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# Is the severity of adolescent conduct disorder associated with the level of nicotine dependence?

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#### Abstract

**Objective:** Our aim was to investigate the relationship between the number of Conduct Disorder (CD) symptoms and specific DSM-IV symptom subscales (i.e. aggression towards people and animals, destruction of property, deceitfulness or theft, and serious violations of rules) and nicotine dependence (ND) among adolescent psychiatric inpatients in Finland.

**Methods:** A total of 171 adolescents with CD (99 boys, 72 girls; age 12-17 years) were admitted to inpatient psychiatric hospitalization between April 2001 and March 2006. Information on their psychiatric DSM-IV diagnoses was obtained using the Schedule for Affective Disorder and Schizophrenia for School-Age Children (K-SADS-PL). The level of ND was assessed with the modified Fagerström Tolerance Questionnaire (mFTQ).

**Results:** The total number of CD symptoms correlated with the level of ND among both the boys (adj. r=0.31, p=0.002) and the girls (adj. r=0.324, p=0.006). For the boys the number of conduct symptoms correlated with the level of ND on all subscales except for aggression, while the only statistically significant correlation for the girls was found with the deceitfulness or theft subscale. A comorbid substance use disorder was statistically significantly associated with a high level of ND among both the boys (p<0.001) and the girls (p=0.019).

**Conclusions**: Our results suggest that both in adolescent boys and girls, the greater the number of CD symptoms, the higher the level of ND. Future studies are needed on the relationship between environmental factors, non-aggressive CD symptoms and the development of ND among adolescents with CD.

Author Keywords: Nicotine dependence, conduct disorder, aggression, adolescent, psychiatric disorders

#### **INTRODUCTION**

Conduct disorder (CD), as defined in the DSM-IV, is characterized by pervasive and persistent patterns of aggressive, deceptive and destructive behaviour with childhood or adolescent onset [1]. The estimated lifetime prevalence of CD in the U.S. is 9.5% (males 12.0%; females 7.1%), with a median age-of-onset of 11.6 years [2].

The prevalence of regular smoking among adolescents with CD has been found to be as high as 48-77% [3, 4, 5]. CD seems to be an independent risk factor for the early initiation of smoking [3, 6] and progression to regular daily smoking [4, 7] or heavy smoking [8], but there have been only a few studies of the association between adolescent nicotine dependence (ND) and CD. Hakko et al. [9] found that the likelihood of a high level of ND as compared with being a non-smoker or having a moderate level of ND was over two-fold among under-aged psychiatric inpatient adolescents with conduct/oppositional disorders. Furthermore, Elkins et al. [10], who were able to investigate prospectively certain dimensional or categorical measures of CD and ADHD in relation to subsequent initiation of smoking and the development of a DSM-IV diagnosis of ND among adolescent twin pairs, found that a diagnosis of CD at the age of 14 years was independently associated with an increased risk of ND (OR 4.27) by 18 years of age even after adjustment for concurrent ADHD.

The DSM IV classifies CD symptoms according to four main subscales: 1) aggression towards people and animals, 2) destruction of property, 3) deceitfulness or theft, and 4) serious violations of rules (DSM IV). As far as we know, there have been no studies to date investigating these CD subscales in relation to adolescent ND. The main goals of the current work were 1) to study whether

the number of CD symptoms is associated with the level of ND as measured by the modified Fagerström Tolerance Questionnaire (mFTQ) [11], 2) to find out whether the type of CD (group type, solitary aggressive type vs. undifferentiated type, and childhood vs. adolescent onset type) is connected with the level of adolescent ND, 3) to investigate whether gender and psychiatric comorbidity among CD adolescents affects the risk of developing ND, and 4) to examine how various CD symptom subscales are associated with the level of ND.

#### **METHODS**

This work is part of the STUDY-70 project, which has been described in detail earlier [12]. The original sample consisted of 508 adolescent inpatients (208 males, 40.9%, and 300 females, 59.1%) aged 12-17 years (mean 15.4 years; sd 1.3) consecutively admitted to Unit 70 at Oulu University Hospital, Department of Psychiatry, between April 2001 and March 2006. The catchment area of Unit 70 covers the regions of Oulu and Lapland, so that all adolescents from this area in need of acute psychiatric hospitalization in a closed ward are initially treated here. Subjects who were over 18 years, mentally retarded, had organic brain disorders or did not give written informed consent to participated in the study. The protocol was approved by the Ethics Committee of Oulu University Hospital, Finland.

#### Subjects with CD

The subjects were interviewed using the Schedule for Affective Disorder and Schizophrenia for School-Age Children, Present and Lifetime (K-SADS-PL), to assess DSM-IV psychiatric diagnoses [13]. K-SADS-PL is a semi-structured interview known to be a reliable method for defining adolescent DSM-IV diagnoses [14, 15]. The interviews were carried out by the treating physician or by trained medical students under the guidance of the treating physician. If data were missing or remained

unreliable after interviewing the adolescent, the material was supplemented by interviewing the parents. Data were recorded on the basis of both information given by the patient and the physician's evaluation of the diagnostic interview. The psychiatric diagnoses of the adolescents were subsequently scrutinized further and were carefully validated against the DSM-IV criteria by two experienced psychiatrists.

A diagnosis of CD required meeting the threshold criteria for at least three of the 15 DSM-IV CD symptoms in the past 12 months, with at least one criterion present in the past 6 months and behaviour causing clinically significant impairment. As the purpose was to investigate pure conduct symptoms, 12 subjects with concurrent ADHD (9 males, 3 females) were excluded from the study. A total of 171 adolescents (99 males and 72 females) met the DSM-IV diagnostic criteria for CD (DSM-IV 312.81, 312.82 or 312.89) and were included in the eventual series. Their mean ages were 15.3 (sd 1.44) and 15.5 (sd 1.29) years for boys and girls respectively (t-test = -0.799, df=169, p=0.425).

#### **CD** subtypes

The cases of CD were categorized into three subtypes based on the adolescents' own reports of whether the conduct symptoms had usually occurred when they were with peers, alone or both with peers and alone, 1) group type, 2) solitary aggressive type, and 3) undifferentiated type, and into two subtypes based on the age of onset of the first CD symptoms, 1) childhood-onset type (onset of at least one criterion prior to 10 years of age), and 2) adolescent-onset type (absence of any criteria prior to 10 years of age). The 15 CD symptoms were investigated in terms of four separate subscales as categorized in DSM-IV: 1) aggression towards people and animals (7 symptoms: initiates physical fights, bullies or threatens others, aggressive stealing, use of a weapon, physical cruelty, forced sexual activity and cruelty to animals), 2) destruction of property (2 symptoms: vandalism and fire setting), 3) deceitfulness or theft (3 symptoms: telling of lies, non-aggressive

stealing and breaking-in), and 4) serious violations of rules (3 symptoms: truancy, frequently staying out at night and running away overnight).

#### **Measure of Nicotine Dependence**

Information on current smoking habits and the level of ND was collected by means of the 7-item modified Fagerström Tolerance Questionnaire (mFTQ) for adolescents [11], the reliability and validity of which have been demonstrated previously [16, 17]. The items in the mFTQ assess the subject's smoking rate, frequency of inhalation, interval between waking up and the first cigarette, level of unwillingness to give up the first cigarette in the morning, difficulty of refraining from smoking in places where it is forbidden, smoking despite medical illness, and smoking more during the first 2 hours than during the rest of the day. The mFTQ sum score can range from 0 to 9. Following Prokhorov et al. (1996), a sum score of 6 or higher was considered to represent a high level of ND in the adolescents.

#### **Comorbid psychiatric diagnoses**

In order to study the association between comorbid psychiatric diagnoses and ND, the diagnoses were categorized into three major groups: 1) affective disorders (DSM-IV 296.2-.3, 300.4, 311), 2) anxiety disorders (300.00-.02, 300.21-.23, 300.29, 300.3, 308.3, 309.81), and 3) substance-related disorders (303.9, 304.0-.6, 304.8-.9, 305.0, 305.2-.7, 305.9). Multiple diagnoses were possible.

#### Family type

Family type was used as a confounding variable in the statistical analysis, since it is known to be associated with both smoking and conduct problems in adolescents [18, 19]. Information on family type was obtained from the K-SADS-PL assessment and covered the adolescents' rearing

environments before admission to hospital. Four family types were recognised for the present purpose: 1) two-parent family (biological mother and biological father), 2) single-parent family (one biological parent), 3) child welfare placement, and 4) other family type (e.g. blended family, foster family).

#### **Statistical Methods**

Statistical significances of group differences were assessed with Pearson's  $\chi^2$  Test or Fisher's Exact Test for categorical variables and with Student's t-Test, the Analysis of Variance (ANOVA) test or the Mann-Whitney U-Test for continuous variables. Partial correlation (adjusted for age) was used to examine the associations between nicotine dependence and the CD subscales. A regression analysis was used to investigate the association of CD symptoms, age and psychiatric disorders (affective, anxiety and substance-related disorders) with the sum score of ND (mFTQ). All the tests were two-tailed and the limit for statistical significance was set at p=0.05. All calculations were carried out using SPSS for Windows, version 18.

#### RESULTS

#### Smoking, comorbid psychiatric diagnoses and ND

The data on family type, the prevalence of regular daily smoking, the level of ND and comorbid psychiatric diagnoses among boys and girls with CD are presented in Table 1. A total 85.9% of the boys and 86.1% of the girls smoked regularly to the extent of at least one cigarette a day, and 40.4% of the boys and 41.7% of the girls reported a high level of ND. The mean ages of the onset of smoking were 11.9 (sd 1.9) and 12.3 years (sd 1.6) for the boys and girls respectively (t-test = -1.33, df=145, p=0.187). The most common comorbid psychiatric diagnosis among both the boys (59.6%) and the girls (66.7%) was substance-related disorders. Comorbid affective and anxiety disorders

were statistically significantly more prevalent among the girls.

Insert Table 1 about here

#### Subtypes of CD and ND

The mean sum score of ND in relation to CD subtypes and comorbid psychiatric diagnoses is presented in Table 2. There was no statistically significant difference in mean sum cores of ND between the types of CD and ages at the onset of CD in either the boys or the girls. A comorbid substance use disorder was statistically significantly associated with a higher level of ND among both the boys (p < 0.001) and the girls (p=0.019). The sum score of ND did not differ significantly between those with or without an affective or anxiety disorder in either the boys or the girls.

Insert Table 2 about here

#### **Correlation between CD and ND**

The mean number of lifetime CD symptoms exceeding the k-SADS threshold level was 6.9 (sd 2.8) among the boys and 5.3 (sd 2.2) among the girls (F= 4.48, df=169, p < 0.001). As seen in Table 3, the total\_number of CD symptoms was positively correlated with the level of ND among both the boys (adj. r=0.310, p= 0.002) and the girls (adj. r=0.324, p= 0.006). Furthermore, the number of CD symptoms correlated with the level of ND among the boys on all subscales except for aggression, whereas the only statistically significant correlation to be found among the girls was on the subscale of deceitfulness or theft

Insert Table 3 about here

#### **Predictors of ND**

A regression analysis was used to examine the association of symptoms of CD, age, affective disorder, anxiety disorder and substance-related disorder with the sum score of ND (Table 4). The model showed statistically significant results in both the boys (F=5.51, p<0.001) and the girls (F=4.53, p=0.001). An increased sum score of ND was statistically significantly associated with an increase in symptoms of CD (p=0.040) and with the presence of a substance-related disorder (p=0.002) in the adolescent boys, while it was shown to be associated with an increase in symptoms of CD in the adolescent girls (p=0.010).

Insert Table 4 about here

#### DISCUSSION

The main finding to emerge from this work was that an increased number of CD symptoms was associated with an increased level of ND in both the adolescent boys and girls. As far as we know, this is the first report of such an association. This association was related to substance use disorder among the boys, but not to any other psychiatric disorders. In the girls psychiatric disorders did not explain the ND-CD association. Also, the number of CD symptoms in the boys correlated with the level of ND on all the subscales except aggression, whereas the only statistically significant correlation for the girls was found with deceitfulness or theft.

Both the initiation of smoking and continuous smoking have been shown to have a strong genetic heritability of around 50%, as also has CD [20, 21, 22], and a group of candidate genes have been studied in an attempt to explain both phenomena [20, 23, 24]. Dopaminergic and serotonergic systems have been considered on account of their influence on smoking/nicotine dependence and CD, in view of the fact that, among many other things, both of these neurotransmitter systems mediate a wide spectrum of cognitive functions such as problem-solving under stress [25, 26], leading to the hypothesis that dysfunction in these systems can cause aggressive behaviour [26]. There have also been suggestions that serotonergic functioning is related to aggression itself [24, 27] and more specifically to a reactive form of aggression, impulsivity and poor emotional regulation [28]. Furthermore, low physiological arousal and reduced noradrenergic function have been shown to be associated with proactive aggression and antisocial behaviour [29]. The DSM-IV criteria for adolescent CD do not differentiate the symptoms by subtypes of aggressive behaviour, i.e. reactive or proactive aggression, and thus future studies with direct behavioural observations and/or valid questionnaires examining reactive vs. proactive aggression in relation to adolescent ND are warranted.

By contrast with the earlier literature, where ND and CD were linked to same genetic background [23, 30], ND was not found here to be related to either the subscale of "aggression towards people and animals" or the "solitary CD" or "childhood-onset CD" subtypes, in spite of the fact that these subtypes are known to be related to life-long persistent antisocial behaviour [31], which has a strong biological background [32]. It is interesting, however, that although the correlation between the number of CD symptoms and the level of ND was present in both genders, our results suggest that aggressive CD and ND are not related, at least in adolescence (before 18 years). On the contrary, ND was related to non-aggressive CD-symptoms of a kind that are often manifested in adolescent peer groups and constitute an only mildly aberrant form of behaviour characteristic of a certain stage in adolescent development. It is possible that heavy smoking and ND among adolescents with CD may be related to familiar factors and peer influences rather than being explained by any single shared genetic factor. A high level of novelty seeking and low avoidance of harm are temperament features that are commonly found to lead to the violation of rules and other disruptive activities in adolescents with CD [33]. This type of behaviour often takes place in peer groups, where both the initiation and continuation of smoking are also more likely to be reinforced. It is also possible that the genetic factor explaining the connection between CD and ND is not associated with aggressive behaviour but with other symptoms of CD.

The strengths of this study were that all the patients were comprehensively interviewed and that the data were gathered using established semi-structured interview techniques [13, 16]. The series consisted of all the psychiatric adolescent patients hospitalized in a large geographical area in northern Finland within a specific space of time and enabled the formation of a reasonably large sample of adolescents with severe conduct disorder and nicotine dependence.

The limitations of our study include the fact that we were unable to study any genetic determinants

of smoking, nor did we have any laboratory tests available to verify the presence of ND. Similarly, no information on parental smoking or other parental substance abuse was available. Furthermore, some authors have criticized the DSM-IV classification of CD symptoms into subscales as being artificial and lacking in empirical justification [2, 34]. It may be difficult to generalize the conclusions drawn here to other settings, due to the fact that the series is a selected sample of adolescents with CD symptoms severe enough to lead to psychiatric hospitalization. Finally, inter-rater agreement was not assessed during the initial data collection phase, because the repeated interviews or videotaping were considered to be too heavy a burden on young adolescents with severe psychiatric symptoms.

In summary, in this study the increased number of CD symptoms was associated with the higher level of ND among underage adolescents. This is as far as we know the first study in which the CD symptom subscales in adolescents have been assessed in relation to the degree of ND. Interestingly, ND was related neither to aggressive features of CD nor to "solitary" or early onset types of CD. We recommend that other substance use habits among adolescents in addition to ND should be investigated in future studies, since comorbid substance use disorders formed a significant covariate in the present analysis. Also of interest in the future would be studies of the genetic relationship between CD and ND - and also the relationship between environmental factors, non-aggressive CD symptoms and the development of ND among adolescents with CD.

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#### **Financial Disclosures**:

The authors have no conflict of interest, financial or otherwise, related directly or indirectly to the submitted work.

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**Table 1.** Family type, smoking status, level of nicotine dependence and comorbid psychiatric diagnoses among boys and girls with conduct disorder.

 Boys	Girls	Gender
(n=99)	(n=72)	difference
n (%)	n (%)	p-value*

Family type			
Two biological parents	20 (20.2)	17 (23.6)	0.257
One biological parent	27 (27.3)	21 (29.2)	
Child welfare placement	43 (43.4)	22 (30.6)	
Other	9 (9.1)	12 (16.7)	
Regular smoking (≥ 1 cig/day)	85 (85.9)	62 (86.1)	0.963
Nicotine dependence			
No ND/Non-smoker	20 (20.2)	12 (16.7)	0.840
Moderate ND	39 (39.4)	30 (41.7)	
High ND	40 (40.4)	30 (41.7)	
Comorbid psychiatric diagnoses			
Affective disorder	30 (30.3)	35 (48.6)	0.015
Anxiety disorder	11 (11.1)	21 (29.2)	0.003
Substance related disorder	59 (59.6)	48 (66.7)	0.346

Note: frequencies indicate positive response if not otherwise specified

\* Pearson's Chi-square Test or Fisher's Exact Test, two-tailed significance.

**Table 2.** Difference of mean sum score of the modified Fagerström Tolerance Questionnaire for nicotinedependence among adolescents in relation to type of conduct disorder and comorbid psychiatric diagnoses.

	Sum score of mFTQ			
	Adolescent boys		Adoles	scent girls
	mean (sd)	p-value*	mean (sd)	p-value*
			GIRLS	
Type of CD		0.120		0.724
Group type	4.4 (2.3)		4.8 (2.3)	
Solitary aggressive type	3.9 (2.7)		4.6 (2.3)	
Undifferentiated type	5.3 (2.3)		5.2 (1.9)	
Type of CD onset		0.807		0.935
Childhood-onset type	4.4 (2.5)		4.7 (2.2)	
Adolescent-onset type	4.5 (2.3)		4.7 (2.3)	
Comorbid psychiatric diagnoses				
Affective disorder		0.371		0.101
Yes	4.2 (2.3)		5.3 (1.9)	
No	4.7 (2.5)		4.4 (2.5)	
Anxiety disorder		0.343		0.209
Yes	3.9 (2.8)		5.3 (2.2)	
No	4.6 (2.4)		4.6 (2.2)	
Substance related disorder		<0.001		0.019
Yes	5.4 (1.9)		5.3 (2.4)	
No	3.3 (2.5)		4.0 (2.0)	

Note: mFTQ = the modified Fagerström Tolerance Questionnaire for nicotine dependence among adolescents [11]

\* Student's t-test or Analysis of Variance (ANOVA) test, two-tailed significance.

**Table 3.** Correlation between the number of symptoms on each Conduct Disorder subscale and the sumscore on the Fagerström Tolerance Questionnaire (mFTQ) .

Number of symptoms	r	p-value	adį r	p-value
		F	,	
BOYS				
Total number of symptoms	0.358	<0.001	0.310	0.002
Aggression	0.140	0.167	0.067	0.514
Destruction of property	0.231	0.022	0.224	0.026
Deceitfulness or theft	0.256	0.011	0.214	0.035
Serious violations or rules	0.297	0.003	0.334	0.001
GIRLS				
Total number of symptoms	0.406	<0.001	0.324	0.006
Aggression	0.169	0.156	0.143	0.235
Destruction of property	0.097	0.419	0.037	0.760
Deceitfulness or theft	0.362	0.002	0.328	0.005
Serious violations or rules	0.244	0.039	0.191	0.110

adj r = partial correlation, age-adjusted

**Table 4.** Predictors for ND among male and female adolescents.

ADOLESCENT BOYS	β	t	p-value
Symptoms of CD Age at admission Affective disorder	0.22 -0.05 -0.09	2.09 -0.43 -0.96	0.040 0.672 0.337
Anxiety disorder	0.03	0.32	0.748
Substance related disorder	0.35	5.25	0.002
ADOLESCENT GIRLS			
Symptoms of CD	0.30	2.66	0.010
Age at admission	0.17	1.41	0.163
Affective disorder	0.14	1.27	0.208
Anxiety disorder	0.01	0.06	0.955
Substance related disorder	0.18	1.59	0.117

Note: Regression analysis, dependent variable was the Fageströn sum score for nicotine dependence.