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ORIGINAL CONTRIBUTION

Subgrouping children and adolescents with disruptive behaviors: symptom profiles and the role of callous–unemotional traits

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Abstract

Disruptive behavior during childhood and adolescence is heterogeneous and associated with several psychiatric disorders. The identification of more homogeneous subgroups might help identify different underlying pathways and tailor treatment strategies. Children and adolescents (aged 8–18) with disruptive behaviors ($N=121$) and healthy controls ($N=100$) were included in a European multi-center cognition and brain imaging study. They were assessed via a battery of standardized semi-structured interviews and questionnaires. *K*-means cluster-model analysis was carried out to identify subgroups within the group with disruptive behaviors, based on clinical symptom profiles, callous–unemotional (CU) traits, and proactive and reactive aggression. The resulting subgroups were then compared to healthy controls with regard to these clinical variables. Three distinct subgroups were found within the group with disruptive behaviors. The High CU Traits subgroup presented elevated scores for CU traits, proactive aggression and conduct disorder (CD) symptoms, as well as a higher proportion of comorbidities (CD + oppositional defiant disorder + attention deficit hyperactivity disorder (ADHD). The ADHD and Affective Dysregulation subgroup showed elevated scores for internalizing and ADHD symptoms, as well as a higher proportion of females. The Low Severity subgroup had relatively low levels of psychopathology and aggressive behavior compared to the other two subgroups. The High CU Traits subgroup displayed more antisocial behaviors than the Low Severity subgroup, but did not differ when compared to the ADHD and Affective Dysregulation subgroup. All three subgroups differed significantly from the healthy controls in all the variables analyzed. The present study extends previous findings on subgrouping children and adolescents with disruptive behaviors using a multidimensional approach and describes levels of anxiety, affective problems, ADHD, proactive aggression and CU traits as key factors that differentiate conclusively between subgroups.

Keywords Callous–unemotional traits · Oppositional defiant disorder · Conduct disorder · Aggression · Psychopathology · Subtyping

Introduction

Disruptive behavior is extremely complex and its diagnosis usually requires the application of categorical criteria. This approach, as we now know, does not accurately reflect the complexity of its etiology. We must ask ourselves to what extent children and adolescents with disruptive behavior can be distinguished. Despite extensive research, there is still an insufficient understanding of these behavioral disorders and, above all, a lack of appropriate individualized treatments. Over the past decades, numerous groups of researchers have attempted to decipher distinctive etiological relationships

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and changes over the life span, given that considerable impairments can also persist in the later lives of individuals with disruptive behavior [1–4].

Overall, the percentage of children and adolescents with externalizing behaviour problems ranges from 3.6% (boys) and 1.5% (girls) [5] up to 6.1% (both sexes) [6], and these features are the most frequent reason for referral of children and adolescents (or youth) to mental health services [7, 8]. According to the current diagnostic categories, most of these children and adolescents are classified as suffering from [9] oppositional defiant disorder (ODD) and conduct disorder (CD). Nevertheless, individuals who exhibit disruptive behaviors display a wide heterogeneity concerning the type and level of maladaptive behaviors and/or aggression, developmental trajectories and treatment response, as well as with regard to social, emotional, and cognitive functioning [10]. Subtyping can be used to identify differences within a largely uniform behavior [11, 12]. Many different approaches have been used to describe different groups of individuals with disruptive behaviors, but there is a lack of multidimensional models to describe this heterogeneous population [e.g. [13]. To date, there is still no clear consensus on the existing subtypes after taking into account a multidimensional range of symptoms that can affect this heterogeneity. Studies have focused mainly on three different subtyping approaches.

One of the most commonly used approaches have focused on the presence of callous–unemotional traits (CU; low guilt and empathy, shallow affect) to define a severe psychopathic-like patient subgroup [1, 14–16]. In this context, after extensive research [see [2, 17, 18], the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) added a specifier to the CD criteria, "With limited prosocial emotions", covering high levels of CU traits, based on evidence indicating that these characteristics define a particularly malignant form of antisocial behavior [9, 15, 19]. Previous studies have found that children and adolescents with CU traits show higher levels of behavioral disinhibition, more severe conduct problems, difficulties in processing punishment cues, reduced psycho-physiological reactivity to emotional and threatening stimuli, and low levels of fear and anxiety [10, 20–22]. Although there is a large number of studies in this field, more investigations are required that combine CU traits with other clinical characteristics to study their relationships and, thus, have a broader understanding of their contribution to this type of disorders.

Another subtyping approach has involved distinguishing between the types of aggression, focusing on the proactive and reactive forms of this behavior. Reactive aggression is defined as uncontrolled, emotional, and fear-induced, and it involves a lack of inhibitory functions, reduced self-control, and increased impulsivity; in contrast, proactive aggression is planned, goal-directed, and "cold-blooded", with little evidence of autonomic arousal [17–19]. However, this dichotomy is not entirely clear [20–22], as some studies have shown that the correlation between these two types of aggression is high, and that those who display proactive aggression most frequently also show reactive aggression [23, 24]. The majority of subtyping studies have identified a subgroup of individuals only displaying reactive aggression and a subgroup with individuals showing both reactive and proactive aggression [23–26]. The display of both reactive and proactive aggression has been linked to increased impulsivity and CU traits [24, 25] and more CD symptoms and antisocial behaviors [26]; whereas the presence of only reactive aggression seems to be associated with more internalizing and attention deficits and hyperactivity disorder (ADHD) problems [23]. Thus, the display of only proactive aggression is rare [27, 28]. Here again, a deeper understanding of these categories and their relationship with other significant variables of aggression is needed to determine their contributions and meaningfulness when studying the heterogeneity of this population.

Another one of the three main subtyping approaches used has focused on co-occurring psychopathological symptoms. Clinical symptoms overlap between disorders [29] and comorbidity rates are high, especially within diagnostic families [30, 31]. Generally, ODD and CD are especially strongly associated with externalizing disorders (such as ADHD) as well as with internalizing disorders such as anxiety and mood disorders [9, 32–34]. The presence of anxiety symptoms alongside disruptive and aggressive behavior has been relatively well studied [35–39], with some consensus on the existence of distinct variants of psychopathy based on the presence of anxiety symptoms. Despite some differences, most studies agree on the existence of two distinct subgroups of individuals with high levels of CU traits and either low (primary variant) or high (secondary variant) anxiety who differ in their levels of psychopathology, personality traits, severity of behavioral problems and gender [13, 16, 40–48]. Comorbid ADHD symptoms have been studied much less in subtyping investigations. Children and adolescents with co-occurring ODD/CD and ADHD symptoms show more severe aggressive and disruptive behaviors [49]. Impulsivity has been associated with the presence of both CU traits and anxiety in disruptive youths [44], the display of both reactive and proactive aggressive behavior [24, 50] as well as with the presence of high levels of CU traits [51–53]. Regarding attention problems, it has been found that children who display reactive aggression may suffer from more attention difficulties than those who show mixed forms of aggression [25]. Specifically, more ADHD diagnoses were found within the subgroup showing high levels of CU traits and increased anxiety in a representative community sample [40]. In conclusion, we

cannot overlook the presence and the role of other comorbid clinical symptoms in the heterogeneity of individuals with disruptive behaviors.

Previous research on the heterogeneity of disruptive and aggressive behaviors has still some limitations. A large number of the studies using cluster analysis to assess disruptive individuals have focused more on boys [26, 43–45, 54–56], with fewer studies involving mixed gender samples [13, 23, 24, 41, 42, 53]. Research has shown that there are important gender differences. Girls with disruptive behaviors have higher levels of anxiety and affective symptoms, and lower scores of CU traits than boys [13, 42, 57–59] but those with high CU traits, display more severe behavioral problems, and aggressive behaviors [24]. Another important limitation in previous research is the small proportion of studies including or focusing on children, as the majority of subtyping research has studied adolescents and youths [25]. Finally, several studies have mainly used simpler cluster models based on single characteristics, with few studies combining these different aspects to develop more complex models [13, 60]. Multidimensional approaches taking into account a broader perspective on the heterogeneity of this population could help move this research field forward and also improve diagnostics and treatment. Therefore, more studies using mixed gender samples and both children and adolescents are greatly needed in the subtyping of this heterogeneous population.

The aims of the present study were: first, using clustering analysis, to subgroup a sample of both male and female European children and adolescents referred for disruptive and aggressive behaviors, taking into account a multidimensional approach including ODD/CD symptoms, CU traits, reactive/proactive types of aggression and comorbid clinical symptoms such as depression, anxiety and ADHD symptoms; and, second, to compare the resulting subgroups between them for descriptive purposes and with a healthy control group.

We hypothesized that we would find three distinct subgroups based on the severity of the ODD/CD symptoms and the presence of CU traits and anxiety. We expected that those with more severe ODD/CD symptoms would also display more ADHD symptoms, both proactive and reactive aggression and more severe antisocial behavior. We also expected to find gender differences across the distinct subgroups. Finally, we hypothesized that all three subgroups would be clinically different from the control group.

Methods

Participants

Two hundred and eighty-three participants aged 8–18 years were recruited across nine sites in Europe (see Supplemental Material for details) and took part in the European MATRICS and Aggressotype projects, which included clinical and neuropsychological assessments, and neuroimaging. One hundred and eighty-three children and adolescents had been clinically referred due to disruptive behaviors and were included as "cases". All of them either had diagnoses of CD and/or ODD, and/or revealed high aggression and disruptive behavior levels determined by means of the instruments used. A high aggression and disruptive behavior level was defined as aggression and/or rule-breaking behavior scores above the clinical range ($T > 70$) in one of the following: the Child Behavior Checklist (CBCL), Youth Self Report (YSR) and/or Teacher Report Form (TRF) [61]. Medication was at a stable dose for at least two weeks prior to assessment. Participants were excluded if they had missing or incomplete data on the clustering variables (34% of the cases group; $n = 62$) (a comparison between included and excluded participants is shown in Supplemental Material). This yielded a final sample of 121 cases. Healthy controls ($n = 100$) were recruited from external institutions such as schools in the same geographical areas. No DSM-psychiatric disorders or scores within the clinical ranges (tested by the Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS) psychiatric interview, and CBCL, YSR and TRF scores) were accepted in this group. An intelligence quotient (IQ) < 80 was an exclusion criterion for all participants in both groups. Ethical approval for the study was obtained from the local ethics committees for each site separately. Written informed consent was given by the participants and their parents or legal representatives.

Measures

Kiddie schedule for affective disorders and schizophrenia (K-SADS)

Symptoms corresponding to the diagnoses of ODD, CD, and/or ADHD were confirmed using the semi-structured interview K-SADS [62]. This instrument assesses psychiatric disorders in children and adolescents according to DSM-IV criteria and is based on information from participants and their parents/caregivers. Screening and disorder-specific modules were administered for CD, ODD, and ADHD. Screening modules were administered to assess the possible presence of other psychiatric diagnoses. Inter-rater reliability (kappa coefficient, 0.855) for all the sites involved in the project showed good reliability.

Child behavior checklist (CBCL)

The CBCL [61] was administered to the parents or caregivers of all participants. This frequently used clinical questionnaire has robust test–retest reliability [63] and assesses

behavioral symptoms, including aggressive and rule-breaking behaviors, mood and anxiety symptoms, and attention problems. It consists of 120 items rated 0–3 on a Likert-type scale. Internal consistency in this sample was excellent ($\alpha = 0.97$).

The SNAP Rating Scale for the diagnosis of the attention-deficit disorder (SNAP-IV-ADHD)

The SNAP rating scale [64] was administered to assess the presence of ADHD symptoms. Parents answered 18 questions concerning inattention, impulsivity, and hyperactivity symptoms (9 for inattention, 9 for hyperactivity/impulsivity). Items were rated on a 4-point scale from 0 (not at all) to 3 (very much). Internal consistency in this sample was excellent ($\alpha = 0.96$).

Inventory of callous–unemotional traits (ICU)

The ICU [14] parent-report version was used to assess CU traits. The ICU includes 24 items (with 4-points scale) on three different subscales: "callousness", which attempts to measure the lack of empathy, guilt, and remorse for misdeeds; "uncaring", which indicates the lack of caring about their performance in tasks and for the feelings of other people; and "unemotional", which reflects the difficulties in sharing emotions or openly expressing feelings. Internal consistency in this sample was excellent ($\alpha = 0.91$).

Reactive–Proactive Questionnaire (RPQ)

The RPQ [65] was used to measure proactive and reactive aggressive behavior. The questionnaire consists of 23 self-report items (3-points scale) distributed between two different subscales: an 11-item subscale collects data on reactive aggression (aggression as a reaction to provocation by others), and a 12-item subscale obtains information on proactive aggression (aggression displayed to get something). This questionnaire showed high internal consistency [66] and internal consistency in this sample was excellent ($\alpha = 0.92$).

Antisocial behavior scale (ABS)

The ABS is an adaptation of the Observed Antisocial Behavior questionnaire (OAB: Vragenlijst Waargenomen AntiSociaal gedrag) [67], which was applied as a child self-report to investigate antisocial behavior. The scores are based on the following subscales: stealing, property damage, violence, substance use, and other antisocial behaviors. Internal consistency in this sample was good ($\alpha = 0.88$).

Wechsler Intelligence Scale for Children-V (WISC-V)/ Wechsler Adult Intelligence Scale-IV (WAIS-IV)

IQ was assessed by the General Ability Index, which was estimated using four subtests (vocabulary, similarities, block design, and matrix reasoning or picture completion) of the WISC-IV [68] for those below 17 years old, or the WAIS-IV [69] for those older than 17 years old. This composite ability score minimizes the impact of tasks involving working memory and processing speed and is recommended for estimating the IQ in populations in whom working memory may be affected (for example, in disruptive disorders) [as suggested in [70].

Statistical analysis

Differences between groups

Demographic and clinical characteristics of the cases and control groups were described as mean and standard deviations for continuous variables and percentages for categorical variables. Student t and chi-square tests were used to compare them between groups.

Identifying subgroups

To address the first aim of our study, we performed a cluster analysis using the K-means algorithm to identify distinct subgroups in our sample of children and adolescents with disruptive and aggressive behaviors. The K-means algorithm is a well-known and tested method that has been used before in other studies in this field [24, 26, 71, 72]. This clustering method aims to partition the data into different clusters and assigns each individual to a single group. The algorithm tests a set of centroids (representing the centers of the clusters), while minimizing the within-cluster squared Euclidean distances from each point, that is, to allot points to the cluster where the distance from the centroid is minimal (for more details on the K-means method, see [73, 74]). Since K-means clustering depends on a previous number of clusters set by the user, we used two different methods to ensure selection of the optimal number of clusters explaining our data: the elbow method and the Bayesian information criterion (BIC). These two techniques are the most popular approaches for selecting the number of groups analytically. The elbow method is the most common approach used in the K-means cluster analysis. It runs the algorithm multiple times over a loop, calculating the total within-cluster sum of squares (WSS), while the best-fitting number of clusters is chosen by the point after which the distortion/inertia starts decreasing

in a linear fashion [75]. The BIC is a less ambiguous formula that subtracts two terms that balances model complexity and model fitting, with the value closest to zero representing the best-fitting model [76, 77]. This method has been widely used in a large number of studies in the field [23, 48, 55]. Principal component analysis was used to project the individuals and variables onto a biplot graph (Figure S3 in Supplemental Material).

The variables (normalized into z-scores) introduced in the cluster analysis were: (a) CU traits: the three subscales of the ICU questionnaire (Callousness, Unemotional and Uncaring); (b) type of aggression: both subscales of the RPQ questionnaire (Proactive and Reactive); (c) the symptoms and severity of the disruptive behaviors: the ODD and CD symptoms subscales of the CBCL questionnaire; (d) affective symptoms: the Affective Problems, Anxiety Problems and Somatic Problems subscales of the CBCL questionnaire; and (e) ADHD symptoms: the Impulsivity-Hyperactivity and Inattention subscales of the SNAP-IV questionnaire. We also used IQ as a variable because a few studies have found differences in the IQ level in patients with CU traits [24, 78, 79]. Age was also added because of the wide age range in our sample (8–18). (Those variables included in the cluster analysis are highlighted in Table 2 with an asterisk and the correlation between the variables used can be found in the Supplemental Material Figure S2).

Outcome analyses

To address the second aim of our study, we conducted univariate analysis of covariance (ANCOVA) and chi-square analyses to describe the main characteristics of the subgroups derived with the cluster variables followed by post-hoc Bonferroni corrected comparisons. In addition, ANCOVAs and chi-square tests were conducted on other external non-clustering variables: gender, antisocial behaviors (ABS questionnaire), type of K-SADS diagnoses and other CBCL subscales not included in the cluster analysis (the Aggressive and Rule-Breaking Behavior subscales, the Externalizing, Internalizing and Total Problems subscales, and the Total subscales of the ICU, RPQ and SNAP-IV). Age and sex were introduced as covariates in the analyses. All analyses were performed using SPSS 23 [80] and R program 3.5.1 [81]. The results are reported at a statistical threshold of $p < 0.05$.

Additional analysis of the specific effects of the age group (children and adolescents) and specific analysis of a sample containing only boys ($n = 100$) are shown in the Supplemental Material.

Results

Characteristics of cases and controls

Table 1 shows the sociodemographic and clinical characteristics of the sample. Cases and controls differed in age and sex, with the control group being older and including more girls than the cases. The groups also differed in IQ, with cases revealing lower scores than controls. Of all cases, 80 (66%) were assigned to ODD, 43 (36%) CD, and 36 (30%) ADHD. Additionally, 54 (45%) suffered from a comorbid condition: 22 (18%) of the participants had both CD and ODD, 2 (2%) had CD and ADHD, and 18 (15%) had ODD and ADHD. Twelve (10%) had all three diagnoses (ODD, CD and ADHD) and 28 (23%) of the cases did not meet the diagnostic criteria for any of the disorders assessed. Information about medication use is shown in Table 1.

Clusters solution

The correlations map showed low to moderate associations between cluster variables (for more details, see Supplemental Material Figure S-2).The elbow method showed a substantial jump from the 1 (WSS = 4391) to the 2 (3322) clusters solution, with a modest gain between the 2 and 3 (2884) clusters solutions that became smaller (below 300) from 4 clusters (2610) and onwards. The BIC identified three clusters (BIC = 2354) as the best solution that minimized the BIC score, with the 2 (2362) and 4 (2363) clusters solutions as the next best-fitting models (See elbow and BIC graphs in Supplemental Material Figure S-1). Based on these findings and taking into account the clinical interpretation, we concluded that the 3 clusters solution was the best-fitting model for our data. A map of the variables and individual factors is presented dimensionally in the Supplemental Material (Figure S3).

Description of the clusters and comparison with controls

Table 2 and Fig. 1 comprise the ANCOVA and chi-square tests to compare the demographic characteristics, cluster variables and non-clustering variables of the 3 resultant cluster subgroups and controls group. All the analyses were controlled for age and sex.

Subgroup 1: the High CU Traits subgroup

We labeled the first subgroup "High CU Traits". This subgroup represented 32% ($n = 39$) of the cases and included the highest proportion of males (90%), significantly more than subgroup 2 (60%). It was characterized by higher scores than

Table 1 Demographics and characteristics by group

	Cases group	Control group	t/x^2	p
N 221	121	100		
Sex (m:f) (more males)	100:21	59:41	15.17	< .001
	Mean (SD)	Mean (SD)		
Age	12.5 (2.7)	13.5 (2.6)	− 2.93	.004
IQ	100.3 (11.1)	107.2 (10.6)	− 4.68	< .001
CBCL				
Rule breaking—T score	67.3 (7.8)	52.3 (3.8)	18.61	< .001
Aggression—T score	74.2 (11.1)	52.2 (3.9)	20.22	< .001
Affective	6.8 (4.1)	1.5 (2.5)	11.76	< .001
Anxiety	3.5 (2.4)	1.1 (1.6)	8.99	< .001
Somatic	2.4 (2.5)	0.9 (1.2)	6.06	< .001
ADHD	9.1 (2.8)	1.8 (2.1)	22.24	< .001
ODD	7.4 (1.9)	1.6 (1.9)	22.66	< .001
CD	11.2 (5.2)	1.1 (1.8)	20	< .001
Externalizing behaviour	28.7 (9.8)	4.3 (4.9)	24.06	< .001
Internalizing behaviour	15.7 (9)	4.8 (5.7)	10.91	< .001
Total CBCL	74.4 (25)	14.4 (13.8)	22.51	< .001
ICU				< .001
Callousness	12.2 (5.7)	4 (3.4)	13.11	< .001
Uncaring	16.5 (4.2)	10.1 (5)	10.25	< .001
Unemotional	7 (3.2)	5.2 (2.8)	4.4	< .001
Total ICU	35.6 (10.2)	19.5 (8.5)	12.29	< .001
SNAP-IV				< .001
Inattention	15.5 (6.2)	3.6 (4)	16.89	< .001
Hyperactivity-impulsivity	13.3 (6.3)	1.9 (2.7)	17.85	< .001
Total ADHD	31.3 (12.3)	5.8 (6.5)	19.56	< .001
RPQ				< .001
Reactive	12 (4.8)	5.7 (3.3)	11.54	< .001
Proactive	3.9 (4.1)	0.8 (1.3)	7.99	< .001
Total RPQ	15.9 (7.9)	6.4 (4.2)	11.41	< .001
ABS				< .001
Stealing	1.3 (1.6)	0.4 (0.9)	5.21	< .001
Violence	3.7 (2.2)	1 (1)	11.86	< .001
Damage	1.5 (1.8)	0.3 (0.6)	6.97	< .001
Subs use	1.2 (1.5)	0.8 (1.2)	2.15	.033
Other antisocial behaviour	2.1 (1.8)	0.7 (1.1)	7.31	< .001
Total ABS	9.9 (6.7)	3.1 (3.1)	9.64	< .001
	N (%)			
ODD	80 (66%)	–		
CD	43 (36%)	–		
ADHD	36 (30%)	–		
None	28 (23%)	–		
Comorbidity	54 (45%)	–		
ODD + CD	22 (18%)	–		
ODD + ADHD	18 (15%)	–		
CD + ADHD	2 (2%)	–		
ODD + CD + ADHD	12 (10%)	–		
Medication	63 (52%)	–		
Stimulants	55 (46%)	–		
Antipsychotics	20 (17%)	–		
Antidepressants	1 (1%)	–		
Others	10 (8%)	–		

Table 1 (continued)

IQ: intelligence quotient; CBCL: Child Behavior Checklist; ADHD: attention-deficit/hyperactivity disorder; ODD: oppositional defiant disorder; CD: conduct disorder; ICU: Inventory of Callous–Unemotional Traits; SNAP-IV: ADHD rating scale; RPQ: Reactive Proactive Aggression Questionnaire. ABS: Antisocial Behavior Scale

the other two subgroups on the Total, Uncaring and Unemotional subscales of the ICU, the Proactive subscale and Total scale of the RPQ, and more CD symptoms measured by the CBCL. Furthermore, the members of this group displayed more aggressive and rule-breaking behaviors based on the CBCL, ODD symptoms, and externalizing problems than subgroup 3; however, they did not differ from subgroup 2 in this respect. This subgroup similarly showed more attention and hyperactivity–impulsivity problems than subgroup 3, but fewer problems of this kind than subgroup 2. Regarding the ABS, more antisocial behaviors were found in this subgroup than in subgroup 3, but did not show significant differences with respect subgroup 2. No differences were found regarding the presence of ODD, CD, or ADHD and use of medication, except for the presence of comorbid ODD + CD + ADHD, which was significantly more frequent within subgroup 1 than subgroup 3.

Subgroup 2: the ADHD and Affective Dysregulation subgroup

The second subgroup, labeled the ADHD and Affective Dysregulation subgroup, included 25% ($n = 30$) of the cases and was characterized by elevated affective and anxiety symptoms, more ADHD symptoms (inattention and hyperactivity–impulsivity) and more total problems assessed by the CBCL than the other two subgroups. This subgroup included a higher proportion of females (40%) than subgroup 1 (10%). Participants also presented more aggressive and rule-breaking behaviors and ODD symptoms than subgroup 3. As for the ICU, this subgroup attained higher scores than subgroup 3 in the Callousness and Total subscales, but lower Total scores than subgroup 1. Concerning the type of aggression, this group displayed less proactive aggression than subgroup 1 and did not differ from the others subgroups with regard to antisocial behaviors measured by the ABS. No differences were found with regard to the presence of ODD, CD, or ADHD and use of medication.

Subgroup 3: The Low Severity subgroup

The third subgroup, labeled "Low Severity", contained the 43% ($n = 52$) of the cases and was distinguished by lower levels of nearly all the variables analyzed compared to the other two subgroups, except IQ and substance abuse. It showed fewer rule-breaking and aggressive behaviors, fewer CD and ODD symptoms, fewer ADHD symptoms, and fewer anxiety and affective problems. Regarding the ABS, this subgroup exhibited fewer antisocial behaviors than subgroup 1, but did not differ from subgroup 2. This subgroup also had fewer CU traits and less reactive and proactive aggression than subgroup 1; nevertheless, it did not differ from subgroup 2. Regarding the presence of psychiatric diagnoses, this subgroup showed less proportion of individuals with a comorbid ODD + CD + ADHD compared to subgroup 1.

Comparison between cases cluster subgroups and healthy controls

Healthy controls showed significantly lower scores for all the problem variables compared to the three subgroups. The only exception was the somatic subscale of the CBCL, for which no significant differences were found compared to subgroup 1. Regarding the sociodemographic characteristics, participants in the control group were older than those in subgroup 3, with a higher proportion of females in the control group than in subgroup 1. Additionally, the control group displayed a higher IQ score compared to the three cluster subgroups.

Discussion

The present European multi-site study aimed to phenotypically differentiate a large clinical referred group of boys and girls between the ages of 8 and 18 years with disruptive behaviors. After conducting a cluster-model analysis, we provide evidence of three subgroups of individuals with disruptive and aggressive behavior in this age group. According to the findings in the literature [13, 41, 42], the compositions of the three clusters suggest a distinction in terms of different comorbidities and the presence of CU traits and proactive aggression, illustrating the dimensional aspect of the conditions under which symptoms arise.

Two of the three resulting subgroups comprised individuals with high levels of rule-breaking, aggressive behaviors, ODD symptoms and antisocial behaviors: one subgroup was distinguished by more males, more CD symptoms, elevated CU traits, and proactive aggression (the High CU Traits subgroup), and the other one with elevated anxiety, affective and ADHD symptoms and represented by more females (the ADHD and Affective

Table 2 ANCOVA of the symptom ratings for the subgroups derived from the cluster analysis and the control group

	1 (HCU)	2 (ADHD + AfD)	3 (LS)	4 (C)	F/χ^2	p	Post-hoc ¥
N 222	39	30	52	100			
Sex (m:f) (more males)	35:4	21:9	44:8	59:41	18.62	< 0.001	1 > 2; 3,1 > 4
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD			
Age*	13.1 (3)	12.4 (3)	12.1 (2.3)	13.5 (2.6)	3.97	0.009	4 > 3
IQ*	100.5 (10.7)	98.9 (8.9)	101 (12.5)	107.2 (10.6)	9.73	< 0.001	4 > 3,1,2
CBCL							
Rule-breaking	11.7 (4.6)	10.1 (5)	6 (3.3)	1.3 (1.9)	124.33	< 0.001	1,2 > 3 > 4
Aggressive	22.7 (5.3)	23.6 (4.8)	15.6 (5.6)	2.8 (3.3)	262.79	< 0.001	2,1 > 3 > 4
Affective*	6.1 (3.7)	10.4 (4.1)	5.3 (3)	1.5 (2.5)	76.21	< 0.001	2 > 1,3 > 4
Anxiety*	2.5 (1.9)	5.8 (2.3)	3 (1.9)	1.1 (1.6)	50.39	< 0.001	2 > 3,1 > 4
Somatic*	1.4 (1.8)	4.5 (2.9)	1.9 (1.9)	0.9 (1.2)	38.95	< 0.001	2 > 3 > 4; 2 > 1
ODD*	8.3 (1.3)	8.4 (1.1)	6.2 (2)	1.6 (1.8)	201.88	< 0.001	2,1 > 3 > 4
CD*	14.8 (4.3)	12.4 (4.4)	7.9 (4)	1.1 (1.8)	186.03	< 0.001	1 > 2 > 3 > 4
Externalizing behaviour	34.3 (7.5)	33.7 (7.4)	21.6 (7.8)	4.3 (4.9)	274.83	< 0.001	1,2 > 3 > 4
Internalizing behaviour	12.2 (6.9)	25.1 (8.3)	12.8 (6.7)	4.8 (5.7)	81.32	< 0.001	2 > 3,1 > 4
Total CBCL	76.1 (18.4)	99.8 (20.4)	58.6 (18.5)	14.4 (13.8)	254.92	< 0.001	2 > 1 > 3 > 4
ICU							
Callousness*	15.7 (5.1)	13.9 (6)	8.5 (3.29)	4 (3.4)	87.36	< 0.001	1, 2 > 3 > 4
Uncaring*	19.4 (2.6)	16.3 (3.6)	14.4 (4.29)	10.1 (5)	42.43	< 0.001	1 > 3 > 4; 2 > 4
Unemotional*	8.5 (2.7)	6.7 (3.7)	6 (2.9)	5.2 (2.7)	10.88	< 0.001	1 > 3, 4; 2 > 4
Total ICU	43.5 (7.8)	36.9 (9.8)	28.9 (7)	19.5 (8.5)	80.97	< 0.001	1 > 2 > 3 > 4
SNAP-IV							
Inattention*	16.8 (5.7)	20.5 (4.3)	11.6 (5)	3.6 (4)	133.22	< 0.001	2 > 1 > 3 > 4
Hyperactivity-impulsivity*	13.4 (6.1)	18.2 (6.1)	10.3 (4.5)	1.9 (2.7)	123.97	< 0.001	2 > 1 > 3 > 4
Total ADHD	33.4 (12.4)	40.1 (9.5)	24.7 (9.9)	5.8 (6.5)	146.45	< 0.001	2 > 1 > 3 > 4
RPQ							
Reactive*	13.4 (4.8)	12.6 (3.8)	10.6 (4.9)	5.7 (3.3)	40.78	< 0.001	1 > 3 > 4, 2 > 4
Proactive*	6.4 (5.2)	3.3 (2.7)	2.5 (2.7)	0.8 (1.3)	31.98	< 0.001	1 > 2,3 > 4
Total RPQ	19.8 (9.3)	15.9 (5.5)	13 (6.7)	6.4 (4.2)	45.43	< 0.001	1 > 3 > 4, 2 > 4
ABS							
Stealing	2.1 (1.8)	1.5 (1.6)	0.7 (1.1)	0.4 (0.9)	16.19	< 0.001	1 > 3,4; 2 > 4
Violence	4.3 (2.7)	3.8 (2)	3.2 (1.9)	1 (1)	37.06	< 0.001	1 > 3 > 4; 2 > 4
Property damage	2.3 (2.2)	1.6 (1.7)	0.9 (1.2)	0.3 (0.6)	20.16	< 0.001	1 > 3 > 4; 2 > 4
Substance use	1.9 (1.7)	1.3 (1.6)	0.6 (0.1)	0.8 (1.2)	9.71	< 0.001	1 > 3,4; 2 > 4
Other antisocial behaviour	2.8 (2)	2.1 (1.6)	1.7 (1.7)	0.7 (1.1)	21.64	< 0.001	1 > 3 > 4; 2 > 4
Total ABS	13.5 (8)	10.2 (5.5)	7.2 (4.9)	3.1 (3.1)	41.42	< 0.001	1,2 > 3 > 4
	N (%)						
ODD	30 (77%)	18 (60%)	32 (62%)	–	3.02	0.221	
CD	18 (46%)	10 (33%)	15 (29%)	–	3	0.223	
ADHD	15 (39%)	10 (33%)	11 (21%)	–	3.44	0.179	
None	7 (18%)	7 (23%)	14 (27%)	–	1.01	0.604	
Comorbidity	23 (59%)	12 (40%)	19 (37%)	–	4.89	0.087	
ODD + CD	9 (23%)	4 (13%)	9 (17%)	–	1.13	0.569	
ODD + ADHD	5 (13%)	4 (13%)	9 (17%)	–	0.43	0.807	
CD + ADHD	1 (3%)	1 (3%)	–	–	1.59	0.451	
ODD + CD + ADHD	8 (21%)	3 (10%)	1 (2%)	–	8.62	0.013	1 > 3
Medication use	24 (62%)	25 (48%)	14 (47%)	–	2.08	0.353	
Stimulants	20 (51%)	25 (48%)	10 (33%)	–	2.46	0.293	

HCU high CU Trait subgroup, *ADHD + AfD* ADHD and Affective Dysregulation subgroup, *LS* low severity subgroup, *C* control group, *IQ* intelligence quotient, *CBCL* Child Behavior Checklist, *ADHD* attention-deficit/hyperactivity disorder, *ODD* oppositional defiant disorder, *CD* conduct disorder, *ICU* Inventory of Callous–Unemotional Traits, *SNAP-IV* ADHD rating scale, *RPQ* Reactive Proactive Aggression Questionnaire, *ABS* Antisocial Behavior Scale

Table 2 (continued)

*Variables included in cluster analysis. All results with age and sex as a covariate

¥Statistical significance set at $p < .05$ with Bonferroni correction

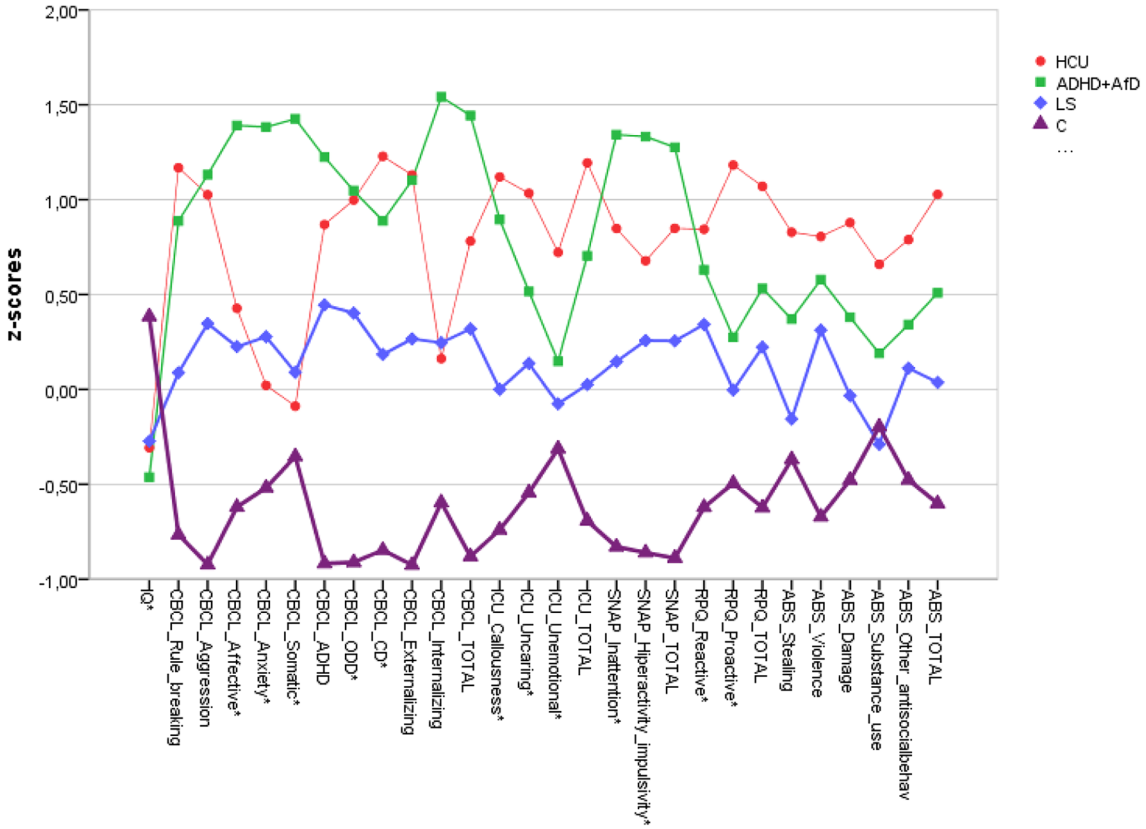

Fig. 1 Mean values for symptoms for the subgroups derived from the cluster analysis and the control group. Mean *z* scores. *HCU* high CU Trait subgroup, *ADHD + AfD* ADHD and Affective Dysregulation subgroup, *LS* low severity subgroup, *C* control group, *CBCL* child behavior checklist, *ADHD* attention-deficit/hyperactivity disorder, *ODD* oppositional defiant disorder, *CD* conduct disorder, *ICU* Inventory of Callous–Unemotional Traits, *SNAP-IV* ADHD rating scale, *RPQ* Reactive Proactive Aggression Questionnaire, *ABS* Antisocial Behavior Scale. *Variables included in the cluster analysis

Dysregulation subgroup). The third subgroup (Low Severity) showed lower levels of symptomatology in almost all the clinical variables analyzed and fewer antisocial behaviors, although this cluster subgroup still displayed significantly more symptoms than the control group. Moreover, there were no in-between differences concerning age, type of disorder, or the amount of medication taken, except for in the High CU Traits subgroup, which contained the highest proportion of individuals with comorbid ODD + CD + ADHD.

Primary and secondary variants

Our results partly agree with those of previous studies in which three similar groups based on primary and secondary variants were found [41, 42]: one group with elevated CU traits and low anxiety, a second with elevated/moderate CU traits and elevated anxiety, and a third with lower CU traits and anxiety. Some studies have found a fourth subgroup that contains individuals with low levels of CU traits and elevated anxiety [54, 55] or has resulted from the splitting of the lower severity group [13]. A fourth subgroup has also been observed in studies that have included community controls in the clustering sample [16, 40, 46, 47]. A separation between CU traits and affective problems has been found in previous studies that linked CU traits with lower levels of anxiety [17, 49, 82] and is also consistent with evidence indicating that low levels of fearfulness may contribute to the development of CU traits [83]. Specifically, Thomson and colleagues [84] reported that youth with CU traits are more able to manage fearful situations. Psychophysiological studies have presented evidence of the

differentiation in these subgroups of patients, indicating that those with CD + internalizing symptoms scored on opposite extremes on physiological measures compared to those with CD + CU [82]. However, contradictory findings have also been reported: there is some evidence that children with CD and elevated CU traits also display anxiety and depressive symptoms equivalent to individuals with CD but without CU traits [1]. Furthermore, since there are very few studies in this field involving children, our results provide evidence that this subgrouping also holds for children. We did not find age differences within our subgroups, indicating that these subgroups were represented equally by children and adolescents. However, we were unable to perform further age-related analyses due to our small sample size.

The comorbidity of ADHD symptoms

In our study, the prevalence of both ADHD symptoms (inattention and hyperactivity–impulsivity) was higher in the subgroup that also displayed anxiety and affective symptoms; in fact, ADHD symptoms appear to co-occur with anxiety traits when subgrouping individuals with aggressive behaviors, regardless of CU traits. Similarly, some studies [42, 85] recorded more ADHD symptoms in the subgroup with elevated anxiety. Specifically, Meehan and colleagues found that the subgroup with high levels of CU traits and anxiety displayed more ADHD symptoms than the other subgroups. However, other studies have observed greater impulsivity in those presenting increased levels of CU traits without anxiety [13]. Additionally, similar to our results, a strong correlation between symptoms of ADHD and reactive aggression, specifically linked with internal frustration, was reported in an adolescent clinical sample with behavioral problems [23]. In this line, ADHD symptoms and specifically impulsivity and elevated reactivity are key factors in a subgroup of individuals who reported disruptive and aggressive behaviors [86, 87]. Their relationship with anxiety and aggressive behavior should help guide specific interventions in this population.

Proactive and reactive aggression

Regarding the type of aggression, we found a 3-subgroup model similar to that of previous studies. One subgroup displayed increased proactive and reactive aggression, another showed only high reactive aggression and the third subgroup presented less aggressive behavior. Interestingly, we found that those with both high proactive and high reactive aggression also exhibited increased levels of CU traits. This is consistent with findings that individuals who display proactive aggression most frequently show reactive aggression as well [23, 88]. Specifically, several studies showed that individuals in combined proactive–reactive groups have higher levels of CU traits [19, 89, 90]. On the other hand, the ADHD and Affective Dysregulation subgroup was affected by a similar level of reactive aggression but lower proactive aggression than the subgroup with high CU traits. This is consistent with previous findings linking anxiety and ADHD with reactive aggression [37, 50, 65] rather than with proactive aggression. Reactive aggressive behaviors may be considered impulsive reactions to a perceived threat or hostility [91].

Gender aspects

Regarding sex, as may be expected, we found that girls were overrepresented in the ADHD and Affective Dysregulation subgroup (which showed moderate levels of CU traits and elevated anxiety, affective and ADHD symptoms), while boys predominated in the other two subgroups. These results are consistent with previous findings indicating that girls with CD have higher levels of anxiety but lower CU scores than boys [42]. Similarly, some studies have found larger proportion of girls in the subgroups with high levels of anxiety and moderate levels of CU traits [13, 42, 58]. Furthermore, Pardini et al. [92] found that girls with CD exhibited elevated depressive symptoms, regardless of whether or not they had CU traits. Girls with CD and CU traits had lower levels of anxiety than girls with CD alone; moreover, girls with high CU traits had low anxiety scores relative to the other group.

Relationship with clinical diagnoses

We did not find a clear relationship between a specific DSM-based diagnosis (ODD, CD or ADHD) and the subgroups derived from our cluster analysis (although we found more CD symptoms in the High CU Traits subgroup and more ADHD symptoms in the ADHD and Affective Dysregulation subgroup). The prevalence of these disorders did not differ between the subgroups, except for comorbid ODD + CD + ADHD being most prevalent in the High CU Traits subgroup, indicating that this subgroup contained more complex and severe cases. These results may have implications in the current diagnostic framework concerning disruptive individuals. Dimensional approaches would be helpful in the diagnostic process of this population.

Strengths and limitations

The most important strength of the current study is the fact that it involved a multi-site assessment of clinically referred subgroups in a large European sample across a wide age range of children and adolescents (8–18) with disruptive

and aggressive behaviors. This enhances the generalizability of our results. Moreover, we showed a comparison with a healthy control group. Another strength is the broad range of problem dimensions assessed, such as CU traits, reactive/proactive aggression and comorbid clinical symptoms. This multidimensional model and the use of a healthy control comparison group are improvements on previous studies in this field.

Some limitations should be mentioned. First, despite the efforts made to match the cases and controls at the outset of the study, both age and the male/female ratio differed between samples; however, both variables were included as covariates in all analyses. Second, the small sample size made it impossible to perform separate sex- and age-related analyses. Third, the inclusion of clinical referrals in our sample could have introduced a selection bias, with only the most severe cases of disruptive behavior from the community included. This must be taken into account when generalizing our results. Another limitation of the present study was that despite the use of a multidimensional approach, we failed to introduce some other important variables such as, for example, possible traumatization or maltreatment [54, 93], personality traits [13], family functioning [59, 94], age of onset [3, 4, 95, 96], symptom dimensions rather than distinct subgroups [97] or symptom criteria like irritable, headstrong or hurtful for ODD [12, 98, 99]. Finally, the possible influence of excluding some participants with incomplete data should be taken into account as a limitation of our study.

Summary and clinical implications

Concluding, our study thus highlights some important aspects that should be taken into account when assessing disruptive and aggressive behaviors in clinically referred children and adolescents. In line with previous studies, it is clear that individuals who display disruptive behaviors form a heterogeneous group who develop conduct and aggression problems for different reasons and, as a consequence, treatment strategies may vary depending on the type of disruptive behavior being targeted. It is now clear that there is a subgroup that displays elevated aggression due to different underlying pathways (e.g., anxiety, affective disorders, impulsivity) from those in the subgroup with high CU traits [86, 87]. This should encourage clinicians to take more account of characteristics such as the new DSM-5 specifier (limited prosocial emotions, CU traits), and comorbid conditions. Comorbidities should not only be taken into account for treatment purposes, but also for diagnosis in disruptive children and adolescents. Disruptive and aggressive conduct in individuals with externalizing behaviors (CD and ODD symptoms) and CU traits should probably be treated differently from the same conduct in individuals with elevated anxiety and/or ADHD symptoms.

Specific treatments for mood dysregulation should focus on teaching skills for coping with anxiety, depression and stressors. By contrast, those with increased levels of CU traits and proactive aggression may benefit from alternative approaches that focus on working on emotional recognition and modify cognitions and behaviors to avoid aggressive behavior. Specifically, although CU traits have been associated with poor and blunted response to behavioral treatment outcomes [20, 100–102], intensive and specialized treatment interventions and social-learning-based parent training are recommended early in childhood and have been proven to be helpful in reducing CU traits [11, 103]. Furthermore, increased impulsivity and attention difficulties should be addressed appropriately with educational resources. Given that the causal processes leading to disruptive and aggressive behaviors appear to differ across subgroups, personalized evaluation and treatment are important prerequisites for favorable developmental and long-term outcomes [11, 25, 103].

In conclusion, the data obtained from our Europe-wide sample enabled us to break disruptive behavior down into coherent subgroups. This kind of distinction between more homogeneous phenotypic subgroups of individuals with disruptive behaviors furthers our understanding of the etiology of aggression and disruptive behaviors. An accurate analysis of the clinical symptoms and types of aggressive and disruptive behavior might help to individualize treatment and thus improve both responses to treatment and prognosis.

Therefore, more research is needed with larger clinically referred samples to assess the replicability of these results, preferably in a longitudinal context, in order not just to improve our understanding of possible age and sex differences (specifically placing a greater emphasis on females and on children), but also to gain a deeper insight into the longitudinal aspects of disruptive behaviors. Longitudinal studies would also help in understanding the stability, course and prognosis of these subgroups to aid in the development of preventive specialized programs. Moreover, there is still a lack of specific studies using a dimensional approach in these populations. In recent years, longitudinal studies and the identification of distinct subgroups have increasingly been taken into consideration, providing further insight into this group of children and adolescents.

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Availability of data and materials The data that support the findings of this study are available on request from the corresponding author.

Code availability The code that support the findings of this study are available on request from the corresponding author.

Compliance with ethical standards

Conflict of interest T Banaschewski has served in an advisory or consultancy role for Lundbeck, Medice, Neurim Pharmaceuticals, Oberberg GmbH, Shire, and Infectopharm. He received conference support or speaker's fee by Lilly, Medice, and Shire. He received royalties from Hogrefe, Kohlhammer, CIP Medien, Oxford University Press; the present work is unrelated to these relationships. C Arango has been a consultant to or has received honoraria or grants from Acadia, Ambrosetti, Caja Navarra, CIBERSAM, Fundación Alicia Koplowitz, Forum, Instituto de Salud Carlos III, Gedeon Richter, Janssen Cilag, Lundbeck, Merck, Ministerio de Ciencia e Innovación, Ministerio de Sanidad, Ministerio de Economía y Competitividad, Mutua Madrileña, Otsuka, Roche, Servier, Shire, Schering Plough, Sumitomo Dainippon Pharma, Sunovio and Takeda. D Brandeis serves as an unpaid scientific advisor for an EU-funded Neurofeedback trial unrelated to the present work. JC Glennon has acted as a consultant for Boehringer Ingelheim GmbH. B Franke received an educational speaking fee from Shire and Medice. JK Buitelaar has been a consultant to/member of the advisory board of, and a speaker for, Janssen Cilag BV, Eli Lilly, Takeda/Shire, Roche, Medice and Servier. He is not an employee of any of these companies, nor a shareholder of any of these companies. He has no other financial or material support, including expert testimony, patents, and royalties. UME Schulze serves as an unpaid ethics advisor for two EU-funded projects unrelated to the present work. She has received a speaker's fee from Shire. The other authors do not report any biomedical financial interests or potential conflicts of interest.

Ethics approval Ethical approval for the study was obtained from the local ethics committees for each site separately.

Consent to participate Written informed consent was given by the participants and their parents or legal representatives.

Consent for publication All authors provided formal written consent to publish before publication of the work.

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