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EXCITABILITY AND IRRITABILITY IN PRESCHOOLERS PREDICTS LATER PSYCHOPATHOLOGY: THE IMPORTANCE OF POSITIVE AND NEGATIVE EMOTION DYSREGULATION

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Abstract

Emotion dysregulation is a risk factor for the development of a variety of psychopathologic outcomes. In children, irritability, or dysregulated negative affect, has been the primary focus, as it predicts later negative outcomes even in very young children. However, dysregulation of positive emotion is increasingly recognized as a contributor to psychopathology. Here we used an exploratory factor analysis and defined four factors of emotion dysregulation-irritability, excitability, sadness, and anhedonia- in the preschool age psychiatric assessment collected in a sample of 302 children ages 3-5 years enriched for early onset depression. The irritability and excitability factor scores defined in preschoolers predicted later diagnosis of mood and externalizing disorders when controlling for other factor scores, social adversity, maternal history of mood disorders, and externalizing diagnoses at baseline. The preschool excitability factor score predicted emotion lability in late childhood and early adolescence when controlling for other factor scores, social adversity, and maternal history. Both excitability and irritability factor scores in preschoolers predicted global functioning into the teen years and early adolescence, respectively. These findings underscore the importance of positive, as well as negative, affect dysregulation as early as the preschool years in predicting later psychopathology, which deserves both further study and clinical consideration.

Keywords

“emotion dysregulation”; preschool; “mood lability”; EFA; depression

INTRODUCTION

Emotion dysregulation has been conceptualized as “a pattern of emotional experiences or expressions that is experienced either too intensely or too enduringly to be adaptive” (Beauchaine, 2015). From a neurobiological perspective, emotion dysregulation can be seen as dysfunctional patterns of bottom up processes, such as those that subserve emotion

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generation, as well as top down processes that subserve emotion regulation (Sheppes, Suri, & Gross, 2015). While there has been much focus on emotion regulatory function, the experience of an emotions' intensity in response to internal and external stimuli is also a key element of understanding this process. Dysregulation of negative emotions such as fear, anxiety, sadness, and anger have been implicated in the development of later psychopathology (Beauchaine, 2001 and 2015). However, there is also evidence that dysregulated positive emotions can result in impairment and psychopathology (Klein, Kotov, & Bufferd, 2011; Putnam & Stifter, 2002; Rydell, Berlin, & Bohlin, 2003). While the focus on dysregulated negative affect in the literature has led to an increasing understanding of risk for and manifestations of psychopathology, including from a young age, the role of positive affect dysregulation in psychopathology remains understudied. Here we aim to expand the study of dysregulation to assess both negatively and positivity valanced emotions in preschoolers, first utilizing exploratory factor analysis to determine if dysregulation for positive and negative emotions are separable and second, if separable, to look at the relationships between these different types of early dysregulation and later outcomes.

Irritability as a paradigm of emotion dysregulation.

The literature on emotion dysregulation and psychopathology in children has been largely focused on the study of irritability, or as Brotman, Kircanski, and Liebenluft (2017) defined, "a low threshold for experiencing anger in response to frustration". This focus is with good reason, as irritability specifically has been related to the concurrent diagnosis or later development of a number of psychiatric disorders, including attention deficit hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), anxiety, and depression (Brotman, Schmajuk, Rich, Dickstein et al., 2006; Copeland, Angold, Costello, and Egger 2013; Copeland, Shanahan, Egger, Angold, and Costello, 2014; Dougherty, Smith, Bufferd, Carlson, et al., 2014; Dougherty, Smith, Bufferd, Kessel, et al., 2016; Ezpelata, Granero, de la Osa, Trepat, and Domenech, 2016; Liebenluft, Cohen, Gorrindo, Brook, and Pine, 2006; Pagliaccio, Pine, Barch, Luby, and Liebenluft, 2018; Stringaris, Cohen, Pine, & Liebenluft, 2009; Wackschlag, Estabrook, Petitclerc, Henry, Burnes, et al., 2015; Whelan, Stringaris, Maughan, & Barker, 2013). The presence of extreme irritability has been such a salient clinical problem that in the latest version of the DSM, disruptive mood dysregulation disorder (DMDD) was included to better describe children who have extremes of irritability but failed to meet criteria for other disorders in which irritability is also present (Roy, Lopes, & Klein, 2014).

Extreme irritability is a robust risk factor to many negative behavioral and developmental outcomes. As early as infancy, proneness to anger is linked to later development of disruptive behavior (He, Degnan, McDermott, Henderson, et al., 2010). Irritability in preschoolers has been linked to not only later psychiatric diagnoses as noted above, but also to poor family relations, school functioning, and suicidality (Belden, Thomson, & Luby, 2008; Dougherty, et al., 2013; Dougherty, et al., 2016; Ezpelata, et al., 2016; Pagliaccio, et al., 2018; Wakschlag, Briggs-Gowen, Carter, Hill, Degnan, Calkins, Keane, 2006; Wakschlag, Choi, Carter, Hullsiek, et al., 2012). Irritability in older children has been linked to increased psychiatric diagnoses and disability as well as increased suicidality, substance use, risky behavior, school drop out, poorer work performance and health outcomes

(Copeland et al., 2013; Copeland et al., 2014; Orri, Galera, Turecki, Forte, et al., 2018). However, expressions of irritability are not necessarily pathologic. Irritability is common and normative during the preschool period (Belden, et al., 2008; Wackschlag et al., 2012) and then typically declines with age (Copeland, Brotman, & Costello, 2015; Liebenluft, et al., 2006; Wackschlag, Perlman, Blair, Liebenluft, et al., 2018). Functionally, irritability conceptualized as a negative response to frustration can be adaptive, in that it may increase efforts to gain a desired outcome. Nonetheless, there is evidence that increased irritability, even in the normative range, is associated with an increased risk of later psychiatric problems (Copeland, et al., 2015, Wackschlag et al., 2015).

Dysregulation of positive emotions.

Dysregulation of positive affect has been understudied relative to negative affect (Forbes, 2009; Forbes & Dahl, 2005; Gilbert, 2012), despite evidence that the general experience of emotion dysregulation writ large, not only the dysregulation of negative emotions, predisposes to psychopathology and impaired social functioning in adolescents (Sallquist, Eisenberg, Spinrad, Reiser, et al., 2009; Silk, Steinberg, & Morris, 2003; Stringaris & Goodman, 2009), including both internalizing and externalizing disorders (Zisner & Beauchaine, 2016). In fact, dysregulated response to reward has also been related to ADHD (Plicta & Scheres, 2014). Conceptually, one might expect to be able to dissociate dysregulation of positive and negative emotion, as neurobiologically these have been thought to be separate processes (Forbes & Dahl, 2005). In the research domain criteria model, negative emotion or valence systems comprise acute, potential and sustained threat, loss, and frustrated nonreward, while positive emotion or valence systems comprise approach motivation, initial and sustained response to reward, reward learning, and habit (Cuthbert & Insel, 2013). However, dysregulation in positive and negative emotion are also likely to be correlated and may be in part subserved by overlapping neurobiological processes, given the overlapping risk for later psychopathology and potential overlap related to abnormal response to reward (Zisner & Beauchaine, 2016).

Like negative emotions, positive emotions also have a normal developmental trajectory. Infants level of expressing positive and negative affect can be differentially studied as early as 4 months of age (Park, Belsky, Putnam, & Crnic, 1997), and while they are correlated, they do not appear to represent a single dimension. The division between state positivity and negativity can be identified in examinations of affect and behavioral inhibition as early as 6-24 months of age (Putnam & Stifter, 2005). Highly reactive infants who have a more positive than negative affect can be identified as early as 4 months of age, are referred to as “exuberant”, and display general phenotypic continuity with increased sociability and low distress at older ages (Fox, Henderson, Rubin, Calkins, & Schmidt, 2001). Positive expressions appear to generally increase throughout toddlerhood before reaching a point of stability in the preschool age range (Sallquist, Eisenberg, Spinrad, Gartner, et al. 2010). However, similar to other forms of emotional expression, there then appears to be a general decrease in positive affect expression throughout childhood (Sallquist et al., 2009).

Positive emotion dysregulation is often studied as a “lack of positivity”, with diminished experiences of positive emotion in children being linked to depression (Forbes, 2009) and to

a lesser degree anxiety (Kashdan, 2007). Consistent with this, Silk et al., (2006) found increased levels of positive emotion in children during a reward task to be associated with a lower level of depressive symptoms. Park et al, (1997) demonstrated that high positive affect in infancy attenuated the effect of high negative affect in the development of behavioral inhibition.

Yet increased experiences of positive emotions are not uniformly adaptive, nor do they always have positive outcomes. In 6-12 month old infants high positive affect predicted externalizing symptoms at age 2 (Putnam & Stifter, 2005). The frequency and intensity of positive affect in 5 year old children, termed “exuberance emotionality”, was positively correlated with anger, negatively correlated with soothability, and predicted externalizing behaviors 18 months later (Rydell et al., 2003). Children with higher parent reported positive anticipation also had higher rates of aggression (Deater-Deckard, Beakman, Wang, Kim, et al., 2010). The irritability literature also implicates dysregulation in reward systems, which have been traditionally linked to positive emotion. There have been some reports of increased activity in the striatum to reward receipt in irritable children (Deveney, Connelly, Haring, Bones, et al., 2013), though the opposite pattern has been seen in other studies (Perlman, Jones, Wakschlag, Axelson, et al., 2015), indicating an excessive response to reward may increase irritable behaviors or outbursts.

Early emotion dysregulation as a risk for later childhood affective diagnoses

Child onset depression is an increasingly recognized developmental diagnosis, with longitudinal continuity and considerable impairment (Gaffrey, Tillman, Barch, & Luby, 2018; Luby, Belden, Pautsch, Si, and Spitznagel, 2009; Luby, Gaffrey, Tillman, April & Belden, 2014; Luby, Heffelfinger, Mrakotsky, Brown, et al., 2003). As reviewed above, there is an extensive literature linking early emotion dysregulation to depressive disorders. Irritability is frequently seen in depressed children (Luby et al., 2009) and is a risk factor for later development of depressive disorders (Ezplata et al., 2016; Paglioccio et al., 2018; Wackshlag et al., 2007, Wackshlag et al., 2012). Dysregulated expressions of sadness and dysregulated-low expressions of positive affect are also seen early childhood depression and continue to be risk factors for later depressive episodes (Luby et al., 2003, 2006, and 2009).

Childhood onset bipolar disorder is also an increasingly recognized developmental disorder, though there continues to be considerable controversy and debate about how narrowly to define criteria for mania in pre-pubertal children (Goldstein, Birmaher, Carlson, DelBello, et al., 2017). While chronic irritability was once considered a potential presentation of childhood bipolar disorder (Biederman, Mick, Farone, Spencer, et al., 2000), some consensus has been reached that children with bipolar disorder I and II should meet criteria similar to adults. Most investigators suggest that when irritability is being used as a central diagnostic criterion, it should wax and wane with the intensity of other manic symptoms rather than have a more chronic presentation (Goldstein et al., 2017). There continues to be debate about how far to extend the “bipolar spectrum”, and whether to include children who may meet criteria for mania but for shorter than four days or who exhibit symptoms consistent with cyclothymia (Goldstein et al., 2017). Notwithstanding these ambiguities on

childhood bipolar disorder, emotion dysregulation in general, and dysregulation of positive affect in particular, are core features of this disorder.

Affective lability in general has been implicated as a risk factor in the development of bipolar disorder (Birmaher, Gill, Axelson, Goldstein, Goldstein, et al., 2014; Hafeman, Merranko, Axelson, Goldstein, et al., 2016). While a long term follow up study showed that more than 50% of children and teens with bipolar disorder will eventually spend most of their time euthymic, increased affective lability was associated with generally worse outcomes (Birmaher, et al., 2014). Further, positive emotion dysregulation has been specifically implicated in childhood bipolar disorder. Extremes of positive emotion dysregulation are diagnostic of bipolar disorder, and even in broad-spectrum characterizations of bipolar disorder 70 −90% of the children will have episodes of elated affect (Kowatch, Youngstrom, Danielyan, Findling, 2005; Geller, Zimmerman, Williams, Bolhofner, et al., 2000). Grandiosity is another more specific marker of dysregulated positive affect. While more challenging to study in early development (Youngstrom, Birmaher, Findling, 2008, but see Luby et al., 2006), grandiosity is also seen in children with mania (Geller et al., 2000, Luby & Belden 2006, Kowatch et al., 2005). However, there is high comorbidity between childhood onset bipolar disorder and other diagnoses, particularly ADHD (Kowatch et al., 2005, Geller et al., 2000, Luby & Belden 2006), and a number of the most common symptoms of mania in children including increased energy, distractibility, pressured speech, and irritability, can also occur in ADHD. This speaks to the potential for dysregulated positive affect to be a more generic potential risk factor for many later forms of psychopathology. Such findings and ambiguities also underscore the need to better identify and characterize these early manifestations of dysregulated positive affect as risk factors and diagnostic markers in early childhood using a dimensional approach to emotion dysregulation.

The Current Study

Given the importance of emotion dysregulation in psychopathology, the well-established impact of dysregulation of negative emotions and irritability on later impairment even in very young children, but the uncertain relationship between positive emotion dysregulation and later adaptive and pathological outcomes, we aimed to better understand whether positive and negative emotion dysregulation were two empirically separable dimensions in preschool children. In a sample enriched for early childhood affective psychopathology, we sought to investigate whether negative and positive affect dysregulation differentially predicted clinical outcomes or global measures of clinical severity in later childhood and adolescence. We utilized a moderately large, longitudinally studied cohort enriched for children with early childhood depression, but not specifically for emotion dysregulation (Luby et al., 2014). We hypothesized that we could separately identify dysregulation in positive and negative emotion. We hypothesized that both types of dysregulation would increase risk for later clinical diagnoses and impairment, but with differential effects. Specifically, we hypothesized that positive affect dysregulation would increase risk for later bipolar disorder and ADHD, while negative affect dysregulation might increase risk for later depressive disorders and ODD. We also hypothesized that negative affect dysregulation

would be more predictive of later global impairment in keeping with the extant literature on irritability.

METHODS

Participants

Study participants were drawn from the Preschool Depression Study (PDS), a longitudinal investigation of children enriched for those with early onset depression that has been extensively described elsewhere (Luby et al., 2014). Our participants included all of those who had reliable Preschool Age Psychiatric Assessment (PAPA; Egger & Angold, 2004) data from the baseline visit (T1), between ages 3-5 years, N= 302, 145F, 157M. These children were then assessed on a regular basis until their late teens (ages 16-19 years), including almost yearly structured interviews and behavioral questionnaires spanning a 15 year period. At the time of this analysis, children had been asked to participate in nine total annual to biannual assessments (T1-T9), with 291 (96%) of the 302 included children returning for at least one later assessment.

Measures

Structured Diagnostic Interviews: In the PDS, children and parents participated in structured diagnostic and developmental interviews annually with a trained clinical interviewer with good interrater reliability (Luby et al., 2014). Initially the interviewers used the PAPA and converted to the Child and Adolescent Psychiatric Assessment (CAPA; Angold, Predergast, Cox, Harrington, et al., 1995) when age appropriate (at age 8). Items from the structured diagnostic interview at T1 were used to both characterize the symptoms and symptom clusters described below, and structured interviews at T1-T9 were also used to derive DSM based diagnoses, using standard DSM-IV criteria.

Global Function: The same trained interviewers who rated the diagnostic interviews also performed global ratings of impairment at T1-T9 using the Preschool and Early Childhood Functional Assessment Scale (PECFAS; Murphy, Pagano, Anaya, Cox, et al., 1999) and Childhood and Adolescent Functional Assessment Scale (CAFAS; Hodges, 1994), generally transitioning when participants were 7 years old. Both are interviewer rated standardized scales that rate the day to day functioning of the child in multiple environments including home, school, and other public environments, as age appropriate. Total impairment scores were utilized in regression analyses. In general, the CAFAS has lower internal reliability (Cronbach's alphas in the development and validation datasets varied between 0.63 and 0.68), thought due to the intended heterogeneity of the included constructs (Bates, 2001).

IQ: IQ was assessed using either the Wechsler Abbreviated Scale of Intelligence II (WASI-II, Wechsler, 2011) at T5 (age 8-12) or the Kaufman Brief Intelligence Test 2 (KBIT-2, Kaufmann & Kaufmann, 2004) at T7 (age 10-14). Later IQ measures were used given that no preschool age IQ measures were available, and IQ is posited to be largely stable (Deary et al., 2000).

Emotion Regulation: Children were assessed with a multitude of other behavioral measures at various time points. In this analysis we have focused on the Emotion Regulation Checklist (ERC, Shields & Cicchetti, 1997), a parent report questionnaire rating both emotion regulation capacity as well as emotion lability and negativity. The ERC was performed at four different times from middle childhood to late teens, and here we report data collected from ages 6-12 years and from 12-19 years of age. In initial validation studies, the emotion regulation subscale had a Cronbach's alpha of 0.83 and the lability/negatively subscale of 0.96 (Shields & Cicchetti, 1997).

Social Adversity: A composite measure of social adversity at age 5 was a sum of yes(1)/no(0) responses to the following: living in a single parent household, a parent having any DSM-IV axis I psychiatric diagnosis, parental arrest, history of foster care placement, physical or sexual abuse, or caregiver reporting being unable to meet the family's financial needs, computed from the timepoint of data collection for each child that occurred closest to age 5. A composite measure was chosen to reflect the diversity of adverse events children might experience, and to account for the potential additive effects of having multiple adverse events, which is a common finding in adults (i.e., Felitti, Anda, Nordenberg, Williamson, et al., 1998).

Maternal History of Depression: Maternal history of depression was assessed using the Family Interview for Genetic Studies (FIGS) and questions about current treatment. We chose to use a relatively conservative measure of maternal history- either meeting criteria for the disorder on the FIGS or being currently under treatment for depression or bipolar disorder with a mental health professional. Possible or presumed diagnoses were coded as negative.

Exploratory Factor Analysis

As we aimed to determine if there was an identifiable difference between positive and negative emotion dysregulation, as well as their relationship to each other and other affective symptoms, an exploratory factor analysis was performed using all items from the PAPA structured clinical interview that addressed emotion dysregulation, including items from the depression, mania, and conduct modules. This allowed us to use a hypothesis neutral approach to data reduction. We performed the EFA on all items that assessed manifestations of emotional experience and regulation from the PAPA depression and mania modules, as well as tantrum related questions from the PAPA conduct module in order to better represent outward displays of emotion dysregulation, using data collected at baseline, when children were age 3 years 0 months through 5 years 11 months (3-5 years) old.

The EFA included intensity based items and also items reflecting overall duration and frequency of affective symptoms, as frequent shifts and/or short duration, may be more reflective of dysregulation or lability than more sustained shifts in affect. For the duration and frequency items, the item responses were divided into deciles and these were converted into a 0-5 rating scale with each decile reflecting 0.5 points on the scale, in order to bring the available range of responses into better alignment with the other items included. A similar method was applied to sleep duration, which was also divided into deciles and converted to a

0-5 scale. All other items were scores as indicated in the PAPA scoring manual. We then excluded 6 items with less than a 50% recorded response rate, which occurred typically due to a negative screen on a preceding question (i.e., delusional guilt was dependent on reporting guilt). 2 items with a pearson's r > .90 with another item were also excluded (spontaneity of elevated mood was correlated at 0.93 with intensity of elevated mood and alleviation of anhedonia was correlated at 0.90 with intensity of anhedonia). This resulted in 78 total items (all shown in Table 1). Responses for any of the variables were included for all 302 children with a PAPA collected at baseline (between age 3-5 years), making a 302 x 78 matrix, allowing for missing values.

EFA was implemented in M-plus, using standard settings and including the geomin oblique rotation due to expected correlations between factors. Missing data was accounted for using FIML. Inspection of the Scree plot and factors resulted in choosing a four factor model, as all factors at this point had eigenvalues > 2, four factors was a noted elbow in the scree plot, and factors demonstrated face validity. Factor assignments for each item and their standardized factor loadings are shown in Table 1.

Computation of Factor Scores

Individual factor scores were calculated for each subject at T1 baseline (age 3-5 years) using all items assigned to a factor with a standardized factor loading greater than 0.35. To account for missing items, data were imputed using the statistical software R (R Core Team, 2017) and the mice package (Burren et al., 2011). Then, structured equation modeling, implemented in R package lavaan (Rosseel, 2012), was used to calculate weighted latent factor scores from the included items for each participant. Four confirmatory factor models were created using the four factor EFA solution established prior. Tests of internal consistency utilizing Cronbach's alpha, distributions of the factor scores and correlations between the scores were calculated.

Relationships between factor scores with both baseline and outcome measures

We hypothesized that factor scores representing emotion dysregulation at baseline would be predicted by cognitive measures such as IQ, age 5 social adversity, and maternal psychiatric history of mood disorder. We conducted linear regressions, implemented in R, predicting each factor score with IQ and the composite measure of social adversity at age 5. The relationship between maternal psychiatric history and the factor scores was tested with first a simple t-test to determine any differences in factor scores between those with and without a maternal history of both bipolar disorder or MDD. In situations where there was a statistical difference between groups, we tested whether this was partially explained by social adversity by performing four separate univariate regressions with the factor scores as the dependent variable, maternal history as a fixed factor, and social adversity as a covariate.

We then utilized logistic regression to determine whether each of the factors predicted later childhood diagnosis of mania, depression, or other externalizing diagnoses including ADHD, ODD, and conduct disorder (CD) at any timepoint after baseline, including all other factor scores, the social adversity score, and maternal history of bipolar disorder as covariates. Social adversity and maternal history of bipolar were entered due to their ability

to predict one or more factor scores. Maternal history of depression and IQ were not included as covariates as they failed to predict any factor score after social adversity was included in the model. A second set of logistic regressions predicting externalizing diagnoses, including ADHD, ODD, and CD, were conducted including all factor scores, maternal history of bipolar disorder, age 5 social adversity, as well as baseline diagnosis of ADHD, ODD, or CD respectively. Baseline diagnosis of the same disorder was included due to potential symptom overlap between items included in the factor scores and diagnostic criteria for these disorders.

For all of the analyses, participants were counted as having a later diagnosis of these disorders if they met DSM-IV criteria for the diagnosis at any subsequent structured diagnostic interview in the study (i.e., timepoints 2-9, ages 4-6 through ages 14-19). Given that several factor scores predicted both later diagnosis of depression and mania, we separately calculated the logistic regression for predicting depression without mania (i.e., meeting criteria for MDD at any later timepoint, but never meeting criteria for mania). Additionally, given the controversy surrounding the diagnosis of pre-pubertal bipolar disorder, we also separately calculated the number of subjects that continued to meet criteria for mania after age 12 (the age at which the diagnosis is more clearcut). Due to the small number of subjects who met such criteria, no further analysis was done.

Next, we performed linear regressions predicting continuous measures of emotion regulation as measured by the ERC and global functioning as measured by the PECFAS and CAFAS. We performed linear regressions predicting ERC emotion regulation and lability/negativity scales in middle childhood (ages 6-12, mean age 10 years) and in the teen years (ages 13-19, mean age 16 years) with all four factor scores, social adversity and maternal history of bipolar disorder as predictors. A similar analysis predicting global impairment as measured by the PECFAS or CAFAS total score (as age appropriate) at each timepoint was conducted with all four factor scores, social adversity and maternal history of bipolar disorder as predictors.

RESULTS

Exploratory Factor Analysis

We performed an exploratory factor analysis using all symptom items from the PAPA depression and mania modules, as well as dysregulation (e.g. irritability, tantrums) items from the PAPA conduct module collected at T1 in order to better represent all manifestations of dysregulated emotion, resulting in 78 total items. We included items with missing data in less than half of the subjects. 17% of items were missing no data, 32% of items were missing data from less than 1% of participants, and 85% of items were missing data from less than 10% of participants. Of the remaining 12 items, 10 were missing data from less than 25% of participants, one from 30% (grandiosity concern to caretakers) and one from 47% of participants (elated/expansive mood alleviation). As above, inspection of the scree plot and factor assignments led us to choose a four factor model. PAPA item content of each factor led to the following naming of the four factors: Sadness, Irritability, Excitability, and Anhedonia, reflecting both negative and positive emotion dysregulation. All items, their factor assignment and loadings can be found in Table 1, correlations between all individual

items can be found in supplementary material. Factor scores were calculated from all items with standardized loading > 0.35.

Characteristics of and Relationships between Factor Scores

Factor scores had acceptable internal consistency. Cronbach's alpha was 0.84 for the excitability factor score, 0.84 for the irritability factor score, 0.77 for the sadness factor score, and 0.75 for the anhedonia factor score.

While not fully normally distributed in our population due to the rightward skew in the excitability (2.26) and anhedonia (3.04) factor scores (which might be predicted in a community population enriched for clinical symptoms), all factor scores had a clear unimodal distribution.

There were significant correlations between factor scores, but these were not fully overlapping constructs. For example, the irritability and excitability factor scores were correlated with a pearson's $r = 0.60$ ($p < 0.001$), which is a moderate correlation but suggests some non-overlapping variance. Excitability was also significantly correlated with the sadness factor score ($r= 0.30$, $p<0.001$) and anhedonia factor score ($r = 0.40$, $p< 0.001$). Irritability was also significantly correlated with Sadness ($r = 0.60$, $p<0.001$) and anhedonia ($r= 0.45$, $p< 0.001$). Sadness and anhedonia were also significantly correlated ($r= 0.60$, $p<0.001$).

Predictors of Factor Scores

Social Adversity: We found via linear regression that social adversity at age 5 significantly predicted excitability ($R^2 = 0.08$, $F=26.42$, $p < 0.001$) and irritability factor scores ($R^2 = 0.08$, $F=24.71$, $p < 0.001$), as well as the sadness factor score ($R^2= 0.02$, $F=6.24$, $p = 0.013$). However, social adversity at age 5 did not significantly predict the anhedonia factor score.

Family History of Mood Disorders: Family history of mood disorders also predicted factor scores. All factor scores were significantly higher in children with a maternal history of bipolar disorder (n=19) relative to those without such a history (as seen in Table 2). The relationships between anhedonia and sadness factor scores and maternal history of bipolar disorder remained significant even when controlling for Age 5 social adversity. In contrast, only the sadness and irritability factor scores were significantly higher when there was a maternal history of MDD (n=101, see Table 2) and this was no longer significant when Age 5 social adversity was included as a covariate.

IQ: While there is some evidence that IQ predicts emotion regulation, only the excitability factor score was predicted by IQ ($r2=0.04$, $F=10.07$, $b= -0.21$, $p=0.002$), and this relationship became non-significant when age 5 social adversity was added to the model ($b= -0.01$, $t=-1.67$, $p=0.09$).

Factor Scores differentially predict later psychiatric diagnosis

Mood Diagnoses: When controlling for all other factor scores as well social adversity and maternal history of bipolar disorder, the excitability factor score significantly predicted ever meeting DSM-IV diagnostic criteria for mania after baseline via binary logistic regression (n=65, diagnosed at any point from T2 (ages 3-5) through T9 (ages 14-19)). The OR of ever having mania as a function of each increased point in the excitability factor score was 2.29 [95% CI 1.49-3.68], p<0.001). The irritability factor score from baseline also significantly predicted ever meeting criteria for mania at later assessment points in this model (OR 1.99 [95% CI 1.19-3.37], p=0.009), again even when controlling for all of the other factors scores, social adversity and maternal diagnosis. The sadness and anhedonia factor scores did not significantly predict later diagnosis of mania in this model. These results are summarized in Figure 2.

When controlling for the contribution of other factor scores, social adversity and maternal mood history, the excitability and irritability factor scores predicted later diagnosis of depression (n= 152, diagnosed at any point T2 (ages 4-7) through T9 (ages 14-19)). The OR of later being diagnosed with depression was 2.55 ([95% CI 1.98-3.36], p=0.01) for each point increase in excitability factor score and OR was 3.11 ([95% CI 1.32-3.27], p=0.002) for each point increase in irritability factor score.

However, when considering only those children that were later diagnosed with depression but never diagnosed with mania (n=91), only the irritability factor score was significantly predictive of later diagnosis of depression (OR 1.77 [95% CI 1.15 – 2.74], p=0.01). Instead, the excitability factor score became predictive of *not* having a later diagnosis of MDD without mania (OR for a later diagnosis of MDD but never mania for each point increase in excitability FS = 0.48 [95% CI 0.30-0.72], p < 0.001). Thus, the predictive ability of the excitability factor score for later diagnosis of depression appeared to be due to the overlap in later diagnosis of mania and later diagnosis of depression.

Externalizing Diagnoses: The excitability factor score from T1 predicted later ADHD diagnosis (n=80, T2 (ages 4-6) through T9 (age 14-19)) via logistic regression, even when all other factor scores, social adversity and maternal history of bipolar disorder were controlled for in the model (OR of ever being diagnosed with ADHD at a later time for each point increase in the excitability FS is 2.20 [95% CI 1.38-3.66], p=0.001).

Both excitability and irritability factor scores at T1 (ages 3-5 years) predicted later diagnosis of ODD (n=61, T2 (ages 4-6) through T9 (age 14-19)) via logistic regression when all factor scores, social adversity, and maternal history of bipolar disorder were controlled for in the model (OR of ever having a diagnosis of ODD with each increased point of the excitability factor score = 1.96 [95% CI 1.23-3.25], p=0.006 and OR for the irritability factor score = 2.25 [95% CI 1.35-3.84], p=0.002), as in figure 3.

The excitability factor score at baseline (ages 3-5 years) also predicted later diagnosis of CD (n=54 with diagnosis at T2 (ages 4-6) through T9 (ages 14-19)) when all factor scores, social adversity, and maternal history of bipolar disorder were in the model. The OR of ever

being diagnosed with CD for each point increase in the excitability factor score = 2.11 (95% CI 1.31-3.51, p=0.003), as in figure 3.

Importantly, while there are overlapping features between the excitability and irritability factor scores and the diagnostic criteria of the externalizing diagnoses, these factor scores predicted later externalizing diagnoses even above and beyond having a baseline diagnosis of the disorder (table 3). The excitability factor score remained predictive of ADHD even when ADHD diagnosis at T1 was added to the full model, with OR =2.08 (95% CI 1.24-3.50 (p=0.006) for the excitability factor score. The excitability factor score was similarly predictive of later ODD even when ODD diagnosis at T1 was entered into the model, with OR of 1.87 (95% CI 1.17-3.01) (p=0.01), though the irritability factor score was no longer predictive (OR = 1.74 [95% CI 0.98-3.11], p=0.06). Once CD at T1 was entered into the model the excitability factor score remained predictive of a later diagnosis of CD above already meeting criteria for a CD diagnosis at age 3-5 (OR 1.92 [95% CI 1.14-3.21], p=0.01).

Affect dysregulation factor scores predict later emotion regulation problems

Emotion Regulation: The excitability factor score predicted ERC lability/negativity score at age 6-12 years (mean 10 years old) and at ages 13-19 years (mean 16 years old) with linear regression (R^2= 0.29 at ages 6-12 and R^2=0.16 at ages 13-19, both p< 0.001), even when the other factor scores, age 5 social adversity, and maternal diagnosis of bipolar disorder were in the model (b = 2.54, t=3.12, p=0.002 at ages 6-12 and b = 2.59 at ages 13-19, t=2.82, p=0.006 in the full model), as seen in figure 4. The other factor scores did not predict later lability/negativity subscale scores when all factor scores were included in the model.

Similarly, only the excitability factor score significantly predicted the ERC emotion regulation score at ages 6 to 12 years when all factor scores were in the model (individual model excitability factor score R^2= 0.16, p<0.001; with all factor scores, excitability factor score b = −1.35, t= −3.08, p=0.003). However, this was no longer significantly predictive once age 5 social adversity was added to the model (t= −1.87, p=0.06). By ages 13-19 (mean age 16 years old), while the direction of the relationship remained similar, excitability factor score at baseline was no longer significantly predictive of the emotion regulation score after accounting for the other factor scores.

Emotion dysregulation factor scores predict concurrent and later measures of global functioning

The excitability and irritability factors scores (R^2=0.37 [95% CI 0.26-0.47] and R^2=0.37 [95% CI 0.25-0.49] respectively, both p< 0.05) predicted concurrent levels of global functioning when all factor scores, age 5 social adversity, and maternal history of bipolar disorder were included in the model. Similarly, later global functioning as measured by the PECFAS or CAFAS total score was predicted by the excitability factor score at all subsequent time points except T3, and PECFAS or CAFAS total score was predicted by the irritability factor score at all time points through T6 when including all factor scores, social adversity and maternal history in the model (see Table 4, Figure 5).

DISCUSSION

Overall, our results demonstrate that two separable manifestations of emotion dysregulation measured during the preschool period predict later psychiatric diagnoses and emotion dysregulation in some specific ways, and global functioning more generally at school age and adolescence. Using an exploratory factor analysis we demonstrated that in preschool children, ages 3-5 years, emotion dysregulation can be divided into separable dimensions of "irritability" related to negative affect and "excitability" related to positive affect, in addition to sadness and anhedonia, consistent with our hypotheses regarding the dual nature of emotion dysregulation. These emotion dysregulation factor scores were influenced by early life social adversity and by maternal mood history, specifically maternal history of bipolar disorder. In turn these emotion dysregulation factor scores, irritability and excitability, predicted later mood and externalizing diagnoses even when controlling for social adversity, maternal history, and presence of the diagnosis at baseline. This suggests that measuring these manifestations of emotion dysregulation in early childhood are robust predictors of later psychopathology and general functioning over and above baseline diagnosis. Contrary to our hypotheses, but particularly notable was that excitability, but not irritability, predicted measures of emotion regulation in later childhood and adolescence. Consistent with our hypotheses, excitability and irritability both predicted concurrent and later global functioning. This finding suggests that the measurement of these dimensions may be important predictors of later risk for psychopathology and adaptive functioning. Further, they also highlight the importance of attention to a novel dimension of emotion dysregulation representing "excitability" in early childhood.

The importance of emotion dysregulation in both positive and negative affect

The exploratory factor analysis described above resulted in a four factor model which we described as "irritability" and "excitability" characterizing negative and positive affect dysregulation as well as "sadness" and "anhedonia". As predicted, irritability items grouped together, including tantrums, irritability, frustration and anger. Interestingly and consistent with the recently defined diagnosis of disruptive mood dysregulation disorder (DMDD, Roy et al., 2014), mood cycling items from the mania module also grouped with this irritability factor. In contrast, the excitability factor was mainly composed of items from the mania module, including elevated mood, inappropriate laughter, grandiosity and gregariousness, along with concentration, motor, and sleep symptoms. Unexpectedly, self-deprecation/self-hatred, and suicide/self-injurious behavior items were also grouped with this factor, illustrative of the detrimental aspects of having dysregulated excitability. The remaining factors, sadness and anhedonia, comprised items commonly associated with depression. Specifically, the sadness factor included not only items related to sad mood, but also loneliness, feeling unloved and pathological guilt, consistent with prior work in preschool onset depression (Luby, Belden, Pautsch, et al., 2009, Luby, Belden, Sullivan et al., 2009). The anhedonia factor included all anhedonia related items as well as loss of interest and anergia; interestingly, this was the least normally distributed factor, perhaps arguing for the clinical importance of this factor in depression pathology, though not in emotion dysregulation, which would also be consistent with prior work (Luby, Belden, Pautsch, et al., 2009).

As hypothesized, separable positive (excitability) and negative (irritability) forms of early emotion dysregulation were found. This expands the conceptualization of emotion dysregulation, which has previously focused largely on irritability or negative affect dysregulation (as reviewed in Brotman et al., 2017; Wackschlag et al., 2018). Such a broader conceptualization is consistent with RDoC positive and negative valence systems (Cuthbert & Insel, 2013), both of which can be dysregulated. In our work, the excitability factor includes theoretically positive attributes such as elevated affect and gregariousness, which have been previously shown to be protective from the development of behavioral inhibition and depression (Park et al., 1997; Silk et al., 2006). Consistent with this work, the excitability factor also proved to be protective against later depression without mania. However, it also contained poor judgement, self-hatred, and suicidality, reflecting the impairment that can come with this form of positive affective dysregulation. That excitability in preschoolers predicts not only later affect lability, but also externalizing diagnoses and global impairment, speaks to the import of better understanding both of these forms of early emotion dysregulation. These findings also suggest that such early symptoms of excitability, which are typically not assessed as a central aspect of clinical interviews in early childhood, are important for clinicians to inquire about in diagnostic interviews of young children.

Predicting later problems with emotion regulation.

Both excitability and irritability predicted meeting criteria for mania at school age and early adolescence (prior to age 12) in our sample. They were not generic affective risk factors, as they did not increase the risk of developing MDD without mania. Despite these relations to mania episodes before age 12, only 2 children went on to meet full criteria for bipolar disorder after age 12, a time frame when the diagnosis becomes clearer and less controversial. This result is consistent with prior longitudinal study of the CBCL- “bipolar profile” (Halperin, Rucklidge, Powers, Miller, et al., 2011), in which many children with the “bipolar profile” were later diagnosed with depression or other externalizing disorders rather than bipolar disorder. Rather, it seems more likely that these factor scores are predicting later problems with emotion dysregulation that are so severe that they are meeting criteria for mania in middle childhood and early adolescence but are not leading to narrow spectrum bipolar disorder as defined by full DSM diagnostic criteria for mania after age 12.

As we conceptualize emotion dysregulation as dimensional, it should confer risk for multiple diagnoses at varying severity rather than one discrete diagnosis of bipolar or bipolar spectrum disorders. Consistent with this, the excitability factor score predicted later lability/negativity as measured by the emotion regulation checklist in both middle childhood and in the teen years. Further study of the relationship between emotion dysregulation and manic symptoms in pre-pubertal children and more strictly defined bipolar disorder in adolescents and adults may help shed further light on the role of emotion dysregulation in childhood bipolar spectrum disorders and whether emotion dysregulation is predictive for the development of bipolar I or II. Moreover, conceptualizing emotion dysregulation dimensionally and occurring in both negative (irritability) and positive (excitability) valence systems may allow for better predictions of overall trajectory toward a variety of diagnostic outcomes beyond bipolar disorder. This is consistent with the extant literature in which

bipolar diagnoses in childhood and adolescence are associated with very high levels of co-morbidity (Geller et al., 2000; Luby & Belden, 2006), a feature that has fueled skepticism about this diagnostic classification in childhood.

Consistent with prior work, early emotion dysregulation predicted multiple types of impairment (Aldao, Gee, de los Reyes, Seager, 2016; Beauchaine & Ziser, 2017; Calkins & Keane, 2004; Vasilev, Crowell, Beauchaine, Mead, et al., 2009). Here we have shown that *both* excitability and irritability in preschoolers predicted global functioning not only concurrently, but also for years into the future. Excitability predicted worse global functioning through adolescence, and irritability predicted worse global functioning through late childhood. The longer duration of excitability predicting global functioning could be related to some level of irritability in preschool years being a normative developmental behavior (Belden et al., 2008; Wakschlag et al., 2012). However, it may also reflect an increased role for excitability in emotion dysregulation in adolescence, a developmental period characterized by increased mood lability, approach behavior, and response to reward (Gilbert, 2012; Ernest, Romeo, & Anderson 2010; van Leijenhorst, Moor, Op de Macks, Rombouts, et al., 2010). Relatedly, while emotion regulation typically improves with development (Blandon, Calkins, Keane, O'Brien, 2008; Calkins & Keane, 2004; Hill et al., 2006; Silvers, McRae, Gabrieli, Gross, et al., 2012; Vasilev et al., 2009), it is notable that variation present at this very young age predicts later outcome, and thus screening for both positive and negative emotion dysregulation as defined here, and targeting interventions for improving emotion regulation in both of these domains should begin in the preschool years.

Early childhood emotion dysregulation increases risk of later externalizing diagnoses

As well established in the extant literature, irritability is related to ADHD diagnosis in our study (Karalunas, Fair, Musser, Aykes, et al., 2014; Shaw, Stringaris, Nigg, Liebenluft, 2014; Steinberg & Drabick, 2015). We found that excitability was also associated with increased risk of later diagnosis of ADHD. Further, only excitability significantly increases the odds of a later ADHD diagnosis above having a diagnosis of ADHD at baseline, suggesting this may be an important and less recognized early predictor of later ADHD. While there is overlap between some items from the excitability factor and ADHD symptoms, such as "motor pressure, hyperactivity, or increased energy", "motor activity, agitation, restlessness", "unusually energetic", "poor judgement", and "decreased concentration", it is notable that the excitability factor score was able to predict later diagnosis of ADHD even when including baseline diagnosis of ADHD in the model, indicating its predictive ability is not solely due to symptom overlap. The excitability factor also contains items regarding elated and expansive mood, grandiosity, self-deprecation and self-hatred, and suicidal and self-injurious behaviors, all of which emphasize the emotion dysregulation component of this factor. Better understanding of the role of early emotion dysregulation in ADHD psychopathology could have significant diagnostic and treatment implications, as currently these are not part of a typical screening for ADHD and addressing emotion dysregulation is often not included in treatment plans for this diagnosis.

Both irritability and excitability factor scores conferred increased risk of later ODD diagnosis, though only excitability above meeting criteria for ODD at baseline. Given the

overlap between items in the irritability factor score and ODD symptoms, including irritability, “touchy or easily annoyed”, being “angry or resentful”, and “temper tantrums”, this might be expected, and there are similar reports in the literature (Wiggins, Mitchell, Stringaris, Liebenluft, 2018). However, it is notable that the excitability factor score was associated with increased risk of later diagnosis of ODD, even when controlling for baseline ODD diagnosis, even though this is a diagnosis meant to describe generally negative or irritable children (Rey, 1993).

The excitability factor score also predicted later diagnosis of CD even when controlling for baseline diagnosis of CD. This is particularly interesting given that at least some children with CD with callous and unemotional traits are thought to have lower emotional reactivity (Beauchaine et al., 2007; Wackschlag et al., 2018). It is possible that excitability is capturing a subset of children that meet criteria for CD who are not callous and unemotional, as we hypothesize the excitability factor score reflects increase emotional reactivity, but this warrants further study.

Early life adversity and family history influence the emotion dysregulation.

Consistent with much prior work, early life adversity, in this case measured by a composite index including items reflecting unstable or stressed caregiving, abuse, and financial stress, is associated with increased excitability and irritability. This finding is consistent with prior literature showing that increased adverse childhood experiences increases the risk of depression (Anda, Felitti, Bremner, Walker, et al., 2003; Chapman, Whitfield, Felitti, Dube, et al., 2004; Luby et al., 2017; Teicher & Samson, 2013), externalizing diagnoses (Cohen, Brown, & Smailes, 2001; Rosen, Handley, Cicchetti, Rogosch, 2018), and overall impairments in functioning (Anda et al., 2006; Edwards, Holden, Felitti, Anda, 2003; Felitti et al., 1998), as well increased risk of early onset depression (Luby et al., 2006) and problems with emotion regulation (Hill et al., 2006; Kim & Cicchetti, 2013) for children in families with lower socioeconomic status. This work extends those findings by showing that social adversity has a marked relationship to behavioral manifestations of emotion dysregulation as early as the preschool period of development.

Family history may impact the development of emotion dysregulation through both genetic and psychosocial mechanisms, and prior work has demonstrated its impact on irritability (Stringaris et al., 2012, Paglioccio et al., 2018). Here we demonstrate that while both a maternal history of bipolar disorder and MDD are associated with increased emotion dysregulation factor scores, only a maternal history of bipolar disorder increases this risk above that accounted for by social adversity. While we have used a conservative estimate of maternal bipolar disorder, including only those who met criteria on the Family Interview for Genetic Studies (FIGS) for parents or were being treated by a mental health professional for this diagnosis, we do not have clear measurements about how impaired mom was by her diagnosis or its impact on the family to better understand variable mechanisms of this risk factor.

The role of sadness and anhedonia in psychopathology

Interestingly, at first glance our results may seem contrary to prior reports of the continuity of pediatric depression through childhood and into later adolescence (Luby et al., 2014; Gaffrey et al., 2018). However, upon closer examination, these findings are largely consistent. Luby et al., (2014) and Gaffrey et al., (2018) both used DSM defined diagnoses in the preschool period to predict later presentations of the same diagnoses. In contrast, the current study investigates symptoms of emotion dysregulation dimensionally, which allows us to identify the impact of empirically defined groups of symptoms. In both Luby et al., (2014) and Gaffrey et al., (2018) ongoing depression in adolescence was predicted by preschool onset depression and preschool onset conduct disorder, which includes a number of the emotion dysregulation symptoms emphasized here. Relatedly, preschool depression predicted later diagnoses of CD, ODD, and ADHD (Gaffrey et al., 2018), again indicating the potential overlap with excitability and irritability. By looking at these symptoms dimensionally, we can see that the component of preschool depression that most strongly predicts later diagnoses of depression may be emotion dysregulation.

Yet, components of sadness, including pathological guilt, and anhedonia have been found to be very specific for childhood depression (Luby et al., 2004), and both symptom reports of anhedonia as well as neural evidence of decreased response to reward in adolescents have been found to predict later depression (Stringaris, Vidal-Ribas, Artiges, Lemairte, et al., 2015; Olino, McMakin, Dahl, Ryan, et al., 2014). The current study did not investigate the predictive role of guilt in risk for later depression, and it is possible that it may carry more predictive power when considered alone than as a part of the sadness factor more broadly. Relatedly, while we identified an anhedonia factor in our EFA, this was the least normally distributed factor with considerable right kurtosis indicating the vast majority of children score very low in this factor score. Thus, we might have been underpowered to detect relationships with later depression, particularly if the relationship was with only a subset of children with later depression. As MDD is a disorder with incredibly variable expression (Zimmerman, Ellison, Young, Chelminksi, Dalrymple, 2015, Fried & Nesse, 2015), it is possible that only a subset is characterized by anhedonia. There are also indications that anhedonia may have a different developmental trajectory than other depressive symptoms (Pine, Cohen, Cohen, Brook, 1999) as well as a differential relationship with other symptoms of depression (Buckner, Joiner, Pettit, Lewinsohn, Schmidt, 2008). It is thus conceivable that anhedonia and even sadness predict subtypes of depression, but due to heterogeneity in diagnoses we were unable to identify such a relationship.

Future Directions

Excitability specifically and dysregulation of positive affect more generally are understudied areas of emotion dysregulation. Clinically, excitability may provide an additional tool for describing potential risk in young children with emotion dysregulation, and further study of the utility of screening for excitability and potential targets interventions such as parent child interaction therapy (PCIT) or dialectical behavior therapy for children (DBT-C) deserve further study. A further description of the longitudinal course of excitability and how this may interact with known developmental changes in emotion regulation, general mood lability, risk taking, and reward sensitivity may help better elucidate whether this is stable

over time, or has developmentally sensitive periods for risk. Examining neurobiological correlates of excitability is an important future direction which is likely to be informative. Excitability might be reflected in broadly increased sensitivity of amygdala response to emotionally salient stimuli as has been seen in children with a bipolar diagnosis and mood lability (Rich et al., 2007; Wiggins et al., 2014). It may also be seen in sensitivity to reward response in the striatum, as seen in some children with irritability (Deveney, et al., 2013).

Further study of how irritability changes across development, given the expected normative decrease with development (Wackschlag et al., 2006), and how this may change its ability to predict later psychopathology will also be relevant. For example, elevated irritability may become more predictive in older children, as it is further from the norm. Further, separating irritability from excitability allows for a more thorough investigation of neurobiological mechanisms of irritability. For example, the increase striatal response that inconsistently seen in irritability (Deveney, et al., 2013; Perlman et al., 2015), may be related to its correlation with excitability and including both in an analysis will allow for finer grain distinctions.

Finally, further study of the development of sadness and anhedonia and their relationship with concurrent and later depression diagnoses will be of interest. Again, depression is a heterogeneous diagnosis, and a better description of these subtypes of problematic emotional responses may allow us to identify reproducible subtypes, for example those with elevated irritability and excitability and those without, which we would predict to be differentially related to anhedonia.

Conclusions

Our work, consistent with the extant developmental literature, clearly emphasizes the importance of early childhood emotion dysregulation in risk for current and later psychopathology and overall well-being. These findings build on and extend prior work by providing data to suggest that there may be two separable and uniquely predictive forms of early emotion dysregulation: irritability and excitability. While both irritability and excitability measured in the preschool years predicted later psychiatric diagnoses and global functioning, excitability predicted overall measures of emotion dysregulation, multiple later psychiatric diagnoses above having a baseline diagnosis of the same, and global functioning into the teen years. Excitability particularly is an understudied area, and a better understanding of this dimensional measure of positive emotion dsyregulation may be important to inform our understanding of psychiatric diagnosis, treatment, and the underlying neurobiology of emotion dysregulation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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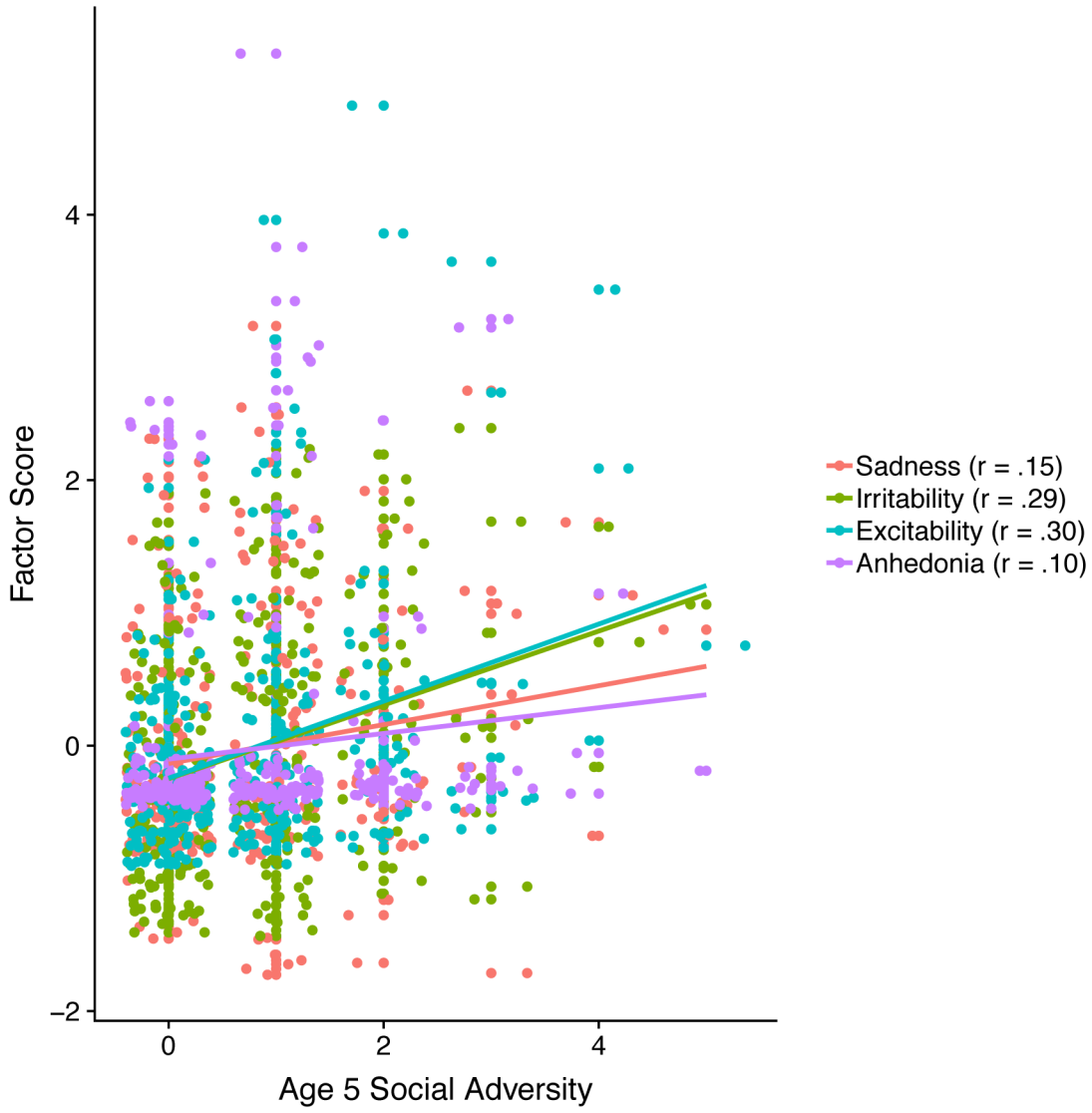

Figure 1.

Factor scores are predicted by age 5 social adversity score. Scatterplots and trend lines for each factor score (on the y axis) plotted by social adversity score (on the x axis). Elevated affect dysregulation factor scores plotted in blue, negative affect dysregulation / irritability factor score plotted in green, sadness factor score plotted in red, and anhedonia factor score plotted in purple..

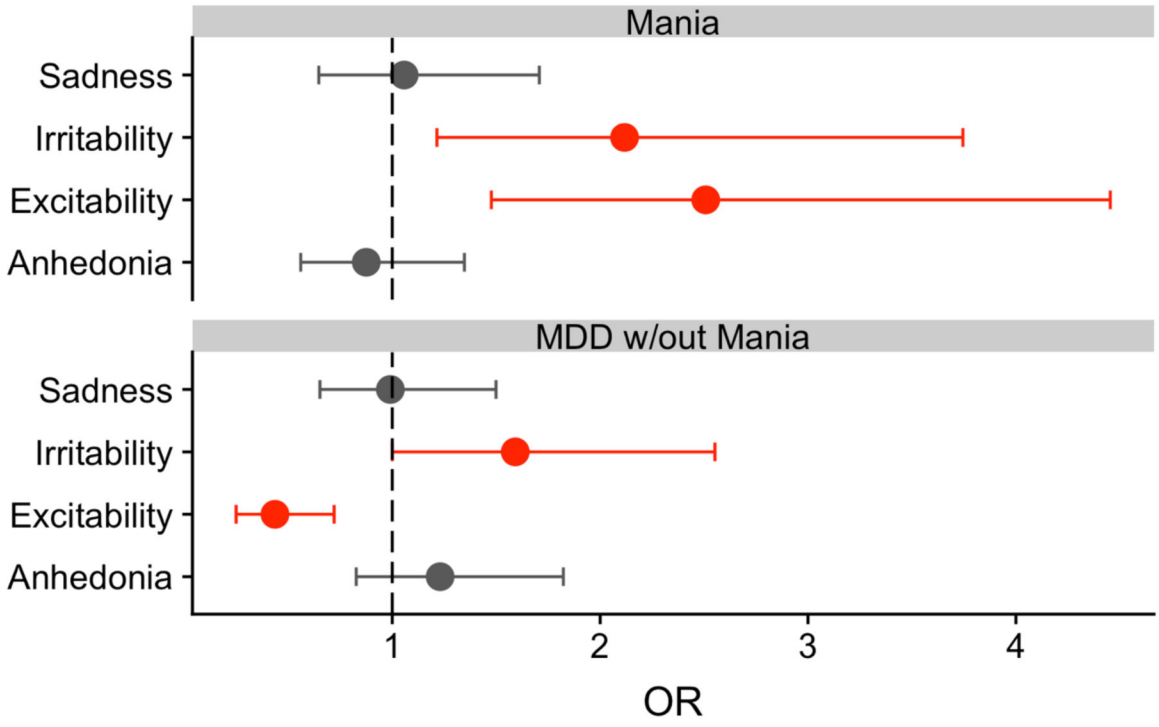

Figure 2.

OR of later developing the diagnosis for each one point increase in factor scores, controlling for all other factor scores, maternal history of bipolar disorder and age 5 social adversity.

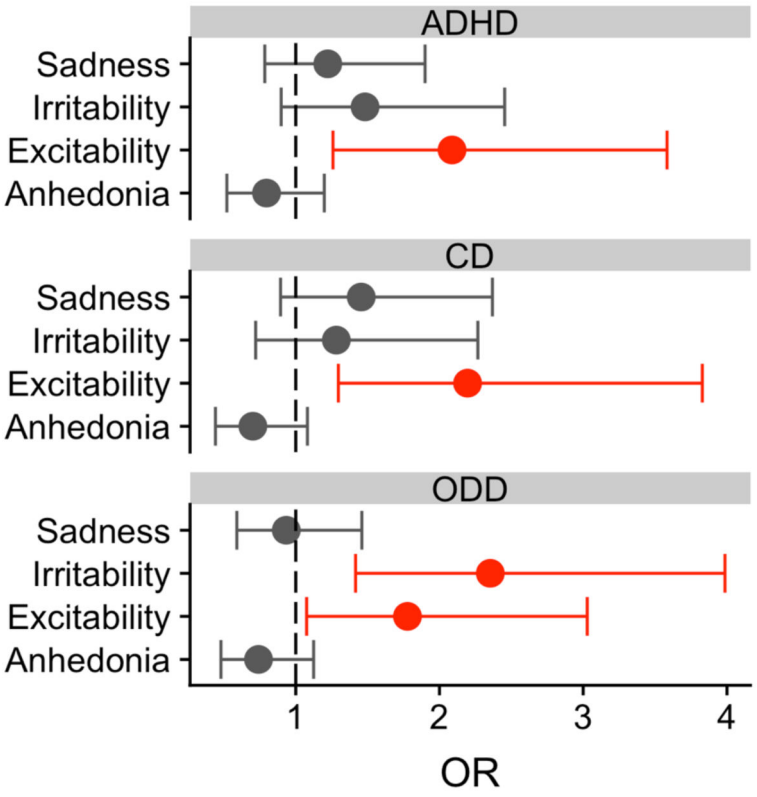

Figure 3.

Odds ratio of later developing the diagnosis for each one point increase in factor scores, controlling for all other factor scores, maternal history of bipolar disorder and age 5 social adversity.

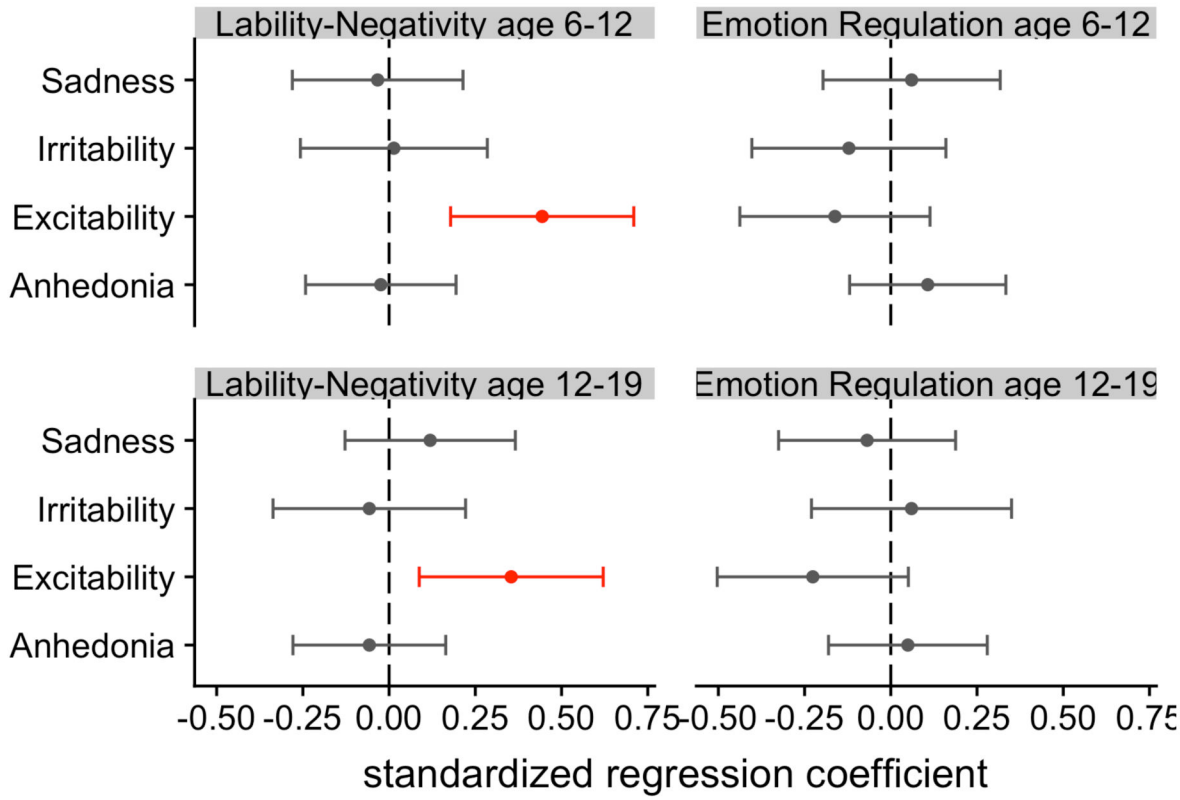

Figure 4.

Excitability factor scores predict later emotion regulation as measured by the ERC. Standardized beta weights in regression models with all 4 factor scores, social adversity and maternal history are shown for each factor score.

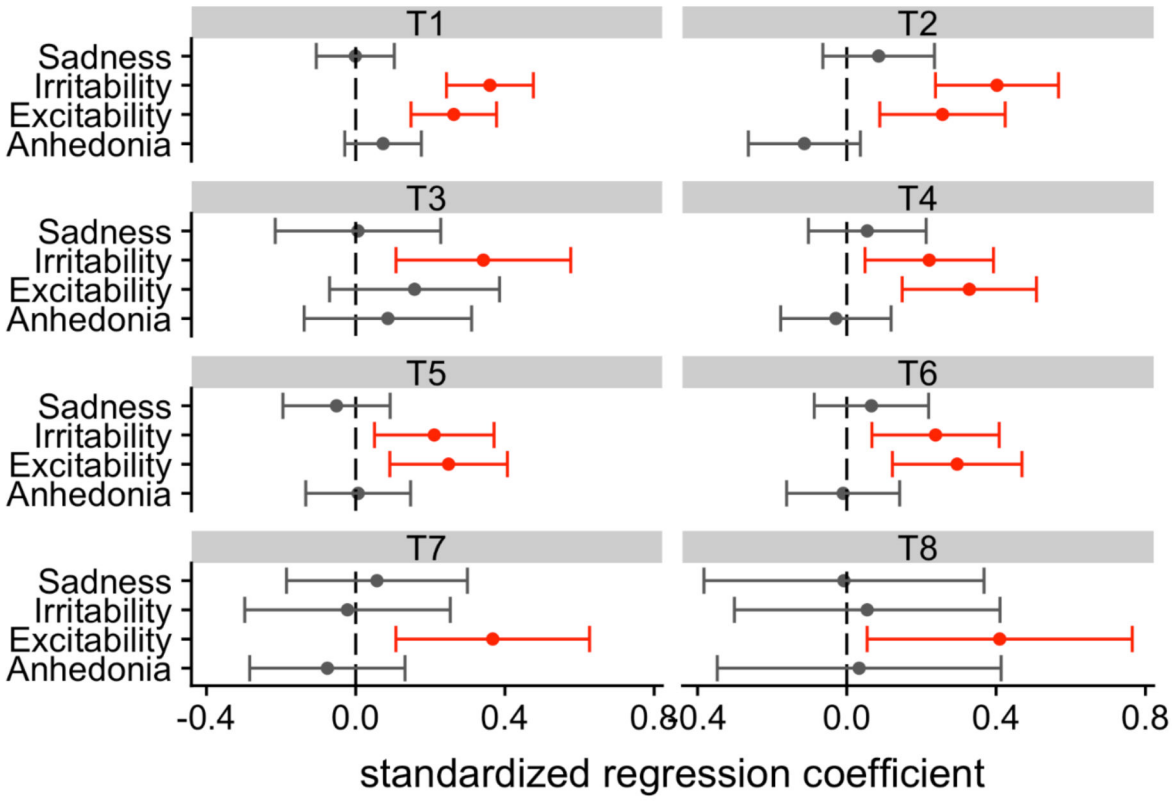

Figure 5.

Excitability and irritability factor scores from T1 (ages 3-5 years) predict concurrent and future global functiong as measured by the PECFAS at T2 (ages 4-7) and T3 (ages 7-10) and CAFAS at T4 (age 7-10) though T6 (age 9-13) and the excitability factor score continues to predict global functioning at T7 (age 10-14) and T8 (age 12-16), even when controlling for the effect of all other factor scores, age 5 social adversity, and maternal history of bipolar disorder.

Table 1.

All included PAPA items sorted and colored by assigned factor in EFA. The sadness factor is denoted in grey, irritability in green, excitability in purple, and anhedonia in blue. Factor loadings for each factor are shown, with all significant loadings denoted with an asterisk and all loadings > 0.30, and thus included in the computation of factor scores, denoted with bold font.

Item	Factor 1 (Sadness)	Factor 2 (Irritability)	Factor 3 (Excitability)	Factor 4 (Anhedonia)
Sad/unhappy intensity	**0.828***	0.058	0.039	0.032
Sad/unhappy spontaneity	**0.767***	0.012	0.064	0.002
Sad/unhappy concern to child	**0.401***	0.097	−0.058	0.07
Sad/unhappy concern to caretaker	**0.516***	0.228*	−0.104	0.198*
Looks unhappy	**0.448***	0.282*	−0.032	0.065
Boredom	0.212*	0.033	0.092	0.152*
Amotivation	0.309*	0.131	−0.035	−0.014
Lack of protest	0.13	−0.078	0.005	0.092
Indecisiveness	0.213*	0.037	0.191*	−0.026
Loneliness	0.307*	−0.057	0.224*	0.068
Feels unloved	0.303*	−0.113	0.230*	0.1
Pathological guilt	**0.351***	0.011	0.086	−0.024
Hopelessness	0.222*	0.115	0.009	−0.079
Suicidal themes in play ever	0.119	0.071	0.021	0.108
Irritability intensity	0.17*	**0.646***	0.044	0.036
Irritability frequency	−0.018	**0.429***	−0.021	0.032
Irritability spontaneity	0.190*	**0.414***	0.024	0.136*
Irritability alleviation	−0.002	0.290*	−0.023	−0.004
Irritability concern to child	0.062	0.225*	0.139	0.113
Irritability concern to caretakers	0.135	**0.580***	0.006	0.082
Sad/unhappy frequency	0.099	0.252*	−0.224*	0.094
Tearfulness & crying	0.294*	**0.457***	−0.086	−0.106
Touchy or easily annoyed	0.095	**0.376***	0.126	0.076
Angry or resentful intensity	−0.013	**0.510***	0.186*	−0.062
Losing temper	−0.033	0.293*	0.167*	−0.195*
Temper tantrums intensity	0.022	**0.433***	0.116	−0.094
Mood cycling intensity	−0.014	**0.697***	0.144*	−0.005
Mood cycling frequency	−0.157*	**0.502***	0.101	0.078
Lack of joyfulness intensity	0.077	0.258*	0.072	0.200*
Easily frustrated intensity	0.145*	**0.395***	0.088	−0.038
Reduced appetite	0.13	0.144	−0.102	0.106
Elated/expansive mood frequency	−0.108	0.219*	0.12	−0.026
Elated/expansive mood concern to caretakers	−0.181*	0.248*	0.219*	0.123

Item	Factor 1 (Sadness)	Factor 2 (Irritability)	Factor 3 (Excitability)	Factor 4 (Anhedonia)
Grandiosity alleviation	0.002	0.234*	0.101	−0.03
Elated/expansive mood	0.015	0.164*	**0.351***	−0.054
Elated/expansive mood alleviation	0.055	0.07	0.152	0.015
More talkative than usual	−0.11	−0.004	**0.686***	0.02
Inappropriate laughing, joking	−0.057	−0.008	**0.641***	0.004
Uninhibited gregariousness	0.052	0.034	**0.488***	−0.035
Motor pressure/hyperactivity/increased energy	−0.220*	0.160*	**0.569***	0.099
Motor activity/agitation/restlessness	−0.109	0.165*	**0.549***	−0.01
Unusually energetic	−0.126*	0.085	**0.550***	0.079
Grandiosity	0.173*	0.026	**0.541***	−0.087
Grandiosity concern to caretakers	0.078	0.021	**0.624***	−0.006
Bragging intensity	0.078	0.028	0.175*	−0.014
Racing thoughts intensity	0.006	0.106	0.306*	−0.01
Flight of ideas intensity	0.009	0.02	**0.570***	0.012
Poor judgment intensity	−0.002	0.113	**0.489***	0
Inappropriate sexual interest	0.032	−0.004	**0.533***	0.003
Inappropriate sexual language	−0.018	−0.022	**0.420***	−0.01
Potty talk	0.043	0.092	0.242*	−0.064
Decreased concentration	0.019	0.011	**0.386***	0.069
Agitation	0.186*	0.053	0.291*	0.076
Motor slowing	0.143*	−0.150*	0.329*	0.267*
Sleep duration	−0.001	−0.052	−0.303*	−0.029
Decreased need for sleep	−0.044	0.129	**0.364***	−0.006
Sleeping more	0.116	0.015	0.239*	0.041
Appetite increase	−0.008	−0.013	0.225*	−0.047
Tantrums difficulty to recovery	−0.001	0.218*	0.236*	0.041
Stoicism	0.125	0.09	−0.147	0.114
Feels sorry for oneself	0.169*	−0.036	0.255*	0.098
Self-deprecation and self-hatred	0.128	0.071	0.321*	0.09
Sad/unhappy duration	0.236*	−0.164*	0.273*	0.098
Negative play themes	0.109	0.216*	0.241*	−0.018
Death themes in play ever	0.043	0.180*	0.236*	−0.009
Thinking/talking about death	0.240*	−0.021	0.279*	−0.186*
Suicide and self injurious behavior screen	0.188*	−0.012	**0.360***	−0.057
Non-suicidal physical self-damaging acts ever	0.138*	0.141*	0.243*	0.018
Anhedonia intensity	−0.047	0.131	0.018	**0.863***
Anhedonia concern to the child	0.05	−0.028	0.140*	**0.552***
Anhedonia concern to caretakers	0.006	0.165	−0.071	**0.854***
Loss of interest	0.038	0.008	0.085	**0.468***

Item	Factor 1 (Sadness)	Factor 2 (Irritability)	Factor 3 (Excitability)	Factor 4 (Anhedonia)
Anergia	0.062	−0.084	0.115	**0.428***
Sleeping less	−0.042	0.007	0.11	0.164*
Fatigability	0.126	−0.071	0.195*	0.261*
Irritability Duration	0.047	−0.086	0.106	0.277*
Sad/unhappy alleviation	0.089	−0.126	0.058	0.153*
Elated/expansive mood duration	−0.015	−0.031	0.026	−0.033

Table 2.

Factor scores differ depending on maternal history of mood disorders. T-tests do not control for age 5 social adversity.

	Maternal History of Bipolar					Maternal History of MDD				
Factor Scores	**No history**	**With history**	**d**	**t**	**p**	**No history**	**With history**	**d**	**t**	**p**
Excitability	−0.04 (SD 0.91)	0.41 (SD 1.19)	.48	2.08	0.04	−0.06 (SD 0.90)	0.07 (SD 0.99)	.13	1.13	0.26
Irritability	−0.06 (SD 0.91)	0.59 (SD 0.82)	.72	3.13	0.00	−0.15 (SD 0.86)	0.20 (SD 0.95)	.40	3.32	0.00
Sadness	−0.07 (SD 0.88)	0.88 (SD 0.93)	1.08	4.67	0.00	−0.10 (SD 0.84)	0.13 (SD 1.00)	.26	2.18	0.03
Anhedonia	−0.06 (SD 0.85)	0.65 (SD 1.45)	.79	3.41	0.00	−0.06 (SD 0.90)	0.06 (SD 0.93)	.13	1.10	0.27

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Table 3.

Elevated affect dysregulation factor scores predict later diagnosis of externalizing disorders above having a baseline (T1) diagnosis of the same

DV: Later Diagnosis of ADHD	**b**	**SE**	**OR**	**95% CI**	**p**
Excitability FS	0.74	0.27	2.09	(0.23-1.28)	0.004
Irritability FS	0.39	0.26	1.48	(−0.11-0.90)	0.15
Sadness FS	0.20	0.22	1.22	(−0.24-0.64)	0.36
Anhedonia FS	−0.23	0.21	0.80	(−0.05-0.18)	0.24
Age 5 Social Adversity	0.29	0.16	1.34	(−0.03-0.62)	0.22
Maternal Bipolar	0.09	0.57	1.10	(−1.06-1.21)	0.31
T1 ADHD	0.11	0.48	1.12	(−0.85-1.04)	0.87
DV: Later Diagnosis of ODD	**b**	**SE**	**OR**	**95% CI**	**p**
Excitability FS	0.63	0.24	1.87	(1.17-3.01)	0.01
Irritability FS	0.55	0.30	1.74	(0.98-3.11)	0.06
Sadness FS	−0.07	0.24	0.93	(0.59-1.48)	0.76
Anhedonia FS	−0.232	0.23	0.79	(0.51-1.24)	0.31
Age 5 Social Adversity	0.19	0.17	1.21	(0.87-1.69)	0.26
Maternal Bipolar	0.38	0.61	1.46	(0.44-4.83)	0.53
T1 ODD	0.90	0.40	2.45	(1.13-5.32)	0.02
DV: Later Diagnosis of CD	**b**	**SE**	**OR**	**95% CI**	**p**
Excitability FS	0.65	0.26	1.92	(1.15-3.21)	0.01
Irritability FS	0.20	0.29	1.22	(0.69-2.18)	0.49
Sadness FS	0.40	0.25	1.49	(0.91-2.43)	0.11
Anhedonia FS	−0.35	0.24	0.71	(0.45-1.12)	0.14
Age 5 Social Adversity	0.42	0.18	1.52	(1.06-2.17)	0.02
Maternal Bipolar	0.88	0.60	2.40	(0.74-7.79)	0.15
T1 CD	0.65	0.52	1.92	(0.69-5.34)	0.21

Table 4.

Factor Scores Predict Measures of Global Functioning as Measured by the PECFAS/CAFAS at Waves T1 – T8 Standardized regression coefficients are presented along with 95% confidence intervals.

	T1 PECFAS		T2 PECFAS		T3 PECFAS		T4 CAFAS	
	Std. b	**95% CI**	**Std. b**	**95% CI**	**Std. b**	**95% CI**	**Std. b**	**95% CI**
Excitability FS	0.368*	0.263- 0.473	0.248*	0.100- 0.396	0.144	−0.069- 0.357	0.324*	0.162- 0.486
Irritability FS	0.371*	0.251-0.491	0.402*	0.239-0.566	0.344*	0.113-0.576	0.220*	0.050-0.391
Sadness FS	0.010	−0.097-0.118	0.084	−0.064- 0.231	0.001	−0.217- 0.219	0.054	−0.102-0.211
Anhedonia FS	0.057	−0.049- 0.162	−0.113	−0.261- 0.036	0.086	−0.136- 0.308	−0.029	−0.176- 0.118
Age 5 Social Adversity	0.107*	0.028- 0.186	0.131*	0.026-0.237	0.211*	0.051- 0.371	0.168*	0.043- 0.293
Maternal Bipolar	0.048	−0.032- 0.129	−0.045	−0.160- 0.070	0.056	−0.087- 0.199	0.187*	0.082- 0.291
Observations	242		240		172		222	
R^2	0.628		0.389		0.257		0.382	
	T5 CAFAS		**T6 CAFAS**		**T7 CAFAS**		**T8 CAFAS**	
	Std. b	**95% CI**	**Std. b**	**95% CI**	**Std. b**	**95% CI**	**Std. b**	**95% CI**
Excitability FS	0.275*	0.137- 0.414	0.259*	0.106-0.412	0.357*	0.131-0.583	0.460*	0.138- 0.783
Irritability FS	0.212*	0.053- 0.371	0.239*	0.069-0.408	−0.023	−0.294-0.248	0.068	−0.277-0.413
Sadness FS	−0.048	−0.190-0.095	0.062	−0.090- 0.214	0.055	−0.182-0.293	0.050	−0.286-0.387
Anhedonia FS	0.002	−0.137-0.141	−0.009	−0.159-0.142	−0.074	−0.278-0.130	−0.027	−0.367-0.312
Age 5 Social Adversity	0.141*	0.035-0.247	0.150*	0.040-0.261	0.281*	0.122-0.440	0.277*	0.071-0.482
Maternal Bipolar	0.036	−0.063-0.135	−0.075	−0.179-0.030	0.140*	0.006-0.275	0.067	−0.241-0.376
Observations	244		218		113		60	
R^2	0.289		0.305		0.342		0.437	

* $p < .05$