Personality Disorders: Theory, Research, and Treatment
2011, Vol. 2, No. 3, 220–229

1949-2715/11/$12.00 DOI: 10.1037/a0022317

BRIEF REPORT

Affective Instability, Family History of Mood Disorders, and Neurodevelopmental Disturbance

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The association between affective instability and both family history of mood disorders and signs of neurodevelopmental disturbance was examined in a sample of 303 adults. Affective instability was measured using the borderline personality disorder "affective instability due to a marked reactivity of mood" diagnostic criterion as assessed dimensionally using the Personality Disorder Interview—IV. Participants were interviewed concerning family history of mood disorders, with family history coded using the Family History Research Diagnostic Criteria. Minor physical anomalies, inconsistent hand use, and dermatoglyphic asymmetries were used to index neurodevelopmental disturbance. Affective instability was associated with elevated rates of family history of mood disorders, particularly among individuals who exhibited inconsistent hand use and greater minor physical anomalies. These associations could not be accounted for by shared variance with age, gender, negative affect, or personal history of mood disorders.

Keywords: affective instability, neurodevelopmental disturbance, borderline personality disorder, mood disorders, family history

Researchers have found that there are a variety of stable emotion-related traits. For example, in addition to varying in the extent to which they experience pleasant and unpleasant mood, individuals vary in the intensity and variability of their emotional experiences (e.g., Eid & Diener, 1999). These two emotional traits tend to be highly correlated (Emmons & King, 1989) and are distinguishable from individual differences in the valence of emotional experience (i.e., pleasant vs. unpleasant mood). Elevated levels of emotional variability (sometimes referred to as *affective lability*) and emotional intensity make up what many psychopathology researchers refer to as *affective instability* (Miller & Pilkonis, 2006).

There are two ways in which affective instability (i.e., elevated levels of emotional variability and intensity) is distinguishable from broader constructs such as emotion dysregulation. First, we consider the components that make up affective instability (i.e., elevated levels of emotional variability and intensity) to be overt behavioral outcomes of perturbations in a variety of emotion regulation processes (e.g., Thompson, Dizen, & Berenbaum, 2009) that collectively make up emotion dysregulation. Second, constructs such as emotion dysregulation include additional characteristics, such as understanding of emotions, and are manifested in additional emotional traits, such as anxiousness and irritability (e.g., Gratz & Roemer, 2004; Livesley, Jang, & Vernon, 1998).

Affective instability is a central feature of borderline personality disorder and bipolar disorders (e.g., Henry et al., 2001). It is also asso-

This article was published Online First March 7, 2011.

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This research was supported by Grant MH62552 from the National Institute of Mental Health. We thank Elaine Walker for her assistance concerning the measurement of neurodevelopmental disturbances and Tom Widiger for his assistance concerning the assessment of personality disorders.

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ciated with a variety of other mental disorders, including the majority of personality disorders (Miller & Pilkonis, 2006) and depression (Angst, Gamma, & Endrass, 2003). In addition, affective instability is associated with functional impairment and suicidal behaviors (Bagge et al., 2004; Miller & Pilkonis, 2006; Yen et al., 2004). As proposed by others (e.g., Siever & Davis, 1991), we hypothesized that affective instability is a stable personality trait that increases vulnerability to a variety of mental disorders (e.g., borderline personality disorder, mood disorders).

Because of its significance, it is important to determine the etiology of affective instability. In the present study, we explored whether affective instability is associated with family history of mood disorders. We hypothesized that the two would be associated based on (a) the findings of past research documenting an association between borderline personality disorder, of which affective instability is a component, and family history of mood disorders (e.g., Links, Steiner, & Huxley, 1988); and (b) our expectation that family history of mood disorders reflects, at least in part, a disposition to emotion dysregulation, which might contribute to affective instability. In fact, some researchers have posited that borderline personality disorder is part of an affective or bipolar spectrum of disorders (e.g., Deltito et al., 2001). To our knowledge, the possibility that affective instability (as opposed to borderline personality disorder more broadly) is associated with a family history of mood disorders has not been examined in past research.

In addition to examining family history of mood disorders, we also explored what we believe is an understudied and potentially important phenomenon—neurodevelopmental disturbances. Given the wide variety of cortical disturbances associated with so many mental disorders, it is not surprising that it has been hypothesized that perturbations in brain development play a role in the etiology of psychopathology (e.g., Fatemi & Folsom, 2009; Sanches, Keshavan, Brambilla, & Soares, 2008; Walker, Sabuwalla, & Huot, 2004). Based on the premise that affective instability reflects, at least in part, one or more disturbances in emotion regulation, and the evidence that various brain regions and neural circuits play a role in emotion regulation (e.g., Davidson, Fox, & Kalin, 2007), it seems plausible that neurodevelopmental disturbances are associated with affective instability.

In the present study, we examined markers of abnormal neurodevelopmental processes that are presumed to have occurred prenatally or during very early childhood. Specifically, we examined minor physical anomalies (MPAs), inconsistent hand use, and dermatoglyphic asymmetries. MPAs are mild errors in morphogenesis (e.g., adherent ear lobes; a large space between the first and second toes). Although the precise etiological origins of MPAs are not fully understood, they are believed to have prenatal origins, most likely during the first or second trimesters of gestation when most ectodermal derivatives are under development (Green, Satz, & Christenson, 1994). Considering that these areas share common embryonic (ectodermal) origins with the brain, MPAs are thought to be biological markers of neurodevelopmental disturbance (Tarrant & Jones, 1999). In fact, MPAs have been found to occur more frequently in individuals with a range of developmental disorders, such as autistic spectrum disorders and mental retardation (e.g., Smith & Bostian, 1964; Tripi et al., 2008), in individuals with schizophrenia (for a review, see Weinberg, Jenkins, Marazita, & Maher, 2007), and in individuals with bipolar disorder (for a review, see Tenyi, Trixler, & Csabi, 2009).

Like MPAs, the precise etiology of atypical hand use (of which inconsistent hand use is one type) has yet to be fully elucidated. However, the most likely time period of this neurodevelopmental deviation is the second trimester, when initial lateralization of the central nervous system occurs (Weinberger, 1995) and the direction of hand preference becomes detectible (Hepper, Shahidullah, & White, 1991). Atypical hand use has been found to be more common among individuals with autism and mental retardation (Soper et al., 1986; Soper, Satz, Orsini, Van Gorp, & Green, 1987) and among individuals with schizophrenia (Green, Satz, Smith, & Nelson, 1989). In a relatively recent study, Fasmer, Akiskal, Hugdahl, and Oedegaard (2008) found that nonrighthandedness was more common among individuals with cyclothymic, hyperthymic, or irritable temperaments.

Like MPAs and inconsistent hand use, the precise etiology of dermatoglyphic asymmetries

is not certain, although dermatoglyphics develop between the 10th and 16th weeks of gestation. Because the skin and brain develop from the same ectoderm, deviations in dermatoglyphics are thought to reflect neurodevelopmental disturbances. Several studies have found that individuals with schizophrenia exhibit greater dermatoglyphic asymmetries (e.g., van Oel et al., 2001).

Most contemporary models of mental disorders posit that psychopathological outcomes are the result of multiple interacting etiological factors. For example, the impact of genetic variations may depend on environmental factors (e.g., Moffitt, Caspi, & Rutter, 2006), and the impact of some genes may depend on the presence of other genes (e.g., Wang et al., 2009). We tested the hypothesis that neurodevelopmental disturbance would moderate the impact of family history of mood disorders on affective instability. This hypothesis was guided by the premise that the impact of family history of mental disorders might be particularly strong among individuals whose brains are not developing in an optimally healthy way and are therefore biologically prone to emotion dysregulation.

Method

Participants

The participants were 303 adults (53.1% women) between the ages of 18 and 89 years (M = 43.2 years, SD = 17.6). Of those who reported their ethnicity (98.7%), the sample was mostly European American (78.9%), with 9.4% African American, 5.4% Asian American/Asian, 2.7% Latino/a, 1.7% biracial, 1.3% Native American, and 0.7% "other." These individuals were participating in a large project examining pathways to disturbed emotions, perceptions, and beliefs (Berenbaum et al., 2008). The only exclusion criteria were inability to speak and understand English and meeting diagnostic criteria for Criterion A of schizophrenia as determined using the psychotic disorders module of the Structured Clinical Interview for *DSM–IV*. Participants were recruited from the general community, although individuals who reported signs of schizotypal traits were oversampled. Despite doing so, only seven individuals met full diagnostic criteria for schizotypal personality disorder. After complete description of the study to participants, written informed consent was obtained.

Procedure

Affective instability and borderline personality disorder traits. Borderline personality disorder traits were assessed using the Personality Disorder Interview—IV (PDI–IV) (PDI–IV; Widiger, Mangine, Corbitt, Ellis, & Thomas, 1995). In this semistructured interview, participants are asked a series of questions. For example, to assess affective instability, participants are asked questions such as "Does your mood tend to shift from one feeling to another, even during the same day?" and "Does it seem to take very little to get you upset, anxious, or angry?" For clarification, these questions are followed up as needed, with the trained interviewers making a single dimensional rating of affective instability (0 = absent; 1 = subthreshold; 2 = present; 3 = severe).[1] Interviewers were trained by Thomas Widiger, the lead developer of the PDI–IV. Interviewers were blind to the participants' family histories of psychopathology and their signs of neurodevelopmental disturbance. A second trained member of the research team (also blind to the same scores) listened to recorded PDI–IV interviews and independently rated the same criteria. When raters disagreed about whether a criterion was above or below threshold or disagreed by more than 1 point, the research team discussed the case and resolved the disagreement by consensus. Other disagreements (e.g., one rater assigned a score of 2, and the second rater assigned a score of 3) were resolved by using the mean of the two raters. Interrater reliability of affective instability ratings, measured using the intraclass correlation coefficient, treating raters as random effects and the mean of the raters as the unit of reliability, was .91.

To test whether associations with affective instability might merely reflect associations with borderline personality disorder traits (rather than being associated specifically with affective instability), we computed a score sum-

[1] In consultation with Thomas Widiger, we changed the original PDI–IV 3-point rating scale (absent, present, severe) to a 4-point scale by adding a subthreshold point to the continuum.

ming across the eight diagnostic criteria other than affective instability. Interrater reliability of this borderline personality disorder eight-criterion score, measured using the intraclass correlation coefficient, treating raters as random effects and the mean of the raters as the unit of reliability, was .96. As expected, in the present sample, affective instability and the borderline personality disorder eight-criterion score were significantly correlated, $r = .52$, $p < .01$.

Family history of mood disorders. We examined the lifetime prevalence of depression and mania in participants' first-degree (i.e., parents, siblings, and children) biological relatives. Participant responses were coded following the Family History Research Diagnostic Criteria (Andreasen, Endicott, Spitzer, & Winokur, 1977). To receive a diagnosis of depression, a family member must have experienced at least one period of 2 weeks or longer with depressed mood co-occurring with at least one other indicator of depression (e.g., suicidal behavior, hospitalization). To receive a diagnosis of mania, a family member must have experienced euphoric or irritable mood with at least two other symptoms of mania (e.g., talkative, decreased need for sleep) co-occurring with one other indicator of mania (e.g., treated for manic-like symptoms).

The interviewers who coded family history of mood disorders were aware of the participants' own history of mood disorders but were blind to the participants' levels of negative affect and borderline traits (including affective instability). Given that not all relatives had lived through the age of risk (e.g., a 20-year-old relative without a history of depression may yet develop the disorder), age-corrected prevalence or morbid risk of mood disorders in biological first-degree relatives was calculated using the Weinberg abridged method (Slater & Cowie, 1971). The risk period for depression and mania was 18–59 years.

Neurodevelopmental disturbance. To assess MPAs, we examined morphology of six specific body regions (head, eyes, mouth, ears, hands, and feet) using the original 18 items from the Waldrop and Halverson scale (1971) supplemented with four additional items from the ear and mouth regions (ear lobe size, anterior ear helix shape, palatal ridges behind upper teeth, and bifid/clefted tongue) in order to improve coverage of minor physical anomalies in these regions. The Waldrop and Halverson scale has been used extensively in previous research on psychopathology (e.g., Green et al., 1994; Weinstein, Diforio, Schiffman, Walker, & Bonsall, 1999). Assessment of MPAs was performed by graduate research assistants who had undergone systematic training in the administration of the scale. Most items were scored as either absent (0) or present (1). In accordance with recent scoring modifications (i.e., Ismail, Cantor-Graae, & McNeil, 1998), specific items (e.g., fine hair) were weighted (and thus were scored 0–2). Head circumference was scored using published norms (Eichorn & Bayley, 1962). Distance between tear ducts was scored using the sample mean and standard deviation. For both head circumference and distance between tear ducts, we coded participants with scores more than 1.5 standard deviations above the mean as having an MPA on these items. Individual item scores were summed to yield a total MPA score. The "number of (ear) asymmetries" item from the original Waldrop scale was not included in final calculations because of problems that arose in assessing and scoring this item. Participants with missing data for three or more of these items were excluded from final analyses.

Inconsistent hand use was measured using the Hand Preference Demonstration Test (Soper et al., 1986). The test consists of eight items that are intended to assess participants' hand preferences over a wide range of activities. For example, participants were asked to pick up a spoon (placed directly in front of them), and the experimenter recorded which hand the participant used. This eight-item task was administered three times over two days. Consistent with past research (Green et al., 1989), the majority of participants rarely, if ever, used different hands to perform the same action across trials. Following Green et al. (1989), we divided participants into those who used different hands on two or more occasions ($n = 48$) and those who used different hands at most one time ($n = 247$); we refer to the former group as the *inconsistent hand use group*.[2]

[2] We chose to use the liberal cutoff of 2 rather than the more conservative cutoff of 3, also used by Green et al. (1989), because relatively few (5.4%) individuals exhibited such high rates of hand use inconsistency.

Ridge count asymmetries were measured to examine dermatoglyphic asymmetries. The number of dermal ridges for each fingertip was counted with the assistance of Afix Comparator software (Lynn Peavey Co., Lenexa, KS). Following Weinstein et al. (1999), we computed the absolute difference between the numbers of ridges on each pair of corresponding fingertips on the right and left hands, which were summed to compute a total asymmetry score.

Negative affect. Negative affect experienced over the past month was measured using the 10 negative affect items from the Positive and Negative Affect Scale (Watson, Clark, & Tellegen, 1988) supplemented with five primarily low arousal negative affect items (i.e., frustrated, down, anxious, grouchy, sad); $\alpha = .94$.

Personal history of mood disorder. Lifetime and current unipolar and bipolar mood disorder diagnoses were assessed using the mood disorders section of the Structured Clinical Interview for the *DSM–IV* (First, Spitzer, Gibbon, & Williams, 1998). Interviews were recorded and were rated by a second diagnostician. Interrater reliabilities, measured using kappa, were 0.90 and 0.95 for current and lifetime major depressive disorder and 1.0 for both current and lifetime bipolar disorder. Approximately half (52%) of participants had lifetime unipolar diagnoses, 5% had lifetime bipolar diagnoses, 9% had current unipolar diagnoses, and 0.67% had current bipolar diagnoses.

Results

We began by examining whether the hypothesized predictors of affective instability, family history of mood disorders, and signs of neurodevelopmental disturbance were associated. Correlations among these variables and descriptive statistics are presented in Table 1. As can be seen in Table 1, as expected, family history of depression and family history of mania were significantly correlated. Also as expected, MPAs and inconsistent hand use were significantly correlated. In contrast, ridge count asymmetries were not significantly correlated with either MPAs or inconsistent hand use. Family history of mood disorders was not significantly associated with signs of neurodevelopmental disturbance.

To examine whether affective instability was associated with family history of mood disorder, neurodevelopmental disturbance, or their interaction, after having taken into account age, gender, and negative affect, we conducted hierarchical regression analyses (using centered variables), entering age, gender, and negative affect in the first step, a family history of mood disorder variable and a neurodevelopmental disturbance variable in the second step, and the interaction between the family history and neurodevelopmental disturbance variables in the third step. Thus, for all three signs of neurodevelopmental disturbance (MPAs, inconsistent hand use, and ridge count asymmetry), we conducted two regression analyses (testing moderation of family histories of depression and mania), for a total of six regression analyses. Ridge count asymmetries were not significantly associated with any of the other variables measured in this study, nor did they significantly moderate any associations. In contrast, as summarized in Tables 2 and 3, family histories of mood disorders interacted with both MPAs and inconsistent hand use to predict affective instability. The sizes of these moderation effects were notable; as pointed out by several researchers (e.g., Champoux & Peters, 1987; McClelland & Judd, 1993), the change in R^2 due to moderation ef-

Table 1
Correlations Among and Descriptive Statistics for Neurodevelopmental Disturbance and Family History Variables

Variable	1	2	3	4	*M*	*SD*
1. Family history of depression	—	—	—	—	0.32	0.33
2. Family history of mania	.28**	—	—	—	0.04	0.13
3. Minor physical anomalies	.09	.08	—	—	4.3	2.9
4. Hand use inconsistency	−.01	.08	.18**	—	16.3[a]	—
5. Ridge count asymmetry	.04	.04	.10	.05	10.5	6.2

[a] Percentage of participants exhibiting inconsistent hand use.
** $p < .01$.

Table 2
Summary of Hierarchical Multiple Regression Analyses Using Family History of Mania and Neurodevelopmental Disturbance (MPAs or Inconsistent Hand Use) To Predict Affective Instability

Variable	MPAs		Inconsistent hand use	
	β	ΔR^2	β	ΔR^2
Step 1		.12**		.12**
Age	.02		.02	
Gender	−.06		−.06	
Negative affect	.34**		.34**	
Step 2		.01		.01
Family history	.08		.07	
Neurodevelopmental disturbance	.01		.06	
Step 3		.02*		.02*
Family History × Neurodevelopmental Disturbance	.13*		.16*	

Note. MPAs = minor physical anomalies.
* $p < .05$. ** $p < .01$.

fects are typically quite small, and changes as low as .01 are usually considered important.

The nature of the moderation effects are illustrated in Table 4. In all cases of moderation, the pattern was remarkably consistent: Family history of psychopathology was associated with affective instability among individuals with higher levels of neurodevelopmental disturbance, but was weakly or not at all associated with affective instability among individuals with lower levels of neurodevelopmental disturbance. On the left side of Table 4, we present the correlations between affective instability and the family history variables separately for individuals with inconsistent and consistent hand use. Among individuals with inconsistent hand use, affective instability was significantly associated with family histories of depression and mania, with the association with family history of depression being particularly strong. In contrast, among individuals with consistent hand use, the associations between affective instability and family history of psychopathology were much smaller, with only family history of depression being statistically significant.

Because MPAs were scored dimensionally (whereas we treated hand use inconsistency dichotomously), we decomposed the interactions between MPAs and family history of mood disorders by computing simple slopes following Aiken and West (1991). To examine the effects of family history of psychopathology when MPAs were low, we conducted regression analyses centering MPAs at 1 standard deviation

Table 3
Summary of Hierarchical Multiple Regression Analyses Using Family History of Depression and Neurodevelopmental Disturbance (MPAs or Inconsistent Hand Use) To Predict Affective Instability

Variable	MPAs		Inconsistent hand use	
	β	ΔR^2	β	ΔR^2
Step 1		.12**		.12**
Age	.02		.02	
Gender	−.06		−.06	
Negative affect	.34**		.34**	
Step 2		.01		.02+
Family history	.12*		.11+	
Neurodevelopmental disturbance	.01		.07	
Step 3		.01		.04**
Family History × Neurodevelopmental Disturbance	.07		.14*	

Note. MPAs = minor physical anomalies.
+ $p < .07$. * $p < .05$. ** $p < .01$.

Table 4
Associations Between Family History of Psychopathology and Affective Instability as a Function of Level of Neurodevelopmental Disturbance

Variable	Hand use		Minor physical anomalies	
	Inconsistent[a]	Consistent[a]	High[b]	Low[b]
Family history: Depression	.59**	.14*	.36**	.12
Family history: Mania	.40**	.04	.27**	–.05

[a] Associations in this column were measured using Pearson correlations. [b] Associations in this column were measured using standardized betas.
* $p < .05$. ** $p < .01$.

below the mean. To examine the effects of family history of psychopathology when MPAs were high, we conducted regression analyses centering MPAs at 1 standard deviation above the mean. The results of these analyses are presented on the right side of Table 4. Predicting affective instability among individuals with high levels of MPAs, the standardized beta coefficients were statistically significant for family histories of depression and mania. In contrast, among individuals with low levels of MPAs, family histories of depression and mania were not significantly associated with affective instability.

We next tested whether the interaction effects predicting affective instability might merely reflect associations with borderline personality disorder traits (rather than being associated specifically with affective instability). We tested this possibility by conducting regression analyses in which we entered on the first step the sum of the remaining eight borderline personality disorder criteria. In three of the four analyses, the interaction of the family history of mood disorder and the neurodevelopmental disturbance variable significantly ($p < .05$) improved the prediction of affective instability. In the fourth analysis, the interaction of family history of mania and inconsistent hand use no longer significantly improved the prediction of affective instability, although the results were in the expected direction ($\Delta R^2 = .01$, $\beta = .09$, $p = .13$).

In our final set of analyses, we conducted regression analyses similar to those described above (i.e., entering potential confounding variables on the first step) to test whether the interaction effects predicting affective instability might merely reflect associations between affective instability and either current or lifetime history of major depressive disorder or bipolar disorder. It was important to examine this because, as expected, levels of affective instability were elevated among individuals with current or lifetime unipolar and bipolar mood disorders (ps $< .01$; effect sizes, measured using Cohen's d, ranged from 0.48 to 3.18). The interactions between neurodevelopmental disturbance variables and family history variables significantly ($p < .05$) predicted affective instability in 13 of the 16 analyses and fell just short of significance ($p = .06$, $p = .06$, and $p = .11$) in the remaining three analyses.

Discussion

Although previous research has found that family history of mood disorders is associated with borderline personality disorder as a whole (e.g., Links et al., 1988), this is the first study to document a link between family history of mood disorders and affective instability. It will be important for future research to determine whether the link between affective instability and family history of mood disorder reflects an association between affective instability and (a) the genes associated with family history of mood disorder or (b) the environmental factors associated with family history of mood disorder. We believe the former is more likely given that the results of past research suggest that affective instability is influenced by genetic factors and not by shared environment (Jang, Livesley, Vernon, & Jackson, 1996; Oniszcenko et al., 2003).

The contribution to affective instability of the interaction between family history of mood disorders and signs of neurodevelopmental disturbance was not eliminated when taking into account (on the first step of the regression equa-

tion) negative affect or the sum of the remaining borderline personality disorder traits. That there may be a specific pathway to affective instability that is independent of related emotion and personality variables is consistent with the findings of Silverman et al. (1991), who found that the familial transmission of affective instability appears to be relatively independent of the familial transmission of impulsivity. Such a possibility is also consistent with the findings of Zanarini et al. (2004) that affective instability is more discriminating between the relatives of individuals with borderline personality disorder and the relatives of individuals with other personality disorders than is borderline personality disorder as a whole.

We tested the hypothesis that affective instability happens to be associated with the interaction of family history of mood disorder and signs of neurodevelopmental disturbance merely because affective instability is a sign of, or is associated with, a personal history of mood disorders. This possibility was rendered less plausible by our finding that the interaction of family history of mood disorder and signs of neurodevelopmental disturbance continued to predict affective instability even after taking personal history of mood disorder into account. These findings are consistent with, but by no means prove, that there is a set of genes that contributes to both affective instability and mood disorders and that plays a particularly important role among those individuals whose neural development is disrupted by factors occurring prenatally or very early in life. Although not directly tested in this study, these results are also consistent with the hypothesis that the links between mood disorders (as well as other disorders such as borderline personality disorder) and the genes that predispose to mood disorders are at least partially mediated by affective instability. Future longitudinal research will be needed to explore such mediational hypotheses.

The present study suffered from several methodological limitations that should be addressed in future research. First, affective instability was measured using a single global rating. Although the rating of affective instability was based on far more information than is provided with a single item from a questionnaire, and these ratings were quite reliable, a global rating leaves unanswered the question of which specific aspect of affective instability was associated with the interaction of family history of mood disorders and signs of neurodevelopmental disturbance. It will therefore be important for future research to measure separately the two facets of affective instability: affect intensity and emotional variability. Second, the reliabilities of MPAs, ridge count asymmetries, and family history variables were not measured. Thus, it is possible that these variables were not rated as reliably as in past research, which could have led us to underestimate the strength of their associations with affective instability. Third, the sample was not representative of the general population. In particular, even though individuals with psychotic disorders were excluded and few individuals met full diagnostic criteria for schizotypal personality disorder, participants tended to exhibit more schizotypal traits than would be found in a representative sample.

In addition to the methodological limitations, there are several additional reasons why it will be important for future research to replicate and extend the results of the present study. First, although we had broad theoretical reasons to expect signs of neurodevelopmental disturbance to moderate the impact of family history of mood disorders, this expectation was not based on specific findings from past research. Second, only two of the three signs of neurodevelopmental disturbance moderated the impact of family history of mood disorders. It is worth noting, however, that the two signs that did moderate family history have the greatest evidence of being associated with developmental and mood disorders. Third, both family history of mood disorders and sign of neurodevelopmental disturbance could reflect both genetic and environmental influences. Ideally, future research will explore which combinations of specific genes and specific environmental factors contribute in which specific ways to affective instability. Although, as is almost always the case, there remain unanswered questions, the findings of the present study provide important clues for understanding the etiology of both affective instability and a variety of different mental disorders (e.g., borderline personality disorder, mood disorders).

References

Aiken, L. S., & West, S. G. (1991). *Multiple regression: Testing and interpreting interactions.* Newbury Park, CA: Sage.

Andreasen, N. C., Endicott, J., Spitzer, R. L., & Winokur, G. (1977). The family history method using diagnostic criteria: Reliability and validity. *Archives of General Psychiatry, 34,* 1229–1235.

Angst, J., Gamma, A., & Endrass, J. (2003). Risk factors for the bipolar and depression spectrum. *Acta Pyschatrica Scandinavica, 108,* 15–19.

Bagge, C., Nickell, A., Stepp, S., Durrett, C., Jackson, K., & Trull, T. J. (2004). Borderline personality disorder features predict negative outcomes 2 years later. *Journal of Abnormal Psychology, 113,* 279–288.

Berenbaum, H., Thompson, R. J., Milanak, M. E., Boden, M. T., & Bredemeier, K. (2008). Psychological trauma and schizotypal personailty disorder. *Journal of Phychology, 117,* 502–519.

Champoux, J. E., & Peters, W. S. (1987). Form, effect size and power in moderated regression analysis. *Journal of Occupational Psychology, 60,* 243–255.

Davidson, R. J., Fox, A., & Kalin, N. H. (2007). Neural bases of emotion regulation in nonhuman primates and humans. In J. J. Gross (Ed.), *Handbook of emotion regulation* (pp. 47–68). New York: Guilford Press.

Deltito, J., Martin, L., Riefkohl, J., Austria, B., Kissilenko, A., Morse, P., & Corless, C. (2001). Do patients with borderline personality disorder belong to the bipolar spectrum? *Journal of Affective Disorders, 67,* 221–228.

Eichorn, D. H., & Bayley, N. (1962). Growth in head circumference from birth to adulthood. *Child Development, 33,* 257–271.

Eid, M., & Diener, E. (1999). Intraindividual variability in affect: Reliability, validity, and personality correlates. *Journal of Personality and Social Psychology, 76,* 662–676.

Emmons, R. A., & King, L. A. (1989). Personal striving differentaion and affective reactivity. *Journal of Personality and Social Psychology, 56,* 478–484.

Fasmer, O. B., Akiskal, H. S., Hugdahl, K., & Oedegaard, K. J. (2008). Non-right-handedness is associated with migraine and soft bipolarity in patients with mood disorders. *Journal of Affective Disorders, 108,* 217–224.

Fatemi, S. H., & Folsom, T. D. (2009). The neurodevelopmental hypothesis of schizophrenia, revisited. *Schizophrenia Bulletin, 35,* 528–548.

First, M. B., Spitzer, R. L., Gibbon, M., & Williams, J. B. W. (1998). *Structured Clinical Interview for DSM–IV Axis I Disorders.* New York: New York State Psychiatric Institute.

Gratz, K. L., & Roemer, L. (2004). Multidimensional assessment of emotion regulation and dysregulation: Development, factor structure, and initial validation of the difficulties in emotion regulation scale. *Journal of Psychopathology and Behavioral Assessment, 26,* 41–54.

Green, M. F., Satz, P., & Christenson, C. (1994). Minor physical anomalies in schizophrenia patients, bipolar patients, and their siblings. *Schizophrenia Bulletin, 20,* 433–440.

Green, M. F., Satz, P., Smith, C., & Nelson, L. (1989). Is there atypical handedness in schizophrenia? *Journal of Abnormal Psychology, 98,* 57–61.

Henry, C., Mitropoulou, V., New, A. S., Koenigsberg, H. W., Silverman, J., & Siever, L. J. (2001). Affective instability and impulsivity in borderline personality and bipolar II disorders. *Journal of Psychiatric Research, 35,* 307–312.

Hepper, P. G., Shahidullah, S., & White, R. (1991). Handedness in the human fetus. *Neuropsychologia, 28,* 1107–1111.

Ismail, B., Cantor-Graae, E., & McNeil, T. (1998). Minor physical anomalies in schizophrenic patients and their siblings. *The American Journal of Psychiatry, 155,* 1695–1702.

Jang, K. L., Livesley, W. J., Vernon, P. A., & Jackson, D. N. (1996). Heritability of personality disorder traits: A twin study. *Acta Psychiatrica Scandinavica, 94,* 438–444.

Links, P. S., Steiner, M., & Huxley, G. (1988). The occurrence of borderline personality disorder in the families of borderline patients. *Journal of Personality Disorders, 2,* 14–20.

Livesley, W. J., Jang, K. L., & Vernon, P. A., (1998). Phenotypic and genetic structure of traits delineating personality disorder. *Archives of General Psychatry, 55,* 941–948.

McClelland, G. H., & Judd, C. M. (1993). Statistical difficulties of detecting interactions and moderator effects. *Psychological Bulletin, 114,* 376–390.

Miller, J. D., & Pilkonis, P. A. (2006). Neuroticism and affective instability: The same or different? *The American Journal of Psychiatry, 163,* 839–845.

Moffitt, T. E., Caspi, A., & Rutter, M. (2006). Measured gene–environment interactions in psychpathology: Concepts, research strategies, and implications for research, intervention, and public understanding of genetics. *Perspectives in Psychological Science, 1,* 5–27.

Oniszcenko, W., Zawadzki, B., Strelau, J., Riemann, R., Angleitner, A., & Spinath, F. M. (2003). Genetic and environmental determinants of temperament: A comparative study based on Polish and German samples. *European Journal of Personality, 17,* 207–220.

Sanches, M., Keshavan, M. S., Brambilla, P., & Soares, J. C. (2008). Neurodevelopmental basis of

bipolar disorder: A critical appraisal. *Progress in Neuro-Psychopharmacology and Biological Psychiatry, 32,* 1617–1627.

Siever, L. J., & Davis, K. L. (1991). A psychobiological perspective on the personality disorders. *The American Journal of Psychiatry, 148,* 1647–1658.

Silverman, J. M., Pinkham, L., Horvath, T. B., Coccaro, E. F., Klar, H., Schear, S., . . . Siever, L. J. (1991). Affective and impulsive personality disorder traits in the relatives of patients with borderline personality disorder. *The American Journal of Psychiatry, 148,* 1378–1385.

Slater, E., & Cowie, V. (1971). *The genetics of mental disorders.* Oxford, England: Oxford University Press.

Smith, D. W., & Bostian, K. E. (1964). Congenital anomalies associated with idiopathic mental retardation. *Journal of Pediatrics, 65,* 189–196.

Soper, H. V., Satz, P., Orsini, D. L., Henry, R. R., Zvi, J. C., & Schulman, M. (1986). Handedness patterns in autism suggest subtypes. *Journal of Autism and Developmental Disorders, 16,* 155–167.

Soper, H., Satz, P., Orsini, D., Van Gorp, W., & Green, M. (1987). Handedness distribution among the severely to profoundly mentally retarded. *American Journal of Mental Deficiency, 92,* 94–102.

Tarrant, C. J., & Jones, P. B. (1999). Precursors to schizophrenia: Do biological markers have specificity? *The Canadian Journal of Psychiatry, 44,* 335–349.

Tenyi, T., Trixler, M., & Csabi, G. (2009). Minor physical anomalies in affective disorders: A review of the literature. *Journal of Affective Disorders, 112,* 11–18.

Thompson, R. T., Dizen, M., & Berenbaum, H. (2009). The unique relations between emotional awareness and facets of affective instability. *Journal of Research in Personality, 43,* 875–879.

Tripi, G., Roux, S., Canziani, T., Brilhault, F. B., Barthelemy, C., & Canziani, F. (2008). Minor physical anomalies in children with autism spectrum disorder. *Early Human Development, 84,* 217–223.

van Oel, C. J., Baare, W. F., Hulshoff Pol, H. E., Haag, J., Balazs, J., Dingemans, A., . . . Sitskoorn, M. M. (2001). Differentiating between low and high susceptibility to schizophrenia in twins: The significance of dermatoglyphic indices in relation to other determinants of brain development. *Schizophrenia Research, 52,* 181–193.

Waldrop, M. F., & Halverson, C. F. (1971). Minor physical anomalies and hyperactive behavior in young children. In J. Hellmuth (Ed.), *Exceptional infant: Studies in abnormalities* (pp. 340–382). New York: Brunner/Mazel.

Walker, E. F., Sabuwalla, Z., & Huot, R. (2004). Pubertal neuromaturation, stress sensitivity, and psychopathology. *Development and Psychopathology, 16,* 807–824.

Wang, Y., Hu, Y., Fang, Y., Zhang, K., Yang, H., Ma, J., . . . Shen, Y. (2009). Evidence of epistasis between the catechol-O-methyltransferase and aldehyde dehydrogenase 3B1 genes in paranoid schizophrenia. *Biological Psychiatry, 65,* 1048–1054.

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: The PANAS scales. *Journal of Personality and Social Psychology, 54,* 1063–1070.

Weinberg, S. M., Jenkins, E. A., Marazita, M. L., & Maher, B. S. (2007). Minor physical anomalies in schizophrenia: A meta-analysis. *Schizophrenia Research, 89,* 72–85.

Weinberger, D. R. (1995). Schizophrenia as a neurodevelopmental disorder. In S. R. Hirsch & D. R. Weinberger (Eds.), *Schizophrenia* (pp. 293–323). Cambridge, England: Blackwell.

Weinstein, D. D., Diforio, D., Schiffman, J., Walker, E., & Bonsall, R. (1999). Minor physical anomalies, dermatoglyphic asymmetries, and cortisol levels in adolescents with schizotypal personality disorder. *The American Journal of Psychiatry, 156,* 617–623.

Widiger, T. A., Mangine, S., Corbitt, E. M., Ellis, C. G., & Thomas, G. V. (1995). *Personality Disorder Interview—IV: A semi-structured interview for the assessment of personality disorders.* Odessa, FL: Psychological Assessment Resources.

Yen, S., Shea, M. T., Sanislow, C. A., Grilo, C. M., Skodol, A. E., Gunderson, J. G., . . . & Morey, L. C. (2004). Borderline personality disorder criteria associated with prospectively observed suicidal behavior. *The American Journal of Psychiatry, 161,* 1296–1298.

Zanarini, M. C., Frankenburg, F. R., Yong, L., Raviola, G., Reich, D. B., Hennen, J., . . . Gunderson, J. G. (2004). Borderline psychopathology in the first-degree relatives of borderline and Axis II comparison probands. *Journal of Personality Disorders, 18,* 449–447.