Externalizing disorders and substance use: Empirically derived subtypes in a population-based sample of adults

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Purpose:

Attention-deficit/hyperactivity disorder (ADHD), conduct disorder (CD), and oppositional defiant disorder (ODD) are common externalizing disorders of childhood. The common effects of these disorders on substance abuse need further investigation. The current study investigated the joint clusters of childhood/adolescence ADHD, CD, and ODD, and their influence on substance abuse/dependence in a population-based sample of adults.

Methods:

The data were drawn from the PsyCoLaus study (*n*=3720) conducted in Lausanne, Switzerland. The population-based sample included 238 subjects meeting criteria for ADHD/ODD/CD diagnoses before the age of 15. Latent class analyses (LCA) were performed in order to derive comorbidity subtypes, which were subsequently characterized with respect to psychosocial correlates and substance use.

Results:

The best fit in LCAs was achieved with three latent classes: an ADHD subtype (35.7%); an externalizing multimorbid subtype (33.6%) involving ODD, ADHD, and CD; and a third subtype with CD (30.7%). The CD subtype showed the highest association with substance use. Apart from this, the externalizing multimorbid subtype was also significantly linked to substance use. The ADHD subtype had only elevated frequencies for alcohol dependence in comparison with subjects that had no history of ADHD, ODD, and CD during childhood or adolescence. Finally, important interactions between subtypes and sex were observed with regard to substance use.

Conclusions:

This study provides evidence showing that subtyping the externalizing disorders, ADHD, ODD and CD, along their comorbidity patterns leads to important differences regarding substance use. This could have implications for the etiology, prevention, and treatment of substance use disorders.

Key words: *Attention-deficit/hyperactivity disorder, conduct disorder, oppositional defiant disorder, latent class analysis, epidemiology*

Introduction

Attention deficit hyperactivity disorder (ADHD) is the most common externalizing disorder of childhood, with prevalence rates between 3 and 7.5%, and, with looser definitions, even up to 17% [1]. Subjects with ADHD frequently remain symptomatic into adulthood. This disorder is associated with adverse long-term functional outcomes, such as poor interpersonal relationships and lower educational qualifications, leading to high economic and social burdens [2]. One of the most controversial issues in the research on ADHD is its relation to comorbid disorders such as substance abuse [3]. A recent meta-analysis demonstrated that childhood ADHD was associated with nicotine use in adolescence and with alcohol and drug use disorders in adulthood [4]. These results were confirmed in a large population-based study [5]. Prevalence rates of substance use disorders were shown to be more than two-fold higher than the 8-15% in the general population [6]. In this context, there is still no consensus on the question whether the ADHD inattention symptoms or the ADHD hyperactivity/impulsivity symptoms are more predictive of substance problems [7-9]. In addition, some studies found a direct association between ADHD and substance abuse [10], while others demonstrated that this relationship disappears when co-occurring conduct disorder (CD) is taken into account [8,11,12]. Flory et al. [3] noted that any observed association between ADHD and substance abuse not considering the overlap of ADHD with CD may be spurious. If ADHD stands as a proxy for CD, the observed relation would be nothing more than the well-replicated association between CD and substance abuse [3]. Furthermore, oppositional defiant disorder (ODD) is likewise highly comorbid with ADHD and could be a predictor for the development of CD [13,9]. There is evidence that ADHD and many comorbid conditions associated with ADHD are heritable [14,15]. One study demonstrated that major genes underlie a broad behavioral phenotype including ADHD, CD, ODD, and alcohol abuse or dependence [16]. A recent controlled study on the offspring of patients with opioid dependence revealed an increased risk of ADHD in the offspring after adjustment for the effects of comorbid ODD and CD in parents, supporting shared etiological factors between ADHD and substance use disorders [17].

Hence, ADHD, CD and ODD show a complex overlap and therefore the common effects of these disorders on substance abuse/dependence need further investigation. This has major implications for etiology, prevention, and treatment of substance use disorders [3]. In particular, population-based samples enabling the examination of the joint relations between these disorders and the risk of substance abuse among adults are lacking [3,8]. A further missing area of research are sex differences in the relations among these externalizing disorders and substance abuse, despite the diverse overall prevalence of these disorders, making differential relations plausible [3].

Accordingly, the major aim of the current study was to analyze the joint clusters of childhood ADHD, CD, and ODD and their influence on substance abuse/dependence in a community-based sample of Swiss adults. In a further step, the resultant subgroups were characterized by psychosocial characteristics and analyzed with regard to further topics of interest.

Methods

Sample and procedures

The sample stemmed from the PsyCoLaus study [18], a subsample of the randomly selected population-based CoLaus survey [19]. Participants in CoLaus were recruited between 2003 and 2006 in the city of Lausanne (Switzerland) and underwent a physical examination in an outpatient clinic [19]. One year later all CoLaus participants in the age range of 35 to 66 years were invited to participate in the psychiatric arm of the study (PsyCoLaus). Among the 5535 subjects participating in the CoLaus study, 3720 individuals (67%) took part in PsyCoLaus [18]. A major aim of the PsyCoLaus study was to establish the prevalences of threshold and subthreshold psychiatric syndromes. For the current paper, a subsample meeting the criteria for ADHD/ODD/CD diagnoses before the age of 15 was selected (*n*=238; 6.4%).

The study was approved by the Ethics Committee of the University of Lausanne, Switzerland. All participants gave their written consent after being informed of the goal and funding of the study [18].

Measures

The psychiatric part of the assessment within the PsyCoLaus study included the French version of the semi-structured Diagnostic Interview for Genetic Studies (DIGS) [20,21]. The DIGS comprises information on a broad spectrum of DSM-IV Axis I diagnoses [18]. Inter-rater and test-retest reliability of the French version were successfully established in a clinical sample of Lausanne for major mood and psychotic disorders [20] as well as for substance use disorders and antisocial personality [22]. The ADHD and ODD sections were translations of the Yale Family Study version of the Schedule for Affective Disorders and Schizophrenia - Lifetime and Anxiety disorder version [SADS-LA; 23]. The ADHD and ODD sections of this interview were developed in analogy to the corresponding sections in the Kiddie-Schedule for Affective Disorders and Schizophrenia [K-SADS-E; 24].

Statistical analysis

Latent Class Analysis

Latent class analyses (LCA) were performed to empirically identify the common patterns of ADHD, CD, and ODD. The goal of person-centered approaches such as LCA is to group individuals into homogeneous categories. In this manner, unobserved population heterogeneity can be captured by qualitatively or quantitatively differing subgroups [25].

The most common statistical model fit indices are the Akaike information criterion [AIC; 26], the Bayesian information criterion [BIC; 27], the sample-size adjusted BIC [ABIC; 28], and the entropy measure. The lower the values of the AIC, BIC and ABIC are, the better is the model fit. The entropy index (range from 0 to 1) measures the precision of classification. High values indicate distinct classes. Based on an extension of a theorem by Vuong [29], Lo, Mendell and Rubin [30] proposed the Lo-Mendell-Rubin likelihood ratio test (LMR-LRT), a test procedure, which compares the model with k classes compared to a model with (k-1) classes [31]. However, as Muthén [32] pointed out, only the consideration of the fit indices in combination with the interpretability and theoretical appropriateness of a given class solution, should guide the final selection. Up to seven latent class models were fitted to the data. These models were compared by the above described model fit indices.

LCA were computed using Mplus version 7 for Macintosh [33]. The number of random starts was set at up to 5000, using the 500 best solutions in the final calculation. Chi-square tests, Fisher's exact tests, Kruskal-Wallis tests, and multinomial logistic regression analyses (odds ratios (OR) with 95% confidence intervals (CI)) adding interaction terms (sex x latent class) were computed using SPSS statistics version 20 for Macintosh (SPSS Inc., USA).

Results

Overall demographics

The demographic distribution of the subsample with externalizing disorders before the age of 15 and the remaining PsyCoLaus sample are shown in Table 1. Sex, age, and socio economic status differed between the two subsamples.

--Insert Table 1 about here--

Model selection

Up to seven LCA models were fitted to the data and compared on the basis of the resulting goodness of fit indices (Table 2). The model fit indices consistently indicated that the three-class solution would provide the best fit to the data. Therefore, the three-class model was chosen for the final analyses.

--Insert Table 2 about here—

Diagnoses profiles

In order to facilitate interpretation, the estimated probabilities of manifesting an externalizing disorder were plotted in Fig. 1. The first class comprised 33.6% of respondents who depicted high probabilities for all three disorders. Accordingly, this class was labeled as 'externalizing multimorbid' subtype. Subjects belonging to the second class (35.7%) showed high probabilities for ADHD disorder, while the probabilities for CD and ODD were only low and zero, respectively. This class was labeled 'ADHD'. Finally, the third class included 30.7% of individuals with high probabilities of having CD, and zero probabilities for the two additional disorders ODD and ADHD. Consequently, this class was labeled 'CD'.

--Insert Fig. 1 about here--

Demographic characteristics

The demographic characteristics of the three empirically derived latent classes are presented in Table 3. The classes did not significantly differ in the distribution of the demographic variables sex, age, religious affiliation,

marital status and occupation. However, the socio economic status (SES) following Hollingshead revealed significant overall differences, which resulted from significant subgroup differences between the ADHD and the CD classes.

-- Insert Table 3 about here--

ADHD subscales inattention, hyperactivity, and impulsivity

The three LCA subtypes displayed significant differences in the ADHD subscales inattention, hyperactivity, and impulsivity. While the values of inattention were highest in the ADHD subtype, both hyperactivity and impulsivity were most pronounced in the externalizing multimorbid subtype (Table 4).

-- Insert Table 4 about here--

Substance abuse/dependence

Table 5 shows the frequencies of alcohol and illicit drug abuse/dependence. Due to the small cell sizes, abuse and dependence of specific illicit drugs were combined to single categories. Alcohol abuse occurred more often in the externalizing multimorbid and the CD subtype compared to the ADHD subtype. The same pattern was observed for marijuana abuse/dependence. However, narcotic dependence was more frequent in the CD class in comparison to the other two subtypes. If all illicit drugs were collapsed into one category, subjects of the CD subtype and the externalizing multimorbid met the criteria for drug abuse or dependence more frequently than the members of the ADHD subtype.

--Insert Table 5 about here--

Table 6 summarizes additional characteristics of the latent classes, including psychopharmaceutical treatment, stationary hospitalization, childhood adversities and further problems during childhood, sleep and traumatic experiences. Subjects with membership in the ADHD class consumed significantly more often sedative, hypnotic drugs or tranquillizers than the CD subgroup. Dyslexia occurred more frequently in the ADHD class compared to both the externalizing multimorbid class and the CD class. Finally, childhood adversities and traumatic experiences revealed merely trend-level associations, e.g. with an unhappier childhood, more running

away from home, more violence in the CD class, and more children's home stays in externalizing multimorbid class.

--*Insert Table 6 about here*--

From the additional internalizing diagnoses, only dysthymia reached the common significant level. Subjects with ADHD more often had a lifetime diagnosis of dysthymia than subjects from the externalizing multimorbid subtype. With regard to antisocial personality disorder, more participants with CD were diagnosed with this disorder compared to subjects with ADHD. Trend-level associations showed more overanxious disorders in the externalizing multimorbid subtype, and more MDD in the ADHD subtype. Familial psychopathology did not significantly differ between the subtypes, apart from more familial anxiety in the CD subtype (trend-level) (Table 7).

--*Insert Table 7 about here*--

Sex differences

The analysis examining interactions between sex and latent class showed differences and similarities between males (m) and females (f) regarding the risk for substance use (data not tabulated). The odds ratios were comparatively lower for both sexes within the ADHD group compared to the male group manifesting CD for substance dependence (m: OR = 0.07, CI = 0.01 – 0.55, $p < 0.05$; f: OR = 0.21, CI = 0.05 – 1.02, $p < 0.05$), substance abuse (m: OR = 0.13, CI = 0.03 – 0.59, $p < 0.01$; f: OR = 0.09, CI = 0.01 – 0.75, $p < 0.05$), and alcohol abuse (m: OR = 0.14, CI = 0.05 – 0.41, $p < 0.001$; f: OR = 0.28, CI = 0.10 – 0.79, $p < 0.05$). In contrast, the externalizing multimorbid subtype only showed a significantly lower odds ratio for females if compared to the subgroup of CD males, and beyond that, was restricted to substance dependence (f: OR = 0.21, CI = 0.04 – 0.99, $p < 0.05$) and alcohol abuse (f: OR = 0.17, CI = 0.05 – 0.55, $p < 0.001$). The results regarding alcohol abuse were not feasible.

Analyses of subtypes including the entire PsyCoLaus sample

In further analyses, the whole PsyCoLaus sample was included. The significant subgroup differences resulting from these comparisons will be listed in the following: Any illicit drug abuse: externalizing multimorbid subtype vs. remaining PsyCoLaus sample ($\chi^2 = 20.828$; df = 1; $p < .001$); CD subtype vs. remaining PsyCoLaus sample ($\chi^2 = 66.324$; df = 1; $p < .001$); illicit drug dependence: externalizing multimorbid subtype vs. remaining

PsyCoLaus sample (χ^2 = 49.332; df = 1; p< .001); CD subtype vs. remaining PsyCoLaus sample (χ^2 = 137.497; df = 1; p< .001); alcohol abuse: externalizing multimorbid subtype vs. remaining PsyCoLaus sample (χ^2 = 35.810; df = 1; p< .001); CD subtype vs. remaining PsyCoLaus sample (χ^2 = 72.033; df = 1; p< .001); alcohol dependence: externalizing multimorbid subtype vs. remaining PsyCoLaus sample (χ^2 = 16.176; df = 1; p< .01); ADHD subtype vs. remaining PsyCoLaus sample (χ^2 = 7.698; df = 1; p< .05); CD subtype vs. remaining PsyCoLaus sample (χ^2 = 35.961; df = 1; p< .001) (data not tabulated).

Discussion

The goal of this population-based study was to empirically derive subtypes of the externalizing disorders ADHD, CD and ODD occurring during childhood/adolescence and to investigate their relation with substance abuse and disorders in adulthood. Community-based studies examining the joint connections of these disorders in adults are lacking. Our data-driven methodological approach found the best fit for a three-class model composed of three approximately equally frequent subtypes: an ADHD subtype, an externalizing multimorbid subtype exhibiting subjects with all three disorders ODD, ADHD and CD, and a third group with subjects manifesting CD. We showed that every perspective is justified regarding the relationship between these externalizing subtypes and substance use: ADHD alone, CD alone, as well as the group manifesting high probabilities for all three disorders ADHD, CD, and ODD were related to substance use in their own specific way. The CD subtype and the externalizing multimorbid subtype revealed significantly higher rates of illicit drug abuse/dependence than the ADHD subtype and subjects without a history of ADHD, ODD, or CD in childhood or adolescence. In addition, subjects belonging to the CD subtype exhibited significantly more narcotic abuse/dependence than the other two subtypes. The only significant association of ADHD with substance use was its higher frequency in alcohol dependence compared to subjects without a history of ADHD, ODD, or CD. The same relation was also found for both the externalizing multimorbid subtype and the CD subtype. Moreover, these two subtypes also showed significantly more alcohol abuse compared to the ADHD subtype. Finally, the present study fills an important research gap by specifying sex-related differences.

The comorbidity of alcohol use and ADHD corroborate the findings of well-performed cross-sectional and prospective longitudinal studies [34,35]. Besides neurobiological and genetic mechanisms, social impairment, symptom persistence, parenting efforts, and delinquency have also been found as possible mediating variables [36,37]. In consideration of comorbid CD, the Danish Longitudinal Study of Alcoholism estimated the highest relative risks for male alcohol dependence at age 30-/40 years for the subgroup with both ADHD and CD (RR = 6.3), followed by the subgroups with only CD (RR = 3.6), and only ADHD (RR = 1.6), compared to a reference group [38]. In the present study, the comparison with subjects without a history of ADHD, ODD, or CD was the crucial feature allowing detection of a link between ADHD and alcohol dependence. Although the lacking association of ADHD und illicit drug use found in the current study differs from some studies [39,40], it is explainable by other research showing that the relation between ADHD and substance use disappeared when the high overlap between ADHD and CD was taken into account [3]. There is some evidence that ADHD and CD may interact to afford a higher risk of substance abuse than either disorder alone [3,41]. While the latter studies focused on the externalizing disorders ADHD and CD, we additionally considered ODD.

The combined effect of ADHD, CD, and ODD on substance use was confirmed by the externalizing multimorbid subtype in our data. A possible explanation for this is provided by the risk-factor model explaining the relation between ADHD and substance abuse as occurring through CD, namely by ADHD increasing the risk for CD, which then increases the risk for substance abuse [3]. An alternative model is the stepping-stone model. This model describes ADHD as the first step in the developmental progression to CD and at the same time explains the high overlap of ADHD and CD. In addition, the stepping-stone model can explain the lack of a direct effect of ADHD on substance abuse once CD is taken into account [3]. From a genetic point of view, Arcos-Burgos et al. [42] provided compiled evidence for common genetic networks underlying a phenotype including the externalizing disorders ADHD, CD, ODD, and substance disorder. However, a community-based case-control study found an association between ADHD and illicit substance use disorders that was not mediated by CD [10]. Yet because the sample consisted of mainly marijuana or marijuana plus cocaine users, the results might not apply to subjects with a different profile of substance abuse or disorders. Furthermore, a meta-analysis and meta-regression investigation concluded that ADHD did not increase the risk of illicit substance use beyond the effects of CD/ODD [11].

ADHD can be defined as extreme values along quantitative dimensions of inattention and hyperactivity/impulsivity [8]. Some studies showed that mainly the inattention symptoms are predictive of substance problems [43,9], while other studies demonstrated that the hyperactivity/impulsivity symptoms are most predictive [44,8]. In the current study, the inattention subscale was highest in the ADHD subtype, and both hyperactivity and impulsivity were most pronounced in the externalizing multimorbid subtype. Because the latter subtype was more associated with substance use than the ADHD subtype, our findings tend to support an association between hyperactivity/impulsivity symptoms and substance use. A recent study, concluded that elevated trait impulsivity is not a specific feature of dependent cocaine use because both recreational and dependent cocaine use were associated with higher trait impulsivity [45]. Whether these findings also apply to other substance classes requires more investigation. Further significant characteristics of the ADHD subtype were dyslexia, a diagnosis of dysthymia, and consumption of sedative, hypnotic, and tranquillizer medications. The comorbid occurrence of learning disabilities and dysthymia of this subtype are in line with the literature [46,47]. The well established correlation between sleep disturbances and ADHD [48] could have resulted in the increased consumption of sedatives, hypnotics, and tranquillizers in our data. Because there were hardly any subjects with stimulant medication, the adverse effect of stimulants on sleep quality could not be examined in the present study.

However, we found the highest risk for substance abuse in the CD subtype. This finding is in accordance with several studies showing that CD is a powerful predictor of substance use and abuse [49,50]. Button et al. [51] concluded that the co-occurrence of CD and alcohol/illicit drug dependence is partly explained by the shared genetic risk of these disorders. In terms of further comorbid diagnoses, only antisocial personality disorder (ASPD) significantly characterized the CD subtype, which was to be expected considering that CD was shown to be a precursor of ASPD [52]. Likewise, a recent study showed strong associations between CD, substance disorders, and ASPD, which may reflect a general vulnerability to externalizing behaviors [53]. A further study revealed that the relationship between childhood CD and adult antisocial behavior was partially mediated by early-onset alcohol abuse [54]. Furthermore, CD had the highest frequencies of childhood adversities in the present study, albeit only on a trend-level. This corresponds with the finding of De Sanctis et al. [6] elucidating an inter-correlation between childhood maltreatment and childhood CD. We could only observe trend-level associations between parental psychopathology and the onset of CD. In this context, particularly associations between parental substance abuse have been demonstrated [55]. This variable was not available in our study. Although, as Burke et al. [56] emphasized in their review article, it is apparent that there is no one single causative factor of CD – the identification of primary risk factors and developmental pathways is much more complex.

Although very few studies have addressed the issue of sex differences of externalizing disorders in substance use [3], one study examining adolescents demonstrated that CD, ADHD and depression were important concomitants in males, while in females depression and not ADHD was the primary variable related to substance dependence [57]. Compared to CD males, we found sex differences for the externalizing multimorbid subtype with a lower association for females but not for males. There were no sex differences within the subgroups of subjects manifesting only ADHD and only CD, respectively – both sexes had significant lower associations within the ADHD subgroup and no significant differences within the CD subgroup compared to CD males. Additionally, there were no sex differences within the subgroup of subjects manifesting only CD. These findings require further replication.

There are some limitations in this study. First, the study design was cross-sectional, and the assessment of the childhood and adolescence diagnoses was carried out retrospectively. Hence, a recall bias cannot be ruled out. Second, the reliabilities of the ADHD and the ODD sections of the diagnostic instrument were not tested in adults. Third, data concerning nicotine use was not available.

To conclude, this community-based study provides evidence that subtyping the externalizing disorders, ADHD, ODD and CD leads to important differentiations regarding substance use. By applying data-driven latent

class methodology we accounted for various possibilities of linkages between ADHD, ODD and CD. Our data indicated that the relation between ADHD and substance use does not entirely disappear when CD is considered –it is simply limited to alcohol dependence and only reaches significance levels in comparison with subjects without ADHD, ODD and CD during childhood/adolescence. Subjects with only CD formed the subgroup with the highest vulnerability to illicit drug use and alcohol use, followed by the multimorbid externalizing subtype. These findings, derived from the unbiased population of adults in Lausanne, Switzerland, might provide basic information for the treatment of persons affected.

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Conflict of interest

All authors declare that they have no conflicts of interest.

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Table 1. Demographic distribution of the subsample of subjects with ADHD/CD/ODD before the age of 15 and the remaining PsyCoLaus sample

	Subjects with ADHD, CD or ODD (*n*=238)	**Others (*n*=3482)**	**Chi^2 statistics/Fisher's statistics *p* value (two-tailed)**
	***n* (%)**	***n* (%)**	
Sex			*p*<.001
Male	149 (62.6)	1601 (46.0)	
Female	89 (37.4)	1881 (54.0)	
Age, y			*p*<.01
36-53	168 (70.6)	2084 (59.9)	
54-66	70 (29.4)	1398 (40.1)	
Religious affiliation			*p*=.237
Catholic	95 (39.9)	15323 (44.0)	
Protestant	73 (30.7)	1101 (31.6)	
Jewish	3 (1.3)	22 (0.6)	
Islamic	3 (1.3)	74 (2.1)	
No religion	52 (21.8)	581 (16.7)	
Other	12 (5.0)	171 (4.9)	
Education[1]			*p*=.516
Compulsory education	39 (16.4)	555 (15.9)	
Apprenticeship/vocational school	92 (38.47)	1279 (36.7)	
Preparatory school for general qualification for university entrance	24 (10.41)	313 (9.0)	
Vocational education	23 (19.7)	327 (9.4)	
Vocational secondary school/intermediate diploma school	12 (15.0)	217 (6.2)	
University/university of applied science	42 (17.6)	756 (21.7)	
Other/NA	1 (0.4)	4 (0.1)	
Income (CHF per y)[1]			*p*=.392
<30'000	21 (8.8)	205 (5.9)	
30 000-49'999	42 (17.6)	535 (15.4)	
50'000-69'999	52 (21.4)	789 (22.7)	
70'000-89'999	44 (18.5)	651 (18.7)	
90'000-109'999	34 (14.3)	474 (13.6)	
>110'000	40 (16.8)	742 (21.3)	

Marital status			*p*=.097
unmarried	46 (19.3)	533 (15.3)	
married	131 (55.0)	2046 (58.8)	
separated	17 (7.1)	154 (4.4)	
divorced	36 (15.1)	642 (18.4)	
widowed	8 (3.4)	107 (3.1)	
SES (quantiles)[1]			*p*<.05
<20	29 (12.2)	376 (10.8)	
20-29	38 (16.0)	427 (12.3)	
30-39	62 (26.1)	1017 (29.2)	
40-55	67 (28.2)	792 (22.7)	
>=55	41 (17.2)	864 (24.9)	

[1] The discrepancy between the total number of persons and the number of persons in the following rows result from missing items
SES: Socio economic status following Hollingshead's index

Table 2. Model fit indices derived from latent class analysis with classing ranging from 1 to 7 for *n*=238 subjects with ADHD, ODD/CD diagnoses in their childhood/adolescence

Fit statistics	1-class	2-class	**3-class**	4-class	5-class	6-class	7-class
AIC	959.143	838.657	**761.219**	769.219	777.219	785.219	793.219
BIC	969.560	862.963	**799.414**	821.303	843.192	865.081	886.970
ABIC	960.051	840.775	**764.547**	773.758	782.968	792.178	801.389
Entropy	N/A	.891	**.998**	.796	.745	.751	.734
LMR-LRT, adj.	N/A	p = .0000	***p* = .0000**	p =.0000	p=.5001	p = .4972	p =.5983

Bayesian Information Criterion (BIC), Sample-Size adjusted Bayesian Information Criterion (ABIC), Lo-Mendell-Rubin likelihood ratio test, adjusted (LMR-LRT adj.)

NA, not applicable

Best-fitting model in bold type

Table 3. Demographic characteristics of the three latent classes (*n*=238)

	Latent Classes			
	Externalizing multimorbid *n* (%)	**ADHD *n* (%)**	**CD *n* (%)**	**Overall Chi[2] statistics/Fisher's statistics *p* value (two-tailed)**
Sex				*p*=.094
Male	45 (56.2)	51 (60.0)	53 (72.6)	
Female	35 (43.8)	34 (40.0)	20 (27.4)	
Age, y				*p*=.384
36-53	54 (67.5)	58 (68.2)	56 (76.7)	
54-66	26 (32.5)	27 (31.8)	17 (23.3)	
Religious affiliation				*p*=.694
Catholic	34 (42.5)	31 (36.5)	30 (41.1)	
Protestant	20 (25.0)	31 (36.5)	22 (30.1)	
Jewish	1 (1.2)	2 (2.4)	0 (0.0)	
Islamic	1 (1.2)	1 (1.2)	1 (1.4)	
No religion	20 (25.0)	14 (16.5)	18 (24.7)	
Other	4 (5.0)	6 (7.1)	2 (2.7)	
Marital status				*p*=.757
unmarried	17 (21.2)	13 (15.3)	16 (21.9)	
married	43 (53.8)	46 (54.1)	42 (57.5)	
separated	6 (7.5)	6 (7.1)	5 (6.8)	
divorced	13 (16.7)	15 (17.6)	8 (11.0)	
widowed	1 (1.2)	5 (5.9)	2 (2.7)	
Education[1]				*p*=.432
Compulsory education	9 (11.4)	19 (22.6)	11 (15.7)	
Apprenticeship/vocational school	27 (34.2)	34 (40.5)	31 (44.3)	
Preparatory school for general qualification for university entrance	8 (10.1)	7 (8.3)	9 (12.9)	
Vocational education	10 (12.7)	7 (8.3)	6 (8.6)	
Vocational secondary school/intermediate diploma school	5 (6.3)	5 (6.0)	2 (2.9)	
University/university of applied science	20 (25.3)	11 (13.1)	11 (15.7)	
Other/NA	0 (0.0)	1 (1.2)	0 (0.0)	
SES (quantiles) [1]				*p*<.05 [III]

<20	7 (8.8)	14 (16.7)	8 (11.0)
20-29	9 (11.2)	16 (19.0)	13 (17.8)
30-39	20 (25.0)	15 (17.9)	27 (37.0)
40-55	26 (32.5)	29 (34.5)	12 (16.4)
>=55	18 (22.5)	10 (11.9)	13 (17.8)

NA, not applicable

[1] The discrepancy between the total number of persons and the number of persons in the following rows result from missing items

SES: Socio economic status following Hollingshead's index

[I] Class 1 significantly differs from class 2; [II] Class 1 significantly differs from class 3; [III] Class 2 significantly differs from class 3

Table 4. Differences in the central tendency for the ADHD subscales inattention, hyperactivity, and impulsivity by the three latent classes (*n*=238)

	Latent Classes			
	Externalizing multimorbid (*n*=80)	**ADHD (*n*=85)**	**CD (*n*=73)**	**Kruskal-Wallis test**
	mean rank	**mean rank**	**mean rank (*n*)**	***p* value**
ADHD subscale				
Inattention	53.4	69.8	50.9	$p<.05$
Hyperactivity	80.6	60.8	53.1	$p<.05$
Impulsivity	82.3	59.1	62.6	$p<.05$

Table 5. Alcohol and illicit abuse/dependence characteristics for the *n*=238 subjects with ADHD, ODD/CD diagnoses in their childhood/adolescence

	Latent Classes			
	Externalizing multimorbid (*n*=80) ***n* (%)**	**ADHD (*n*=85)** ***n* (%)**	**CD (*n*=73)** ***n* (%)**	**Overall Chi[2] statistics/Fisher's statistics *p* value (two-tailed)**
Alcohol abuse/dependence				
Alcohol abuse	22 (27.5)	11 (12.9)	27 (37.0)	$p<.01$ [I, III]
Alcohol dependence	11 (13.8)	9 (10.6)	14 (19.2)	$p=.296$
Illicit drug abuse/dependence				
Marijuana abuse/dependence	16 (20.0)	3 (3.5)	21 (28.8)	$p<.001$ [I, III]
Hallucinogen abuse/ dependence	2 (2.5)	1 (1.2)	3 (4.1)	$p=.448$
Stimulants abuse/ dependence	0 (0.0)	0 (0.0)	1 (1.4)	$p=.307$
Cocaine abuse/ dependence	7 (8.8)	3 (3.5)	10 (13.7)	$p=.074$
Narcotic abuse/ dependence	2 (2.5)	1 (1.2)	12 (16.4)	$p<.001$ [II, III]
Any illicit drug abuse[1]	12 (15.0)	3 (3.5)	18 (24.7)	$p<.001$ [I, III]
Any illicit drug dependence[1]	11 (13.8)	3 (3.5)	17 (23.3)	$p<.01$ [I, III]

[1] Marijuana, hallucinogens, cocaine, stimulants, narcotics
[I] Class 1 significantly differs from class 2; [II] Class 1 significantly differs from class 3; [III] Class 2 significantly differs from class 3

Table 6. Additional characteristics for the *n*=238 subjects with ADHD, ODD/CD diagnoses in their childhood/adolescence

	Latent Classes			
	Externalizing multimorbid (*n*=80) ***n* (%)**	**ADHD (*n*=85)** ***n* (%)**	**CD (*n*=73)** ***n* (%)**	**Overall Chi[2] statistics/Fisher's statistics *p* value (two-tailed)**
Psychotropic drugs [1]				
Antidepressants	15 (18.8)	27 (31.8)	17 (23.3)	*p*=.145
Sedative, hypnotic, tranquillizer	24 (30.0)	38 (44.7)	20 (27.4)	*p*<.05 [III]
Antipsychotic drugs	1 (1.2)	5 (5.9)	5 (6.8)	*p*=.178
Stimulants [2]	0 (0.0)	0 (0.0)	1 (1.4)	*p*=.307
Antimanic drugs	0 (0.0)	2 (2.4)	2 (2.7)	*p*=.466
Stationary hospitalization [3]	6 (8.7)	10 (14.3)	12 (23.1)	*p*=.089
Childhood adversities				
General childhood [4]	7 (8.8)	3 (3.5)	10 (13.7)	*p*=.074
Death mother	3 (3.8)	0 (0.0)	1 (1.4)	*p*=.161
Death father	7 (9.1)	5 (6.0)	3 (4.2)	*p*=.531
Divorce parents	22 (27.5)	24 (28.2)	20 (27.4)	*p*=0.99
Children's home	21 (26.6)	11 (13.1)	12 (16.4)	*p*=.077
Runaway from home	12 (15.0)	8 (9.4)	17 (23.3)	*p*=.059
Migration	7 (11.5)	11 (17.7)	10 (18.5)	*p*=.519
Other childhood problems				
Bed-wetting	16 (20.0)	22 (25.9)	16 (22.2)	*p*=.662
Dyslexia	6 (7.6)	19 (22.4)	3 (4.1)	*p*<.001 [I, III]
Sleep				
Nightmares	17 (21.8)	25 (29.8)	19 (26.4)	*p*=.528
Sleepwalking	9 (11.4)	13 (15.3)	7 (9.6)	*p*=.528
Traumatic experiences [5]				
Accident	5 (23.8)	6 (22.2)	2 (8.0)	*p*=.274
Crime	2 (9.5)	8 (29.6)	3 (12.0)	*p*=.172
Sexual abuse	6 (7.5)	8 (9.4)	2 (2.7)	*p*=.227
War	1 (4.8)	3 (11.1)	3 (12.0)	*p*=.783
Violence	9 (42.9)	12 (44.4)	19 (73.1)	*p*=.056
Overall trauma	19 (90.5)	25 (92.6)	24 (92.3)	*p*=0.99

[1] Lifetime consumption
[2] Ritalin, Amphetamine, others
[3] Due to emotional/psychological problems, lifetime
Mean age of first hospitalization (years): Externalizing multimorbid=13.67 y; pure ADHD=17.10y; pure CD=11.36y (overall Kruskal-Wallis test: $\chi^2 = 2.758$; df = 2; p = 0.252)
[4] General childhood, rated from 1=happy to 4=very unhappy (mean rank): Externalizing multimorbid=128.44; pure ADHD=121.49; pure CD=107.38 (overall Kruskal-Wallis test: $\chi^2 = 4.291$; df = 2; p = 0.117)
[5] Lifetime

[I] Class 1 significantly differs from class 2; [II] Class 1 significantly differs from class 3; [III] Class 2 significantly differs from class 3

Table 7. Additional diagnoses for the *n*=238 subjects with ADHD, ODD/CD diagnoses in their childhood/adolescence

	Latent Classes			
	Externalizing multimorbid (*n*=80) ***n* (%)**	**ADHD (*n*=85)** ***n* (%)**	**CD (*n*=73)** ***n* (%)**	**Overall Chi^2 statistics/Fisher's statistics *p* value (two-tailed)**
PTSD [1, 2]	7 (8.8)	7 (8.2)	8 (11.0)	*p*=.850
Internalizing disorders [3]				
GAD	3 (3.8)	4 (4.7)	0 (0.0)	*p*=.202
Overanxious disorder	17 (21.2)	12 (14.1)	6 (8.2)	*p*=.075
Panic disorder	6 (7.5)	8 (9.4)	3 (4.1)	*p*=.439
Separation anxiety disorder	8 (10.0)	11 (12.9)	4 (5.5)	*p*=.271
Simple phobia	17 (21.2)	19 (22.4)	9 (12.3)	*p*=.230
Social phobia	11 (13.8)	19 (22.4)	11 (15.1)	*p*=.290
Agoraphobia	6 (7.5)	6 (7.1)	2 (2.7)	*p*=.396
Dysthymia	0 (0.0)	6 (7.1)	1 (1.4)	*p*<0.05 [I]
MDD	36 (45.0)	49 (57.6)	29 (39.7)	*p*=.065
OCD	4 (5.0)	3 (3.5)	0 (0.0)	*p*=.181
Antisocial personality disorder	14 (17.5)	6 (7.1)	18 (24.7)	*p*<0.01 [III]
Familiar psychopathology				
Anxiety	5 (6.4)	2 (2.4)	8 (11.4)	*p*=.079
Depression	17 (21.8)	16 (19.0)	16 (22.2)	*p*=.863
Bipolar	2 (2.6)	5 (6.0)	3 (4.2)	*p*=.612
OCD	2 (2.6)	1 (1.2)	0 (0.0)	*p*=.647
Schizophrenia	1 (1.3)	2 (2.4)	2 (2.7)	*p*=.867

Abbreviations: Post traumatic stress disorder (PTSD); generalized anxiety disorder (GAD); major depression disorder (MDD); obsessive-compulsive disorder (OCD)

[1] PTSD onset (mean, years): externalizing multimorbid=20.43; pure ADHD=16.57; pure CD=13.88 (Kruskal-Wallis test: χ^2 = 0.996; df = 2; p = 0.608)
[2] PTSD offset (mean, years): externalizing multimorbid=37.03; pure ADHD=47.63; pure CD=35.60 (Kruskal-Wallis test: χ^2 = 8.688; df = 2; p < 0.05)
[3] Lifetime

[I] Class 1 significantly differs from class 2; [II] Class 1 significantly differs from class 3; [III] Class 2 significantly differs from class 3

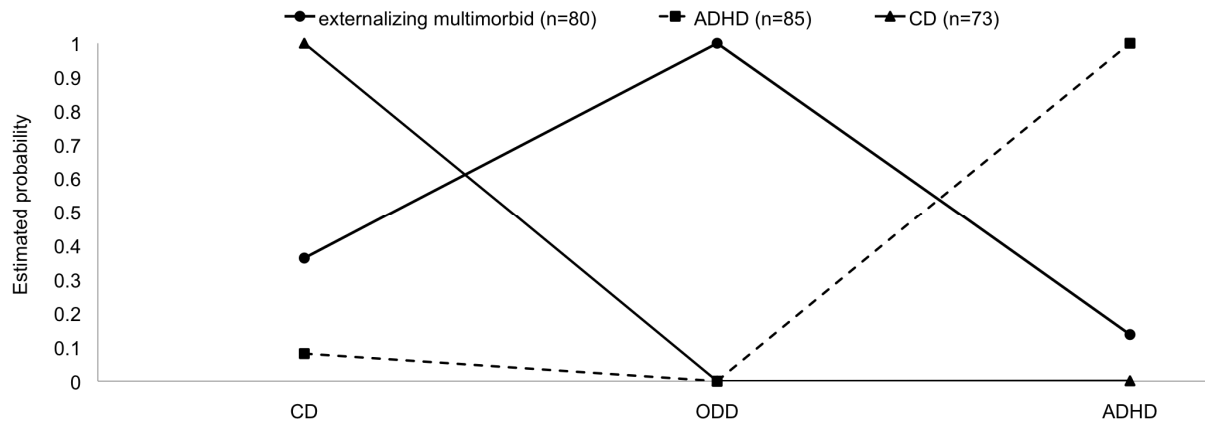

Figure 1. Three latent classes derived from the subsample of subjects having a diagnoses of conduct disorder (CD), oppositional defiant disorder (ODD)/ attention-deficit/hyperactivity disorders (ADHD) during their childhood/adolescence