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ADHD in adults: clinical subtypes and associated characteristics

L'ADHD negli adulti: sottotipi clinici e caratteristiche associate

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SUMMARY. Introduction. Attention Deficit Hyperactivity Disorder (ADHD) is an early onset clinical condition characterized by attention difficulties, hyperactivity and impulsivity which can persist across the lifespan, significantly influencing the evolutionary course and facilitating the rise of psychiatric comorbidities. The presence of different ADHD subtypes in adults is a heterogeneity factor to be recognized in order to orient prognosis and treatment, as indicated by studies that described differences in the characterization of different subtypes in relation to both severity and comorbidities. **Materials and methods.** In the present study we evaluated the socio-demographic and clinical characteristics of a sample of adults with ADHD and the characteristics associated with the different disorder subtypes. We described 60 patients aged between 18 and 65 years (mean age 34.1) with primary diagnosis of ADHD consecutively admitted to the Regional Centre for diagnosis and treatment of ADHD in adults in Milan. **Results.** We observed high severity of symptoms and low quality of life, in particular in the "life outlook" dimension. The subtypes distribution was the following: 18.3% inattentive subtype, 8.3% hyperactive/impulsive subtype and 70% combined subtype. The hyperactive/impulsive subtype showed a significantly higher frequency in females, while the inattentive subtype was more frequent in males. Patients with the hyperactive/impulsive subtype showed worse quality of life and more frequent anxiety disorders. **Conclusions.** Considering the different clinical profiles among various subtypes, these data add relevance to subtypes classification of adult ADHD.

KEY WORDS: ADHD, adults, subtypes, comorbidity.

RIASSUNTO. Introduzione. Il disturbo da deficit di attenzione e iperattività (ADHD) è un disturbo a esordio nell'infanzia caratterizzato da deficit dell'attenzione, iperattività e impulsività che può persistere in età adulta, complicandosi con altri disturbi in comorbilità. La presenza di sottotipi nell'ADHD costituisce un fattore di eterogeneità che va riconosciuto in quanto i diversi sottotipi possono associarsi a profili di gravità e comorbilità differenti. **Materiali e metodi.** In questo studio abbiamo valutato le caratteristiche socio-demografiche e cliniche di un gruppo di pazienti adulti con ADHD, nonché le caratteristiche associate ai sottotipi del disturbo. Abbiamo reclutato 60 pazienti di età compresa fra i 18 e i 65 anni (età media 34,1) con diagnosi primaria di ADHD consecutivamente afferiti al Centro Regionale per la diagnosi e il trattamento dell'ADHD a Milano. **Risultati.** Il campione si caratterizza per un'elevata gravità sintomatologica e una bassa qualità di vita, in particolare nella dimensione "prospettive di vita". La distribuzione in sottotipi è la seguente: 18,3% con sottotipo disattento, 8,3% con sottotipo iperattivo/impulsivo, 70% con sottotipo combinato. I pazienti con sottotipo iperattivo/impulsivo sono più frequentemente di sesso femminile, manifestano una peggiore qualità di vita e una più frequente comorbilità con disturbi d'ansia. **Conclusioni.** Considerando le diversità nelle manifestazioni cliniche associate, i dati presentati confermano l'utilità della classificazione in sottotipi dell'ADHD.

PAROLE CHIAVE: ADHD, adulti, sottotipi, comorbilità.

INTRODUCTION

Attention Deficit Hyperactivity Disorder (ADHD) is a clinical condition with onset in childhood and pre-adolescence characterized by attention deficits, hyperactivity and impulsivity leading to significant impairment in academic/occupational, familiar and social functioning[1]. ADHD does not only affect childhood; indeed several studies found that it often persists into adult age[2-5], with prevalence rates ranging between 1% and 5%[6]. The most significant clinical symptoms in adulthood are the difficulties in planning/organizing daily activities, an extreme restlessness and damaging impulsivity, all of which contribute to the challenge in keeping stable job and relationships[7]. Moreover, adults with ADHD often present with concurrent psychiatric disorders[8], to the extent that up to two thirds of adults with ADHD show at least one comorbid psychiatric condition[6]. Similarly, ADHD is found in approximately 15% of adults with other psychiatric disorders[8,9]. Comorbid disorders often mask ADHD core symptoms, with the result that only a minority of these patients are correctly diagnosed and receive appropriate treatment[10,11].

In addition to comorbid disorders, the presence of different subtypes of ADHD in adults – hyperactive/impulsive,

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inattentive and combined subtypes – is a further element of heterogeneity to be recognized in order to orient prognosis and treatment. Recent studies demonstrated an association between the combined subtype and some severity indices of ADHD such as a higher frequency of comorbid disorders[12], substance abuse[13] and neuroticism[14], underlining the importance of subtype classification for prognostic purposes.

Aim of the present study is to describe the socio-demographic and clinical characteristics of ADHD in a sample of adult patients in charge of a regional reference center, and to evaluate their association with the different subtypes of the disorder.

MATERIALS AND METHODS

Subjects with a primary diagnosis of ADHD[1] aged between 18 and 65 years consecutively referred to the regional center for the diagnosis and treatment of ADHD in adults in Milan were recruited during a period of 2 years.

Patients included in the study were administered the following scales:

- MINI Neuropsychiatric Inventory 5.0.0[15] and SCID-II[16] for the diagnosis of psychiatric disorders;
- Diagnostic Interview for ADHD in adults (DIVA)[17] for the diagnostic evaluation of ADHD subtypes;
- Adult ADHD Self Report scale (ASRS)[18] to evaluate ADHD symptomatology in adulthood;
- Wender Utah ADHD rating scale (WURS)[19] to evaluate ADHD symptomatology in childhood;
- Adult ADHD Quality of Life Questionnaire (AAQoL)[20] to evaluate the impact of ADHD symptomatology on quality of life;
- State Trait Anxiety Inventory (STAI-Y)[21] to evaluate the presence of comorbid anxiety symptoms;
- Beck Depression Inventory II (BDI-II)[22] to evaluate the presence of comorbid depressive symptoms.

Statistical analyses

Socio-demographic and clinical characteristics of the sample were described through mean and standard deviation. Socio-demographic characteristics included age, gender, biological or adoptive parents, education, occupation, civil status. Clinical characteristics included ADHD subtype, age of onset, comorbid psychiatric and medical diseases, family history of ADHD and other psychiatric disorders, suicidal ideation or attempts, traumatic episodes in childhood, severity of illness (scores at ASRS, CGI, WURS), quality of life (AAQoL), severity of anxiety symptoms (STAI-Y), and severity of depressive symptoms (BDI-II).

Socio-demographic and clinical characteristics were then compared in the three ADHD subtypes (inattentive, hyperactive/impulsive, combined). Between-group comparison of categorical variables were made with Pearson's Chi-square test. Comparisons of continue variables were performed using ANOVA.

Given the exploratory nature of our study, we decided to use a 2-tailed significance level of $p<.05$. All statistical analyses were performed using the IBM SPSS 20.0 software[23].

RESULTS

Sixty adult patients with ADHD consecutively admitted at the center from June 2015 to June 2017 were recruited for the present study. Thirty-two patients were referred by the Italian Association of Families with ADHD (AIFA), 16 patients self-referred to the center, 10 were referred by their general practitioner, while only 2 were referred by the local Child and Adolescent Mental Health Service. Forty-one (68.3%) were males, mean age was 34.1±12.0 years. Four (6.7%) were adopted during childhood. Mean education was 13.5±3.4 years. The majority were single. All socio-demographic characteristics of the sample are reported in Table 1.

Mean age of onset of the ADHD was 7.5±2.2 years. Thirteen patients reported a family history of ADHD. Thirty-eight were diagnosed with at least one comorbid psychiatric disorder.

The most frequently associated disorders were personality disorders (20 patients), among which the majority was diagnosed with cluster B (17 patients) and the remaining with cluster C personality disorders. The following most frequent comorbidities were affective (16 patients) and anxiety disorders (10 patients). Less frequently comorbid were substance abuse (8 patients) and specific learning disorders such as dyslexia (5 patients) and dyscalculia (1 patient).

Severity of illness was measured referring to both the symptomatology recalled from childhood (WURS) and the current symptomatology (ASRS). Mean WURS score was 46.3±16.2, mean ASRS score was 41.3±15.4. Mean number of positive criteria at the ASRS was 12.1±3.7.

Looking at the severity of associated depressive and anxious symptoms, the mean BDI-II score was 27.4±13.5 and the mean STAI-Y scores were 49.6±14.1 (state anxiety) and 57.3±11.2 (trait anxiety). Finally, the total mean quality of life score (AAQoL) was 44.3±14.8; subscale scores were 41.3±18.6 for 'Life productivity', 42.6±25.7 for 'Psychological health', 36.5±14.0 for 'Life outlook' and 53.3±22.9 for 'Relationships'. All clinical characteristics of the sample are reported in Table 2.

Table 1. Socio-demographic characteristics of the sample (N=60).

	N (%) / mean (SD)
Age, years	34.1 (12.0)
Education, years	13.5 (3.4)
Gender	
females	19 (31.7)
males	41 (68.3)
Adopted	4 (6.7)
Occupation	
White collar	22 (36%)
Blue collar	4 (6,7%)
Housewife	1 (1,7%)
Student	16 (26,7%)
Unemployed	17 (28,3%)
Civil status	
Single	43 (71,7)
Married/partner	16 (26,7)
Divorced	1 (1,7)

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ADHD subtypes and associated socio-demographic and clinical characteristics

Regarding ADHD subtypes, eleven patients (18.3%) were diagnosed the inattentive type, five (8.3%) the hyperactive/impulsive type and forty-two (70%) the combined type.

The subtypes did not differ in socio-demographic characteristics except for gender: we observed higher prevalence of females in the hyperactive/impulsive in comparison to the inattentive subtype (4 vs. 0 patients, p=0.005) and higher prevalence of males in the inattentive in comparison to the hyperactive/impulsive subtype (11 vs. 1 patient, p=0.005).

Hyperactive/impulsive subtype was more frequently associated with comorbid anxiety disorders (60% hyperactive/impulsive vs. 27% inattentive and 9.5% combined; p=0.011).

Hyperactive/impulsive type was also associated with worse quality of life in the Relationships domain in comparison to the other subtypes (5.00 hyperactive/impulsive vs. 60.43 inattentive and 55.45 combined; p=0.004).

The other variables were not significantly different in the three subtypes. ASRS and WURS total scores tended to be higher in the combined subtype, but the difference with other subtypes did not reach the statistical significance.

All socio-demographic and clinical characteristics associated with ADHD subtypes are reported in Table 3.

Table 2. Clinial characteristics of the sample (N=60).

	N (%) / media (DS)
Suicidal ideation	6 (10)
Suicidal attempts	2 (3.3)
Traumatic episodes in childhood	8 (13.3)
ADHD familiarity	13 (21.1)
ADHD age of onset	7,5 (2.2)
DIVA *Inattentive* *Hyperactive/Impulsive* *Combined* *Not determined*	 11 (18.3) 5 (8.3) 42 (70.3) 2 (3.3)
Comorbidity Personality disorders Affective disorders Anxiety disorders Substance abuse SLD Psychotic disorders	38 (63.3%) 20 (33.3%) 16 (26,7%) 10 (16.7%) 8 (13.3%) 6 (10%) 1 (1.7%)
WURS	46.3 (16.2)
BDI_II	27.4 (13.5)
STAI	I: 49.6 (14.1) II: 57.3 (11.2)
ASRS *18 criteria:* *Positive criteria* *Total score* *6 criteria:* *Positive criteria* *Total score*	 12.1 (3.7) 41.3 (15.4) 4.6 (1.1) 15.9 (3.1)
AAQoL *Total* *Life productivity* *Psychological health* *Life outlook* *Relationships*	 44.3 (14.8) 41.3 (18.6) 42.6 (25.7) 36.5 (14.0) 53.3 (22.9)

Table 3 (part I). Socio-demographic and clinical charateristics of the main subtypes (N=58).

	Inattentive subtype	Iperact/ impuls subtype	Combined subtype		
	N=11	N=5	N=42	χ^2 / F	p
Gender *females* *males*	 0 11 (100%)	 4 (80.0%) 1 (20%)	 14 (33.3%) 28 (66.7%)	10.655	0.005*
Adopted	1 (9.1%)	0	3 (7.1%)	0.457	0.796
Age, mean (SD)	33.2 (11.8)	44.4 (20.5)	33.4 (10.7)	1.964	0.150
Civil status *Single* *Married/ partner* *Divorced*	 10 (90.9%) 1 (9.1%) 0	 4 (80.0%) 1 (20%) 0	 27 (64.3%) 14 (33.3%) 1 (2.4%)	3.293	0.510
Education, mean (SD)	14.2 (4.7)	12.4 (2.6)	13.6 (3.1)	0.477	0.623
Age of onset, mean (SD)	7.0 (1.9)	9.2 (2.9)	7.4 (2.0)	1.981	0.148
Occupation *White collar* *Blue collar* *Housewife* *Student* *Unemployed*	 3 (27.3%) 1 (9.1%) 0 4 (36.4%) 3 (27.3%)	 3 (60.0%) 0 0 1 (20.0%) 1 (20.0%)	 16 (38.1%) 3 (7.1%) 1 (2.4%) 10 (23.8%) 12 (23.8%)	2.501	0.962
ADHD familiarity	2 (20%)	2 (40%)	8 (20%)	1.066	0.587
Comorbid psychosis	0	0	1 (2.4%)	0.388	0.824
Comorbid affective disorder	4 (36,4%)	3 (60%)	9 (21.4%)	3.851	0.146
Comorbid anxiety disorder	3 (27.3%)	3 (60.0%)	4 (9.5%)	8.936	0.011*
Comorbid SLD	2 (18.2%)	0	4 (9.5%)	1.336	0.513
Comorbid substance abuse	0	0	7 (16,7%)	3.033	0.220
Comorbid personality disorder	2 (18.2%)	0	16 (38.1%)	4.077	0.130
Suicidal ideation	0	1 (20.0%)	5 (11.9%)	1.882	0.390
Suicidal attempts	0	1 (20.0%)	1 (2.4%)	4.651	0.098
Traumatic episodes in childhood	0	0	7 (16.7%)	3.033	0.220

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Table 3 (part II). Socio-demographic and clinical charateristics of the main subtypes (N=58).

	Inattentive subtype	Iperact/ impuls subtype	Combined subtype		
	N=11	N=5	N=42	χ^2 / F	p
WURS	41.80	32.25	49.14	2.582	0.087
ASRS-18 total score	30.00	37.33	45.14	2.648	0.089
ASRS-6 total score	13.50	14.67	16.40	1.785	0.189
ASRS-18 n° positive items	10.40	13.00	12.39	0.642	0.534
ASRS- 6 n° positive items	5.00	4.33	4.60	0.316	0.732
AAQoL Total score	47.56	31.08	46.18	1.463	0.248
AAQoL Life productivity	46.35	53.40	39.91	0.812	0.454
AAQoL Psychologica l health	44.04	8.50	46.91	2.447	0.104
AAQoL Life outlook	33.58	38.42	37.28	0.195	0.824
AAQoL Relatioships	60.43	5.00	55.45	6.784	0.004*
BDI_II	16.00	37.50	28.46	1.824	0.195
STAI_I	51.86	66.00	47.58	2.641	0.084
STAI_II	56.57	64.33	56.88	0.614	0.546

DISCUSSION

This study aimed at characterizing a clinical sample of accurately diagnosed adults with ADHD referred to a regional specialist center in Italy. We also aimed at further validating the diagnostic construct of subtypes in our sample.

Several studies demonstrated the usefulness of assessing ADHD subtypes in adults, in particular for their impact on the prognosis. As far back as 20 years ago, a DSM-IV field trial found that 66% of children and adolescents with ADHD displayed the combined subtype[24]. Our finding that the two thirds of adults with ADHD still present with the combined subtype, in agreement with other studies on adults with ADHD[12,25-27], suggests a stability of subtypes over time.

It is noteworthy that almost 90% of patients show inattentive symptoms, confirming the observation by Wilens and colleagues[27] that attention deficit tends to be far more prevalent than other symptom domains. On the other hand, the hyperactive/impulsive type appears to be the less represented, characterizing only the 8% of the patients' sample.

Regarding the gender distribution males were over represented, with a 2:1 male/female ratio in line with the 1.6:1 ratio indicated in the DSM-5[1]. Although it tends to decrease over time[28], a predominance of males is confirmed also in adult patients with ADHD[12,29]. In our sample we observed a higher prevalence of females in the hyperactive/impulsive type; this observation is in contrast to several studies that showed higher levels of inattention in females, suggesting that in women the symptomatology is more internalized[25-27,30]. According to some researchers this would lead to less frequent access to care and therefore to a reduced recognition of ADHD in females, resulting in a biased evidence of males preponderance in ADHD samples[31,32]. In line with this hypothesis, our finding of hyperactive/impulsive type prevalence in females could mean that women asking for treatment in our center are those with the most evident clinical presentation, characterized by hardly tolerated hyperactivity and impulsive behaviors and for this reason either seeking treatment or being induced to treatment by their family members.

Looking at severity of illness, the mean score obtained at the WURS, administered to adults in order to retroactively report ADHD symptoms in childhood, was 46. The value matches those reported in Korean and Spanish samples[33,34], thus demonstrating the high consistency of the scale in different populations. Although the difference did not reach statistical significance, most likely because of the small sample size, we found that WURS scores were higher in the combined type, thus confirming the more severe progression of disease in this subtype. This result is in line with a German study, the only one that examined WURS scores in ADHD subtypes, also finding higher scores in the combined type versus the other subtypes[14].

The ASRS total score, which evaluates the intensity of current symptomatology, was well beyond the cut-off of 32, further validating the diagnosis of ADHD[35], As well as with the WURS, although not reaching significance we found higher ASRS scores in the combined type. We also found higher total scores in females than in males; this finding, which confirms the hypothesis that mainly women with more severe ADHD clinical conditions and more externalized symptoms ask for clinical attention, is in accordance with a recent Norwegian study in adults with ADHD that showed greater severity of illness in females[36].

In our study the 63% of patients, about two thirds, present at least one comorbid psychiatric disease, thus confirming the high tendency in adults with ADHD to show a broad symptomatology. This phenomenon has been described in several studies, which indicated comorbidity rates between 57% and 92%[12,25,27].

Personality disorders appear to be the most frequent ones (33%, most of which cluster B disorders), in accordance with an Italian study indicating that up to 60% of patients with borderline personality disorder reported childhood behaviors and symptoms compatible with a diagnosis of ADHD[37].

The comorbidity of ADHD with depressive disorders in our sample is also in line with previous clinical observations reporting depression rates between 18% and 53% in adults with ADHD[12,38,39]. Comorbid depression implies an increased burden of illness with further deterioration of the quality of life, which is worse in patients with ADHD and depression than in patients with depression alone[40]. The co-occurrence between depressive disorders and ADHD can be explained by shared etiopathogenetic factors, both genetic[41,42] and related to pregnancy, such as preterm birth, smoking or pathological conditions during pregnancy[43]. Some authors have proposed that the development of depressive

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symptoms represents an adaptive strategy for compensating hyperstimulation through a reduced "hedonic tone"[44]. Moreover, impairment of functioning in all areas and the worsening of the quality of life brought by ADHD can induce secondary demoralization with associated decreased hedonic ability, sleep disorders and irritability[45,46].

Looking at the association between ADHD subtypes and comorbid disorders, we found a higher frequency of anxiety disorders (60%) in patients with hyperactive/impulsive ADHD. This results are partially consistent with those by Soendergaard and colleagues, in which 20% of hyperactive/impulsive patients showed anxiety disorders against 7% of patients with the combined subtype[12]. However it substantially differs from two US studies in which anxiety disorders were mostly associated with the combined subtype[27,47].

Self-reported quality of life is consistent with two studies conducted on a sample of US college students and Spanish adults with ADHD[34,48]. In both studies particularly low scores were found in the "Life outlook" subscale, while better quality of life was perceived in the "Relationships" dimension, suggesting that subjects perceive the impact of illness mainly in academic/occupational functioning. Our patients with hyperactive/impulsive subtype showed worse quality of interpersonal relationships in comparison to the other subtypes: this appears coherent with the clinical experience, which describes impulsive subjects as complicated ones, who have difficulty in waiting for their turn, often talk over other speakers and occasionally show aggressive behaviors, thus pushing others away.

The main strength of our study is the broad range of scales adopted and administered by expert psychologists in a regional reference center. The main limitation is the small sample size; accordingly, the observed higher frequency of depressive disorders and higher intensity of the depressive symptoms in this subtype as well as the observed higher severity of ADHD symptomatology in the combined subtype could not reach the statistical significance. Another limit of the study is the cross-sectional design, which cannot inform about the effectiveness of pharmacological treatments in the different subtypes.

CONCLUSIONS

We observed an ADHD subtype distribution similar to that evidenced in most previous studies, with a clear preponderance of the combined type and a reduced prevalence of the hyperactive/impulsive type. Besides the combined subtype, which appears to be characterized by higher severity of symptoms, the hyperactive/impulsive subtype also shows severe features such as a higher frequency of comorbid anxiety disorders and the worst quality of life in interpersonal relationships. Finally, the observation that women referred to our center more frequently present with hyperactivity and impulsive behaviors suggests the need for a better screening of symptoms of inattention (difficulties in attention, planning, organizing), which particularly in women are probably not recognized, although they can be associated to poor quality of life and to the development of secondary psychiatric symptoms and disorders[49,50].

Conflict of interests: the authors declare no conflict of interests.

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