The Dysregulation Profile in Young Children: Empirically-Defined Classes in the Generation R Study

Ms. Maartje M. G. J. Basten, M.Sc.,
Erasmus University Medical Center

Dr. Robert R. Althoff, M.D., Ph.D.,
University of Vermont College of Medicine

Dr. Henning Tiemeier, M.D., Ph.D.,
Erasmus University Medical Center

Dr. Vincent W. V. Jaddoe, M.D., Ph.D.,
Erasmus University Medical Center

Dr. Albert Hofman, M.D., Ph.D.,
Erasmus University Medical Center

Dr. James J. Hudziak, M.D.,
Erasmus University Medical Center. University of Vermont College of Medicine

Dr. Frank C. Verhulst, M.D., Ph.D., and
Erasmus University Medical Center

Mr. Jan van der Ende, M.Sc.
Erasmus University Medical Center

Abstract

Objective—Children with co-occurring internalizing and externalizing problems have higher levels of impairment and worse outcomes later in life, but it is unclear whether these children can be distinguished validly from children who have problems in a single domain. We used a person-centered statistical approach to examine whether a group of children with co-occurring internalizing and externalizing problems can be identified in a general-population sample of young children.

Method—This study included a population-based sample of 6,131 children, aged 5 to 7 years. Mothers (92.6%) reported emotional and behavioral problems using the Child Behavior Checklist/

1.5–5 (CBCL). A latent profile analysis was performed on the CBCL syndrome scales. Identified classes were compared on early socioeconomic and parental risk factors using multinomial logistic regression.

Results—We identified 4 classes: 1) a class scoring high on all internalizing and externalizing scales (1.8%), 2) a class with internalizing problems (5.3%), 3) a class with externalizing problems and emotional reactivity (7.3%), and 4) a class without problems (85.6%). The first class, with co-occurring problems, was associated with higher levels of maternal and paternal affective symptoms and hostility than the other 3 classes.

Conclusions—The class with co-occurring internalizing and externalizing problems appears to be highly similar to the CBCL Dysregulation Profile described in older children. This empirically-based dysregulation profile offers a promise to the study of the development of poor self-regulation.

INTRODUCTION

Internalizing and externalizing problems co-occur at rates that are much higher than expected by chance. Co-occurrence of internalizing and externalizing problems has been associated with higher levels of impairment and higher risk for adult psychiatric disorders, criminal offences and suicide.[1–3] Studying co-occurrence may increase our understanding of the etiology, course, and treatment of psychiatric disorders.[1] So far, most research on the co-occurrence of internalizing and externalizing problems has been done in school-age children and adolescents. However, since psychiatric symptoms begin in the preschool period, research on co-occurrence should also start at an early age.[4]

One of the methodological challenges to investigating children with co-occurring internalizing and externalizing problems is validly distinguishing them from children who have problems in a single domain. Co-occurring problems are often defined using cut-points on internalizing and externalizing dimensions.[2,5,6] However, the use of cut-points on continuous variables results in loss of information. In addition, it is debatable as to which cut-points should be used. Lastly, it is unclear how many groups are needed to adequately describe these co-occurring problems in children. Person-centered methods, such as latent class analysis (LCA) or latent profile analysis (LPA) help to identify homogeneous groups of individuals with similar patterns of psychopathology.

Person-centered methods have previously been used to examine children with co-occurring internalizing and externalizing problems. To our knowledge, these studies focused only on high-risk samples, and not on the general population. Connell *et al.*[7] performed LCA on the preschool Child Behavior Checklist (CBCL)[8] in a sample of preschool children with behavioral problems, family problems, and/or low socioeconomic status. They identified 4 classes: a) comorbid internalizing and externalizing, b) externalizing only, c) internalizing only, and d) normative. Interestingly, children with comorbid internalizing and externalizing problems appeared to benefit more from a family-centered intervention than children with problems in a single domain.[7] Tolan and Henry[9] found four very similar patterns of psychopathology using LCA in urban poor school-age children. The class of children with high scores on internalizing and externalizing scales was most strongly associated with poor psychosocial functioning 2 years later. These studies showed the importance of identifying children with co-occurring internalizing and externalizing problems for examining

intervention effects and prognosis. However, the selection of children who are at high risk might have resulted in biased prevalence and patterns of co-occurring problems[1].

In school-age children LCA has also been used to identify the CBCL Dysregulation Profile, a phenotype that is characterized by co-occurring internalizing and externalizing problems.[10] The CBCL Dysregulation Profile latent class captures children with high scores on the items of Anxiety/Depression, Attention Problems, and Aggressive Behavior scales.[11–13] This class was associated with suicidal behavior and predicted increased rates of anxiety, mood and disruptive behavior disorders in adulthood.[12,13]

The co-occurrence of internalizing and externalizing problems presented in the CBCL Dysregulation Profile is thought to stem from an underlying syndrome of poor self-regulation.[10] A common factor underlying internalizing and externalizing problems has been studied by others using related concepts such as irritability[14] and mood lability[15]. In preschool children, self-regulation is often studied from a temperamental perspective.[16] At this young age, poor self-regulation has also been shown to be a key feature of emerging and persisting internalizing and externalizing problems.[5,16] The identification of the CBCL Dysregulation Profile in young children would allow continued study of poor self-regulation from preschool to adolescence using an empirically-based measure.

In person-centered methods it is important to study risk factors or other correlates of classes. External validity can be demonstrated if class membership can be predicted from variables other than the ones used to create the classes.[17] Studying risk factors can also aid to understand differential etiology of classes. Many family and environmental factors such as parental psychopathology, poverty, and stressful life events are related to both internalizing and externalizing problems.[18] Co-occurring internalizing and externalizing problems, in comparison with problems on a single domain, have been associated with higher levels of risk factors.[18]

In the present study, we used a person-centered method to examine whether a group of children with co-occurring internalizing and externalizing problems can be distinguished in a general population sample of young children. We performed LPA on the syndrome scales of the preschool CBCL in a large sample of 5 to 7-year-old children. A wide range of continuously measured psychological problems was used to overcome the limitations of previous studies that used LCA based on dichotomized scale scores[7,9], or that investigated only a subset of problems.[11–13] We hypothesized to find a highly problematic group of children scoring high on internalizing and externalizing scales. We were interested in whether this group would have elevated scores on all scales or only on the Anxious/Depressed, Attention Problems, and Aggressive Behavior scales contributing to the CBCL Dysregulation Profile. We also hypothesized to observe a group of children with mainly internalizing problems and a group of children with mainly externalizing problems. We expected the majority of the children to be in a class characterized by no psychopathology. To examine external validity and differential etiology, the classes were examined in relation to known risk factors of psychopathology, i.e. gender, ethnicity, maternal education, family income, and parental psychological problems. We expected the highly problematic class to be most strongly associated with these socioeconomic and parental risk factors.

METHOD

Setting and population

This study was embedded in the Generation R study, a multi-ethnic population-based cohort from fetal life onwards. The Generation R Study has been described in detail previously.[19,20] Briefly, all pregnant women living in Rotterdam, the Netherlands, with an

expected delivery date between April 2002 and January 2006 were invited to participate. The study was approved by the Medical Ethics Committee of the Erasmus Medical Center, Rotterdam. Written informed consent was obtained from all adult participants. At birth, 9,749 children participated in the study (participation rate 61%). When the children reached the age of 5 years, 8,305 parents gave consent for further participation. At this time point, 6,210 primary caregivers completed the CBCL. We excluded 79 children who were 8 years or older, which resulted in a study sample of 6,131 children (63% of the original sample). Table 1 presents sample characteristics.

Child Behavior Checklist/1.5–5

We assessed emotional and behavioral problems using the 100-item Child Behavior Checklist for ages 1.5 to 5 (CBCL).[8] The CBCL/1.5–5 was chosen because we expected most children to be younger than 6 years at assessment. At the end of the assessment, while most children were 5 years old (58%), some were 6 (38%) or 7 (4%) years old. The CBCL was completed by the primary caregiver (92.6% mothers). Based on the behavior of the child in the preceding 2 months, each item was rated as 0 for not true, 1 for somewhat or sometimes true, and 2 for very true or often true. We used syndrome scales that are part of the Internalizing and Externalizing broad-band scales. The Internalizing scale consists of 4 scales: Emotionally Reactive (e.g. 'rapid shifts between sadness and excitement,' 'disturbed by any change in routine'), Anxious/Depressed (e.g. 'Looks unhappy without good reason,' 'nervous, highstrung or tense'), Somatic Complaints (e.g. 'headaches' 'nausea, feels sick'), and Withdrawn (e.g. 'refuses to play active games,' 'seems unresponsive to affection'). The Externalizing scale contains two scales: Attention Problems (e.g. 'can't concentrate,' 'wanders away') and Aggressive Behavior (e.g. 'angry moods', 'defiant'). Good reliability and validity have been reported for the CBCL/1.5–5[8], and the syndrome scales were found to be generalizable across 23 societies.[21] In our sample, for all scales Cronbach's alphas were the same in 5-year-old children and in children older than 5, indicating that problems were also reliably measured in children older than 5.

Early Risk Factors

Information on risk factors was obtained by questionnaires. Ethnicity of the child was defined by the country of birth of the parents.[22] Children were classified as non-Dutch if one of the parents was born abroad. Three categories were defined: Dutch, other Western, and non-Western. Maternal education level was examined at time of enrollment. It was defined as highest education finished and was classified into 3 categories[23]: low (primary school or lower vocational education), medium (intermediate vocational education), and high (higher vocational education or university). Family income was also examined at enrollment. It was defined by the total net month income of the household and categorized as '< €1200' (below social security level), '€1200–2000,' and '> €2000' (more than modal income). When the child was 3 years old (mean=3.1±0.1), psychological problems of both parents were measured using the Brief Symptom Inventory (BSI), a validated self-report questionnaire.[24] The BSI consists of 53 items that have to be answered on a 5-point scale and can be classified in 8 subscales; Depression, Hostility, Anxiety, Phobic Anxiety, Paranoid Ideation, Psychoticism, Interpersonal Sensitivity, and Obsessive-Compulsive. We aimed to focus on internalizing and externalizing symptoms. Therefore, we calculated a mean affective symptom score, which included the items from the Depression and Anxiety scales, and the mean symptom score on the Hostility scale.

Data Analysis

We conducted latent profile analysis (LPA) using Mplus version 6.[25] LPA is a person-centered method using continuous variables as indicators. LPA identifies classes of individuals with similar scoring patterns. T-scores on the syndrome scales, which have the

same norms for boys and girls on the CBCL/1.5–5, were used as indicators. To reduce the influence of skewed variables, a maximum likelihood estimator with robust standard errors was used. We started with a 1-class model and increased the number of classes until a stable, best fitting model was achieved. The best fitting model was determined by looking at the Bayesian information criterion (BIC) and the Bootstrapped Likelihood-Ratio Test (BLRT) as these fit indices appeared to perform best in a simulation study by Nylund *et al.*[26] For the BIC, a lower value represents a better fitting model, taking parsimony into account. The BLRT tests if the addition of a class leads to a significant improvement in model fit. In determining the number of classes we also considered the rule of parsimony and the substantive relevance of a class. Entropy, a measure of how well the children were classified, was also taken into account. We tested whether age entered as a covariate would improve model fit. Once the best fitting model was determined, we assigned each individual to the class for which the individual had the highest probability of membership. To examine the relationship between risk factors and the latent classes, we performed multinomial logistic regression in SPSS (IBM SPSS Statistics, version 20.0). First, we made pairwise comparisons between classes on each risk factor. Second, to examine which factors were most strongly associated, we made pairwise comparisons between classes on each risk factor while adjusting for other factors. Maternal education and family income were not adjusted for each other because they are highly related. For similar reasons parental affective and hostility symptoms were not adjusted for each other. All analyses were also adjusted for age child. Scores on the BSI were transformed to z scores to facilitate the interpretation of the findings. Percentages of missing data on early risk factors were 4.7% for child ethnicity, 6.6% for maternal education, 21.1% for family income, 31.5% for maternal psychological symptoms, and 43.3% for paternal psychological symptoms. To avoid selection bias due to missing data, we used multiple imputations. It has been shown that missing values up to 60% can be adequately dealt with using multiple imputations.[27,28] We imputed missing values using a fully conditional specification method in SPSS. Because a large fraction of the data was imputed, we generated 20 imputed data sets.[29] Imputations were based on class membership and all risk factors in the model. We added prenatal parental BSI as additional indicators to improve the imputation model. We imputed parental psychological symptoms regardless of whether the parent was present in the home, to account for a possible genetic effect of parental psychological symptoms. To examine if the multiple imputations were not fatal, analyses were repeated in a sample with complete paternal psychological symptoms data (n=3,475).

Nonresponse Analysis

We compared child and maternal characteristics of the children included in the analysis (n=6,131) with those excluded because of missing data on CBCL (n=3,618). Children of responding mothers were more likely to be Dutch (60.6% vs. 30.8%, x^2=1,062, df=3, p<0.001). Responding mothers were more likely to be high educated (48.7% vs. 18.9%, x^2=1,250, df=3, p<0.001) and to have a high family income (55.2% vs. 20.3%, x^2=1,328, df=3, p<0.001).

RESULTS

Table 2 presents the model fit indices for 1 to 5 class solutions of the LPA. According to the BIC and the BLRT, more classes resulted in better model fit. The 4-class solution resulted in clearly distinct classes. A comparison of the 4-class and 5-class solutions showed that the 5-class solution included an additional class with a profile that was not clearly different from that of the lowest scoring class. Furthermore the probability of membership in the highest scoring class decreased to include only 0.9% of the sample. Because of minimal

differentiation from four to five classes we chose the 4-class solution. The entropy was 0.98. Adding age as a covariate did not improve model fit.

Figure 1 and Table 3 show the mean T-scores for the classes. Table 3 also provides standard deviations of the T-scores. The first class, containing 1.8% of the sample, showed the highest scores on all scales ranging from 62 on Somatic Complaints to 73 on Emotionally Reactive. We labeled this class "highly problematic." As shown in Figure 1, there were 2 intermediate classes with elevations around 60, which corresponds to 1 SD above the mean. Class 2, including 5.3% of the sample, showed T-scores around 60 on the internalizing scales Emotionally Reactive, Anxious/Depressed, Somatic Complaints, and Withdrawn, and was labeled "internalizing." Class 3 showed elevations around 60 on Emotionally Reactive and Aggressive Behavior, moderate elevations on Somatic Complaints, Withdrawn, and Attention Problems (range:57–58), but no elevation on Anxious/Depressed. Because of the elevation on the Emotionally Reactive scale, the relatively higher scores on Attention Problems and Aggressive Behavior in comparison with the internalizing class, and the absence of problems on Anxious/Depressed, we labeled this class "externalizing/emotionally-reactive." This class contained 7.3% of the children. Class 4, including 85.6% of the children, scored low on all scales (range: 50–52) and was labeled "no problems."

We examined the relationship between risk factors and class membership using multinomial logistic regression. In the unadjusted analyses, all risk factors predicted membership to the 3 problem classes (Table S1, available online). To investigate which risk factors were most strongly associated with the classes, we controlled effects for other factors. Table 4 reports the results for each problem class relative to the no problems class. The highly problematic class included more boys (OR=2.10, p<0.01) and more mothers with a low education level (OR=1.97, p<0.05) than the no problems class. Both mothers and fathers of the highly problematic class reported higher levels of affective symptoms (mother OR=1.54, p<0.001; father OR=1.40, p<0.001) and hostility (mother OR=1.60, p<0.001; father OR=1.47, p<0.001) than the no problems class. The internalizing class was associated with non-Western ethnicity (OR=1.53, p<0.01), low maternal education (OR=1.76, p<0.001), and low family income (OR=1.63, p<0.05) in comparison with the no problems class. The internalizing class was also related to higher levels of maternal affective symptoms (OR=1.32, p<0.001), maternal hostility (OR=1.30, p<0.001) and paternal affective symptoms (OR=1.13, p<0.05). The externalizing/emotionally-reactive class included more boys (OR=1.92, p<0.001) and was associated with higher levels of maternal affective symptoms (OR=1.29, p<0.001) and maternal hostility (OR=1.43, p<0.001) than the no problems class. Next, we made pairwise comparisons between the highly problematic class and the internalizing and externalizing/emotionally-reactive classes. Results are shown in Table 5. Mothers and fathers of the highly problematic class reported higher levels of affective symptoms (mother OR=1.17, p<0.05; father OR=1.24, p<0.01) and hostility (mother OR=1.24, p<0.05; father OR=1.36, p<0.01) than the internalizing class. Mothers and fathers of the highly problematic class reported also more psychological symptoms than the externalizing/emotionally-reactive class (maternal affective symptoms OR=1.19, p<0.05; paternal affective symptoms OR=1.32, p<0.01; paternal hostility OR=1.33, p<0.01). All significant associations between parental psychological symptoms and class membership were also found in the sample with complete data on paternal psychological symptoms (Tables S2–S4, available online).

DISCUSSION

In this study, we aimed to identify a pattern of co-occurring internalizing and externalizing problems in a large population-based sample of 5 to 7-year-old children. Using latent profile analysis on the CBCL/1.5–5 syndrome scales, we identified 4 classes: 1) a class scoring high

on all internalizing and externalizing scales, 2) an intermediate class with internalizing problems, 3) an intermediate class with predominantly externalizing problems and emotionally reactive behavior, and 4) a class without problems. The highly problematic class was associated with high levels of maternal and paternal psychological symptoms.

This study was performed in a population-based sample of young children. In general, the selection of the sample may affect the structure and the prevalence of the latent classes.[17] Interestingly, the identified patterns of emotional and behavioral problems in our study are largely in line with the 4 identified classes in high risk samples.[7,9] Additionally, we found that internalizing and externalizing problems were always accompanied by emotional reactivity, which was less clear in the study of Connell *et al.*[7] The agreement across studies suggests that the structure of the classes is less dependent on the socioeconomic background of the sample. In our study we found a lower prevalence rate for the highly problematic class than other studies in high risk samples.[7,9] The internalizing and externalizing/emotionally-reactive classes were also smaller in our study than in the study by Connell *et al.*[7] The prevalences of the three problem classes in our study may be somewhat lower than in our target population because of a higher nonresponse among non-Western and low socioeconomic families.

The CBCL Dysregulation Profile captures children with elevations on the Anxious/Depressed, Attention Problems, and Aggressive Behavior scales.[11–13] The highly problematic class in our study also showed elevations on the Emotionally Reactive, Somatic Complaints, and Withdrawn scales. The question arises whether the highly problematic class identifies the same children as the CBCL Dysregulation Profile. There could be several explanations why we did not find a Dysregulation Profile. First, Althoff *et al.* identified a dysregulation class by performing latent class analyses based on the items from the Anxious/Depressed, Attention Problems, and Aggressive Behavior scales.[11–13] We based our analyses on a broader spectrum of emotional and behavioral problems using all internalizing and externalizing scales. Second, the content of the CBCL/1.5–5 differs from the school-age CBCL/6–18. Five of the 6 scales used in our study have comparable counterparts on the CBCL/6–18.[8] The scale Emotionally Reactive is only present in the CBCL/1.5–5, but includes items from the Anxious/Depressed and Aggressive Behavior scales of the CBCL/6–18. This makes it likely that the Dysregulation Profile in preschool children would also include elevations on the Emotionally Reactive scale. Third, the Dysregulation Profile might emerge only at an age later than 5 to 7 years. However, confirmatory factor analyses on symptoms from *DSM* disorders in 2 to 5-year-old children have shown that differentiation of syndromes is visible at this young age[30], suggesting that the Dysregulation Profile may also appear at a young age. Fourth, LPA might have been unable to detect different patterns within the 1.8% of children with co-occurring internalizing and externalizing problems. This is possible if one assumes a Dysregulation Profile prevalence of 0.7–1.0%, which was reported in studies that based the Dysregulation Profile on cut-points on the scales.[31,32] However, according to the LCA studies the prevalence of the Dysregulation Profile is 4–8%.[11–13] This makes it less likely that the LPA in our study could not identify a Dysregulation Profile. At the same time, there is little evidence that children who fulfill the Dysregulation Profile only have elevations on Anxious/Depressed, Attention Problems, and Aggressive Behavior. Several studies found that children with dysregulation also have high scores on other scales, including Somatic Complaints and Withdrawn/Depressed.[31,33,34] Based on these findings, the current study, and the studies of Connell *et al.*[7] and Tolan and Henry[9], we propose that, even though the profiles differ, children in the highly problematic class are similar to children who meet the CBCL Dysregulation Profile. At least for very young children, dysregulation should not be restricted to elevations on the Anxious/Depressed, Attention Problems, and Aggressive Behavior scales. Children with

dysregulation show high levels of problems across the range of both internalizing and externalizing problems.

All three of the problem classes were related to several socioeconomic and parental risk factors. Pairwise comparisons between the classes showed that the highly problematic or 'dysregulation' class was most strongly associated with parental psychological symptoms. Maternal and paternal psychological symptoms independently contributed to the risk of dysregulation. These results are in-line with evidence that parents of children with co-occurring internalizing and externalizing disorders are more likely to show psychological symptoms than parents of children with a single disorder.[18] Because of the high correlation between affective symptoms and hostility in this study, the specificity of these symptoms remains unclear. The results suggest that psychological symptoms of both parents play a role in the development of dysregulation. More research is needed to understand the genetic and environmental mechanisms that operate in the transmission of psychological symptoms to children with dysregulation.

Gender was also related to class membership. Dysregulation was more prominent in boys. This has also been reported in another sample[11], though others did not find a predominance of boys.[31,32] These mixed results might be related to age or could be explained by the use of cut-points to define dysregulation.[31,32] The externalizing/emotionally-reactive class was also associated with male gender and gender was equally distributed in the internalizing class. This is consistent with male preponderance of externalizing disorders at early age while gender differences in internalizing disorders arise only in adolescence.[35]

This study has limitations. First, we relied only on parental report. However, we included both maternal and paternal psychological symptoms and variables were measured at different time points. Second, data on parental psychological symptoms were missing in 32–43% of the cases. We used multiple imputations to account for the missing data. To examine possible biases of the multiple imputations, we repeated the analyses in a sample with complete paternal data. Similar results were found regarding the association between parental psychological symptoms and dysregulation. The most important reasons for missing data on parental psychological symptoms were that part of the Generation R sample was not reached at 3 years[19] or that parents refused to fill out the questionnaire. However, it was also possible that the parent was not involved in raising the child which might in itself be a risk for the development of dysregulation. Third, we measured parental psychological symptoms only when the child was 3 years old. Thus, we were unable to study the effects of the development of parental psychological symptoms over time on dysregulation. Fourth, our nonresponse analysis demonstrated that our study included relatively more families with a Dutch background and higher socioeconomic status. Because ethnicity and socioeconomic status were associated with class membership, the nonresponse might have led to an underestimation of the associations between sociodemographic risks and class membership.

In conclusion, we identified a pattern of co-occurring internalizing and externalizing problems in a general-population sample of 5 to 7-year-old children. This class seems to be highly overlapping with the CBCL Dysregulation Profile. The profile provides an empirically-based measure to study poor self-regulation at an early age. It allows characterizing poor self-regulation in relation to typically developing children of the same age and gender. A new diagnosis that covers both internalizing and externalizing symptoms is proposed for the *DSM-5*, namely Disruptive Mood Dysregulation Disorder. Future studies should examine to what extent this new diagnosis identifies these children with poor self-regulation.

Previous research on the CBCL Dysregulation Profile has shown a heterotypic development from self-regulatory problems in childhood to different forms of adult psychiatric disorders.[13] Continued empirically-based investigation of self-regulation is necessary to determine how and why children with dysregulation will proceed down a particular course towards psychiatric illness and may provide insights into prevention. Our results suggest that parental psychological symptoms play a role in the etiology of dysregulated behavior. Although more research is needed to understand which mechanisms are involved, it suggests that intervention strategies for dysregulated behavior should focus on psychological symptoms of both parents to prevent these children from developing severe psychopathology later in life.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

References

1. Angold A, Costello EJ, Erkanli A. Comorbidity. J Child Psychol Psychiatry. 1999; 40(1):57–87. [PubMed: 10102726]

2. Sourander A, Jensen P, Davies M, et al. Who is at greatest risk of adverse long-term outcomes? The Finnish From a Boy to a Man study. J Am Acad Child Adolesc Psychiatry. 2007; 46(9):1148–1161. [PubMed: 17712238]

3. Fombonne E, Wostear G, Cooper V, Harrington R, Rutter M. The Maudsley long-term follow-up of child and adolescent depression. 2. Suicidality, criminality and social dysfunction in adulthood. Br J Psychiatry. 2001; 179:218–223. [PubMed: 11532798]

4. Egger HL, Angold A. Common emotional and behavioral disorders in preschool children: presentation, nosology, and epidemiology. J Child Psychol Psychiatry. 2006; 47(3–4):313–337. [PubMed: 16492262]

5. Briggs-Gowan MJ, Carter AS, Bosson-Heenan J, Guyer AE, Horwitz SM. Are infant-toddler social-emotional and behavioral problems transient? J Am Acad Child Adolesc Psychiatry. 2006; 45(7): 849–858. [PubMed: 16832322]

6. Youngstrom EA, Findling RL, Calabrese JR. Who are the comorbid adolescents? Agreement between psychiatric diagnosis, youth, parent, and teacher report. J Abnorm Child Psychol. 2003; 31(3):231–245. [PubMed: 12774858]

7. Connell A, Bullock BM, Dishion TJ, Shaw D, Wilson M, Gardner F. Family intervention effects on co-occurring early childhood behavioral and emotional problems: a latent transition analysis approach. J Abnorm Child Psychol. 2008; 36(8):1211–1225. [PubMed: 18473160]

8. Achenbach, TM.; Rescorla, LA. Manual for the ASEBA Preschool Forms and Profiles. Burlington, VT: University of Vermont, Research Center for Children, Youth, and Families; 2000.

9. Tolan PH, Henry D. Patterns of psychopathology among urban poor children: comorbidity and aggression effects. J Consult Clin Psychol. 1996; 64(5):1094–1099. [PubMed: 8916642]

10. Ayer L, Althoff R, Ivanova M, et al. Child Behavior Checklist Juvenile Bipolar Disorder (CBCL-JBD) and CBCL Posttraumatic Stress Problems (CBCL-PTSP) scales are measures of a single

dysregulatory syndrome. J Child Psychol Psychiatry. 2009; 50(10):1291–1300. [PubMed: 19486226]

11. Althoff RR, Rettew DC, Ayer LA, Hudziak JJ. Cross-informant agreement of the Dysregulation Profile of the Child Behavior Checklist. Psychiatry Res. 2010; 178(3):550–555. [PubMed: 20510462]

12. Althoff RR, Rettew DC, Faraone SV, Boomsma DI, Hudziak JJ. Latent class analysis shows strong heritability of the child behavior checklist-juvenile bipolar phenotype. Biol Psychiatry. 2006; 60(9):903–911. [PubMed: 16650832]

13. Althoff RR, Verhulst FC, Rettew DC, Hudziak JJ, van der Ende J. Adult outcomes of childhood dysregulation: a 14-year follow-up study. J Am Acad Child Adolesc Psychiatry. 2010; 49(11): 1105–1116. [PubMed: 20970698]

14. Stringaris A. Irritability in children and adolescents: a challenge for DSM-5. Eur Child Adolesc Psychiatry. 2011; 20(2):61–66. [PubMed: 21298306]

15. Stringaris A, Goodman R. Mood lability and psychopathology in youth. Psychol Med. 2009; 39(8): 1237–1245. [PubMed: 19079807]

16. Eisenberg N, Spinrad TL, Eggum ND. Emotion-related self-regulation and its relation to children's maladjustment. Annu Rev Clin Psychol. 2010; 6:495–525. [PubMed: 20192797]

17. Lenzenweger MF. Consideration of the challenges, complications, and pitfalls of taxometric analysis. J Abnorm Psychol. 2004; 113(1):10–23. [PubMed: 14992653]

18. Oland AA, Shaw DS. Pure versus co-occurring externalizing and internalizing symptoms in children: the potential role of socio-developmental milestones. Clin Child Fam Psychol Rev. 2005; 8(4):247–270. [PubMed: 16362255]

19. Jaddoe VW, van Duijn CM, Franco OH, et al. The Generation R Study: design and cohort update 2012. Eur J Epidemiol. 2012; 27(9):739–756. [PubMed: 23086283]

20. Tiemeier H, Velders FP, Szekely E, et al. The Generation R Study: A Review of Design, Findings to Date, and a Study of the 5-HTTLPR by Environmental Interaction From Fetal Life Onward. J Am Acad Child Adolesc Psychiatry. 2012; 51(11):1119–1135. e1117. [PubMed: 23101739]

21. Ivanova MY, Achenbach TM, Rescorla LA, et al. Preschool psychopathology reported by parents in 23 societies: testing the seven-syndrome model of the child behavior checklist for ages 1.5–5. J Am Acad Child Adolesc Psychiatry. 2010; 49(12):1215–1224. [PubMed: 21093771]

22. Statistics Netherlands. Migrants in the Netherlands 2004 (Allochtonen in Nederland 2004). Voorburg/Heerlen: 2004. http://www.cbs.nl [Accessed June 4, 2012.]

23. Statistics Netherlands. Standard classification of education 2003 (Standaard Onderwijsindeling 2003). Voorburg/Heerlen: 2004. http://www.cbs.nl [Accessed June 4, 2012.]

24. De Beurs, E. Brief symptom inventory, handleiding. Leiden; The Netherlands: 2004.

25. Muthén, LK.; Muthén, BO. Mplus User's Guide. 6. Los Angeles, CA: Muthén and Muthén;; 1998–2010.

26. Nylund KL, Asparouhov T, Muthén BO. Deciding on the Number of Classes in Latent Class Analysis and Growth Mixture Modeling: A Monte Carlo Simulation Study. Structural Equation Modeling. 2007; 14(4):535–569.

27. Barzi F, Woodward M. Imputations of missing values in practice: results from imputations of serum cholesterol in 28 cohort studies. Am J Epidemiol. 2004; 160(1):34–45. [PubMed: 15229115]

28. Janssen KJ, Donders AR, Harrell FE Jr, et al. Missing covariate data in medical research: to impute is better than to ignore. J Clin Epidemiol. 2010; 63(7):721–727. [PubMed: 20338724]

29. Sterne JA, White IR, Carlin JB, et al. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. BMJ. 2009; 338:b2393. [PubMed: 19564179]

30. Sterba S, Egger HL, Angold A. Diagnostic specificity and nonspecificity in the dimensions of preschool psychopathology. J Child Psychol Psychiatry. 2007; 48(10):1005–1013. [PubMed: 17915001]

31. Holtmann M, Bolte S, Goth K, et al. Prevalence of the Child Behavior Checklist-pediatric bipolar disorder phenotype in a German general population sample. Bipolar Disord. 2007; 9(8):895–900. [PubMed: 18076540]

32. Hudziak JJ, Althoff RR, Derks EM, Faraone SV, Boomsma DI. Prevalence and genetic architecture of Child Behavior Checklist-juvenile bipolar disorder. Biol Psychiatry. 2005; 58(7): 562–568. [PubMed: 16239161]

33. Biederman J, Petty CR, Day H, et al. Severity of the aggression/anxiety-depression/attention child behavior checklist profile discriminates between different levels of deficits in emotional regulation in youth with attention-deficit hyperactivity disorder. J Dev Behav Pediatr. 2012; 33(3):236–243. [PubMed: 22278125]

34. Holtmann M, Goth K, Wockel L, Poustka F, Bolte S. CBCL-pediatric bipolar disorder phenotype: severe ADHD or bipolar disorder? J Neural Transm. 2008; 115(2):155–161. [PubMed: 17994189]

35. Rutter M, Caspi A, Moffitt TE. Using sex differences in psychopathology to study causal mechanisms: unifying issues and research strategies. J Child Psychol Psychiatry. 2003; 44(8): 1092–1115. [PubMed: 14626453]

Clinical Guidance

- In 5 to 7-year-old children from the general population three empirically-based patterns of elevated emotional and behavioral problems can be distinguished:

    – A pattern of high levels of internalizing and externalizing problems (1.8%)

    – A pattern characterized by internalizing problems (5.3%)

    – A pattern of externalizing problems accompanied by emotional reactivity (7.3%)

- The pattern of co-occurring internalizing and externalizing problems was labeled dysregulation as it was considered to be similar to the Child Behavior Checklist (CBCL) Dysregulation Profile in older children.

- Parental psychopathology was more strongly associated with the dysregulation pattern than with the other problem patterns. Socio-economic status and ethnicity were not differentially associated to the 3 problem patterns.

- Children with poor self-regulation, characterized by internalizing and externalizing problems, have previously been shown to be most likely to develop psychopathology in adulthood. Parental psychopathology may be a target for prevention and intervention.
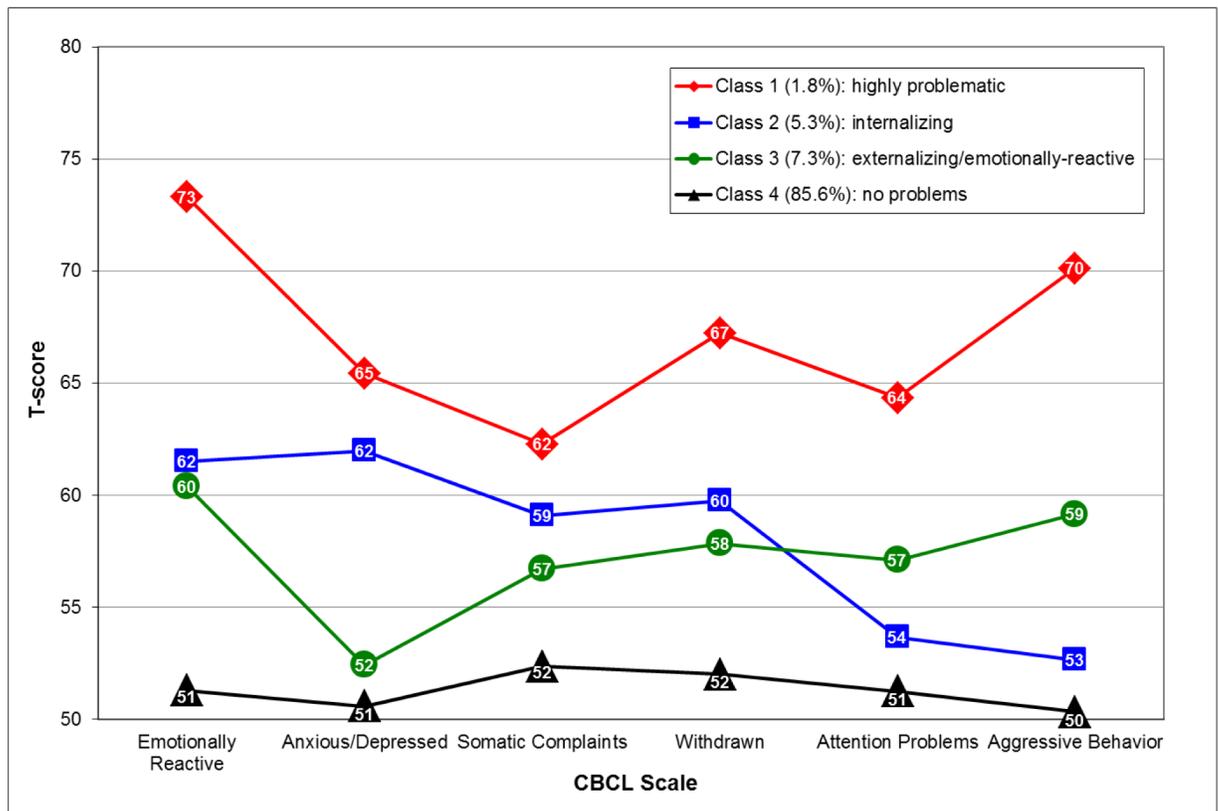
Figure 1.
Mean T-scores from the latent profile model with 4 classes. Note: CBCL = Child Behavior
Checklist 1.5-5.

Table 1

Sample Characteristics.

	n=6,131
Child age in years, mean (sd)	6.0 (0.4)
Child gender, %	
Girls	49.7
Boys	50.3
Child ethnicity, %	
Dutch	62.5
Other Western	9.2
Non-Western	28.4
Maternal education, %	
High	50.2
Medium	29.2
Low	20.6
Family income, %	
> €2000	66.0
€1200–€2000	17.4
< €1200	16.6
Maternal psychological symptoms, mean (SD)	
Affective symptoms	0.18 (0.33)
Hostility	0.19 (0.29)
Paternal psychological symptoms, mean (SD)	
Affective symptoms	0.14 (0.25)
Hostility	0.18 (0.28)

Note: Missing values: child ethnicity 4.7%, maternal education 6.6%, family income 21.1%, maternal psychological symptoms 31.5%, paternal psychological symptoms 43.3%.

Table 2

Fit Statistics for Latent Profile Models.

Number of Classes	BIC	BLRT	Entropy
1 class	217,304	—	—
2 class	204,285	<0.001	0.98
3 class	199,746	<0.001	0.97
4 class	196,759	<0.001	0.98
5 class	194,392	<0.001	0.99

Note: BIC = Bayesian information criterion; BLRT = bootstrapped likelihood-ratio test.

Table 3

Mean T-scores From the Latent Profile Model With 4 Classes.

	Highly problematic **n=110, m (SD)**	**Internalizing** **n=326, m (SD)**	**Externalizing/emotionally-reactive** **n=443, m (SD)**	**No problems** **n=5,252, m (SD)**
Emotionally Reactive	73.4 (9.0)	61.5 (6.1)	60.4 (5.9)	51.3 (2.9)
Anxious/Depressed	65.4 (8.1)	62.0 (4.8)	52.4 (2.7)	50.6 (1.4)
Somatic Complaints	62.2 (9.2)	59.1 (8.0)	56.7 (7.4)	52.4 (4.5)
Withdrawn	67.2 (8.5)	59.7 (7.3)	57.9 (6.7)	52.0 (3.3)
Attention Problems	64.3 (8.1)	53.7 (5.1)	57.1 (6.8)	51.2 (2.8)
Aggressive Behavior	70.2 (7.9)	52.7 (3.1)	59.2 (3.7)	50.3 (1.0)

Table 4

Adjusted Associations Between Risk Factors and Class Membership: The Highly Problematic, Internalizing, and Externalizing/Emotionally-Reactive Classes Compared With the No Problems Class.

	No problems (reference)	Highly problematic		Internalizing		Externalizing/ emotionally-reactive	
	OR	OR	95% CI	OR	95% CI	OR	95% CI
Child gender							
Girls (reference)							
Boys	1.00	2.10 **	1.37–3.23	1.00	0.80–1.26	1.92 ***	1.56–2.36
Child ethnicity							
Dutch (reference)							
Other Western	1.00	1.00	0.46–2.14	0.97	0.61–1.56	0.88	0.53–1.48
Non-Western	1.00	0.92	0.53–1.61	1.53 **	1.13–2.07	1.07	0.81–1.41
Maternal education							
High (reference)							
Medium	1.00	1.45	0.87–2.40	1.16	0.86–1.56	1.14	0.90–1.46
Low	1.00	1.97 *	1.15–3.36	1.76 ***	1.29–2.41	1.31	0.94–1.83
Family income							
> €2000 (reference)							
€1200 – €2000	1.00	1.52	0.84–2.76	1.50 *	1.06–2.11	1.16	0.83–1.62
< €1200	1.00	2.29	0.91–5.78	1.63 *	1.13–2.36	1.40	0.92–2.12
Maternal psychological symptoms							
Affective symptoms	1.00	1.54 ***	1.37–1.73	1.32 ***	1.19–1.46	1.29 ***	1.16–1.43
Hostility	1.00	1.60 ***	1.40–1.83	1.30 ***	1.14–1.48	1.43 ***	1.30–1.56
Paternal psychological symptoms							
Affective symptoms	1.00	1.40 ***	1.22–1.61	1.13 *	1.00–1.28	1.07	0.93–1.22
Hostility	1.00	1.47 ***	1.26–1.72	1.08	0.95–1.24	1.11	0.98–1.26

Note: The model was based on multinomial logistic regression analysis. The no problems class is the reference group against which the odds ratios (OR) are calculated.

*
$p<0.05$,

**
$p<0.01$,

***
$p<0.001$

Table 5

Adjusted Associations Between Risk Factors and Class Membership: The Highly Problematic Class Compared With the Internalizing and Externalizing/Emotionally-Reactive Classes.

	Highly problematic versus Internalizing			Highly problematic versus Externalizing/emotionally-reactive		
	Internalizing (reference)	Highly problematic		Externalizing/emotionally-reactive (reference)	Highly problematic	
	OR	OR	95% CI	OR	OR	95% CI
Child gender						
Girls (reference)						
Boys	1.00	2.10**	1.31–3.36	1.00	1.09	0.69–1.74
Child ethnicity						
Dutch (reference)						
Other Western	1.00	1.02	0.42–2.49	1.00	1.13	0.45–2.84
Non-Western	1.00	0.60	0.33–1.12	1.00	0.86	0.48–1.55
Maternal education						
High (reference)						
Medium	1.00	1.25	0.70–2.24	1.00	1.26	0.73–2.19
Low	1.00	1.12	0.61–2.04	1.00	1.50	0.82–2.75
Family income						
> €2000 (reference)						
€1200 – €2000	1.00	1.02	0.53–1.95	1.00	1.32	0.69–2.51
< €1200	1.00	1.40	0.54–3.63	1.00	1.64	0.62–4.33
Maternal psychological symptoms						
Affective symptoms	1.00	1.17*	1.02–1.34	1.00	1.19*	1.04–1.38
Hostility	1.00	1.24*	1.03–1.48	1.00	1.12	0.97–1.30
Paternal psychological symptoms						
Affective symptoms	1.00	1.24**	1.07–1.44	1.00	1.32**	1.10–1.57
Hostility	1.00	1.36**	1.14–1.62	1.00	1.33**	1.10–1.60

Note: The model was based on multinomial logistic regression analysis. The internalizing class and externalizing/emotionally-reactive class are the reference groups against which the odds ratios (OR) are calculated.

*
p<0.05,

**
p<0.01,

***
p<0.001