



# Suicidal ideation in adult ADHD: Gender difference with a specific psychopathological profile

Brigitta Kakuszi, István Bitter, Pál Czobor \*

Semmelweis University, Department of Psychiatry and Psychotherapy, Budapest, Hungary

## ARTICLE INFO

## ABSTRACT

**Objective:** To investigate suicidal ideation (SI) in patients with adult ADHD (aADHD), and its association with gender and psychopathology.

**Methods:** Case-control study with 206 participants (patients = 103/healthy controls = 103; matched on gender, age, and education). SI was assessed by the Beck-I Depression-Inventory. The Conners' Adult ADHD Rating Scale (CAARS) was used to characterize the ADHD symptom-domains.

**Results:** Compared to controls, the likelihood of SI was significantly higher in females with ADHD (odds ratio[OR] = 25.0 (95%CI:2.98–200.0); the difference was not significant in males (OR = 2.09 (95%CI:0.75–5.81)). In females, “Problems with Self-Concept” scores on the CAARS showed the closest association with SI (OR = 5.60,95%CI:2.34–13.41)], while in males it was “Impulsivity” scores (OR = 3.01,95%CI:1.50–6.06).

**Conclusion:** Our findings extend previously described transdiagnostic associations of specific psychopathological risk factors to aADHD, including problems with self-concept and impulsivity, which are robustly associated with suicidality across diagnostic boundaries. In addition, they indicate that these associations exhibit pronounced gender-specificity in aADHD.

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## 1. Introduction

Suicide is one of the leading causes of mortality worldwide, and it ranks among the first three causes of death for both men and women between the ages of 15–44 in the majority of countries [1]. Accumulating evidence indicates that Attention Deficit Hyperactivity Disorder (ADHD), a common neurodevelopmental disorder, which typically starts at young ages and persists in a high percentage in adulthood, is associated with a high prevalence of suicidal behaviors, such as ideation, planning, attempts and completed suicides [2]. This can be attributable to the specific psychopathology of the disorder that includes symptoms of impulsivity and hyperactivity as well as problems with self-concept and low self-esteem [3], which may increase the risk of suicidal behaviors [4–6].

Suicidal behaviors are characterized by a pronounced gender difference: females attempt suicide more frequently than males in most western countries, while male suicide rates are substantially higher from adolescence to adulthood [1,7,8]. ADHD exhibits a marked gender difference both in terms of symptom presentation [9,10] and

neurobiological background (e.g., different morphometric changes between boys and girls with ADHD in the ventral anterior cingulate, a brain area involved in emotion regulation) [6,11]). With respect to gender-specific symptom presentation, females with ADHD tend to have lower ratings on hyperactivity, impulsivity, and externalizing problems as compared to males. In addition, females with ADHD are found to manifest more inattention, anxiety and affective symptoms, and internalizing problems [4,12]. Despite these observations, investigation of gender difference in suicidal behaviors in ADHD has been a neglected area of research [2]. Our goal was to study the question of how gender influences the risk of suicidal ideation (SI) in adult ADHD (aADHD), and whether the psychopathological profiles that underlie SI differ between male and female patients.

Investigation of suicidal ideation in a population at risk is essential since SI is postulated as the starting point of a key pathway, which progresses, via a continuum of suicide behaviors, to completed suicide [13–15]. Indeed, SI has been shown to be a powerful predictor of completed suicide [16,17]; therefore, the knowledge of the risk factors for SI is important in suicide prevention. Study of suicidal ideation in adults with ADHD is particularly important since patients with ADHD receive negative feedback during their course of the disease, which results in negative self-referential thinking with a deleterious impact on self-esteem [4,5]. This puts them at increased risk for suicidal behaviors, which escalate over time and frequently lead to completed suicide

\* Corresponding author at: Semmelweis University, Department of Psychiatry and Psychotherapy, Budapest, Balassa u. 6., 1083, Hungary.

E-mail address: [czobor.pal@med.semmelweis-univ.hu](mailto:czobor.pal@med.semmelweis-univ.hu) (P. Czobor).

[4,18]. A systematic review on suicidality in ADHD noted that one third of ADHD patients had suicidal ideation in adulthood, and that the rate of previous suicide attempts was the highest (16%) in adults as compared to children or adolescents [19].

As shown by a series of systematic reviews of the literature starting from the early 2000s [13,19–21], evidence for the association between increased suicidality with ADHD has grown considerably during the past fifteen years. Nevertheless, the issue of the potential gender difference in suicidal behaviors in aADHD remains unaddressed. The most recently published systematic review of the literature on the connection between ADHD and suicidality [2], covering the period after 2011, identified a total of 26 studies as potentially relevant from the published literature. However, as stated in the review, only three of these studies dealt with sex differences in ADHD with respect to suicidality [22–24]. Taken together, these studies yielded inconsistent findings, and had certain limitations.

In particular, one of the above mentioned studies [24] was a large register-based full population study from Sweden, which revealed a substantially greater increase in females than in males in the risk of suicide attempts in aADHD patients as compared to matched control subjects from the general population. The study, however, did not yield data on suicidal ideation. The second study [22] analyzed data from the US National Comorbidity Survey Replication (NCS-R), and reported a numerically higher proportion of females than males in patients with aADHD who attempted suicide as compared to those who did not. It also found an elevated risk of SI in females as compared to males in the pooled sample of aADHD and control subjects, but could not detect a gender-specific interaction with diagnostic status. The third study [23] was conducted in children with ADHD (average age 8.8 years), and had no control group. Therefore, it is difficult to establish whether a greater increase in the risk of SI in ADHD compared to controls occurred in females than in males. In terms of absolute (%) prevalence of SI, the study did not find a statistically significant difference between males and females. Overall, neither of the above studies relied on a clinical diagnosis of ADHD, or had a detailed assessment of various dimensions of psychopathology of ADHD.

Mounting evidence supports the idea that potential psychopathological risk factors may make a differential contribution to suicidal behaviors in women and men in non-psychiatric populations and across various nosological entities [25]. For example, self-esteem was found to be lower in females than in males among healthy individuals [26], and the relationship between self-esteem and depression, which is closely associated with suicidal behaviors, is more pronounced in females [27]. In general, female as compared to male patients may have a higher severity on certain psychopathological traits and have a higher proportion of comorbidities that predispose for suicidal behaviors (e.g., depressive traits, affective comorbidities). With respect to differential psychopathological contributions, Verona et al.'s study [28] based on a large epidemiological (community) sample found that “women, more than men, showed strong relationships between comorbid externalizing and internalizing psychopathology and suicide attempt history”, while externalizing psychopathology uniquely predicted suicidal behaviors in both genders (even though women showed fewer externalizing symptoms).

However, despite the aforementioned findings, it remains unclear how gender interacts with psychopathology in determining suicidal behaviors in patients with ADHD. Thus, in the current article, we will first analyze whether female and male patients with aADHD differ in their propensity to engage in suicidal thoughts and ideation. Second, we will examine whether women and men with aADHD show a different pattern of association between basic psychopathological dimensions in ADHD, as measured by the four symptoms domains of the Conners' Adult ADHD Rating Scale (CAARS), and suicidal ideation.

## 2. Methods

### 2.1. Participants

A total of 206 subjects participated in this matched case-control investigation: 103 ADHD patients and 103 healthy controls. The data collection took place between 07/01/2012 and 06/31/2017. The rationale for the sample size was guided by consideration of statistical power. A cross-sectional study conducted in 17 countries [29] estimated that the lifetime prevalence of suicidal ideation as 9.3% in the general population. We used this estimate for the control group for the determination of statistical power, and posited a medium effect size (odds ratio [OR] = 3.0) for an increase in the likelihood of suicidal ideation in patients with ADHD vs. controls. Results indicated that 103 subjects/group would yield approximately 80% statistical power to detect a difference (i.e.,  $OR \geq 3$ ) between the ADHD and control group at the alpha threshold of 0.05 [30].

Patients with aADHD were recruited from the Department of Psychiatry and Psychotherapy, Semmelweis University, Budapest, which provides an outpatient service for adults with ADHD in Hungary. Controls were recruited from the office and medical staff at the University and their acquaintances, using the 90-item Symptom-CheckList (SCL-90R) [31] to exclude psychiatric comorbidity.

Inclusion criteria for patients were a diagnosis of ADHD according to the DSM IV criteria, confirmed with a semi-structured interview with the treating physician; lack of history of any psychotic disorder; and current age at enrollment into the study in the range of  $\geq 18$ –65 years. Exclusion criteria for all participants (both patients and healthy controls) included a history of severe neurological or somatic disorder, or severe head trauma. This criterion was adopted since certain neurological illnesses (e.g., epilepsy and other seizure disorders, sensory integration disorder) and head trauma (especially if it involves the frontal cortex) may produce symptoms that mimic and overlap symptoms with ADHD (e.g., distractibility, deficits in attention, hyperactivity and/or impulsiveness); moreover, they are likely to receive concomitant pharmacological treatment, which may confound the findings [32].

Additional exclusion criteria for control subjects were (a) a history of psychiatric illness; and (b) the presence of severe psychiatric symptom distress, as measured by a score outside the normal range on the SCL-90R scale [31]. Psychiatric distress outside the normal range was defined according to the Derogatis criteria [33], as either a Global Severity Index (GSI) score of 2 or more subscale scores on the SCL-90 scale at or above a T score of 63. Normalized and standardized T scores were derived using Unoka et al.'s data [34] who examined the validity of the Hungarian version of SCL-90 in a normative sample. Raw score cutoffs for psychiatric distress outside the normal range have been published (Table 2, [34]). Finally, controls with a prior history of ADHD in childhood were excluded from our study.

We applied a matched case-control design since this design may increase efficiency when the distribution of the matching covariate can differ considerably between the case and control populations [35], e.g., gender, age and education attainment with regard to ADHD and healthy control subjects. These variables were selected for matching because available data indicate (e.g., a cross-national study including 17 countries [29]) that common and consistent risk factors in the general population for suicidal behaviors include gender (females are more at risk), younger age, lower level of education, and unmarried status. Moreover, these risk factors, such as gender, age and education level, also play a fundamental role in the course and symptom manifestation of ADHD. Control subjects were individually matched to ADHD patients at a one-to-one ratio on the basis of gender, age (within 5 years), and education achievement (no college vs. college education or higher).

Participants gave written consent according to a protocol approved by the institutional review board (Permission#:015340-004/2015/OTIG), and compliant with the Declaration of Helsinki.

## 2.2. Measures

The Beck Depression Inventory (BDI) (Beck-I, 21-item version, item range: 0–3) [36] was applied to assess the presence of suicidal thoughts. In particular, item 9 characterizes suicidal thoughts and motivation on a 4-point scale: 0- “I don’t have any thoughts of killing myself.”; 1- “I have thoughts of killing myself, but I would not carry them out.”; 2- “I would like to kill myself”; and 3 - “I would kill myself if I had the chance.”

This item has been used in earlier research as a stand-alone measure of suicidal ideation [37]. In our study, similar to prior research [37], responses to item 9 of the BDI (“suicide question”) were dichotomized, contrasting those subjects who had a score of 0 with those who had a score > 0 on BDI item 9 (i.e., subjects who endorsed suicidal thoughts) [37]. This measure of SI has been validated in Hungary [38,39].

The total score on the SCL-90R was used to describe the severity on general domains of psychopathology.

The Conners' Adult ADHD Rating Scale (CAARS) [40–42] was used to characterize the four ADHD symptom domains, including Inattention, Hyperactivity, Impulsivity and Problems with Self-Concept. We used the Self-Report, Long Version form of the scale in our study [42]. The scale has 66 items, each scored on a 4-point range from 0 through 3. The CAARS has a 4-factor structure that characterizes symptoms across the following core psychopathological domains: Inattention (12 items, domain score range: 0–36), Hyperactivity (12 items, domain score range: 0–36), Impulsivity (11 items, domain score range: 0–33) and Problems with Self-Concept (6 items, domain score range: 0–18). CAARS is a psychometrically sound scale with good internal-consistency (coefficient-alpha ranging from 0.86 to 0.92 for the 4 factors) and test-retest reliability (median = 0.93 [42]). The four-factor structure of the CAARS Scale that we adopted for our analyses and its external validity with regard to functional impairment have been assessed and confirmed in two of our prior studies that focused on an aADHD population [43,44].

The clinical and psychometric data were collected by personnel of the Outpatient Service trained in the administration of the clinical interviews and questionnaires used in the study. Face-to-face interviews were conducted at the Department of Psychotherapy and Psychiatry, Semmelweis University, Budapest, Hungary, which provides an outpatient service for patients with adult ADHD in Hungary.

## 2.3. Statistical analysis

We applied logistic regression (LR), using the Statistical Analysis System v9.4 GLIMMIX Procedure [45]. The presence of suicidal ideation was used as the dependent variable. Grouping (aADHD vs. control), gender and their interaction served as independent variables. Age was a covariate. We applied a hierarchical matched-pair analysis design in order to take into account the lack of independence of patient cases and individually matched controls in the sample. Accordingly, case-control cluster (“pair-id”) was applied as a stratifying (subject-level) factor in the analyses. The association of suicidal ideation with the independent variables was characterized by the odds ratio (OR). LR analyses were also applied to test the association between the ADHD symptom domains and the presence of suicidal ideation. Moreover, we investigated whether the presence of comorbidities (any comorbidity [yes/no], affective comorbidity [yes/no]) and medication status (methylphenidate medication [yes/no]) influenced the findings. Since prior data indicate that unmarried status and divorce may serve as risk factors for suicidal ideation [29,46,47], we also explored whether these factors are associated with suicidal ideation.

## 3. Results

### 3.1. Demographic characteristics

As shown by Table 1, due to the individual one-to-one matched-pair design patients with aADHD (N = 103) and controls (N = 103) had no difference in the proportion of males (58.3% in both groups).

The mean age was also virtually identical in the two samples (approximately 31 years in each group;  $F = 0.01$ ,  $df = 102$ ,  $p = 0.94$ ). Almost half of the sample attained college or higher education in both groups (aADHD = 47.57%, Control = 45.63%; Chi-square = 0.08,  $df = 1$ ;  $p = 0.78$ ). The two groups were similar in marital status, with a little more than one-fourth of the sample being married in both groups. There were 7 subjects who underwent divorce (6 with ADHD, and 1 control subject). In the divorced group, there was a higher proportion of patients with suicidal ideation (57.1%, 4/7) than in the non-divorced group (16.6%, 33/166); the difference was statistically significant (Fisher's exact test, two-sided  $p = 0.0201$ ).

Patients with aADHD showed a numerically higher divorce rate (5.83%, 6/103) than controls (0.97%, 1/103), but the difference was not statistically significant ( $p = 0.12$ ). In the aADHD group, 66.7% (4 of 6) of subjects with divorce endorsed suicidal ideation as compared to 25.8% (25 of 97) with no divorce (Fisher's Exact Test,  $p = 0.051$ ). The analogous numbers in the control group were 0% (0 of 1 with divorce) and 7.84% (8 of 102 with no divorce) (Fisher's Exact Test,  $p = 1$ ).

There was a significant group-difference in the CAARS symptom domains: as expected, patients showed higher severity in all domains. A total of 24 (23.3%) of 103 patients had comorbidity according to the DSM-IV system. The majority of comorbidities (18[17.48%] of 103 patients) fell into DSM-IV affective-categories, including, depressive, bipolar and anxiety disorders; the remaining conditions included substance use, obsessive-compulsive, and personality disorders. Approximately half of the patients received methylphenidate treatment ( $n = 52$ , 50.49%), with no significant difference between females (55.81%) and males (46.67%) (Chi-square = 0.84,  $df = 1$ ;  $p = 0.36$ ).

### 3.2. Suicidal ideation in aADHD group vs. controls

As shown by Table 1, the proportion of suicidal ideation was 28.16% and 7.77% in the aADHD and control groups, respectively (OR = 4.65, 95%CI = 2.01–10.78; Chi-square = 14.53,  $df = 1$ ,  $p < 0.0001$ ).

To examine whether SI varied as a function of diagnostic group, gender and group-by-gender interaction, we applied LR models both without and with adjustments for potentially important covariates including comorbidities, methylphenidate treatment and marital status.

The LR analysis without covariate adjustment (see Table 2, 1st row) revealed that the likelihood of SI varied significantly with diagnostic status (aADHD vs. control) ( $F = 11.08$ ,  $df = 1,97$ ,  $p = 0.0012$ ), with no main effect for gender. The interaction with gender was significant ( $F = 4.37$ ,  $df = 1,97$ ,  $p = 0.0398$ ), indicating that the association of diagnostic group with SI was different in men and women. Thus, we performed post-hoc analyses to delineate differences in the increase of SI between female and male patients as compared to controls. These analyses indicated that females with aADHD exhibited approximately 16-fold increase in the likelihood of suicidal ideation vs. controls (from 2.33% to 37.21%), with an OR of 25.0 (95%CI: 2.98–200.0) ( $t = 3.0$ ,  $df = 97$ ,  $p = 0.0034$ ). By contrast, in males the increase was more modest (from 11.67% to 21.67%; OR = 2.09 (95%CI: 0.75–5.81)), and was not significant ( $t = 1.44$ ,  $df = 97$ ,  $p = 0.15$ ).

The LR analyses with covariate adjustment (see Table 2, rows 2 through 5) showed that the main effect of diagnostic group, and the group-by-gender interaction remained significant in all analyses. Furthermore, the adjustment for comorbidities, MPH treatment and marital status did not substantively change the results, i.e., both in males and females the adjusted ORs for the diagnostic group difference (aADHD vs. control) remained similar in magnitude to the unadjusted ORs. The effect of covariates was not significant in any of the analyses; nonetheless, it is noteworthy the comorbidities were associated with a moderate numerical increase in the risk of SI while married status was accompanied with a numerical decrease.

**Table 1**  
Basic demographic and clinical characteristics of the study sample.

Characteristic	Healthy Control N = 103	ADHD N = 103	Test-statistic <sup>a</sup> F/Chi <sup>2</sup>	p
Age (mean, SD) <sup>b</sup>	30.92 (9.84)	30.82 (10.39)	0.01 <sup>c</sup>	0.94
Male, N (%)	60 (58.25%)	60 (58.25%)	0.00 <sup>d</sup>	1.00
Education level (college or higher), N (%)	47 (45.63%)	49 (47.57%)	0.08 <sup>d</sup>	0.78
Marital status (married), N(%)	29 (28.16%)	26 (25.24%)	0.22 <sup>d</sup>	0.64
Divorced (Yes), N(%)	1 (0.97%)	6 (5.83%)	-. <sup>e</sup>	0.12
Score on CAARS subscales <sup>f,g</sup>				
Inattention	9.6 (6.02)	23.8 (7.2)	228.40 <sup>c</sup>	<0.0001
Hyperactivity	10.5 (6.0)	21.1 (6.6)	141.87 <sup>c</sup>	<0.0001
Impulsivity	8.3 (4.8)	19.2 (6.1)	197.03 <sup>c</sup>	<0.0001
Problems with self-concept	4.4 (3.9)	10.7 (4.7)	105.65 <sup>c</sup>	<0.0001
Stimulant medication, N (%) <sup>h</sup>	-	52 (50.49%)	-	-
Affective comorbidity N (%) <sup>i</sup>	-	18 (17.5%)	-	-
Any comorbidity N (%) <sup>j</sup>	-	24 (23.3%)	-	-
Suicidal ideation (SI) present N (%) <sup>j</sup>	8 (7.77%)	29 (28.16%)	14.53	0.0001
			OR: 4.65 (CI: 2.01–10.78)	

Abbreviations: OR, odds ratio; CI, 95% confidence interval; SD, standard deviation.

<sup>a</sup> Chi-square test for categorical, ANOVA for continuous variables.

<sup>b</sup> Inclusion criterion for age: ≥18–65 years. Actual age range for controls and patients with ADHD was 19–59 and 19–64 years, respectively.

<sup>c</sup> ANOVA, F.

<sup>d</sup> Chi-square test, Chi-square.

<sup>e</sup> Fisher's Exact Test.

<sup>f</sup> CAARS=Conners' Adult ADHD Rating Scale. CAARS subscale score ranges: Inattention = 0–36; Hyperactivity = 0–36; Impulsivity = 0–33; Problems with Self-Concept = 0–18.

<sup>g</sup> No significant difference between males and females was present on any of the CAARS subscales in the ADHD or Control group ( $p > 0.05$  in all comparisons).

<sup>h</sup> Methylphenidate (MPH). The proportion of subjects with MPH treatment did not differ significantly between females (55.81%) and males (46.67%) (Chi-square = 0.84,  $df = 1$ ;  $p = 0.36$ ).

<sup>i</sup> Affective-comorbidities included DSM-IV depressive, bipolar and anxiety disorders; the remaining conditions included substance use, obsessive-compulsive, and personality disorders.

<sup>j</sup> SI was measured by item 9 on the Beck Depression Inventory, which captures suicidal thoughts and motivation on a 4-point scale: 0-“I don't have any thoughts of killing myself.”; 1-“I have thoughts of killing myself, but I would not carry them out.”; 2-“I would like to kill myself”; and 3-“I would kill myself if I had the chance.” The dichotomous variable, presence of SI (i.e., score of 0 vs. score > 0 on item 9) was investigated.

### 3.3. ADHD symptom domains vs. suicidal ideation

Similar to the analyses of the diagnostic group effects, we applied LR models both without and with adjustments for potentially important covariates to examine whether SI varied as a function of symptom severity, gender and symptom severity-by-gender interaction.

In the unadjusted LR models, analyses of the association of CAARS symptom domains with SI revealed a significant main effect of symptom severity in all four domains. Furthermore, symptom severity had significant gender interactions in two domains: Problems with Self-Concept and Hyperactivity (see Table 3). The strengths of the association of symptom severity with suicidal ideation, as indexed by the ORs, are illustrated in Fig. 1 for females and males, respectively.

It is noteworthy that for each domain the OR was higher for females than for males. Furthermore, the pattern of associations of suicidal ideation with the four basic ADHD symptom domains reveals a specific psychopathological profile in females and males (Fig. 1). In females, Problems with Self-Concept scores on the CAARS manifested a close association with suicidal ideation, although symptom severity in other symptom domains, especially in impulsivity, also had a relationship. In

males, Impulsivity had the closest association; Problems with Self-Concept and Inattention had a modest relationship, while Hyperactivity was not significantly related.

Adjustment for covariates, including comorbidities and MPH treatment, did not substantially change the results. We found that all main effects and interactions that were significant in the unadjusted LR models were significant or marginally significant after the adjustment (see Online Table 1). In addition, the adjusted ORs in males and females for the diagnostic group difference were comparable to the unadjusted ORs. The covariates did not reach significance in any of the analyses.

### 3.4. Subsidiary analyses

In subsidiary analyses we explored whether our main findings remain significant if we contrasted controls with subgroups of aADHD based on comorbidities (comorbidity present/absent) or MPH treatment status (MPH treatment yes/no). We also examined whether subgroups of ADHD based on comorbidities or MPH treatment (yes/no) differed from each other. Our results indicate that in females the difference between the aADHD and control subjects in the likelihood

**Table 2**  
Association of suicidal ideation (SI) with diagnostic group, gender and covariates in patients with ADHD and matched healthy control subjects<sup>a</sup>.

Covariate	Group	Gender	Group × Gender	ADHD vs. Control: OR (95% CI) <sup>c</sup>		Covariate effect	
	F/p <sup>b</sup>	F/p <sup>b</sup>	F/p <sup>b</sup>	Male	Female	F/p <sup>b</sup>	OR (95% CI) <sup>c</sup>
-	11.08 0.0012	0.64 0.425	4.34 0.043	2.09 (0.75–5.81)	25.00 (2.98–200)	n/a	n/a
Any comorbidity, yes/no	8.99 0.0034	0.65 0.421	4.26 0.042	1.83 (0.63–5.32)	21.28 (2.50–200)	1.15 0.295	1.73 (0.60–4.98)
Affective comorbidity, yes/no	9.38 0.0028	0.64 0.426	4.29 0.0411	1.87 (0.65–5.38)	22.22 (0.63–200)	1.12 0.306	1.81 (0.55–5.99)
MPH treatment, yes/no	9.57 0.0026	0.64 0.427	4.32 0.040	2.09 (0.69–6.33)	25.00 (2.79–200)	0.00 0.999	1.00 (0.40–2.48)
Marital status, married/unmarried	10.92 0.0013	0.64 0.426	4.41 0.038	2.05 (0.73–5.81)	26.32 (3.01–250)	0.29 0.592	0.78 (0.31–1.96)

Abbreviations: OR = odds ratio; 95%CI = 95% confidence interval; MPH = Methylphenidate; n/a = not applicable.

<sup>a</sup> Logistic regression (LR) based on a hierarchical matched-pair design was used. SI (present/absent) served as the dependent variable. Grouping (ADHD/control), gender and their interaction were used as independent variables. The analyses were conducted without (1st row in Table) and with adjustment for potentially important variables (see subsequent rows).

<sup>b</sup> Test-statistic (F) and alpha-error (p) from the LR model.

<sup>c</sup> The association of SI with model with independent variables and covariates was characterized by the OR. A value of OR > 1 and OR < 1, respectively, indicate an increase or decrease in the likelihood of SI.

**Table 3**  
Association of suicidal ideation (SI) with symptom severity on CAARS subscales, gender, and symptom severity-by-gender interaction<sup>a</sup>.

Symptom domain (CAARS Subscale)	Effect of symptom severity on CAARS subscale	Gender	CAARS severity × Gender	OR (95% CI) <sup>c</sup>	
	F/p <sup>b</sup>	F/p <sup>b</sup>	F/p <sup>b</sup>	Male	Female
Inattention	17.5 0.0001	0.4 0.526	0.7 0.406	2.95 (1.45–6.00)	3.63 (1.43–9.24)
Hyperactivity	8.6 0.0041	4.2 0.043	4.3 0.041	1.54 (0.61–3.89)	4.14 (1.68–10.16)
Impulsivity	23.4 0.0001	1.8 0.180	1.4 0.233	3.01 (1.50–6.06)	4.40 (1.82–10.65)
Problems with self-concept	11.7 0.0009	2.5 0.116	4.2 0.040	2.61 (1.28–5.30)	5.60 (2.34–13.41)

Abbreviations: CAARS=Conners' Adult ADHD Rating Scale. OR = odds ratio; 95% CI = 95% confidence interval.

<sup>a</sup> Logistic regression (LR) based on a hierarchical matched-pair design. SI (present/absent) was used as the dependent variable. Symptom severity on CAARS subscales, gender and their interaction were the independent variables. A separate analysis was conducted for each CAARS subscale.

<sup>b</sup> Test-statistic (F) and alpha-error (p) from the LR model.

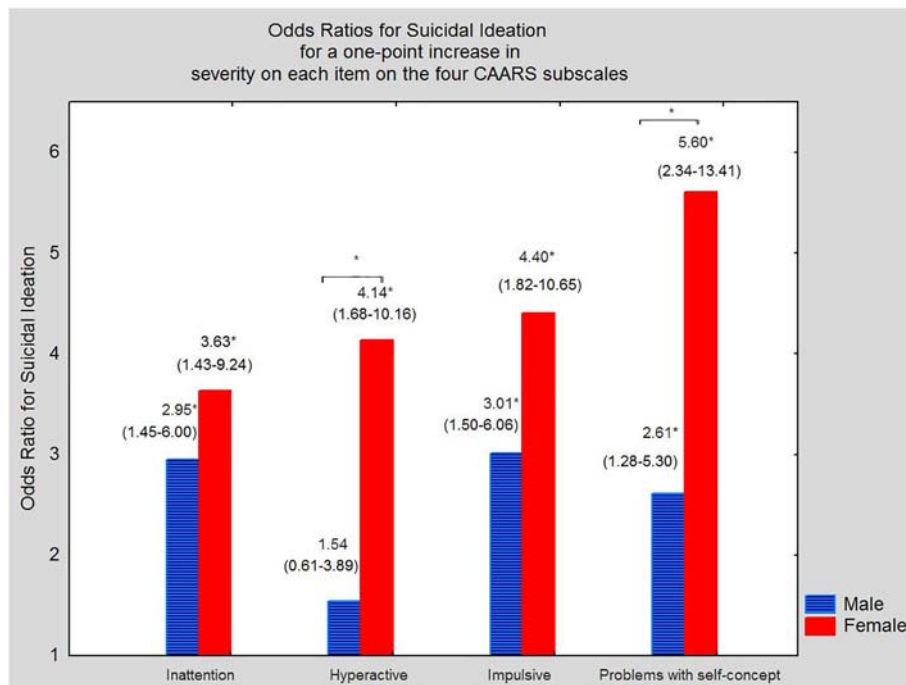
<sup>c</sup> Association of SI with symptom severity on CAARS subscales was characterized by the OR. ORs for the increase in the likelihood of suicidal ideation were computed for a 1-point increase across all constituting items of a given CAARS subscale in order to assure comparability among the subscales. OR > 1 and OR < 1, respectively, indicate an increase or decrease in the likelihood of SI with symptom severity.

of SI remained significant irrespective of comorbidity (present or absent) or MPH treatment (yes/no) status (see Online Table 2). Additionally, we note that even though the effect of comorbidities was not significant, the presence of comorbidities was associated with numerically higher ORs for SI. Furthermore, while MPH treatment was associated with a numerical decrease in the OR for SI, this finding did not obtain statistical significance. In males, similar to our principal results detailed in Table 2, the analyses with respect to diagnostic status did not reach statistical significance.

**4. Discussion**

Suicidal ideation is significantly increased in adult ADHD patients compared to controls and the increase is considerably higher in females than males. The finding that the increase is present regardless of comorbidities indicates that ADHD in itself is associated with markedly increased suicidality.

Our results with regard to gender difference are consistent, at least in part, with two prior investigations of suicidal attempts in aADHD. Specifically, one investigation [22], using data from the US National Comorbidity Survey Replication reported a numerically higher proportion (%) of females relative to males in ADHD patients with attempted suicide as compared to patients who had no suicide attempt. The study also found a higher risk of suicidal ideation in females as compared to males in the pooled sample of ADHD and control subjects. However, it could not demonstrate a gender-specific difference in the association between ADHD and suicidal ideation. It remains unclear to what extent this was due to the small sample size, or a small effect size, and/or to the fact that the criteria used for ADHD in that study were developed for children, and may not be applicable to adults [22]. The other study [24], similar to our results, found that the risk of suicide attempts among aADHD patients was significantly higher in females (ORs were 5.41[95%CI:4.60–6.36] and 2.93[95%CI:2.60–3.29] for females and males, respectively).



**Fig. 1.** Relationship between the likelihood of suicidal ideation and symptom severity on the four CAARS subscales (Inattention, Hyperactivity, Impulsivity, Problems with Self-Concept) in females and males, respectively. Logistic regression (LR) analysis revealed, both for females and males, a positive association between the likelihood of suicidal ideation and symptom severity. The association was statistically significant ( $p < 0.05$ ) for each of the four symptom domains, with the exception of Hyperactivity, which did not obtain significance in males. The interaction of gender with symptom severity reached statistical significance in the LR for the Problems with Self-Concept and Hyperactivity subscales, indicating that symptom severity was differentially related to suicidal ideation in females and males on these two subscales. The strength of the association between symptom severity and suicidal ideation is indicated by the odds ratio (OR) statistic; the numbers in parentheses depict 95% confidence limits. ORs for the increase in the likelihood of suicidal ideation were computed for a 1-point increase across all constituting items of a given CAARS subscale in order to assure comparability among the four subscales. Abbreviations: Conners' Adult ADHD Rating Scale, CAARS. Asterisks (\*) indicate statistical significance ( $p < 0.05$ ) for a main effect in LR, horizontal square-brackets with asterisks indicate a significant interaction.

The fact that the association between diagnostic status and suicidal ideation did not reach statistical significance for males is due to the markedly lower effect size (males OR = 2.09, 95%CI: 0.75–5.81) as compared to females (OR = 25.0, 95%CI: 2.98–200.0). In interpreting this result, we also considered the fact that prior literature showed that women were more likely to engage in suicidal behaviors than men because they had a higher prevalence of depression, which is a strong predictor of suicide attempts. However, in our study the proportion of comorbidities was relatively low, and the results remained significant after the adjustment for comorbidities.

Additionally, we considered that the gender difference in the increased risk of suicidal ideation in patients with ADHD may be attributable to the fact that women are more likely than men to engage in self-directed aggression and suicidal behaviors [28], whereas men are much more likely than women to exhibit aggression and assaultive behavior against others [48]. There is evidence that externalizing psychopathology in men is associated not only with self-directed [28] but with other directed aggression as well [37]. On the other hand, women, as compared to men, have been found to exhibit strong relationships between co-occurring externalizing and internalizing psychopathology and suicide attempt history [28]. Thus, the finding that compared to controls female patients with ADHD showed a substantially greater increase in the risk of suicidal ideation than males may be due to the fact that female patients manifested high levels on both externalizing (hyperactivity, impulsivity) and internalizing psychopathology (problems with self-concept).

The association of suicidal ideation with the basic ADHD symptom domains suggests a differential psychopathological pattern for suicidality in females and males. Specifically, in females, Problems with Self-Concept scores on the CAARS had a close association with suicidal ideation, albeit symptom severity in other domains (especially in Impulsivity) also had a relationship. In males, Impulsivity had the closest association with suicidal ideation; Problems with Self-Concept and Inattention exhibited a modest relationship, while Hyperactivity was unrelated.

Our results, with the specific pattern of psychopathology that underlies suicidal ideation in females and males, are in line with emerging functional Magnetic Resonance Imaging (fMRI) data [6]. The latter indicate significant gender-by-brain volume interaction in the ventral ACC (vACC) in children with ADHD. Specifically, never-medicated boys exhibited decreased grey matter (GM) volume in vACC, which has been associated with increased aggression in those who manifested pathological levels of impulsive aggression. By contrast, never-medicated girls with ADHD showed increased GM volumes when compared to typically-developing girls. vACC and medial Prefrontal Cortex (mPFC) activity have been found to be involved in negative self-referential thinking; thus, the increased GM volumes in females with ADHD may be related, at least in part, to suicidal ideation. This relationship may represent a transdiagnostic association, as the vACC and mPFC have been found to be involved in negative self-referential bias in depression and mood disorders [49–51], and treatment with CBT in depression improved vACC and mPFC activation [49].

Overall, our findings extend some of the previously described transdiagnostic associations of specific psychopathological risk factors to patients with ADHD, including problems with self-concept and impulsivity, which are strongly related to suicidal behaviors across psychiatric disorders (e.g., depressive, bipolar, psychotic, anxiety, substance use, and impulse-control disorders) [7,52]. Moreover, they indicate that these transdiagnostic associations exhibit pronounced gender-specificity in aADHD.

The study was limited to a clinically-referred population. While this limits generalizability, it provides an added strength by means of the availability of detailed psychopathological and clinical evaluations, which typically cannot be obtained in epidemiological studies. Moreover, the results may be particularly relevant since this population manifests high symptom severity, which leads to an increased risk of

suicidality. Another limitation that should be kept in mind is that, while patients and controls were matched on basic demographic variables and controlled for key clinical variables including comorbidities and stimulant treatment, it is conceivable that our investigation may have missed some of the relevant covariates. For example, ADHD patients are known to experience more stress and negative life events in their everyday lives [4], which in turn may increase negative affect [53] that leads to suicidal ideation [54]. Accordingly, future research should evaluate the role of further potentially important variables, including the ratings of negative and positive affect. Finally, statistical power to contrast controls with subgroups of aADHD based on comorbidity strata (present/absent) or MPH treatment status (yes/no) was limited due to the small sample size for subgroup analyses in our study. This rendered the subsidiary analyses exploratory. Larger studies are therefore needed to further delineate the role of these factors (comorbidities, stimulant treatment) in the gender specific increase in SI we identified in this study, and to improve the precision of the OR estimates.

Despite these limitations, the results of this study highlight the importance of a gender-specific strategy for risk evaluation and prevention. In particular, the strong association of Problems with Self-Concept with suicidal ideation may be critically important for females with ADHD, since it may provide information for the early recognition of those who are at risk of suicide. This association can also be important for prevention as there is evidence that, while untreated ADHD is associated with poorer long-term self-esteem, a beneficial response to treatment (pharmacological or nonpharmacological) can be elicited for the majority of self-esteem outcomes [55]. It is recommended that future research should focus on the evaluation of therapy that targets difficulties with self-esteem, especially in females.

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.comppsy.2018.06.003>.

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## Ethical standards

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## Conflict of interest

Authors B. Kakuszi, I. Bitter and P. Czobor, declare that they have no conflict of interest.

## Informed consent

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, and the applicable revisions at the time of the investigation. Informed consent was obtained from all patients for being included in the study.

## References

- [1] White A, Fawcner HJ, Holmes M. Is there a case for differential treatment of young men and women? *Med J Aust* 2006;185:454–5.
- [2] Balazs J, Keresztesy A. Attention-deficit/hyperactivity disorder and suicide: a systematic review. *World J Psychiatry* 2017;7:44–59.

- [3] Harpin V, Mazzone L, Raynaud JP, Kahle J, Hodgkins P. Long-term outcomes of ADHD: a systematic review of self-esteem and social function. *J Atten Disord* 2016;20:295–305.
- [4] Cook J, Knight E, Hume I, Qureshi A. The self-esteem of adults diagnosed with attention-deficit/hyperactivity disorder (ADHD): a systematic review of the literature. *Atten Defic Hyperact Disord* 2014;6:249–68.
- [5] Knouse LE, Safren SA. Current status of cognitive behavioral therapy for adult attention-deficit hyperactivity disorder. *Psychiatr Clin North Am* 2010;33:497–509.
- [6] Villemonteix T, De Brito SA, Slama H, Kavec M, Baleriaux D, Metens T, et al. Grey matter volume differences associated with gender in children with attention-deficit/hyperactivity disorder: a voxel-based morphometry study. *Dev Cogn Neurosci* 2015;14:32–7.
- [7] Mann JJ. Neurobiology of suicidal behaviour. *Nat Rev Neurosci* 2003;4:819–28.
- [8] Moscicki EK. Gender differences in completed and attempted suicides. *Ann Epidemiol* 1994;4:152–8.
- [9] Gershon J. A meta-analytic review of gender differences in ADHD. *J Atten Disord* 2002;5:143–54.
- [10] Hinshaw SP, Owens EB, Zalecki C, Huggins SP, Montenegro-Nevado AJ, Schrodek E, et al. Prospective follow-up of girls with attention-deficit/hyperactivity disorder into early adulthood: continuing impairment includes elevated risk for suicide attempts and self-injury. *J Consult Clin Psychol* 2012;80:1041–51.
- [11] Mahone EM, Wodka EL. The neurobiological profile of girls with ADHD. *Dev Disabil Res Rev* 2008;14:276–84.
- [12] Gershon J. A meta-analytic review of gender differences in ADHD. *J Atten Disord* 2002;5:143–54.
- [13] Impey M, Heun R. Completed suicide, ideation and attempt in attention deficit hyperactivity disorder. *Acta Psychiatr Scand* 2012;125:93–102.
- [14] Brent DA, Baugher M, Bridge J, Chen T, Chiapetta L. Age- and sex-related risk factors for adolescent suicide. *J Am Acad Child Adolesc Psychiatry* 1999;38:1497–505.
- [15] Shaffer D, Gould MS, Fisher P, Trautman P, Moreau D, Kleinman M, et al. Psychiatric diagnosis in child and adolescent suicide. *Arch Gen Psychiatry* 1996;53:339–48.
- [16] Ludwig B, Roy B, Wang Q, Birur B, Dwivedi Y. The life span model of suicide and its neurobiological foundation. *Front Neurosci* 2017;11:74.
- [17] Turecki G, Brent DA. Suicide and suicidal behaviour. *Lancet* 2016;387:1227–39.
- [18] Copeland WE, Goldston DB, Costello EJ. Adult associations of childhood suicidal thoughts and behaviors: a prospective, longitudinal analysis. *J Am Acad Child Adolesc Psychiatry* 2017;56:958–65.
- [19] Balazs J, Miklosi M, Keresztesy A, Dallos G, Gadoros J. Attention-deficit hyperactivity disorder and suicidality in a treatment naive sample of children and adolescents. *J Affect Disord* 2014;152–154:282–7.
- [20] James A, Lai FH, Dahl C. Attention deficit hyperactivity disorder and suicide: a review of possible associations. *Acta Psychiatr Scand* 2004;110:408–15.
- [21] Furczyk K, Thome J. Adult ADHD and suicide. *Atten Defic Hyperact Disord* 2014;6:153–8.
- [22] Agosti V, Chen Y, Levin FR. Does attention deficit hyperactivity disorder increase the risk of suicide attempts? *J Affect Disord* 2011;133:595–9.
- [23] Mayes SD, Calhoun SL, Baweja R, Mahr F. Suicide ideation and attempts in children with psychiatric disorders and typical development. *Crisis* 2015;36:55–60.
- [24] Jung T, Chen Q, Lichtenstein P, Larsson H. Common etiological factors of attention-deficit/hyperactivity disorder and suicidal behavior: a population-based study in Sweden. *JAMA Psychiatr* 2014;71:958–64.
- [25] Nigg JT. Attention-deficit/hyperactivity disorder and adverse health outcomes. *Clin Psychol Rev* 2013;33:215–28.
- [26] Bleidorn W, Arslan RC, Denissen JJ, Rentfrow PJ, Gebauer JE, Potter J, et al. Age and gender differences in self-esteem—a cross-cultural window. *J Pers Soc Psychol* 2016;111:396–410.
- [27] Derdikman-Eiron R, Indredavik MS, Bratberg GH, Taraldsen G, Bakken IJ, Colton M. Gender differences in subjective well-being, self-esteem and psychosocial functioning in adolescents with symptoms of anxiety and depression: findings from the Nord-Trøndelag health study. *Scand J Psychol* 2011;52:261–7.
- [28] Verona E, Sachs-Ericsson N, Joiner Jr TE. Suicide attempts associated with externalizing psychopathology in an epidemiological sample. *Am J Psychiatry* 2004;161:444–51.
- [29] Nock MK, Borges G, Bromet EJ, Alonso J, Angermeyer M, Beautrais A, et al. Cross-national prevalence and risk factors for suicidal ideation, plans and attempts. *Br J Psychiatry* 2008;192:98–105.
- [30] Chow SC, Shao J, Wang H. Sample size calculations in clinical research. New York: Marcel Dekker; 2003.
- [31] Derogatis LR, Cleary PA. Factorial invariance across gender for the primary symptom dimensions of the SCL-90. *Br J Soc Clin Psychol* 1977;16:347–56.
- [32] Barkley RA. Attention-deficit hyperactivity disorder. A handbook for diagnosis and treatment. New York: London: The Guilford Press; 2006; 610.
- [33] Derogatis LR. SCL-90-R: symptom Checklist-90-R. Administration, scoring, and procedures manual. Minneapolis (Minn): National Computer Systems1994.
- [34] Unoka ZS, Rózsa S, Kő N, Kállai J, Fábíán Á, Simon L. Validity and reliability of the SCL-90 in a Hungarian population sample. *Psychiat Hung* 2004;19:235–43.
- [35] Rose S, Laan MJ. Why match? Investigating matched case-control study designs with causal effect estimation. *Int J Biostat* 2009;5 (Article).
- [36] Beck AT, Rush AJ, Shaw BF, Emery G. Cognitive therapy of depression. New York: Guilford Press; 1979.
- [37] Paradiso S, Beadle JN, Raymont V, Grafman J. Suicidal thoughts and emotion competence. *J Clin Exp Neuropsychol* 2016;38:887–99.
- [38] Beck Depresszió Kérdőív Kopp M. (The Beck depression questionnaire.) In Hungarian. In: Perczel-Forintos D, Ajtay Gy, Kiss Zs, editors. *Kérdőívek, becslőskálák a klinikai pszichológiában.* (Questionnaires, rating scales in clinical practice.) In Hungarian. Budapest: Semmelweis Kiadó; 2007.
- [39] Rózsa S, Szádóczy E, Füredi JA. Beck Depresszió Kérdőív rövidített változatának vizsgálata hazai mintán. (Investigation of the short version of Beck depression questionnaire in a Hungarian sample). In Hungarian. , vol. 16*Psychiatria Hungarica*; 2001; 379–97.
- [40] Conners CK. Clinical use of rating scales in diagnosis and treatment of attention-deficit/hyperactivity disorder. *Pediatr Clin North Am* 1999;46:857–70 [vi].
- [41] Conners CK, Erhardt D, Epstein J. Self-ratings of ADHD symptoms in adults I: factor structure and normative data. *J Atten Disord* 1999;3:141–51.
- [42] Erhardt D, Epstein J, Conners CK, Parker J, Sitarenios G. Self-ratings of ADHD symptoms in adults II: reliability, validity, and diagnostic sensitivity. *J Atten Disord* 1999;3:158.
- [43] Balogh L, Czobor P, Simon V, Bitter I. Neuropsychological functioning and clinical symptoms in adult ADHD: a multidimensional analysis. *EUNETHYDIS, 1st ADHD international conference Amsterdam, vol. 201; 2010, 26–28 May* (poster abstracts E 31).
- [44] Szuromi B, Bitter I, Czobor P. Functional impairment in adults positively screened for attention-deficit hyperactivity disorder: the role of symptom presentation and executive functioning. *Compr Psychiatry* 2013;54:974–81.
- [45] Zhu M. Analyzing multilevel models with the GLIMMIX procedure. Cary, NC: SAS Institute Inc; 2014.
- [46] Corcoran P, Nagar A. Suicide and marital status in Northern Ireland. *Soc Psychiatry Psychiatr Epidemiol* 2010;45:795–800.
- [47] Fukuchi N, Kakizaki M, Sugawara Y, Tanji F, Watanabe I, Fukao A, et al. Association of marital status with the incidence of suicide: a population-based cohort study in Japan (Miyagi cohort study). *J Affect Disord* 2013;150:879–85.
- [48] Swanson JW, Holzer III CE, Ganju VK, Jono RT. Violence and psychiatric disorder in the community: evidence from the epidemiologic catchment area surveys. *Hosp Community Psychiatry* 1990;41:761–70.
- [49] Yoshimura S, Okamoto Y, Onoda K, Matsunaga M, Okada G, Kunisato Y, et al. Cognitive behavioral therapy for depression changes medial prefrontal and ventral anterior cingulate cortex activity associated with self-referential processing. *Soc Cogn Affect Neurosci* 2014;9:487–93.
- [50] Marchand WR. Self-referential thinking, suicide, and function of the cortical midline structures and striatum in mood disorders: possible implications for treatment studies of mindfulness-based interventions for bipolar depression. *Depress Res Treat* 2012;2012:246725.
- [51] Lemogne C, Gorwood P, Bergouignan L, Pelissolo A, Lehericy S, Fossati P. Negative affectivity, self-referential processing and the cortical midline structures. *Soc Cogn Affect Neurosci* 2011;6:426–33.
- [52] Schaffer A, Levitt AJ, Bagby RM, Kennedy SH, Levitan RD, Joffe RT. Suicidal ideation in major depression: sex differences and impact of comorbid anxiety. *Can J Psychiatry* 2000;45:822–6.
- [53] Payne TW, Schnapp MA. The relationship between negative affect and reported cognitive failures. *Depress Res Treat* 2014;2014:396195.
- [54] Yamokoski CA, Scheel KR, Rogers JR. The role of affect in suicidal thoughts and behaviors. *Suicide Life Threat Behav* 2011;41:160–70.
- [55] Harpin V, Mazzone L, Raynaud JP, Kahle J, Hodgkins P. Long-term outcomes of ADHD: a systematic review of self-esteem and social function. *J Atten Disord* 2016;20:295–305.

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