (Bonanno et al. 2004; Coifman and Bonanno 2010) by providing one numerical score to indicate positive emotion facial behaviors and one numerical score to indicate negative emotion facial behaviors, resulting in a positive and a negative emotion expression score for each participant. Coders were sufficiently reliable (average ICC = 0.80, range 0.74–0.90), and ratings were averaged across coders to increase reliability.

To measure emotional experience, participants were instructed to self-report their emotional response immediately following each film by rating emotion-words on a 7-point Likert scale. Emotion-words were of both negative (fear, sadness, disgust, guilt, distress, anger) and positive (happiness, enjoyment, amusement, affection, relief) valence. Self-reported ratings of negatively valenced words were utilized to generate a mean negative affect score in response to both negative (*The Road to Guantanamo*) and positive (*Alive*) emotion contexts, for each participant.

[1] Evidence suggests that facial coding by relatively naïve coders may be as valid as highly trained coders (e.g., Dondi et al. 2007).

Similarly, self-reported ratings of positively valenced words were used to generate a mean positive affect score in response to both negative (*The Road to Guantanamo*) and positive (*Alive*) emotion contexts, for each participant. Emotion-words were chosen from contemporary circumplex models of affect (e.g. Rafaeli et al. 2007; Russell 1980). These emotion-words have been used reliably in prior studies (e.g. Coifman and Bonanno 2010), and demonstrated sufficient internal consistency in this sample (negative emotion experience in response to negative emotion context; $\alpha = 0.88$, and positive emotion experience in response to positive emotion context; $\alpha = 0.85$).

Procedure

Participants were recruited over the course of two academic years from the Psychology department subject pool. Upon arrival at the laboratory, all participants gave informed consent. After informed consent was obtained, participants provided demographic information, and then completed the CES-D to index depressive symptoms. Following completion of questionnaires, saliva (2 mL) was collected using Oragene-DNA Self-Collection Kits. Samples were then stored at − 20 °C. Saliva was processed following established procedures (Gilman et al. 2015). Once saliva collection was complete, the participant was seated in a private 4′ × 4′ study room where they completed the emotion response assessment. Approval for the study was obtained by the university's institutional review board governing research involving human subject. Upon completion of the study session, all participants were compensated with research credits.

Data cleaning and processing

Missing data

Data from n = 27[2] participants were dropped from some of the final analyses (resulting in a sample size of $N = 120$). Data were dropped for the following reasons. ECG signal data was lost due to equipment malfunction (e.g. detachment of electrodes, large muscle movements disrupting signal recording) that resulted in lack of a detectable signal. EDA signal data was lost due to equipment malfunction resulting in lack of a detectable signal and naturally occurring irregular or low skin conductance.[3] Physiological data (ECG and EDA signals) was lost for one participant due to administration error (electrodes not placed properly). Facial behavior data was lost due to unsuccessful video recording following camera software malfunction, and facial data was dropped for one participant upon their request. No significant differences on key study variables emerged between participants who were included in final analyses for the present study and participants with some missing data points.

Manipulation check

Validity of the emotion response assessment was confirmed in this sample by conducting paired samples *t* tests on negative and positive self-reported affect and negative and positive emotional facial behavior in response to each emotional context. Participants were found to report significantly more negative than positive affect during the negative emotion video (*The Road to Guantanamo*) and significantly more positive than negative affect during the positive emotion video (*Alive*) (see Table 2). Moreover, a significant change in negative affect emerged across the task, such that negative affect increased from baseline to the negative video [$t(118) = -16.33$, $p = .00$] and decreased from the negative video to the positive video [$t(118) = 16.22$, $p = .00$]. To further confirm the intensity of the emotion response assessment, Pearson correlations between affect and facial behavior in response to positive and negative stimuli were examined. A significant positive correlation emerged between negative affect and negative facial behavior in response to the negative video, suggesting intense negative emotion (*The Road to Guantanamo*) ($r = .30$, $n = 115$, $p < .01$). Further, a significant positive correlation was found between positive affect and positive facial behavior in response to the positive film, suggesting intense positive emotion (*Alive*) ($r = .25$, $n = 114$, $p < .01$). These findings are in line with past research suggesting that emotions manifest as a more organized response at high intensity, as compared to emotions at low intensity (Mauss et al. 2005).

[2] Note regarding missing data for this study: pairwise deletion was utilized for missing data and resulted in deletion of data from a total of n = 27 participants according to the following. ECG data was lost for n = 21 participants due to equipment malfunction, n = 4 of these participants were also missing EDA data. EDA data was lost for an additional n = 3 participants due to equipment malfunction, and EDA data for n = 2 participants was lost due to naturally occurring skin conductance (see below footnote). Facial behavior data was lost for n = 5 research participants. For n = 4 participants, video recording was unsuccessful due to camera software malfunction, and n = 1 participant requested deletion of their video data. Two of the participants with missing facial behavior data were also dropped from ECG or EDA analyses.}

[3] Notably, due to individual skin conductance variation within the general population, some people naturally show irregular or low skin conductance (termed "nonresponders") (Dawson et al. 2007). When such irregularities were discovered during data collection for the present study, the research investigator attempted to adjust the electrodes and massage fingers of the participant in order to better collect the EDA data. Adjustments were unsuccessful for n = 2 participants, resulting in lack of a detectable signal.

Table 2 Paired sample *t* tests for manipulation check of emotion responses to emotion response assessment

Condition	Mean (SD)	*t* test
Negative affect during baseline video	1.07 (0.17)	$t(118) = -17.51$, p = .00
Positive affect during baseline video	3.05 (1.22)	
Negative facial behavior during baseline video	1.71 (0.55)	$t(114) = .85$, p = .40
Positive facial behavior during baseline video	1.62 (0.89)	
Negative affect during negative emotion video (*The Road to Guantanamo*)	2.91 (1.23)	$t(118) = 10.28$, p = .00
Positive affect in during negative emotion video (*The Road to Guantanamo*)	1.47 (0.69)	
Negative facial behavior during negative emotion video (*The Road to Guantanamo*)	2.74 (1.10)	$t(114) = 15.10$, p = .00
Positive facial behavior during negative emotion video (*The Road to Guantanamo*)	1.10 (0.28)	
Negative affect during positive emotion video (*Alive*)	1.18 (0.32)	$t(118) = -13.58$, p = .00
Positive affect during positive emotion video (*Alive*)	2.60 (1.25)	
Negative facial behavior during positive emotion video (*Alive*)	2.29 (0.67)	$t(114) = 12.84$, p = .00
Positive facial behavior during positive emotion video (*Alive*)	1.25 (0.51)	

Data analytic strategy

We first tested for baseline differences in each of the emotion response indicators using ANOVA. Then we performed four repeated measures analysis of covariance (ANCOVA) tests to analyze group differences (BDNF ValVal versus ValMet/MetMet) in patterns of emotion output measured during the videos of interest, controlling for baseline levels. These omnibus ANCOVA tests followed a 2 (video type: negative emotion video [*The Road to Guantanamo*), positive emotion video (*Alive*)] × 1 (response type: RSA or skin conductance) × 2 (genotype: ValVal versus ValMet/MetMet) design, or a 2 (video type) × 2 (response type: positive emotion expression and positive emotion experience, or negative emotion expression and negative emotion experience) × 2 (genotype) design. Hence, a total of four omnibus tests were conducted to examine group differences in (1) RSA, (2) skin conductance, then (3) positive emotion expression and positive emotion experience were tested in the same model, and (4) negative emotion expression and negative emotion experience were tested in the same model. Baseline differences in emotional responding were controlled for by including emotion output during the baseline video as a covariate in these analyses. Demographic variables (age, sex, race, and ethnicity) and depressive symptoms (CES-D) were also entered into all analyses as covariates. For each test, if the omnibus model was significant, then follow-up univariate tests were examined to better understand group differences. This would allow for a preliminary test of both hypotheses. If the results suggested a need for additional testing, we would conduct additional univariate ANCOVA to examine differences in the positive film, while controlling for responses to the negative film. This was specifically for Hypothesis 2 (e.g., to test if negative emotion persisted during the positive film and if this differed by group).

Due to the number of follow-up tests, we controlled for the false discovery rate (FDR; Benjamini and Hochberg 1995, 2000) resulting in the first test being declared significant based on a p value of .05 and subsequent tests being declared significant based on increasingly smaller p values. For example, the set of follow-up univariate tests of the first hypothesis involved three tests, hence we would apply the following alpha levels: .050, .033, .016.[4] The set of follow-up univariate tests of the second hypothesis involved two tests, hence we would apply the following alpha levels: .050, .025.[5] For our exploratory analyses for positive emotional responses and RSA, we applied the same "family-based" rule for three tests (applying alpha levels: .050, .033, .016). Effect sizes are reported as *partial*^{2}. Assumptions of ANCOVA were met, including sphericity and equality of error variances. All with PASW Statistics 21 (SPSS Inc., Chicago, IL, USA).

[4] As per Benjamini and Hochberg (1995), unadjusted p values were ranked by hypothesis. Adjusted p values were then calculated using the following formula: $p(j) \leq \alpha\left(\frac{j}{m}\right)$, where $\alpha = .05$, j = rank, and $m = 3$, the total number of hypothesis tests conducted. For the first hypothesis and exploratory analysis, rank order was as follows: emotional expression (1), autonomic activity (2), and emotional experience (3).

[5] Adjusted p values were then calculated using the following formula: $p(j) \leq \alpha\left(\frac{j}{m}\right)$, where $\alpha = .05$, j = rank, and $m = 2$, the total number of hypothesis tests conducted. For the second hypothesis, rank order was as follows: emotional expression (1), emotional experience (2).

Table 3 Val66Met genotype differences in mean emotional responses during the baseline video of the emotion response task

Baseline video emotional responses	ValVal mean (SD)	ValMet/MetMet mean (SD)	
Negative emotion experience	1.04 (.10)	1.12 (.24)	$F(1,119) = 6.32$, p = .013
Negative emotion expression	1.65 (.49)	1.80 (.64)	$F(1,115) = 1.95$, p = .165
Positive emotion experience	3.12 (1.18)	2.99 (1.32)	$F(1,119) = .32$, p = .575
Positive emotion expression	1.62 (.85)	1.61 (.95)	$F(1,115) = .00$, p = .96
RSA	6.57 (1.19)	6.25 (1.16)	$F(1,108) = 1.77$, p = .186
SC	4.56 (2.83)	5.38 (2.92)	$F(1,112) = 2.18$, p = .143

Results

Baseline differences

We first conducted ANOVA to test for genotype differences during the baseline neutral film. There was an effect of genotype on negative emotion experience during the baseline video $F(1,119) = 6.32$, p = .013 such that Met carriers reported greater negative emotion experience at baseline (M = 1.12, SD = .24), as compared to Val homozygotes (M = 1.04, SD = .10). No other baseline effects emerged in this sample. Indeed, no significant effect of genotype was found on baseline emotion output including negative emotion expression $F(1,115) = 1.95$, p = .165, positive emotion experience $F(1,119) = .32$, p = .575, positive emotion expression $F(1,115) = .00$, p = .96, RSA $F(1,108) = 1.77$, p = .186, or skin conductance $F(1,112) = 2.18$, p = .143 (see Table 3).

Omnibus tests

Examination of group differences (BDNF ValVal versus ValMet/MetMet) in emotion output during the task, utilizing four repeated measures ANCOVA tests, resulted in the following. First, using Pillai's trace, a significant omnibus effect of genotype emerged on RSA across the emotion response assessment $F(1,97) = 5.01$, p = .027, $partial^2 = .05$, while controlling for RSA in response to the baseline video. A within-subjects effect also emerged, $F(1,97) = 5.01$, p = .027, $partial^2 = .05$, such that Val homozygotes had significantly greater RSA during the negative video (see Fig. 1a). Second, a significant between-subjects effect emerged on positive emotion expression and positive emotion experience across the emotion response assessment, $F(1,103) = 3.62$, p = .06, $partial^2 = .03$, while controlling for positive emotion expression and positive emotion experience during the baseline video (see Fig. 1b). No significant effect of genotype emerged on skin conductance across the emotion response assessment $F(1,105) = 2.39$, p = .125, $partial^2 = .02$, while controlling for skin conductance in response to the baseline video. Moreover, no significant effect of genotype emerged on negative emotion expression and negative emotion experience across the emotion response assessment $F(1,103) = .48$, p = .49, $partial^2 = .01$ Regarding the video stimuli that were not included in the present analyses (*The Champ* and *Between Two Ferns*), non-significant trends of a similar pattern as reported results, emerged across the emotion response assessment.[6]

Follow-up tests

Follow-up univariate tests were examined for significant omnibus tests (i.e. genotype effects on RSA and positive emotion expression and positive emotion experience) in order to better understand group differences during each film or emotion context. These follow-up tests revealed a significant difference between Val homozygotes and Met carriers in RSA during the negative video (*The Road to Guantanamo*), $t(97) = 2.04$, p = .044, $partial^2 = .04$, 95%CI .01–.35. Specifically, Val homozygotes displayed significantly higher RSA in response to a negative context (M = 6.61, SD = 1.19) as compared to Met carriers (M = 6.10, SD = 1.27). Follow-up contrasts also revealed a significant difference between Val homozygotes and Met carriers in positive emotion expression $t(103) = 2.30$, p = .024, $partial^2 = .05$, 95%CI .02–.21, such that Val homozygotes showed significantly greater positive emotion expression during the negative video (M = 1.14, SD = .35), as compared to Met carriers (1.04,

[6] Specifically, Val homozygotes showed higher RSA in response both excluded videos, as compared to Met carriers. Val homozygotes also showed an increase in reported negative emotion expression and negative emotion experience in response to the negative emotion context (*The Champ*) which then decreased as the context shifted to positive emotion (*Between Two Ferns*). Met carriers were observed to follow a similar pattern of negative emotion expression and negative emotion experience. Val homozygotes showed a decrease in positive emotion expression as the context shifted to negative (*The Champ*), followed by an increase in positive emotion expression in response to the positive emotion context (*Between Two Ferns*). Met carriers were observed to follow a more blunted pattern of responding, with a less pronounced decrease in positive emotion expression as the context shifted to negative (*The Champ*). Lastly, Val homozygotes and Met carriers were also shown to follow a similar pattern of positive emotion experience.

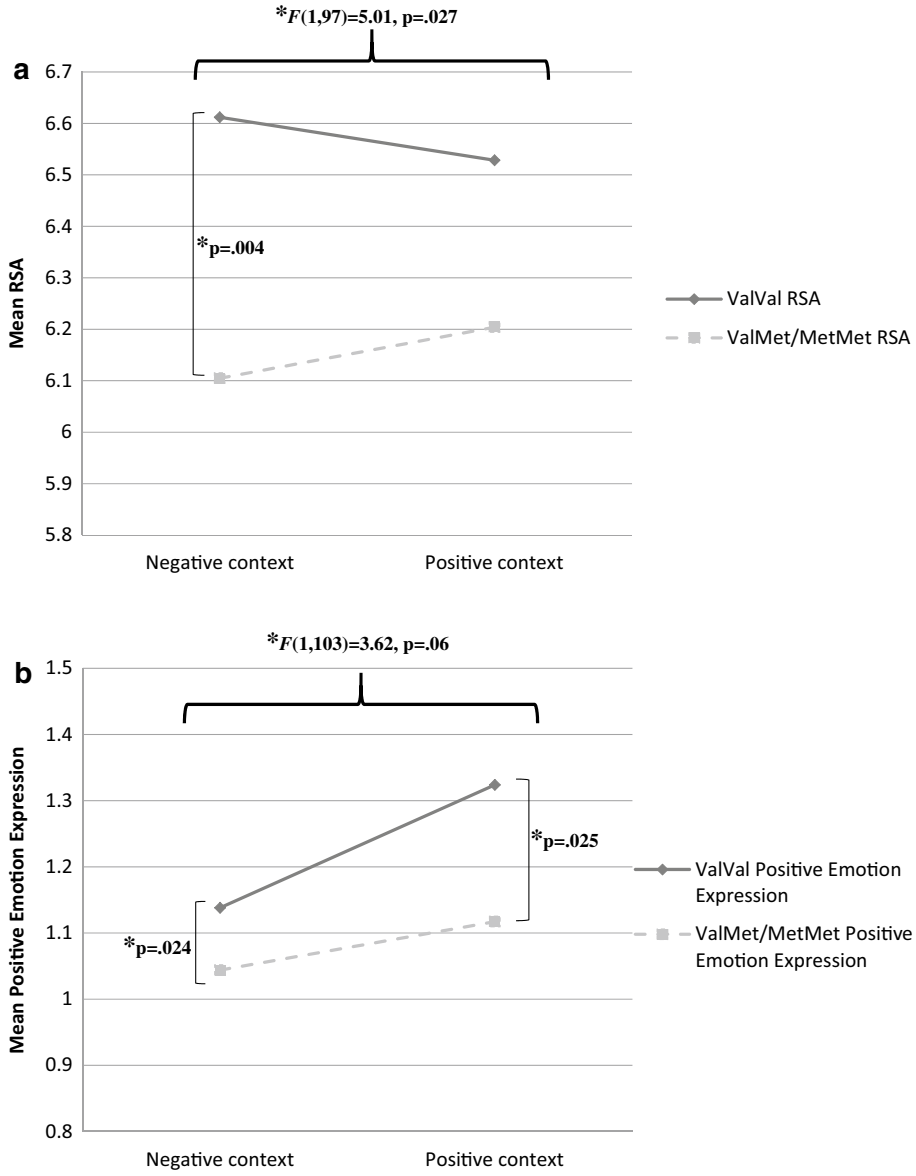

Fig. 1 **a** Val66Met genotype differences in mean respiratory sinus arrhythmia (RSA) during the emotion response task. **b** Val66Met genotype differences in mean positive emotion expression during the emotion response task

SD = .08). Moreover, Val homozygotes showed greater positive emotion expression during the positive video (M = 1.32, SD = .62), as compared to Met carriers (M = 1.12, SD = .23), $t(103) = 2.28$, p = .025, $partial^2 = .05$, 95%CI .03–.37. There were no significant differences in reported positive emotion experience by genotype.

Overall, these findings did not support the two stated hypotheses. Indeed, no evidence emerged to suggest that Val homozygotes show greater negative emotion reactivity in response to negative emotion context (first hypothesis). These results also did not suggest that Val homozygotes show greater down-regulation of negative emotion in response to positive emotion context (second hypothesis). However, significant findings did emerge from the exploratory analyses conducted in this study. Indeed, Val homozygotes in this sample demonstrate higher RSA and greater positive emotion expression across the emotion response assessment.

Discussion

The impact of genetic variation on psychological illness has received much research attention over the past decade, and there is evidence to suggest that variation in the BDNF gene might play a role in emotion-linked psychological disorders (Colzato et al. 2011; Lotrich et al. 2013; Notaras et al. 2015). The current investigation expands this work by examining the influence of the Val66Met polymorphism on emotion flexibility by measuring emotion behaviors (emotional facial behaviors and autonomic activity) in response to changing emotional contexts in a lab-based task. The results of the

present study were surprising, and although they did not support the stated hypotheses, they were broadly consistent with the literature. In particular, unlike some previous research, no evidence of greater negative emotional reactivity in Val homozygotes emerged in this sample as well as no evidence of negative emotion inflexibility in Met carriers. However, exploratory analyses, based on extensive research on autonomic flexibility (Porges 2009; Thayer et al. 2012) and benefits of increased positive emotion generation (Coifman and Bonanno 2010; Fredrickson et al. 2003), revealed findings that may provide more nuance to what is known about genetic influence on emotion flexibility. Specifically, the current findings show a pattern in which Met carriers in this sample appear to exhibit broadly decreased regulatory resources, as compared to Val homozygotes. Indeed, Met carriers in this sample exhibited less parasympathetic nervous system activation across the task, as compared to Val homozygotes. Met carriers also generated less positive emotion facial behaviors in response to an explicit positive emotion context. In contrast, Val homozygotes in this sample were able to adaptively generate and maintain positive emotion facial behaviors across the task during both the negative emotion and the positive emotion context. Indeed, Val homozygotes showed greater positive emotion facial behavior in response to the negative emotion context, a response that might indicate greater ability to down-regulate negative emotion (Papa and Bonanno 2008). Both parasympathetic activation and positive emotion generation have been clearly shown to provide expansive physical and emotional health benefits, most notably, in the form of increasing regulatory resources (Bonanno et al. 2004; Fredrickson and Levenson 1998; Porges 2009; Thayer et al. 2012). Although these indicators could not be hypothesized a priori in the current study, our findings may indeed indicate greater emotion flexibility in Val homozygotes.

That we did not find effects relating to negative emotion or skin conductance is surprising. Measurement of skin conductance was included in the present study based on previous evidence that suggest a link between the Val allele and greater stress reactivity. Non-significant findings might reflect a similarity between the genotype groups on sympathetic activation in an emotion context, but call for further research on specific patterns of autonomic activity and reduced BDNF. Moreover, inconsistent with the present study hypothesis, and apart from reports at baseline, Met carriers in this sample were not found to demonstrate less ability to down-regulate negative emotion in response to changes in emotional context. Non-significant findings might reflect a similarity between the genotype groups on ability to effectively down-regulate negative emotion, given that negative emotions were explicitly elicited. Finally, it may be that the operationalization of emotion flexibility used in this paradigm was not sufficiently sensitive to the question of genetic variation. We did find evidence of flexibility differences, but not in the hypothesized ways. Certainly, this suggests that future work is needed to verify and perhaps adjust application of the construct of emotion flexibility to questions of genetic variation. Indeed, our team is already at work on this challenge.

The present findings are of particular interest due to the comprehensive measurement of emotional responses, captured in a well-vetted emotion-elicitation paradigm targeting objective indicators of emotion processing, as opposed to retrospective self-report of emotion which can present important methodological problems (e.g. demand characteristics) (Messner and Wanke 2011; Schwarz and Clore 1983). Thus, this study captures emotional processes, more broadly including those response channels that may be outside of awareness (e.g. autonomic activity and emotional facial behaviors). Interestingly, Met carriers in this sample self-reported greater negative emotion in response to a neutral emotion context (baseline video) but did not report more negative emotion throughout the emotion elicitation. This finding is consistent with prior research suggesting an association between presence of the Met allele and elevated report of neuroticism in the absence of stress-evoking contexts (Lehto et al. 2016). Indeed, low concentrations of BDNF in serum have also been found to predict elevated report of neuroticism (Terracciano et al. 2011). Neuroticism is a well-known predictor of emotion-linked psychopathology. Thus, the current findings also echo previous studies that have found greater self-report of psychological symptoms in Met carriers (Beevers et al. 2009; Lotrich et al. 2013), although we did not find elevated reports of psychological symptoms in Met carriers in this sample. Importantly, no baseline genotype differences were found for RSA or positive emotion expression in this sample, but effects only emerged during emotionally evocative contexts. Although previous research has shown increased parasympathetic activity at rest in Val homozygotes, relative to Met *homozygotes* (obtained from ECG monitoring for 2 h while participants remained in resting state) (Yang et al. 2010), our findings point more clearly to potential genotype difference in emotional regulatory processing such that Val/Met carriers may have diminished regulatory resources, as compared to Val homozygotes.

Clinical implications

Clinically, the main findings of the present study, decreased parasympathetic activity and decreased positive emotion facial expression in Met carriers, suggest a pattern of weaker emotional regulatory resources in these individuals, and might indicate a higher risk for emotion-linked psychological illness. Such emotion responses have indeed been

both theorized and demonstrated to contribute to higher risk for psychological illness (e.g., Barlow et al. 2013; Kendall et al. 2015). Furthermore, decreased parasympathetic activity has been consistently linked to increased psychiatric risk (Beauchaine and Thayer 2015). More broadly, these findings contribute to the understanding of dominant models of psychopathology, which have demonstrated that psychological disorders likely develop from complex interactions between genetically predisposed vulnerability and environmental factors (Cuthbert and Insel 2013; Insel et al. 2010).

Limitations

This study had some limitations. Primarily, the sample size of this study was relatively small, and consisted largely of college-aged Caucasian individuals. The costly nature of In vivo measurement of emotion makes the sample size necessarily limited. Indeed, such ecologically valid measurement of emotion is crucial in order to better understand the complex patterns of emotion linked to genetic variation, but it is time intensive and laborious. Furthermore, it restricts detection of potentially distinct emotional profiles of low frequency genotypes (i.e., MetMet), an inherent challenge in the broader realm of SNP research. Weighting the MetMet genotype group with greater Ns would be ideal for evaluating how behaviorally and physiologically distinguishable this genotype is from ValVal and ValMet, but such an endeavor is presently too cost- and time-prohibitive given the low prevalence of the MetMet genotype (e.g., three individuals in our $N = 120$).

Another limitation of the present study was the sole focus on Val66Met, without consideration of potential interactions of this polymorphism with other SNPs within the BDNF gene, or other related genes. Evaluations of emotional and autonomic responses associated with one polymorphism in isolation should certainly be interpreted with caution. Though we have implemented rigorous controls in our study, it remains possible that the surprising effects we discovered are a consequence of an as-yet-unidentified gene or polymorphism that is in linkage disequilibrium with the BDNF Val66Met polymorphism. Moreover, while BDNF is certainly an important component of brain development and activity, we recognize that it interacts with myriad other systems and polymorphisms, such that the effects we observe here are psychological and physiological manifestations far downstream from a single nucleotide difference. Indeed, there is a small body of research that has examined interactions between BDNF Val66Met and other genes (Bredemeier et al. 2014; Dougherty et al. 2010; Nederhof et al. 2010; Latsko et al. 2016). Although results are generally mixed, there is a clear need for more methodologically complex studies on the BDNF gene and emotion responses. Additionally, it is essential that future research take epistatic interactions into account in such investigations, particularly through studying populations with more diverse ages and racial backgrounds. Finally, participants in this study were not evaluated, prior to study participation, for common psychological illnesses (e.g. depression). This could potentially influence study results. However, survey data (using, for example, the CES-D, see above for sample details) indicated that the sample was, overall, healthy.

Conclusion

Results from the present study suggest an association between presence of the Met allele at the Val66Met polymorphism and decreased emotional regulatory resources. This difference was clearly evident in behavioral expressions of emotion, via autonomic nervous system responsivity and coded facial behavior. These findings echo patterns found in emotion-linked disorders, where greater inflexibility in emotion responses often is found in individuals who suffer from both depression and anxiety-related illnesses, as well as research suggesting the role of emotion inflexibility in prospective prediction of emotion-linked disorders (Coifman and Bonanno 2010; Rottenberg and Hindash 2015). Undeniably, BDNF plays an essential role in synaptic plasticity, learning, and thereby psychiatric risk. Thus, it is essential to gain further understanding about how reduced BDNF influences clinically relevant emotion responses. Greater specificity in the present study was achieved by exploring these associations in healthy individuals, where the effect of genotype could be further isolated. Given the complexity of BDNF and the call for replication within candidate gene research, further exploration of associations between genetic variation in the BDNF gene and clinically relevant emotion responses is necessary.

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References

Aldao, A., Sheppes, G., & Gross, J. J. (2015). Emotion regulation flexibility. *Cognitive Therapy and Research, 39*, 263–278.

Alexander, N., Osinsky, R., Schmitz, A., Mueller, E., Kuepper, Y., & Hennig, J. (2010). The BDNF Val66Met polymorphism affects HPA-axis reactivity to acute stress. *Psychoneuroendocrinology, 35*(6), 949–953. https://doi.org/10.1016/j.psyneuen.2009.12.008.

Anastasia, A., Deinhardt, K., Chao, M. V. S., Will, N. E., Irmady, K., Lee, F. S., Hempstead, B. L., & Bracken, C. (2013). Val66Met polymorphism of BDNF alters prodromal structure to induce neuronal growth cone retraction. *Nature Communications, 4*, 2490.

Asthana, M. K., Brunhuber, B., Mühlberger, A., Reif, A., Schneider, S., & Herrmann, M. J. (2016). Preventing the return of fear using reconsolidation update mechanisms depends on the Met-allele of the brain derived neurotrophic factor Val66Met polymorphism. *The International Journal of Neuropsychopharmacology I: Official Scientific Journal of the Collegium Internationale Neuropsychopharmacologicum (CINP)*. https://doi.org/10.1093/ijnp/pyv137.

Barlow, D. H., Sauer-Zavala, S., Carl, J. R., Bullis, J. R., & Ellard, K. K. (2013). The nature, diagnosis, and treatment of neuroticism: Back to the future. *Clinical Psychological Science, 2*(3), 344–365.

Bath, K., Chuang, J., Spencer-Segal, J. L., Amso, D., Altemus, M., McEwen, B., & Lee, F. (2012). Variant BDNF (Val66Met) polymorphism contributes to developmental and estrous-stage-specific expression of anxiety-like behavior in female mice. *Biological Psychiatry, 72*(6), 499–504. https://doi.org/10.1016/j.biopsych.2012.03.032.

Beauchaine, T. P., & Thayer, J. F. (2015). Heart rate variability as a transdiagnostic biomarker of psychopathology. *International Journal of Psychophysiology*. https://doi.org/10.1016/j.ijpsycho.2015.08.004.

Beevers, C. G., Wells, T. T., & Mcgeary, J. E. (2009). The BDNF Val66Met polymorphism is associated with rumination in healthy adults. *Emotion*, 9(4), 579–584. https://doi.org/10.1037/a0016189.

Benjamini, Y., & Hochberg, Y. (1995). Controlling the False-Discovery Rate : A new and powerful approach to multiple testing. *Journal of the Royal Statsitical Society B, 57*, 289–300.

Benjamini, Y., & Hochberg, Y. (2000). On the adaptive control of the False Discovery rate in multiple testing with independent statistics. *Journal of Educational and Behavioral Statistics, 25*(1), 60–83.

Bonanno, G. A., & Burton, C. L. (2013). Regulatory flexibility: An individual differences perspective on coping and emotion regulation. *Perspectives on Psychological Science, 8*, 591–612.

Bonanno, G. A., Papa, A., Lalande, K., Westpal, M., & Coifman, K. (2004). The importance of being flexible: The ability to enhance and suppress emotional expression as a predictor of long-term adjustment. *Psychological Science, 15*(7), 482–487.

Bradley, M. M., Codispoti, M., Sabatinelli, D., & Lang, P. J. (2001). Emotion and motivation II: Sex differences in picture processing. *Emotion, 1*(3), 300–319.

Bredemeier, K., Beevers, C. G., & McGeary, J. E. (2014). Serotonin transporter and BDNF polymorphisms interact to predict trait worry. *Anxiety, Stress, & Coping, 27*(6), 712–721. https://doi.org/10.1080/10615806.2014.909928.

Buss, K. A. (2011). Which fearful toddlers should we worry about? Context, fear, regulation, and anxiety risk. *Developmental Psychology, 47*(3), 804–819.

Buss, K. A., Davidson, R. J., Kalin, N. H., Goldsmith, H. H. (2004). Context-specific freezing and associated physiological reactivity as a dysregulated fear response. *Developmental Psychology, 40*(4), 583–594.

Bylsma, L. M., Morris, B. H., & Rottenberg, J. (2008). A meta-analysis of emotional reactivity in major depressive disorder. *Clinical Psychology Review, 28*(4), 676–691. https://doi.org/10.1016/j.cpr.2007.10.001.

Caspi, A., Hariri, A. R., Holmes, A., Uher, R., & Moffitt, T. E. (2010). Genetic sensitivity to the environment: The case of the serotonin transporter gene and its implications for studying complex diseases and traits. *American Journal of Psychiatry, 167*, 509–527. https://doi.org/10.1176/appi.ajp.2010.09101452.

Chen, L., Lawlor, D. A., Lewis, S. J., Yuan, W., Abdollahi, M. R., Timpson, N. J., … Shugart, Y. Y. (2008). Genetic association study of BDNF in depression: Finding from two cohort studies and a meta-analysis. *American Journal of Psychiatric Genetics Part B: Neuropsychiatric Genetics, 821*, 814–821. https://doi.org/10.1002/ajmg.b.30686.

Chen, Z.-Y., Jing, D., Bath, K. G., Ieraci, A., Khan, T., Siao, C.-J., … Lee, F. S. (2006). Genetic variant BDNF (Val66Met) polymorphism alters anxiety-related behavior. *Science, 314*(5796), 140–143. https://doi.org/10.1126/science.1129663.

Chhatwal, J. P., Stanek-Rattiner, L., Davis, M., & Ressler, K. J. (2006). Amygdala BDNF signaling is required for consolidation but not encoding of extinction. *Nature Neuroscience, 9*(7), 870–872.

Chourbaji, S., Brandwein, C., Vogt, M. A., Dormann, C., Hellweg, R., & Gass, P. (2008). Nature vs. nurture: Can enrichment rescue the behavioural phenotype of BDNF heterozygous mice? *Behavioural Brain Research, 192*(2), 254–258. https://doi.org/10.1016/j.bbr.2008.04.015.

Coifman, K. G., & Almahmoud, S. Y. (2016). Emotion flexibility in psychological risk and resilience. In U. Kumar (Ed.), *Handbook of resilience: A psychosocial perspective*. New York: Routledge.

Coifman, K. G., & Bonanno, G. A. (2010). When distress does not become depression: Emotion context sensitivity and adjustment to bereavement. *Journal of Abnormal Psychology, 119*(3), 479.

Coifman, K. G., Bonanno, G. A., Ray, R., & Gross, J. (2007). Does repression lead to recovery and resilience? Affective-autonomic response discrepancy in bereavement. *Journal of Personality and Social Psychology, 92*(4), 745–758.

Colzato, L. S., Van der Does, A. J. W., Kouwenhoven, C., Elzinga, B. M., & Hommel, B. (2011). BDNF Val66Met polymorphism is associated with higher anticipatory cortisol stress response, anxiety, and alcohol consumption in healthy adults. *Psychoneuroendocrinology, 36*, 1562–1569.

Cuthbert, B. N., & Insel, T. R. (2013). Toward the future of psychiatric diagnosis: The seven pillars of RDoC. *BMC Medicine, 11*(126), 1–8.

Da Silveira Da Luz, Dias, G. P., do Nascimento Bevilaqua, M. C., Cocks, G., Gardino, P. F., Thuret, S., & Nardi, A. E. (2013). Translational findings on brain-derived neurotrophic factor and anxiety: Contributions from basic research to clinical practice. *Neuropsychobiology, 68*(3), 129–138. https://doi.org/10.1159/000353269.

Dawson, M. E., Schell, A. M., & Filion, D. L. (2007). The electrodermal system. In J. T. Cacioppo, L. G. Tassinary & G. G. Berntson (Eds.), *Handbook of psychophysiology* (3rd ed., pp. 159–181). New York: Cambridge University Press.

Dondi, M., Messinger, D., Colle, M., Tabasso, A., Simion, F., Barba, D., B., & Fogel, A. (2007). A new perspective on neonatal smiling: Differences between the judgments of expert coders and naive observers. *Infancy, 12*(3), 235–255. https://doi.org/10.1111/j.1532-7078.2007.tb00242.x.

Dougherty, L. R., Klein, D. N., Congdon, E., Canli, T., & Hayden, E. P. (2010). Interaction between 5-HTTLPR and BDNF Val66Met polymorphisms on HPA axis reactivity in preschoolers. *Biological Psychology, 83*(2), 93–100.

Duman, R. S., Aghajanian, G. K., Sanacora, G., & Krystal, J. H. (2016). Synaptic plasticity and depression: New insights from stress and rapid-acting antidepressants. *Nature Medicine, 22*(3), 238–249. https://doi.org/10.1038/nm.4050.

Egan, M. F., Kojima, M., Callicott, J. H., Goldberg, T. E., Kolachana, B. S., Bertolino, A., … Weinberger, D. R. (2003). The BDNF val66met polymorphism affects activity-dependent secretion of BDNF and human memory and hippocampal function. *Cell, 112*(2), 257–269. https://doi.org/10.1016/S0092-8674(03)00035-7.

Ekman, P. (1992). Are there basic emotions? *Psychological Review, 99*(3), 550–553.

Fredrickson, B. L., & Levenson, R. W. (1998). Positive emotions speed recovery from the cardiovascular sequelae of negative emotions. *Cognition and Emotion, 12*, 191–220.

Fredrickson, B. L., Tugade, M. M., Waugh, C. E., & Larkin, G. R. (2003). What good are positive emotions in crises? A prospective study of resilience and emotions following the terrorist attacks on the United States on 11th September, 2001. *Journal of Personality and Social Psychology, 84*(2), 365–376.

Friedman, B. H. (2007). An autonomic flexibility-neurovisceral integration model of anxiety and cardiac vagal tone. *Biological Psychology, 74*(2), 185–199. https://doi.org/10.1016/j.biopsycho.2005.08.009.

Gatt, J. M., Nemeroff, C. B., Dobson-Stone, C., Paul, R. H., Bryant, R. A., Schofield, P. R., … Williams, L. M. (2009). Interactions between BDNF Val66Met polymorphism and early life stress predict brain and arousal pathways to syndromal depression and anxiety. *Molecular Psychiatry, 14*(7), 681–695. https://doi.org/10.1038/mp.2008.143.

Gaunt, T. R., Rodríguez, S., & Day, I. N. (2007). Cubic exact solutions for the estimation of pairwise haplotype frequencies: implications for linkage disequilibrium analyses and a web tool 'CubeX'. *BMC Bioinformatics, 8*(1), 428.

Gilman, T. L., Latsko, M., Matt, L., Flynn, J., Cabrera, OdlC., Douglas, D., Jasnow, A. M., & Coifman, K. G. (2015). Variation of 5-HTTLPR and deficits in emotion regulation: A pathway to risk? *Psychology & Neuroscience, 8*(3), 397.

Gilman, T. L., Shaheen, R., Nylocks, K. M., Halachoff, D., Flynn, J. J., Matt, L. M., & Coifman, K. G. (2017). A film set for the elicitation of emotion in research: A comprehensive catalogue derived from four decades of investigation. *Behavior Research Methods, 49*(6), 2061–2082.

Gotlib, I. H., & Joormann, J. (2010). Cognition and depression: Current status and future directions. *Annual Review of Psychology, 6*, 285–312.

Graham, B. M., & Milad, M. R. (2011). The study of fear extinction: Implications for anxiety disorders. *American Journal of Psychiatry, 168*, 1255–1265.

Hollenstein, T. (2015). This time. It's real: Affective flexibility, time scales, feedback loops, and the regulation of emotion. *Emotion Review, 7*, 308–315.

Hollenstein, T., & Lewis, M. D. (2006). A state space analysis of emotion and flexibility in parent–child interactions. *Emotion, 6*, 663–669.

Hollenstein, T., Lichtwarck-Aschoff, A., & Potworowski, G. (2013). A model of socioemotional flexibility at three time scales. *Emotion Review, 5*, 397–405.

Holtmaat, A., & Svoboda, K. (2009). Experience-dependent structural synaptic plasticity in the mammalian brain. *Nature Reviews Neuroscience, 10*(9), 647–658. https://doi.org/10.1038/nrn2721.

Insel, T., Cuthbert, B., Garvey, M., Heinssen, R., Pine, D. S., Quinn, K., Sanislow, C., & Wang, P. (2010). Research domain criteria (RDoC): Toward a new classification framework for research on mental disorders. *American Journal of Psychiatry, 167*(7), 748–751.

Insel, T. R., & Cuthbert, B. N. (2009). Endophenotypes: Bridging genomic complexity and disorder heterogeneity. *Biological Psychiatry, 66*, 988–989.

Johnson, D. C., & Casey, B. J. (2015). Easy to remember, difficult to forget: The development of fear regulation. *Developmental Cognitive Neuroscience, 11*, 42–55. https://doi.org/10.1016/j.dcn.2014.07.006.

Joorman, J., Siemer, M., & Gotlib, I. H. (2007). Mood regulation in depression: Differential effects of distraction and recall of happy memories on sad mood. *Journal of Abnormal Psychology, 116*(3), 484–490.

Kashdan, T. B., & Rottenberg, J. (2010). Psychological flexibility as a fundamental aspect of health. *Clinical Psychology Review, 30*(7), 865–878. https://doi.org/10.1016/j.cpr.2010.03.001.

Kashdan, T. B., & Steger, M. F. (2006). Expanding the topography of social anxiety: An experience sampling assessment of positive emotions and events, and emotion suppression. *Psychological Science, 17*, 120–128.

Kendall, A. D., Zinbarg, R. E., Mineka, S., Bobova, L., Prenoveau, J. M., Revelle, W., & Craske, M. G. (2015). Prospective Associations of Low positive emotionality with first onsets of depressive and anxiety disorders: Results from a 10-Wave Latent Trait-State Modeling Study. *Journal of Abnormal Psychology*. https://doi.org/10.1037/abn0000105.

Koenen, K., Duncan, L. E., Liberson, I., & Ressler, K. (2015). From candidate genes to genome-wide association: The challenges and promise of posttraumatic stress disorder genetic studies. *Biological Psychiatry, 74*(9), 634–636. https://doi.org/10.1016/j.biopsych.2013.08.022.

Kok, B. E., & Fredrickson, B. L. (2010). Upward spirals of the heart: Autonomic flexibility, as indexed by vagal tone, reciprocally and prospectively predicts positive emotions and social connectedness. *Biological Psychology, 85*(3), 432–436.

Kovacs, M., Bylsma, L. M., Yaroslavsky, I., Rottenberg, J., George, C. J., Kiss, E., Halas, K., Benak, I., Baji, I., Vetro, A., & Kapornai, K. (2015). Positive affectivity is dampened in youths with histories of major depression and their never-depressed adolescent siblings. *Clinical Psychological Science, 4*(4), 661–674.

Kreibig, S. D. (2010). Autonomic nervous system activity in emotion: A review. *Biological Psychology, 84*(3), 394–421. https://doi.org/10.1016/j.biopsycho.2010.03.010.

Kring, A. M., & Gordon, A. H. (1998). Sex differences in emotion: Expression, experience, and physiology. *Journal of Personality and Social Psychology, 74*(3), 686–703.

Latsko, M. S., Gilman, T. L., Matt, L. M., Nylocks, K. M., Coifman, K. G., Jasnow, A. M., & Hashimoto, K. (2016). A novel interaction between tryptophan hydroxylase 2 (TPH2) gene polymorphism (rs4570625) and BDNF Val66Met predicts a high-risk emotional phenotype in healthy subjects. *PLOS ONE, 11*(10), e0162585.

LeDoux, J. E. (1995). Emotion: Clues from the brain. *Annual Review of Psychology, 46*, 209–235.

Lehto, K., Mäestu, J., Kiive, E., Veidebaum, T., & Harro, J. (2016). BDNF Val66Met genotype and neuroticism predict life stress: A longitudinal study from childhood to adulthood. *European Neuropsychopharmacology, 26*(3), 562–569. https://doi.org/10.1016/j.euroneuro.2015.12.029.

Liebl, D. J., Tessarollo, L., Palko, M. E., & Parada, L. F. (1997). Absence of sensory neurons before target innervation in brain-derived neurotrophic factor-, neurotrophin 3-, and TrkC-deficient embryonic mice. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience, 17*(23), 9113–9121.

Lissek, S., Rabin, S., Heller, R. E., Lukenbaugh, D., Geraci, M., Pine, D. S., & Grillon, C. (2010). Overgeneralization of conditioned fear as a pathogenic marker of panic disorder. *American Journal of Psychiatry, 167*, 47–55.

Lopez-Leon, S., Janssens, A. C., Ladd A. G., Del-Favero, J., Claes, S. J., Oostra, B., & van Duijn, C. M. (2008). *Meta-analyses of genetic studies on major depressive disorder. Molecular Psychiatry, 13*(8), 772–785. https://doi.org/10.1038/sj.mp.4002088.

Lotrich, F. E., Albusaysi, S., & Ferrell, R. E. (2013). Brain-derived neurotrophic factor serum levels and genotype: Association with depression during interferon: A treatment. *Neuropsychopharmacology, 38*(6), 985–995. https://doi.org/10.1038/npp.2012.263.

Mathews, A., & MacLeod, C. (2005). Cognitive vulnerability to emotional disorders. *Annual Review of Clinical Psychology, 1*(1), 167–195.

Mauss, I. B., Levenson, R. W., McCarter, L., Wilhelm, F. H., & Gross, J. J. (2005). The tie that binds? Coherence among emotion experience, behavior, and physiology. *Emotion, 5*(2), 175–190.

Messner, C., & Wanke, M. (2011). Good weather for Schwarz and Clore. *Emotion, 11*(2), 436–437.

Mühlberger, A., Andreatta, M., Ewald, H., Glotzbach-Schoon, E., Tröger, C., Baumann, C., … Pauli, P. (2014). The BDNF Val-66Met polymorphism modulates the generalization of cued fear responses to a novel context. *Official Publication Of The American College Of Neuropsychopharmacology, 39*(5), 1187–1195. https://doi.org/10.1038/npp.2013.320.

Nederhof, E., Bouma, E. M. C., Riese, H., Laceulle, O. M., Ormel, J., & Oldehinkel, A. J. (2010). Evidence for plasticity genotypes in gene-gene-environment interaction: The TRAILS study. *Genes, Brain, and Behavior, 9*, 968–973.

Notaras, M., Hill, R., Gogos, J. A., & van den Buuse, M. (2016). BDNF Val66Met genotype determines hippocampus-dependent behavior via sensitivity to glucocorticoid signaling. *Molecular Psychiatry, 21*(6), 730–732. https://doi.org/10.1038/mp.2015.152.

Notaras, M., Hill, R., & van den Buuse, M. (2015). The BDNF gene Val66Met polymorphism as a modifier of psychiatric disorder susceptibility: Progress and controversy. *Molecular Psychiatry, 20*(8), 916–930. https://doi.org/10.1038/mp.2015.27.

Ochsner, K. N., Ray, R. R., Hughes, B., McRae, K., Cooper, J. C., Weber, J., & … Gross, J. J. (2009). Bottom-up and top-down processes in emotion generation: Common and distinct neural mechanisms. *Psychological Science, 20*(11), 1322–1331.

Öhman, A., & Mineka, S. (2001). Fears, phobias, and preparedness: Toward an evolved module of fear and fear learning. *Psychological Review, 108*(3), 483–522. https://doi.org/10.1037/0033-295X.108.3.483.

Papa, A., & Bonanno, G. (2008). Smiling in the face of adversity: The interpersonal and intrapersonal functions of smiling. *Emotion, 8*(1), 1–12. https://doi.org/10.1037/1528-3542.8.1.1.

Porges, S. W. (1995). Orienting in a defensive world: Mammalian modifications of our evolutionary heritage: A polyvagal theory. *Psychophysiology, 32*(4), 301–318.

Porges, S. W. (2007). The polyvagal perspective. *Biological Psychology, 74*, 116–143.

Porges, S. W. (2009). The polyvagal theory: New insights into adaptive reactions of the autonomic nervous system. *Cleveland Clinic Journal of Medicine, 76*(Suppl 2), S86-S90.

Porges, S. W., Doussard-Roosevelt, J. A., & Maiti, A. K. (1994). Vagal tone and the physiological regulation of emotion. *Monographs of the Society for Child Development, 59*(2–3), 167–186.

Radloff, L. S. (1977). The CES-D scale a self-report depression scale for research in the general population. *Applied Psychological Measurement, 3*(1), 385–401.

Rafaeli, E., Rogers, G. M., & Revelle, W. (2007). Affective synchrony: Individual differences in mixed emotions. *Personality and Social Psychology Bulletin, 33*(7), 915–932.

Rattiner, L. M., Davis, M., French, C. T., & Ressler, K. J. (2004). Brain-derived neurotrophic factor and tyrosine kinase receptor B involvement in amygdala-dependent fear conditioning. *Journal of Neuroscience, 24*(20), 4796–4806.

Rattiner, L. M., Davis, M., & Ressler, K. J. (2004). Differential regulation of brain-derived neurotrophic factor transcripts during the consolidation of fear learning. *Learning & Memory, 11*(6), 727–731.

Rottenberg, J., Gross, J. J., & Gotlib, I. H. (2005). Emotion context insensitivity in major depressive disorder. *Journal of Abnormal Psychology, 114*(4), 627–639. https://doi.org/10.1037/0021-843X.114.4.627.

Rottenberg, J., & Hindash, A. C. (2015). Emerging evidence for emotion context insensitivity in depression. *Current Opinion in Psychology, 4*, 1–5.

Rottenberg, J., Kasch, K. L., Gross, J. J., & Gotlib, J. H. (2002). Sadness and amusement reactivity differentially predict concurrent and prospective functioning in major depressive disorder. *Emotion, 2*(2), 135–146. https://doi.org/10.1037/1528-3542.2.2.135.

Russell, J. A. (1980). A circumplex model of affect. *Journal of Personality and Social Psychology, 39*(6), 1161.

Schwarz, N., & Clore, G. L. (1983). Mood, misattribution, and judgments of well-being: Informative and directive functions of affective states. *Journal of Personality and Social Psychology, 45*(3), 513–523.

Shean, G., & Baldwin, G. (2008). Sensitivity and specificity of depression questionnaires in a college-age sample. *The Journal of Genetic Psychology, 169*(3), 281–288.

Sheppes, G., Scheibe, S., Suri, G., Blechert, J., & Gross, J. J. (2014). Emotion regulation choice: A conceptual framework and supporting evidence. *Journal of Experimental Psychology: General, 143*, 163–181.

Singh, J. P., Larson, M. G., O'Donnell, C. J., Tsuji, H., Evans, J. C., & Levy, D. (1999). Heritability of heart rate variability: The Framingham Heart Study. *Circulation, 99*, 225–2254.

Soliman, F., Glatt, C. F., Bath, K. G., Levita, L., Jones, R. M., Pattwell, S. S., Jing, D., Tottenham, N., Amso, D., Somerville, L. H., Voss, H. U., Lover, G., Ballon, D. J., Liston, C., Teslovich, T., van Kempen, T., Lee, F. S., & Casey, B. J. (2010). A genetic variant BDNF polymorphism alters extinction learning in both mouse and human. *Science, 327*, 863–867.

Sravish, A. V. S., Tronick, E., Hollenstein, T., & Beeghly, M. (2013). Dyadic flexibility during the face-to-face still-face paradigm: A dynamic systems analysis of its temporal organization. *Infant Behavior and Development, 36*, 432–437.

Stange, J. P., Alloy, L. B., & Fresco, D. M. (2017). Inflexibility as a vulnerability to depression:A systematic qualitative review. *Clinical Psychology: Science and Practice*. https://doi.org/10.1111/j.1469-8986.2005.00347.x.

Stifter, C. A., Fox, N. A., & Porges, S. W. (1989). Facial expressivity and vagal tone in 5- and 10-month old infants. *Infant Behavior and Development, 12*(2), 127–137.

Tabor, H. K., Risch, N. J., & Meyers, R. M. (2001). Candidate-gene approaches for studying complex genetic traits: Practical considerations. *Nature Reviews Genetics, 7*, 263–272.

Terracciano, A., Lobina, M., Piras, M. G., Mulas, A., Cannas, A., Meirelles, O., … Schlessinger, D. (2011). Neuroticism, depressive symptoms, and serum BDNF. *Psychosomatic Medicine, 73*(8), 638–642. https://doi.org/10.1097/PSY.0b013e3182306a4f.

Thayer, J. F., Åhs, F., Fredrikson, M., Sollers, J. J., & Wager, T. D. (2012). A meta-analysis of heart rate variability and neuroimaging studies: Implications for heart rate variability as a marker of stress and health. *Neuroscience & Biobehavioral Reviews, 36*(2), 747–756.

Thayer, J. F., Hansen, A. L., Saus-Rose, E., & Johnsen, B. H. (2009). Heart rate variability, prefrontal neural function, and cognitive performance: The neurovisceral integration perspective on self-regulation, adaptation, and health. *Annals of Behavioral Medicine, 37*(2), 141–153. https://doi.org/10.1007/s12160-009-9101-z.

Tugade, M. M., & Fredrickson, B. J. (2007). Regulation of positive emotions: Emotion regulation strategies that promote resilience. *Journal of Happiness Studies, 8*, 311–333.

Van Winkel, M., Peeters, F., van Winkel, R., Kenis, G., Collip, D., Geschwind, N., … Wichers, M. (2014). Impact of variation in the BDNF gene on social stress sensitivity and the buffering impact of positive emotions: Replication and extension of

a gene-environment interaction. *European Neuropsychopharmacology, 24*(6), 930–938. https://doi.org/10.1016/j.euroneuro.2014.02.005.

Verhagen, M., van der Meij, A., van Deurzen, PaM., Janzing, J. G. E., Arias-Vásquez, A., Buitelaar, J. K., & Franke, B. (2010). Meta-analysis of the BDNF Val66Met polymorphism in major depressive disorder: Effects of gender and ethnicity. *Molecular Psychiatry, 15*(3), 260–271. https://doi.org/10.1038/mp.2008.109.

Vrana, S. R., & Rollock, D. (2002). The role of ethnicity, gender, emotional content, and contextual differences in physiological, expressive, and self-reported emotional responses to imagery. *Cognition and Emotion, 16*(1), 165–192. https://doi.org/10.1080/02699930143000185.

Waugh, C. E., Thompson, R. J., & Gotlib, I. H. (2011). Flexible emotion responsiveness in trait resilience. *Emotion, 11*, 1059–1067.

Westphal, M., Seivert, N. H., & Bonanno, G. A. (2010). Expressive flexibility. *Emotion, 10*(1), 92–100.

Wichers, M., Kenis, G., Jacobs, N., Myin-Germeys, I., Schruers, K., Mengelers, R., … van Os, J. (2008). The psychology of psychiatric genetics: Evidence that positive emotions in females moderate genetic sensitivity to social stress associated with the BDNF Val-sup-6-sup-6Met polymorphism. *Journal of Abnormal Psychology, 117*(3), 699–704. https://doi.org/10.1037/a0012909.

Yang, A. C., Chen, T. J., Tsai, S. J., Hong, C. J., Kuo, C. H., Yang, C. H., & Kao, K. P. (2010). BDNF Val66Met polymorphism alters sympathovagal balance in healthy subjects. *American Journal of Medical Genetics B. Neuropsychiatric Genetics, 153B*, 1024–1030.

Yu, H., Wang, D., Wang, Y., Liu, T., Lee, F. S., & Chen, Z. (2012). Variant brain-derived neurotrophic factor Val66Met polymorphism alters vulnerability to stress and response to antidepressants. *The Journal of Neuroscience, 32*(12), 4092–4101. https://doi.org/10.1523/JNEUROSCI.5048-11.2012.

Zimmerman, P., & Iwanski, A. (2014). Emotion regulation from early adolescence to emerging adulthood and middle adulthood: Age differences, gender differences, and emotion-specific developmental variations. [Special section: Emotion regulation across the life span]. *International Journal of Behavioral Development, 38*(2), 182–194.