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ORIGINAL ARTICLE

Dysfunctional Attitudes and Affective Responses to Daily Stressors: Separating Cognitive, Genetic, and Clinical Influences on Stress Reactivity

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Abstract Despite decades of research examining diathesis-stress models of emotional disorders, it remains unclear whether dysfunctional attitudes interact with stressful experiences to shape affect on a daily basis and, if so, how clinical and genetic factors influence these associations. To address these issues, we conducted a multi-level daily diary study that examined how dysfunctional attitudes and stressful events relate to daily fluctuations in negative and positive affect in 104 young adults. Given evidence that clinical and genetic factors underlie stress sensitivity, we also examined how daily affect is influenced by internalizing and externalizing symptoms and brain-derived neurotrophic factor (BDNF) genotype, which have been shown to influence neural, endocrine, and affective responses to stress. In multivariate models, internalizing symptoms and BDNF Val66Met genotype independently predicted heightened negative affect on stressful days, but dysfunctional attitudes did not. Specifically, the BDNF Met allele and elevated baseline internalizing symptomatology predicted greater increases in negative affect in stressful circumstances. These data are the first to demonstrate that BDNF genotype and stress are jointly associated with daily fluctuations in negative affect, and they challenge the assumption that maladaptive beliefs play a strong independent role in determining affective responses to everyday stressors. The results may thus inform the development of new multi-level theories of psychopathology and guide future research on predictors of affective lability.

Keywords Cognitive vulnerability · Brain-derived neurotrophic factor · Internalizing · Externalizing · Emotion · Stress

Introduction

Cognitive theories of psychopathology posit that negative thinking styles operate as a diathesis that, when activated by stress, leads to the onset, maintenance, and recurrence of psychiatric and behavioral problems that cause substantial distress and morbidity (Abramson et al. 1989; Alloy et al. 2006; Beck 1967, 1983; Ingram et al. 1998). A common focal point for research on this topic involves assessing the extent to which people harbor dysfunctional attitudes, which are conceptualized as rigid and maladaptive beliefs about oneself, the world, and the future. Examples of dysfunctional attitudes include "My value as a person depends entirely on what others think of me" and "If I fail at my work, then I am a failure as a person." Early research on these cognitive biases demonstrated that dysfunctional attitudes are more frequently endorsed by clinical than non-clinical populations, especially in the context of depression (e.g., Eaves and Rush 1984; Ilardi and Craighead 1999). More recently, research has suggested

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that these maladaptive beliefs may serve as an antecedent vulnerability factor for the development of psychopathology, and may also contribute to the maintenance and recurrence of psychiatric and behavioral problems over time (Hankin and Abramson 2001).

The most well-established organizing framework for research on this topic is cognitive theory (Beck 1967; Clark et al. 1999). According to cognitive theory, dysfunctional attitudes are embedded in a diathesis-stress framework that aims to explain the development, maintenance, and recurrence of psychopathology, particularly anxiety disorders and depression. The underlying cognitive schemas that give rise to dysfunctional attitudes are hypothesized to remain latent until an individual experiences a stressor that activates the schemas. When activated by stress, the dysfunctional attitudes become salient to the individual and increase risk for affective and behavioral disturbance. Supporting this diathesis-stress perspective, several, but not all, longitudinal studies have demonstrated an interactive effect between dysfunctional attitudes and major stressful life events in predicting emotional pathology (Alloy et al. 2006; Brown et al. 1995; Gibb et al. 2001; Lewinsohn et al. 2001; Monroe et al. 2007; cf. Otto et al. 2007).

One issue not frequently discussed in this literature concerns the fact that the vast majority of stressors that individuals respond to on a daily basis are not major stressful life events, but rather events in the minor-to-moderate severity range (e.g., daily hassles, minor life events). Despite this fact, we are aware of only one study (i.e., Hankin 2010) that has gone beyond examining major stressful life events to focus on how dysfunctional attitudes are influenced by more minor stressors occurring on a daily basis, and data from this study indicated that dysfunctional attitudes potentiate the depressogenic effects of daily stressors. A lack of research on associations between everyday stress exposure and maladaptive cognitions is surprising for at least two reasons. First, daily stressors have the potential to shape individuals' affective states on a more frequent and ongoing basis than major stressful life events, which occur relatively infrequently; and second, understanding relations between dysfunctional attitudes and daily stressors may provide important new information about how to conceptualize relations between stress and dysfunctional attitudes in etiologic theories of psychopathology, which posit that daily fluctuations in mood are central to emotional disorders (Hankin et al. 2005).

Another critical issue in research on cognitive theory concerns whether dysfunctional attitudes exert unique effects on affective responses to stress after accounting for other factors that are known to influence stress reactivity. Some prior research has challenged the view that dysfunctional attitudes are conceptually independent from broader vulnerabilities for internalizing distress. For example, irrational thinking, low self-esteem, and pessimism have all been considered facets of neuroticism (Costa and McCrae 1992; Eysenck and Eysenck 1975; Scheier et al. 1994). Moreover, although this issue has been examined only minimally, at least one study has shown that dysfunctional attitudes are related to depression through their association with neuroticism (Zinbarg et al. 2014). Therefore, much more research is needed to demarcate the influence that dysfunctional attitudes have on affective responses to daily stressors while adjusting for other personality and clinical factors that also shape peoples' affective lives (Clark et al. 1994; Hankin and Abramson 2001).

Dysfunctional attitudes are a potentially important factor that can contribute to a person's vulnerability for stress-induced changes in affect, but they nevertheless represent functioning at only one level of analysis—namely, the cognitive level. To address this issue, some investigators have recently broadened the scope of research on vulnerability for affective lability to account for the fact that cognitive factors interact with biological processes and social-environmental exposures to shape risk for affective disorders. Indeed, several multi-factorial models of psychopathology have now been proposed (e.g., Gibb et al. 2013; Kendler 2008; Slavich and Irwin 2014; Slavich et al 2010). The most rapidly growing body of research in this context focuses on how genetic factors interact with environmental exposures to shape risk for affective disorders (e.g., Caspi et al. 2010; Munafó et al. 2009). Although this work has received criticism (e.g., Risch et al. 2009), several meta-analytic reviews have demonstrated that when a priori hypotheses and good measurement techniques are employed (especially for assessing stress), some key hypothesized gene–environment interactions tend to replicate and predict biological and affective outcomes, including prospective risk for depression (Hosang et al. 2014; Karg et al. 2011; see also Monroe and Reid 2008).

One genetic factor that has received substantial attention, given that it has been implicated in shaping affective responses to stress, involves variation in the gene that encodes brain-derived neurotrophic factor (BDNF). BDNF plays a critical role in neurogenesis (i.e., the creation of new neurons) and long-term potentiation (i.e., the increase in signal transmission between neurons), which in turn influence several higher-order processes such as learning and memory, especially in the hippocampus and cerebral cortex. BDNF may also be related to the plasticity and survival of dopaminergic, cholinergic, and serotonergic neurons in the brain, which can greatly affect risk for major psychological disorders, including anxiety disorders, depression, and schizophrenia (Angelucci et al. 2005). Early research on this topic using animal models of depression implicated BDNF in shaping rodents'

depression-like responses to stress (for a review, see Duman and Monteggia 2006). More recently, this work has been extended into humans to test multi-factorial models of psychopathology.

The majority of research on BDNF in humans has focused on a single nucleotide polymorphism in the BDNF gene called Val66Met (rs6265). Several well-controlled experimental studies have examined biological and affective correlates of variation at this genetic locus and found that Val66Met genotype modulates neural, endocrine, and affective responses to emotional and stressful stimuli (Gatt et al. 2009; Lau et al. 2010; Montag et al. 2008; Mukherjee et al. 2011; Schofield et al. 2009; Wang et al. 2012). The majority of this research has linked the Met (vs. the Val) allele with greater reactivity to emotional or stressful events (cf. Perroud et al. 2008). Similar findings have emerged from a growing line of research on the molecular genetic correlates of cognitive vulnerability for emotional disorders. In this context, presence of the Met allele, in contrast to Val allele homozygosity, has been associated with elevated levels of rumination in response to life stress (Clasen et al. 2011) and diminished recall of positive words in a self-referent encoding task (van Oostrom et al. 2012), although not all studies have found this effect (e.g., Haeffel et al. 2012).

Most relevant for psychopathology research is the fact that several longitudinal studies have now shown that Val66Met genotype predicts risk for major depression following exposure to severe stressful life events, with Met carriers exhibiting a greater likelihood of developing depression following major life stress compared to their Val/Val counterparts (e.g., Aguilera et al. 2009; Brown et al. 2014; Wichers et al. 2008). Although some contradictory results have been reported (e.g., Bresin et al. 2013) and some evidence suggests that BDNF gene–environment interactions may be more pronounced for childhood than for adulthood life stress (Perea et al. 2012), a recent meta-analytic review of 22 studies found that having a Met allele at the Val66Met locus is a reliable marker of risk for stress-induced depression (Hosang et al. 2014). As discussed earlier in regard to dysfunctional attitudes, however, no studies to date have examined the role that variation at this important genetic locus plays in influencing affective responses to daily stressors, nor have any studies examined how dysfunctional attitudes and BDNF Val66Met genotype interact to predict differences in affective responses to daily life stress.

Present Study

To address these limitations in existing research, we conducted a multi-level daily diary study, which integrated information from cognitive, genetic, and social-environmental levels of analysis, and used hierarchical linear modeling (HLM) techniques to elucidate the independent and joint effects that dysfunctional attitudes, BDNF genotype, and daily life stress have on daily fluctuations in negative affect. This paradigm enabled us to examine for the first time diathesis-stress predictions within the context of an expanded cognitive vulnerability framework that incorporates a genetic factor that has been shown to predict affective, biological, and clinical responses to stress. Given evidence showing that blunted positive emotional responses to stress are associated with increased risk for affective disorders such as depression (e.g., Mineka et al. 1998; Watson and Naragon-Gainey 2010), we also examined the independent and joint effects that dysfunctional attitudes, BDNF genotype, and life stress have on daily fluctuations in positive affect.

Based on findings from between-subjects research linking attitudinal biases with clinical depression (Alloy et al. 2006; Brown et al. 1995; Gibb et al. 2001; Monroe et al. 2007), and the only other daily process study that has examined dysfunctional attitudes (i.e., Hankin 2010), we hypothesized that greater levels of dysfunctional attitudes would potentiate negative affective responses to daily stressors. Regarding BDNF genotype, consistent with prior laboratory-based studies linking BDNF variation with differential psychological and biological reactivity to emotional stimuli (e.g., Gatt et al. 2009; Wang et al. 2012), we predicted that Met allele carriers would report higher levels of negative affect on stressful days compared to their Val/Val counterparts. Although dysfunctional attitudes and the Val66Met polymorphism have not been investigated in direct relation to positive affect, both of these risk markers—either in isolation, or jointly with life stress—have been previously associated with depression, a hallmark feature of which is anhedonia. Therefore, we also predicted that more extreme dysfunctional attitudes and Met allele status would be associated with diminished positive affect on high stress days.

Finally, to delineate the boundaries of attitudinal influences on daily negative and positive affect, we compared the effects of dysfunctional attitudes on affective responses to daily stressors with the effects attributable to trait levels of internalizing and externalizing symptoms. As discussed earlier, cognitive biases, including dysfunctional attitudes, are sometimes conceptualized as facets of an overarching internalizing spectrum, as opposed to independent vulnerability factors (e.g., Costa and McCrae 1992), and studies have found that the depressogenic effects of dysfunctional attitudes may be accounted for by co-occurring processes such as subclinical depression and personality pathology (e.g., Ilardi et al. 1997; Otto et al. 2007). We therefore examined the effects dysfunctional attitudes have on stress-affect relations while statistically adjusting for baseline levels of internalizing and externalizing symptomatology.

We hypothesized that internalizing symptoms would potentiate the effects of daily stress on negative and positive affect due to the close correspondence of internalizing pathology and trait neuroticism, which is known to predict exaggerated affective responses to minor stress (Lahey 2009). If cognitive effects were found to be robust while controlling for internalizing and externalizing features, this would suggest that dysfunctional attitudes operate as a unique risk factor independent of clinical symptomatology.

Methods

Participants

Participants were 104 young adults enrolled in an introductory psychology course at a large, ethnically diverse university on the west coast. The sample included 76 females (73.1 %) and 28 males (26.9 %), with a mean age of 19.64 years ($SD = 4.61$). Forty-seven participants (45.2 %) self-identified as Caucasian, 45 (43.3 %) as Latino/a, 5 (4.8 %) as biracial, 3 (2.9 %) as Asian, 1 (1.0 %) as Native American, and 3 (3.0 %) as "other."

Procedures

During a baseline study visit, participants completed self-report assessments of dysfunctional attitudes and internalizing and externalizing symptomatology. They also provided a saliva sample for genotyping and were instructed on how to complete the online daily diary questionnaire. Participants were emailed a link to the online diary on the evening of the baseline session and the 13 subsequent nights. Diaries were intended to be completed as late at night as was convenient; the admissible period for responses was 8PM to 3AM. All study procedures were approved by the institutional review board of the University of California, Los Angeles, and all participants provided informed consent at study entry.

Measures

Baseline Measures

Dysfunctional Attitudes The Dysfunctional Attitude Scale (DAS; Weissman and Beck 1978) is a 40-item questionnaire designed to measure cognitive vulnerability to internalizing pathology. It includes items indexing a variety of rigid, negative, and perfectionistic attitudes. The DAS is widely used in psychopathology research, and prior studies have reported good-to-excellent levels of internal consistency, test–retest reliability, and criterion validity (e.g., Dobson and Breiter 1983). In the present sample, Cronbach's alpha for the DAS was .87. Based on evidence for the scale's unidimensionality (Zuroff et al. 1999), DAS total score was used to index overall dysfunctional attitudes in the present analyses.

Internalizing and Externalizing Symptoms The Young Adult Self Report questionnaire (YASR; Achenbach 1997) includes 119 items that assess internalizing symptoms, externalizing symptoms, and a variety of other clinical domains that were not considered in the present analyses (e.g., somatic complaints, attention problems). Achenbach (1997) has compiled extensive data to support the predictive validity, internal consistency, and test–retest reliability of the YASR scales. In the present sample, Cronbach's alpha values for the internalizing and externalizing scales were .87 and .72, respectively. We used clinical cutoffs recommended by Achenbach (1997) for descriptive purposes to indicate the portion of the sample in the clinical or borderline clinical range on internalizing and/or externalizing symptoms (see Results).

Assessment of Daily Affect and Stressful Events

Stressful Events Participants completed a daily survey inquiring about their possible experience of 16 different stressful events. The survey was modeled off of previous self-report instruments designed to elicit information about a wide range of stressors that are frequently experienced by undergraduate populations (e.g., Seidlitz and Diener 1993; Shahar et al. 2003). Stressors included in the stress assessment inventory covered several core life domains, such as interpersonal, occupational, academic, financial, and health. Example items included "Was rejected or excluded by others (group, significant other, friend, etc.)," "Fight or argument among social group to which you belong," and "Did poorly on, or failed, an important exam or major project" (see Appendix for complete inventory). Participants indicated the number of times each stressful event occurred per day. This information was then used to compute a total daily stress burden, indexed as the sum of all stressors occurring on a given day.

Daily Positive and Negative Affect We used a short form of the Positive and Negative Affect Schedule (PANAS), which was originally developed by Watson et al. (1988) and is widely used in the affective sciences. The Short PANAS (Kercher 1992; Mackinnon et al. 1999) includes five items indexing positive affect and five items indexing negative affect. Its internal consistency and criterion validity have been documented in several large-scale studies (e.g., Mackinnon et al. 1999). In the present project, participants were asked to rate the extent to which they experienced each emotion over the course of each day on a

scale from 1 (*very slightly or not at all*) to 5 (*very much*). Averaged across the 14 days of the study, the positive affect scale (including the adjectives Inspired, Alert, Excited, Enthusiastic, and Determined) and negative affect scale (including the adjectives Afraid, Upset, Nervous, Scared, and Distressed) had internal consistency reliabilities of .91 and .92, respectively.

Genotyping

Saliva samples for DNA analyses were collected under researcher observation using Oragene saliva collection kits (DNA Genotek, Kanata, Canada). Genotyping was performed at the UCLA Genotyping and Sequencing Core. The Val66Met polymorphism (rs6265) was genotyped using a 5′ nuclease assay to discriminate between the two alleles (i.e., Val vs. Met; Taqman SNP Genotyping Assay C__11592758_10, Applied Biosystems, Grand Island, NY). Polymerase chain reactions were performed using 5-μL reaction volumes in 384-well plates with 5 ng of DNA and Taqman genotyping master mix from Applied Biosystems. The standard protocol provided with the kit was followed. End point reads of fluorescence levels were obtained with an ABI 7900HT Sequence Detection System. The genotype frequencies at Val66Met in the present sample were Val/Val = 73, Val/Met = 28, and Met/Met = 3, and did not deviate from Hardy–Weinberg equilibrium, χ^2 (1, 104) = 0.03, p = .99.

Data Analytic Plan

HLM was used to analyze the daily influences of stress, dysfunctional attitudes, BDNF genotype, and clinical symptoms on positive and negative affect. Associations between same-day stress exposure and positive and negative affect were examined using the following HLM functions:

$$\mathrm{NA}_t = \pi_0 + \pi_1(\mathrm{Stress}_t) + \pi_2(\mathrm{NA}_{t-1}) + e_t$$

$$\begin{aligned}\pi_{0j} = {} & \beta_{00} + \beta_{01}\left(\mathrm{Gender}_j\right) + \beta_{02}\left(\mathrm{Internalizing}_j\right) \\ & + \beta_{03}\left(\mathrm{Externalizing}_j\right) + \beta_{04}\left(\mathrm{Dysfunctional\ Attitudes}_j\right) \\ & + \beta_{05}\left(\mathrm{BDNF}_j\right) + u_{0j}\end{aligned}$$

$$\pi_{1j} = \beta_{10} + u_{1j}$$

$$\pi_{2j} = \beta_{20} + u_{2j},$$

where NA_t represents negative affect on Day_t (an equivalent set of functions was specified for the positive affect analyses), Stress_t represents the count of stressors on Day_t, NA_{t-1} represents levels of negative affect reported on Day_{t-1}, $\mathrm{Internalizing}_j$ and $\mathrm{Externalizing}_j$ represent responses to the YASR clinical scales, $\mathrm{Dysfunctional\ Attitudes}_j$ reflects DAS score, and BDNF_j represents the contrast between Val homozygotes and Met allele carriers.

All Level 1 variables were person-mean centered, such that Stress_t indicated the difference between the number of stressors occurring on Day_t for a given participant and that participant's mean number of daily stressors across all 14 days. Gender and BDNF genotype contrasts were entered un-centered into Level 2 equations, whereas baseline YASR and DAS scores were grand-mean centered.

Cross-level interactions of DAS and BDNF with the total number of daily stressors were specified using the same Level 1 and Level 2 equations specified above, except that gender, YASR clinical scales, DAS, and BDNF genotype were added as Level 2 predictors of the Level 1 coefficient representing the stress-affect association (π_1), as shown below:

$$\mathrm{NA}_t = \pi_0 + \pi_1(\mathrm{Stress}_t) + \pi_2(\mathrm{NA}_{t-1}) + e_t$$

$$\begin{aligned}\pi_{0j} = {} & \beta_{00} + \beta_{01}\left(\mathrm{Gender}_j\right) + \beta_{02}\left(\mathrm{Internalizing}_j\right) \\ & + \beta_{03}\left(\mathrm{Externalizing}_j\right) \\ & + \beta_{04}\left(\mathrm{Dysfunctional\ Attitudes}_j\right) \\ & + \beta_{05}\left(\mathrm{BDNF}_j\right) + u_{0j}\end{aligned}$$

$$\begin{aligned}\pi_{1j} = {} & \beta_{10} + \beta_{11}\left(\mathrm{Gender}_j\right) + \beta_{12}\left(\mathrm{Internalizing}_j\right) \\ & + \beta_{13}\left(\mathrm{Externalizing}_j\right) + \beta_{14}\left(\mathrm{Dysfunctional\ Attitudes}_j\right) \\ & + \beta_{15}\left(\mathrm{BDNF}_j\right) + u_{1j}\end{aligned}$$

$$\pi_{2j} = \beta_{20} + u_{2j}.$$

Results

Descriptive Statistics

Responses to the YASR indicated a moderate degree of clinical symptomatology in the present sample (see Table 1). Following Achenbach's (1997) guidelines, 18 participants qualified for clinically significant internalizing pathology and four participants qualified for clinically significant externalizing pathology. The level of dysfunctional attitudes observed was consistent with prior research in non-clinical samples (e.g., Hankin 2010). Table 1 presents descriptive statistics for all between-person variables, stratified by BDNF genotype. None of the main predictors (i.e., YASR scales, DAS, or count of daily stressors) were significantly related to BDNF genotype. The weak association between daily stress and genotype ruled out the possibility of gene–environment correlation, which can be problematic for the interpretation of gene–environment interactions (Moffitt et al. 2005). As can be seen in

Table 1 Descriptive statistics for primary study variables by BDNF genotype

	BDNF genotype			Contrast (χ^2 or t)
	Val/Val	Met/+	Total	
N	73	31	104	
Mean (*SD*) DAS	123.51 (23.72)	127.23 (33.31)	124.62 (26.82)	0.65
Mean (*SD*) YASR internalizing	15.74 (7.72)	15.84 (7.30)	15.76 (7.56)	0.61
Mean (*SD*) YASR externalizing	7.73 (4.43)	8.32 (5.10)	7.90 (4.62)	0.60
Mean (*SD*) daily stressors	1.23 (1.04)	1.37 (1.15)	1.27 (1.07)	0.63
Mean (*SD*) daily positive affect	11.11 (3.07)	11.17 (4.10)	11.12 (3.39)	0.09
Mean (*SD*) daily negative affect	8.59 (2.29)	9.43 (3.71)	8.84 (2.79)	1.43
Number (%) female	55 (75.3)	21 (67.7)	76 (73.1)	0.64
Number (%) White	36 (49.3)	11 (35.5)	47 (45.2)	1.68

Met/+ represents the combination of Met/Met ($n = 3$) and Val/Met ($n = 28$) genotypes; *N*, sample size; *DAS* Dysfunctional Attitude Scale, *YASR* Young Adult Self Report. Descriptive statistics for daily variables were computed by first calculating the within-person value for each participant across time-points and then averaging across participants. Contrasts reflect mean (*t*-tests) or frequency (Pearson Chi square tests) comparisons between the Val/Val and Met/+ groups. None of the contrasts approached statistical significance ($ps > .10$)

Table 2 Correlations among between-person factors

	1	2	3	4
1. DAS	–			
2. YASR internalizing	.62***	–		
3. YASR externalizing	.14	.29**	–	
4. Gender	−.14	−.16	−.03	–
5. Ethnicity	−.10	−.15	−.11	.03

For gender, female = 0, male = 1. For ethnicity, White = 0, other ethnicities = 1

DAS Dysfunctional Attitude Scale, *YASR* Young Adult Self Report

** $p < .01$, *** $p < .001$

Table 2, internalizing and externalizing symptoms were moderately correlated ($r = .29$, $p < .01$). Additionally, dysfunctional attitudes were strongly correlated with internalizing symptoms ($r = .62$, $p < .001$), but not externalizing symptoms ($r = .14$, $p = .44$).

The daily affect scales demonstrated excellent internal consistency. Averaged across 14 days, Cronbach's alpha values for negative affect and positive affect were .92 and .91, respectively. Participants reported 1.27 stressors per day, on average. The most prevalent stressors were school-related events and medical problems (a rate of approximately one event every three days); in contrast, damaged or lost property events occurred least frequently (one event every 100 days). Participants completed an average of 11.63 diaries on time (i.e., before 3AM the day after they were mailed). This response rate of 83.1 % is similar to that of prior studies in similar samples (e.g., Sahl et al. 2009). Compliance rates were unrelated to DAS score, BDNF genotype, or YASR scores ($ps > .10$). In addition, the pattern and statistical significance of results were unaltered when participants who missed more than 3 surveys were omitted from analyses. Therefore, the results presented below reflect analyses involving the entire sample.

Dysfunctional Attitudes, BDNF, and Affective Reactivity to Daily Stress

Before testing our main hypotheses regarding the relations between dysfunctional attitudes, BDNF, and clinical dimensions with stress responsivity, we first examined their main effects on average levels of negative and positive affect over the course of the entire study. As shown in Table 3, neither dysfunctional attitudes nor BDNF variation were directly associated with mean affect levels (π_0). The relation between baseline internalizing symptoms and mean daily levels of negative affect was the only statistically significant association between baseline characteristics and affect over the 14-day study period ($b = 1.23$, $SE = 0.34$, $p < .001$).

Next, we examined daily (within-person) relations between stress and negative and positive affect. As hypothesized, stressful events on Day t were positively associated with negative affect and inversely associated with positive affect on Day t (see Table 3, row β_{10}). Inconsistent with the cognitive vulnerability hypothesis, DAS scores were not related to the strength of association between daily stress exposure and daily levels of either negative or positive affect. In contrast, BDNF genotype was a statistically significant moderator of the effects of the daily stress exposure on daily negative affect. Simple effects analyses designed to probe this effect revealed that, as hypothesized, Met allele carriers exhibited greater negative affective reactions to daily stressors ($b = 1.09$, $SE = 0.13$, $p < .001$) than Val homozygotes ($b = 0.56$,

Table 3 Hierarchical linear models of BDNF, dysfunctional attitudes, and daily stress predicting daily negative and positive affect

Predictors	Negative affect$_t$			Positive affect$_t$		
	b	*SE*	*p*	*b*	*SE*	*p*
For overall intercept, π_0						
Intercept, β_{00}	8.54	0.20	<.001	10.85	0.36	<.001
Gender, β_{01}	−0.58	0.45	.195	0.49	0.78	.527
Internalizing, β_{02}	1.23	0.34	<.001	−0.53	0.43	.225
Externalizing, β_{03}	0.22	0.22	.312	−0.27	0.30	.375
Dysfunctional attitudes, β_{04}	0.34	0.38	.376	−0.15	0.46	.746
BDNF, β_{05}	−0.83	0.59	.164	−0.23	0.79	.768
For stress$_t$ slope, π_1						
Intercept, β_{10}	1.06	0.13	<.001	−0.54	0.11	<.001
Gender, β_{11}	−0.18	0.22	.413	0.29	0.23	.206
Internalizing, β_{12}	0.32	0.15	.030	0.21	0.11	.061
Externalizing, β_{13}	−0.28	0.11	.011	0.11	0.10	.281
Dysfunctional attitudes, β_{14}	−0.10	0.12	.411	−0.15	0.11	.190
BDNF, β_{15}	0.46	0.20	.023	−0.26	0.22	.238
For affect$_{t-1}$ slope, π_2						
Intercept, β_{20}	0.10	0.03	.004	0.24	0.04	<.001

For gender, female = 0, male = 1. For BDNF, Val/Val = 0, Met/+ = 1. Affect$_{t-1}$ represents the prior day's levels of negative affect or positive affect. All continuous variables were standardized prior to entry in the model

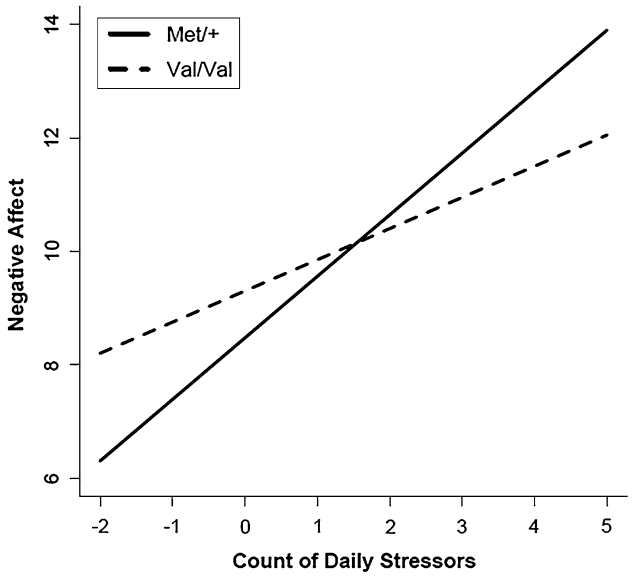

Fig. 1 Within-person associations between daily stress exposure and negative affect as a function of BDNF genotype. On the *x*-axis, the count of daily stressors is person-centered, such that 0 represents a person's average count of daily stressors

$SE = 0.19$, $p < .01$). The nature of this BDNF Genotype × Stress Exposure interaction in the prediction of daily negative affect is illustrated in Fig. 1.

Visual inspection of the pattern of interaction suggested that the gene–stress interaction effect might be more consistent with a differential susceptibility model than a diathesis-stress model (Belsky and Pluess 2013). We thus performed follow-up analyses to determine whether the Met allele conferred statistically significant protection from negative affect at low levels of stress exposure but also vulnerability to negative affect at high levels of stress exposure, as would be predicted by the differential susceptibility hypothesis. We followed the procedures outlined by Roisman et al. (2012) to establish regions of significance (RoS) for the BDNF genotype—that is, areas wherein the Val and Met genotype groups exhibited statistically significant (at a .05 alpha level) differences on negative affect—at both the low and high poles of the daily stress exposure dimension (i.e., *x*-axis of Fig. 1). The RoS at the low pole of stress encompassed the area at −0.47 and below, whereas the RoS at the high pole of stress exposure included the area at 20.22 and above. Specifically, the Val homozygotes endorsed greater NA under conditions of low stress, and the Met carriers endorsed greater NA under extremely stressful conditions. However, because the stress variable was person-centered in HLM analyses with a mean of 0 and a standard deviation of 1.07, the RoS at the high end of stress exposure (starting at a value of 20.22) was outside the *research range of interest* of our independent variable (Pedhazur 1982, p. 461). Overall, then, the pattern of interaction was not consistent with a differential susceptibility model.

BDNF genotype did not moderate the effects of daily stress exposure on positive affect (see Table 3, row β_{15}). Table 3 also shows that internalizing symptoms ($b = 0.32$, $SE = 0.15$, $p < .05$) and externalizing symptoms ($b = -0.28$, $SE = 0.11$, $p < .05$) predicted the magnitude of negative affect responses to daily stress, but in opposite directions. As expected, participants who were high on the internalizing dimension experienced greater stress-linked increases in negative affect. Additionally, participants who were low on the externalizing dimension similarly exhibited potentiated negative affect responses to daily stress.

To test for a possible joint influence of cognitive and genetic vulnerabilities on daily affective responses to stress, we examined the three-way interaction between dysfunctional attitudes, BDNF genotype, and daily stress exposure in predicting negative and positive affect. Neither of these interactions approached statistical significance (*p*s > .10), indicating that dysfunctional attitudes did not augment the effect of the Met allele on affective responses to daily stress. Likewise, gender did not moderate the Dysfunctional Attitudes × Stress Exposure or BDNF Genotype × Stress Exposure interactions in predicting daily negative or positive affect (*p*s > .10). It is also important to note that the BDNF × Stress Exposure interaction did not vary across

Caucasian versus Latino ethnic groups (which collectively made up approximately 93 % of our sample) for either negative affect ($b = -0.79$, $SE = 0.52$, $p = .13$) or positive affect ($b = -0.78$, $SE = 0.53$, $p = .15$).

Secondary Analyses

Given the strong correlation between dysfunctional attitudes and internalizing symptoms ($r = .62$) reported above, we conducted secondary analyses to examine the effects of dysfunctional attitudes on affective reactivity to daily stress without adjusting for concurrent clinical symptomatology. This analysis revealed that, when only dysfunctional attitudes, BDNF genotype, and gender were entered as between-subjects predictors, dysfunctional attitudes were positively associated with average levels of negative affect over the 14-day study period (equivalent to Table 3, row β_{05}; $b = 1.10$, $SE = 0.25$, $p < .001$), but they did not moderate the association between daily stress exposure and negative affect ($b = 0.06$, $SE = 0.11$, $p = .57$). In contrast, dysfunctional attitudes were unrelated to average levels or stress-related changes in positive affect ($b = -0.48$, $SE = 0.35$, $p = .17$ and $b = -0.01$, $SE = 0.10$, $p = .95$, respectively). The full results from these reduced models are available upon request.

Discussion

Longitudinal research has demonstrated that dysfunctional attitudes interact with stressful circumstances to prospectively predict higher rates of psychopathology, particularly depression (e.g., Alloy et al. 2006; Lewinsohn et al. 2001). The present study extends this important body of work by evaluating the diathesis-stress hypothesis in a novel context–namely, affective responses to everyday stressful events. More specifically, we assessed participants' stress exposure and affective experiences over 14 consecutive days and examined whether stress–affect associations were magnified for persons endorsing more dysfunctional attitudes. We also tested these predictions within an expanded, multi-level cognitive vulnerability framework that incorporated internalizing symptoms, externalizing symptoms, and a genetic polymorphism in the BDNF gene (i.e., Val66Met, rs6265). There were two main findings: first, consistent with hypotheses, BDNF Met allele carriers exhibited more intense negative affective responses on stressful days than Val homozygotes; and second, contrary to expectations, dysfunctional attitudes did not moderate daily associations between stress exposure and negative or positive affect.

Research over the past several decades has generally supported the hypothesis that rigid and perfectionistic patterns of thinking confer vulnerability for emotional distress in the face of environmental adversity (Ingram et al. 1998). Therefore, the relatively weak association that we observed between dysfunctional attitudes and affective responses to daily life stress was unexpected. At least two explanations are possible. First, there was sizeable overlap between our measures of dysfunctional attitudes and internalizing symptoms at baseline ($r = .62$), and this shared element necessarily was partialled out in our multivariate analysis. In fact, internalizing symptoms increased negative affect reactivity to daily stress in multivariate analyses, suggesting that, in this sample, general internalizing dysfunction was a stronger predictor of stress-linked changes in affect than dysfunctional attitudes. This interpretation is consistent with prior theorizing about the hierarchical relations between neuroticism, which is known to serve as the personologic foundation for internalizing spectrum disorders (e.g., Krueger 1999), and attitudinal biases (e.g., Clark et al. 1994). Indeed, a recent latent variable study found that prospective associations between dysfunctional attitudes and depressive and anxiety disorders were largely accounted for by their overlap with neuroticism (Zinbarg et al. 2014). Along these same lines, several longitudinal studies have demonstrated that dysfunctional attitudes do not predict risk for new onsets or recurrences of depression after adjusting for subclinical depressive symptoms, prior syndromal depression history, and/or personality pathology (e.g., Hart et al. 2001; Ilardi et al. 1997). We conducted secondary analyses to examine these issues and found that when baseline clinical symptoms were omitted from the predictive model, dysfunctional attitudes predicted *average levels* of negative affect over the 14-day study period, but did not moderate associations between daily stress exposure and affect. Therefore, in the present data, dysfunctional attitudes predicted average levels of negative affect over time (when not adjusting for baseline clinical symptoms), but had only a small effect on stress reactivity even when their overlap with internalizing symptoms was ignored.

The second possible reason for the relatively weak association observed between dysfunctional attitudes and affective responses to daily life stress may have to do with the fact that nearly all prior studies of life stress, dysfunctional attitudes, emotion dysregulation, and emotional disorders have investigated individuals' enduring affective responses to major life events. Consequently, dysfunctional attitudes may exert greater effects in the context of major life stressors than in the context of more frequently occurring, but less severe, daily events and hassles that might be expected to influence day-to-day fluctuations in affect. At the same time, it must be noted that at least one prior study has investigated associations between dysfunctional attitudes and affective responses to daily

stressors and found that within-person associations between daily life stress and depressive symptoms are greatest for persons exhibiting more dysfunctional attitudes (Hankin 2010). Given these mixed findings, additional research is clearly needed to examine the unique effects dysfunctional attitudes have on daily stress responsivity.

In addition to examining associations between dysfunctional attitudes and affective responses to daily stressors, the present study is one of the first to integrate genetic risk factors into the cognitive diathesis-stress framework (Beevers et al. 2007; for a review, see Gibb et al. 2013). As hypothesized, we found that Met allele carriers at the Val66Met locus in the BDNF gene exhibited greater negative affective responses to increasing levels of daily life stress relative to Val homozygotes. However, the pattern of interaction was not consistent with a diathesis-stress model (wherein the Met genotype serves as the diathesis), in that the only meaningful statistically significant genotype difference was the higher NA level reported by *Val* homozygotes at below-average levels of stress exposure. Nevertheless, this pattern of interaction is also at variance with a differential susceptibility model (Belsky and Pluess 2013), according to the standards offered by Roisman et al. (2012), in that the same BDNF variant does not predict better *and* worse outcomes at different levels of stress exposure (at least at meaningful levels of stress exposure). In sum, the Met allele confers greater within-person reactivity to daily stress in this sample (i.e., greater changes in NA from low- to high-stress days), but not in a manner predicted by diathesis-stress *or* differential susceptibility hypotheses.

The finding of greater within-person stress reactivity among Met carriers is generally consistent with the growing body of research showing that BDNF influences neural, endocrine, and affective responses to emotional and stressful stimuli and, more specifically, that Met allele carriers exhibit exaggerated responses in these stress-related psychological and neurobiological systems relative to Val homozygotes (e.g., Gatt et al. 2009; Montag et al. 2008; Wang et al. 2012). Converging evidence for these effects comes from naturalistic studies of life stress and depression, which have fairly consistently, but not uniformly, demonstrated that Met allele carriers are more vulnerable to depression following major stressful life events than Val homozygotes (for a recent meta-analytic review, see Hosang et al. 2014; cf. Bresin et al. 2013). The present study, however, is the first to document a stress sensitizing effect of the BDNF Met allele on negative affect in the context of daily stressful life events—an effect that was robust even when adjusting for other known determinants of stress reactivity, such as dysfunctional attitudes and internalizing and externalizing symptomatology. The findings thus support the construct validity of the BDNF gene–environment interaction hypothesis (Brown et al. 2014). Considered more broadly, the findings add to an emerging line of research on the dynamic associations between cognitive vulnerability, molecular genetics, and emotional disorders (Gibb et al. 2013), which is part of a general push toward a greater rapprochement of genetics, neuroscience, and psychology in the service of building more comprehensive, integrative explanatory models of mental and physical health (e.g., Caspi and Moffitt 2006; Kendler 2008; Slavich and Cole 2013).

Although support for the construct validity of the BDNF gene–environment interaction hypothesis to some extent mitigates the danger of false positive results, it is important to note that the sample size for the present genetic analyses was modest, increasing the likelihood of Type I error (Duncan and Keller 2011). Therefore, results involving BDNF should be interpreted with caution until replications in larger samples are available. Additionally, BDNF genotype may confer different degrees of sensitivity to various types of stressors. As a result, additional research is needed to replicate the present findings in populations with higher rates and different types of stress exposure (e.g., romantic, financial, illness-related stressors, etc.).

Several other limitations should also be noted. First, participants reported on stressors and affect at the same time, and it was therefore impossible to determine the temporal ordering of stress exposure vis-à-vis participants' affective responses. Additional research involving multiple assessment points per day (e.g., using ecological momentary assessment strategies) is necessary to resolve this issue. Second, due to time constraints on the daily assessment procedure, our inventory of stressful events was fairly brief (i.e., 16 items). Future studies with more detailed stress assessment procedures could be conducted to examine the precise severity levels and forms of daily stress that are most relevant for daily fluctuations in negative and positive affect, both in isolation and jointly with cognitive, clinical, and genetic vulnerabilities. Third, the present study examined the stress sensitizing effects of only one cognitive vulnerability factor (i.e., dysfunctional attitudes) and one genetic locus (i.e., Val66Met). Future research is thus needed to examine how other cognitive factors, such as maladaptive inferential styles or implicit attentional and memory biases, and other genetic variation influence affective responses to daily life stress. Fourth, it is possible that the Val66Met genotype was associated with some unmeasured genetic variant (i.e., linkage disequilibrium) that produced the observed effects. Likewise, although we ruled out gene–environment correlation with the daily stress measure, Val66Met may predispose to some environmental circumstances that affect daily stress reactivity. Experimental designs involving BDNF, standardized stressors, and affective outcomes are needed to

resolve these potential confounds. Fifth, although supplementary analyses in the present sample indicated that the strength of the BDNF gene–stress interaction effect was not significantly different across ethnic groups, we recommend that future research employ genomic control methods to more rigorously account for the potentially confounding influence of population stratification on genetic analyses (Devlin, Roeder, and Wasserman Devlin et al. 2001). Finally, our test of the differential susceptibility model of BDNF–environment interaction was limited because the environmental factor was not designed to have well-defined opposite poles of "stressful" versus "enriching" conditions. As such, low scores on the daily stress assessment instrument did not necessarily reflect particularly supportive or stimulating conditions. Future studies aiming to compare diathesis-stress and differential susceptibility models of gene-stress interplay should measure both positive and negative features of the environment (Roisman et al. 2012).

In summary, the present study is the first to test a diathesis-stress model of affective responses to daily stressors while incorporating cognitive, genetic, and clinical markers of risk for emotional disorders. We found that elevated internalizing symptoms and the Met allele at the BDNF Val66Met locus were both associated with heightened negative affect on stressful days. When examined in isolation, dysfunctional attitudes predicted average levels of negative affect over the entire study period, but they did not play a role in affective responses to stress in either bivariate or multivariate models, raising important questions about the role maladaptive beliefs play in shaping affective responses to everyday stressful events. The genetic findings replicate prior research implicating the Met allele in potentiated reactivity to stress, but extend this work in an important new direction by documenting the phenomenon in the flow of daily life and in the context of other factors that are known to predict affective responsivity to stress, specifically dysfunctional attitudes and internalizing and externalizing symptomatology. Additional research is needed to replicate these effects and to examine the relevance of these findings for the development and maintenance of emotional disorders. Conducting multi-factorial studies of this sort may inform the next generation of multi-level theories of psychopathology and potentially help clinicians identify new targets for treating emotional disorders that cause substantial disease burden and public concern.

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Conflict of Interest Christopher C. Conway, George M. Slavich, and Constance Hammen declare that they have no conflict of interest.

Informed Consent All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. Informed consent was obtained from all patients before their inclusion in the study.

Animal Rights No animal studies were carried out by the authors for the purposes of this article.

Appendix: Daily Stressful Life Events

- Did not have enough money to do something or buy something.
- Lost money or something important.
- Property was damaged or stolen.
- Was sick or had a medical issue.
- Did poorly on, or failed, an important exam or major project.
- Failed to achieve an important school related goal that does not involve GPA.
- Problems at work (e.g., didn't get the schedule that you requested, couldn't find someone to fill in for you).
- Problems with co-workers or boss (if different from above).
- An event that happened today related to a family member or close friend having a medical or emotional problem.
- Had an argument/problem with significant other.
- Had an argument/problem with a friend.
- Had an argument/problem with family member.
- Had an argument/problem with a professor, or project group.
- Fight or argument among social group to which you belong.
- Was rejected or excluded by others (group, significant other, friend, etc.).
- Was criticized by others (project group, significant other, friend, professor, etc.).

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