Empirically Determined, Psychopathological Subtypes in Children With ADHD

Yvonne Zenglein1, Christina Schwenck1, Eva Westerwald1, Catharina Schmidt2, Sonja Beuth1, Jobst Meyer3, Haukur Palmason3, Christiane Seitz4, Susann Hänig4, and Christine M. Freitag1

Abstract

Objective: The aim of this study was to empirically determine subgroups of ADHD defined by specific patterns of psychopathology. Method: A clinical sample of 223 children with ADHD, aged 5 to 14 years, was examined with the Child Behavior Checklist (CBCL). In addition, comorbid psychiatric disorders, psychosocial risk factors, and socioeconomic status were assessed. Results: Cluster analysis of CBCL subscales yielded a solution with four distinct subgroups. While “externalizers” showed a high rate of comorbid oppositional defiant disorder (ODD) and conduct disorder (CD), “obsessive-compulsives” exhibited thought problems, low rates of comorbid CD, and high symptoms of inattention. “High psychiatric symptom carriers” had high rates of familial risk factors, acute life events, comorbid ODD, and CD. “Low psychiatric symptom carriers” also scored low in all other variables studied. Conclusion: Children with ADHD can be divided into four subgroups according to their CBCL-based psychopathology, and these subgroups differ in their risk factor profiles. (J. of Att. Dis. 2013; XX(X) XX-XX)

Keywords
ADHD, subtypes, comorbidity, risk factors

Introduction

In preparation for the new Diagnostic and Statistical Manual of Mental Disorders (5th ed.; DSM-V; American Psychiatric Association [APA], 2013), many attempts have been made to identify subgroups of patients with ADHD according to their psychopathology that differs with regard to associated risk factors. The intent was to better understand the disorder and to be able to treat patients with targeted treatment approaches. Because ADHD is a heterogeneous disorder, homogeneous subgroups according to different psychopathological criteria have been proposed. In accordance with International Classification of Diseases (10th rev.; ICD-10; Dilling, 2008), two categories for hyperkinetic disorders do exist (“attention deficit and hyperactivity disorder” [F90.0] and “hyperkinetic conduct disorder” [F90.1]). In contrast, DSM-IV-TR–based subtypes of ADHD, results are inconsistent, especially regarding psychosocial risk factors. Some researchers found family adversity and low family cohesion being associated with an increased risk of the inattentive type (Pheula, Rohde, & Schmitz, 2011) and severity of inattentive symptoms in ADHD (Freitag et al., 2012). In contrast, others discovered more family dysfunction and histories of physical or sexual abuse in the combined type compared with the inattentive type (Hinshaw, 2002; Lewis, 1992). Psychosocial risk factors have shown a strong influence on overall ADHD severity in some previous studies and three severe classes of ADHD. These classes were not only highly heritable, but also relatively unstable over 5 years time (Rasmussen et al., 2002; Todd et al., 2008; Todd et al., 2001). With respect to associated risk factors of DSM-IV-TR–based subtypes of ADHD, results are inconsistent, especially regarding psychosocial risk factors. Some researchers found family adversity and low family cohesion being associated with an increased risk of the inattentive type (Pheula, Rohde, & Schmitz, 2011) and severity of inattentive symptoms in ADHD (Freitag et al., 2012). In contrast, others discovered more family dysfunction and histories of physical or sexual abuse in the combined type compared with the inattentive type (Hinshaw, 2002; Lewis, 1992). Psychosocial risk factors have shown a strong influence on overall ADHD severity in some previous studies.
Irrespective of the subtypes described in the diagnostic manuals, there has been some research on subgroups of ADHD according to the profiles of comorbidities. Jensen and colleagues (2001) recommended differentiating between patients with ADHD plus anxiety disorders, ADHD plus oppositional defiant disorder or conduct disorder (ODD/CD), and ADHD plus anxiety disorders and ODD/CD, because these subgroups responded differently to treatment in the Multimodal Treatment Study of Children With ADHD (MTA) study. This approach, to differentiate between comorbidity patterns, seems to be particularly interesting for clinicians, because comorbid disorders are also associated with reduced treatment response to stimulants (Chazan et al., 2011). ADHD is a disorder with a high rate of comorbidities, and many children with ADHD show comorbid ODD (50%; Greene, Beszterczez, Katzenstein, Park, & Goring, 2002) and CD (30%; Willcutt, Pennington, Chhabildas, Friedman, & Alexander, 1999), autism spectrum disorders (20%; Ronald, Simonoff, Kuntsi, Asherson, & Plomin, 2008), or internalizing disorders such as anxiety disorders (30%; The MTA Cooperative Group, 1999) and obsessive-compulsive disorder (OCD; 10%; Arnold, Ickowicz, Chen, & Schachar, 2005). Regarding ADHD subtypes, there seems to be a stronger, probably genetically determined association between ODD and especially CD and hyperactivity/impulsivity and therefore the combined type of ADHD compared with the inattentive type (Barkley, DuPaul, & McMurray, 1990; Freitag, Rohde, Lempp, & Romanos, 2010; Gaub & Carlson, 1997). In contrast, studies did not find differences between subtypes concerning rates of comorbid anxiety disorders (Milich et al., 2001; Power, Costigan, Eiraldi, & Leff, 2004). Because comorbid disorders, namely, ODD, CD, and anxiety disorders, as well as parental psychopathology were found to serve as predictors for the persistence of ADHD (Biederman, Petty, Clarke, Lomedico, & Faraone, 2011), comorbid disorders are of high relevance when differentiating between subgroups of ADHD. Psychosocial risk factors, such as familial adversity, violence, and dysfunction, as well as abuse and neglect have been shown to be correlated with comorbidities of ADHD rather than with ADHD itself (Blanz et al., 1991; Deault, 2010; Johnston, 1996). An attenuated cortisol awakening response was observed in children with ADHD compared with control children by one research group (Blomqvist et al., 2007), while others found a lower cortisol awakening response in children with aggressive or oppositional behavior with or without ADHD (Fairchild et al., 2008; Freitag et al., 2009; Yang, Won Shin, Sun Noh, & Stein, 2007). At the same time, an increased cortisol awakening response was detected in patients with anxiety disorders (Vreeburg et al., 2010). Several studies tried to define more homogeneous ADHD subtypes by statistically analyzing psychopathological patterns of children with ADHD. Bauermeister, Alegría, Bird, Rubio-Stipec, and Canino (1992) performed a cluster analysis on 170 participants with and without ADHD using 17 items representing ADHD criteria from DSM-III-R; APA, 1987) that resulted in five clusters (“hyperactive,” “inattentive,” “inattentive-hyperactive,” and “normal,” “highly adapted”). In contrast, Lahey et al. (1988) derived three clusters (“no ADD,” “inattention and hyperactivity,” and “inattention and sluggish tempo”) from a mixed clinical sample based on clinician’s ratings of 20 items consisting of ADHD symptoms. So far no study has aimed at subdividing a clinical sample of children with ADHD using the Child Behavior Checklist for children and adolescents aged 4 to 18 years (CBCL/4-18; Achenbach, 1991; Döpfner, 1998) and thereby using different aspects of psychopathology, such as social problems, anxious-depressed, and aggressive behavior, in addition to attention problems. Because aspects of psychopathology are often signs of comorbid disorders and these disorders influence the treatment of the children, using the CBCL to describe more homogeneous subgroups of ADHD is of strong clinical relevance. Furthermore, it is highly efficient and valuable, as the CBCL is widely known, used, and relatively easy to apply.

For that reason, the aim of the current study was to empirically determine subgroups of ADHD using the parent-rated CBCL and to compare them with the DSM-IV-TR subtypes. To our knowledge, this is the first time that subgroups are empirically determined by statistical methods according to their CBCL profiles. Contrary to assuming certain subgroups hypothetically, this method has the advantage that it prevents a biased analysis. Given that a large number of children show comorbid ODD and CD, we hypothesize that the cluster analysis will show a substantial group of children with delinquent and aggressive behavior. In comparison with former studies that conducted cluster and latent class analysis, we expect to find a group of children with ADHD without further comorbidities. The former attempts of cluster analysis (Bauermeister et al., 1992; Lahey et al., 1988) were based on ADHD symptoms only. In contrast, the CBCL measures different aspects of psychopathology as well as attention problems. A second aim of the study was to compare the cluster groups with the DSM-IV-TR subtypes. Because comorbid disorders, and biological and psychosocial risk factors influence severity and persistence of ADHD symptoms and the outcome of treatment, a third goal of the study was to describe factors associated with the empirically derived subgroups. Comorbid disorders, namely, ODD, CD and anxiety disorders, autistic symptoms, biological and psychosocial risk factors, and the cortisol awakening response were analyzed.
hypotheses in regard to differences in these variables between cluster groups are not formulated, because cluster groups cannot be predicted concisely in advance.

**Method**

**Sample**

The sample comprises 223 children with ADHD aged 5 to 14 years. Children were recruited from the Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy, Goethe-University, Frankfurt, the Department of Neurobehavioral Genetics, University of Trier, Trier, and the Department of Child and Adolescent Psychiatry and Psychotherapy, Saarland University Hospital, Homburg, as part of genetic studies on ADHD. The mean age was 9.7 years ($SD = 1.9$ years) with a range of 5.4 to 14.7 years, and mean IQ was 100.0 ($SD = 12.6$) with a range of 70 to 139. In the sample, 147 children (65.9%) were diagnosed with the combined type of ADHD, 19 (8.5%) with the predominantly hyperactive-impulsive type, and 57 (25.6%) with the predominantly inattentive type. Socioeconomic status (SES) of the parents ranged from lowest (unskilled worker = 1) to highest SES (highly skilled, employment with high income in a leading position = 5) with a mean of 2.74. Data of subsamples of this study have already been published (Freitag et al., 2009, 2012). Ethical approval was obtained from the ethical committee of the Ärztekammer des Saarlandes and the Medical Faculty of the Goethe University Frankfurt am Main.

**Inclusion and Exclusion Criteria**

Children with ADHD according to DSM-IV-TR, combined subtype (314.01), hyperactive-impulsive subtype (314.01), or inattentive subtype (314.00) were included. The following criteria led to study exclusion: birth weight below 2,000 g, IQ below 70, bipolar disorder, schizophrenia, autism spectrum disorder, history of epilepsy, chronic medical or neurological condition, and current medication treatment except for stimulant medication.

**Instruments**

ADHD was diagnosed according to DSM-IV-TR by a structured child psychiatric interview with a parent or primary caregiver (Kinder-DIPS; Schneider, Unnewehr, & Margraf, 1998). The interview Kinder-DIPS was also used to collect data with regard to comorbid psychiatric disorders according to DSM-IV-TR. The retest reliability of the Kinder-DIPS parent version ranges from moderate to perfect agreement ($\kappa = .49$–1.0), and the interrater reliability ranges from substantial to almost perfect agreement ($\kappa = .74$–.96). External validity has been established using the CBCL and other disorder-specific questionnaires (Schneider et al., 1998). In the present study, CD, ODD, and anxiety disorders were analyzed, as these were the most frequent comorbid disorders in this sample. Children diagnosed with CD did not receive a diagnosis of ODD. Anxiety disorders include separation anxiety, social phobia, generalized anxiety disorder, agoraphobia, and panic disorder.

The DCL-ADHS, a German diagnosis checklist for ADHD (Döpfner & Lehmkuhl, 1998), was filled in by a trained clinician, based on information from the Kinder-DIPS and from direct observation of the child. It was used to describe ADHD symptom severity. The child behavior was rated not taking medication effects into account. In the DCL-ADHS, all DSM-IV-TR-derived ADHD symptoms are rated on a Likert-type scale ranging from 0 to 3. The Inattentive subscale is composed of nine items, the Hyperactivity subscale of five items, and the Impulsivity subscale of four items. Item scores were summarized to gain subscale scores. The summary score consists of the scores on the Inattentive, Hyperactivity, and Impulsivity subscales. The summarized subscale scores were used as dependent measures indicating severity of ADHD in three different areas.

Parents completed the German version of CBCL/4-18 (Achenbach, 1991; Döpfner, 1998), a standardized parent rating scale about psychopathological problems of children and adolescents. The questionnaire consists of 113 items concerning behavior problems that are rated on a 3-point Likert-type scale. For the current study, the eight second-order subscales (Withdrawn, Somatic Complaints, Anxious/Depressed, Social Problems, Thought Problems, Attention Problems, Delinquent Behavior, and Aggressive Behavior) were used. All indices are $t$ standardized, and $t$ scores above 70 are considered as clinically relevant (Achenbach, 1991). The evaluation of the CBCL data was based on the German norms. Reliability, and factorial and discriminant validity of the different scales of the German version have been confirmed by German clinical and field samples (Döpfner, Schmeck, Berner, Lehmkuhl, & Poustka, 1994; Schmeck et al., 2001). The $t$ scores of all CBCL subscales served as variables to discriminate subgroups of ADHD in cluster analysis.

To quantify the number of autistic symptoms, parents completed the Fragebogen zur sozialen Kommunikation (FSK; Bölte & Poustka, 2006), the German version of the Social Communication Questionnaire (SCQ; Rutter, Bailey, & Lord, 2003). FSK is a parent-report questionnaire used to screen for autism spectrum disorders in persons aged 4 years or older with 40 dichotomous items. It is based on the Autism Diagnostic Interview—Revised (ADI-R; Lord, Rutter, & Couteur, 1994) and is available in a current and a lifetime version. Summary scores of 15 or above are recommended as cutoffs for autism spectrum disorder (Rutter et al., 2003). Reliability and validity of the SCQ and its
German version FSK have been proved by several studies (Bölte & Postuksa, 2006; Chandler et al., 2007; Rutter et al., 2003). In the present study, the summary score of the lifetime version rated by the mother was used as the dependent measure. Data were available for 168 children.

To assess psychosocial risk factors, a structured interview with the primary caregiver on Axis V of the World Health Organization (WHO) multiaxial classification system (Goor-Lambo, 1987; Postuksa, 1994) was completed. Psychosocial risk factors were evaluated for six periods of children’s lives (1st year, 1-3 years, 4-6 years, 7-9 years, 10-12 years, and the last 6 months) in nine different domains (e.g., abnormal intrafamiliar relationship patterns). These data were aggregated into summary scores of early (20 items) and current (10 items) familial risk factors (abnormal intrafamiliar relationship patterns, distorted communication within the family, parental separation/divorce, or institutional education outside the family), early (6 items) and current (3 items) psychiatric disorders or disability in parent or sibling, current abnormal parenting (7 items), and current acute life events independent of the child (6 items). Early risk factors were assessed for the first 3 years of life, and current risk factors were assessed for the previous 6 months (Freitag et al., 2009). Each item was either rated as present or not, and summary scores were calculated subsequently. Data of psychosocial risk factors were available for 180 children with ADHD.

SES of the family was assigned based on occupational status of both parents. It was rated on a Likert-type scale ranging from 1 to 5 with 1 as lowest and 5 as highest SES. The values of both parents were added and divided by 2 and the result was used as an indicator of the SES of the family. If only one parent was available, the value of this parent was used as an indicator of the SES of the family. In the current study, SES values served as dependent measure. SES was available for 198 participants.

Intelligence was measured by standardized German intelligence tests (Kaufman, Kaufman, & Melchers, 1991; Petermann, 2008; Rossmann, Schallberger, Twes, & Wechsler, 2000; Weiss, 2006). Medical history with pre-, peri-, and postnatal risk factors (including maternal smoking and alcohol use during pregnancy) were assessed using a semistructured interview that had been developed for the current study, and was carried out by the primary caregiver. For further information, see Freitag et al. (2009).

The cortisol awakening response was obtained in a subsample of 98 children on 2 consecutive weekend days. Children collected saliva directly after awakening as well as 30, 45, and 60 min later. Parents who were instructed in detail supervised collection. They filled in a protocol about the collection times. Analysis of the saliva cortisol was done using DELFIA (a time-resolved immunoassay with fluorescence detection). The procedure is explained in detail elsewhere (Dressendorfer, Kirschbaum, Rohde, Stahl, & Strasburger, 1992). The intra- and interassay coefficients of variance were below 6.7% and 9.0%, respectively (Freitag et al., 2009). Mean values of the four measures of both days were used, when available. Missing values of 1 day were replaced by the values of the other day (for details, see Freitag et al., 2009). The mean increase, MnInc = (AC45 + AC60)/3 − AC0, and the area under the curve with reference to zero, AUC = (AC × 30) + ((AC45 − AC0) × 30 / 2) + (AC × 15) + (AC45 − AC0) × 15 / 2) + (AC × 15) + ((AC45 − AC60) × 15 / 2), where AC is awakening cortisol, and index is minutes after awakening, were calculated and used as dependent measures. The AUC predicts the mean cortisol levels over 12 hr and serves as an indicator of relative basal cortisol activity.

**Statistical Analysis**

IBM SPSS Statistics version 19 (IBM SPSS, Chicago, Illinois) was used for statistical analysis. For scale internal consistencies of the CBCL subscales, Cronbach’s α was calculated. Only the Aggressive Behavior subscale showed an acceptable reliability (α = .75). All other subscales of the CBCL had questionable (Complaints: α = .61; Anxious/Depressed: α = .67; Thought Problems: α = .62) to very low reliabilities (Withdrawn: α = .50; Somatic Social Problems: α = .48; Attention Problems: α = .54; Delinquent Behavior: α = .52). This is probably due to the small number of items in most of the subscales. To examine subgroups with different patterns of behavior problems within the ADHD sample, we performed a series of three cluster analyses with the t values of the eight CBCL second-order subscales. The first cluster analysis was a single linkage procedure and was carried out to identify outliers for elimination. Examination of the dendrogram using the elbow criterion showed two spikes. The two indicated participants presented atypical profiles compared with the rest of the sample. Thus, they were excluded from further analysis. Next, a cluster analysis with the Ward method (Blashfield, 1976; Wiedenbeck & Züll, 2010) was conducted using the squared Euclidian distance as the proximity measure. A four cluster solution was determined by the elbow criterion. Finally, the nearest centroid sorting method (Bortz & Schuster, 2010; Scheibler & Schneider, 1985) was used to optimize the cluster solution identified by the Ward method. The cluster centers of the previous analysis served as the starting position for this analysis. A MANOVA with cluster affiliation as an independent variable and CBCL subscales as dependent variables was administered to control the quality of the clustering solution. In addition, discriminant analysis was used to validate the results of the cluster analysis. If 90% to 95% of cases are correctly classified by this analysis, the clustering solution is considered as satisfying (Steinhäuser & Langer, 1977). To check if clusters differed concerning IQ, age, and gender, an ANOVA with cluster affiliation as an independent variable and IQ and age as dependent variables was calculated.
A chi-square test was used to compare clusters regarding gender. Because no between-group differences were found, data sets were collapsed across IQ, age, and gender. Cluster groups then were compared regarding the severity of ADHD symptoms, autistic symptoms, psychosocial risk factors, SES, and cortisol measures. Three MANOVAs and two ANOVAs were conducted with the cluster group as factor and dependent variables of each of the five fields as dependent measures. Post hoc t tests using Bonferroni adjustment were carried out. To compare the four clusters with regard to the frequency of the DSM-IV-TR subtypes and comorbid psychiatric disorders (ODD, CD, and anxiety disorders), chi-square tests were used. Bonferroni procedure was applied to control for multiple testing. Effect size was calculated by partial η² (ANOVA) or Cohen’s φ (χ² tests).

Results

Cluster Analysis

Figure 1 shows the t scores of the CBCL subscales regarding the final cluster solution.

Cluster 1 (n = 77) of the final solution was characterized by high values on the Attention Problems, Delinquent Behavior, and Aggressive Behavior subscales. Furthermore, children assigned to this cluster showed low values on the Thought Problems subscale. This cluster was labeled as externalizers, because it mainly represented aspects of externalizing behavior. Children belonging to the second cluster (n = 54) showed high values regarding attention problems and thought problems. They scored low on the Delinquent Behavior and Aggressive Behavior subscales. Therefore, this group can be summarized with regard to the item content as obsessive-compulsives. Cluster 3 (n = 64) includes participants with t values below 60 in all subscales except for Attention Problems and was labeled as low psychiatric symptom carriers. In contrast, Cluster 4 (n = 26; high psychiatric symptom carriers) was characterized by high values on all subscales, particularly on Social Problems, Attention Problems, and Aggressive Behavior. For these three subscales, the group showed t values above 75. Children in this cluster scored lowest on the Somatic Complaints subscale. Most CBCL data were filled in by mothers and were therefore mainly used for analysis. Thirty children were lacking CBCLs completed by mothers. For these participants, CBCL data completed by fathers were available. A chi-square test showed no differences between cluster groups regarding the distribution of CBCLs completed by fathers. Therefore, these data were included in the further analysis.

A MANOVA with cluster affiliation as an independent factor and CBCL subscales as dependent variables showed significant differences, F(24, 546) = 20.873, p < .001, partial η² = 0.478, between all clusters for the subscales Withdrawn, Anxious/Depressed, Attention Problems, and Aggressive Behavior. Post hoc analysis indicated that the “externalizer” and the “low psychiatric symptom carriers” groups on one hand and the “obsessive-compulsive” and “high psychiatric symptom carriers” groups on the other hand did not differ with regard to somatic complaints and thought problems. We found the “externalizer” and the “obsessive-compulsive” groups to be comparable concerning the Social Problems subscale. The “obsessive-compulsive” and the “low psychiatric symptom carriers” groups scored comparably low on the Delinquent Behavior subscale. Means, standard deviations, and between-group comparisons are demonstrated in Table 1.

A discriminant analysis was computed to confirm the results of the cluster analysis. The first discriminant function explained 72.2% of the variance (p < .001), the second explained 22.7% (p < .001), and the third only 1.0%. Thus, the third discriminant function did not add much further information and showed only a trend for significance (p = .051). Calculation of the averaged discriminant coefficients of the first discriminant function showed the highest scores for the Social Problems (0.47), Anxious/Depressed (0.45), Withdrawn (0.42) and Somatic Complaints (0.16) subscales with the last subscale showing the smallest impact on the distinction between clusters. The second discriminant function was most strongly influenced by the Thought Problems (0.67), Aggressive Behavior (0.53), and Delinquent Behavior (0.48) subscales, and the third discriminant function by the Attention Problems subscale (0.87). Results of the classification according to the discriminant function analysis showed that 96.8% of the children were reclassified correctly.

Characteristics of Cluster Groups

MANOVAs and ANOVAs with cluster affiliation as the independent variable and severity of ADHD symptoms,
Table 1. Comparison of CBCL Subscale t Scores Between Cluster Groups.

<table>
<thead>
<tr>
<th>CBCL subscales</th>
<th>Cluster 1 externalizer (n = 77)</th>
<th>Cluster 2 obsessive-compulsive (n = 54)</th>
<th>Cluster 3 low psychiatric symptom carriers (n = 64)</th>
<th>Cluster 4 high psychiatric symptom carriers (n = 26)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M (SD)</td>
<td>M (SD)</td>
<td>M (SD)</td>
<td>M (SD)</td>
</tr>
<tr>
<td>Withdrawn</td>
<td>58.8 (6.0)</td>
<td>65.2 (7.3)</td>
<td>53.9 (5.2)</td>
<td>72.5 (7.9)</td>
</tr>
<tr>
<td>Somatic Complaints</td>
<td>57.4 (7.7)</td>
<td>62.7 (9.5)</td>
<td>56.5 (7.3)</td>
<td>66.1 (8.7)</td>
</tr>
<tr>
<td>Anxious/Depressed</td>
<td>60.7 (6.9)</td>
<td>64.1 (6.2)</td>
<td>54.3 (5.1)</td>
<td>73.4 (5.5)</td>
</tr>
<tr>
<td>Social Problems</td>
<td>63.7 (6.7)</td>
<td>66.6 (7.8)</td>
<td>54.2 (5.1)</td>
<td>78.2 (7.4)</td>
</tr>
<tr>
<td>Thought Problems</td>
<td>51.7 (3.9)</td>
<td>67.4 (7.7)</td>
<td>53.6 (5.4)</td>
<td>69.2 (9.6)</td>
</tr>
<tr>
<td>Attention Problems</td>
<td>70.4 (6.2)</td>
<td>73.7 (6.1)</td>
<td>61.4 (6.3)</td>
<td>79.0 (6.8)</td>
</tr>
<tr>
<td>Delinquent Behavior</td>
<td>66.8 (6.4)</td>
<td>60.4 (6.4)</td>
<td>57.1 (6.4)</td>
<td>72.6 (6.2)</td>
</tr>
<tr>
<td>Aggressive Behavior</td>
<td>72.2 (7.2)</td>
<td>64.3 (6.3)</td>
<td>59.1 (6.2)</td>
<td>78.5 (9.5)</td>
</tr>
</tbody>
</table>

Note. For post hoc tests, numbers indicate cluster groups. CBCL = Child Behavior Checklist.

Table 2. Psychopathology, Psychosocial Risk Factors, and CAR Measures Between Cluster Groups.

<table>
<thead>
<tr>
<th></th>
<th>Cluster 1 externalizer (n = 77)</th>
<th>Cluster 2 obsessive-compulsive (n = 54)</th>
<th>Cluster 3 low psychiatric symptom carriers (n = 64)</th>
<th>Cluster 4 high psychiatric symptom carriers (n = 26)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M (SD)</td>
<td>M (SD)</td>
<td>M (SD)</td>
<td>M (SD)</td>
</tr>
<tr>
<td>DCL-ADHS inattention (n = 216)</td>
<td>18.5 (4.5)</td>
<td>19.9 (4.1)</td>
<td>17.7 (4.3)</td>
<td>20.1 (3.5)</td>
</tr>
<tr>
<td>DCL-ADHS hyperactivity (n = 216)</td>
<td>9.8 (3.6)</td>
<td>8.8 (4.0)</td>
<td>8.3 (4.4)</td>
<td>9.3 (4.5)</td>
</tr>
<tr>
<td>DCL-ADHS impulsivity (n = 216)</td>
<td>7.9 (2.9)</td>
<td>7.3 (3.6)</td>
<td>7.2 (3.5)</td>
<td>9.0 (2.3)</td>
</tr>
<tr>
<td>FSK (n = 168)</td>
<td>6.9 (4.2)</td>
<td>7.5 (4.9)</td>
<td>6.1 (3.6)</td>
<td>9.0 (4.2)</td>
</tr>
<tr>
<td>Early familial risk factors (n = 180)</td>
<td>3.4 (3.7)</td>
<td>2.4 (3.3)</td>
<td>2.1 (2.8)</td>
<td>6.2 (4.9)</td>
</tr>
<tr>
<td>Current familial risk factors (n = 180)</td>
<td>2.6 (2.1)</td>
<td>2.2 (2.0)</td>
<td>1.6 (2.1)</td>
<td>3.9 (3.0)</td>
</tr>
<tr>
<td>Early psychiatric disorders (n = 180)</td>
<td>0.9 (1.4)</td>
<td>1.1 (1.6)</td>
<td>1.3 (2.1)</td>
<td>1.8 (1.9)</td>
</tr>
<tr>
<td>Current psychiatric disorders (n = 180)</td>
<td>0.5 (0.8)</td>
<td>0.7 (1.1)</td>
<td>0.7 (1.0)</td>
<td>0.7 (0.8)</td>
</tr>
<tr>
<td>Abnormal parenting (n = 180)</td>
<td>0.8 (1.1)</td>
<td>1.1 (1.3)</td>
<td>0.8 (1.2)</td>
<td>1.0 (1.3)</td>
</tr>
<tr>
<td>Acute life events (n = 180)</td>
<td>0.8 (1.0)</td>
<td>0.5 (1.1)</td>
<td>0.6 (1.1)</td>
<td>1.1 (1.6)</td>
</tr>
<tr>
<td>Cortisol awakening response –AUC (n = 98)</td>
<td>491.6 (208.3)</td>
<td>542.4 (249.5)</td>
<td>481.0 (403.3)</td>
<td>578.5 (182.7)</td>
</tr>
<tr>
<td>Cortisol awakening response–mean increase (n = 98)</td>
<td>-0.4 (4.6)</td>
<td>-1.4 (4.1)</td>
<td>-2.0 (3.6)</td>
<td>1.1 (4.1)</td>
</tr>
</tbody>
</table>

Note. Means and standard deviations of measures compared in a MANOVA are given in the upper section and absolute and relative frequencies in subgroups compared in chi-square tests are in the lower section. Effect sizes (partial η²) for MANOVAs and Cohen’s ϕ for chi-square tests were calculated and post hoc comparisons were made. ADHD-I = ADHD predominantly inattentive type; ADHD-HI = ADHD hyperactive, impulsive type; ADHD-C = ADHD combined type; FSK = Fragebogen zur sozialen Kommunikation; MANOVA = multivariate analysis of variance; CBCL = Child Behavior Checklist; ODD = oppositional defiant disorder; CD = conduct disorder; SES = socioeconomic status; AUC = area under the curve.

$F(9, 636) = 2.35, p = .013$, partial $\eta^2 = 0.032$; autistic symptoms, $F(3, 164) = 2.22, p = .088$, partial $\eta^2 = 0.039$; psychosocial risk factors, $F(21, 516) = 1.89, p = .010$, partial $\eta^2 = 0.072$; SES, $F(3, 194) = 1.65, p = .180$, partial $\eta^2 = 0.025$; and cortisol measures, $F(6, 188) = 1.08, p = .378$, partial $\eta^2 = 0.033$, as dependent variables yielded significant differences regarding the severity of inattention in the DCL-ADHS (small effect size) and early and current familial risk factors (medium effect sizes; see Table 2). Post hoc $t$ tests were conducted. We found more early and current familial risk factors in the “high psychiatric symptom carriers” cluster than in all other groups. Participants in the “obsessive-compulsive” group showed significantly more symptoms of inattention than participants in the “low psychiatric symptom carriers” group. Only trends were found regarding acute life events in the post hoc test, with “obsessive-compulsives” scoring lower than “high psychiatric symptom carriers” ($p = .059$). In addition, impulsive behavior...
symptoms were slightly more frequent (trend only, \( p = .080 \)) in “high psychiatric symptom carriers” than in “low psychiatric symptom carriers” and “obsessive-compulsives,” and “low psychiatric symptom carriers” scored lower than “high psychiatric symptom carriers” with regard to autistic symptoms (trend only, \( p = .088 \)). There were no between-group differences regarding early and current psychiatric disorders in the family, current abnormal parenting, SES, cortisol measures, and frequency of maternal alcohol use or smoking during pregnancy. Chi-square tests did not show significant differences between groups regarding ADHD subtypes according to DSM-IV-TR. Groups differed in rates of comorbid ODD (small effect size) with a higher frequency than expected in the “externalizers” and “high psychiatric symptom carriers” groups, and lower rates in children of the “obsessive-compulsive” group. CD was more prevalent in the “externalizers” and the “high psychiatric symptom carriers” groups than in the “obsessive-compulsive” and the “low psychiatric symptom carriers” groups (medium effect size). The between-group difference regarding anxiety disorders resulted from a lower frequency of anxiety disorders in the “low psychiatric symptom carriers” group than in all other groups (small effect size). Details are given in Table 2.

**Discussion**

The aims of the present study were, first, to describe empirically derived homogeneous subgroups in a clinical sample of children with ADHD according to their parent-rated CBCL profiles; second, to contrast the empirically derived subgroups with the DSM-IV-TR subtypes; and third, to compare the subgroups with regard to the severity of ADHD symptoms, comorbid disorders, biological and psychosocial risk factors, and the cortisol awakening response. Cluster analysis resulted in four subgroups, which were labeled as “externalizers,” “obsessive-compulsives,” “low psychiatric symptom carriers,” and “high psychiatric symptom carriers” with regard to their main characteristics.

Comparing CBCL profiles of the subgroups with each other indicated that the “low psychiatric symptom carriers” group consisted of children with “pure” ADHD with only very few psychopathological symptoms or comorbid disorders. These children represent an ADHD subgroup without comorbidities as has also been described by Jensen et al. (2001) in the children participating in the MTA study. This is confirmed by the results of the comparisons between the cluster groups, which showed that the “low psychiatric symptom carriers” group had also lower scores regarding symptoms of inattention, hyperactivity and impulsivity, comorbid ODD, CD and anxiety disorders, and early and current familial risk factors. This group seems to show a high overall functioning in spite of suffering from ADHD. Therefore, as recommended by Jensen et al., this subgroup might respond best to medical treatment and a behavioral treatment might not be necessary.

Contrasting the profile of the “externalizers” group with the other subgroups, the members of this subgroup showed ADHD with comorbid aggressive and/or delinquent behavior and also exhibited social problems. This group is partly consistent with the ADHD + ODD/CD groups proposed by Jensen et al. (2001) from the MTA study, and also reflects the ICD-10 classification of hyperkinetic conduct disorder (F90.1). In accordance with CBCL profiles, children in the “externalizers” subgroup were more likely to show comorbid ODD and CD in diagnostic interview “Kinder-DIPS.” Children in the “externalizers” group were exposed to less early and current familial risk factors compared with the “high psychiatric symptom carriers” group, but did not differ from the other two subgroups. This might be due to genetic risk factors especially influencing children with ADHD + ODD/CD (e.g., Tuvblad, Zheng, Raine, & Baker, 2009), while the “high psychiatric symptom carriers” group might be more strongly influenced by genetic as well as familial risk factors. Findings concerning treatment response in children with ADHD + ODD vary. While children with ADHD + ODD/CD in the MTA study responded well to medication treatment (Jensen et al., 2001), Chazan et al. (2011) found a reduced treatment response in these children. For this reason, a stepwise approach in treating children with ADHD + ODD/CD seems appropriate, taking medical and behavioral treatment into account.

While children in the “obsessive-compulsive” group showed a similar amount of social problems as the “externalizers,” their social problems were more strongly correlated with thought problems than with delinquent or aggressive behavior. These children show ADHD with comorbid obsessive-compulsive symptoms. This group is in accordance with the ADHD + OCD subgroup suggested by Geller et al. (2007) in a family study of children with ADHD with and without OCD matched with controls. “Obsessive-compulsives” were more inattentive than “low psychiatric symptom carriers,” and were less likely to suffer from CD, but not ODD. This corresponds with a subgroup of children with OCD and ADHD, described by Masi et al. (2006). “Obsessive-compulsives” also showed less familial risk factors and acute life events than “high psychiatric symptom carriers.” Higher scores of inattention in the “obsessive-compulsive” subgroup may be due to attentional deficits caused by obsessions (Abramovitch, Dar, Hermesh, & Schweiger, 2012; de Geus, Denys, Stiksrorn, & Westenberg, 2007). Less familial risk factors and acute life events compared with the “high psychiatric symptom carriers” subgroup can be explained by a high heritability of ADHD and OCD (Geller et al., 2007) and therefore a smaller impact of environmental risk factors than in “high psychiatric symptom carriers.” As children with OCD plus ADHD have a worse outcome when treated with serotonergic agents alone (Masi et al., 2006), screening children.
with the CBCL could improve the treatment outcome. Because therapy with serotonergic agents and psychostimulants are the best pharmacological treatments for OCD and ADHD, a combined medical treatment supported by a behavior therapy might be helpful.

The smallest group, the so-called “high psychiatric symptom carriers,” exhibited a high amount of psychopathological symptoms in nearly all second-order subscales of the CBCL. These children are the most impaired participants with high scores of attention problems, aggressive behavior, and social problems. In addition to the highest scores on the externalizing behavior scales, they also showed the highest scores of internalizing behavior of the whole sample at the same time, with the $t$ score on all CBCL subscale means above 70, except the Somatic Complaints subscale. In addition, a trend for the highest autistic symptoms compared with the other three clusters was observed in this group, which likely did not become fully significant because of the small sample size of the “high psychiatric symptom carriers” group. These children also displayed more often comorbid ODD and CD and early and current familial risk factors compared with other groups. The latter indicate that combined severe externalizing and internalizing behavior in children with ADHD are strongly related to early and chronic ongoing familial risk factors. Our findings are in line with previous studies that found a stronger correlation between psychosocial risk factors and comorbidities of ADHD compared with ADHD alone (Blanz et al., 1991; Deault, 2010; Johnston, 1996). Children showing the highest psychopathology partly consist of the ADHD + anxiety disorders + ODD/CD group proposed by Jensen et al. (2001) from the MTA study. Because this group responded best to a combined treatment and also because of the high amount of psychosocial risk factors, a regimen combining medical and behavioral treatment seems to be inevitable. As externalizing behavior is often more apparent, screening children with the CBCL and particularly taking internalizing behavior into account is reasonable. This could avoid a reduced treatment response caused by overseen internalizing problems.

Several aspects confirm the meaning and the benefit of the found cluster groups: Compared with the established literature, they seem to be valid and have all been found in former samples of children with ADHD. The prevalence of the subgroups in this clinical sample reflects the prevalence of comorbid disorders in ADHD in general, with the externalizing behavior problems being the most common (Greene et al., 2002), internalizing behavior problems being found in about one third of the children (The MTA Cooperative Group, 1999), and a considerably smaller group of children showing a mixture of both. About one third of the children belonged to the “low psychiatric symptom carriers” cluster with only few comorbid disorders. The found cluster groups also differ regarding familial risk factors that may influence treatment, as they may influence the resources of the family in using treatment offers. It seems possible to deduce diagnostic and treatment recommendations for the cluster groups that might outrun the classifications in the DSM-IV-TR and the ICD-10, because they are more specific and therefore might promise a better treatment outcome. This makes them particularly valuable for clinicians. They may also outreach the former attempts of cluster and latent class analysis, because they take several aspects of psychopathology into account. Three of the cluster groups are quite similar to the groups based on comorbidity patterns proposed by Jensen et al. (2001), but a fourth group (“obsessive-compulsives”) is added, that completes the range of psychopathology most frequently found in children with ADHD.

The second aim of the present study was to evaluate the accordance of the determined subgroups with the DSM-IV-TR derived subtypes of ADHD. The prevalence of the different subtypes in our study is similar to that in other clinical samples (Greene et al., 2002; Lahey et al., 2005), with ADHD-C as the most frequent diagnosis. The empirically derived CBCL-based subgroups did not correspond to a specific pattern of DSM-IV-TR subtypes. This likely resulted from the content of the CBCL, which is mainly a screening instrument for various psychopathological problems in addition to some symptoms of ADHD, and which does not differentiate inattentive and hyperactive/impulsive symptoms. Due to the relatively small frequency of the inattentive and the hyperactive-impulsive type, we also may not have picked up expected DSM-IV-TR subtype differences with regard to the two CBCL-derived clusters with increased rates of ODD/CD. Previous studies regularly observed a higher frequency of the combined and hyperactive-impulsive type in children with ADHD and ODD/CD, with less frequent inattentive type (Barkley et al., 1990; Gaub & Carlson, 1997). However, the cluster groups are partly in accordance with the classification of the ICD-10, where the two categories “attention deficit and hyperactivity disorder” and “hyperkinetic conduct disorder” do exist. The cluster groups “externalizers” and “low psychiatric symptom carriers” do reflect these two categories.

No differences between subgroups were found regarding the severity of hyperactivity or impulsivity, psychiatric disorders in the family, abnormal parenting, SES, cortisol measures, and maternal alcohol use or smoking during pregnancy. The missing difference regarding the severity of hyperactivity or impulsivity could be either due to the small sample size of single clusters, because the smallest “high psychiatric symptom carriers” group showed more severe symptoms of impulsivity descriptively, and this difference nearly approaches significance ($p = .08$). Another explanation is the high prevalence of children with the combined type in this sample and therefore a relatively equally distributed amount of hyperactive and impulsive symptoms.
Possibly due to selection effects, SES did not vary much throughout the sample; thus, power was low to detect differences between cluster groups. Current abnormal parenting as well as smoking during pregnancy may be more specifically related to comorbid CD (Freitag et al., 2012) than to the CBCL-derived ADHD subtypes of the present study. We were also not able to replicate prior research results regarding the cortisol awakening response (Freitag et al., 2009; Vreeburg et al., 2010; Yang et al., 2007), though the subgroups differed concerning externalizing behavior. This might be due to the fact that children with ADHD + ODD and ADHD + CD were overrepresented in two subgroups, namely, the “high psychiatric symptom carriers” and the “externaliser” subgroup, which reduces the likelihood to observe subgroup differences based on comorbid ODD or CD respective aggressive behavior, which was also equally high in both CBCL-derived clusters.

Limitations of this study include the limited number of items in the CBCL and in parts of the Axis V interview, leading to low internal consistencies. Furthermore, parts of the Axis V interview are retrospective, which may have led to recall bias. The detailedAxis V interview still was chosen for the study as it is a structured interview assessing a large and differential number of psychosocial risk factors during different ages of the child, which is a quality of the study. Another limitation is that 30 children were lacking CBCLs completed by mothers. For these participants, CBCL data completed by fathers were available. As the number of CBCLs filled by the fathers did not differ between cluster groups, it is unlikely that the different raters may have influenced study results. Another limitation of the study represents the diverging sizes of the data sets of the dependent measures. This is especially true of the cortisol measures as they were only available for a subsample of 98 children out of 223 of the whole sample. Thus, power was only around 20% to detect the small, and around 40% to detect the medium effect sizes, which were observed for different cortisol awakening response measures in our study. Furthermore, the current study exclusively investigated a sample of children with ADHD, while past studies on the cortisol awakening response examined mixed samples with and without ADHD.

A clear strength of this study is the thorough diagnostic workup of the children with ADHD and comorbid disorders by using a structured child psychiatric interview as this increases the accuracy of the diagnoses.

In conclusion, the results of the current study suggest the existence of four CBCL-derived subgroups of ADHD, which can be identified by specific profiles of co-occurring behavior problems. These subgroups differ mainly regarding the amount of externalizing behavior problems and obsessive-compulsive symptoms, which were related to specific comorbid disorders pattern, as well as the amount and severity of psychopathological symptoms in general. In addition, as subgroups differed regarding familial risk factors, our findings may have implications for prevention and targeted treatment especially of the children with ADHD with high comorbid psychiatric symptoms. The results of this study should be replicated in another sample of children with ADHD to validate the observed clusters and subgroups.

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References


**Author Biographies**

**Yvonne Zenglein**, MA, is a PhD student and clinical assistant in the Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy, Goethe University, Frankfurt am Main. Her research interests include subtypes of ADHD and differences regarding comorbidities and risk factors between them.

**Christina Schwenck**, PhD, is a post doc in the Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy, Goethe University, Frankfurt am Main. Her research interests are social cognition, neuropsychology and psychopathology of ADHD, Autism, and Conduct Disorder.

**Eva Westerwald**, MA, is a PhD student and clinical assistant in the Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy, Goethe University, Frankfurt am Main. Her research interests is the differential diagnosis and neuropsychology of ADHD and Autism Spectrum Disorders.

**Catharina Schmidt**, MD, is a clinical assistant in the Department of Psychiatry and Psychotherapy, University of Mainz. Her research interest is on the neuropsychology of ADHD.

**Sonja Beuth**, MA, is a clinical assistant in the Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy, Goethe University, Frankfurt am Main. Her research interests is the differential diagnosis and neuropsychology of ADHD and Autism Spectrum Disorders.

**Jobst Meyer**, PhD, is head of the Department of Neurobehavioral Genetics at the University of Trier, Germany. His research interests comprise gene regulation, stress research and monogenous forms of psychiatric disorders.

**Haukur Palmason** is a PhD from the University of Trier, Department of Neurobehavioral Genetics. He is currently working as a neuropsychologist at the Department of Child and Adolescent Psychiatry, in the National Hospital of Iceland. His research interests is the neuropsychology of ADHD and Autism Spectrum Disorders.

At the time of the study, **Christiane Seitz**, MD, was an MD student and clinical research worker in the Department of Child and Adolescent Psychiatry, Saarland University Hospital, Homburg, Germany. Her research interest is on cortisol measures in ADHD and comorbid disorders.

**Susann Hänig**, MA, is a PhD student and clinical research worker in the Department of Child and Adolescent Psychiatry and Psychotherapy, Saarland University Hospital, Homburg, Germany. Her research interest is on the psychopathology and neuropsychology of ADHD.

**Christine Freitag**, MD, MA is the director of the Department of Child and Adolescent Psychiatry and Psychotherapy, Goethe University, Frankfurt am Main, and Chair and Professor of Child and Adolescent Psychiatry and Psychotherapy. Her main research areas are genetics, psychopathology, differential diagnosis, and therapy of ADHD and Autism Spectrum Disorders.