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ORIGINAL PAPER

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Lack of gender effects on subtype outcomes in adults with attention-deficit/hyperactivity disorder

Support for the validity of subtypes

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Abstract The aim of the present study is to verify if gender modifies the clinical, adaptative and psychological outcomes of adult attention-deficit/hyperactivity disorder (ADHD) subtypes. We evaluated 219 clinically referred adult patients. The interviews followed the DSM-IV criteria, using the K-SADS-E for ADHD and oppositional defiant disorder and SCID-IV for comorbidities. Regression models were used to analyze gender and subtype main effects and interactions in psychiatric outcomes. In the initial sample, 117 patients (53.5 %) were of the combined subtype, 88 (40 %) were inattentives and 14 (6.5 %) hyperactives. There were no significant interactions between gender and subtype in any variable assessed. Men and women did not differ in the relative frequency of each subtype. Patients of the combined subtype in both genders presented a higher severity and increased rates of conduct and ODD disorders than inattentives. The main effects of gender and subtype in this sample are similar to those previously reported in other countries, suggesting the cross-cultural equivalence of the phenotype. The absence of significant interactions between gender and subtype suggests that, at least in clinical-based samples, DSM-IV adult ADHD subtypes present cross-gender validity.

Key words ADHD · adults · DSM-IV · sex · subtype

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Introduction

Attention-deficit/hyperactivity disorder (ADHD) is highly prevalent in children and adolescents worldwide (Biederman and Faraone 2004; Rohde et al. 1999). The disorder is associated with both a broad range of negative outcomes for affected subjects (Dulcan 1997; Swanson et al. 1998; McGough et al. 2005) and a serious financial burden to families and society (National Institutes of Health 2000), characterizing a major public health problem (Lesesne et al. 1999). Several investigations have documented a high rate of persistence into adulthood (Hechtman et al. 1984; Mannuzza et al. 1991; Biederman et al. 1996; Barkley et al. 2002; Mannuzza et al. 2003; McGough and Barkley 2004). Recent population surveys in adults found estimated DSM-IV prevalences of ADHD between 1 % and 2.5 % in the Netherlands (Kooij et al. 2005) and 4.1 % in the USA (Kessler et al. 2005).

Despite of the growing interest in the diagnosis of ADHD in adults, most of the knowledge in ADHD still relies on research with children. The extrapolation of information generated from children to adults has been a subject of great debate (McGough and Barkley 2004; Barkley and Biederman 1997; Wilens et al. 2004).

The DSM-IV (American Psychiatric Association 1994) divides ADHD into three subtypes for children and adults (inattentive, hyperactive and combined). Unlike childhood ADHD, there is a shortage of investigations on adult ADHD subtypes (Murphy et al. 2002). Millstein et al. (1997) classified 56 % of patients as combined, 37 % as inattentive, and only 2 % as the hyperactive-impulsive subtype. They detected that individuals of the combined subtype had a higher prevalence of comorbid oppositional defiant disorder (ODD), substance abuse and dependence disorders, and more educational

problems. Murphy et al. (2002) reported similar rates with 60 % of combined, 38 % of inattentive and 2 % of hyperactive subtype subjects. The combined/hyperactive cluster was more likely to have ODD, to experience police arrests, interpersonal hostility, and to have attempted suicide compared to the inattentive subtype.

Adult ADHD patients are more impaired than controls, regardless of gender (Biederman et al. 1994). Biederman et al. (2004) also verified that the increase in the frequency of psychiatric disorders in ADHD patients compared with the control group was equivalent in men and women. Therefore, the lack of interaction between diagnosis and gender on clinical outcomes supported the cross-gender validity of adult ADHD diagnosis. However, although there is evidence that the ADHD diagnosis is valid in both genders, it is not clear if subtypes in adults present cross-gender validity.

Only two investigations assessed the cross-gender validity of ADHD subtypes, both with children. The first study reported significant interactions between gender and ADHD subtype for social problems, schoolwork difficulties, and self-esteem (Graetz et al. 2005). The results suggested the existence of gender-specific risks for symptom expression that may possibly have been overlooked in previous studies failing to separate by subtype or including only those with the combined subtype. On the other hand, a second investigation did not indentify interaction effects (Biederman et al. 2005). These studies were based on the same rationale suggested by Biederman et al. (2004). According to the authors, one way to validate a clinical entity is to determine if the clinical phenotype is different for male cases versus female cases. If the association between the subtypes and clinically relevant outcomes is not moderated by gender, it would be reasonable to interpret the findings to be supportive of the validity of ADHD subtypes for both genders (cross-gender validity).

The two objectives of the present study were 1) assess the main effects of gender and current ADHD subtypes on clinical, adaptative and psychological outcomes in a Latin American culture, and 2) test for interactions between gender and subtypes, contributing to the cross-gender validation of ADHD subtypes.

Methods

Sample

The recruitment process started with local newspaper articles on ADHD including the telephone number of the adult ADHD outpatient clinic of the Clinical Hospital of Porto Alegre (a major teaching hospital). Two hundred and nineteen self-referred adult ADHD patients of European descent, recruited from September 2002 to July 2004, comprised the initial sample. Patients were investigated and treated after a screening interview that confirmed ADHD diagnosis. All measurements were performed after recruitment, prior to the initiation of treatment for ADHD. Subjects of the hyperactive subtype (N = 14) were excluded from the analyses due to the small size of this group. Therefore, the final sample size was 205. Other exclusion criteria were evidence of clinically significant neurological diseases, current or past history of psychosis and IQ ≤ 70 (Kaplan et al. 1991). The project was approved by the Ethics Committee of the Hospital, and all patients signed an informed consent.

Diagnostic process

The interviewers in this research were all psychiatrists extensively trained in the application of all instruments in the research protocol. The diagnostic procedures for ADHD and ODD followed the DSM-IV criteria (American Psychiatric Association 1994) using the respective sections of the Portuguese version of K-SADS-E (Mercadante et al. 1995). The K-SADS-E is a semi-structured interview for children and adolescents aged 6 to 18 years which assesses current episodes and the severest episode in the past (lifetime) of DSM-IV psychiatric disorders in children (Ambrosini 2000). The only adaptation to adulthood symptoms (Grevet et al. 2005) was the adjustment of the criterion for onset of symptoms to age 12 or earlier instead of 7 or earlier as reported by others (Murphy and Barkley 1996; Murphy et al. 2002). In clinical practice, adolescents and adults frequently fail to provide precise recall on age of onset (Rohde et al. 2000). This adjustment is justified because no evidence exists to show that this criterion of onset by age 7 distinguishes valid from invalid cases (Barkley and Biederman 1997; Rohde et al. 2000). Moreover, the DSM-IV field trial also found that use of this criterion significantly diminished the reliability of the diagnosis (Applegate et al. 1997). The Kappa coefficients of interrater agreement for the K-SADS-E were 1.00 ($z = 8.19$; $p < 0.001$) for the childhood ADHD diagnosis, 0.91 ($z = 20.19$; $p < 0.001$) for childhood subtype, 1.00 ($z = 13.66$; $p < 0.001$) for current ADHD diagnosis and 0.95 ($z = 14.78$; $p < 0.001$) for current subtype diagnosis. Kappa coefficients regarding ODD were 1.00 ($z = 10.64$; $p < 0.001$) for the childhood diagnosis and 0.89 ($z = 9.10$; $p < 0.001$) for the current ODD diagnosis (Grevet et al. 2005).

All comorbid psychiatric disorders presented in Tables 3 and 4, except ADHD, ODD and anti-social personality disorder were derived from the structured interview SCID-IV-R (First et al. 1998). The diagnosis of conduct and anti-social personality disorder was obtained using the appropriate sections of the Mini-International Neuropsychiatric Interview (M. I. N. I.). This instrument is a short structured diagnostic interview for DSM-IV and ICD-10 psychiatric disorders (Sheehan et al. 1998).

The severity of current ADHD and ODD symptoms was assessed by the self-administered SNAP-IV Rating Scale (Swanson 1992). The instrument includes items from the DSM-IV criteria for ADHD and ODD. It is based on a 0 to 3 rating scale: Not at All = 0, Just a Little = 1, Quite a Bit = 2, and Very Much = 3. Scores on the SNAP-IV are calculated by summing the scores on the items in the subset and dividing by the number of items in the subset.

Barkley's current and childhood symptoms scales (self-report forms) address current and past ADHD symptoms listed in the DSM-IV diagnostic criteria (Barkley and Murphy 1998). The subset of the scale used in our study asks patients to report how often their symptoms interfere in ten areas of life activities.

The research protocol also included the assessment of demographic and education data, medical history and social problems. Socio-economic status was scored in five major cathegories according to the Brazilian Institute of Geography and Statistics census protocol (IBGE 2002).

Statistical analysis

The gender differences according to current ADHD subtype were assessed by the Pearson chi-square test. Continuous and categorical outcomes were analyzed by linear and logistic regressions, respectively.

The regression analyses were performed in two steps for each dependent variable (clinical data, psychological and adaptative functioning). The first step assessed the effects of gender, subtype and the interaction between gender and subtype. If the interaction were significant, it would be kept in the model, and the main effects of gender and subtype would be evaluated in the same analysis. If the interaction term were not significant, it would be removed in order to obtain more precise values for the main effects of gender and subtype, as re-

ported by Biederman et al. (2004). All tests were 2-tailed and significance level was set at 0.05. The analyses were performed with the SPSS statistic software.

Results

Sample and demographic characteristics

Considering the initial sample of 219 patients, 117 (53.5 %) were of the combined subtype, 88 (40 %) were inattentives and 14 (6.5 %) hyperactives. The final sample resulted in 205 individuals, with 57 % of the combined subtype and 43 % of the inattentive subtype.

The male:female ratio of the sample was 1.1:1. Fifty of the 109 men (45.9 %) presented the ADHD inattentive subtype while 59 (54.1 %) had the combined subtype. Among the 96 women, 38 (39.6 %) presented the inattentive and 58 (60.4 %) had the combined subtype. Men and women did not differ in relation to current subtype diagnosis ($\chi^2 = 0.82$, $p = 0.36$).

The average age of the sample was 34.45 years (± 10.89). Women were significantly older than men ($w = -3.23$, $p = 0.001$). Men and women did not differ in income ($w = 1.67$, $p = 0.10$) and education ($t = -1.49$, $p = 0.14$) (Table 1).

Interaction effects

There were no significant gender by subtype interaction effects in any variable assessed (see Tables 1–4). Therefore, the interaction terms were excluded in subsequent analyses focusing on effects of gender and ADHD subtypes separately.

Medical, adaptative and psychological history

Gender. Males with ADHD presented a higher incidence of past occurrence of head traumas ($w = 5.88$, $p = 0.01$), bone fractures ($w = 16.59$, $p < 0.001$), school suspensions ($w = 9.25$, $p = 0.002$), school expulsions ($w = 4.13$, $p = 0.04$) and car accidents ($w = 6.44$, $p = 0.01$) than women with the disorder. Men also received earlier ADHD diagnosis ($t = -3.03$, $p = 0.003$) and psychiatric treatment ($t = -2.56$, $p = 0.01$).

Subtype. Individuals of the combined subtype presented more school suspensions ($w = 11.64$, $p = 0.001$), school expulsions ($w = 4.36$, $p = 0.04$) and problems with authority and discipline ($w = 15.83$, $p < 0.001$) than those presenting the inattentive subtype (Table 1).

Severity of the disorder

Gender. Males and females did not differ on the severity of any current ADHD and ODD symptoms as assessed by the SNAP-IV Rating Scale. However, women reported more problems in functioning in areas of life activity for the last 6 months ($t = -3.36$, $p = 0.001$).

Subtype. Individuals of the combined subtype presented higher SNAP-IV ODD scores ($t = 5.61$, $p < 0.001$). They also reported higher problems in functioning in life activity for the last 6 months ($t = 2.06$, $p = 0.04$), and during childhood ($t = 2.60$, $p = 0.01$). As expected, patients of the combined subtype presented higher scores in hyperactivity ($t = 10.80$, $p < 0.001$), impulsivity ($t = 9.76$, $p < 0.001$) and overall SNAP-IV scores ($t = 7.03$, $p < 0.001$) (Table 2).

Lifetime comorbidities

Gender. Females had a higher prevalence of multiple (> 2) anxiety disorders ($w = 5.30$, $p = 0.02$) and generalized anxiety disorder (GAD) ($w = 4.00$, $p = 0.04$). Males presented a higher frequency of any substance use disorders ($w = 15.37$, $p < 0.001$), alcohol dependence ($w = 7.61$, $p = 0.006$) and alcohol abuse ($w = 4.08$, $p = 0.04$).

Subtype. The combined subtype had increased prevalence of conduct disorder ($w = 7.96$, $p = 0.005$) diagnoses.

There were no gender or subtype differences in the following diagnoses: Any comorbidity, MDD, bipolar disorder (BD), panic disorder, agoraphobia, social phobia, obsessive-compulsive disorder (OCD), post-traumatic stress disorder (PTSD), substance abuse and dependence and childhood ODD (Table 3).

Current comorbidities

Gender. Females presented more comorbidity with specific phobias ($w = 4.35$, $p = 0.04$) and GAD ($w = 5.20$, $p = 0.02$). Males had more substance use disorder ($w = 7.34$, $p = 0.007$), alcohol abuse ($w = 4.55$, $p = 0.03$) and anti-social personality disorder ($w = 5.93$, $p = 0.01$).

Subtype. The combined ADHD subtype was associated with more frequent current ODD diagnosis ($w = 6.37$, $p = 0.01$).

The presence of MDD, dysthymia, BD, multiple anxiety disorders, panic disorder, agoraphobia, social phobia, OCD, alcohol dependence, substance abuse and dependence did not differ in relation to subtype or gender (Table 4).

Discussion

The results of this study suggest two major findings: (a) gender does not moderate the effect of adult ADHD current subtypes on clinically relevant outcomes, support-

Table 1 Demographics and medical, adaptative and psychological history in adult males and females by subtype

	Males			Females			Statistical analysis					
	Inattentive (n = 50, 45.9 %) Mean (± SD)	Combined (n = 59, 54.1 %) Mean (± SD)	Total (n = 109) Mean (± SD)	Inattentive (n = 38, 39.6 %) Mean (± SD)	Combined (n = 58, 60.4 %) Mean (± SD)	Total (n = 96) Mean (± SD)	Interaction		Gender effect		Subtype effect	
							t	p	t	p	t	p
Demographic data												
Age	31.50 (11.63)	32.70 (10.64)	32.10 (11.1)	36.52 (10.30)	37.50 (10.32)	37.0 (10.3)	0.08	0.93	−3.23	0.001*	0.73	0.46
Monthly income	6.34 (14.87)	7.29 (9.45)	6.81 (12.1)	3.80 (4.22)	4.73 (11.31)	4.25 (7.75)	0.01	0.99	1.67	0.10	0.61	0.54
Years of schooling	13.28 (3.39)	14.07 (3.54)	13.67 (3.46)	15.52 (4.68)	13.99 (5.27)	14.75 (4.97)	1.92	0.06	−1.49	0.14	−0.45	0.65
Medical history												
Age at first treatment	23.80 (12.77)	20.88 (14.49)	22.34 (13.63)	29.34 (14.34)	25.43 (13.74)	27.38 (14.04)	0.25	0.80	−2.56	0.011*	−1.73	0.09
Age at ADHD diagnosis	28.58 (12.73)	27.45 (14.27)	28.01 (13.50)	32.76 (14.39)	34.31 (12.60)	33.53 (13.49)	−0.70	0.49	−3.03	0.003*	0.05	0.96
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	w	p	w	p	w	p
Nicotine use	21 (42.0)	30 (50.8)	51 (46.8)	10 (26.3)	26 (44.8)	36 (37.5)	0.70	0.40	1.96	0.16	3.38	0.07
Childhood seizures	5 (10.0)	3 (5.1)	8 (7.3)	2 (5.3)	1 (1.7)	3 (3.1)	0.08	0.77	1.50	0.22	1.72	0.19
Head traumas	9 (18.0)	15 (25.4)	24 (22.0)	4 (10.5)	5 (8.6)	9 (9.4)	0.60	0.44	5.88	0.015*	0.37	0.54
Bone fractures	31 (62.0)	39 (66.1)	70 (64.2)	13 (34.2)	21 (36.2)	34 (35.4)	0.02	0.88	16.59	0.001*	0.21	0.64
School problems												
Grade repetition	36 (72.0)	39 (66.1)	75 (68.8)	22 (57.9)	37 (63.8)	59 (61.4)	0.77	0.38	1.20	0.27	0.00	0.94
Suspensions	12 (24.0)	33 (55.9)	45 (41.3)	6 (15.8)	16 (27.6)	22 (22.9)	1.01	0.32	9.25	0.002*	11.64	0.001*
Expulsions	3 (6.0)	13 (22)	16 (14.7)	2 (5.3)	4 (6.9)	6 (6.2)	1.15	0.28	4.13	0.04*	4.36	0.04*
Social problems												
Problems with authority and discipline	20 (40.0)	34 (57.6)	54 (49.5)	6 (15.8)	33 (56.9)	39 (40.6)	3.64	0.06	2.53	0.11	15.83	< 0.001*
Problems with the law and police	10 (20.0)	15 (25.4)	25 (22.9)	0 (0.0)	0 (0.0)	0 (0.0)	0.00	0.99	0.13	0.72	0.45	0.50
Car accidents	22 (44.0)	32 (54.2)	54 (49.5)	12 (31.6)	19 (32.8)	31 (32.3)	0.36	0.55	6.44	0.01*	0.78	0.38

For binary outcomes we reported w (Wald chi-square scores) and for continuous outcomes t scores

* $p < 0.05$

ADHD attention-deficit/hyperactivity disorder

Table 2 Severity measures in adult males and females by subtype

Severity measures	Males			Females			Statistical analysis					
	Inattentive (n = 50, 45.9 %) Mean (± SD)	Combined (n = 59, 54.1 %) Mean (± SD)	Total (n = 109) Mean (± SD)	Inattentive (n = 38, 39.6 %) Mean (± SD)	Combined (n = 58, 60.4 %) Mean (± SD)	Total (n = 96) Mean (± SD)	Interaction		Gender effect		Subtype effect	
							t	p	t	p	t	p
Snap scores												
Inattention	1.68 (0.57)	1.80 (0.59)	1.74 (0.58)	1.91 (0.43)	1.89 (0.57)	1.90 (0.50)	0.96	0.34	−1.91	0.06	0.71	0.48
Hyperactivity	0.91 (0.55)	1.77 (0.51)	1.34 (0.55)	0.92 (0.56)	1.73 (0.58)	1.32 (0.57)	0.31	0.76	0.23	0.82	10.80	< 0.001*
Impulsivity	0.94 (0.69)	1.87 (0.58)	1.40 (0.63)	1.10 (0.78)	2.03 (0.63)	1.56 (0.70)	−0.00	0.99	−1.73	0.09	9.76	< 0.001*
ODD	0.73 (0.54)	1.16 (0.56)	0.94 (0.55)	0.68 (0.48)	1.13 (0.60)	0.90 (0.54)	−0.16	0.87	0.47	0.64	5.61	< 0.001*
Total	1.12 (0.44)	1.59 (0.46)	1.35 (0.45)	1.19 (0.36)	1.60 (0.49)	1.39 (0.42)	0.48	0.63	−0.54	0.59	7.03	< 0.001*
Barkley and murphy problem areas												
Self report last 6 months	1.42 (0.55)	1.73 (0.56)	1.58 (0.57)	1.87 (0.51)	1.88 (0.61)	1.85 (0.59)	1.83	0.07	−3.36	0.001*	2.06	0.04*
Self report childhood	1.10 (0.53)	1.30 (0.56)	1.22 (0.58)	1.13 (0.52)	1.35 (0.61)	1.27 (0.59)	−0.12	0.90	−0.53	0.60	2.60	0.01*

* $p < 0.05$
ODD oppositional defiant disorder

ing the cross-gender validity of adult ADHD subtypes; and (b) the main effects of gender and subtype are similar to those reported in other samples, suggesting a cross-cultural equivalence of the ADHD phenotype.

Gender and subtype distribution

The frequencies of each subtype in this study are very similar to those reported in other samples (Millstein et al. 1997; Murphy et al. 2002). Our results from a different culture also reinforce previous findings suggesting that clinically referred male and female adults have similar prevalences of ADHD diagnosis (Wender et al. 1981, 1985; Biederman et al. 1993, 1994; Murphy and Barkley 1996). In addition, men and women did not differ in the relative frequency of each subtype, consistent with previous findings (Millstein et al. 1997; Biederman et al. 2004). The adult pattern in all mentioned studies contrasts with the childhood ADHD pattern, where boys have a higher rate of the combined subtype than girls (Biederman et al. 2002).

Main effect of gender

Our data confirm previous reports showing that ADHD females present a higher frequency of simple phobia (Millstein et al. 1997), GAD and multiple anxiety disorders (McGough et al. 2005), and males more antisocial and substance use disorders (Millstein et al. 1997; Biederman et al. 2004; McGough et al. 2005). The fact that males reported more childhood medical and behavioral problems is consistent with other studies suggesting that ADHD boys are more likely to have disruptive behavioral disorders compared with girls (Biederman et al. 2002; Abikoff et al. 2002). In our study, women were older at the first ADHD diagnosis and treatment, and at the time of enrollment in this study. These findings are also consistent with previous findings showing that ADHD boys have an earlier average age at ADHD diagnosis and treatment. The most feasible explanation could be the increased frequency of disruptive and externalizing behavior and substance abuse in boys compared to girls that would develop more serious problems later in adolescence and adulthood (Gaub and Carlson 1997).

Main effect of subtypes

The results regarding the main effect of subtype agree with previous findings suggesting that individuals of the combined subtype present higher frequencies of ODD (Murphy et al. 2002; Millstein et al. 1997), school (Millstein et al. 1997) and social problems (Murphy et al. 2002). Consistent with these outcomes, combined individuals in our study also presented impaired functioning in areas of life activities. However, there were no sub-

Table 3 Lifetime psychiatric diagnoses in adult males and females by subtype

Lifetime comorbidities	Males			Females			Statistical analysis					
	Inattentive (n = 50, 45.9 %) n (%)	Combined (n = 59, 54.1 %) n (%)	Total (n = 109) n (%)	Inattentive (n = 38, 39.6 %) n (%)	Combined (n = 58, 60.4 %) n (%)	Total (n = 96) n (%)	Interaction		Gender effect		Subtype effect	
							w	p	w	p	w	p
Any comorbidity	29 (58.0)	43 (72.9)	72 (66.0)	29 (76.3)	45 (77.6)	74 (77.0)	0.79	0.37	2.86	0.91	1.70	0.19
Major depression	11 (22.0)	10 (16.9)	21 (19.2)	13 (34.2)	16 (27.6)	29 (30.2)	0.00	0.98	3.49	0.06	0.92	0.34
Bipolar disorder (I and II)	6 (12.0)	8 (13.6)	14 (12.8)	4 (10.5)	11 (19)	15 (15.6)	0.41	0.52	2.59	0.61	0.91	0.34
Multiple (> 2) anxiety disorders	6 (12.0)	5 (8.5)	11 (18.6)	8 (21)	14 (24.1)	22 (22.9)	0.07	0.79	5.30	0.02*	0.00	0.97
Panic disorder	2 (4.0)	4 (6.8)	6 (5.5)	2 (5.3)	8 (13.8)	10 (10.4)	0.17	0.68	1.45	0.23	1.97	0.16
Agoraphobia	0 (0.0)	1 (1.7)	1 (0.9)	0 (0.0)	3 (5.2)	3 (3.1)	0.00	0.99	0.97	0.32	0.03	0.85
Social phobia	9 (18.0)	7 (11.9)	16 (14.6)	10 (26.3)	9 (15.5)	19 (19.8)	0.05	0.81	1.14	0.28	2.40	0.12
OCD	4 (8.0)	2 (3.5)	6 (5.5)	3 (7.9)	2 (3.4)	5 (5.2)	0.00	0.98	0.00	0.99	1.92	0.17
GAD	5 (10.0)	9 (15.3)	14 (12.8)	9 (27.3)	14 (24.1)	23 (23.9)	0.35	0.55	4.00	0.04*	0.32	0.57
PTSD	0 (0.0)	1 (1.7)	1 (0.9)	2 (5.3)	0 (0)	2 (2.1)	0.04	0.84	0.53	0.47	0.72	0.40
Any substance use disorder[a]	15 (30.0)	20 (33.9)	35 (32.1)	3 (7.9)	5 (8.6)	8 (8.3)	0.01	0.92	15.37	< 0.001*	0.20	0.66
Alcohol dependence	6 (12.0)	11 (18.6)	17 (15.6)	1 (2.6)	2 (3.4)	3 (3.1)	0.03	0.86	7.61	0.006*	0.91	0.34
Alcohol abuse	7 (14.0)	5 (8.5)	12 (11.0)	0 (0.0)	3 (5.2)	3 (3.1)	0.09	0.77	4.08	0.04*	0.03	0.87
Substance dependence[b]	3 (6.0)	9 (15.3)	12 (11.0)	2 (5.3)	3 (5.2)	5 (5.2)	0.82	0.37	2.39	0.12	1.58	0.21
Substance abuse[b]	3 (6.0)	4 (6.8)	7 (6.4)	0 (0.0)	0 (0.0)	0 (0.0)	0.00	0.99	0.09	0.76	0.03	0.87
ODD	19 (38.0)	27 (45.8)	46 (42.2)	16 (42.1)	29 (50.0)	45 (46.9)	0.00	0.99	0.36	0.55	1.24	0.26*
Childhood conduct disorder	8 (16.0)	20 (33.9)	28 (25.6)	3 (7.9)	14 (24.1)	17 (15.5)	0.18	0.67	2.34	0.13	7.96	0.005*

* $p < 0.05$

[a] alcohol or drug abuse or dependence

[b] other than alcohol

OCD obsessive-compulsive disorder; *GAD* generalized anxiety disorder; *PSTD* post-traumatic stress disorder; *ODD* oppositional defiant disorder

Table 4 Current psychiatric diagnoses in adult males and females by subtype

	Males			Females			Statistical analysis					
	Inattentive (n = 50, 45.9 %)	Combined (n = 59, 54.1 %)	Total (n = 109)	Inattentive (n = 38, 39.6 %)	Combined (n = 58, 60.4 %)	Total (n = 96)	Interaction		Gender effect		Subtype effect	
Current comorbidities	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	w	p	w	p	w	p
Major depressive episode	7 (14.0)	11 (18.6)	18 (16.5)	10 (26.3)	15 (25.9)	25 (26.0)	0.26	0.61	2.66	0.10	0.16	0.69
Dysthymia	3 (6.0)	3 (5.1)	6 (5.5)	4 (10.5)	6 (10.3)	10 (10.4)	0.02	0.87	1.68	0.19	0.02	0.88
Bipolar disorder (I and II)	0 (0.0)	1 (1.7)	1 (0.9)	1 (2.6)	1 (1.7)	2 (2.1)	0.04	0.84	0.43	0.51	0.09	0.77
Multiple (> 2) anxiety disorders	4 (8.0)	3 (5.1)	7 (6.4)	6 (15.8)	8 (13.8)	14 (14.6)	0.11	0.74	3.64	0.06	0.34	0.56
Panic disorder	1 (2.0)	3 (5.1)	4 (3.7)	2 (5.3)	6 (10.3)	8 (8.3)	0.03	0.87	1.72	0.20	1.41	0.23
Agoraphobia	0 (0.0)	2 (3.4)	2 (1.8)	2 (5.3)	2 (3.4)	4 (4.2)	0.05	0.83	0.87	0.35	0.18	0.67
Social phobia	7 (14.0)	3 (5.1)	10 (9.2)	7 (18.4)	7 (12.1)	14 (14.6)	0.44	0.51	1.70	0.19	2.84	0.09
Specific phobia	1 (2.0)	1 (1.7)	2 (1.8)	1 (2.6)	8 (13.8)	9 (9.4)	1.18	0.28	4.35	0.04*	2.28	0.13
OCD	3 (6.0)	0 (0.0)	3 (2.7)	3 (7.9)	0 (0.0)	3 (3.1)	0.00	0.99	0.12	0.73	0.05	0.82
GAD	5 (10.0)	6 (10.2)	11 (10.1)	9 (23.7)	12 (20.7)	21 (21.9)	0.06	0.81	5.20	0.02*	0.06	0.80
Any substance abuse disorder[a]	8 (16.0)	9 (15.3)	17 (15.6)	1 (2.6)	2 (3.4)	3 (3.1)	0.06	0.80	7.34	0.007*	0.00	0.99
Alcohol dependence	3 (6.0)	2 (3.4)	5 (4.6)	1 (2.6)	0 (0.0)	1 (0.9)	0.04	0.84	1.76	0.18	1.13	0.29
Alcohol abuse	5 (10.0)	5 (8.5)	10 (9.2)	0 (0.0)	1 (1.7)	1 (0.9)	0.06	0.81	4.55	0.03*	0.00	0.99
Substance dependence[b]	1 (2.0)	5 (8.5)	6 (5.5)	0 (0.0)	1 (1.7)	1 (0.9)	0.03	0.86	2.73	0.10	2.29	0.13
Substance abuse[b]	2 (4.0)	3 (5.1)	5 (4.6)	0 (0.0)	0 (0.0)	0 (0.0)	0.00	0.99	0.04	0.84	0.07	0.79
ODD	8 (16.0)	17 (28.8)	25 (22.9)	7 (18.4)	22 (37.9)	29 (30.2)	0.12	0.73	1.06	0.30	6.37	0.01*
Anti-social personality	4 (8.0)	10 (16.9)	14 (12.8)	0 (0.0)	3 (5.2)	3 (3.1)	0.06	0.81	5.93	0.01*	3.26	0.07

* $p < 0.05$

[a] alcohol or drug abuse or dependence

[b] other than alcohol

OCD obsessive-compulsive disorder; *GAD* generalized anxiety disorder; *ODD* oppositional defiant disorder

type differences in the frequencies of bipolar and substance use disorders, as opposed to previous data (Millstein et al. 1997). We think that sample size is a likely reason for the discrepancies among studies regarding the frequencies of less common comorbidities. In addition, the comorbidity pattern of each subtype in a multifactorial disorder like ADHD may be influenced by genetic or environmental differences in each country.

Interaction effects

There are no previous gender by subtype interaction analyses on adult ADHD. For this reason, the only possible comparison with the present data is with samples of children. The two previous gender by subtype interaction analyses on ADHD conducted using samples of children (Biederman et al. 2005; Graetz et al. 2005) did not find interactions involving comorbidities. More research is needed in order to confirm the cross-gender validity of ADHD subtypes in children and adults.

Limitations

Our results should be understood in the context of some methodological limitations. We assessed a clinical referred sample. Thus, our findings should not be extrapolated to the general population. In addition, the present sample was limited to patients of European descent because the vast majority of the population of Porto Alegre, the capital of the southernmost state of Brazil, is European derived (Salzano and Freire-Maia 1970). For this reason, these results should not be generalized to the Brazilian population as a whole, since other regions have a more complex ethnic composition. Despite our relatively large sample, the stratification of genders, subtypes and comorbid diagnoses generated some low cell values, especially in less prevalent disorders. These results should be interpreted with caution, until another study with a larger sample size is performed. This kind of inherently detailed analysis generates a large set of comparisons. However, we regarded adjustment methods such as Bonferroni correction not applicable in this case since the objective is the careful description of frequency distributions, including small differences.

The absence of a control group might limit the precise estimative on the increased comorbidity rates of adult ADHD. Nevertheless, an additional comparison of our data with a population-based survey in Porto Alegre (Almeida-Filho et al. 1997) revealed a higher psychiatric morbidity in both genders in our study. For example, in the population-based sample, the prevalence of MDD was 5.2 % in males and 8.8 % in females (Almeida-Filho et al. 1997), while in the ADHD sample the respective frequencies are 19.2 % and 30.2 %. These prevalences are parallel with a US study of gender effects on ADHD (Biederman et al. 2004), where the MDD prevalences in the control sample were 5 % (males) and 7 % (females), while in the ADHD sample, 21 % and 23 %.

Finally, we restricted our analysis to current ADHD subtype. Since hyperactivity symptoms decrease over time, some patients met criteria for combined subtype as children, but are currently categorized as inattentives. Future studies should evaluate the clinical outcomes of individuals that change of subtype.

Conclusions

Adult ADHD is a relatively new diagnosis in psychiatry (Wender et al. 1985) and little studied outside the US, especially in developing countries. These findings in a Latin American sample agree with previous characterizations of the main effects of gender and subtype on adult ADHD, supporting the cross-cultural equivalence of the adult ADHD phenotype. Another noteworthy point is that the pure hyperactive subtype is rare in this and other samples. The existence and validity of a pure hyperactive subtype should thus be further clarified in larger samples.

Adults of both genders presented a worse outcome pattern if they were of the combined subtype. The absence of interaction effects between gender and subtype suggest that, at least in clinical-based samples, DSM-IV adult ADHD inattentive and combined subtypes present cross-gender validity.

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References

1. Abikoff HB, Jensen PS, Arnold LL, Hoza B, Hechtman L, Pollack S, Martin D, Alvir J, March JS, Hinshaw S, Vitiello B, Newcorn J, Greiner A, Cantwell DP, Conners CK, Elliott G, Greenhill LL, Kraemer H, Pelham WE Jr, Severe JB, Swanson JM, Wells K, Wigal T (2002) Observed classroom behavior of children with ADHD: relationship to gender and comorbidity. J Abnorm Child Psychol 30:349–359
2. Almeida-Filho N, Mari Jde J, Coutinho E, Franca JF, Fernandes J, Andreoli SB, Busnello ED (1997) Brazilian multicentric study of psychiatric morbidity. Methodological features and prevalence estimates. Br J Psychiatry 171:524–529
3. Ambrosini PJ (2000) Historical development and present status of the schedule for affective disorders and schizophrenia for school-age children (K-SADS). J Am Acad Child Adolesc Psychiatry 39:49–58
4. American Psychiatric Association (1994) Diagnostic and statistical manual of mental disorders. 4th ed. APA Washington DC
5. Applegate B, Lahey BB, Hart EL, Biederman J, Hynd GW, Barkley RA, Ollendick T, Frick PJ, Greenhill L, McBurnett K, Newcorn JH, Kerdyk L, Garfinkel B, Waldman I, Shaffer D (1997) Validity of the age-of-onset criterion for ADHD: a report from the DSM-IV field trials. J Am Acad Child Adolesc Psychiatry 36:1211–1221

6. Barkley RA, Biederman J (1997) Toward a broader definition of the age-of-onset criterion for attention-deficit hyperactivity disorder. Am Acad Child Adolesc Psychiatry 36:1204–1210
7. Barkley RA, Fischer M, Smallish L, Fletcher K (2002) The persistence of attention deficit/hyperactivity disorder into young adulthood as a function of reporting source and definition of disorder. J Abnorm Psychol 111:279–289
8. Barkley RA, Murphy KR (1998) Attention deficit hyperactivity disorder: a clinical workbook. Second edition. The Guilford Press New York
9. Biederman J, Faraone S, Milberger S, Curtis S, Chen L, Marrs A, Ouellette C, Moore P, Spencer T (1996) Predictors of persistence and remission of ADHD into adolescence: results from a four-year prospective follow-up study. J Am Acad Child Adolesc Psychiatry 35:343–351
10. Biederman J, Faraone SV, Monuteaux MC, Bober M, Cadogen E (2004) Gender effects on attention-deficit/hyperactivity disorder in adults, Revisited. Biol Psychiatry 55:692–700
11. Biederman J, Faraone SV, Spencer T, Wilens T, Mick E, Lapey KA (1994) Gender differences in a sample of adults with attention deficit hyperactivity disorder. Psychiatry Res 53:13–29
12. Biederman J, Faraone SV, Spencer T, Wilens T, Norman D, Lapey KA (1993) Patterns of psychiatric comorbidity, cognition, and psychosocial functioning in adults with attention deficit hyperactivity disorder. Am J Psychiatry 150:1792–1798
13. Biederman J, Faraone SV (2004) Attention deficit hyperactivity disorder: a worldwide concern. J Nerv Ment Dis 192:453–454
14. Biederman J, Kwon A, Aleardi M, Chouinard V, Marino T, Cole H, Mick E, Faraone SV (2005) Absence of gender effects on attention deficit hyperactivity disorder: findings in nonreferred subjects. Am J Psychiatry 162:1083–1089
15. Biederman J, Mick E, Faraone SV, Braaten E, Doyle A, Spencer T, Wilens TE, Frazier E, Johnson MA (2002) Influence of gender on attention deficit hyperactivity disorder in children referred to a psychiatric clinic. Am J Psychiatry 159:36–42
16. Dulcan M (1997) Practice parameters for the assessment and treatment of children, adolescents, and adults with attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry 36(Suppl):85S–121S
17. First MB, Spitzer RL, Gibbon M, Williams JB (1998) Structured clinical interview for DSM-IV axis I disorders, patient edition (SCID-I/P, Version 2.0, 8/98 revision). Biometric Research Department, New York State Psychiatric Institute New York
18. Gaub M, Carlson CL (1997) Gender differences in ADHD: A meta-analysis and critical review. J Am Acad Child Adolesc Psychiat 36:1036–1045
19. Graetz BW, Sawyer MG, Baghurst P (2005) Gender differences among children with DSM-IV ADHD in Australia. J Am Acad Child Adolesc Psychiatry 44:159–168
20. Grevet EH, Bau CHD, Salgado CAI, Ficher A, Victor MM, Garcia C, de Sousa NO, Nerung L, Belmonte-de-Abreu P (2005) Inter-rater reliability for diagnosis in adults of attention deficit hyperactivity disorder and oppositional defiant disorder using K-SADS-E. Arq Neuropsiquiatr 63:307–310
21. Hechtman L, Weiss G, Perlman T, Amsel R (1984) Hyperactives as young adults: Initial predictors of adult outcome. J Am Acad Child Psychiatry 23:250–260
22. IBGE – Instituto Brasileiro de Geografia e Estatística (2002) Censo demográfico 2000. IBGE Rio de Janeiro
23. Kaplan E, Fein D, Morris R, Delis DC (1991) WAIS-R: Manual. Psychological Corporation San Antonio
24. Kessler RC, Chiu WT, Demler O, Merikangas KR, Walters EE (2005) Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry 62:617–627
25. Kooij JJS, Buitelaar JK, Van Den Oord EJ, Furer JW, Rijnders CAT, Hodiamont PPG (2005) Internal and external validity of attention-deficit hyperactivity disorder in a population-based sample of adults. Psychol Med 35:817–827
26. Lesesne C, Abramowitz A, Perou R, Brann E (1999) Attention deficit/hyperactivity disorder: A public health research agenda. Available at: http://www.cdc.gov/ncbddd/adhd/dadphra.htm
27. Mannuzza S, Gittelman Klein R, Bonagura N, Malloy P, Giampino TL, Addalli KA (1991) Hyperactive boys almost grown up: V Replication of psychiatric status. Arch Gen Psychiatry 48:77–83
28. Mannuzza S, Klein RG, Moulton JL (2003) Persistence of attention-deficit/hyperactivity disorder into adulthood: what have we learned from the prospective follow-up studies? J Attent Disor 7:93–100
29. McGough JJ, Barkley RA (2004) Diagnostic controversies in adult attention deficit hyperactivity disorder. Am J Psychiatry 161:1948–1956
30. McGough JJ, Smalley SL, McCracken JT, Yang M, Del'homme M, Lynn DE, Loo S (2005) Psychiatric comorbidity in adult attention deficit hyperactivity disorder: findings from multiplex families. Am J Psychiatry 162:1621–1627
31. Mercadante MT, Asbahar F, Rosário MC, Ayres AM, Karman L, Ferrari MC, Assumpção FB, Miguel EC (1995) K-SADS, entrevista semi-estruturada para diagnóstico em psiquiatria da infância, versão epidemiológica. FMUSP São Paulo
32. Millstein RB, Wilens TE, Biederman J, Spencer TJ (1997) Presenting ADHD symptoms and subtypes in clinically referred adults with ADHD. J Attention Dis 2:159–166
33. Murphy K, Barkley RA (1996) Attention deficit hyperactivity disorder adults: comorbidities and adaptive impairments. Comp Psychiatry 37:393–401
34. Murphy KR, Barkley RA, Bush T (2002) Young adults with attention deficit hyperactivity disorder: subtype differences in comorbidity, educational, and clinical history. J Nerv Ment Dis 190:147–157
35. National Institutes of Health Consensus Development Conference Statement (2000) Diagnosis and treatment of attention-deficit/hyperactivity disorder (ADHD). J Am Acad Child Adolesc Psychiatry 39:182–193
36. Rohde LA, Biederman J, Busnello EA, Zimmermann H, Schimitz M, Martins S, Tramontina S (1999) ADHD in school sample of Brazilian adolescents: a study of prevalence, comorbid condition, and impairments. J Am Acad Child Psychiatry 38:716–722
37. Rohde LA, Biederman J, Zimmermann H, Schmitz M, Martins S, Tramontina S (2000) Exploring ADHD age-of-onset criterion in Brazilian adolescents. Eur Child Adolesc Psychiatry 9:212–218
38. Salzano FM, Freire-Maia N (1970) Problems in human biology: a study of Brazilian populations. Wayne State University Press Detroit
39. Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, Hergueta T, Baker R, Dunbar GC (1998) The mini-international neuropsychiatric interview (M. I. N. I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry 59(Suppl) 20: 22–33
40. Swanson JM (1992) School-based assessments and interventions for add students. KC Publishing Irvine
41. Swanson JM, Sergeant JA, Taylor E, Sonuga-Barke EJ, Jensen PS, Cantwell DP (1998) Attention-deficit hyperactivity disorder and hyperkinetic disorder. Lancet 351:429–433
42. Wender PH, Reimherr FW, Wood DR (1981) Attention deficit disorder ("minimal brain dysfunction") in adults. A replication study of diagnosis and drug treatment. Arch Gen Psychiatry 38:449–456
43. Wender PH, Wood DR, Reimherr FW (1985) Pharmacological treatment of attention deficit disorder, residual type (ADD, RT, "minimal brain dysfunction," "hyperactivity") in adults. Psychopharmacol Bull 21:222–231
44. Wilens TE, Faraone SV, Biederman J (2004) Attention-deficit/hyperactivity disorder in adults. JAMA 292:619–623