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The dysregulation profile in preschoolers with and without a family history of autism spectrum disorder

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Abstract

Background: The "dysregulation profile" (DP) is a measure of emotional and behavioral dysregulation that may cut across diagnostic boundaries. Siblings of children with autism spectrum disorder (ASD) who do not develop ASD themselves are at risk for atypical outcomes including behavioral challenges and therefore may be a useful population in which to investigate the structure of the DP in preschoolers.

Methods: We sought to examine the factor structure and predictors of the DP in a sample enriched for a wide range of phenotypic variation—36-month-olds with and without family histories of ASD—and to determine whether children with genetic liability for ASD are at risk for a phenotype characterized by elevated dysregulation. Data were collected from 415 children with (n=253) and without (n=162) an older sibling with ASD, all without ASD themselves, at 18, 24, and 36 months of age.

Results: Our findings replicate prior reports, conducted in predominantly clinically-referred and older samples, supporting the superiority of a bifactor model of the DP in the preschool period compared to second-order and one-factor models. Examiner ratings were longitudinally and concurrently associated with the DP at 36 months of age. Family history of ASD was associated with higher dysregulation in the Anxious/Depressed dimension.

Conclusions: These findings support the relevance of examining the structure of psychopathology in preschoolers and suggest that examiner observations as early as 18 months of age, particularly of overactivity, may help identify risk for later DP-related concerns. Non-ASD preschoolers with family histories of ASD may be at risk for a phenotype characterized by elevated dysregulation particularly in the anxious/depressed dimension by age 3.

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Keywords

Dysregulation; preschool; high-risk; siblings; autism spectrum disorder

Although identifying risk for specific *DSM-5* diagnoses is valuable, prior research has suggested the relevance of identifying behavioral phenotypes that cut across multiple diagnostic categories. Building on work by Lahey and colleagues (Lahey et al., 2012), Caspi and colleagues (Caspi et al., 2014) demonstrated that a single general psychopathology factor (or "p factor"), rather than distinct symptom dimensions, best described the structure of psychiatric symptoms among adults. Similar findings have been documented in childhood and adolescence (Laceulle, Vollebergh, & Ormel, 2015; Lahey et al., 2015). Recent work has emphasized that the superior fit of models featuring these general factors is likely not merely a result of measurement artifact (Lahey et al., 2015). The presence of a 'general psychopathology' factor could explain the persistent difficulties related to identifying specific and reliable biological markers of, and treatments for, individual diagnostic categories (Caspi et al., 2014; Lahey et al., 2015; Lahey, Krueger, Rathouz, Waldman, & Zald, 2017).

A related construct in child psychopathology has been termed the "dysregulation profile" (DP) (Bellani, Negri, & Brambilla, 2012). Typically measured using select items or subscales from the Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2000), the DP is generally viewed as a measure of broad-based, generalized emotional and behavioral dysregulation (Holtmann et al., 2011; Kim et al., 2012) and has been shown to be highly heritable (Althoff, Rettew, Faraone, Boomsma, & Hudziak, 2006). It predicts a variety of outcomes both concurrently and longitudinally including general functional impairment (Althoff, Verhulst, Rettew, Hudziak, & Van Der Ende, 2010; Holtmann et al., 2011; Kim et al., 2012), substance use (Holtmann et al., 2011), self-harm and suicidality (Althoff, 2010; Deutz, Geeraerts, van Baar, Deković, & Prinzie, 2016), and psychiatric diagnoses spanning mood disorders and ADHD (Bellani et al., 2012; Masi, Pisano, Milone, & Muratori, 2015). In measuring and defining the DP, most approaches have relied on three subscales from the CBCL emphasizing affective (Anxious/Depressed subscale), behavioral (Aggressive Behavior subscale), and cognitive (Attention Problems subscale) symptoms.

A key question with critical implications for the conceptualization of childhood psychopathology is whether the DP constitutes a syndrome in its own right, versus merely reflects comorbidity among the three subscales of which it is comprised (described in Geeraerts et al., 2015). This can be addressed by examining the factor structure of the DP. Two recent studies explicitly did this: one focusing on a sample of 247 predominantly clinically-referred preschoolers ages 3.5–5.5 years (Geeraerts et al., 2015) and the other utilizing a community sample of 697 school-age children and adolescents (Deutz et al., 2016). Both found that a bifactor model—in which the items comprising these three CBCL subscales load both on their respective subscales as well as on a general "DP factor"—best described the structure of the DP compared to one-factor (all items load on a single general factor) or second-order (all items load on their respective factors, which load on a general factor) models (Deutz et al., 2016; Geeraerts et al., 2015).

To our knowledge, the only study that has examined the factor structure of the DP in preschoolers in this way was conducted in a predominantly clinically-referred sample of children with externalizing problems (Geeraerts et al., 2015), although we note that several studies have examined the factor structure of psychopathology more broadly—beyond the DP per se—in community samples of preschoolers (e.g., Olino et al., 2018). Because predominantly clinically-referred samples may be biased toward elevations across all of the CBCL subscales, it is important to also assess the factor structure of the DP in non-referred preschoolers originally ascertained in early childhood, before psychopathology symptoms emerge.

Samples of younger siblings of children with and without autism spectrum disorder (ASD) are especially well-suited for addressing such questions given the wide range of phenotypic variation across the dimensions comprising the DP among such cohorts, potentially providing a more generalizable window into the early development of psychopathology. Indeed, younger siblings of children with ASD who do not develop ASD themselves are at greater risk for atypical developmental outcomes than those without family histories of ASD (Charman et al., 2017; Landa, Gross, Stuart, & Bauman, 2012; Messinger et al., 2013; Miller et al., 2015; Ozonoff et al., 2014; Schwichtenberg et al., 2013) spanning ASD-related symptoms, language delay, and/or general developmental functioning. Large epidemiological studies have demonstrated siblings of children with ASD to be at elevated risk for a variety of psychiatric and neurodevelopmental disorders beyond ASD, including attention-deficit/hyperactivity disorder (ADHD), oppositional defiant and conduct disorders, and mood and anxiety disorders (Jokiranta-Olkoniemi et al., 2016). Heightened risk for psychiatric disorders has also been documented among parents of individuals with ASD (Daniels et al., 2008; Sucksmith, Roth, & Hoekstra, 2011), suggesting the possibility of shared genetic liability among these conditions. Several studies have found elevated levels of behavioral dysregulation and psychopathology symptoms in at least a subset of school-aged siblings of children with ASD (Griffith, Hastings, & Petalas, 2014; Miller et al., 2016), but little work has been done to identify *preschool* manifestations of non-ASD psychopathology in these at-risk children. Determining the earliest expressions of disorders typically not diagnosed until middle childhood or adolescence—but to which younger siblings of children with ASD may be particularly vulnerable—is critical to enhancing early screening, detection, and intervention for psychopathology. So-called “infant sibling samples” are also particularly well-suited to understanding early predictors of preschool psychopathology because they are recruited in infancy and assessed repeatedly over the first several years of life.

In this study, we sought to (1) examine the factor structure of the DP in a large sample of 36-month-olds enriched for a wide range of phenotypic variation by including preschoolers with and without a family history of ASD (but without ASD themselves), all of whom were originally ascertained in infancy well before symptoms of childhood psychopathology emerge thereby reducing the risk of a biased sample; (2) assess longitudinal and concurrent associations between examiner-rated behavior and 36-month DP scores; and (3) determine whether children with genetic liability for ASD are at risk for a phenotype characterized by elevated dysregulation. We expected (1) to replicate prior research conducted primarily in clinically-referred or older samples on the factor structure of the DP; (2) that examiner

ratings of overactivity, disruptive behavior, anxiety, and clinical best estimate outcomes would be associated with 36-month DP scores; and (3) that children who have an older sibling with ASD would exhibit elevated dysregulation.

Method

Participants

Participant characteristics are included in Table 1. The sample included 415 children enrolled in a prospective longitudinal study of younger siblings of children with ASD (n=253) or typical development (n=162), conducted across two sites. We excluded children in the larger study who had ASD themselves since we were specifically interested in examining the DP outside of the context of ASD in order to better understand the structure and predictors of non-ASD psychopathology. Children were enrolled before 18 months of age with 95% of the sample having their first assessment by 12 months. Data from assessments conducted at 18, 24, and 36 months of age are reported here.

Inclusion criteria for the group with a family history of ASD included confirmed diagnosis of ASD in an older sibling (proband) by meeting ASD criteria on the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2000) and the Social Communication Questionnaire (SCQ; Rutter, Bailey, & Lord, 2003); exclusion criteria included birth before 32 weeks gestation or a known genetic disorder in the proband. Status as a younger sibling of children without ASD was confirmed by an intake screener and proband SCQ scores below the ASD range; exclusion criteria included birth before 37 weeks gestation, developmental/learning/medical conditions in any older siblings, and ASD in first-, second-, or third-degree relatives. The study was approved by the universities' Institutional Review Boards.

Measures

Child Behavior Checklist (CBCL 1.5–5; Achenbach & Rescorla, 2000).—The preschool form of this standardized parent rating scale was used to assess child behavior problems when participants were 36 months old. Parents rate items based on the child's behavior during the prior six months. It has good internal consistency (0.78–0.97) and test-retest reliability (0.68–0.92). Individual items comprising the three DP-related syndrome scales (Anxious/Depressed, Attention Problems, Aggressive Behavior) were used in confirmatory factor analyses. All participants had complete CBCL data.

Autism Diagnostic Observation Scale (ADOS; Lord et al., 2000, 2012).—This semi-structured interaction and observation measures symptoms of autism. It was administered at 18, 24, and 36 months of age by examiners trained to reliability and unaware of the child's risk status or history. Psychometric studies report high inter-rater reliability and agreement in diagnostic classification. Three item scores from the ADOS were selected to assess examiner-rated behaviors that map on, conceptually, to the CBCL DP specific factors: (1) ADOS Item E1—Tantrums, Aggression, Negative or Disruptive Behavior—represented the CBCL DP factor "Aggressive Behavior;" (2) ADOS Item E2 (Modules 1–2)/E3 (Toddler Module)—Anxiety—corresponded with the CBCL DP factor "Anxious/

Depressed;" and (3) ADOS Item E3 (Modules 1–2)/E4 (Toddler Module)—Overactivity—mapped on to the CBCL DP factor "Attention Problems." These ADOS items are scored on a 0–2 (Tantrums, Aggression, Negative or Disruptive Behavior) or 0–3 (Anxiety) scale. ADOS scores of 0 generally indicate no problem in that area, whereas scores of 1, 2, and 3 represent differing degrees of problematic behavior. Given the relative infrequency of scores of 2 and 3, we collapsed across the "problematic" scoring options (i.e., 1, 2, and 3), resulting in a dichotomous score for each ADOS item with "0" representing no problem and "1" representing at least a minor problem. The Overactivity item has an additional scoring option of "7" to represent underactive; the two instances of 7s were treated as 0s, per ADOS scoring guidelines (Lord et al., 2000, 2012). Missingness resulted from missed visits or incomplete scoring by the examiner; 32 cases were missing these ADOS items at 18 months, n=37 were missing at 24 months, and n=13 were missing at 36 months.

The ADOS was also used for diagnostic classification purposes in both the proband (to verify inclusion criteria) and the participant (to determine outcome and subsequently exclude those with ASD from the present analyses). The 3 ADOS items selected to map on to the DP (i.e., E-codes) do not contribute to the diagnostic algorithm and thus none of the items used in analyses focused on associations between examiner-rated behavior and the DP informed outcome determination.

Clinical Best Estimate (CBE) Classification—At the end of the 36-month visit, examiners classified each child into one of eight clinically-defined outcome categories: ASD (excluded), Typically Developing (n=308), Broader Autism Phenotype (BAP; n=42), Speech-Language Problems (n=25), ADHD Concerns (n=16), Other Externalizing Behavior Problems (n=13), Learning Difficulties (n=3), or Anxiety or Mood Problems (n=2). We dichotomized CBE outcomes as Typically Developing or Non-Typically Developing (i.e., BAP, Speech-Language Problems, ADHD Concerns, Other Externalizing Behavior Problems, Learning Difficulties, and Anxiety or Mood Problems; n=101). CBE outcomes were missing for 6 children, all of whom were confirmed to be below the autism spectrum cutoff on the ADOS. These outcomes were not necessarily intended to map on to specific *DSM* categories, but rather to capture categories of clinical concern based on clinician judgment. The dichotomized CBE outcome rating was used to provide a clinician observation of typical versus non-typical development, capturing similar behavioral dimensions to those that are probed in the parent-reported CBCL.

Data Analytic Plan

In order to directly assess whether the DP factor structure would replicate prior work in our sample, we modeled our data analytic strategy after Geeraerts et al. (2015) using statistical code developed by their group. As described in Deutz et al. (2016) and Geeraerts et al. (2015), we first conducted a confirmatory factor analysis (CFA) using weighted least-squares means and variance adjusted (WLSMV) estimators with delta-parameterization. Consistent with previous studies (Deutz et al., 2016; Geeraerts et al., 2015), we tested three CFA models (bifactor, second-order, and one-factor) for the 32 items comprising the CBCL Anxious/Depressed, Attention Problems, and Aggressive Behavior subscales. Multiple indices were used to assess model fit: Comparative Fit Index (CFI), Tucker-Lewis Index

(TLI), and Root Mean Square Error of Approximation (RMSEA), with RMSEA values <0.05 and CFI and TLI values >0.95 indicating good model fit (Byrne, 2012). To compare the three models, we used χ^2 difference tests for WLSMV estimator, with significant values reflecting diminished model fit.

Next, to examine associations between the DP measured at 36 months and demographic, longitudinal (i.e., 18 and 24 months), and concurrent (i.e., 36 months) variables, regression paths were computed for child demographic factors, CBE outcome, and examiner-rated behavior scores from the ADOS within the bifactor model. Four separate models were constructed based on age: One containing child demographic factors (familial risk status, sex, ethnicity, maternal education, household income), one including 18-month examiner ratings, a comparable 24-month model, and a 36-month model which additionally included dichotomized child CBE outcome. Note that the 6 children without CBE outcomes were excluded from the 36-month model.

Analyses were conducted in *Mplus* version 8 (Muthén & Muthén, 2011).

Results

Factor structure of the DP

Table 2 displays the results of the CFA. The bifactor and second-order models fit the data particularly well, with RMSEA values below 0.05 and CFI and TLI values above 0.95. The one-factor model resulted in a RMSEA value slightly greater than 0.05 and CFI and TLI values slightly below 0.95. Comparisons between the models revealed that, although both the bifactor and second-order models fit the data well, the bifactor model fit the data significantly better than the second-order model (which fit the data better than the one-factor model).

Standardized factor loadings, extracted from the bifactor model, for the CBCL items comprising the three DP subscales are presented in Table 3. Consistent with Geeraerts et al. (2015), factor loadings of the individual subscale items were more robust for the DP than for their respective CBCL subscales. All items from these three subscales significantly loaded on the DP factor, but not all items loaded appropriately on their respective scales; this was especially true for the Aggressive Behavior subscale, consistent with what has been demonstrated previously (Geeraerts et al., 2015).

Longitudinal and concurrent predictors of the DP

Table 4 displays the associations (fully standardized regression paths) between the four DP-related factors in the bifactor model (i.e., general DP factor, plus three specific subscale factors) and child demographic factors (familial risk status, sex, ethnicity, maternal education, household income), CBE outcome (Typically Developing versus Non-Typically Developing), and examiner ratings resulting from separate models based on the age at which examiner-rated measurements were acquired. These models took into account all predictors and outcomes simultaneously.

Within the child demographic factors model, genetic liability for ASD was significantly positively associated with the Anxious/Depressed factor, male sex was associated with lower scores on the Anxious/Depressed and Aggressive Behavior factors, and lower household income was associated with higher DP scores. Maternal education and non-white ethnicity were not associated with any of the DP factors.

In terms of examiner ratings, overactivity at the 18-month visit significantly predicted the 36-month DP factor, and ratings of anxiety significantly predicted the Anxious/Depressed factor. At 24 months, examiner ratings of overactivity again predicted the DP. At 36 months, examiner ratings of aggressive/negative/disruptive behavior and anxiety significantly predicted the DP (positive association for aggressive behavior, negative association for anxiety); ratings of anxiety were also negatively associated with the 36-month Aggressive Behavior and positively associated with 36-month Anxious/Depressed behavior. Non-Typical CBE outcomes were associated with all but the Anxious/Depressed factors.

Discussion

In this study, we sought to (1) examine the factor structure of the DP in a sample of preschoolers enriched with a wide range of variation across dysregulation-related domains, (2) evaluate longitudinal and concurrent predictors of the DP, and (3) determine whether children with genetic liability for ASD are at risk for a phenotype characterized by elevated dysregulation at age 3.

The results of the CFA replicated those of Geeraerts et al. (2015) in our non-clinically-referred sample of preschoolers, all initially ascertained before 18 months of age, well before symptoms of psychopathology are first evident. The present findings further support the superiority of a “general-specific” bifactor model of the DP when compared to one-factor and second-order factor models. That is, in 3-year-olds, the structure of the DP consists of a general syndrome of dysregulation as well as individual (specific) syndromes characterized by anxious/depressed behavior, aggressive behavior, and attention problems (Deutz et al., 2016; Geeraerts et al., 2015). The factor loadings for items comprising the three relevant CBCL subscales were more robust and consistent for the DP than for their own respective subscale factors, consistent with prior reports (Geeraerts et al., 2015). These findings have implications for the conceptualization and measurement of early childhood psychopathology. Clinically, nonspecific factors that account for comorbidity between, or co-occurrence of, various disorders have the potential to lead to the development of transdiagnostic treatments, which could have broader impacts than those that focus on specific syndromes. This may be especially important in the preschool period, during which many forms of psychopathology are just beginning to emerge and have not yet become clinically differentiable, as well as for early detection of meaningful clinical constructs that confer longitudinal risk and are characterized by multifinality over time, such as the DP (e.g., Bellani et al., 2012; De Caluwé et al., 2013; Deutz et al., 2016; Holtmann et al., 2011). Notably, our sample is not a community sample and the degree to which our findings would generalize to such a sample is unknown. We also did not assess measurement invariance across groups due to sample size limitations in subgroups and because doing so would be inconsistent with the conceptualization of the DP as a dimension of emotional and

behavioral dysregulation *that may cut across diagnostic boundaries*. However, future studies in true community samples may be able to address the important issue of measurement invariance across different subgroups.

We also found that examiner ratings of specific behaviors selected, a priori, to closely map on to the constructs that comprise the DP were longitudinally and/or concurrently associated with the general DP factor as well as several of the specific factors. Among the examiner-rated behaviors considered, overactivity constituted a consistent early predictor of the DP, although was not concurrently associated with the DP at 36 months, instead perhaps being captured by the Non-Typical CBE predictor. Our findings expand on prior work documenting the external validity of the DP (Geeraerts et al., 2015) by demonstrating that examiner observations as early as 18 months of age are longitudinally associated with 36-month parent-rated broad-based dysregulation, and that CBE outcome ratings of non-typical development are concurrently associated with elevated, generalized dysregulation. More specifically, these findings suggest that overactivity may be a viable early marker of generalized dysregulation. This is consistent with prior research which has found that parent-rated infant activity level is predictive of childhood conduct problems (Lahey et al., 2008).

Finally, this study found a significant association between familial risk for ASD and greater dysregulation in the affective dimension. After accounting for aspects of dysregulation shared across the affective, behavioral, and cognitive domains (i.e., the general DP factor) as well as unique dysregulation in the Aggressive Behavior and Attention Problems dimensions, young children with a family history of ASD exhibited elevations specifically in the Anxious/Depressed dimension. Put another way, the two groups were differentiated only by “pure” Anxious/Depressed dysregulation. This is consistent with research in school-aged and adolescent siblings of children with ASD documenting vulnerabilities to a variety of challenges, including affective problems (Drumm, Bryson, Zwaigenbaum, & Brian, 2015; Gamliel, Yirmiya, Jaffe, Manor, & Sigman, 2009; Miller et al., 2016). Our findings also fit with large, population-based studies documenting elevated rates of a range of psychiatric disorders in family members of individuals with ASD (Daniels et al., 2008; Jokiranta-Olkoniemi et al., 2016), extending this downward to preschoolers, all of whom were originally ascertained by 18 months of age. Moreover, the Anxious/Depressed factor was predicted by examiner-rated anxiety at 18 months and concurrently, indicating that examiner observations as early as 18 months of age may help to identify early risk for preschool affective symptoms, to which high-risk infant siblings may be especially vulnerable. Given the established longitudinal associations between the DP and psychopathology (Althoff et al., 2010; De Caluwé et al., 2013; Deutz et al., 2016; Geeraerts et al., 2015; Holtmann et al., 2011), these findings may suggest increased risk for later psychopathology for younger siblings of children with ASD beyond the preschool years. This may also imply that the syndromes comprising such nonspecific factors and ASD are influenced by shared etiologies (Lahey et al., 2017; Lahey, Van Hulle, Singh, Waldman, & Rathouz, 2011).

Although our findings of elevated affective dysregulation among younger siblings of children with ASD are at least partially consistent with prior research, it is somewhat surprising that we did not find elevations *across* the DP dimensions in this group particularly

since studies utilizing a temperament framework in infant sibling samples have documented broader dysregulation in this population (Clifford, Hudry, Elsabbagh, Charman, & Johnson, 2013; Garon et al., 2009). Differences in measurement approaches may explain this. Whereas temperament measures are designed to assess trait-like "individual differences in reactivity and self-regulation" (Rothbart, 1981, p. 569), the CBCL was developed specifically to identify symptoms of psychopathology.

Future investigations should examine the predictive validity of the DP at age 3 to later outcomes, particularly among younger siblings of children with ASD. Further follow-up of a subset of this sample into middle childhood and adolescence, which is ongoing, will provide an opportunity to determine whether the DP at age 3 is predictive of later diagnostic, symptom, or functional outcomes, as has been demonstrated in older samples and in studies of similar constructs in preschoolers (Althoff et al., 2010; De Caluwé et al., 2013; Holtmann et al., 2011; Olino et al., 2018). Such investigations, in cohorts of children expected to demonstrate a wide range of phenotypic variation (e.g., high-risk infant sibling samples), may contribute to a more complete understanding of the developmental unfolding of emotional and behavioral dysregulation and psychopathology in children.

Ultimately, the present findings support the utility of examining the structure of psychopathology in preschoolers. These results suggest that preschool-aged siblings of children with ASD may be at elevated risk not only for ASD and other related challenges (e.g., speech-language delays, broader autism phenotype) but also for broader dysregulation problems, with an emphasis on the affective domain, as early as age 3 years. Our findings also indicate the utility of observer-rated overactivity during a semi-structured assessment as an early marker of later generalized dysregulation. Given what is known about the elevated rates of, and long-term disability associated with, psychopathology in families of individuals with ASD (Howlin, Moss, Savage, Bolton, & Rutter, 2015; Jokiranta-Olkoniemi et al., 2016; Sucksmith et al., 2011), these results point to the need for close monitoring of preschool-aged siblings of children with ASD in order to facilitate earlier detection and treatment of a number of behavioral and emotional challenges.

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Key Points

- The “dysregulation profile” (DP) is a measure of broad-based dysregulation that may cut across diagnostic boundaries. Siblings of children with autism spectrum disorder (ASD) are at increased risk for a broad range of atypical developmental outcomes providing a unique opportunity to explore the DP in a population enriched for dysregulation.
- We examined the factor structure of the DP in preschool-aged siblings of children with and without ASD, finding that a bifactor model best fit the data. This supports the relevance of examining the structure of psychopathology in preschoolers.
- Examiner ratings as early as 18 months of age were associated with the DP at 36 months of age, suggesting that examiner observations early in life may help identify risk for later DP-related concerns.
- Family history of ASD was associated with higher dysregulation in the Anxious/Depressed dimension, suggesting the need to closely monitor preschool-aged siblings of children with ASD in order to facilitate earlier detection and treatment of behavioral and emotional challenges.

Table 1.

Sample characteristics by familial risk status for ASD.

	Low-Risk (*n*=162)	High-Risk (*n*=253)	*p*-value[a]
Male sex (*n*, %)	97 (59.88%)	131 (51.78%)	0.11
Ethnicity (*n*, % non-white)[b]	39 (24.07%)	112 (44.62%)	<0.001
Household income (*n*, % over $100,000)[c]	81 (54.73%)	128 (54.70%)	0.99
Maternal education (*n*, % college degree or higher)[d]	125 (80.13%)	171 (71.25%)	0.05
Mullen Scales of Early Learning[e]			
Nonverbal Composite (mean, *SD*)	56.90 (9.62)	55.44 (11.41)	0.18
Verbal Composite (mean, *SD*)	54.47 (7.14)	51.25 (8.93)	<0.001

[a] *p*-values from chi-square (for categorical variables) and independent samples *t*-tests (for continuous variables).

[b] Missing/decline to state *n*=2 for High-Risk.

[c] Missing/decline to state *n*=14 for Low-Risk and *n*=19 for High-Risk.

[d] Missing/decline to state *n*=6 for Low-Risk and *n*=13 for High-Risk.

[e] Scores at 36 months of age. Nonverbal Composite=Average of Visual Reception and Fine Motor subscale *T*-scores; missing *n*=5 for Low-Risk and *n*=4 for High-Risk. Verbal Composite=Average of Receptive Language and Expressive Language subscale *T*-scores; missing *n*=5 for Low-Risk and *n*=6 for High-Risk.

Table 2.

Model fit indices for bifactor, second-order, and one-factor models.

Model	χ^2	*df*	RMSEA	RMSEA 90% CI	CFI	TLI	$\Delta\chi^2$ (significant values reflect diminished model fit)
Bifactor	649.81***	432	0.035	0.029–0.040	0.976	0.972	--
Second-order[a]	788.51***	461	0.041	0.036–0.046	0.963	0.961	Second-order vs. bifactor (29) = 144.36***
One-factor	962.71***	464	0.051	0.046–0.055	0.944	0.940	One-factor vs. second-order (3) = 92.92***

Note. RMSEA=Root Mean Square Error of Approximation; CI=Confidence Interval; CFI=Comparative Fit Index; TLI=Tucker-Lewis Index.

[a]Latent variable covariance matrix was not positive definite.

*** *p*<.001

Table 3.

Standardized factor loadings for relevant Child Behavior Checklist items.

Item	Description	Scale-Specific Loading	DP Loading
Anxious/Depressed			
10	Clings	0.550***	0.474***
33	Feelings hurt	0.469***	0.477***
37	Upset by separation	0.437***	0.600***
43	Looks unhappy	0.155	0.725***
47	Nervous	0.404***	0.745***
68	Self-conscious	0.630***	0.225**
87	Fearful	0.580***	0.542***
90	Sad	0.123	0.611***
Aggressive Behavior			
8	Can’t stand waiting	−0.247***	0.757***
15	Defiant	0.204**	0.817***
16	Demands met	−0.275***	0.817***
18	Destroys others’	0.235**	0.737***
20	Disobedient	0.223**	0.769***
27	Lacks guilt	0.185**	0.663***
29	Easily frustrated	−0.143*	0.801***
35	Fights	0.279***	0.824***
40	Hits others	0.600***	0.669***
42	Hurts accidentally	0.309***	0.627***
44	Angry moods	−0.022	0.807***
53	Attacks people	0.431***	0.728***
58	Punishment doesn’t change	0.221**	0.753***
66	Screams	0.021	0.745***
69	Selfish	0.042	0.631***
81	Stubborn/sullen/irritable	0.041	0.797***
85	Temper	0.010	0.752***
88	Uncooperative	0.050	0.806***
96	Wants attention	−0.090	0.644***
Attention Problems			
5	Can’t concentrate	0.594***	0.610***
6	Can’t sit still	0.625***	0.649***
56	Clumsy	0.333***	0.444***
59	Quickly shifts	0.279***	0.529***

Item	Description	Scale-Specific Loading	DP Loading
95	Wanders away	0.318***	0.539***

Note: DP=Dysregulation Profile.

*$p<.05$;

**$p<.01$;

***$p<.001$

Table 4.

Standardized regression coefficients (standard errors) for associations between demographic and examiner-rated observed behavior predictors and dysregulation profile (DP) factors at 36 months within the bifactor model.

	DP	Aggressive Behavior	Anxious/Depressed	Attention Problems
Model 1: Child demographic factors[a]				
ASD Risk Status	0.02 (0.05)	−0.04 (0.08)	0.28 (0.08)***	0.06 (0.09)
Male Sex	0.01 (0.06)	−0.16 (0.08)*	−0.18 (0.08)*	0.02 (0.08)
Non-white ethnicity	0.06 (0.06)	0.04 (0.07)	0.08 (0.08)	−0.06 (0.08)
Maternal education: College degree or higher	−0.11 (0.06)	0.11 (0.07)	−0.00 (0.08)	−0.05 (0.08)
Household income: Over $100,000	−0.17 (0.06)**	0.12 (0.08)	0.02 (0.08)	−0.10 (0.08)
Model 2: 18-month examiner ratings[b]				
Overactivity	0.18 (0.05)**	−0.00 (0.07)	−0.09 (0.08)	0.09 (0.08)
Aggressive/negative/disruptive	0.01 (0.06)	0.05 (0.07)	0.03 (0.08)	0.03 (0.08)
Anxiety	−0.04 (0.05)	−0.01 (0.07)	0.17 (0.08)*	0.01 (0.08)
Model 3: 24-month examiner ratings[c]				
Overactivity	0.17 (0.05)**	0.06 (0.07)	−0.12 (0.08)	0.06 (0.07)
Aggressive/negative/disruptive	0.02 (0.06)	−0.04 (0.07)	−0.10 (0.08)	0.05 (0.07)
Anxiety	0.02 (0.05)	0.03 (0.07)	0.13 (0.08)	−0.04 (0.007)
Model 4: 36-month examiner ratings[d]				
Non-Typical CBE Outcome	0.15 (0.06)**	0.19 (0.07)**	0.03 (0.07)	0.21 (0.08)**
Overactivity	0.05 (0.06)	0.10 (0.07)	−0.06 (0.07)	0.01 (0.07)
Aggressive/negative/disruptive	0.11 (0.06)**	−0.09 (0.07)	−0.03 (0.08)	0.04 (0.07)
Anxiety	−0.13 (0.06)*	−0.13 (0.06)*	0.18 (0.08)*	0.02 (0.08)

^ $p<.10$;

* $p<.05$;

** $p<.01$;

*** $p<.001$.

Note. ASD=Autism Spectrum Disorder; CBE=Clinical Best Estimate. Fully standardized regression coefficients were extracted from linear regression models; all predictor variables are dichotomous. Separate models computed for child demographic variables (sex, ASD risk status), and examiner ratings collected at 18 months, 24 months, and 36 months.

[a] Missing *n*=46;

[b] Missing *n*=32;

[c] Missing *n*=38;

[d] Missing *n*=18.