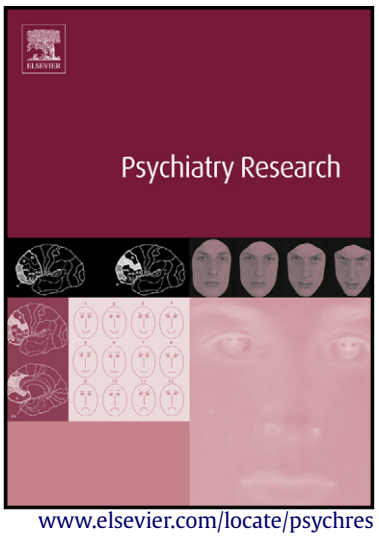

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PII: S0165-1781(15)00099-2
DOI: http://dx.doi.org/10.1016/j.psychres.2015.02.010
Reference: PSY8777

To appear in: *Psychiatry Research*

Received date: 2 May 2014
Revised date: 22 January 2015
Accepted date: 14 February 2015

Cite this article as: F. López Seco, J. Aguado-Gracia, P. Mundo-Cid, S. Acosta-García, S. Martí-Serrano, A.M. Gaviria, E. Vilella, A. Masana-Marín, Maternal psychiatric history Is associated with the symptom severity of ADHD in offspring, *Psychiatry Research,* http://dx.doi.org/10.1016/j.psychres.2015.02.010

Maternal psychiatric history is associated with the symptom severity of ADHD in offspring.

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Abstract

Controversy exists about the role of parent psychopathology in persistence and severity of attention deficit hyperactivity disorder (ADHD) symptoms in their children. Here we aimed to analyse the potential association between the severity of ADHD symptoms in children and the presence of psychiatric and ADHD symptoms in their biological parents. Seventy-three triads of children and their parents who were in active treatment for their diagnosed ADHD were evaluated in our Child and Adolescent Mental Health Centers. The mental health of the parents was also assessed. The general psychopathology of the parents was evaluated using the Symptom Checklist-90-R (SCL-90-R), and symptoms of hyperactivity were examined using the Adult ADHD Self-Report Scale (ASRSv.1.1). The severity of symptoms in children was assessed using the ADHD Rating Scale-IV (ADHD-RS-IV). Variables that could have affected the clinical development of ADHD such as sex, evolution time, age, academic level and the presence of comorbidities were controlled. The severity of the symptoms in children with ADHD was significantly related to the psychiatric history of their mother, the younger age of the child and the presence of a comorbid conduct disorder in the child. We discussed the importance of screening for parental psychopathology in clinical practice.

Key words: ADHD, prognosis, family risk factors, adult ADHD

1. Introduction

Attention deficit hyperactivity disorder (ADHD) is characterised by a persistent pattern of inattention and/ or hyperactivity-impulsivity that is more frequently displayed and is more severe than is typically observed in individuals at comparable developmental levels. Some hyperactive-impulsive symptoms must present before 12 years of age. Some impairment from the symptoms must be present in at least two settings. There must be clear evidence of interference with developmentally appropriate social, academic or occupational functioning (American Psychiatric Association, 2013). The prevalence of this disorder is estimated to be between 3 and 5% in the school population (Biederman and Faraone, 2005; Cardo et al., 2007). Because the course of ADHD can be persistent (Biederman et al., 1996, 2010, 2012), different authors have studied the factors that are associated with poor prognoses. The persistence of ADHD has been associated with a number of patient characteristics, including parents' social, educational and psychopathological status (mood disorders, ADHD, anxiety, antisocial disorder, substance abuse and dependence, rate of exposure to maternal psychopathology) (Biederman et al., 1996). Lara et al. (2009) reported a higher rate of symptomatic persistence of ADHD into adulthood (50% of cases) depending on the profile of

childhood symptoms, comorbidities and the presence of maternal and paternal psychopathology. Similarly, Gau and Chang (2013) found that ADHD persistence is related to the presence of comorbidities, neuroticism and depression in the mother, which could potentially lead to impaired parenting skills. Other authors have also reported that maternal depression is related to poor evolution of ADHD in the offspring (Gerdes et al., 2007; Goodman et al., 2011). Factors that appear likely to mediate this association include impairments in the mother's educational style, emotional involvement and depressive symptoms (Gerdes et al., 2007). In general, parental psychopathology is thought to be a significant risk factor for psychopathology in children (Vidair et al., 2011). Parents of children with ADHD frequently exhibit significant psychological problems, including ADHD, mood disorders, anxiety, behavioural and substance abuse, neuroticism, and personality disorders, especially when the offspring's ADHD is associated with other comorbid externalising disorders (Johnston and Mash, 2001; Harvey et al., 2003; Deault, 2010; Steinhausen et al., 2012; Margari et al., 2013).

Having a parent with ADHD is also associated with increased dysfunction in children with ADHD. Parental ADHD predicts a wide range of internalising and externalising problems (Chronis-Tuscano et al., 2011; Humphreys et al., 2012). Parental ADHD problems indicate a higher risk for a more severe clinical presentation of ADHD in children and higher levels of family conflict. Parental ADHD is associated with a more severe clinical presentation in children with ADHD; maternal ADHD was associated with an increased severity of overall ADHD, inattention and conduct symptoms and an increased likelihood of CD in children. Paternal ADHD was found to be associated with the severity of children's ADHD symptoms and a trend towards higher rates of CD for children in the paternal ADHD group (Agha et al., 2013). Children's overall functioning was related to the presence of executive functioning in their parents with ADHD (Chronis-Tuscano et al., 2011; Humphreys et al., 2012)]

Because of the high heritability of ADHD, the co-occurrence of ADHD in parents and their offspring is fairly common. Approximately half of all adults with ADHD have at least one child with ADHD, and between 35 and 50% of children with ADHD have one parent who has been diagnosed with this disorder. It is possible that the literature describing the difficulties faced by the families of children with ADHD at least partially reflects the presence of ADHD in the parents (Johnston et al., 2012)

Many domains of functioning have been shown to be affected in parents with ADHD: more family stress, negative parental functioning, psychosocial adversity, difficulty in organising parenting tasks, wavering parenting style, high emotional expression, coercive behaviour, family conflict, low cohesion, psychological problems, authoritarian and over-

reactive discipline, low levels of involvement and repeating orders before giving the child time to fulfil them (Harvey et al., 2003; Chronis-Tuscano et al., 2008; Deault, 2010). The presence of ADHD symptoms in mothers can interfere with monitoring and implementing parenting training and tracking coping strategies and lead to abandoning training programs (Sonuga-Barke et al., 2002; Murray and Johnston, 2006; Griggs and Mikami, 2011; Margari et al., 2013). The presence of ADHD in parents can also have consequences for emotional development and has been associated with problems in bonding and emotional regulation in adulthood (Edel et al., 2010). A number of authors have suggested that pharmacological treatments for parents with ADHD can improve their parenting styles (Chronis-Tuscano et al., 2008, 2011; Chronis-Tuscano and Stein, 2012). However, the detection of symptoms in parents of patients with ADHD is not protocolised in our setting. Similarly, the prevalence and impact of parental psychopathology on the course of ADHD are not sufficiently studied in our clinical context. Studies of parental clinical variables that aim to help fulfil the healthcare requirements of this population have gained interest, perhaps owing to the interest generated by studies on the influence of parental stress and educational styles as prognostic elements (Raya Trenas et al., 2008; Miranda et al., 2009).

Overall, only a small number of studies have analysed psychiatric and ADHD symptoms in both biological parents of children with ADHD. With the hypothesis that an association exists between parental psychopathology and ADHD symptom severity in the child, we designed the present study to analyse the potential relationship between the current severity of ADHD symptoms measured by the cut-point and the ADHD-RS total score in the offspring and parental psychopathology and/or parental ADHD symptoms in a sample of patients following treatment.

2. Material and Methods

2.1 Participants

The current study followed a cross-sectional design and was composed of 73 children with ADHD and their biological parents (73 fathers and 73 mothers). The children comprised a sample of patients who were in active treatment for ADHD. The clinical and socio-demographic data of the study sample are shown in Table 1. All patients who were included in the current study were in active follow-up in January 2011 and had been attended to for the first time between January 1999 and January 2010 in our Child and Adolescent Mental Health Centres. Patient selection was performed via the incidental sampling of patients who

had received a minimum of one year of multimodal treatment and had received a confirmed diagnosis of ADHD based on a structured clinical interview (Mini-Kid)(Sheehan et al., 2010). The following inclusion criteria were used: an initial clinical diagnosis of ADHD according to the DSM-IV(American Psychiatric Association, 1994) criteria with or without comorbidities, a medical history including at least one year of treatment and the persistence of the ADHD diagnosis at the one-year mark and the completion of the questionnaires by both parents. Exclusion criteria included the presence of any of the following comorbidities: mental retardation, autism, psychosis or organic brain disorder. Of the sample, 46 subjects (63%) presented comorbid diagnoses, the most frequent being oppositional defiant disorder (28.8%), phobic disorders (19.1%), affective disorders (16.4%), anxiety disorders (15%), behavioural disorders (8.2%) and tic disorders (6.8%). In addition, 13.3% of the patients had at least one other, less common comorbidity. Of the total sample, 80.8% were receiving pharmacological treatment for ADHD, of whom 91.4% were treated with methylphenidate and 8.6% were treated with atomoxetine. Of the subjects in pharmacological treatment, 1.6% had concomitant antidepressant treatment, 11.5% had neuroleptic treatment, 4.9% had mood stabilisers treatment and 1.6% had some combination of these drugs. Children's current ADHD symptom severity was obtained by the ADHD Rating-Scale-IV (ADHD-RS-IV)(Du Paul, G.J., Power, T.J., Anastopoulos, A.D., Reid, 1998).

Patient variables such as sex, comorbidity, age and treatment length were also examined to determine their potential relationship to ADHD severity (Lara et al., 2009; Goodman et al., 2011; López Seco et al., 2012).

To observe the influence of potential predictor variables on the current severity of ADHD symptoms according to the ADHD Rating-Scale-IV (ADHD-RS-IV), we compared subjects with scores below the cut-off of the original scale adjusted for age and sex (Du Paul, G.J., Power, T.J., Anastopoulos, A.D., Reid, 1998). Symptomatic children (N = 38) obtained a mean score of 33.3 ± 7.7 on the ADHD-RS-IV questionnaire, whereas the non-symptomatic group (N = 35) obtained a mean score of 14.6 ± 5. ($t=-11.6$, $p<0.001$).

Parental psychopathology was assessed with the Symptom Checklist-90-R (SCL-90-R)(Derogatis, 2002). Symptoms of inattention and hyperactivity/impulsivity were assessed with the World Health Organisation Adult ADHD Self-Report Scale (ASRS v.1.1) (Kessler et al., 2005, 2007; Ramos-Quiroga et al., 2009). A semi-structured interview was administered to all parents to assess their personal psychiatric histories (presence/absence) with the following general categories: anxiety disorders, affective disorders, psychosis, personality disorders, substance abuse and dependence, eating disorders, and adjustment disorders.

We found that 41.1% of mothers and 20.5% of parents had a psychiatric history. In mothers, depression (17.8%) and anxiety (13.7%) were the most common disorders. In fathers, adjustment disorders (4.1%) were the most common. Parental characteristics were categorised into potential predictor variables. Parents were divided into two categories based on their results from the World Health Organisation Adult ADHD Self-Report Scale (ASRS v.1.1)(Kessler et al., 2005, 2007) for hyperactivity symptoms in adults: those who exceeded the screening cut-off (raw score ≥ 12) according to the Spanish adaptation of the scale (Ramos-Quiroga et al., 2009) and those who did not. Similarly, the Symptom Checklist-90 R (SCL-90-R)(Derogatis, 2002) was used to divide parents into two categories based on their psychopathological profiles. Specifically, one group of parents comprised individuals who had obtained scores within the normal range, and the second group comprised individuals who had obtained scores equal to or exceeding the 80th percentile on at least two scales or on the global severity index.

The present study was evaluated and approved by the research committee of our hospital and by the local Clinical Research Ethics Committee. All families and all children over 12 years of age signed an informed consent form that was specifically designed for the current study.

2.2 Statistical analysis

The socio-demographic and clinical variables (Table 1) of children and parents were recorded. Qualitative variables are presented as percentages, and quantitative variables are presented as the means and standard deviations.

Using bivariate analyses to explore the relationship between all socio-demographic and clinical variables and children's ADHD symptom severity, the dependent variable was studied as a categorical (symptomatic vs. non-symptomatic children) and a continuous variable. Thus, a chi-square test was used to compare the distribution of categorical qualitative variables across the symptomatic and non-symptomatic child groups. The results were adjusted using the Yates correction for continuity. We used Student's T test to compare continuous variables. We conducted Pearson correlations to obtain associations among the continuous variables including the ADHD-RS score. To adjust for multiple comparisons, we used the Bonferroni correction. A binary logistic regression model was created for child ADHD symptom severity and the variable symptom severity was shown to be associated with in the bivariate analyses (i.e., psychiatric history of the mother, child's age and paternal psychiatric history, although this was not significantly associated). The children's time in drug

treatment was not included in the model because it was not associated with ADHD severity and it had high correlation with age (see Supplementary Table 3).The *Enter* method was used to adjust the model, and the Hosmer–Lemeshow chi-square test was used to assess the model's goodness of fit. The Wald test was used to evaluate the odds ratios (ORs) and 95% confidence intervals (CIs) that described the strength of each association and the ADHD symptom severity risk conferred by each variable. The results are presented in accordance with the suggestions of Franco (2007) regarding the quality of reports.

Potential collinearity between children's symptom severity, age, and months of treatment as well as both parents' ADHD symptoms was assessed using Pearson's correlation. A linear regression model was created for each of the predictor variables identified in the bivariate analyses (i.e., child's conduct disorder and mother's psychiatric history).

All two-tailed P-values < 0.05 were considered to be statistically significant. We used SPSS/PC^{TM}, version 17.0 (Arkmonk, NY,IBM Corp, USA) for all statistical analyses.

3. Results

Of the entire sample of children in the current study, 46.6% had at least one parent with a history of psychiatric treatment and 75.3% of the children had at least one parent with current psychopathology according to the SCL-90-R. In addition, 34.2% had at least one parent who exceeded the cut-off value on the adult ADHD scale. The number of children who exceeded the cut-off value on the ADHD-Rating Scale was 38 (52.1%), and 35 (47.9%) children had scores below the cut-off point. The differences in parental characteristics between the two groups are shown in Figure 1. Our results demonstrate that children with symptomatic severity were more likely to have mothers with a psychiatric history (70.4% vs. 29.6%, $\chi^2 = 4.6$, $p = 0.03$).

Regarding the current parental psychopathology, we did not find differences between the symptomatic and non-symptomatic groups in either mothers ($\chi^2 = 0.000$, p=1) or fathers ($\chi^2 = 0.31$, p=0.57); see Figure 1 and supplementary Table 1.

The symptomatic children were more likely to have a mother or a father with ADHD symptoms, but these differences did not reach statistical significance. There were nearly

twice as many fathers and twice as many mothers with ADHD symptoms in the group of symptomatic children (Figure 1).

The child's age was the only control variable that was significantly associated with symptom severity in our sample (Supplementary Table 3). The mean age of the symptomatic children was 10.4 years and that of the non-symptomatic children was 12.1 ($t = 2.6$, $p = 0.009$). There were no differences between the two groups with respect to sex, treatment length, comorbidity rates, academic level or the percentage of patients who continued drug therapy.

Logistic regression analysis with categorical ADHD child severity as the dependent variable revealed that younger children had an increased risk of more severe ADHD symptoms. Maternal psychiatric history showed a trend towards association with child's symptom severity, but it was not significant. The ORs and 95% CIs for this analysis are shown in Table 2.

A linear regression analysis with the continuous child ADHD severity score as the dependent variable also revealed that the mother's psychiatric history was associated with the child's ADHD severity even when the co-variable conduct disorder was entered into the analysis (Table 3, step 2).

4. Discussion

To our knowledge, the present study is the first to examine the prevalence of ADHD symptoms and psychopathology in the parents of children following treatment for ADHD and the relationships between these parental characteristics and symptom severity in children in a Spanish population. The results revealed high levels of past psychopathology (20.5% of fathers and 41.1% of mothers), current psychopathology (46.6% of fathers and 57.5% of mothers) and adult ADHD symptoms (21.9% of fathers and 17.8% of mothers) in our study sample. These data are consistent with results obtained in other countries (Gerdes et al., 2007; Chronis-Tuscano and Stein, 2012; Margari et al., 2013).

At the time of the study, both mothers and fathers from the sample exhibited a high incidence of psychopathology, but our analysis was not associated with offspring's symptom severity. In our sample, maternal but not paternal psychiatric history was associated with ADHD severity. Taken together, our findings are consistent with at least two hypotheses. First, one might hypothesise that other factors and not only the severity of the child's ADHD symptoms explain the presence of psychopathology in the parents of children with ADHD (Steinhausen et al., 2012). One might also hypothesise that the mother's current

psychopathological status is not important for symptom severity in the offspring but that maternal symptoms of psychopathology during a specific developmental period may play an important role in the development of psychopathology in the offspring (Stevens et al., 2008; Bagner et al., 2010; Thorell et al., 2012). A maternal history of psychiatric disturbances, which is associated with increased symptom severity, may contribute to offspring psychopathology via genetic and/or environmental influences or through other variables, such as attachment processes and/or emotional regulation (Bagner et al., 2010). These hypotheses require additional studies to evaluate them, and our study is not conclusive in this regard.

It is worth noting that both fathers and mothers showed similarly high percentages of ADHD symptoms (21.9% fathers and 17.8% mothers) that were consistent with those observed in clinical samples (Ramos-Quiroga et al., 2012) but much higher than the prevalence that has been described in the general population (Simon et al., 2009), suggesting the importance of ADHD detection in parents for the treatment prognoses of children with ADHD (Harvey et al., 2003; Chronis-Tuscano et al., 2011; Agha et al., 2013).

The fact that the current severity of ADHD symptoms in the parents of our study sample is not related to the severity of symptoms in their offspring could also be attributable to our selection of a sample of patients who were in ongoing treatment. It is possible that parental symptoms did not result in increased symptom severity among the offspring in our sample because these parents were being supported by a therapeutic team. However, one might expect that being in treatment could have helped improve these symptoms. This alerts us to a potential need for systematic pathology screening protocols for the parents of childhood ADHD patients to facilitate the development of health guidelines for parents. Improving coordination between the mental health services offered to childhood psychiatric patients and those offered to their mentally ill parents could be highly relevant, especially for pathologies with a strong genetic basis such as ADHD. On one hand, we have to notice that the global index of psychopathology may be an overall global concept to show associations. This could be a better explanation for the absence of differences in ADHD severity in offspring in our sample, and it is a limitation of our study. On the other hand, we would add the hypotheses that in a treated sample (more than three years of treatment), it is possible that some patients with few or mild symptoms are not treated in primary care because of parental psychopathology. This fact is congruent with our clinical impression and shows the importance of evaluating parents.

Of the children in our sample, 52.1% remained above the symptomatic cut-off point, whereas 47.9% remained below it. This finding also has significant welfare implications because ADHD is a highly prevalent and persistent pathology (Lara et al., 2009; Biederman et al., 2010), and thus it is important to design programs that include monitoring these patients once clinical stability has been reached at the primary care level. At this time, there is no formalised process for monitoring these patients in our setting.

We believe that the primary importance of this study is its clinical applicability. Specifically, it is important to know whether it would be appropriate to screen for psychopathology or ADHD symptoms in fathers and mothers to identify cases with poor prognoses, especially in samples who are receiving treatment at public mental health centres, which typically have very high workloads. Our results suggest that obtaining maternal psychiatric histories can be useful in identifying cases with worse symptom severity, a subgroup that might require additional specific attention. High rates of ADHD-like symptoms in parents suggest it is important to screen for parental ADHD. It would be useful to identify and treat parental ADHD and to adapt multimodal treatment programs for parents with ADHD as described in the literature (Chronis-Tuscano et al., 2008, 2011; Chronis-Tuscano and Stein, 2012).

In our sample, the presence of a conduct disorder was also associated with poor symptomatic prognosis of ADHD. Children with both ADHD and a conduct disorder have more severe symptoms and worse prognoses than do children with either disorder alone. Additionally, ADHD symptom severity and pervasiveness predict the development of antisocial behaviour through a gene-environment correlation (Thapar et al., 2006).

The main limitations of the present study include its variable treatment time, sampling type and relatively small sample size. It is a cross-sectional design, and we did not measure the previous severity. The children's ADHD symptom severity was assessed by a questionnaire completed by parents, and it could be interpreted that the scores reflected the parents' psychopathology more than the children's given that the parents reported the same symptom rates for themselves and for their children. However, in our sample, the presence of current parental psychopathology did not allow us to distinguish symptomatic from non-symptomatic cases. Symptomatic and non-symptomatic children had similar scores on the ADHD-RS based on current parental psychopathology (Supplementary Material, Table 1). The presence and type of parents' psychopathological history were gathered using a collection protocol for socio-demographic data that was designed for the study and that collected parental psychiatric history but did not take into account the type of pathology

treated. The children's overall functioning and degree of impairment were not assessed. In addition, the parents' psychopathology and ADHD symptoms were obtained using questionnaires and were not subsequently confirmed in clinical interviews. Consequently, we cannot definitively report parents' clinical diagnoses but only their compatible symptoms. Another potential source of bias derives from the type of parents examined. Because this study required the collaboration of both parents, it is possible that our sample consisted of highly involved families. In this sense, it should be noted that if higher rates of parental psychopathology are observed in a study with nuclear families that maintain therapeutic follow-up, efforts should be devoted to detecting parental psychopathology in less collaborative families. The participation of both parents is the strongest point of the study because the majority of the literature includes only female parents. An additional strength of the present study is that it pertains to a clinical sample that had been in follow-up for over a year (the mean was three years of treatment).

In conclusion, the presence of maternal psychiatric history and paternal ADHD symptoms were associated with greater ADHD severity in the offspring during clinical follow-up appointments in our setting. This finding supports the results described in the literature about ADHD psychosocial risk factors and suggests the need to formalise screening for psychopathology in parents with children who are in treatment for ADHD. Additional studies that examine therapeutic approaches to parental psychopathology and their influence on children's prognoses are needed to improve the overall management of this condition.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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Figure legends

Figure 1. Percentage of children in symptomatic and non-symptomatic subgroups according to parental psychiatric history, current presence of psychopathology and ADHD symptoms.

PH= presence of psychiatric history (obtained by semi-structured research interview); C-P= current presence of psychiatric symptoms (according to SCL-90-R), ADHD = Current presence of ADHD symptoms (according to ASRS-v1.1). See more details in Material and Methods section. *$\chi^2 = 4.6$, $p = 0.03$

Table 1. Socio-demographic and clinical variables of the total sample of children and parents

Children (N=73)	**Age (Mean±SD)**	11.2 ± 2.7
	Months of treatment (Mean±SD)	35.5 ± 28.7
	Sex (%)	
	Males	80.8
	Females	19.1
	Academic level (%)	
	Normal	71.2
	Low	20.7
	Presence of comorbidity (%)	63
	Pharmacotherapy (%)	80.8
	Current ADHD	24.5 ± 11.9
Parents (N= 146)	**Age of parents**	
	Mother	41.5±4.9
	Father	43.9±5.4
	Mother's education level (%)	
	Low	17.8
	Medium	67.1
	High	15.1
	Father's education level (%)	
	Low	43.8
	Medium	43.8
	High	12.3
	Family monthly income (%)	
	Low	6.8
	Medium-low	72.7
	Medium-high	16.4
	High	3.4
	Psychiatric history (%)	
	Mother	41.1
	Father	20.5
	ADHD symptoms (ASRS>12) (%)	
	Mother	17.8
	Father	21.9

Current psychopathology (%)	
Mother	57.1
Father	46.6

Table 2. Binary logistic regression analysis of the relationship between parental psychopathology and covariables and child's current ADHD symptom severity[a]

Regression model	Variables of the equation	β	Wald statistic	p	OR (CI 95%)
Binary logistic[b]	Age of the child	-0.2	4.6	0.03	0.8 (0.67-0.97)
	Psychiatric history of the mother	0.88	2.5	0.10	2.4 (0.82-7.2)
	Psychiatric history of the father	0.45	0.52	0.46	1.5 (0.46-5.4)

[a]ADHD symptom severity rated with the ADHD Rating-Scale-IV (ADHD-RS-IV) were dichotomised according to the cut-off of the original scale adjusted for age and sex (Du Paul, G.J., Power, T.J., Anastopoulos, A.D., Reid, 1998). See Material and Methods section

[b]Enter method. Hosmer-Lemeshow statistic $\chi^2 = 14.2$. $p>.05$. Naglekerke $R^2 = 0.10$.

Table 3. Linear regression analysis of the relationship between child conduct disorder, maternal psychiatric history and child's ADHD symptom severity

Variables in the equation[a]	B	SE B	β	p
Step 1				
Constant	23.4	1.37		
Child conduct disorder [b]	11.9	4.7	0.28	0.01
Step 2				
Constant	21.4	1.6		
Child conduct disorder	11.1	4.7	0.26	0.02
Psychiatric history of the mother	5.47	2.6	0.22	0.04

[a]Stepwise method

[b]Child conduct disorder was the only child covariable associated with child ADHD symptom severity (see supplementary Table 4).

We introduced parental psychiatric history, but these results were excluded from the analysis.

- Maternal psychiatric history was associated with an increased risk of greater symptom severity in the offspring.
- It will be important to screen for past and current psychopathology or ADHD symptoms in fathers and mothers to identify cases with poor prognoses, especially in samples undergoing treatment at public Mental Health Centres
- It would be useful to identify and treat paternal ADHD, to screen mothers with psychopathological history and to adapt multimodal treatment programs for parents with ADHD as described in the literature.