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Trait-based Dimensions Discriminating Adults with Attention Deficit Hyperactivity Disorder (ADHD), Autism Spectrum Disorder (ASD) and Co-occurring ADHD/ASD

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Abstract: The study assesses the co-occurrence of ADHD and ASD in newly diagnosed adults of normal intelligence and the contribution of trait-based dimensions deriving from the Barkley Adult ADHD Rating Scale-IV (BAARS-IV), the Autism-Spectrum Quotient (AQ) and the Empathy Quotient (EQ) to the differentiation of patients with ADHD, ASD and ADHD/ASD. 16.1% of patients with ADHD received a co-occurring ASD diagnosis while 33.3% of patients with ASD an ADHD diagnosis. Subjects with ADHD or ADHD/ASD had higher scores in all ADHD traits compared to ASD ones. The ASD compared to the ADHD group had AQ scores significantly greater except from Attention to Details. ADHD/ASD co-occurrence significantly increased the score of Attention to Details. Total EQ score was greater in the ADHD group. In stepwise logistic regression analyses past Hyperactivity, current Inattention and Impulsivity, Attention Switching, Communication, Imagination and EQ Total score discriminated ADHD from ASD patients. Attention to Details, Imagination and Total EQ score discriminated ADHD from ADHD/ASD cases, while past Hyperactivity and current Impulsivity discriminated ASD from ADHD/ASD subjects. Our findings highlight the importance of particular trait-based dimensions when discriminating adults with ADHD, ASD and co-occurring ADHD/ASD.

Keywords: attention deficit hyperactivity disorder (ADHD); autism spectrum disorder (ASD); adults; self-report dimensions

1. Introduction

Attention deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) are amongst the most prevalent neurodevelopmental disorders. ADHD is characterized by developmentally inappropriate inattention, impulsiveness, and/or hyperactivity that remain relatively persistent over time and result in impairment across multiple domains of life activities. ASD is characterized by persistent deficits in social interaction and communication as well as restrictive, repetitive patterns of behavior or interests [1]. These disorders typically have a childhood onset and persist into adult life, but there is a significant unmet clinical and research need to

understand the persistence into adulthood [2-7]. In clinical practice a notable symptom overlap between ASD and ADHD symptoms, may lead to diagnostic overshadowing of ADHD symptoms in ASD and vice versa. Despite the fact that prior to the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) [1], a diagnosis of ASD precluded a diagnosis of ADHD, there has been a considerable amount of research focusing on the co-occurrence between ADHD and ASD and many questions have been posed about the relationship between the two disorders. So far, the body of literature is for the vast majority based on childhood data. Research data show that 18% to 50% of children with ADHD present with clinical levels of ASD symptoms [7-10]. Conversely, ADHD is the most common co-occurring disorder in children with ASD with co-occurrence rates in the 40-70% range [11-13]. Moreover, it has been reported that the overshadowing of symptoms in co-occurring cases that had been diagnosed with ADHD first, may lead to a delay in the diagnosis of ASD [14]. Research data on the co-occurrence of ADHD and ASD in adulthood are scarce. Current or past diagnosis of ADHD in ASD adult patients has been reported to be from 9.7% to 43% with most reports being within the range of 37-43% [6,15-19] while Edvinsson et al. [20] in a sample of patients diagnosed with ADHD in adulthood found that over 10% of the sample had a current and past diagnosis of ASD. Some researchers have even categorized ADHD and ASD as falling on the same continuum of neurodevelopmental disorders, with ADHD representing a less severe presentation of ASD [21, 22].

Although diagnosis following DSM or ICD criteria has been the norm in child and adult psychiatry, a dimensional or hybrid model approach has been adopted for polythetic syndromes [23]. There is increasing recognition that dimensions of behavior can cut across diagnostic categories and those dimensions can be helpful in successfully categorizing individuals with neurodevelopmental disorders. Consistent with the hypothesis that co-occurrence of ADHD and ASD is better examined by dimensional traits are studies that investigate mechanisms underlying the co-occurrence of the two disorders. Polderman et al. [24] investigated specific patterns in the co-occurrence of ASD and ADHD traits in adults. Five trait-based dimensions of ASD (social skill impairments, strong routine preferences, attentional switching problems, imagination impairments and a strong fascination for numbers and patterns), and two dimensions of ADHD (Inattentive (IA) and Hyperkinetic/Impulsive (HI)) were jointly examined in a population-based adult sample. HI problems did not correlate substantially with the ASD trait dimensions, whereas IA problems correlated only with the ASD dimension assessing attentional switching difficulties. Furthermore Polderman et al. [25] examined the genetic and environmental etiology of the association between specific ASD and ADHD disorder dimensions. In a community sample of adult twins they assessed self-reported data on ASD dimensions social and communication difficulties (ASDsc), repetitive and restricted behavior and interests (ASDr) and ADHD dimensions (IA) and (HI). They concluded that ASDr problems form an important link between ASD and ADHD comorbidity. Ghirardi et al. [26] studied individuals aged 20–28 years from the Swedish Study of Young Adult Twins. They estimated the phenotypic and etiological overlap between self-rated trait dimensions of ADHD and ASD. At the phenotypic level HI was correlated more strongly with repetitive and restricted behaviors (RRB) than social interaction and communication (SIC), whereas IA was equally associated with both dimensions of ASD traits. Their findings suggest a dimension-specific phenotypic and etiological overlap between ADHD and ASD traits.

It has been also reported that ADHD prevalence in ASD decreases with age and preliminary data suggest that the association between ASD and ADHD traits may be somewhat lower in adult age than in childhood/adolescence [27]. Hartman et al. [28] reported that both ADHD and ASD symptom constellations are not at all stable across development with some symptom dimensions (attention problems and social problems) being much more persistent than other symptom dimensions (hyperactivity/impulsivity and repetitive behaviors). In a meta-analysis of social cognition [29], it was reported that developmental trajectories of social cognition probably differ between ADHD and ASD as social cognitive deficits in ADHD might be improving with age in most individuals. Lai & Baron-Cohen [6] state that ADHD is seen in up to 40% of adults with ASD and support the view that important point of differentiation is the nature of surface-level inattentiveness.

In ASD inattentiveness is characterized by slowness or difficulty in attention disengagement and switching, whereas in ADHD the main characteristic is difficulty in maintaining focused attention. They suggest that a dimensional perspective can be adopted.

The concept of empathy includes the identification of another's mental state and the appropriate response to their mental state [30]. Abnormalities in empathy have been reported in various psychiatric disorders [31-33]. Individuals with ASD have repeatedly reported to show impairments in empathy across the life span relative to typical controls [30, 34] and in their ability to maintain selective attention when it concerns emotional stimuli [35]. The notion of empathy has not been adequately studied in adult patients with ADHD. There has been only one study [36] reporting that adults with a subclinical ADHD diagnosis had reduced levels of the Empathy Quotient (EQ) scores compared to the control group. To our knowledge there are no reports on the possible role of empathy in diagnosing co-occurring ADHD and ASD in adults.

Data from studies that try to estimate the phenotypic and etiological overlap between self-rated trait dimensions of ADHD and ASD derive from a general population sample and, as such, results might not be extrapolated directly to clinical settings. Clinicians performing an ASD/ADHD assessment are able to use their judgment to distinguish between ASD/ADHD and other conditions that can mimic ASD/ADHD symptoms [6] but often struggle deciding which disorder better describes the patient's problems. They also acknowledge that when ASD and ADHD co-occur, each becomes more difficult to diagnose than when they occur in isolation [37]. Antshel et al. [11] comment that the base rate of ADHD symptoms for children, adolescents and adults with ASD has never been firmly established and the extent to which those symptoms are inherent to ASD is not clear. Establishing symptom profiles for making a diagnosis of ADHD in individuals with ASD remains an important area of research. Of particular interest is the less studied group of the less impaired adult patients who are overlooked until adulthood and pose complex diagnostic issues [38].

As part of a comprehensive assessment of adults self-rated questionnaires are often used. They can be useful either for screening purposes or in support of the diagnostic procedure. We hypothesize that individual trait dimensions that derive from questionnaires with widely accepted psychometric properties may offer helpful information for the differential diagnosis of adults with normal intelligence that are referred with a suspected ADHD or ASD or ADHD/ASD diagnosis.

The aim of the present study is twofold: first, to estimate the rate of co-occurrence of ADHD and ASD in adults with normal intelligence referred for the first time in their lives to an Adult Neurodevelopmental Department; and second to examine how the total score and individual trait dimensions such as the current and past inattention, hyperactivity and impulsivity that derive from the Barkley Adult ADHD Rating Scale-IV (BAARS), the five subscales deriving from Autism-Spectrum Quotient (AQ) and the total score of EQ could help a clinician in everyday clinical practice to identify variables that could differentiate patients with ADHD, ASD and ADHD/ASD. We particularly focus on the extent to which these trait dimensions can be helpful in disentangling the most puzzling group of patients with a dual ADHD/ASD diagnosis.

2. Materials and Methods

2.1. Recruitment

The present study was part of a larger research project on de novo diagnosed adults with ADHD and ASD [38]. The research group included 238 adults who were assessed at the Adult Neurodevelopmental Department in the 1st Department of Psychiatry at the National and Kapodistrian University of Athens and received a de novo ADHD and/or ASD diagnosis during a three-year period. The Adult Neurodevelopmental Department is the only nation-wide center that accepts referrals from the general population across Greece for the diagnosis of ASD and ADHD in adults. It used to be specialized for the diagnosis and treatment of adult ADHD [38,39] but during the last ten years the increased needs for diagnosis and treatment of adults with ASD resulted to the broadening of referral criteria in order to include suspected ASD cases. The multi-disciplinary team that carries out all assessments consists of: psychiatrists who have extended experience in the

diagnosis and treatment of Neurodevelopmental Disorders in adults and are trained in ADOS [40,41], ADI-R [42,43] and DIVA [3,5,44]; clinical psychologists; a speech and language therapist; an occupational therapist; and a social worker. In order to be included in the study subjects had to be adults with normal intelligence and fluent phrase speech that received for the first time in their life an ADHD and/or ASD diagnosis. Exclusion criteria were a previous ADHD and/or ASD diagnosis, the presence of acute psychopathology requiring urgent psychiatric treatment, IQ <70 according to WAIS and a known genetic cause.

Written consent was obtained from all participants. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of the National and Kapodistrian University of Athens, Eginition Hospital (10549/17.10.2016)

2.2. Procedure

The assessment procedure is built on a standard diagnostic routine described in detail in Pehlivanidis et al [38]. Initially, all referred patients have to complete a questionnaire that comprises demographic, educational, occupational and clinical data and a battery of screening instruments including a modified version of BAARS-IV [45], the AQ [46], and the EQ [47]. The completed questionnaire is sent via e-mail to our clinic.

Responses to the questionnaire are then discussed with the patient and a family member when possible. Patients undergo a thorough psychiatric examination by experienced psychiatrists of our Department exploring the existence and pervasiveness of a suspected neurodevelopmental disorder and the presence of co-occurring psychopathology. If needed, patients are referred to other members of the multidisciplinary team or for a laboratory workout. The semi-structured interview DIVA is administered to all patients while the ADOS and ADI-R are administered to selected cases considered to be more complicated. The final diagnosis regarding the presence of ADHD and/or ASD is given during a consensus meeting of the multidisciplinary team and is based on DSM-5 criteria while taking into consideration all available information.

2.3. Measures of ADHD and ASD dimensions

2.3.1. BAARS-IV

A modified version of BAARS-IV was used in order to assess self-report ADHD traits. This 18-item questionnaire assesses the DSM-IV criteria for ADHD, with clinical response and recovery cutoffs derived from population-based norms. The BAARS-IV shows adequate internal consistency and test–retest reliability, and strong construct validity and discriminant validity [45]. It comprises 18 items for both current (last 6 months) and childhood (for age 5-12) behavior, using a 4-point (0, 1, 2, 3) rating scale. A score of two or above indicates the presence of a symptom. Nine items assess the presence of inattentive symptoms and nine the hyperactive/impulsive symptoms. For the needs of our study we divided the Hyperactivity/Impulsivity items in two subscales: Impulsivity (4 items) and Hyperactivity (5 items). The following ADHD traits subscales: Inattention for age 5-12 (0 to 9 points), Hyperactivity for age 5-12 (0 to 5 points), Impulsivity for age 5-12 (0 to 4 points), Inattention at last 6 months (0 to 9 points), Hyperactivity at last 6 months (0 to 5 points), Impulsivity at last 6 months (0 to 4 points), Total score for age 5-12 (0 to 18 points) and Total score at last 6 months (0 to 18 points) entered the analysis. In our sample Cronbach's α for all scales was between 0.70 and 0.91

2.3.2. Autism Quotient (AQ)

The AQ was originally developed to identify ASD among adults with normal intelligence [48]. It consists of 50 items, 10 items per subscale. Participants responded to each of 50 statements on a four-point Likert scale (1 “strongly agree”, 2 “slightly agree”, 3 “slightly disagree”, 4 “strongly disagree”). Total AQ, as well as the five subscale scores namely Social Skills (SS), Attention Switching (AS), Attention to Detail (AD), Communication (C) and Imagination (I) were calculated using the relevant key. Woodbury-Smith et al. [49] were the first to evaluate AQ for its potential as a screening questionnaire in clinical practice and concluded that AQ is strongly predictive of who receives a

diagnosis of ASD in normal intelligence and high functioning adults. Other researchers [50] questioned the utility of AQ to predict ASD caseness in patients seen at an adult ASD diagnostic service when using the total AQ score. Moreover, in a more recent analysis [51], it was suggested that several measurement properties of the AQ are good and have adequate sensitivity and specificity to distinguish people with ASD from those without ASD but noted that AQ cannot be described as a unidimensional measurement. In our study the following five AQ subscales entered the analysis: Social Skills, Attention Switching, and Attention to Details, Communication, Imagination and the AQ Total score. In our sample Cronbach's α for the total score and the subscales was between 0.73 and 0.84 except from Imagination and Attention Switching subscales where Cronbach's α was 0.59 and 0.50 respectively.

2.3.3. Empathy Quotient (EQ)

EQ is a self-assessment instrument for measuring the construct of empathy in adults of normal intelligence both as a one-factor and three-factor dimension [52-54]. It comprises 40 questions tapping empathy and 20 filter items [35, 47]. Responses are given on a 4-point Likert scale and scores can range from 0 to 80 points. Reduced levels of EQ scores reflecting deficits in empathy have been repeatedly reported for individuals with ASD, relative to typical controls [55]. EQ is inversely correlated with the AQ [55]. The EQ has been validated in a Greek adult population, demonstrating good psychometric properties and supporting both the one and the three-factor models [56]. In the present study the Total EQ score entered the analysis. Cronbach's α was 0.71.

2.4. Statistical analysis

Normal distribution of the variables was evaluated using Kolmogorov -Smironov test. Qualitative variables are expressed as absolute and relative frequencies. Chi-square test was used for the comparison of proportions. For the comparison of continuous variables between the three study groups one-way analysis of variance (ANOVA) was used. Bonferroni correction was applied in case of multiple testing in order to eliminate type I error. Multiple logistic regression analyses with a stepwise method (p for removal was set at 0.1 and p for entry was set at .05) was also performed, in order to identify the variables that could differentiate the study disorders. Adjusted odds ratios with 95% confidence intervals were computed from the results of the logistic regression analyses. We performed a series of multiple logistic regression analyses with dependent variables those defined from groups with different disorders. All reported p values are two-tailed. Statistical significance was set at $p \leq 0.05$ and analyses were conducted using SPSS statistical software (version 22.0).

3. Results

The sample consisted of 238 participants (172 men and 66 women) with mean age 30.2 years (SD=9.8). 151 subjects (63.4%) were diagnosed with ADHD, 58 (24.4%) with ASD and 29 (12.2%) with both ADHD and ASD. Of the total number of patients that received an ADHD diagnosis either as a sole or co-occurring diagnosis (n=180), 29 (16.1%) received a comorbid ASD diagnosis while of the 87 subjects diagnosed with ASD, 29 (33.3%) fulfilled the criteria for an ADHD diagnosis. Sample characteristics of all groups are shown in Table 1. The three groups of patients were similar in terms of sex, and age (Table 1).

Table 1. Sample characteristics by group.

	Diagnosis			Test statistic (df)	
	ADHD	ASD	ADHD+ASD		p

	N=151	N=58	N=29		
Age (years), mean (SD)	31.0(10.0)	28.7(9.2)	28.8(10)	1.41 (2, 234)	0.246
Sex, N (%)					
Men	106(70.2)	47(81)	19(65.5)	3.21 (2)	0.201
Women	45(29.8)	11(19)	10(34.5)		

F (df1, df2) for ANOVA; X^2 (df) for Pearson's chi-square test

Self-report measures of ADHD subscales for the three study groups are shown in Table 2. As expected, subjects with ADHD had significantly greater score on all ADHD traits as compared to ASD ones. Also, subjects having both ADHD and ASD diagnoses had significantly greater score on all ADHD traits as compared to ASD ones. No significant differences concerning ADHD traits scores were found between subjects with ADHD and those having both ADHD and ASD.

Table 2. Comparison of self-report number of ADHD traits between the three study groups.

	ADHD	ASD	ADHD+ASD					
	A	B	C			A vs. B	A vs. C	B vs. C
ADHD TRAITS	Mean(SD)	Mean(SD)	Mean(SD)	F (df_1, df_2)	*p*	*p*	*p*	*p*
INATTENTION AT AGE 5-12	6.2(2.4)	3.9(2.6)	6.6(2.5)	20.00 (2 , 229)	<0.001	<0.001	>0.999	<0.001
HYPERKINETIC AT AGE 5-12	2.7(1.6)	1.5(1.6)	3.1(1.6)	15.36 (2 , 229)	<0.001	<0.001	0.716	<0.001
IMPULSIVITY AT AGE 5-12	2.1(1.4)	1.1(1.3)	2.6(1.3)	15.35 (2 , 229)	<0.001	<0.001	0.360	<0.001
TOTAL SCORE AT AGE 5-12	11(4.4)	6.4(4.4)	12.4(4.3)	27.90 (2 , 229)	<0.001	<0.001	0.399	<0.001
INATTENTION AT LAST 6 MONTHS	5.8(2.5)	3.1(2.6)	5.5(2.9)	22.75 (2 , 231)	<0.001	<0.001	>0.999	<0.001
HYPERKINETIC AT LAST 6 MONTHS	2.7(1.5)	1.6(1.4)	2.9(1.5)	12.56 (2 , 231)	<0.001	<0.001	>0.999	0.001
IMPULSIVITY AT LAST 6 MONTHS	1.8(1.4)	0.8(1)	2.2(1.5)	15.12 (2 , 231)	<0.001	<0.001	0.328	<0.001

TOTAL SCORE AT LAST 6 MONTHS	10.3(4.3)	5.4(4)	10.6(5)	27.17 (2 , 231)	<0.001	<0.001	>0.999	<0.001

F (df1, df2) for ANOVA; p values after multiple comparisons using Bonferroni correction.

Comparison of self-report measures of AQ and EQ scores between the three study groups are presented in Table 3. Scores in AQ traits were found to be significantly greater in ASD subjects as compared to ADHD ones –as expected-, with the exception of Attention to Details. Additionally, all AQ traits scores were found to be significantly greater in those having both ADHD and ASD in comparison to those having ADHD alone. Furthermore, Attention to Details score was found to be greater in those having both ADHD and ASD as compared to those with ASD. Total EQ score was greater in ADHD subjects as compared to ASD cases and those that had both ADHD and ASD.

Table 3. Comparison of self-report number of ASD traits between the three study groups.

	Diagnosis							
	ADHD	ASD	ADHD+ASD					
	A	B	C			A vs. B	A vs. C	B vs. C
ASDTRAITS	Mean(SD)	Mean(SD)	Mean(SD)	F (df_1, df_2)	*p*	*p*	*p*	*p*
SOCIAL SKILLS SCORE	4(2.4)	6.1(2.5)	6(2.4)	19.25 (2 , 223)	<0.001	<0.001	<0.001	>0.999
ATTENTION SWITCHING SCORE	5.8(1.8)	6.8(1.7)	6.9(1.8)	9.38 (2 , 223)	<0.001	0.001	0.010	>0.999
ATTENTION TO DETAILS SCORE	4.8(2.4)	4.7(2.4)	6.3(2.1)	7.84 (2 , 223)	<0.001	>0.999	0.008	0.020
COMMUNICATION SCORE	4.5(2.4)	5.8(2.6)	6.7(2.1)	13.19 (2 , 223)	<0.001	0.001	<0.001	0.412
IMAGINATION SCORE	3.6(1.9)	5.3(2.2)	5.1(2.1)	17.94 (2 , 223)	<0.001	<0.001	0.001	>0.999
AQ TOTAL SCORE	22.7(6.2)	28.9(6.9)	30.9(7.2)	30.22 (2 , 223)	<0.001	<0.001	<0.001	0.529
EMPATHY TOTAL SCORE	31.7(10.5)	23.4(10.1)	19.7(6)	26.61 (2 , 223)	<0.001	<0.001	<0.001	0.307

F (df1, df2) for ANOVA; *p* values after multiple comparisons using Bonferroni correction.

Results from stepwise logistic regression analyses (Table 4) showed that Hyperactivity at age 5-12, Inattention at the last 6 months, Impulsivity at the last 6 months, Attention Switching, Communication, Imagination and EQ total score could discriminate ADHD from ASD patients. Also, multiple analysis showed that Attention to Details, Imagination and Total EQ score could discriminate ADHD cases from those having both ADHD and ASD, while Hyperactivity at age 5-12 and Impulsivity at the last 6 months were found to significantly discriminate between ASD and ADHD/ASD subjects.

Table 4. Results from stepwise logistic regression analysis for the discrimination of ADHD, ASD and ADHD/ASD group of patients from the self-reported number of ADHD and ASD traits.

	OR(95% CI)	***p***
ADHD vs. ASD		
HYPERKINETIC AT AGE 5-12	1.68(1.22-2.32)	0.001
INATTENTION AT LAST 6 MONTHS	1.50(1.22-1.84)	<0.001
IMPULSIVITY AT LAST 6 MONTHS	1.77(1.1-2.84)	0.019
ATTENTION SWITCHING SCORE	0.68(0.51-0.9)	0.008
COMMUNICATION SCORE	0.76(0.6-0.97)	0.025
IMAGINATION SCORE	0.74(0.59-0.92)	0.007
EMPATHY QUOTIENT	1.08(1.02-1.15)	0.012
ADHD+ASD vs. ADHD		
ATTENTION TO DETAILS SCORE	1.25(1.00-1.55)	0.050
IMAGINATION SCORE	1.38(1.09-1.74)	0.007
EMPATHY QUOTIENT	0.87(0.81-0.93)	<0.001
ADHD+ASD vs. ASD		
HYPERKINETIC AT AGE 5-12	1.72(1.22-2.42)	0.002
IMPULSIVITY AT LAST 6 MONTHS	2.13(1.41-3.24)	<0.001

Odds Ratio (95% Confidence Interval).

4. Discussion

In our study we estimated the rate of co-occurrence of ADHD and ASD in patients referred to an Adult Neurodevelopmental Department and explored dimensions of self-rated screening instruments that could help a clinician discriminate between patients with ADHD, ASD and ADHD/ASD.

4.1. Co-occurrence of ADHD and ASD

Among the 238 normal intelligence adults that were assessed during a three-year period, 63.4% received an ADHD diagnosis only, 24.4% an ASD diagnosis only and 12.2% a dual ADHD/ASD

diagnosis. 16.1% of the 180 patients with an ADHD diagnosis received a co-occurring ASD diagnosis while of the 87 subjects diagnosed with ASD 33.3% fulfilled the criteria for an ADHD diagnosis. Our findings are in line with previous findings showing elevated ratings of ADHD symptoms in ASD patients and elevated but lower rates of ASD symptoms in ADHD patients. Anckarsäter et al [57] reported that from 260 consecutive adults assessed for current and lifetime ADHD and ASD 113 subjects had ASD, 147 had ADHD while in 46 (19.2%) there was an overlap between ASD and ADHD. In a naturalistic study in an adult psychiatric population, from the 84 patients diagnosed with ASD 37% fulfilled criteria for comorbid ADHD [19]. In Hofvander et al. study [15], an ADHD clinical diagnosis was given in 43% of 122 adult outpatients with ASD. Johnston et al., [16] reported that from the 31 adults with ASD and average intellectual function who completed self-report measures of ADHD symptoms, 36.7% met DSM-IV criteria for current ADHD "caseness". Lai & Baron-Cohen [6] state that ADHD is seen in up to 40% of adults with ASD. The only study showing low rates of comorbid ADHD in ASD adult patients is a retrospective case review [18] where only 9.7% from those who met ICD-10 criteria for ASD received the diagnosis of ADHD, a rate that was not significantly greater compared to general population data. The authors commented though that there was an associated specialist ADHD clinic within the same set of services and many referrals were possibly diverted away from the ASD clinic. Regarding co-occurring ASD in adults with ADHD, a study [20] examining the prevalence and gender differences of DSM-IV axis I and II comorbidity in a clinical cohort of patients diagnosed with ADHD in adulthood, found that over 10% of the sample had a current and past diagnosis of ASD which is comparable to the rate of 16.1% found in our study.

4.2. BAARS dimensions

Patients with confirmed ADHD diagnosis scored higher in the Total number of self-reported ADHD symptoms compared to ASD patients -as expected- but not higher compared to ADHD/ASD patients. The same applied to all ADHD traits subscales (Table 2). In the stepwise logistic regression analysis (Table 4) ADHD traits subscales scores that could discriminate ADHD patients from ASD were Hyperactivity at age 5-12, Inattention at last 6 months and Impulsivity at last 6 months. Also, the scores of Hyperactivity at age 5 -12 together with Impulsivity at last 6 months could discriminate ADHD/ASD from ASD patients. It seems that the following four ADHD items that describe current Impulsivity 1) Talked excessively, 2) Blurted out answers before questions had been completed (completed others' sentences, or jumped the gun), 3) Had difficulty awaiting my turn and 4) Interrupted or intruded on others (butted into conversations or activities without permission or took over what others were doing) may be very useful for the discrimination between adults with a dual ADHD/ASD diagnosis and those patients having ASD as sole diagnosis. The fact that Impulsivity at age 5-12 was not among the discriminant factors could be explained by the suggestion made by Barkley [45] that symptoms of impulsivity, especially verbal impulsivity, begin to emerge as a semi distinct dimension of ADHD symptoms in adulthood and is not so distinct from hyperactivity in children's ratings or in the retrospectively recalled symptoms of childhood, as reported by adults. Also, in accordance to our findings, Barkley et al. [58] noted that in a free interview context patients' responses for the symptoms 1) Making decisions impulsively and 2) Having difficulty stopping activities or behavior when should do so, are the best discriminating symptoms for ADHD from other forms of psychopathology. The above symptoms were also found useful in order to screen for ADHD among anxious and depressive adult psychiatric outpatients [39]. There are very few disorders apart from ADHD where impulsivity is part of the diagnostic criteria, such as the borderline personality disorder or some obsessive-compulsive spectrum disorders [1,59]. Therefore, current impulsivity may be viewed as a red flag for a possible co-occurring ADHD in patients with other diagnoses. Impulsivity is also considered to play a central role in understanding ADHD/ASD comorbidity. Sokolova et al.[60] studied the relationship between ASD and ADHD symptoms by applying causal modeling. They used a large phenotypic data set of 417 children with ASD and/or ADHD, 562 affected and unaffected siblings, and 414 controls, to infer a structural equation model using a causal

discovery algorithm. The strongest links they found were between social communication difficulties, inattention and impulsivity and suggested that impulsivity has a causative effect on social ineptness.

In clinical practice the finding that self-report of current impulsivity can discriminate ASD patients from ASD/ADHD patients has both diagnostic and treatment implications. Interviewing adults of normal intelligence with an ASD diagnosis for current impulsivity may lead to a co-occurring ADHD diagnosis which has to be treated accordingly (i.e. with stimulants).

4.3. AQ dimensions

As expected, the total AQ score and most of the AQ subscales scores were higher in adults with ASD compared to adults with ADHD, with the exception of the subscale score of Attention to Details. Also, patients with ADHD/ASD compared to patients with ADHD scored higher in all AQ scores.

When comparing patient with ASD to patients with ADHD/ASD no difference was found with the exception of the subscale Attention to Details whose scores were higher in the combined group. It seems that Attention to Details scores do not significantly differ between ADHD and ASD but the co-occurrence of the two disorders significantly increases the score in this subscale. Also, stepwise logistic regression multiple analysis showed that Attention to Details along with Imagination were two of the three dimensions (the third one being EQ score) discriminating ADHD/ASD cases from those having ADHD, with Imagination being lower while Attention to Details higher in the dual diagnosed group.

Our results on "Attention to Details" are in line with previous reports separating this subscale from the other subscales of AQ. In a confirmatory factor analyses in both a general population and a student sample [60] four out of the five domains of the AQ (Social skill, Communication, Attention Switching, and Imagination) were highly correlated. The authors proposed a hierarchical model allowing these four domains to cluster together as a ''Social Interaction'' factor, while a small second factor, consisting of items focusing on a preference for details and patterns (the domain ''Attention to Details'') was also identified. The usefulness of the AQ in differentiating between adult ASD and adult ADHD was also studied by Sizoo et al. [62] who explored whether Substance Use Disorders (SUD) comorbidity affects the AQ scores. Once more Total AQ score and most of the AQ subscale scores were higher in adults with ASD compared to adults with ADHD, except for the subscale score Attention to Details. Attention to Details subscale is composed of items referring to a perceptual style with a preference for details and patterns. It might be that this autistic dimension scale does not discriminate between patients with ASD and patients with ADHD because it refers to a strategy for dealing with aspects of attention deficit that is common to both disorders. Patients with ASD present attention deficit distress when they are overwhelmed by perceptual stimuli. The distress is said to reduce, when focusing on logical sequences such as patterns, telephone numbers or car license plates. On the other hand patients with ADHD might try to compensate for their attention deficits by focusing on patterns and details. It seems that co-occurrence of ADHD/ASD further increases the attention deficit and consequently a stereotyped behavior that is registered as an increased score in the Attention to Details subscale. Attention to detail could also be an underlying psychological mechanism explaining why ASD repetitive and restricted behavior and interests seem to form a link between ASD and ADHD [24, 26].

Imagination was the other dimension deriving from AQ that differentiated individuals with ADHD from individuals with ASD or ADHD/ASD, indicating that lack of imagination could be considered as a discriminating trait in adults with ASD regardless of ASD being a sole or co-occurring diagnosis. It is well known that people with ASD form a group of individuals for whom spontaneous and fantastical acts of imagination appear to be a challenge. Children with autism do not engage in spontaneous pretend play in the ways that typically-developing children do, engaging instead in repetitive activities; and adults with autism are less interested in fiction [63-66].

4.4. EQ score

The EQ total score was lower in ASD and in ADHD/ASD patients compared to ADHD patients while no difference was found between ASD and ADHD/ASD patients (Table 3). Also, stepwise

logistic regression multiple analysis showed that EQ score was among the factors that discriminate both ASD and ADHD/ASD cases from ADHD cases (Table 4). It seems that low EQ score similarly to low Imagination is indicative of the presence of ASD either as a sole diagnosis or as co-occurring disorder.

The EQ has not been systematically studied in adults with clinical ADHD diagnosis. Groen et al [36] reported reduced EQ scores in adults with a subclinical DSM-5 ADHD diagnosis compared to the control group, although still within the normal range. They considered that the reduced EQ score may be related either to a reduced emotion regulation/emotional lability in patients with ADHD or to ASD comorbidities. The latter is supported by our finding that EQ was reduced only in the group with ADHD/ASD co-occurrence and not the ADHD group.

EQ is designed to measure how easily a person can detect other people's feelings and is affected by them. Since empathy is a core skill that facilitates effective social interaction [30], lower empathetic ability may reflect less social adaptability and may be the key factor in understanding reasons for referrals in adulthood [67]. Lower empathizing traits as measured by EQ in individuals referred and diagnosed in adulthood may be especially important in understanding challenges with social adaptability. Measures assessing social-cognition may not be sensitive enough to detect difficulties in functioning for adults of normal intelligence because of the "camouflaging" of ASD-related characteristics in social situations where a patient is motivated by the desire to fit in with others [68].

The finding that EQ discriminates adults of normal intelligence with co-occurring ADHD/ASD from patients with ADHD has important clinical implications. Interviewing for the capacity to detect other people's feelings when assessing adults for a possible ADHD diagnosis might reveal symptoms indicating the possible co-occurrence of ASD. Treating ADHD with co-occurring ASD is much more complex than treating ADHD as a sole diagnosis.

4.5. Limitations

A number of limitations of the study should be taken in consideration. First, our subjects represent a specific clinical population and results cannot be generalized to other samples such as community or low functioning ones. Second, the study population is not very large, especially the combined ADHD/ASD population. Third, we used structured interviews only in selected cases considered to be more complicated. Previous research though has shown that there is moderate agreement between clinical diagnoses and ADOS4 while ADI-R might not be reliable in adults without intellectual disability [69-71]. An extended psychiatric interview made by an experienced psychiatrist combined with collateral information is probably the most essential part of the diagnostic assessment in high functioning adults. Also, BAARS-IV is based on the DSM-IV criteria for ADHD. Nevertheless, the18 items of BAARS-IV are similar in terms of number and quality to the DSM-5 items and BAARS-IV is the only screening instrument where the three dimensions of ADHD (Inattention, Hyperactivity and Impulsivity) are considered separately [45]. Another limitation of the study is the low Cronbach's α for the Attention Switching and the Imagination subscale of the AQ. It is noteworthy that a low degree of internal consistency for some subscales of the AQ and in particular for the Imagination subscale has been reported in previous studies too [61, 72-75]. Therefore, findings regarding these particular dimensions should be considered with caution. Finally, researchers must always be prudent with the interpretation of results of self-report questionnaires when used for individuals with neurodevelopmental disorders where self-reflection and meta-cognitive skills might be impaired. This is particularly an issue with people having an ASD diagnosis where poor awareness of autism related traits may lead to an under-reporting of autism symptoms and over-reporting of social competency [50,76].

5. Conclusions and Research Implications

Despite the limitations, our results illustrate that apart from considering diagnostic categories, individual trait-based dimensions deriving from screening instruments (BAARS-IV, AQ, and EQ) might be of particular help in the comprehensive assessment and differential diagnosis of adults of normal intelligence with a suspected ADHD or ASD diagnosis and in particular of those with the

more perplexing ADHD/ASD diagnosis. Being able to successfully categorize individuals with ADHD, ASD or ADHD/ASD by using clinical dimensions is an important first step towards identifying atypical brain function and structure underlying these clinical features. Our findings highlight the importance of the dimensions current impulsivity, attention to details, imagination and empathy when discriminating adults with ADHD, ASD and co-occurring ADHD/ASD. They also suggest the need to study the neural underpinnings of these particular traits using a lifespan approach, in order to understand the persistence and co-occurrence of ADHD and ASD in adulthood.

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