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Childhood Trajectories of Inattention, Hyperactivity and Oppositional Behaviors and Prediction of Substance Abuse/Dependence: A 15-Year Longitudinal Population-Based Study

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Abstract

Numerous prospective studies have shown that children diagnosed with ADHD are at higher risk of long-term substance abuse/dependence. However, there are two important limits to these studies: a) most did not differentiate the role of hyperactivity and inattention; b) most did not control for associated behavioral problems; c) most did not consider females. Our aim was to clarify the unique and interactive contributions of childhood inattention and hyperactivity symptoms to early adulthood substance abuse/dependence. Behavioral problems of 1804 participants (814 males) in a population-based longitudinal study were assessed yearly between 6 and 12 years by mothers and teachers. The prevalence of substance abuse/dependence at age 21 years was 30.7% for nicotine, 13.4% for alcohol, 9.1 % for cannabis and 2.0% for cocaine. The significant predictors of nicotine dependence were inattention (OR: 2.25; 95% CI: 1.63–3.11) and opposition (OR: 1.65; 95%: 1.20–2.28). Only opposition contributed to the prediction of cannabis dependence (OR: 2.33; 95% CI: 1.40–3.87) and cocaine dependence (OR: 2.97; 95% CI: 1.06–8.57). The best behavioral predictor of alcohol abuse/dependence (opposition) was only marginally significant (OR: 1.38; 95% CI: 0.98–1.95). Frequent oppositional behaviors during elementary school were clearly the most pervasive predictors of substance abuse/dependence in early adulthood. The association of childhood ADHD with substance abuse/dependence is largely attributable to its association with opposition problems during childhood. However, inattention

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Conflict of interest

The authors declare no conflict of interest.

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remained a key predictor of nicotine dependence, in line with genetic and molecular commonalities between the two phenotypes suggested in the literature.

Keywords

Nicotine; cannabis; alcohol; inattention; hyperactivity; opposition

Attention Deficit/Hyperactivity Disorder (ADHD) has been shown to predict many long-term negative outcomes,¹⁻⁵ including substance abuse/dependence.^{6, 7} However, past research suffers from several shortcomings that limit our understanding of the specific role of ADHD symptoms. Of interest is whether inattention and/or hyperactivity symptoms are responsible for the association between ADHD and substance abuse/dependence and if this association remains significant after controlling for other behavioral problems. We address these and other questions in a large population-based sample of boys and girls followed between the ages of 6 and 21 years.

In a recent meta-analytic review⁶ including 13 prospective studies of participants diagnosed with ADHD in childhood and followed after age 18 years, ADHD children were found to be at higher risk of alcohol, cannabis, nicotine as well as drug use disorder (non alcohol). Not all of these results were robust to meta-analysis control procedures (e.g. removing one study and re-estimating the effect). In another recent meta-analysis⁷ including 27 prospective studies assessing substance disorders in adolescence and adulthood, childhood ADHD prospectively predicted adolescent/adult nicotine, alcohol, cannabis, and cocaine use disorders (i.e., abuse or dependence). Analyses were more robust to meta-analysis control procedures. Thus, there is solid evidence to demonstrate that children diagnosed with ADHD are at higher risk of long-term substance disorders. However, a number of conceptual and methodological problems in previous studies limit the conclusions that can be drawn about the unique role of inattention and hyperactivity symptoms as predictors of substance abuse/dependence.

First, few studies distinguished between inattention and hyperactivity symptoms.^{7, 8} This distinction appears essential as the two dimensions of ADHD can make specific contributions depending on the substance outcome.^{9, 10} For instance, it has been suggested that inattention symptoms play a specific role in the prediction of nicotine dependence. Based on the genetic and molecular commonalities between nicotine use and hyperactivity (i.e. dopaminergic and nicotinic-acetylcholinergic circuits), some authors hypothesized that nicotine use may help the self-regulation of inattention.^{7, 10, 11} Second, few studies have adequately controlled for other externalizing problems⁷ which have also been found to predict substance abuse/dependence. In studies which did control for the co-occurrence of other externalizing problems, the unique predictive contribution of ADHD symptoms was less evident.⁷ Consequently, it has been suggested that the role of ADHD symptoms in the prediction of substance abuse/dependence has been overstated.⁸ In addition, the few studies accounting for the comorbidity of other externalizing problems mostly considered conduct disorder, overlooking the putative role of opposition. Yet, opposition appears to be an important possible confounder since its prevalence is higher and mostly stable in childhood, in particular for girls.¹² Furthermore, ADHD seems more strongly linked with oppositional than with conduct disorder symptoms.¹² Third, it has also been suggested that ADHD symptoms act as a trigger to early onset of substance abuse^{7, 10} and more studies are needed to verify this possibility. Fourth, most studies were conducted with clinically based samples and few included girls. Thus, studies with population-based samples are needed to verify whether the findings hold true in the general population and are similar for boys and girls.^{8, 11, 13} Fifth, there is considerable evidence to show that ADHD symptoms are

continuously distributed in the population,¹⁴ the same being true for substance abuse/dependence.⁷ Diagnoses, compared to dimensional measures, might lead to underestimate the association between ADHD symptoms and substance abuse/dependence symptoms.¹⁰ Finally, the role of moderators must be considered because they may diminish (e.g. anxiety) or exacerbate (e.g. opposition) the role of ADHD symptoms in the prediction of substance abuse/dependence.^{13, 15, 16}

Two studies have tackled some of these issues. The Minnesota Twin Family Study followed¹³ a population-based sample of 1512 children from 11 to 18 years and showed that hyperactivity/impulsivity symptoms predicted most substance abuse/dependence outcomes. Inattention did not contribute except possibly for nicotine dependence. The Christchurch Health and Development Study¹⁵ followed a cohort of 1265 children from 7 to 25 years and found that attentional problems (including hyperactivity) did not predict most substance abuse/dependence outcomes after adjustment for externalizing behaviors, anxiety and adversity. Therefore, whereas the first study found a prominent role for hyperactivity/impulsivity, this was not the case for the second study. Several aspects of these two studies may explain the discrepant findings. First, in adolescence, rates of substance abuse/dependence have not yet reached their peak,¹⁰ and only the Christchurch study followed the children until adulthood. Furthermore, the Christchurch study controlled for more variables – anxiety, adversity as well as a measure of externalizing behaviors which included opposition. However, the Christchurch study did not distinguish between inattention and hyperactivity symptoms, which may have prevented the detection of associations.

In the present study we followed longitudinally a population-based sample of male and female participants from 6 years to early adulthood to verify: 1) whether inattention and hyperactivity symptoms differentially predict substance abuse/dependence diagnoses; age at onset of first symptom; and a dimensional measure of substance abuse/dependence (i.e. count of lifetime symptoms); 2) whether these predictions are independent from oppositional behaviors, anxiety and adversity; 3) whether these relationships are moderated by sex or levels of oppositional or anxious behaviors.

Method

Participants

The 1803 participants (814 males) belonged to a large cohort of kindergarten children in Quebec's French-speaking public schools (Canada) who were first assessed in 1986–1987 (for details^{17, 18}). For the present study, we selected the 1803 participants who had a valid diagnosis of substance abuse/dependence in early adulthood. To characterize the present sample, we compared it to a sample of 2,000 (1001 males) children belonging to the same cohort and who were selected to be representative of kindergarten children Quebec's French-speaking public schools (Canada).¹⁹ Table 1 presents the characteristics of the two samples: no significant difference was found on initial socioeconomic characteristics (e.g. income, education, intact families). Children did not differ on several behavioral characteristics (anxiety, teachers' rated inattention). Small significant differences (Cohen $d < .20$) were noted for mothers' rated inattention and for hyperactive and oppositional behaviors, more frequent in the study sample. The percentage of males was also lower in the present study (45.1%) than in the representative sample (50.1%). Overall, the study sample was highly similar to the representative sample of the initial cohort.

Measures

Substance abuse/dependence—To assess abuse/dependence, we used the Diagnostic Interview Schedule (DIS), based on DSM-III-R criteria.^{20, 21} The interview took place when

participants were aged between 19 and 23 years (Mean = 20.88; SD = 0.85). Regarding diagnosis, the absence of abuse/dependence was coded 0; presence of either abuse, mild, moderate, severe dependence was coded 1. The count of lifetime symptoms was also available. Finally, for each diagnosis, participants were asked their age at onset of first symptom.

Behaviors—Children were rated by teachers using the SBQ²² each year between kindergarten and sixth grade, providing seven assessment points from the age of 6 to 12 years (in Quebec, at this age, a teacher teaches only at one level so that the assessments were made by a different teacher each year). Mothers also rated children with the SBQ each year. The SBQ is based upon the Children’s Behavior Questionnaire²³ and the Preschool Behavior Questionnaire²⁴ which both demonstrated good psychometric properties, which was also true for the SBQ.²² Each item of the SBQ was rated from 0 to 2 (“never applies” to “frequently applies”). Four items assessed inattention: 1) weak capacity for concentration 2) easily distracted 3) absentmindedness 4) gives up easily (Cronbach’s alphas for the seven assessments ranged between 0.84 and 0.90 for teachers and between .71 and .81 for mothers). Hyperactivity was assessed with two items: 1) restless, runs about, or jumps up and down, does not keep still 2) squirmy, fidgety child (alphas for the seven assessments ranged between 0.83 and 0.88 for teachers and between .76 and .79 for mothers). For the last 5 years (8 to 12 years), three additional items were available to assess hyperactivity/impulsivity, which we used in sensitivity analyses restricted to this period. These additional items were: 3) Jumps from one activity to another 4) Shouts to draw attention 5) Acts without thinking (alphas for the 5 items of hyperactivity/impulsivity ranged between .82 and .86 for teachers; .75 and .76 for mothers). Opposition included 5 items available at all ages: 1) Irritable, quick to “fly off the handle” 2) Is disobedient 3) Doesn’t share toys 4) Blames others 5) Inconsiderate of others (alphas between 0.80 and 0.85 for teachers; .63 and .69 for mothers). Anxiety-depressive symptoms consisted of five items available at all ages: (a) Is worried. Worries about many things (b) Tends to do things on his own, rather solitary (c) Appears miserable, unhappy, tearful, or distressed (d) Tends to be fearful or afraid of new things or new situations (e) Cries easily (alphas between 0.72 and 0.76 for teachers; 0.58 and 0.66 for mothers).

Family Adversity Index—The index was based on information collected at the start of the study when the children were finishing kindergarten. The index was created by averaging the following indices: 1) family structure (intact or not intact), 2) parents’ levels of education, 3) parents’ occupational status,²⁵ and 4) parents’ age at the birth of the first child. Families at or below the 30th percentile for each of these indices (or a non intact family) were coded as having 1 adversity point. The family adversity score ranges from 0 to 1.

Data Analysis

Trajectories—To take into account the richness of the seven yearly teachers’ and mothers’ ratings of behavioral problems, we utilized developmental trajectory analyses. We estimated trajectories of inattention, hyperactivity, opposition and anxiety/depressive symptoms using k-means for longitudinal data.²⁶ In this procedure, participants who are homogenous in their behavioral evolution are assigned to a given trajectory. In the present study, we employed a three-dimensional version of this procedure to estimate joint trajectories that relied on the repeated assessments of both teachers and mothers. This procedure is original as it provides developmental trajectories of each behavior (e.g. inattention) relying on two types of informants instead of one; mental health data from multiple informants is considered more valid than data from a single informant.²⁷

Prediction of substance abuse/dependence—We utilized a logistic regression to examine the predictive links between the trajectories and diagnoses of abuse/dependence. Survival models (Cox regression²⁸) were used to examine the behavioral trajectories as predictors of age at first symptom. We used the diagnosis as the survival binary variable and age at first symptom as the time variable.

Missing data and complementary analyses—All children but 5 had at least one teacher's and one mother's assessment for each of the 4 behavioral dimensions and were included in the estimation of the trajectories.²⁶ The 5 children were removed. Of the remaining children, 82 (4.6%) had missing data for the family adversity index. We conducted a single imputation of the index missing values by utilizing the constituent variables of the index as well as behavioral characteristics of the child at age 6 years as assessed by teachers and mothers (later behaviors and adult data were not used in the imputation).²⁹

To test whether the results were sensitive to the statistical techniques we utilized, we averaged the behavioral scores over five years (8 to 12 years) instead of using trajectories. We conducted these analyses separately with mothers' and teachers' ratings and used assessments of hyperactivity/impulsivity (with the 5 items available between 8 and 12 years). We estimated two-way interactions between all variables included in the model. Given the number of interactions tested for each substance abuse/dependence model (6 variables, 15 two-ways interactions), we calculated false discovery rates.³⁰ Finally, we wanted to ascertain whether childhood behaviors were predictive of the severity of substance abuse/dependence. Therefore, we modeled the count of lifetime symptoms using hurdle regression models³¹, which are detailed in the online material.

Results

Behavioral trajectories—Percentages of participants in each trajectory are presented in Table 2 (first column). We provide an online file which allows the reader to explore the three-dimensional trajectories in a dynamic fashion (see Supplemental Figure 1). Of interest is the fact that 17.9% of children had high levels of hyperactivity as assessed by both mothers and teachers. However, 30.8% children were rated almost as highly hyperactive by mothers than the previous group but manifested almost no hyperactivity according to teachers' ratings. This discrepancy in ratings is interesting as it shows that children in this group are found hyperactive only by mothers. A similar group was observed for both oppositional and anxiety/depressive behaviors whereas it was not the case for inattention.

Prediction of substance abuse/dependence—A total of 30.7% of the participants reported nicotine dependence (mild, moderate or severe); 13.4% of the participants reported alcohol abuse or dependence (mild, moderate or severe). Cannabis abuse or dependence (mild, moderate or severe) affected 9.1% of the participants. Regarding other illicit drug use, only cocaine was used by at least 1% of the participants. Consequently, we restricted the analyses to cocaine abuse/dependence (2.0%).

We report the predictive values of the trajectories in Table 2. Regarding nicotine dependence, inattention was a key predictor. Children in the high (OR: 2.25; 95%: 1.63–3.11) and medium (OR: 1.78; 95%: 1.37–2.32) trajectories of inattention were at a higher risk of nicotine dependence. Opposition trajectories were, to a smaller extent, also significantly associated with nicotine dependence. Hyperactivity trajectories did not contribute.

For cannabis, only opposition trajectories made a significant contribution (high trajectory, OR: 2.33; 95% CI: 1.4–3.87). Interestingly children rated as oppositional by mothers only were also at higher risk of cannabis abuse/dependence (OR: 2.01; 95% CI: 1.33–3.05). Regarding cocaine, only the high trajectory of opposition made a significant contribution (OR: 2.97; 95% CI: 1.06–8.57). Finally, for alcohol, only one of the opposition trajectories – children rated high only by mothers – made a contribution that was marginally significant: (OR: 1.38; 95% CI: 0.98–1.95). As relative merits of Odds Ratios and Risk Ratios are debated³² we also present Risk Ratios (see online comments and Supplemental Table 1) along with percentages of substance abuse/dependence in each trajectory.

Survival models' results are reported in Table 3. Inattention trajectories were predictive of nicotine dependence. Figure 1 illustrates the adjusted contribution of inattention to age at onset of first symptoms from early adolescence to early adulthood for girls. The contributions of hyperactivity and opposition trajectories were also very similar to their contributions estimated from logistic regressions.

Complementary analyses

Analyses with average means of behaviors instead of trajectories yielded very similar results overall (see online comments & Supplemental Table 2). To summarize, mothers' and teachers' ratings of inattention were still predictive of nicotine dependence. The use of the five items measure of hyperactivity/impulsivity did not change the fact that this dimension was never predictive. Mother-rated opposition significantly predicted most outcomes whereas teacher-rated opposition was less predictive.

We tested two-way interactions between all variables included in the model, using average means of behaviors. Very few interactions were significant: accepting even only one interaction in each substance abuse/dependence model would have yielded unacceptably high false discovery rate (superior to .10 in most models). Furthermore, the few significant interactions between behavioral variables were negative, contrary to the hypothesis of a synergic effect but coherent with results from a previous study.¹⁵ Regarding sex, very few interactions were significant with the exception of a negative interaction with opposition in the prediction of alcohol abuse/dependence, suggesting that opposition was a significant predictor for women and not for men.

Finally, we modeled the count of lifetime symptoms with hurdle models (see comments and Supplemental Table 3 & 4). To summarize, inattention predicted the absence/presence of symptom(s) but also the count of lifetime symptoms, suggesting that inattention predicts the severity of nicotine dependence. In these analyses, opposition appeared as a predictor of the count of symptoms in the case of cannabis and alcohol abuse/dependence. Anxiety/depressive symptoms appeared as a protective factor against the presence of symptom(s) in the case of nicotine, cannabis and alcohol.

Discussion

The aim of the present study was to clarify the contributions of inattention and hyperactivity symptoms to early adulthood substance abuse/dependence, net of possible confounders and in combination with possible moderators. In particular, we wanted to verify whether inattention and hyperactivity symptoms played a different role depending on the type of substance; whether that role was maintained when opposition, anxiety and adversity were controlled for; and whether interactive effects with sex, family adversity and with other behavioral dimensions could be detected. We found that oppositional behaviors were the most pervasive predictors of substance abuse/dependence, i.e. for nicotine, cannabis, cocaine and alcohol. However, for the latter outcome, the results were less consistent across

analyses. Inattention was a key predictor of the diagnosis of nicotine abuse/dependence as well as its severity assessed by the number of lifetime symptoms. Hyperactivity did not predict any outcome nor did it predict age at onset of first symptom. We found no consistent interactive effects.

The results of the present study are coherent with studies casting doubt on the real contribution of ADHD symptoms to later substance abuse/dependence when comorbid externalizing behaviors are controlled for.^{7, 8, 15} Fergusson et al.^{15, 33} proposed a dual-pathway model where attentional problems contribute to academic achievement whereas conduct problems contribute to substance abuse/dependence and criminality. In their model, crossed contributions (e.g. contributions of attentional problems to substance abuse) are viewed as a collateral effect of their comorbidity with other externalizing problems and, therefore, spurious. In their model, each of the two childhood behavioral dimension (i.e. attentional problems and disruptive behaviors) has its own specific consequences on adult outcomes.^{15, 19, 33, 34} Our study partially supports this model as hyperactivity and inattention did not contribute to most substance outcomes when opposition and other control variables were taken into account.

Nevertheless, some studies have reported a contribution of inattention and/or hyperactivity symptoms to substance abuse/dependence even after controlling for conduct disorders. In particular, the Minnesota Twin Family Study,¹³ a large population-based prospective study reported that hyperactivity/impulsivity symptoms predicted most substance abuse/dependence outcomes in adolescence even after controlling for conduct disorders. However, this study had less control variables (i.e. adversity and anxiety) than the present study and controlled for conduct disorder which may represent a less stringent control than opposition because it is less frequent during childhood, in particular for girls.¹² Thus, some significant contributions reported in the literature may have come from insufficient control for comorbid behaviors as well as adversity. Furthermore, even in the Minnesota Twin Family Study, the contribution of hyperactivity/impulsivity symptoms to adult substance use disorders was smaller than the contribution of conduct disorders. Overall, we are tempted to share Looby's concern that the role of ADHD symptoms in the development of substance use disorders has been overstated.⁸

Albeit true for most outcomes, the previous statement is not supported in the case of nicotine dependence. Indeed, we found a solid association of inattention symptoms with nicotine dependence. Such an association has been reported in the literature^{7, 10, 11} and our study offers a confirmation of this association in a 15 years prospective study of a population-based sample of boys and girls followed into early adulthood. Furthermore, we demonstrated that inattention symptoms were associated not only with the presence of nicotine dependence but also with the severity of this dependence as assessed by the number of lifetime symptoms. People with inattention symptoms may initiate smoking to alleviate symptoms of inattention as well as to improve executive functions and working memory.^{10, 13, 35} This mitigation of impairing symptoms by nicotine could involve dopamine reward processing system and nicotinic-acetylcholinergic circuits, with a possible interaction with ovarian hormones in women.^{11, 36, 37} If this causal pathway between ADHD symptoms and smoking is verified, prevention aiming at diminishing inattention symptoms should reduce the development of nicotine dependence. Furthermore, in people with both smoking dependence and inattention symptoms, treating the inattention symptoms should help in the success of smoking dependence treatment.¹¹

Strengths and Limitations

To the best of our knowledge, this study is the first prospective population-based study to assess the contribution of both inattention and hyperactivity symptoms to substance abuse/

dependence in early adulthood, whilst controlling for opposition, anxiety and adversity. Despite its strengths, some limitations need to be acknowledged.

Because of their low prevalence, we were unable to model abuse/dependence to illicit drugs other than cannabis and cocaine. Regarding survival models, we used participants' retrospective recollection of age at first symptom and not repeated diagnoses over the years. Additionally, the instrument used to assess childhood externalizing problems was not a diagnostic tool. However, it has proven to be predictive of a range of adult and adolescent outcomes in numerous studies,^{18, 34, 38, 39} and our predictive results were based on seven repeated assessments over a 7-year period from mothers and teachers.

Conclusion

We demonstrated in a large prospective sample that childhood inattention made a unique contribution to early adulthood nicotine dependence; that oppositional behaviors represented a predictor of nicotine, cannabis, cocaine and alcohol abuse/dependence whereas hyperactivity was not. In terms of theory, these findings argue in favor of specific childhood behavioral predictors for specific substance abuse/dependence outcomes, in particular regarding the link between inattention and nicotine dependence. In terms of practice, the results suggest that prevention or treatment of externalizing problems prior to the initiation of substance use could reduce the risk for substance use disorders.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Frazier TW, Youngstrom EA, Glutting JJ, Watkins MW. ADHD and achievement: Meta-analysis of the child, adolescent, and adult literatures and a concomitant study with college students. *J Learn Disabil.* 2007 Feb;40:49-65. [PubMed: 17274547]
2. Polderman TJC, Boomsma DI, Bartels M, Verhulst FC, Huizink AC. A systematic review of prospective studies on attention problems and academic achievement. *Acta Psychiatr Scand.* 2010 Oct;122:271-84. [PubMed: 20491715]
3. Hofvander B, Ossowski D, Lundström S, Anckarsäter H. Continuity of aggressive antisocial behavior from childhood to adulthood: The question of phenotype definition. *Int J Law Psychiatry.* 2009 Aug;32:224-34. [PubMed: 19428109]
4. Mannuzza S, Klein RG, Moulton JL III. Lifetime criminality among boys with attention deficit hyperactivity disorder: A prospective follow-up study into adulthood using official arrest records. *Psychiatry Res.* 2008 Sep;160:237-46. [PubMed: 18707766]
5. Rasmussen P, Gillberg C. Natural outcome of ADHD with developmental coordination disorder at age 22 years: A controlled, longitudinal, community-based study. *J Am Acad Child Adolesc Psychiatry.* 2000 Nov;39:1424-31. [PubMed: 11068898]

6. Charach A, Yeung E, Climans T, Lillie E. Childhood attention-deficit/hyperactivity disorder and future substance use disorders: Comparative meta-analyses. *J Am Acad Child Adolesc Psychiatry*. 2011 Jan;50:9–21. [PubMed: 21156266]
7. Lee SS, Humphreys KL, Flory K, Liu R, Glass K. Prospective association of childhood attention-deficit/hyperactivity disorder (ADHD) and substance use and abuse/dependence: A meta-analytic review. *Clin Psychol Rev*. 2011 Apr;31:328–41. [PubMed: 21382538]
8. Looby A. Childhood attention deficit hyperactivity disorder and the development of substance use disorders: Valid concern or exaggeration? *Addict Behav*. 2008 Mar;33:451–63. [PubMed: 18037571]
9. Lee SS, Hinshaw SP. Predictors of adolescent functioning in girls with attention deficit hyperactivity disorder (ADHD): The role of childhood ADHD, conduct problems, and peer status. *J Clin Child Adolesc Psychol*. 2006 Sep;35:356–68. [PubMed: 16836474]
10. Molina BSG, Pelham WE Jr. Childhood predictors of adolescent substance use in a longitudinal study of children with ADHD. *J Abnorm Psychol*. 2003 Aug;112:497–507. [PubMed: 12943028]
11. McClernon FJ, Kollins SH. ADHD and smoking: From genes to brain to behavior. *Ann N Y Acad Sci*. 2008 Oct;1141:131–47. [PubMed: 18991955]
12. Maughan B, Rowe R, Messer J, Goodman R, Meltzer H. Conduct disorder and oppositional defiant disorder in a national sample: Developmental epidemiology. *J Child Psychol Psychiatry*. 2004 Mar;45:609–21. [PubMed: 15055379]
13. Elkins IJ, McGue M, Iacono WG. Prospective effects of Attention-Deficit/Hyperactivity Disorder, conduct disorder, and sex on adolescent substance use and abuse. *Arch Gen Psychiatry*. 2007 Oct;64:1145–52. [PubMed: 17909126]
14. Snowling M. Editorial: Multiple perspectives on ADHD: Implications for future research. *J Child Psychol Psychiatry*. 2009 Sep;50:1039–41. [PubMed: 19709089]
15. Fergusson DM, Horwood LJ, Ridder EM. Conduct and attentional problems in childhood and adolescence and later substance use, abuse and dependence: Results of a 25-year longitudinal study. *Drug Alcohol Depend*. 2007 Apr; 88(Suppl 1):S14–26. [PubMed: 17292565]
16. Levy F. Synaptic gating and ADHD: A biological theory of comorbidity of ADHD and anxiety. *Neuropsychopharmacology*. 2004 Sep;29:1589–96. [PubMed: 15114344]
17. Zoccolillo M, Vitaro F, Tremblay RE. Problem drug and alcohol use in a community sample of adolescents. *J Am Acad Child Adolesc Psychiatry*. 1999 Jul;38:900–7. [PubMed: 10405509]
18. Vitaro F, Brendgen M, Larose S, Tremblay RE. Kindergarten disruptive behaviors, protective factors, and educational achievement by early adulthood. *J Educ Psychol*. 2005 Nov;97:617–29.
19. Pingault JB, Tremblay RE, Vitaro F, Carbonneau R, Genolini C, Falissard B, et al. Childhood trajectories of inattention and hyperactivity and prediction of educational attainment in early adulthood: A 16-year longitudinal population-based study. *Am J Psychiatry*. 2011; 168:1164–70. [PubMed: 21799065]
20. Breton JJ, Bergeron L, Valla JP, Berthiaume C, St-Georges M. Diagnostic Interview Schedule for Children (DISC-2.25) in Quebec: Reliability findings in light of the MECA study. *J Am Acad Child Adolesc Psychiatry*. 1998 Nov;37:1167–74. [PubMed: 9808928]
21. Shaffer D, Fisher P, Dulcan MK, Davies M, Piacentini J, Schwab-Stone ME, et al. The NIMH Diagnostic Interview Schedule for Children Version 2.3 (DISC-2.3): Description, acceptability, prevalence rates, and performance in the MECA Study. *J Am Acad Child Adolesc Psychiatry*. 1996 Jul;35:865–77. [PubMed: 8768346]
22. Tremblay RE, Loeber R, Gagnon C, Charlebois P, Larivée S, LeBlanc M. Disruptive boys with stable and unstable high fighting behavior patterns during junior elementary school. *J Abnorm Child Psychol*. 1991 Jun;19:285–300. [PubMed: 1865046]
23. Rutter M. A children's behaviour questionnaire for completion by teachers: Preliminary findings. *J Child Psychol Psychiatry*. 1967 May;8:1–11. [PubMed: 6033260]
24. Behar L, Strinfield S. A behavior rating scale for the preschool child. *Dev Psychol*. 1974; 10:601–10.
25. Blishen BR, Carroll WK, Moore C. The 1982 socioeconomic index for occupations in Canada. *Can Rev Soc Anthropol*. 1987; 24:465–88.
26. Genolini C, Falissard B. KmL: K-means for longitudinal data. *Comput Stat*. 2010; 25:317–28.

27. Achenbach TM, McConaughy SH, Howell CT. Child/adolescent behavioral and emotional problems: Implications of cross-informant correlations for situational specificity. *Psychol Bull.* 1987 Mar.101:213–32. [PubMed: 3562706]
28. Fox, J. *An R and S-Plus companion to applied regression.* Sage Publications; CA: 2002. Cox Proportional-Hazards Regression for Survival Data. Appendix.
29. van Buuren S, Groothuis-Oudshoorn K. mice: Multivariate Imputation by Chained Equations in R. *J Stat Softw.* 2011 Dec.45:1–67.
30. Falissard, B. *Comprendre et utiliser les statistiques dans les sciences de la vie [Understanding and use of statistics in life sciences].* Paris: Masson; 2005.
31. Zeileis A, Kleiber C, Jackman S. Regression models for count data in R. *J Stat Softw.* 2008; 27:2–25.
32. Cummings P. The relative merits of risk ratios and odds ratios. *Arch Pediatr Adolesc Med.* 2009 May.163:438–45. [PubMed: 19414690]
33. Fergusson DM, Horwood LJ. Early disruptive behavior, IQ, and later school achievement and delinquent behavior. *J Abnorm Child Psychol.* 1995 Apr.23:183–99. [PubMed: 7642833]
34. Nagin DS, Tremblay RE. Trajectories of boys' physical aggression, opposition, and hyperactivity on the path to physically violent and nonviolent juvenile delinquency. *Child Dev.* 1999 Oct. 70:1181–96. [PubMed: 10546339]
35. Swan GE, Lessov-Schlaggar CN. The effects of tobacco smoke and nicotine on cognition and the brain. *Neuropsychol Rev.* 2007 Sep.17:259–73. [PubMed: 17690985]
36. Gehricke J-G, Whalen CK, Jamner LD, Wigal TL, Steinhoff K. The reinforcing effects of nicotine and stimulant medication in the everyday lives of adult smokers with ADHD: A preliminary examination. *Nicotine Tob Res.* 2006 Feb.8:37–47. [PubMed: 16497598]
37. Van Voorhees EE, Mitchell JT, McClermon FJ, Beckham JC, Kollins SH. Sex, ADHD symptoms, and smoking outcomes: An integrative model. *Med Hypotheses.* In Press.
38. Côté S, Tremblay RE, Nagin DS, Zoccolillo M, Vitaro F. Childhood behavioral profiles leading to adolescent conduct disorder: Risk trajectories for boys and girls. *J Am Acad Child Adolesc Psychiatry.* 2002 Sep.41:1086–94. [PubMed: 12218430]
39. Fontaine N, Carbonneau R, Barker ED, Vitaro F, Hébert M, Côté SM, et al. Girls' hyperactivity and physical aggression during childhood and adjustment problems in early adulthood: A 15-year longitudinal study. *Arch Gen Psychiatry.* 2008 Mar.65:320–8. [PubMed: 18316678]

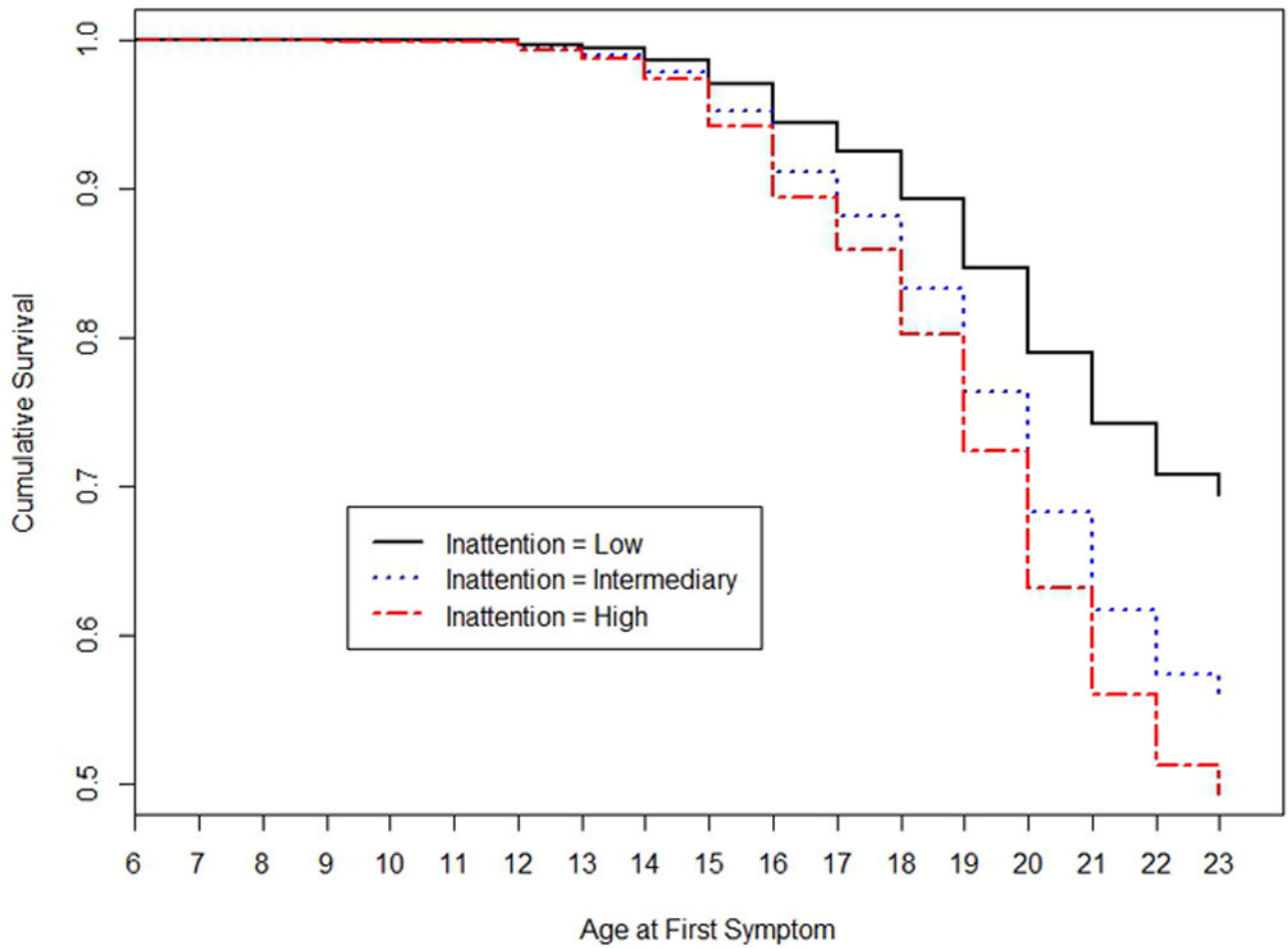


Figure 1. Survival Model: Predictive Value of Female Inattention for Age at First Symptom of Nicotine Dependence

The adjusted effect of inattention was plotted from a multivariate Cox model. The values for covariates were kept at the mean for the adversity index and at the low trajectory level for behavioral variables other than inattention.

Table 1

Comparison of the Study Sample and the Representative Sample

	Study Sample (N = 1803)		Representative sample (N = 2000)		Cohen d (or Phi)
	Mean (or %)	SD	Mean (or %)	SD	
Maternal socioeconomic status	44.25	12.90	43.99	13.00	0.02
Paternal socioeconomic status	44.75	14.63	43.92	14.86	0.05
Maternal education	12.08	2.59	11.95	2.59	0.05
Paternal education	12.27	3.41	12.15	3.44	0.04
Intact family	16.70	-	16.24	-	0.01
Maternal age first child	24.60	3.94	24.58	3.87	0.00
Paternal age first child	26.80	4.11	26.92	4.04	-0.03
Overall family adversity index	0.27	0.25	0.28	0.25	-0.02
Inattention (teacher, 6 years)	1.85	1.31	1.83	1.28	0.01
Hyperactivity (teacher, 6 years)	1.02	1.31	0.91	1.28	0.09**
Opposition (teacher, 6 years)	1.83	2.31	1.41	2.04	0.19***
Anxiety/Depressive symptoms (teacher, 6 years)	1.74	2.03	1.75	2.01	0.00
Inattention (mother, 6 years)	2.58	1.34	2.42	1.31	0.12*
Hyperactivity (mother, 6 years)	1.81	1.34	1.64	1.31	0.13***
Opposition (mother, 6 years)	3.45	1.89	3.11	1.81	0.18***
Anxiety/Depressive symptoms (mother, 6 years)	3.47	2.01	3.38	2.01	0.04
Sex of the child	45.1	-	50.1	-	0.05**

Note. The table presents a comparison between the study sample and a sample from the same cohort (N = 2000) which was selected to be representative of the Kindergarten children in Quebec. Phi coefficients are proposed instead of Cohen d for the variables: intact family; sex of the child.

*** p<.001;

** p<.01;

* p<.05;

† p<.10

Table 2
 Prediction of Substance Abuse/dependence Diagnoses with Behavioral Trajectories

	Nicotine		Cannabis		Cocaine		Alcohol	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Inattention trajectories								
Low ¹ (41.4%) ²								
Medium (33.0%)	1.78***	1.37–2.32	0.84	0.55–1.27	1.18	0.48–3.07	0.91	0.63–1.29
High (25.7%)	2.25***	1.63–3.11	0.72	0.43–1.19	0.80	0.26–2.46	0.93	0.61–1.43
Hyperactivity trajectories								
Low (51.3%)								
High mother only (30.8%)	0.81 [†]	0.63–1.03	0.95	0.64–1.42	1.22	0.51–2.91	0.98	0.70–1.37
High (17.9%)	0.74 [†]	0.53–1.04	1.08	0.64–1.81	1.62	0.57–4.65	0.98	0.62–1.52
Opposition trajectories								
Low (48.0%)								
High mother only (32.3%)	1.33*	1.03–1.71	2.01***	1.33–3.05	1.88	0.75–4.89	1.38 [†]	0.98–1.95
High (19.7%)	1.65**	1.20–2.28	2.33**	1.40–3.87	2.97*	1.06–8.57	1.43	0.93–2.19
Anxiety trajectories								
Low (50.3%)								
High mother only (28.9%)	0.93	0.73–1.19	0.85	0.57–1.25	0.89	0.38–2.04	0.81	0.58–1.13
High (20.8%)	0.76 [†]	0.57–1.01	0.73	0.45–1.17	1.27	0.53–2.96	0.72	0.48–1.06
Adversity	1.66*	1.11–2.49	0.73	0.37–1.4	5.28**	1.60–17.1	1.22	0.70–2.11
Sex	0.77*	0.62–0.96	2.11***	1.49–3.00	0.74	0.36–1.51	2.30***	1.71–3.09

Note. The table presents Odds ratios (OR) and 95% Confidence intervals (CI) from logistic regressions. Behavioral trajectories relying on mothers' and teachers' assessments were used to predict diagnoses of substance abuse/dependence. Analyses were conducted on the 1798 participants with data for behavioral trajectories and diagnoses.

¹Low trajectories are the contrast.

²The percentages in this column correspond to the number of participants in each trajectory. The sum is 100% for each behavior.

*** p<.001;

** p<.01;

0.1 > d
; 50 > d
*

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Table 3

Survival Models of Abuse/Dependence

	Nicotine		Cannabis		Cocaine		Alcohol	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
<i>Inattention trajectories</i>								
Medium	1.61 ^{***}	1.30–2.01	0.85	0.57–1.27	1.18	0.47–2.94	0.90	0.65–1.25
High	1.94 ^{***}	1.49–2.51	0.74	0.46–1.2	0.82	0.27–2.44	0.92	0.62–1.36
<i>Hyperactivity trajectories</i>								
High mother only	0.83 [†]	0.68–1.02	0.95	0.65–1.39	1.23	0.53–2.86	0.98	0.72–1.34
High	0.81	0.62–1.06	1.07	0.66–1.73	1.60	0.57–4.47	0.97	0.65–1.46
<i>Opposition trajectories</i>								
High mother only	1.24 [*]	1.01–1.52	1.96 ^{***}	1.32–2.9	1.86	0.74–4.66	1.35 [†]	0.99–1.86
High	1.47 ^{**}	1.14–1.88	2.21 ^{**}	1.37–3.57	2.92 [*]	1.05–8.14	1.39	0.94–2.06
<i>Anxiety trajectories</i>								
High mother only	0.94	0.77–1.15	0.86	0.6–1.24	0.90	0.39–2.05	0.82	0.60–1.11
High	0.81 [†]	0.65–1.02	0.74	0.47–1.17	1.25	0.54–2.87	0.73	0.51–1.06
Adversity	1.36 [†]	0.98–1.89	0.72	0.38–1.36	5.1 ^{**}	1.61–16.17	1.23	0.74–2.02
Sex	0.78 ^{**}	0.65–0.93	2.01 ^{***}	1.44–2.8	0.74	0.37–1.50	2.15 ^{***}	1.63–2.83

Note. The table presents Hazard Ratios (HR) and 95% Confidence Interval (CI) from Cox models. The time variable is the age at first symptom for each outcome as reported by the young adult at the time of diagnosis. Analyses were conducted on the 1798 participants with data for behavioral trajectories and diagnosis.

*** p<.001;

** p<.01;

* p<.05;

[†] p<.10