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Co-existing psychiatric problems in ADHD in the ADORE cohort

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Abstract *Objective* To study the impact of co-existing psychiatric problems with ADHD on behavioural features, psychosocial functioning and quality of life in subjects of the ADORE cohort (N = 1,478). *Methods* The following six groups of associated psychiatric problems with ADHD were compared: oppositional-defiant disorder or conduct disorder only (ODD/CD); anxiety or depressive disorder only (ANX/DEP); tic/Tourette's disorder only (TIC/Tourette's); developmental co-ordination disorder only (DCD); two or more associated conditions; and none. Dependent variables included the ADHD Rating Scale-IV, the Strengths and Difficulties Questionnaire, the Clinical Global Impression-Severity scale, the Children's Global Assessment Scale and the Child Health Illness Profile-Child Edition. *Results* Having multiple co-existing psychiatric problems increased the severity of ADHD in all domains, be it behavioural features, psychosocial impairment or deterioration of quality of life. A similar though less consistent pattern applied to subjects with co-existing ODD/CD. *Conclusions* The ADORE study provides impressive evidence for the far-reaching consequences of co-existing psychiatric problems in children with ADHD that warrant intensive consideration in clinical assessment and treatment.

Key words ADHD – children – co-existing disorders – Europe

Abbreviations

ADHD	Attention-Deficit/Hyperactivity Disorder
ADORE	Attention-deficit/hyperactivity Disorder Observational Research in Europe
ADHD-RS-IV	ADHD Rating Scale-IV
ANX	Anxiety
CD	Conduct Disorder
CHIP-CE	Child Health and Illness Profile – Child Edition
CGAS	Children's Global Assessment Scale
CGI-S	Clinical Global Impression-Severity scale
DCC	Developmental Co-ordination Disorder
ODD	Oppositional Defiant Disorder
RD	Reading Disabilities
SDQ	Strengths and Difficulties Questionnaire
SLD	Specific Learning Disorder

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Introduction

Co-morbidity is a common phenomenon in medicine. However, the application of the term "co-morbidity" to psychopathology is problematic because it is meaningful only in the context of well-validated disease entities with reasonably well-understood pathology and aetiology. "Co-existence" or "co-variation" would be more appropriate terms to use in psychopathology. This is particularly true for the ADORE study because clinical ratings of associated mental problems were made rather than detailed clinical assessments of additional psychiatric disorders. However, the distinction between co-existence and co-morbidity has rarely been made in the literature.

Both large-scale epidemiological surveys [3, 16, 27] and the MTA study [13] have shown that co-existing problems are frequent in ADHD. A large number of clinical studies have found that co-existing oppositional defiant (ODD) and conduct disorder (CD) are common (occurring in more than 50 % of cases); specific learning disorders (SLD), anxiety disorders (ANX) and developmental co-ordination disorders (DCD) are frequent (occurring in up to 50 % of cases); tic disorders and depressive disorders are occasionally present (in up to 20 % of cases); and autism spectrum disorders and mental retardation are infrequent. Over 85 % of patients with ADHD have at least one co-existing psychiatric condition and approximately 60 % of patients have at least two co-existing conditions. Thus, in clinical practice, co-existing psychiatric problems are the rule rather than the exception.

Co-existing problems in ADHD have implications for research. For example, there is sufficient evidence to delineate two new sub-classifications of ADHD: (a) ADHD aggressive subtype; and (b) ADHD anxious subtype [14]. Findings from neurophysiological studies support the validity of the aggressive or externalising subtype of ADHD [2, 4]. In addition, family genetic and prevalence studies point to the genetic and phenotypic heterogeneity of ADHD [9], and behavioural genetic studies are trying to identify the genetic liability of various co-existing conditions, e.g. ODD/CD [6, 7, 18] or SLD, namely, reading disability (RD) [28]. With recent advances in molecular genetics, the search for specific candidate genes has provided initial insights that genes can affect several disorders and functions, e. g. in ADHD and RD [29], or ADHD and autism [26].

Most importantly, the co-existence of ADHD with other psychiatric problems has strong implications for clinical practice. Physicians are not only confronted with rather complex conditions for referral and assessment, but also face the challenge of developing adequate treatment guidelines [19] and intervention schemes [1, 13]. Effective interventions are particularly important because there is evidence from research that co-existing forms of psychopathology in children and adolescents are associated with increased psychosocial impairment [17]. So far, psychosocial impairment has not been well studied in ADHD. Thus, the ADORE study with its large sample size, rich cultural diversity and longitudinal structure, allows study of the impact of various co-existent psychiatric problems with ADHD on clinical features, behavioural dimensions, psychosocial functioning and quality of life. The present analysis of the impact of ADHD and co-existing psychiatric problems is based on the results of the various scales measured at the baseline assessment of the ADORE cohort.

Methods

The background, rationale and design of the ADORE study on 1,478 children with ADHD have been described in detail in a previous paper [21], and the baseline characteristics of the study population are reported in a separate paper of this issue [20]. In the present analysis, we have divided the subjects with ADHD into the following six groups according to the absence or presence of co-existing psychiatric problems: (a) ADHD only (N = 471), (b) ADHD with ANX/DEP (N = 59), (c) ADHD with ODD/CD (N = 244), (d) ADHD with TIC/Tourette's (N = 33), (e) ADHD with COORD (co-ordination problems) (N = 200), and (f) ADHD with two or more of these conditions (N = 363). Anxiety, depression, CD and ODD were defined by clinical ratings based on a 7-point Likert scale, whereas tic disorders and co-ordination problems were assessed as either 'present' or 'not present'. A co-existing problem was considered clinically significant when rated as present or as at least moderately impaired (i. e. score ≥ 4) on the 7-point scale.

The dependent variables in the analyses were grouped into three domains: [1] behavioural features as measured by the ADHD Rating Scale-IV (ADHD-RS-IV) [8], including the overall score and the two subdomain scores for inattention and hyperactivity-impulsivity, and the Strengths and Difficulties Questionnaire (SDQ) [11, 24], consisting of five subscales measuring emotional symptoms, conduct problems, hyperactivity/inattention, peer relationship problems, and prosocial behaviour; [2] psychosocial functioning, including the Clinical Global Impression-Severity (CGI-S) scale [12] and the Children's Global Assessment Scale (CGAS) [25]; and [3] quality of life as measured by the Child Health and Illness Profile-Child Edition (CHIP-CE) [22], which is composed of the five domains of Satisfaction, Comfort, Risk Avoidance, Resilience and Achievement.

Statistical analyses

Comparisons of the six groups of subjects across each of the three dependent variable domains (behavioural fea-

tures, psychosocial functioning and quality of life) were made by multivariate analyses of covariance (ANCOVA), with gender, age and co-existing psychiatric problems (present/absent) as covariates. These analyses were followed by univariate ANCOVA for each individual dependent variable, adjusting for multiple pairwise comparisons between the different subgroups of co-existing psychiatric problems using the Tukey test to identify homogenous subsets.

Results

In the entire ADORE sample at the baseline assessment (N = 1,478), the distribution of co-existing symptoms of any degree was as follows: anxiety (44 %), depression (32 %), CD (46 %), ODD (67 %), tics (8 %), Tourette's (1 %) and co-ordination problems (33 %). Further co-existing problems not considered in the present analyses included obsessive compulsive disorders (2 %), bronchial asthma (8 %) and epilepsy (less than 1 %).

A comparison of the scores across the six groups for behavioural features (ADHD-RS-IV) and psychosocial functioning (CGI-S and CGAS) is given in Table 1. For all variables, the group with multiple psychiatric problems (ADHD + ≥ 2 COND, Group F) was significantly more impaired than the ADHD-only group (Group A) and most other groups. A similar but less consistent pattern emerged for the ADHD plus ODD/CD group (Group C), which showed worse scores than the ADHD-only group and some (though not all) of the other groups. Thus, subjects with multiple psychiatric problems (and less consistently those with ADHD plus ODD/CD) had higher scores on all ADHD scales, a more severe overall clinical picture (CGI-S) and poorer psychosocial functioning (CGAS) than the other groups.

A similar picture emerged from the comparison of the SDQ scores among the six groups, as shown in Table 2. Again, the multiple psychiatric problems group and the ADHD plus ODD/CD group stood out as being different from the other groups. The multiple problems group (Group F) showed more 'abnormal' scores than the ADHD-only group (Group A) and most of the other groups on the SDQ subscales measuring total difficulties, emotional symptoms, conduct problems, hyperactivity/inattention, peer relationship problems, and prosocial behaviour. In addition, the ADHD plus ODD/CD group (Group C) had significantly worse scores for total difficulties, conduct problems, peer relationship problems and prosocial behaviour than the

Table 1 Adjusted mean scores for the ADHD-RS-IV, CGI-S, and CGAS scales across the six groups with co-existing disorders

	ADHD-only (A)	ADHD + ANX/DEP (B)	ADHD + ODD/CD (C)	ADHD + TIC/ Tourette's (D)	ADHD + COORD (E)	ADHD + ≥2 COND (F)	Homogenous subsets
ADHD-RS-IV Overall[a]	33.6 (8.9)	34.2 (9.0)	37.3 (8.9)	33.9 (9.0)	34.1 (8.9)	38.8 (8.9)	F > A,B,D,E; C > A,E
ADHD-RS-IV Inattention subscale[a]	17.9 (4.6)	19.1 (4.6)	19.1 (4.6)	17.5 (4.6)	19.0 (4.6)	20.4 (4.6)	F > A,C,D,E; C > A
ADHD-RS-IV Hyperactivity-Impulsivity subscale[a]	15.6 (5.9)	15.1 (5.9)	18.2 (5.9)	16.4 (6.0)	15.1 (5.9)	18.4 (5.9)	C,F > A,B,E
CGI-S[a]	4.1 (0.8)	4.3 (0.8)	4.6 (0.8)	4.0 (0.8)	4.1 (0.8)	4.8 (0.8)	F > A,B,C,D,E; C > A,D,E
CGAS[b]	58.5 (10.1)	55.8 (10.2)	53.3 (10.2)	54.8 (10.3)	57.2 (10.2)	50.7 (10.1)	F < A,B,E; C < A,E

Data are presented as mean (standard deviation); [a] higher scores indicate worse health; [b] lower scores indicate poorer functioning
WILKS LAMBDA 0.80, F = 11.97, num df = 20; den df = 3546.4; p < 0.001

Table 2 Adjusted mean scores for the SDQ scale across the six groups with co-existing disorders

SDQ scale	ADHD-only (A)	ADHD + ANX/DEP (B)	ADHD + ODD/CD (C)	ADHD + TIC/ Tourette's (D)	ADHD + COORD (E)	ADHD + ≥2 COND (F)	Homogenous subsets
Total Difficulties[a]	18.6 (5.6)	20.1 (5.7)	21.5 (5.6)	19.3 (5.7)	18.4 (5.6)	23.1 (5.6)	F > A,B,C,D,E; C > A,E
Emotional Symptoms[b]	3.7 (2.3)	5.1 (2.3)	4.1 (2.3)	4.6 (2.4)	3.9 (2.3)	5.1 (2.3)	B,F > A,C,E
Conduct Problems[b]	3.9 (2.2)	3.6 (2.2)	5.4 (2.2)	3.8 (2.3)	3.5 (2.2)	4.9 (2.2)	F > A,B,E; C > A,B,D,E
Hyperactivity/Inattention[b]	7.9 (1.7)	7.9 (1.7)	8.2 (1.7)	7.7 (1.7)	8.0 (1.7)	8.5 (1.7)	F > A,E
Peer Relationship Problems[b]	3.1 (2.4)	3.5 (2.4)	3.8 (2.4)	3.3 (2.4)	3.1 (2.4)	4.6 (2.4)	F > A,B,C,D,E; C > A,E
Prosocial Behaviour[b]	7.4 (2.2)	7.5 (2.2)	6.4 (2.2)	7.5 (2.3)	7.5 (2.2)	6.5 (2.2)	C,F < A,B,E

Data are presented as mean (standard deviation)
[a] range 0–40, 'abnormal' score ≥ 17 [based on UK norms]
[b] range 0–10, 'abnormal' score ≥ 4 (conduct problems), ≥ 5 (emotional symptoms), ≥ 7 (hyperactivity/inattention), > 4 (peer relationship problems), ≤ 4 (prosocial behaviour) [based on UK norms]
WILKS LAMBDA 0.82, F = 10.58, num df = 25; den df = 4797.4; p < 0.001

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ADHD-only group (Group A) and various other groups on the SDQ subscale. As expected, the ADHD plus ANX/DEP group (Group B) scored significantly worse on the emotional symptoms scale compared with the ADHD-only group and the groups with either co-existing ODD/CD or co-ordination problems.

Finally, comparisons of the six groups with co-existing disorders for the quality of life domains of the CHIP-CE are shown in Table 3. Once again, the pattern was consistent with the findings for the other scales. The multiple problems group (Group F) displayed significantly greater quality of life impairment (i. e. lower scores) in all CHIP-CE domains compared with most other groups. For the two domains of Risk Avoidance and Resilience, the ADHD plus ODD/CD group (Group C) showed the same pattern and this group also had significantly more impairment in the Comfort and Achievement domains than the ADHD-only group (Group A). The ADHD only group had significantly higher scores (indicating better quality of life) in the Satisfaction domain than all other single co-existing problems groups except the ADHD plus COORD problems (Group E) and ADHD plus tics/Tourette's (Group D).

Discussion

Co-existing problems not only represent an important issue of theoretical reasoning, but also are common both in the general population and in clinical samples. The ADORE study, with its large sample taken from 10 European countries, has allowed us to investigate the impact of co-existing psychiatric problems on the expression of ADHD and overall functioning. The term "co-existence" was preferred over "co-morbidity" in the present paper because it is more appropriate for mental disorders in general and for the design of the ADORE study specifically. The ADORE study did not perform a detailed assessment of associated mental disorders, but rather only asked for clinical overall ratings of various other psychiatric conditions. Besides sample differences, this difference in methods may be one of the reasons why the present study had a rather high proportion of coexisting problems rather than the much lower rate of comorbid anxiety, depression, and ODD ranging between 1.5 and 4.5 % in a recent European drug study based on structured psychiatric interviews [30]. The overall findings were consistent across multiple measures of severity and functioning. ADHD with multiple co-existing psychiatric problems had important clinical consequences in terms of greater severity of ADHD and behavioural problems, poorer psychosocial functioning and greater impairment of quality of life. To our knowledge, such a consistent picture has not been demonstrated before for ADHD. However, there is much concordance with individual findings in the literature. The Oregon Adolescent Depression Project demonstrated the varying clinical consequences of different patterns of co-existing psychiatric conditions, but did not include ADHD [17].

The evidence that ADHD in combination with ODD/CD represents a valid subtype [2, 4, 14] is supported by the present study. In contrast, we found no evidence to support the subtype of ADHD plus ANX/DEP. The present findings also do not support the hypothesis that ADHD in combination with tics/Tourette's or DCDs form valid nosological subtypes or increase the severity of the clinical disorder. However, various studies have found that the combination of ADHD and Tourette's syndrome is associated with more psychopathology and poorer social adaptation than Tourette's syndrome alone [5, 10, 23]. Whilst ADHD and DCD are strongly correlated and together are strongly associated with ODD [15], this study indicates that their combination does not necessarily lead to more behavioural problems. The combination of ADHD with either tics/Tourette's or DCD may only exert a strong impact when multiple psychiatric problems are present. Furthermore, the differences in findings from other studies may be also due to different approaches in study design and assessment.

In conclusion, the present findings in the large ADORE cohort provide impressive evidence for the far-reaching consequences of co-existing psychiatric problems in ADHD that need to be taken into account in clinical practice.

Table 3 Adjusted mean scores (standardised) for the CHIP-CE scale across the six groups with co-existing disorders

CHIP-CE domain	ADHD-only (A)	ADHD + ANX/DEP (B)	ADHD + ODD/CD (C)	ADHD + TIC/ Tourette's (D)	ADHD + COORD (E)	ADHD + ≥2 COND (F)	Homogenous subsets
Satisfaction[a]	36.1 (13.7)	30.0 (13.8)	32.4 (13.7)	35.6 (13.9)	32.7 (13.7)	25.1 (13.7)	F < A,C,D,E; A > B,C,F
Comfort[a]	44.3 (10.2)	41.2 (10.3)	41.0 (10.2)	42.0 (10.4)	43.0 (10.3)	37.5 (10.2)	F < A,C,E; C < A
Risk Avoidance[a]	34.5 (12.9)	35.5 (13.0)	25.7 (12.9)	36.8 (13.1)	34.7 (12.9)	27.4 (12.9)	C,F < A,B,D,E
Resilience[a]	38.6 (11.9)	36.4 (12.0)	33.4 (11.9)	37.0 (12.1)	37.8 (11.9)	33.3 (11.9)	C,F < A,E
Achievement[a]	33.2 (10.2)	30.9 (10.2)	29.6 (10.2)	34.5 (10.3)	31.4 (10.2)	25.6 (10.2)	F < A,B,C,D,E; C < A

Data are presented as mean (standard deviation); [a] higher scores mean better quality of life
WILKS LAMBDA 0.82, F = 10.27, num df = 25; den df = 4626.5; $p < 0.001$

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