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Developmental trajectories of childhood symptoms of hyperactivity/inattention and suicidal

behaviour during adolescence

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Abstract

Hyperactive/inattentive symptoms (ADHD symptoms) are associated with suicidal behaviour in clinical studies, but

there is still a lack of population-based longitudinal investigations on the developmental aspects of this association.

Additionally, it is unclear whether the association is similar for boys and girls. The objectives of the study were to test

the association between the ADHD symptoms during childhood and suicidal ideation and attempt during adolescence,

and to investigate sex differences. 1407 children from the Québec Longitudinal Study of Child Development were

followed up from 5 months to 17 years of age. We used teacher-reports of ADHD symptoms from 6 to 12 years, and

self-report of suicidal ideation and attempt at 13, 15, and 17 years. We identified 3 ADHD symptoms trajectories: low

(boys: 32.2%, girls: 48.7%), moderate (boys: 44.6%; girls: 42.2%) and high (boys: 23.2%; girls: 9.1%). Compared to

boys on a low trajectory, boys on a moderate trajectory were at higher risk for suicidal ideation (OR=4.2, 95% CI=1.2-

14.8), and boys on a high trajectory were at higher risk for suicide attempts (OR: 4.5, 95%CI: 1.1-17.9). Girls on

moderate or high ADHD symptoms trajectories were not at higher risk for suicidal ideation or attempts than girls on

low trajectories.

For boys, but not for girls, moderate-to-high ADHD symptoms increased the suicidal risk in adolescence. Interventions

with boys showing ADHD symptoms should include a suicide prevention component.

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Introduction

Suicidal behavior is most prevalent during adolescence (lifetime prevalence of suicide ideation, plans, and attempts is 12.1%, 4.0%, and 4.1% respectively) [1], and main risk factors for suicide mortality - the second leading cause of death among adolescents [2]. Attention deficit hyperactivity disorder (ADHD), a common disorder affecting 5.3% of children and adolescents [3], is associated with several adult negative outcomes including suicide mortality, suicide attempt and suicidal ideation (SB) [4]. Despite a few reports, there is still a lack of longitudinal investigations on the association between the course of ADHD symptoms during childhood and SB in adolescents at the population level. Indeed, hyperactive and inattentive symptoms were associated with increased risk for SB in some clinical and population-based samples [5-7]. However only a few longitudinal population-based studies investigated the specific association between hyperactivity/inattention and SB [8-10]. Hurtig et al. conducted a population-based study on a Finnish birth cohort and showed an association between a diagnosis of ADHD and suicidal ideation and deliberate self-harm; however, they took into account only clinically relevant ADHD diagnosis without including developmental traits of hyperactivity and inattention throughout childhood. Sourander and colleagues [8] investigated the association between psychopathology at the age of 8 years and later suicide mortality, but did not focus specifically on the association between the development of hyperactivity/inattention and SB. Finally, Galera et al. found that the association between ADHD and SB held only for males [9], but there seem to be not clear consensus regarding sex differences since another study reported opposite results [10]. Given the importance of individualized preventive intervention taking into account sex differences in adolescent SB [11], it is relevant to clarify the extent to which sex differences play a role in SB of children showing hyperactive/inattentive symptoms. The objective of this study was to clarify the predictive association between childhood symptoms of hyperactivity/impulsivity and inattention (ADHD

symptoms) and suicidal ideation and attempt in adolescence. Especially, we investigated whether this association is different among girls and boys. We relied on longitudinal data from a population sample from Québec, Canada, using person-centered methods allowing us to identify children with atypically high ADHD symptoms over the course of childhood, and teacher-assessment of children behaviors.

Methods

Sample

Participants were drawn from the Quebec Longitudinal Study of Child Development (QLSCD), a representative sample of 2120 infants born in Québec, Canada, in 1997/98 and followed up between 5 months and 17 years. Random selection of the initial representative sample was made through the birth registry and following a procedure based on living area and birth rate. Mothers giving birth after 24 weeks of gestation and speaking French or English were eligible to participate in the study. Data were collected annually or bi-yearly from 1998 through 2015. We used teacher-reports of ADHD symptoms from 6 to 12 years, and self-report of suicidal ideation and attempt from 13 to 17 years. The final sample comprised of N=1407 participants for which data were available on SB (Table 1).

[Table 1 about here]

Ethical Consideration

Ethical approval was given by the Quebec Statistics Institute and the St-Justine Hospital Research Centre. Written informed consent was obtained from all participants and their parents at each assessment. All adolescents and their parents were provided with a list of resources in case of needing help.

Measures

Outcome: Past-Year Suicidal Ideation and Suicide Attempt. Suicidal ideation was assessed at 13, 15, and 17 years using the question: "in the past 12 months, did you ever seriously think of attempting suicide" (yes coded 1, no coded 0; answering "don't know" or refusal was coded as missing). If they answered affirmatively, they were asked: "in the past 12 months, how many times did you attempt suicide", dichotomized as 0 versus ≥1. As in our previous publications [12, 13] the following variables were derived: lifetime suicidal ideation (i.e., reporting ≥1 suicide ideation at 13 or 15 or 17 years but never suicide attempt) and lifetime suicide attempt (i.e., reporting ≥1 suicide attempt at 13 or 15 or 17 years).

Exposure: ADHD symptoms during childhood. ADHD symptoms were rated by schoolteachers when participants were 6, 7, 8, 10, and 12 years of age. Items were derived from the Behavior Questionnaire created for the Canadian National Longitudinal Study of Children and Youth, which incorporates items from the Child Behavior Checklist [14], the Ontario Child Health Study Scales [15], and the Preschool Behavior Questionnaire [16]. The following items were used and summedup to obtain the hyperactivity/inattention score at each year (range: 0 to 18; Cronbach's alpha range: 0.74-0.79), for hyperactivity-impulsivity: 1) could not sit still, was restless and hyperactive; 2) was impulsive, acted without thinking; 3) had difficulty waiting for his/her turn in games; 4) couldn't settle down to do anything for more than a few moments; For inattention: 1) was unable to concentrate, could not pay attention for long 2) was easily distracted, had trouble sticking to any activity 3) was inattentive. Each year, a different teacher rated the frequency of these behaviours in the past 6 months (0=never, 1=sometimes, 2=often).

Covariates. We used a parsimonious set of covariates for our multiple regression models, all measured before the exposure variable (i.e. age 6 years). Variables were selected on the basis of the literature [9, 17, 18] and previous studies on the same sample [12, 19, 20]: maternal depressive symptoms, assessed using a short version of the Centre for Epidemiological Study Depression Scale [21]; children depression-anxiety symptoms, assessed by teachers at age 6 and measured with 5 items (3 for anxiety, e.g., "was too fearful or anxious" and 2 for depression, e.g., "seemed to be unhappy or sad;"); family socioeconomic status (SES) at 5 months, an aggregate index of annual gross income, parental education level, and occupational prestige, based on Willms and Shields (range -3=low SES to 3=high SES, centered at zero) and dichotomized into low (i.e, 0-25th percentile) vs non-low (25th-75th percentile). [22]. All questionnaires are available online (http://www.jesuisjeserai.stat.gouv.qc.ca).

Statistical Analyses

First, we estimated the developmental trajectories of ADHD symptoms among girls and boys, using Group based-trajectory modeling [23]. This approach is based on semiparametric mixture models, and allows us clustering children according to the similarities of their developmental pattern of ADHD symptoms from 6 to 12 years. Both the best number of trajectories and the polynomial order of the trajectories (i.e., intercept only, linear or quadratic; determining the shape of the trajectory) were defined by comparing multiple models on the Bayesian Information Criterion [23].

Second, we used binary logistic regressions to test the predictive association between trajectory membership and suicidal ideation and attempt. We estimated unadjusted models as well as models adjusted for the influence of the selected covariates. Missing data on these covariates were handled using multiple imputations by chained equation: the models were estimated on 50 complete

datasets, and the results were pooled. Data analysis was performed using Stata version 14, and the trajectories were estimated using the *traj* procedure.

Results

Prevalence of suicidal ideation and suicide attempt

At 13, 15, and 17 years respectively, 23 (1.9%), 43 (3.3%), and 51 (4.3%) adolescents reported suicidal ideation in the past year, while at those same ages respectively 28 (2.4%), 37 (2.8%), and 28 (2.4%) adolescents reported suicide attempt in the past year. In total, 29 boys (4.3%) and 60 girls (8.1%) reported suicidal ideation at least at one assessment (i.e., lifetime suicidal ideation), while 19 boys (2.8%) and 61 girls (8.2%) reported suicide attempt at least at 1 assessment (i.e., lifetime suicide attempt; **Table 2**).

[Table 2 about here]

Developmental trajectories of ADHD symptoms

For both boys and girls, we identified a 3-group model as having the best fit (**Figure 1**): low trajectory (boys: 32.2%, girls: 48.7%), moderate trajectory (boys: 44.6%; girls: 42.2%), high trajectory (boys: 23.2%; girls: 9.1%). The trajectories showed similar developmental patterns for boys and girls. However, boys on the high trajectory had higher ADHD symptoms scores than girls on the high trajectory. Additionally, the proportion of children within each trajectory was different, with the high trajectory being larger for boys than for girls, and the low trajectory being larger for girls than for boys.

[Figure 1 about here]

Association between ADHD symptoms trajectories and suicidal ideation

Prevalence of suicidal ideation and attempt in each trajectory are shown in **Table 2**. For girls, the highest prevalence of suicidal ideation was found in the high trajectory (11.1%), while girls in the moderate and low trajectories had a slightly lower suicide ideation rate (7.3% and 8.1%, respectively). Logistic regression analyses (**Table 3**) showed that, girls in the low, moderate, and high trajectories were at similar risk of suicidal ideation (moderate vs low, OR=0.9, 95%CI=0.5-1.5; high vs low, OR=1.4, 95%CI=0.6-3.3), even after adjustment for the selected covariates (moderate vs low, OR=1.0, 95%CI=0.5-1.7; high vs low, OR=1.8, 95%CI=0.7-5.0).

Boys in the high and moderate trajectories had a similar suicidal ideation rate (5.3% and 5.9%, respectively), which was higher than that of boys in the low trajectory (1.4%). Consistently, logistic regression analysis showed that boys in the moderate and high trajectories had a 4-fold increased risk of suicide ideation compared to boys in the low trajectory (moderate, OR: 4.4, 95%CI: 1.3-15.1; high, OR=3.9, 95%CI=1.0-14.9). Odds ratios remained similar after adjustment for the selected covariables, although below the significance threshold for the high trajectory (moderate, OR: 4.2, 95%CI: 1.2-14.8; high, OR=3.6, 95%CI=0.8-15.1).

Association between ADHD symptoms trajectories and suicide attempt

There was a dose-response pattern indicating that the higher the ADHD symptoms, the higher the rate of suicide attempts (girls: 5.1%, 9.9%, 17,4%; boys: 1.9%, 2.6%, 4.6%, respectively for the low, moderate, and high trajectories; **Table 2**). Logistic regression (**Table 3**) showed that girls in both high (OR=3.9, 95%CI=1.7-8.6) and moderate trajectory (OR=2.0, 95%CI=1.1-3.6) had a higher crude risk for attempting suicide compared to girls in the low trajectory. However, those risks decreased and became non-significant after adjustment for the covariates (moderate, OR=1.6, 95%CI=0.8-3.0; high, OR=2.3, 95%CI=0.9-5.8).

A different pattern was observed for boys. Compared to boys in the low trajectory, boys in the moderate and high trajectories had, respectively, 1.4-fold (OR=1.4, 95%CI=0.4-4.7) and 2.5-fold (OR=2.5, 95%CI=0.7-8.7) increased risk for suicide attempt. After accounting for the confounding role of the covariates, the risk became statistically significant for the boys in the high trajectory (OR: 4.5, 95%CI: 1.1-17.9), but not for the boys in the moderate trajectory (OR=1.8, 95%CI=0.5-6.3).

[Table 3 about here]

Discussion

The objectives of this population-based study were to test the predictive association between childhood ADHD symptoms and suicide ideation and attempts in adolescence, and to test whether the suicidal risk differed by sex. Our analyses showed that moderate to high levels of ADHD symptoms did not convey the same suicidal risk for boys and girls. We found that boys following moderate and high ADHD symptoms trajectories during the course of childhood (6-12 years) had a higher risk of suicidal ideation in adolescence (13-17 years), compared to boys following a low ADHD symptoms trajectory. In contrast, girls following a moderate or high ADHD symptoms trajectory did not have a heightened risk for suicidal ideation, compared to girls following a low ADHD symptoms trajectory. These associations were of similar magnitude after taking into account the confounding effects of childhood depressive symptoms, socioeconomic status, and maternal depression.

For suicide attempts, only boys following a high ADHD symptoms trajectory showed an increased (4.5 times higher) risk of suicide attempt compared to boys following a low trajectory. The risk of suicide attempts was not higher for girls on the high ADHD symptoms trajectory compared to girls on the low trajectory.

Our results are consistent with previous studies suggesting that ADHD symptoms might be considered early risk factors for suicide attempts during adolescence, especially among boys.[8, 9]

Our findings also extend prior knowledge in several ways. First, to our knowledge, this is the first population-based study to investigate the association between ADHD symptoms and SB using group-based trajectory modeling [23]. Given the developmental origins of suicidal behaviour, it is important to identify the developmental aspects of ADHD symptoms and its longitudinal association with suicidal behaviour using statistical techniques that account for population heterogeneity in the long term development of ADHD symptoms [7–9]. Specifically, such techniques rely on a data driven approach that allows one to identify homogeneous group of children with typical and atypically high levels of symptoms without using arbitrary classifications. Second, previous studies were mainly based on cross-sectional designs and focused on clinical populations [6, 7, 10]. Third, as previous studies mainly documented the association between ADHD symptoms and suicide mortality or serious attempts (i.e., requiring hospitalization) [8] in boys, our findings extend previous reports by showing that the association also holds for selfreported suicidal ideation and self-reported attempt. This is important because suicidal ideation precede suicide attempt in most cases. Only one previous population-based study found a positive association between childhood ADHD symptoms and SB among boys, although it was not based on a birth cohort [8, 9].

The underlying mechanisms of the sex difference in the association between ADHD symptoms and SB are still unclear, but they might be related to the type of ADHD symptoms that boys and girls experience. Boys with ADHD are more likely than girls with ADHD to display hyperactive-impulsive symptoms and less likely to experience inattentive symptoms [24]. Previous studies indicated that impulsivity is one of the pathway to suicidal behaviors, both in boys and girls [25–27], and a recent study also highlighted that different domains of impulsivity are connected to suicidal ideation and suicide attempt (respectively Pervasive Influence of Feelings and Feelings Trigger Action) [28]. Thus boys' higher levels of ADHD symptoms may explain why the association between hyperactivity-inattention and suicidal outcomes holds mainly for boys [28, 29].

Moreover, the same level of suicidal ideation may convert more easily into the acting out of suicide attempts in boys than in girls being facilitated by higher levels of hyperactivity-impulsivity, as previously suggested [12, 30–32]. Previous studies distinguishing the role of impulsivity and inattention show that those symptoms have different long term effect on educational and mental health outcome [33, 34] but to our knowledge no study investigated suicidal outcomes. Therefore, studies distinguishing the role of inattention from that of hyperactive/impulsive symptoms in boys and girls are needed to clarify the origin of the sex difference that we observed. The lack of risk awareness which can be part of ADHD itself might also explain the finding that ADHD symptoms are risk factors for suicide attempt and ideation among boys [4, 9], as these symptoms may confer to adolescents a higher risk of acting without considering the consequences of their acts. However, further studies are needed to clarify the underlying mechanisms of this association.

Our findings have clear clinical and preventive implications: boys presenting with moderate or high levels of ADHD symptoms throughout elementary school, might be considered more at risk for suicidal ideation and attempt later in life. These findings may guide clinicians to a more focused detection and prevention of SB in adolescents who manifested these symptoms throughout elementary school.

To our knowledge this is the first population-based study using trajectory modelling to clarify the association between ADHD symptoms during childhood and suicidal behaviour during adolescence, with a focus on sex differences. Strengths of the study include: the use of a population-based sample followed-up from birth to 17 years; the yearly or bi-yearly assessments of hyperactivity/impulsivity and inattention by 5 different teachers providing independent assessments by adults with a good sense of normative behaviours in a group context [35], and the assessment of suicidality at 3 time points during adolescence.

However, caution in interpreting the results is warranted in light of the following limitations. First, attrition (eg, emigration, loss to follow-up, and refusal) is a limitation of all longitudinal

cohort studies including this one. To limit the loss of data, we used multiple imputations to deal with missing on the covariates. Moreover, as the participants with the more severe mental health symptoms tended to drop out, our models are likely to provide conservative estimate of the association between ADHD symptoms and suicidality in the population. Second, we focused on symptoms of hyperactivity/impulsivity and inattention, as the prevalence of ADHD diagnoses is low in population-based samples and we did not obtain clinical mental health evaluation during childhood.

This population-based study showed that boys with high and moderate levels of ADHD symptoms during childhood are at higher risk for later suicidal behaviour. In particular, boys with moderate and high level of ADHD symptoms exhibited a higher risk for suicidal ideation, and a 4.5 times higher risk of suicide attempts in adolescence compared to those with low levels of ADHD symptoms. Interventions with pre-adolescent and adolescent boys showing ADHD symptoms should include a suicide prevention component. Population level suicide prevention for adolescents should particularly target boys with a history of ADHD problems.

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Table 1. Socio-demographic characteristics of the sample

	Attempt (N=80)	Ideation (N=89)	No attempt/ideation (N=1238)	<i>p</i> -value
Child characteristics				
Sex male, N (%)	19 (23.7)	29 (32.6)	617 (49.8)	0.000
Depressive/anxiety symptoms	2.4 (1.4)	2.1 (1.6)	2.1 (1.6)	0.255
ADHD medication use, N (%)	15 (18.7)	14 (15.7)	152 (12.2)	0.121
Opposition	3.8 (1.5)	3.5 (1.5)	3.6 (1.5)	0.363
Low birth weight (<2500g), N (%)	3 (3.7)	1 (1.1)	40 (3.2)	0.515
Parents and family characteristics				
Low Socioeconomic Status, N (%)	28 (35.9)	21 (23.6)	265 (21.5)	0.013
Maternal age at child birth	28.5 (5.5)	30.0 (5.3)	29.3 (5.1)	0.191
Paternal age at child birth	31.6 (5.5)	32.9 (4.7)	32.2 (5.5)	0.315
Family dysfunction	2.0 (1.5)	1.7 (1.4)	1.7 (1.4)	0.115
Family structure non-intact, N (%)	22 (37.5)	13 (14.6)	215 (17.4)	0.053
Smoking during pregnancy, N (%)	24 (30.7)	18 (20.2)	299 (24.2)	0.276
Parental mental health				
Maternal suicide attempt, N (%)	3 (3.8)	2 (2.2)	19 (1.5)	0.387
Maternal depression	1.6 (1.1)	1.4 (1.1)	1.4 (1.1)	0.207

The table provides basic socio-demographic characteristics of the sample. Descriptive statistics are mean (standard deviations) if not otherwise indicated. P-values are based on ANOVA (continuous variables) or Chi-squares (categorical variables).

Data were compiled from the final master file of the Québec Longitudinal Study of Child Development (1998-2015), Québec Government, Québec Statistic Institute.

Table 2. Prevalence of suicidal ideation and attempt by trajectory and sex

	Suicidal behavior Entire sample		Suicidal behavior by trajectory						
			Low trajectory		Moderate trajectory		High tr	High trajectory	
	Boys n=665	Girls n= 742	Boys n= 211	Girls n= 367	Boys n= 303	Girls = 312	Boys n= 151	Girls n= 63	
Ideation	29 (4.3)	60(8.1)	3 (1.4)	30 (8.1)	18 (5.9)	23 (7.3)	8 (5.3)	7 (11.1)	
Attempt	19 (2.8)	61(8.2)	4 (1.9)	19 (5.1)	8 (2.6)	31 (9.9)	7 (4.6)	11(17.4)	

The table provides count (N) and percentage (%) of adolescents reporting suicide ideation and attempt at 13-17 years for each trajectory and by sex.

 $\begin{tabular}{ll} Table 3. Logistic regression models predicting suicidal ideation and suicide attempt at 13-17 years \end{tabular}$

	Suicidal	ideation	Suicide attempt		
ADHD symptoms trajectory	Unadjusted OR (95%CI)	Adjusted OR (95%CI) ^a	Unadjusted OR (95%CI)	Adjusted OR (95%CI) ^a	
Boys (665)					
Low ADHD symptoms	1 [reference]	1 [reference]	1 [reference]	1 [reference]	
Moderate ADHD symptoms	4.4 (1.3-15.1)	4.2 (1.2-14.8)	1.4 (0.4-4.7)	1.8 (0.5-6.3)	
High ADHD symptoms	3.9 (1.0-14.9)	3.6 (0.8-15.1)	2.5 (0.7-8.7)	4.5 (1.1-17.9)	
Girls (742)					
Low ADHD symptoms Moderate ADHD	1 [reference]	1 [reference]	1 [reference]	1 [reference]	
symptoms	0.9 (0.5-1.5)	1.0 (0.5-1.7)	2.0 (1.1-3.6)	1.6 (0.8-3.0)	
High ADHD symptoms	1.4 (0.6-3.3)	1.8 (0.7-5.0)	3.9 (1.7-8.6)	2.3 (0.9-5.8)	

^a Odds ratios adjusted for child depressive symptoms, socioeconomic status, and maternal depression

Figure 1. Trajectories of ADHD symptoms among boys and girls



