Journal of Affective Disorders 200 (2016) 82–88

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research paper

Temperament and major depression: How does difficult temperament affect frequency, severity, and duration of major depressive episodes among offspring of parents with or without depression?

Brian J. Sherman [a,*,1], Eleni Vousoura [a], Priya Wickramaratne [b,c], Virginia Warner [b,c], Helen Verdeli [a,b]

[a] Department of Counseling and Clinical Psychology, Teachers College, Columbia University, United States
[b] Division of Child and Adolescent Psychiatry, New York State Psychiatric Institute, United States
[c] Department of Psychiatry, College of Physicians and Surgeons, Columbia University, United States

ARTICLE INFO

Article history:
Received 10 February 2016
Received in revised form
8 April 2016
Accepted 16 April 2016
Available online 20 April 2016

Keywords:
Temperament
Depression
High-risk
Psychopathology
Difficult temperament

ABSTRACT

Introduction: The current study examined the relationships between parental depression, offspring depression, and offspring temperament among 203 offspring of parents with or without depression. The specific aim was to investigate how parental depression and offspring difficult temperament affect frequency, severity, and duration of offspring major depressive episodes (MDEs).

Methods: As part of an ongoing multigenerational study assessing familial transmission of depression, offspring were assessed over a 20-year study period. Offspring temperament was assessed at baseline using the Dimensions of Temperament Survey and diagnostic interviews were conducted at each of the four waves using best estimate procedures.

Results: Difficult temperament predicted greater frequency of lifetime MDEs. Parental depression moderated the relationship between offspring difficult temperament and severity of MDEs, such that difficult temperament was associated with increased severity ratings among high-risk, but not low-risk offspring. Dimensional analysis revealed that lower rhythmicity and adaptability were associated with greater number of lifetime MDEs, higher inattention/distractibility was associated with shorter duration of MDEs, and greater activity was associated with decreased severity of MDEs.

Discussion: Certain limitations must be noted, namely the self-report nature of temperament data and the relatively small sample size drawn from a clinical and predominantly Caucasian and Christian sample. Notwithstanding these limitations, our results suggest that the clinical presentation of major depression may reflect temperamental profiles and should be considered in diagnostic and treatment settings.

Since the four classical temperaments of Hippocratic medicine and the writings of Galen, individual differences in human behavior have been an area of great debate. The last century has witnessed tremendous growth in defining and categorizing psychopathology, yet only recently has the study of temperament become an integral part of the developmental psychopathology literature (Nigg, 2006; Rettew and McKee, 2005). Integrating the historical debate on individual differences with present-day taxonomies of psychopathology is increasingly important as we delineate developmental profiles of typical and atypical development.

Temperament is currently best understood as behaviorally observable individual differences that a) have a strong genetic basis, b) manifest early in life, and c) are relatively stable over the lifespan (Nigg, 2006; Rettew and McKee, 2005; Rothbart and Bates, 2006). The construct of 'difficult temperament' was first introduced by Thomas and Chess in their seminal New York Longitudinal Study (1977), and is now generally characterized by a tendency for intense emotional and physiological reactivity with poor self-regulation (Buss and Plomin, 1984; Rothbart and Bates, 2006; Thomas and Chess, 1977). Difficult temperament has been associated with a wide range of psychological problems across the lifespan including conduct disorders, attention-deficit/hyperactivity disorder, substance abuse, and internalizing disorders (Bruder-Costello et al., 2007; Chronis-Tuscano et al., 2009; Schwartz et al., 1999; Watson et al., 2005; Windle and Windle, 2006). A large body of research supports a strong link between dimensions of difficult temperament and increased risk for

* Corresponding author.
E-mail address: shermanb@musc.edu (B.J. Sherman).
[1] Current address: Medical University of South Carolina, 125 Doughty Street, Suite 190, Charleston, SC, 29425, USA.

http://dx.doi.org/10.1016/j.jad.2016.04.033
0165-0327/

depressive and anxiety disorders. Results from prospective studies have identified several temperamental profiles associated with affective and anxiety disorders in childhood and adolescence. In a longitudinal birth cohort study, social reticence, behavioral inhibition, and fear/avoidance at age 3 was associated with increased risk of major depression by age 21 (Caspi et al., 1996). In another longitudinal study, behavioral inhibition assessed multiple times from age 4 months to 7 years increased the risk for adolescent social anxiety disorder almost 4-fold (Chronis-Tuscano et al., 2009). Likewise, children, particularly girls, with high levels of negative emotionality were more likely to manifest emotional problems in adolescence (Goodyer et al., 1993).

Parental depression is also an important factor to consider when examining developmental pathways to depression. Parental depression significantly increases risk of offspring lifetime depression (Weissman et al., 2006, 1997) and this relationship is mediated by negative maternal behavior, harsh parenting, and disengagement (see Lovejoy et al., 2000 for review; Radke-Yarrow and Klimes-Dougan, 2002). Interestingly, a recent study found that remission of maternal depression was associated with decreased depressive symptoms in offspring, a relationship partially mediated by improved parenting behaviors (Weissman et al., 2014). Moreover, upon relapse to maternal depression, offspring depressive symptoms increased as well, suggesting a strong influence of maternal depression on offspring depression.

Despite ample evidence linking specific dimensions of temperament and parental depression to offspring depressive disorders, most temperament research focuses on child and adolescent development. However, given its biological basis and relative stability over time, temperament lends itself particularly well to exploration across the lifespan (Rothbart et al., 2000). The transition from adolescence to adulthood comes with increasing pressures of individuation, intimacy, and autonomy, and structural neuroimaging evidence confirms that the frontal lobe continues to develop well into the third decade of life (Conklin et al., 2007). In addition, this developmental period witnesses high rates of first-onset mental illness (Kessler et al., 2007). Therefore, it is important to examine the relationship between temperament and psychopathology during this critical period of development.

The current study aims to address this critical gap in the literature by analyzing data from the ongoing multigenerational High Risk Study designed to explore the intergenerational transmission of depression and its correlates (Weissman et al., 2006, 1997, 1987). Findings from the first 20 years of data show that offspring of parents with depression (high-risk offspring) are at three-fold higher risk for lifetime major depression than offspring of parents without depression (low-risk offspring) (Weissman et al., 2006, 1997) and that offspring difficult temperament is associated with lifetime major depressive disorder (MDD) in both high and low-risk offspring (Bruder-Costello et al., 2007).

The current study builds on these findings and examines how parental depression and offspring temperament affect the frequency, severity, and duration of major depressive episodes (MDEs), rather than just lifetime incidence, over a 20-year study period from adolescence to adulthood. To our knowledge this is the longest follow-up study comparing high- versus low-risk offspring and first to examine the relationship between temperament and features of depressive episodes among such a sample. In addition, the current study addresses an important and oft-understudied period of temperamental development from adolescence to adulthood.

1. Method

1.1. Participants and procedures

The current study utilized a subsample of a longitudinal, multigenerational study of individuals at high- and low-risk for major depression by Weissman and colleagues (2006, 1997, 1987). A full description of the study procedures has been published elsewhere (Weissman et al., 2006, 1997, 1987). The original study sample consisted of adults with depression recruited from the Yale University Depression Research Unit, an outpatient specialty clinic for the treatment of mood disorders. They had moderate to severe depression and significant functional impairment as assessed by the Schedule for Affective Disorders and Schizophrenia – Lifetime Version (SADS-L; Mannuzza et al., 1986). Healthy controls without a history of depression were also recruited from a large epidemiological survey in the same community (Weissman et al., 1987). The healthy probands had no lifetime diagnosis of mental illness assessed in four separate interviews. Probands and their offspring completed assessments at Baseline (Wave 1), 2 years later (Wave 2), 10 years later (Wave 3), and 20 years later (Wave 4).

The sample for the current study is comprised of 203 offspring who completed (1) a diagnostic interview at baseline and again at the 10-or 20-year follow-up; and (2) an assessment of temperament at baseline. The study was approved by the Institutional Review Board at both Yale University and Columbia University/York State Psychiatric Institute. Following a detailed description of the study procedures, written consent was obtained from adults, and assent was obtained from minors accompanied by written consent from their parents.

2. Measures

2.1. Diagnostic assessments

Offspring and parents completed up to four diagnostic assessments (Waves 1–4); adult participants were assessed using the SADS-L (Mannuzza et al., 1986) and children aged 6 through 17 were administered the K-SADS-E (Kaufman et al., 1997). Trained doctoral and master's level mental health professionals conducted all interviews, and all interviewers were blind to lifetime diagnostic status of either parent or child. Best estimate (BE) procedure (Leckman et al., 1982) was used to diagnose MDEs, and all final BE diagnoses were made by psychiatrists or doctoral level psychologists blind to risk status. At the initial baseline interview (wave 1 or wave 2) BE lifetime diagnoses were made to determine lifetime history of major depression prior to beginning the study. Subsequent assessments noted diagnoses of all MDEs occurring in the interim.

2.2. Temperament

High- and low-risk offspring completed the Dimensions of Temperament Scale (DOTS; Lerner et al., 1982) at Wave 1 or Wave 2. Of the 203 participants, 155 completed the DOTS at Wave 1 and 48 at Wave 2. The DOTS is a self-report measure that consists of 34 “true” or “false” items representing five dimensions: 1) Activity Level (during sleep); 2) Attention span/distractibility (task persistence in the face of distracting stimuli); 3) Adaptability/approach-withdrawal (response to novel situations); 4) Rhythmicity (regularity of eating and sleeping patterns); and 5) Irritability (restlessness, reactivity to sensory stimuli, intensity of reactivity). The DOTS provides subscale scores for each of the five dimensions, as well as a total temperament score, produced by summing all subscale scores, with higher scores reflecting a more difficult

temperament. The median total temperament score (current study = 15) was used as a cutoff for categorical analyses (Bruder-Costello et al., 2007; Thomas and Chess, 1977). Participants with a score ≥ 15 were designated as having a "difficult temperament" and those with a score < 15 were designated as having an "easy temperament."

2.3. Major depression features

BE data on frequency, severity, and duration of lifetime MDE were compiled across the four waves to create three continuous outcome variables:

2.3.1. Frequency

Total number of MDEs was derived from summing the number of reported lifetime MDEs. Waves 1 and 2 assessed for current and lifetime MDE; for those who did not complete a Wave 1 interview, Wave 2 assessment served as the baseline interview. At Wave 3 (10-year follow-up) and Wave 4 (20-year follow-up) participants were asked to report the number of MDEs occurring since their last assessment. Total number of lifetime MDEs was then standardized by dividing the total number of MDEs by the number of years in the study. Participants who missed one of the middle waves (Wave 2 or 3) were considered 20-year participants as long as they had completed a Wave 4 assessment.

2.3.2. Duration

Duration of all reported MDEs (coded into days) was assessed at each study wave. An Average Duration of MDEs variable was computed for each participant by summing the total days with a MDE and dividing by the number of lifetime MDEs. Due to a positively skewed distribution (Skewness = 4.6, Kurtosis = 25) data were log linear transformed.

2.3.3. Severity

Severity of lifetime MDEs was assessed at each wave using a self-report 3-point scale (1 = Mild, 2 = Moderate, 3 = Severe). Waves 1 and 2 assessed for severity of current episode (if present) and most severe lifetime MDE; Wave 3 assessed for severity of each MDE since the previous wave; at Wave 4 severity of worst episode between Wave 3 and Wave 4 was assessed. An Average Worst Severity variable was created to examine intensity of depression among offspring with depression.

3. Data analysis

Mixed Model procedures were used to examine the impact of difficult temperament and parental depression (i.e., risk status) on features of major depression. MIXED command in SPSS version 20 was used to adjust for nested family effect. Nested family effect suggests non-independence of outcome; having multiple offspring from the same high-risk family artificially increases the chances of finding a significant association between parental depression, offspring depression, and difficult temperament (i.e., Type I error) due to shared biological and environmental factors. For each outcome (frequency, severity, and duration of MDEs) we ran three models: Model 1-Temperament alone, Model 2-Risk Status alone, and Model 3-Temperament, Risk Status, and the interaction of Temperament X Risk Status. As a methodological check, the same set of analyses were rerun using temperament as a continuous variable rather than categorical variable. For exploratory analysis we again used MIXED procedure and entered all 5 DOTS dimensions into separate models predicting each of the 3 outcomes. This procedure was then repeated separately for high and low-risk offspring. All analyses adjusted for baseline age.

4. Results

4.1. Participants

The current study sample consists 203 offspring from 80 families, including 138 high-risk offspring (at least one parent with depression) and 65 low-risk offspring (no history of parental depression). All participants were Caucasian and group matched for age and sex and proband groups did not differ on any key demographic variables (see Table 1). Participants completed a diagnostic interview at Wave 1 and/or Wave 2, and subsequently at Wave 3 and/or Wave 4, and an assessment of temperament at Wave 1 or Wave 2. Fifty-six percent were female. One hundred sixty-nine participants completed a Wave 1 diagnostic interview and 34 completed an initial diagnostic interview at Wave 2 yielding a total baseline sample of 203. There were no significant differences in sex, level of education, household income, or religious beliefs between those who completed an initial interview at Wave 1 and those who completed an initial interview at Wave 2. However, participants with initial interview at Wave 1 were more likely to be younger and single/never married than those initially interviewed at Wave 2. Retention was high with 99% (202/203) completing the study through Wave 3 (10 years) and 85% (173/203) completing the study through Wave 4 (20 years). There were no significant differences in age, marital status, household income, religious beliefs, or highest level of education between Wave 3 and Wave 4 completers. Women were more likely than men to complete the study through Wave 4 ($\chi^2 = 14.4$, df = 1, $p < .01$).

One hundred fifty-five participants completed the DOTS at Wave 1, while the remaining 48 completed the DOTS at Wave 2. These initial DOTS interview data were combined and used as the baseline assessment of temperament. Offspring who completed the DOTS at Wave 2 were significantly older ($M = 25$, $SD = 8.0$) than those who completed the DOTS at Wave 1 ($M = 17$, $SD = 4.5$; $p < .001$); there were no significant differences between these groups on demographic variables of level of education, marital

Table 1
Descriptives for entire sample and by risk group.

	Entire sample ($N = 203$)	High risk ($n = 138$)	Low risk ($n = 65$)
Age[a] *M*(SD)	18.7(6.5)	19.2(6.9)	17.6(5.6)
	N (%)	N (%)	N (%)
Sex[a]: Female	114(56)	79(57)	35(54)
Male	88(43)	58(42)	30(46)
Marital Status[b]			
Married	113(56)	74(54)	39(60)
Never married	61(30)	43(31)	18(28)
Separated/divorced	27(13)	20(14)	7(11)
Highest level of education[b]			
No high school diploma	7(3.5)	5(4)	2(3)
High school diploma	54(27)	37(27)	17(26)
Tech school or 2-yr college	57(28)	37(27)	20(31)
Four-year college	56(27)	42(30)	14(22)
Graduate/professional	29(14)	17(12)	12(18)
Religious affiliation[b]			
Roman Catholic	120(59)	75(54)	45(69)
Protestant	31(15)	25(18)	6(9)
Jewish	9(4.4)	5(4)	4(6)
Personal religious	15(7.4)	9(7)	6(9)
Agnostic/atheist	4(2)	4(3)	0(0)
Other	18(9)	15(11)	4(6)
Household income[b]			
< $30,000	48(24)	37(27)	11(17)
30,000–49,000	44(22)	30(22)	14(21)
50,000–89,000	56(27)	38(27)	18(28)
90,000 or greater	52(26)	31(22)	21(32)

[a] Assessed at initial interview (Wave 1 or 2).
[b] Assessed at last interview (Wave 3 or 4).

Table 2
Mixed models analyses examining how difficult temperament and risk status predict frequency, duration, and severity of lifetime major depressive episodes.

		Total # MDEs per study year ($N=97$)		Average Duration MDE [a] ($N=97$)		Average Worst Severity ($N=92$)	
		M (SD)	*F*	*M* (SD)	*F*	*M* (SD)	*F*
Model 1							
Temperament	Easy ($n=37$)	.13 (.08)	4.00*	5.1 (1.0)	.90	($n=35$) 2.4 (.57)	1.97
	Difficult ($n=60$)	.17 (.12)		4.8 (1.4)		($n=57$) 2.2 (.64)	
Model 2							
Risk Status	Low ($n=17$)	.15 (.08)	.12	4.8 (1.2)	.35	($n=16$) 2.4 (.60)	1.23
	High ($n=80$)	.16 (.11)		4.9 (1.3)		($n=76$) 2.2 (.62)	
Model 3							
Temperament		–	3.27+	–	.58	–	.09
Risk Status		–	.04	–	.48	–	.55
Temperament x Risk Status		–	.21	–	.01	–	4.06*
Low Risk	Easy ($n=8$)	.11 (.06)	–	5.0 (1.1)	–	($n=7$) 2.2 (.70)	n.s.
	Difficult ($n=9$)	.18 (.09)		4.6 (1.3)		($n=9$) 2.6 (.50)	
High Risk	Easy ($n=29$)	.13 (.09)	–	5.1 (1.0)	–	($n=28$) 2.4 (.54)	$p=.06$
	Difficult ($n=51$)	.17 (.12)		4.8 (1.4)		($n=48$) 2.1 (.65)	

Notes. Mixed model analyses are adjusting for family effect and baseline age.
* $p<.05$.
+ $p=.07$.
[a] Log linear transformation adjusting for positive skew.

status, household income, or religious affiliation. Combined, mean age at baseline interview was 18.6 ($SD=6.5$).

4.2. Primary outcomes

Please see Table 2 for full summary of primary outcomes.

4.2.1. Frequency of MDEs

As shown in Table 2, offspring with difficult temperament had significantly more lifetime MDEs per study year ($M=0.17$, $SD=.12$) than those with an easy temperament ($M=0.13$, $SD=.08$), $F(1, 94)=4.00$, $p<.05$. When adjusting for risk status (model 3), difficult temperament continued to show a trend in predicting lifetime MDEs (p=.07). There was no main effect of risk status on frequency of MDEs independently or when adjusting for temperament. The interaction of difficult temperament by risk status on frequency of MDEs was not significant. Analyses using temperament as a continuous variable supported these results.

4.2.2. Duration of MDEs

There were no main effects of difficult temperament or risk status on duration of MDEs either independently or when adjusting for each other. Nor did the interaction of temperament by risk status significantly predict duration of MDEs. Analysis using temperament as a continuous variable supported these results.

4.2.3. Severity of MDEs

There were no main effects of difficult temperament or risk status on severity of MDEs. However, there was a significant interaction effect of difficult temperament by risk status on severity of MDEs ($F(1, 87)=4.06$, $p<.05$). Post-hoc mixed model analyses revealed a marginally significant effect among high-risk offspring, $F(1, 73)=3.6$, $p=.06$, but no effect among low-risk offspring. High-risk offspring with an easy temperament reported more severe MDEs ($M=2.4$, $SD=.54$) than high-risk offspring with a difficult temperament ($M=2.1$, $SD=.65$). Among low-risk offspring there was no significant difference in severity score between offspring with easy vs. difficult temperament. Analysis using temperament as a continuous predictor did not fully support severity results. First, difficult temperament assessed continuously predicted decreased severity of MDEs ($b=-.025$, $p<.05$). Second, the interaction effect of difficult temperament and risk status on MDE severity was not significant when temperament was assessed continuously.

4.3. Exploratory analyses

As a follow up, exploratory analyses examined the relationship between the five dimensions of temperament assessed by the DOTS and features of depression. Using a Mixed Model procedure separately for each outcome, all five dimensions were entered while adjusting for family effect and baseline age. Results are found in Table 3. Low rhythmicity and low adaptability were associated with greater frequency of MDEs ($b=.016$, $p<.01$ and $b=.014$, $p<.05$, respectively). Greater inattention/distractibility was inversely associated with average duration of MDEs ($b=-.116$, $p<.05$). Finally, greater activity was inversely associated with average worst severity of MDEs ($b=-.093$, $p<.05$). The same analyses were then run separately for high risk and low risk offspring (see Table 4). Results indicate that among high-risk offspring low adaptability ($b=.013$, $p<.05$) and low rhythmicity ($b=.016$, $p<.01$) were positively associated with frequency of MDEs. For low-risk offspring, low rhythmicity alone was positively associated with frequency of MDEs ($b=.024$, $p<.05$), and greater inattention/distractibility was inversely associated with severity of

Table 3
Mixed model analyses examining the association between dimensions of temperament and features of MDEs among entire sample.

N=203	***Total MDEs***	***Average duration***	***Worst severity***
DOTS dimension	***B (s.e.)***	***B (s.e.)***	***B (s.e.)***
Activity	.009 (.007)	.004 (.08)	-.093 (.05)*
Inattention/distractibility	-.003 (.004)	-.116 (.04)*	-.044 (.02)+
Adaptability	.014 (.006)*	.010 (.07)	.012 (.03)
Rhythmicity	.016 (.005)**	-.051 (.06)	-.007 (.03)
Irritability	.008 (.007)	.071 (.08)	.021 (.04)

Notes. Mixed model analyses are adjusting for baseline age and family effect. Higher subscale scores reflect more difficult temperament. Higher score on activity=more active/restless, higher adaptability=less adaptive, higher inattention/distractibility=less attentive/more distractible, higher rhythmicity=less rhythmic, higher irritability=more irritable.
* $p<.05$.
** $p<.01$.
+ $p<.07$.

Table 4
Mixed model analyses examining the association between DOTS dimensions of temperament and features of MDEs among high and low-risk offspring effect.

High Risk (n=138)	*Total MDEs*	*Average Duration*	*Worst Severity*
DOTS dimension	***B (s.e.)***	***B (s.e.)***	***B (s.e.)***
Activity	.014 (.008)	-.006 (.102)	-.094 (.052)$^{+}$
Inattention/distractibility	-.004 (.005)	-.101 (.055)$^{+}$	-.031 (.028)
Adaptability	.013* (.006)	.108 (.077)	.028 (.038)
Rhythmicity	.016** (.005)	-.051 (.064)	-.018 (.032)
Irritability	.008 (.008)	.078 (.097)	.004 (.050)
Low Risk (n=65)			
Activity	-.025 (.004)	-.252 (.268)	-.127 (.111)
Attention/distractibility	-.018 (.011)	-.387 (.176)$^{+}$	-.174 (.070)*
Adaptability	.008 (.013)	-.080 (.186)	-.061 (.088)
Rhythmicity	.024 (.010)*	.031 (.170)	.146 (.066)$^{+}$
Irritability	-.030 (.020)	-.391 (.318)	-.170 (.130)

Notes. Mixed model analyses are adjusting for baseline age and family. Higher subscale scores reflect more difficult temperament. Higher score on activity = more active/restless, higher adaptability = less adaptive, higher inattention/distractibility = less attentive/more distractible, higher rhythmicity = less rhythmic, higher irritability = more irritable.

* $p < .05$,
$^{+}$ $p < .07$.

MDEs ($b = -.174$, $p < .05$).

5. Discussion

The current study examined the relationships between parental depression, offspring depression, and offspring temperament over a 20-year developmental period from adolescence to adulthood. We extended existing findings by examining how offspring difficult temperament and parental depression affect qualitative features of major depression rather than just lifetime incidence. Several important results were found.

Offspring difficult temperament was associated with more frequent MDEs, but not with episode severity or duration. Previous findings showed that difficult temperament increased risk for lifetime depression (Bruder-Costello et al., 2007; Weissman et al., 2006), while current findings show more specifically that difficult temperament is associated with recurrent depressive episodes over time. Parental depression (i.e., offspring risk status) did not predict frequency, severity, or duration of offspring MDEs, which is notable given that parental depression is a robust predictor of offspring lifetime depression (Bruder-Costello et al., 2007; Weissman et al., 1997; 2006). Together, these findings suggest that while parental depression may predict whether a child ever develops MDD, offspring temperament may be more predictive of MDD recurrence.

While there was no main effect of risk status on the three primary outcomes, there was a significant interaction between risk status and temperament on severity of MDEs. Risk status moderated the relationship between temperament and severity of MDEs among high-risk, but not low-risk offspring. High-risk offspring with an easy temperament reported more severe MDEs than those with a difficult temperament; there was no difference among low-risk offspring. One possible explanation for this finding is that since high-risk offspring with difficult temperament have more frequent MDEs they habituate to depression resulting in lower subjective reports of distress. In contrast, offspring with an easy temperament are more sensitive to depression and may perceive their episodes as more disruptive and severe.

To better understand the nuanced relationship between risk status and temperament on the clinical presentation of MDEs, we explored individual dimensions of temperament. For the overall sample, difficulty adapting to new situations and irregular sleeping and eating patterns predicted greater frequency of MDEs. Lower adaptability has been linked with depression among school-aged children (Lee et al., 2015), and young adults (age 20–35), specifically in regard to social situations (Elovainio et al., 2015). In addition, poor sleep patterns are diagnostic of depression, and are evidenced by disruptions in biological mechanisms that regulate sleep, primarily the suprachiasmatic nucleus (SCN), which regulates the neurohormone melatonin. Significant evidence links the dysregulation of melatonin release and reuptake with depression (see Srinivasan et al., 2009 for review). Changes in the hypothalamic-pituitary-adrenal axis (HPA), which regulates cortisol secretion and corticotrophin releasing hormone (Stetler and Miller, 2005), reduction in slow wave sleep, and decreased latency of rapid eye movement (REM) sleep are also commonly found in people with depression (Srinivasan et al., 2009). A predisposition to arhythmicity as assessed by the DOTS may reflect a vulnerability to changes in biological mechanisms affecting the sleep-wake cycle, putting individuals at increased risk for frequent depressive episodes.

Regarding duration of MDEs, we found that individuals who report being more easily distracted and less attentive as measured by the DOTS have MDEs of shorter duration. This appears a curious finding since high inattention is loaded towards difficult temperament and there exists high comorbidity between attention-related disorders such as adult ADHD and major depression (Klassen et al., 2010). We might expect inattention to predict longer duration of MDEs. However, the tendency to be easily distracted (distractibility) may actually serve a protective function, particularly against the deleterious effects of rumination so common in depression. Response styles theory (Nolen-Hoeksema, 1991) has demonstrated that rumination, which involves repetitively and passively focusing on distressing symptoms and their causes and consequences, exacerbates and prolongs depressed mood states (Kuehner and Weber, 1999; Nolen-Hoeksema and Parker, 1994; Nolen-Hoeksema et al., 1993), while distraction activities in response to negative mood state have been shown to reduce severity and duration of depressed mood (Joormann and Siemer, 2004; Trask and Sigmon, 1999). Response styles theory could explain why greater distractibility in our sample was associated with shorter and less severe depressive episodes. Therapeutic interventions that include distraction techniques may therefore be effective for individuals with low temperamental distractibility.

Regarding severity of MDEs, greater activity level was associated with reduced episode severity. Higher activity scores on the DOTS are loaded towards difficult temperament, however, the tendency towards activation may prove to be protective as well. Indeed evidence suggests that deficits in behavioral activation system (BAS; Gray, 1991), have been consistently linked to increased risk for depression (Pinto-Meza et al., 2006), while diminished BAS sensitivity has been found to predict the course and severity of depression (Kasch, Rottenberg, Arnow, and Gotlib, 2002; McFarland, Shankman, Tenke, Bruder, Klein, 2006). Therefore, individuals with depression who have a temperamental vulnerability to low levels of activation may be particularly responsive to interventions targeting dysregulated BAS, most notably Behavioral Activation, which has been established as an effective therapeutic strategy (Dimidjian et al., 2006).

The implications of our results are two-fold. First, just as not all depression is created equally, not all depression can be treated equally. A person with irregular biological rhythms may be best served by treating sleep problems first, with the indirect benefit of improving their overall mood state, while a ruminative individual may require distraction or behavioral activation techniques. Second, the results speak to a broader discussion about dimensional

versus categorical models of psychopathology (Krueger, Watson, and Barlow, 2005; Widiger and Gore, 2015). If certain dimensions of temperament predict certain characteristic features of depression, then it behooves us as clinicians to pay closer attention to dimensional aspects of temperament/personality rather than diagnostic categories of mental disorders. Interestingly, psychiatry and clinical neuroscience recognize the importance of dimensional approaches even as they work explicitly within the medical model. For example, psychotropic medication is largely prescribed based on side effect profiles, which serve as clinical indicators for different types of depression. The anxious-depressed person may be prescribed paroxetine because of its sedating properties (Fava et al., 2000), while the lethargic-depressed person may be prescribed escitalopram because of its activating effects (Uher, Maier, Hauser, et al., 2009).

Taken together, the current study holds potential in clarifying the link between temperament and psychopathology, a complex relationship for which various models have been proposed (Tackett, 2006). In brief, the *vulnerability model* posits that underlying temperamental traits evident early in life increase the likelihood of later developing a mental disorder, while the *scarring model* suggests that a permanent alteration of an individual's temperament occurs following the remission of an acute mental disorder. The *spectrum/continuum model* posits that temperament and psychopathology have a shared underlying structure and taxonomic distinctions are artificial, whereas, the *pathoplasty model* suggests a significant temporal relationship between temperament and psychopathology in which the presentation, course, and prognosis of a mental disorder are affected by the pre-existing temperament of the individual.

The current study may provide evidence for the pathoplasty and spectrum/continuum models. For the combined sample dimensional analysis, low rhythmicity and adaptability were associated with greater frequency of MDEs, higher inattention/distractibility was associated with shorter duration, and higher activity was associated with lower severity. This suggests that underlying dimensions of temperament affected the clinical presentation of depressive episodes (pathoplasty model). In addition, our finding that offspring with low rhythmicity, which may reflect a vulnerability to changes in biological mechanisms affecting the sleep-wake cycle, had an increased risk for recurrent depressive episodes suggests the possibility of a shared etiology (spectrum/continuum model). Importantly, these models are not necessarily mutually exclusive and perhaps a more thorough integrative perspective will emerge with continued research. It may be that different models are more relevant at different developmental stages, that certain models better account for specific disorders, or that a combination of models is most appropriate.

The current study is the longest reported follow-up of high-risk offspring and comparison offspring that we are aware of and the attrition rate was exceptionally low over the 20 years. However, there are important limitations to consider. First, temperament data is all self-report and required recollection of childhood behavioral styles. While temperament was assessed at the initial interview, it was subject to various biases including memory distortion, current or previous psychopathology, and subclinical symptoms. These reflect potential state-dependent factors (as opposed to trait, i.e., temperament). However, the relative stability of temperament is widely accepted, and has been shown even within the current study sample (Mufson et al., 1990). Thus we can assume with relative confidence that our results reflect trait-dependent rather than state-dependent constructs. Second, the external validity (generalizability) is limited. The original proband sample of parents with depression was recruited from a treatment center and all met criteria for moderate to severe MDD. Therefore, we cannot generalize to a community sample of people with milder forms of depression who are not receiving treatment. However, given we are examining the impact of biological predisposition to depression and that temperament has a biological component, using a sample with more severe depression is arguably a more desirable choice. Third, the relatively small sample size reduced power and limited our ability to conduct additional analyses by gender or other demographic variables. Finally, certain characteristics of the study sample may limit the generalizability of our findings. The sample was entirely Caucasian and predominantly Christian, and while this provides a more genetically uniform sample, it precludes the examination of racial or ethnic variations in depression and temperament. In addition, the age range was large and while we adjusted for baseline age in our analyses, a larger more tight-knit age cohort may have allowed us to draw more firm conclusions about developmental processes related to temperament and depression.

In light of these limitations, the current study provides important evidence that dimensions of temperament are uniquely associated with the features of MDEs. Greater rhythmicity is associated with decreased frequency of MDEs, greater inattention/distractibility is associated with decreased episode duration, and higher activity is associated with lower severity. These important findings suggest that variations in the phenomenology of depression may reflect specific temperamental profiles which are important to consider above and beyond basic diagnoses.

6. Conclusion

The period from adolescence to adulthood is one of increased responsibility and autonomy. Given the onset of depression peaks during this time, it is crucial to understand how an individual's constitutional makeup (i.e., temperament) impacts the onset, course, and prognosis of disorder. The current study examined the relationships between parental depression, offspring depression, and offspring temperament. As far as we know it is the longest multigenerational follow-up study with high- and low-risk comparison groups and retention was exceptionally high over the 20-year study period. Our findings provide important evidence that the relationship between temperament and depression is far more nuanced than simply difficult temperament predicting lifetime incidence of depression. Biological rhythms appear strongly related to recurrence of depression, while a tendency towards distraction and activation may serve a protective function. Continued research on the relationship between temperament and depression over the lifespan can inform more accurate and effective diagnostic and treatment strategies, as well as prevention initiatives geared towards minimizing the impact of temperamental risk factors.

References

Bruder-Costello, B., Warner, V., Talati, A., Nomura, Y., Bruder, G., Weissman, M., 2007. Temperament among offspring at high and low risk for depression. Psychiatry Res. 153, 145–151. http://dx.doi.org/10.1016/j.psychres.2007.02.013.

Buss, A.H., Plomin, R., 1984. Temperament: early developing personality traits. Psychol. Behav. Sci. http://dx.doi.org/10.11648/j.pbs.20140304.12.

Caspi, A., Moffitt, T.E., Newman, D.L., Silva, P.A., 1996. Behavioral observations at age 3 years predict adult psychiatric disorders: longitudinal evidence from a birth cohort. Arch. Gen. Psychiatry 53, 1033–1039. http://dx.doi.org/10.1001/archpsyc.1996.01830110071009.

Chronis-Tuscano, A., Degnan, K.A., Pine, D.S., Perez-Edgar, K., Henderson, H.A., Diaz, Y., Raggi, V.L., Fox, N.A., 2009. Stable early maternal report of behavioral inhibition predicts lifetime social anxiety disorder in adolescence. J. Am. Acad. Child Adolesc. Psychiatry 48, 928–935. http://dx.doi.org/10.1097/CHI.0b013e3181ae09df.

Conklin, H.M., Luciana, M., Hooper, C.J., Yarger, R.S., 2007. Working memory performance in typically developing children and adolescents: behavioral evidence

of protracted frontal lobe development. Dev. Neuropsychol. 31, 103–128. http://dx.doi.org/10.1207/s15326942dn3101_6.
Dimidjian, S., Hollon, S.D., Dobson, K.S., Schmaling, K.B., Kohlenberg, R.J., Addis, M. E., Gallop, R., McGlinchey, J.B., Markley, D.K., Gollan, J.K., Atkins, D.C., Dunner, D. L., Jacobson, N.S., 2006. Randomized trial of behavioral activation, cognitive therapy, and antidepressant medication in the acute treatment of adults with major depression. Annual Convention of the Association for the Advancement of Behavior Therapy. Nov 2003, Boston, MA, US. vol. 74, p. 658. Doi: http://dx.doi.org/10.1037/0022-006X.74.4.658.
Elovainio, M., Jokela, M., Rosenström, T., Pulkki-Råbäck, L., Hakulinen, C., Josefsson, K., Hintsanen, M., Hintsa, T., Raitakari, O.T., Keltikangas-Järvinen, L., 2015. Temperament and depressive symptoms: what is the direction of the association? J. Affect. Disord. 170, 203–212. http://dx.doi.org/10.1016/j.jad.2014.08.040.
Goodyer, I.M., Ashby, L., Altham, P.M.E., Vize, C., Cooper, P.J., 1993. Temperament and major depression in 11 to 16 year olds. J. Child Psychol. Psychiatry Allied Discip. 34, 1409–1423. http://dx.doi.org/10.1111/j.1469–7610.1993.tb02099.x.
Gray, J., 1991. The neuropsychology of temperament. In: Strelau, J., Angleitner, A. (Eds.), Explorations in Temperament: International Perspectives on Theory and Measurement. Plenum, New York.
Joormann, J., Siemer, M., 2004. Memory accessibility, mood regulation, and dysphoria: difficulties in repairing sad mood with happy memories? J. Abnorm. Psychol. 113, 179–188. http://dx.doi.org/10.1037/0021–843X.113.2.179.
Kasch, K.L., Rottenberg, J., Arnow, B.A., Gotlib, I.H., 2002. Behavioral activation and inhibition systems and the severity and course of depression. J. Abnorm. Psychol. 111, 589–597. http://dx.doi.org/10.1037/0021–843X.111.4.589.
Kaufman, J., Birmaher, B., Brent, D., Rao, U., Flynn, C., Moreci, P., Williamson, D., Ryan, N., 1997. Schedule for affective disorders and schizophrenia for school-age children-present and lifetime version (K-SADS-PL): initial reliability and validity data. J. Am. Acad. Child Adolesc. Psychiatry 36, 980–988. http://dx.doi.org/10.1097/00004583–199707000–00021.
Kessler, R.C., Amminger, G.P., Aguilar-Gaxiola, S., Alonso, J., Lee, S., Ustün, T.B., 2007. Age of onset of mental disorders: a review of recent literature. Curr. Opin. Psychiatry 20, 359–364. http://dx.doi.org/10.1097/YCO.0b013e32816ebc8c.
Klassen, L.J., Katzman, M.A., Chokka, P., 2010. Adult ADHD and its comorbidities, with a focus on bipolar disorder. J. Affect. Disord. http://dx.doi.org/10.1016/j.jad.2009.06.036.
Krueger, R.F., Watson, D., Barlow, D.H., 2005. Introduction to the special section: toward a dimensionally based taxonomy of psychopathology. J. Abnorm. Psychol. 114 (4), 491–493. http://dx.doi.org/10.1037/0021–843X.114.4.491.
Kuehner, C., Weber, I., 1999. Responses to depression in unipolar depressed patients: an investigation of Nolen-Hoeksema's response styles theory. Psychol. Med. 29, 1323–1333. http://dx.doi.org/10.1017/S0033291799001282.
Leckman, J.F., Sholomskas, D., Thompson, W.D., Belanger, A., Weissman, M.M., 1982. Best estimate of lifetime psychiatric diagnosis: a methodological study. Arch. Gen. Psychiatry 39, 879–883. http://dx.doi.org/10.1001/archpsyc.1982.04290080001001.
Lee, S.A., Rice, K., Callan, S.M., Brame, B.M., Lee, C.A., 2015. Temperament and depressive symptoms in at-risk children: aggression and learning problems as mediating factors. Personal. Individ. Differ. 87, 35–38. http://dx.doi.org/10.1016/j.paid.2015.07.018.
Lerner, R.M., Palermo, M., Spiro III, A., Nesselroade, J.R., 1982. Assessing the dimensions of temperamental individuality across the life span: The dimensions of Temperament Survey (DOTS). Child Development 53, 149–159.
Lovejoy, M.C., Graczyk, P.A., O'Hare, E., Neuman, G., 2000. Maternal depression and parenting behavior: a meta-analytic review. Clin. Psychol. Rev. 20, 561–592. http://dx.doi.org/10.1016/S0272–7358(98)00100–7.
Mannuzza, S., Fyer, A.J., Klein, D.F., Endicott, J., 1986. Schedule for affective disorders and schizophrenia-lifetime version modified for the study of anxiety disorders (SADS-LA): rationale and conceptual development. J. Psychiatr. Res. 20, 317–325. http://dx.doi.org/10.1016/0022–3956(86)90034–8.
McFarland, B.R., Shankman, S.A., Tenke, C.E., Bruder, G.E., Klein, D.N., 2006. Behavioral activation system deficits predict the six-month course of depression. J. Affect. Disord. 91, 229–234. http://dx.doi.org/10.1016/j.jad.2006.01.012.
Mufson, L., Fendrich, M., Warner, V., 1990. The stability of temperament by child and mother reports over two years. J. Am. Acad. Child Adolesc. Psychiatry 29, 386–391. http://dx.doi.org/10.1097/00004583–199005000–00009.
Nigg, J.T., 2006. Temperament and developmental psychopathology. J. Child Psychol. Psychiatry Allied Discip. http://dx.doi.org/10.1111/j.1469–7610.2006.01612.x.
Nolen-Hoeksema, S., 1991. Responses to depression and their effects on the duration of depressive episodes. J. Abnorm. Psychol. 100, 569–582. http://dx.doi.org/10.1037/0021–843X.100.4.569.
Nolen-Hoeksema, S., Morrow, J., Fredrickson, B.L., 1993. Response styles and the duration of episodes of depressed mood. J. Abnorm. Psychol. 102, 20–28. http://dx.doi.org/10.1037/0021–843X.102.1.20.
Nolen-Hoeksema, S., Parker, L., 1994. Ruminative coping with depressed mood following loss. J. Personal. Soc. Psychol. 67, 92–104. http://dx.doi.org/10.1037/0022–3514.67.1.92.
Pinto-Meza, A., Caseras, X., Soler, J., Puigdemont, D., Pérez, V., Torrubia, R., 2006. Behavioural inhibition and behavioural activation systems in current and recovered major depression participants. Personal. Individ. Differ. 40, 215–226. http://dx.doi.org/10.1016/j.paid.2005.06.021.
Radke-Yarrow, M., Klimes-Dougan, B., 2002. Parental depression and offspring disorders: a developmental perspective. In: Sherryl, H., Gotlib, I.H. (Eds.), Children of Depressed Parents: Mechanisms of Risk and Implications for Treatment. American Psychological Association, Washington, DC, pp. 155–173. http://dx.doi.org/10.1037/10449–006.
Rettew, D.C., McKee, L., 2005. Temperament and its role in developmental psychopathology. Harv. Rev. Psychiatry 13, 14–27. http://dx.doi.org/10.1080/10673220590923146.
Rothbart, M.K., Bates, J.E., 2006. Temperament. In: Handbook of Child Psychology: Vol. 3: Social, Emotional, and Personality Development, pp. 99–166.
Rothbart, M.K., Derryberry, D., Hershey, K., 2000. Stability of temperament in childhood: Laboratory infant assessment to parent report at seven years. In: Temperament and Personality Development across the Life Span, pp. 85–119.
Schwartz, C.E., Snidman, N., Kagan, J., 1999. Adolescent social anxiety as an outcome of inhibited temperament in childhood. J. Am. Acad. Child Adolesc. Psychiatry 38, 1008–1015. http://dx.doi.org/10.1097/00004583–199908000–00017.
Srinivasan, V., Pandi-Perumal, S.R., Trakht, I., Spence, D.W., Hardeland, R., Poeggeler, B., Cardinali, D.P., 2009. Pathophysiology of depression: role of sleep and the melatonergic system. Psychiatry Res. 165, 201–214. http://dx.doi.org/10.1016/j.psychres.2007.11.020.
Stetler, C., Miller, G.E., 2005. Blunted cortisol response to awakening in mild to moderate depression: regulatory influences of sleep patterns and social contacts. J. Abnorm. Psychol. 114, 697–705. http://dx.doi.org/10.1037/0021–843X.114.4.697.
Thomas, A., Chess, S., 1977. Temperament and development. Brunner/Mazel, New York, NY.
Trask, P.C., Sigmon, S.T., 1999. Ruminating and distracting: The effects of sequential tasks on depressed mood. Cogn. Ther. Res. 23, 231–246. http://dx.doi.org/10.1023/A:1018787430249.
Uher, R., Maier, W., Hauser, J., Marušič, A., Schmael, C., Mors, O., Zobel, A., 2009. Differential efficacy of escitalopram and nortriptyline on dimensional measures of depression. Br. J. Psychiatry 194 (3), 252–259.
Watson, D., Gamez, W., Simms, L.J., 2005. Basic dimensions of temperament and their relation to anxiety and depression: a symptom-based perspective. J. Res. Pers. 39, 46–66. http://dx.doi.org/10.1016/j.jrp.2004.09.006.
Weissman, M.M., Gammon, G., John, K., et al., 1987. Children of depressed parents: Increased psychopathology and early onset of major depression. Arch. Gen. Psychiatry 44, 847–853. http://dx.doi.org/10.1001/archpsyc.1987.01800220009002.
Weissman, M.M., Warner, V., Wickramaratne, P., Moreau, D., Olfson, M., 1997. Offspring of depressed parents. 10 Years later. Arch. Gen. Psychiatry 54, 932–940. http://dx.doi.org/10.1001/archpsyc.1997.01830220054009.
Weissman, M.M., Wickramaratne, P., Nomura, Y., Warner, V., Pilowsky, D., Verdeli, H., 2006. Offspring of depressed parents: 20 Years later. Am. J. Psychiatry 163, 1001–1008. http://dx.doi.org/10.1176/appi.ajp.163.6.1001.
Weissman, M.M., Wickramaratne, P., Pilowsky, D.J., Poh, E., Hernandez, M., Batten, L. A., Flament, M.F., Stewart, J.W., Blier, P., 2014. The effects on children of depressed mothers' remission and relapse over 9 months. Psychol. Med. 44, 2811–2824. http://dx.doi.org/10.1017/S003329171400021X.
Widiger, T.A., Gore, W.L., 2015. Dimensional versus Categorical Models of Psychopathology. In: The Encyclopedia of Clinical Psychology. John Wiley & Sons, Inc, Hoboken, NJ, USA, pp. 1–12. http://dx.doi.org/10.1002/9781118625392.wbecp108.
Windle, M., Windle, R.C., 2006. Adolescent temperament and lifetime psychiatric and substance abuse disorders assessed in young adulthood. Personal. Individ. Differ. 41, 15–25. http://dx.doi.org/10.1016/j.paid.2006.01.005.