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Characteristics of DSM-IV Attention Deficit Hyperactivity Disorder Combined and Predominantly Inattentive Subtypes in a Turkish Clinical Sample

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Abstract

Consecutively referred subjects ($N = 537$) to an outpatient clinic were evaluated to compare the Attention Deficit Hyperactivity Disorder Combined (ADHD-C) and predominantly inattentive (ADHD-PI) subtypes using parent and teacher ratings and neuropsychological variables. Statistical significance was at $P < 0.002$ adjusted for multiple comparisons. ADHD-PI subjects were older, more likely to be female, higher socioeconomic status, had lower Child Behavior Checklist and Teacher Report Form Aggression, Delinquency and Social Problems scores, and higher Withdrawal and Competence scores, compared to ADHD-C subjects. Comorbid conduct problems were more common among ADHD-C subjects. There were no differences in terms of anxiety/depression, and neuropsychological measures. The study is unique in that it provides data on a broad range of measures from a middle income developing country with important confirmation of similar pattern of differences and similarities between ADHD-C and ADHD-PI subtypes previously reported in North American and Western European samples.

Keywords

Attention Deficit Hyperactivity Disorder; Inattentive; Combined

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Conflicts of interest There are no conflicts of interest.

Introduction

Attention Deficit Hyperactivity Disorder (ADHD) is one of the most common psychiatric disorders of childhood. According to the DSM-IV-TR there are three mutually exclusive subtypes: combined (ADHD-C), predominantly inattentive (ADHD-PI) and predominantly hyperactive-impulsive (ADHD-HI). Several studies investigated the relationship between ADHD-HI and ADHD-C, suggesting that ADHD-HI may be a precursor of ADHD-C and raising questions about the validity of the ADHD-HI and ADHD-C distinction [1]. On the other hand there have been significant differences reported that distinguish between the ADHD-PI and ADHD-C subtypes. The discussion between similarities and difference between ADHD-C and ADHD-PI predates the DSM-IV, with its origins in the DSM-III classification of Attention Deficit Disorder (ADD) with and without hyperactivity; the latter *inattentive* DSM-III ADD subtype considered somewhat akin to the DSM-IV ADHD-PI. When compared to ADHD-PI subjects, those with ADHD-C have been reported to be more aggressive [2, 3], have higher rates of comorbid oppositional defiant (ODD) and conduct (CD) disorders [4–6], social problems in response inhibition, and peer rejection [7, 8]. In addition, the ADHD-PI subjects have been found to be comparably more likely to be female patients [9, 10], older [5, 10, 11], have higher socioeconomic status (SES) [5] and comorbid learning disabilites (LD) [12]. Subjects with ADHD-PI have also been noted to have more inhibited and withdrawn social style and less popular social demeanor among their peers [7, 8, 13]. The question as to whether there are differences in medication treatment response between the ADHD-C and ADHD-PI subtypes remains a matter of further debate.

From a neuropsychological perspective, ADHD-PI subjects are reported to have less response inhibition problems but have a sluggish cognitive tempo, meaning that they are slower and have less energy and have impaired focused attention [14]. Nevertheless, some recent studies have suggested that sluggish cognitive tempo may be correlated with inattentiveness regardless of ADHD subtype and that it is highest in the comorbid anxiety group [15]. Other studies have reported a range of differences between the subtypes including higher level of difficulty in interference inhibition, working memory [16], and motor planning [17] among the ADHD-PI subjects; although these findings have not been consistently supported by other studies (see review, [7]).

Previous studies conducted in a number of other countries in the Middle East region have shown that the overall ADHD prevalence was lower in Yemen [18] and United Arab Emirates [19] while the rate was found to be higher in Oman [20]. In a recent study conducted in Iran the prevalence of ADHD was 9.7% among children in primary schools [21], with 77.9% of the subjects reported to be of combined subtype, with ADHD-PI and ADHD-HI subtypes rates at 10.5 and 11.6%, respectively. Comorbidity with ADHD and other psychiatric disorders was noted to be high in clinical study sample in Saudi Arabia [22]. In an epidemiological study using standardized parent and teachers scales, we compared the attention problems scores among Turkish children and adolescents with scores among youth in other European countries [23]. Our national sample had higher mean attention problems scores than the Scandinavian but lower mean scores than the former Soviet Union samples.

In the present study, our aim was to investigate the subtype differences specifically between ADHD-PI and ADHD-C in terms of social competence, emotional and behavioral problems, rates of psychiatric comorbidity, cognitive measures, and SES within a clinical sample. To our knowledge, this is one of the largest scale studies comparing ADHD-PI and ADHD-C subtypes differences in children and adolescents in a middle income developing country. We predicted that, consistent with the previous studies, subjects with ADHD-PI will be older, include more females, have lower ODD/CD and higher LD rates, compared to subjects with ADHD-C. Eiraldi et al. [5] suggested that low SES significantly predicted a comorbidity of ODD/CD in subjects with ADHD-C. Therefore, in this study we also evaluated the effect of SES on psychiatric comorbidity across subtype.

Methods

Participants

We approached 739 subjects among consecutive referrals to the outpatient clinic in a general public pediatric hospital between September 2009 and June 2010. The primary referral reason was related to concerns about attention, hyperactivity and impulsivity. The eligible subjects fulfilled the study inclusion criteria: DSM-IV-TR diagnosis of ADHD; age between 6 and 15 years; and being medication free for at least 15 days prior to enrollment. Subjects with diagnosis of ADHD-HI (n = 124) were excluded, since prior research has shown that this subtype is akin, i.e., milder or subthreshold form of ADHD-C [1] and ADHD-HI children did not meet full criteria for ADHD-C. The present study objective therefore pertains to the comparison of distinct characteristics among ADHD-PI and ADHD-C subtypes. In addition, among the consecutive referred children, we excluded those with concurrent medication treatment (n = 23), major sensory neural (visual and hearing) impairments (n = 6), documented history of brain injury (n = 7) and those whose parents/teachers did not fill in the requisite rating scales (n = 78). The remaining sample in the analysis included 537 subjects.

ADHD and comorbid psychiatric diagnoses (anxiety, mood, oppositional defiant/conduct, tic and elimination disorders) were also assessed by the authors, who are experienced child psychiatrists certified in the use of the Schedule for Affective Disorders and Schizophrenia for School-Age Children—Present and Lifetime Version (K-SADS-PL), a semistructured interview validated in Turkish [24, 25]. The study was approved by the institutional ethics board of the Yildirim Bayazit Hospital, a large public training hospital in Ankara. The study participation was voluntary. The informed consent process was verbal as is customary given the literacy level of the parents. Given the predominance of illiteracy among the parents attending a large public pediatric hospital, the checklist questionnaires were administered verbally using a standardized format, that allow for repetition of questions. The semi-structures interviews were conducted with formalized probing using a limited set of questions. The parents, and assenting older children and adolescents (12 years and over) had the opportunity to opt out from the study at any time.

Measures

Schedule for Affective Disorders and Schizophrenia for School-Age Children: Present and Lifetime Version (K-SADS-PL)—K-SADS-PL is a semi-structured interview used by the clinicians to make DSM-III-R and DSM-IV diagnosis. The first part is for screening and this is followed by 5 modules. For the diagnostic modules the inter-rater relibility is high 90–100%. Kappa value indicating the test–retest reliability is between 0.63 and 1.00. The Turkish form has shown to be valid and reliable [24, 25].

Child Behavioral Checklist (CBCL)—The 118 items describe a wide array of problems rated on a 3-point scale [26]. There are eight syndrome scales: Withdrawn, Somatic Complaints, Anxiety/Depression, Thought Problems, Attention Problems, Social Problems, Aggressive Behavior, and Delinquent Behavior. Back translation, bilingual retest method, and pretest field study have been used for the translation of the CBCL [27]. The test–retest reliability of the Turkish form was 0.84 for the Total Problems, and the internal consistency was adequate (Cronbach's alpha = 0.88) [27].

Teacher Report Form (TRF)—The 118 items describe array of behavioral and emotional problems [28]. Ninety-three TRF items have counterparts on the CBCL. The syndrome scales and broadband syndromes are identical with the CBCL. The same translation methods were used for the translation of TRF [29]. The test–retest reliability of the Turkish form was 0.88 for Total Problems, and the internal consistency was adequate (Cronbach's alpha = 0.87) [29].

Wechsler Intelligence Scale for Children-Revised form (WISC-R)—WISC-R is consisted of 12 subtests assessing verbal and performance abilities. Verbal subtests include: Information, Similarities, Vocabulary, Comprehension and Digit Span. Performance subtests include: Picture completion, Picture Arrangement, Block Design, Object Assembly, and Digit Symbol. Verbal and Performance IQ scores were assessed. The WISC-R Turkish-version has adequate reliability and validity [30]. While WISC-R is a relatively outdated form of the test, it is widely used; and the updated forms have not yet been translated into Turkish.

Trail Making Test A–B (TMT A–B)—The basic task involves connecting a series of stimuli (numbers expressed as numerals) in a specified order as quickly as possible. The score is the number of seconds required to complete the task. In TMT B, the patients have to alternate between numbers and letters in a specified order, which taps mental tracking ability. Trail making test performance is heavily influenced by attention. The overall test takes 5–12 min. Higher scores in these two tests indicate worse performance. The Comprehensive Trail Making Test [31] was utilized with TMT A and TMT B results from 491 to 273 subjects, respectively.

Procedure

All cognition tests and neuropsychological assessments were administered by study psychologists blind to subtype status of study subjects. These assessments were done as a part of the clinical work up for the patients seen in the clinic. Typically it took two to three

assessment sessions to complete the neuropsychological tests. Teacher data was obtained, with parental consent, from the classroom teachers by the study staff. For subjects in the higher grades, teacher ratings were obtained from the teacher who knows the subject best (usually the teacher who spends more hours with the subject).

Data Analysis

The categorical variables such as gender, and psychiatric comorbidity were compared with Chi-square and Fisher Exact tests. CBCL (School Competence, Social Competence, Activities, Social Problems, Withdrawal, Anxiety/Depression, Attention Problems, Delinquency, Aggression); TRF (Total Competence, Social Problems, Withdrawal, Anxiety/Depression, Attention Problems, Delinquency, Aggression); Trail Making Tests A–B (TMT-A and TMT-B) (time to complete, seconds); and WISC-R (Freedom from Distractibility, Verbal, Performance, Total) scores were compared with analysis of variance with Bonferroni correction for significance for multiple comparisons (0.05/23 = 0.002). We used only two groups and did not make any post hoc ANOVA comparisons. We analyzed whether SES significantly predicted ODD/CD comorbidity in logistic regression analysis including ADHD subtype, gender and age as independent factors with SPSS 13.0 program (Chicago, IL). All *P* values were two-tailed.

Results

Of the total 537 (85.1% male patients, $n = 457$; 14.9% female patients, $n = 80$) in the study, 87.7% ($n = 471$) had ADHD-C and 12.3% ($n = 66$) had ADHD-PI. First we tested the hypothesis that subjects with ADHD-PI will be older with over representation of females. Although there were more female subjects in the ADHD-PI group, the finding did not reach statistical significance ($P = 0.07$). Age range of subjects was 6–15 years (mean 9.2, SD 2.1). Group comparisons indicated that ADHD-PI subjects were older (ADHD-C, mean 9.1, SD 2.1 vs. ADHD-PI, mean 10.0, SD 2.2 years; F = 9.7, $P = 0.002$; $df = 1,536$).

Second, we tested our hypothesis that comorbidity with ODD/CD, based on the K-SADS-PL, is more common in ADHD-C group. The overall distribution of comorbid conditions and gender are summarized in Table 1. The comorbidity with ODD/CD was significantly more common in the ADHD-C group ($P < 0.001$; $\chi^2 = 38.9$; $df = 1$). In addition, the ADHD-C subjects were more likely to be from lower SES background ($\chi^2 = 13.8$; $P = 0.008$, $df = 4$) and also had lower maternal (ADHD-C, mean 7.4, SD 3.2 years vs. ADHD PI: mean 8.9, SD 3.1 years; F = 10.8; $P = 0.001$, $df = 1,536$) education. As a post hoc explanatory analysis, we controlled for age, gender and SES in the logistic regression analyses and found that ADHD-C subtype was still significantly associated with ODD/CD comorbidity (OR = 6.6; 95% CI, 3.0–14.5; $P < 0.001$).

Third, we compared the parent and teacher ratings and cognitive test scores. CBCL, TRF, and TMT-A and TMT-B, and WISC-R scores by subtype are summarized in Tables 2 and 3. Analysis of variance results indicated that ADHD-C subjects had significantly higher CBCL Social Problems (F = 9.9, $P < 0.002$, $df = 1,536$), Aggression (F = 31.1, $P < 0.001$, $df = 1,536$) and Delinquency (F = 17.1, $P < 0.001$, $df = 1,536$) scores, as well as lower CBCL

Social Competence (F = 18.5, $P < 0.001$, $df = 1,536$) and Withdrawal scores (F = 10.5, $P < 0.001$, $df = 1,536$). The same pattern was also detected for TRF scores: ADHD-C subjects had higher Social Problems (F = 15.7, $P < 0.001$, $df = 1,536$), Aggression (F = 46.9, $P < 0.001$, $df = 1,536$), Attention Problems (F = 26.5, $P < 0.001$, $df = 1,536$), and Delinqunecy (F = 25.2, $P < 0.001$, $df = 1,536$) scores, and lower Total competence (F = 12.2, $P = 0.001$, $df = 1,536$) and Withdrawal (F = 17.0, $P < 0.001$, $df = 1,536$) scores.

TMT-A score was lower, i.e., indicating better performance (F = 6.4, $P = 0.01$, $df = 1,461$); and WISC-R Performance IQ score (F = 4.7, $P = 0.03$, $df = 1,430$) was higher in the ADHD-PI group. However, these latter differences did not reach the defined statistical significance. WISC-R Freedom from Distractibility, Performance IQ, Total IQ, and TMT-B scores were also not significantly different. Since it is know that Trail Making Test scores are heavily influenced by age and IQ, we also conducted a post hoc covariance analysis with TMT-A score as dependent variable, subtype as independent variable, and age and Total IQ, as covariates. This analysis showed that after age and IQ were controlled, there were no differences between the ADHD-PI subtype and the ADHD-C group.

Discussion

To our knowledge, this is the largest scale study examining subtype differences among consecutively referred children and adolescents in a general public pediatric hospital in a middle income developing country. Our results are consistent with prior results comparing ADHD-C and ADHD-PI subject characteristics in North American and West European samples. The distribution of the subtypes was similar to the Iranian study, suggesting that our results might also be consistent with the Middle East studies [21]. Also consistent with previous studies, we found several differences between the two study groups: the subjects with the ADHD-PI subtype were older [5, 10, 11], more likely to be female [9, 10] and from higher SES families [5]. Again, in line with previous research [4–6] our results also showed that the ADHD-C subjects had significantly higher rate of comorbidity with ODD/CD. When gender, age and SES were controlled through multivariate analysis ADHD-C subjects were in fact more than six times more likely to have comorbidity with ODD/CD. On the other hand, ADHD-C subjects had higher Social Problems, Aggression, and Delinquency scores by both parent and teacher reports. Consistent with previous research, our finding indicate that that such behaviors could be observed in different settings and might be considered not to be dependent on informant reports [2, 3].

It has been previously shown that both ADHD-C and ADHD-PI subjects exhibited social problems. Furthermore, ADHD-C subjects had problems with inhibition while ADHD-PI subjects had a withdrawn style [8, 13]. Our results were consistent with this pattern. We found that ADHD-C subjects had higher Social Problems scores, and ADHD-PI subjects had higher Withdrawal and Competence scores, based both in CBCL and TRF ratings. The consistency of this observation between teachers and parents therefore also indicated the pervasiveness of these behaviors. These results clearly support the previous studies that ADHD-C and ADHD-PI subjects exhibit different pattern of social problems.

The ADHD-C subjects were noted to take longer time to complete TMT-A [32], but not so to complete the TMT-B, indicating problems in perceptual motor planning. However, when we controlled for age, there was no significant group differences. We found that Verbal IQ score was higher among the ADHD-PI subjects, although our finding did not reach statistical significance. There were no differences in Freedom from Distractibility, Performance, and Total IQ scores.

There were number of important implications of the present study. Our results showed that ADHD-C subjects had a significantly higher risk of having ODD/CD as well as higher rate of parent and teacher rated aggression and delinquency. Therefore the ADHD-C subjects might need behavioral interventions targeting their externalizing behaviors. Second, the different nature of the social problems seen in subjects with ADHD-C and ADHD-PI might suggest that while the predominantly inattentive ADHD subjects need interventions to help them focus more on social contexts and to be more assertive, the combined ADHD subjects need training in response inhibition. In future studies, the effects of behavioral interventions targeting disruptive behaviors and social problems in different ADHD subtypes must be directly evaluated.

Our results involving a clinical sample in a large public pediatric hospital in Turkey are consistent with those reported in North American and Western European samples, supporting notion that the findings may indeed be robust in different cross-national settings. Our sample was ascertained among consecutive referrals in a large public pediatric hospital. Nevertheless, an important limitation of a clinic based study is that the results may not be applicable for the general population. Another limitation of the study was our use of the relatively outdated form of the WISC-R IQ test by North American and Western European norms, since an updated Turkish version is currently not yet available.

Despite these important important limitations, there were considerable strengths of the present study. First, our sample was considerably large. Second, the sample was recruited from a single site among consecutively referred subjects in a public hospital setting and all the subjects were evaluated in a standardized way using highly reliable and validated semistructured instruments and checklists. Third, comprehensive categorical diagnoses and dimensional measures were obtained from both parent and teacher informants. Some of the previous studies have found that different informants may contradict each other [33]. It was therefore important to show that the differences between combined and predominantly inattentive subjects were consistently reported by both teachers and parents, indicating the pervasiveness of these behaviors across informant. Fourth, systematic neuropsychological data was obtained. The study is unique in that it provides data on a broad range of measures from a middle income developing country with important confirmation of pattern of differences and similarities between ADHD-C and ADHD-PI subjects previously reported in North American and Western European samples.

Summary

In summary, the results suggest the combined and predominantly inattentive ADHD subtypes are different in terms of referral age, gender distribution, SES, comorbidity, parent

and teacher reported behavioral and social problems. On the other hand, there are no significant differences in neuropsychological performance, and internalization problems. To our knowledge, this is one of the largest scale studies comparing combined and predominantly inattentive ADHD subjects for any clinical sample. Although the diagnosis of predominantly inattentive ADHD was less frequently endorsed than the combined ADHD subtype, nevertheless it remains an important diagnosis in clinically relevant large sample. We recognize that the current subtype structure in the DSM-IV-TR may not accurately allow for 'purely' predominantly inattentive children. Hence the complex relationship in the pattern of similarities and differences observed between the combined and predominantly inattentive ADHD subtypes as confirmed in this study. It is all the more important that the distinctness of the relationship between combined and predominantly inattentive ADHD subtypes be further elucidated by means of application of additional methods, including neuroimaging and genetic studies involving large sample sizes. Such approaches will also be important to test the utility of the proposed changes in the classification of the predominantly inattentive and combined ADHD subtypes for the upcoming changes in the DSM5 [34] and beyond.

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Table 1

Gender and comorbidity of subjects with attention deficit hyperactivity disorder (ADHD) combined (C) or predominantly inattentive (PI) subtypes

	ADHD C (%)	ADHD PI (%)	χ^2; *P* (*df* = 1)
Gender (male)	86.2	77.3	3.6; 0.07
ODD/CD	54.4	13.6	38.4; <0.001
AD	19.3	22.7	.42; 0.51
LD	33.3	39.4	.95;0.34

ODD/CD oppositional defiant disorder/conduct disorder, *AD* anxiety disorders, *LD* learning disorders. Chi-square analysis

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Table 2

Child Behavior Checklist and Teacher Report Form scores for subjects with attention deficit hyperactivity disorder combined (C) and predominantly inattentive (PI) subtypes

Subtype	Child Behavior Checklist								
	Activities	Social competence*	School	Anxiety/depression*	Social withdrawal*	Social problems	Attention problems	Aggression*	Delinquency*
ADHD C	8.1 ± 2.9	5.6 ± 2.3	3.3 ± 1.0	8.0 ± 4.3	4.2 ± 2.7	8.6 ± 4.0	12.0 ± 3.3	16.7 ± 8.1	6.5 ± 4.5
ADHD PI	8.5 ± 2.6	7.0 ± 2.2	3.5 ± .7	7.6 ± 4.9	5.3 ± 3.0	6.9 ± 3.9	11.2 ± 3.4	10.7 ± 7.2	4.0 ± 4.5

ADHD subtype	Teacher Report Form						
	Competence*	Anxiety/depression*	Social withdrawal*	Social problems*	Attention problems*	Aggression*	Delinquency*
ADHD C[a]	12.1 ± 3.6	5.8 ± 4.2	3.5 ± 2.9	6.2 ± 4.0	28.8 ± 9.7	15.7 ± 9.3	5.0 ± 3.9
ADHD PI[b]	13.8 ± 3.5	6.1 ± 4.8	5.2 ± 4.0	4.1 ± 3.9	22.0 ± 9.6	7.2 ± 6.7	2.4 ± 2.4

Analysis of variance.

*$P < .001$

Table 3

Trail making test A and B and Weschler Intelligence Scale for Children-Revised scores for subjects with attention deficit hyperactivity disorder (ADHD) combined (C) or predominantly inattentive (PI) subtypes

ADHD subtype	Trail making test (TMT)		Weschler Intelligence Scale for Children-Revised			
	TMT-A	TMT-B	Freedom from distractiblity	Verbal IQ	Performance IQ	Total IQ
ADHD C	100.3 ± 56.2	171.0 ± 78.8	24.8 ± 6.9	84.7 ± 16.8	91.2 ± 17.7	87.2 ± 16.1
ADHD PI	81.6 ± 41.6	160.2 ± 86.0	26.3 ± 6.3	86.2 ± 16.4	97.0 ± 15.0	90.1 ± 14.6

No significant differences after statistical correction

TMT-A and TMT-B Trail making test A and B, respectively