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ORIGINAL ARTICLE

Types of adult attention-deficit hyperactivity disorder (ADHD): baseline characteristics, initial response, and long-term response to treatment with methylphenidate

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Abstract Much recent research describes the importance of emotional symptoms in ADHD. While there is no accepted system for including emotionality in diagnosing ADHD, the Wender–Reimherr Adult Attention Deficit Disorder Scale (WRAADDS) provides a tool to facilitate this. It assesses a range of adult ADHD symptoms which load on two factors: inattentive and emotional dysregulation. The consistently high inattentive factor was used to define significant elevation on the more variable emotional dysregulation factor (which contains four WRAADDS domains: hyperactivity/restlessness, temper, affective lability, and emotional over-reactivity) allowing the definition of two ADHD diagnostic types. We compared these two types on a broad range of adult subject characteristics, including response to methylphenidate (MPH) treatment assessed during two clinical trials. Marked impairment in three of the four emotional domains reflected a symptom severity level equivalent to that of the inattentive factor. 59 % met this threshold, defining them as ADHD emotion dysregulation presentation, as opposed to 41 % with ADHD inattentive presentation. Cluster analysis validated these groups by generating similar clusters with 85 % agreement regarding membership. ADHD emotional dysregulation presentation subjects showed more childhood ADHD symptoms, adult symptoms of oppositional defiant disorder, and evidence of personality disorder. Both types showed similar improvement during the double-blind MPH arm of the trials and during a 6-month open-label phase. Based on the presence of symptoms of emotional dysregulation, ADHD in adults can be conceptualized as two types. Impairment and comorbidity in adults with ADHD are largely concentrated in ADHD emotional dysregulation presentation patients.

Keywords ADHD · Emotional dysregulation · Diagnosis · Adult

Introduction

The 1980 publication of the DSM-III (American psychiatric Association) (APA 1980) codified an understanding of ADHD as a disorder of childhood, and the criteria for this diagnosis were based on children with ADHD having some combination of inattentive and/or hyperactive-impulsive symptoms. This conceptualization, carried forward in subsequent editions of the DSM, has proven less useful for adults with ADHD, who tend to display fewer hyperactive symptoms and more emotional symptoms as age increases (Barkley et al. 2008). Beginning in the 1970s, investigators at the University of Utah, led by Paul Wender, started to develop the Utah Criteria for the diagnosis of ADHD based on the study of adults (Wood et al. 1976). These criteria were an outgrowth of our studies in which we attempted to define the multiplicity of symptoms found in adults with ADHD.

In 1993 we published and made publicly available the Wender Utah Rating Scale (WURS) to help identify

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individuals whose childhood ADHD symptoms were likely to persist into adulthood. We found that this scale, which assesses childhood retrospectively, better separated adults with ADHD from patients with depression than did self-rating instruments assessing current symptoms. This scale has been perceived as sensitive, but not sufficiently specific (Glöckner-Rist et al. 2013; Rodriguez and Simon-Dack 2013; Roy-Byrne et al. 1997). Conversely, it contains mood and conduct factors linked to persistence of ADHD into adulthood (Oncü et al. 2005; Stein et al. 1995; Trujillo-Orrego et al. 2009; Wierzbicki 2005).

A later step was the development of the Wender–Reimherr Adult Attention Deficit Disorder Scale (WRAADDS) which examines the symptoms covered by the DSM criteria, but also emotionality, as represented by temper, affective lability, and emotional over-reactivity (Marchant et al. 2013; Wender et al. 1981).

In 2005, we reported that within a large multicenter study of adults with ADHD selected using the Diagnostic and Statistical Manual IV (DSM-IV) (American Psychiatric Association 1994) criteria and excluding other Axis I disorders, we could identify a subgroup of adults with ADHD characterized by high levels of these emotional symptoms, which we labeled as ADHD-related emotional dysregulation (Reimherr et al. 2005). Compared to the rest of the sample, these patients showed higher levels of ADHD symptoms and more impairment in work, family, and social functioning.

In a later clinical trial we reported that a majority of adults with ADHD evidenced a combination of emotional and/or oppositional symptoms (Reimherr et al. 2007). Subsequently, we described the feasibility of applying oppositional defiant disorder criteria to adults (Marchant et al. 2011; Reimherr et al. 2013). We have also documented that much of the symptom load in adults with ADHD, including personality disorder and substance abuse, is associated with this cluster of emotional symptoms (Reimherr et al. 2010a, b).

Since our initial reports on ADHD-related emotional symptoms, additional publications have appeared exploring their pivotal role in ADHD. Sobanski et al. (2010) in a very large sample of European ADHD children found that most had high levels of emotional lability, which was associated with increased impairment. Barkley and Fischer (2010) showed that emotional lability made a unique contribution to impairment in a population of young adults with ADHD, while Spencer et al. (2011) reported a similar finding in children. In 2012, Biederman et al. showed that high levels of emotionality led to a more adverse outcome in children with ADHD. Surman et al. (2013) also reported higher emotional symptoms leading to increased impairment in adults with ADHD. Corbisiero et al. (2013) and Barkley (2010) argued that emotional symptoms are a fundamental part of the disorder, and Merwood et al. (2014) presented genetic data pointing to a close association between hyperactivity/restlessness, impulsivity, inattention, and emotional dysregulation. Several studies have found that during treatment, emotional symptoms improve in parallel with the conventional symptoms of inattention, hyperactivity/restlessness, and impulsivity (Marchant et al. 2011; Reimherr et al. 2007; Rösler et al. 2010; Wender et al. 2011).

While the literature broadly supports the importance of emotional symptoms in ADHD, two recent reviews note the absence of consensus as to how emotional dysregulation in ADHD should be defined and how it should be measured (Manos et al. 2011; Shaw et al. 2014). Most studies have used rating scales completed by patients in the case of adults with ADHD, or by parents when children are studied. In this research, the overlapping of symptoms of an emotional nature with symptoms of oppositional defiant disorder has been extensive, and much of the research on emotional dysregulation in ADHD has focused narrowly on temper/irritability.

Recently we reported that in assessing over 700 ADHD adults with the WRAADDS, two symptom factors were detected. Attention and disorganization items loaded on one factor, while emotional symptoms—temper control, mood lability, emotional over-reactivity, and hyperactivity/restlessness—loaded on a second factor (Marchant et al. 2013). Prior to this investigation, we assumed that emotional symptoms stood apart from hyperactivity/restlessness and that ADHD symptoms in adults sorted onto three main symptoms factors: attention disorganization, restlessness impulsivity, and emotional dysregulation.

While an arithmetic procedure based on the WRAADDS factor scores could be used to assign an adult with ADHD to one of these two groups, such an approach would be contrary to the diagnostic process commonly used in psychiatry. Typically, a diagnostic interview assesses salient patient symptoms to arrive at a psychiatric diagnosis. This process might be aided by rating scales, but the clinician interview is the ultimate guide. In this report we seek to define a type of ADHD based on emotional symptoms in a categorical, and therefore more clinically useful, manner. This research utilized data from two crossover studies of methylphenidate (MPH) response in adults with ADHD (Marchant et al. 2011; Reimherr et al. 2007), both involving a short-term double-blind phase and a long-term open-label follow-up.

The following questions are addressed:

1. Using WRAADDS factor scores as a guide, how should types of adult ADHD be defined clinically?
2. After dividing adults with ADHD in this manner, are there important differences historically and cross-

sectionally between these two groups of ADHD subjects?

3. Are there differences in short- or long-term treatment response between these two groups of subjects?

Methods

Procedure

The University of Utah Institutional Review Board reviewed and approved each study. They were double-blind, placebo-controlled, crossover trials of either MPH transdermal system or MPH oral release osmotic system (Concerta). Each contained a screening/baseline phase followed by a double-blind crossover phase with two four-week arms.

During the crossover phase subjects were randomly assigned in a double-blind manner to either placebo or active medication. After 4 weeks, subjects were crossed to the other treatment arm for an additional 4 weeks. Subjects were assessed weekly. Doses were adjusted based on treatment response and tolerability. When a subject was rated as much improved or better on the Clinical Global Impression-Improvement Scale or improved by 50 % or more on the WRAADDS, the dose remained constant for the remainder of that treatment arm. Generally, a stable dose was achieved in 2 weeks and held constant the last 2 weeks. Details of the initial portion of each study, including subject selection, have been published previously (Marchant et al. 2011; Reimherr et al. 2007).

Following the double-blind, crossover phase, all subjects were invited to enter a 6-month open-label extension. During this phase, subjects were seen monthly, and methylphenidate dosing was flexible.

Study population

Subjects were required to have a current diagnosis of ADHD using DSM-IV-Text Revision (APA 2000) criteria for current ADHD based on the Conners' Adult ADHD Diagnostic Interview for DSM-IV and/or meet the Utah Criteria for adult ADHD. [The Utah Criteria require a childhood diagnosis of ADHD as reflected by either the Wender Utah Rating Scale (WURS) or the Parent Rating Scale (PRS) (Wender 1995)]. The Utah Criteria also require the presence, as reflected by the WRAADDS, of both attentional difficulties and hyperactivity/restlessness along with two of the following characteristics: affective lability, disorganization or inability to complete tasks, hot temper or explosive short-lived outbursts, emotional over-reactivity, or impulsivity. Participants were obtained from clinic patients, referrals, and a limited amount of advertising in the greater Salt Lake City, Utah community. Subjects were between 18 and 65 years of age.

The following DSM-IV-Text Revision, Axis I diagnoses were exclusionary: current diagnosis of major depressive disorder, panic disorder, obsessive compulsive disorder, post-traumatic stress disorder, bipolar disorder, schizophrenia, or other psychotic disorder. Subjects with significant medical conditions likely to become unstable during the trial or likely to be destabilized by treatment with MPH (for example, cardiovascular disease) were excluded.

Whenever possible, the subjects' partners participated in all visits, a procedure employed in the development of the WRAADDS and an approach that has been endorsed by McGough and Barkley (2004). These informants were often able to view more keenly the subjects' behavior and symptoms, as well as treatment response, than were the subjects themselves.

Measures

The WURS was used to help ascertain childhood symptoms of ADHD. We have reported that a 26-item subset of WURS items should be used in scoring the WURS (Ward et al. 1993). Hereafter, reference to the WURS will denote this 26-item set; a score at or above the 95th percentile on these items has been demonstrated to indicate that ADHD was present during childhood.

The WRAADDS was used as the primary outcome measure in each study. The WRAADDS is an interviewer-administered scale assessing the adult ADHD symptoms identified in the Utah Criteria. Symptoms are grouped into seven domains: attention difficulties, hyperactivity/restlessness, temper, affective lability, emotional over-reactivity, disorganization, and impulsivity. This scale was completed at each visit. A copy of this scale is included as appendix to this article.

The Self-Report WRAADDS (SR-WRAADDS) mirrors items from both the WRAADDS and the WURS. It is being developed as an adult-oriented questionnaire that assesses the seven domains of the WRAADDS, as well as problems in three other areas: oppositional defiant symptoms, academic impairment, and social functioning. Its scoring permits a diagnosis of oppositional defiant disorder. Items are rated using a five-point scale ranging from 0 = none to 4 = very much. It was completed at screening and the end of each study phase. Copies of this scale are available from the corresponding author.

The Clinical Global Impression Scale-Severity (CGI-S) (Guy 1976) was completed at all visits. Subjects were assessed on severity of ADHD at the time of rating: 1, normal, not at all ill; 2, borderline ill; 3, mildly ill; 4,

moderately ill; 5, markedly ill; 6, severely ill; or 7, extremely ill. In this analysis, scores of 5 (markedly ill) or higher were categorized as significant impairment when comparing the two groups at baseline. Scores of 3 (mildly ill) or lower were used to categorize improvement during the double-blind phase.

The interviewer-administered version of the Conners' Adult ADHD Rating Scale (CAARS) (Conners et al. 1999) consists primarily of the DSM-IV ADHD symptoms modified to better assess adults. It was administered in the MPH transdermal system trial at baseline, at the end of both the medication and placebo arms, and at the end of the open-label phase. The Adult Investigator Symptom Rating Scale (AISRS) (Spencer et al. 2010) is an interviewer-administered scale that assesses the 18 items of the DSM-IV. It includes a total score and the subscales of inattention and hyperactivity/impulsivity. Like the CAARS, it was administered in the OROS MPH trial at baseline, at the end of both the medication and placebo arms, and at the end of the open-label phase. In the tables reporting treatment outcome, we calculated percentage change on these scales and combined them.

Two measures were used in the assessment of personality disorder. The Structured Clinical Interview for DSM-IV Axis II personality disorders (SCID-II) is an interview-based assessment approach to personality disorder using a two-step system (Jacobsberg et al. 1995). The subjects complete a screening questionnaire, and then a follow-up interview is conducted to check on areas that the subjects have rated above a threshold level. Its administration was amended in these trials by including their partners as an informant in the assessment. The Wisconsin Personality Inventory-IV (WISPI-IV) is a self-administered scale consisting of 214 items derived from viewing personality disorders from an interpersonal perspective; its validity has been demonstrated (Smith et al. 2003). It evaluates pathology associated with the 10 DSM personality disorder categories, as well as passive aggressive personality. For each diagnostic category, it generates *z*-scores relative to norms for age and sex.

At the end of both studies, information from all sources, including the SCID-II, WISPI-IV, and general observation of the subjects over the study course, was utilized by the treating psychiatrists to make a DSM-IV Text Revision personality disorder (PD) diagnosis. Subjects were then segregated into three post hoc categories: PD-negative (subjects without a personality disorder), PD-positive (subjects meeting diagnostic criteria for only one personality disorder), and PD-plus (subjects meeting diagnostic criteria for two or more personality disorders); this characterization has shown validity in prior research (Olsen et al. 2012; Robison et al. 2010; Williams et al. 2010).

Data analysis

All statistical testing was done with SPSS. A cluster analysis based on the two-factor scores was used to validate the diagnostic groups. The clustering methodology consisted of a two-step model-based clustering framework with the number of clusters chosen according to the Bayesian Information Criterion.

The two ADHD groups were compared on a broad range of subject characteristics by examining individual variables using a Chi-square test or Fisher's exact test for categorical variables and ANOVA for continuous variables. The false discovery rate (Benjamini–Hochberg procedure) was used to control for multiple comparisons at baseline.

Repeated-measures ANOVA was employed to assess group differences in the double-blind phase using treatment (active medication versus placebo) and ADHD diagnostic categories (ADHD inattentive presentation versus ADHD emotional dysregulation presentation) as the independent variables. Subsequently, the impact of treatment upon symptoms was assessed within each ADHD diagnostic group using the Chi-square test or Fisher exact test for categorical variables and using repeated-measures ANOVA for the total WRAADDS and the factor scores. Treatment effect as measured by the CGI-S was assessed within each diagnostic group using Chi-square test. The false discovery rate (Benjamini–Hochberg procedure) was used to control for multiple comparisons during the double-blind phase.

Change during the open-label phase was assessed using a repeated-measures ANOVA comparing the amount of change between the end of the medication arm of the double-blind phase and the final open-label visit for the two diagnostic groups. A second repeated-measures ANOVA addressed change in WRAADDS scores from baseline to open-label endpoint; both included diagnostic group as a fixed effect.

Data from the double-blind and open-label portions of the studies were analyzed on the basis of last observation carried forward (LOCF). There was no control for multiple measures applied.

Results

Combining data from both studies, 139 individuals signed consent agreements and entered the screening phase, of which 126 began the double-blind phase. 74 % ($n = 93$) completed both double-blind arms, and from this group, 71 subjects subsequently chose to enter the open-label phase.

In establishing a group of subjects high in emotional dysregulation, we wished to arrive at a method that, unlike calculating factor scores, might be easily used by

clinicians. We first examined the distribution of ADHD symptoms as assessed by the WRAADDS domains presented in Table 1. In almost 100 % of the sample, a rating of "quite a bit" or higher is obtained on both the attention and disorganization domains (Table 1 Part A) which constitute core criteria for adults with ADHD. The average factor score on the inattentive factor is 8.9, which is 83 % of the maximum possible.

In contrast to these uniformly high ratings, the other five domains show much more diversity. We noted previously that the emotional dysregulation factor of the WRAADDS contains mainly hyperactivity/restlessness, temper, mood lability, and emotional over-reactivity. In part B of Table 1, we present the number of subjects rated as "quite a bit" or "very much" from none up to all four of the emotionality domains. We then present the average emotional dysregulation factor scores for individuals rated as "quite a bit" or "very much" on none up to all four of these domains. As displayed in Table 1 part B, only those individuals rated as "quite a bit" or "very much" on at least three of these domains obtained an emotional dysregulation factor score of the same magnitude as the inattentive factor (the equivalent of "quite a bit").

Consequently, being categorized as having ADHD emotional dysregulation presentation should require a rating of "quite a bit" or "very much" at least on three of the four emotional domains. This allowed us to divide our population into two groups: ADHD inattentive presentation and ADHD emotional dysregulation presentation.

Confirmation of the results of this procedure was achieved through the use of a model-based cluster analysis, with the number of clusters chosen via the Bayesian information criterion. This supported the creation of two categories that closely resembled the separation based on factor scores and symptom domains. Cluster 1 was similar to ADHD inattentive presentation, having 52 subjects with average factor scores of inattentive factor 7.8 ± 1.2 and emotional dysregulation factor score 8.0 ± 1.7. Cluster 2 was similar to ADHD emotional dysregulation presentation having 84 subjects with an average inattentive factor score of 9.7 ± 0.7 and emotional dysregulation factor score 10.8 ± 2.7. There was 85 % agreement in membership between the two classification techniques, with 44 of the 56 ADHD attentive presentation subjects having membership in cluster 1 and 72 of the 80 ADHD emotional dysregulation presentation subjects having membership in cluster 2.

Baseline measures

Characteristics of the two diagnostic groups are presented in Table 2. The subjects with emotional dysregulation presentation were rated as more severely ill on the CGI-S. Of the 67 subjects rated markedly ill or higher, 81 % were in the emotional dysregulation presentation group, while 19 % were in the inattentive presentation group ($p < .001$).

As displayed in Table 2, numerous variables displayed significant differences ($p \leq .05$) between the two diagnostic types in bivariate analyses. These include the WRAADDS inattentive factor, impulsivity, childhood ADHD reflected by WURS scores, and measures of PD, as well as most SR-WRAADDS measures, including oppositional defiant disorder manifestations.

Table 1 Domain responses

Domain rankings	None (%)	Mild (%)	Moderate (%)	Quite a bit (%)	Very much (%)
Part A: Percentage of subjects with each specific rating for the seven WRAADDS domains ($n = 136$)					
Attention	0	1	1	30	68
Disorganization	1	2	4	26	66
Hyperactivity/restlessness	1	10	17	41	32
Temper (one subject not scored)	12	22	18	24	23
Mood lability (one subject not scored)	1	5	21	31	41
Emotional over-reactivity	2	6	21	28	43
Impulsive (one subject not scored)	1	6	16	39	39

Number of elevated ED domains	0	1	2	3	4
Part B: Average factor scores subjects with a specific number of emotional dysregulation domain scores rated as "quite a bit" or "very much" on none up to all four of these domains					
Number of subjects	9	21	26	36	44
Percentage of subjects	7 %	15 %	19 %	26 %	32 %
Average emotional dysregulation factor score mean ± SD (maximum possible score for this factor is 14.9)	6.2 ± 1.3	7.6 ± 1.4	9.4 ± 1.4	11.6 ± 1.1	13.5 ± 0.9
Percentage of maximum factor score	42 %	52 %	63 %	78 %	91 %

Table 2 Baseline attributes of subjects displaying the inattentive presentation versus emotional dysregulation presentation

	ADHD inattentive presentation 41 % ($n = 56$)	ADHD emotional dysregulation presentation 59 % ($n = 80$)	p value[a]
Sex—male ($n = 96$)	42.7 % ($n = 41$)	57.3 % ($n = 55$)	$\chi^2 = .3$, $p =$ ns
Female ($n = 40$)	37.5 % ($n = 15$)	62.5 % ($n = 25$)	
Age	35.3 ± 12.7	32.6 ± 10.9	$t = 1.4$, $p = .2$
DSM-IV diagnosis			
Inattentive	30 %	4 %	na[d]
Hyperactive-impulsive	0 %	1 %	
Combined type	70 %	95 %	
CGI-S—average	4.3 ± 0.6	5.0 ± 0.6	$t = 5.4$, $p < .001$*
CGI-S—percentage rated "markedly ill" (4) or higher	23 % ($n = 13$)	68 % ($n = 54$)	$\chi^2 = 25.8$, $p < .001$*
Retrospective childhood ADHD			
Wender Utah Rating Scale	45.9 ± 16.4	58.8 ± 14.9	$t = 4.6$, $p < .001$*
Wender Utah Rating Scale % (N) ≥ 46[b]	49 % ($n = 25$)	84 % ($n = 62$)	$\chi^2 = 17.2$, $p < .001$*
WRAADDS total	17.8 ± 3.1	24.1 ± 2.2	$t = 14.1$, $p < .001$*
Inattentive factor	8.1 ± 1.3	9.5 ± 1.0	$t = 7.8$, $p < .001$*
Percentage of maximum score (10.7)	76 %	89 %	
Emotionality factor	8.2 ± 1.8	12.7 ± 1.4	$t = 16.1$, $p < .001$*
Percentage of maximum score (14.9)	55 %	85 %	
Inattentive factor domains % (n) "quite a bit"			
Attention	98 % ($n = 55$)	98 % ($n = 78$)	na[d]
Disorganization	89 % ($n = 50$)	94 % ($n = 75$)	na[d]
Emotional dysregulation factor domains % (n) "quite a bit"			
Hyperactivity/restlessness	52 % ($n = 29$)	89 % ($n = 71$)	na[d]
Temper	5 % ($n = 3$)	75 % ($n = 60$)	na[d]
Affective lability	34 % ($n = 19$)	98 % ($n = 78$)	na[d]
Emotional over-reactivity	39 % ($n = 22$)	94 % ($n = 75$)	na[d]
Other domains %(n) "quite a bit"			
Impulsivity	58 % ($n = 32$)	91 % ($n = 73$)	$t = 4.7$, $p < .001$*
AISRS	32.7 ± 9.7	37.3 ± 7.7	$t = 1.8$, $p = .07$
CAARS	47.5 ± 15.0	59.7 ± 14.7	$t = 3.3$, $p = .002$*
SR-WRAADDS (item average scores)			
Total ADHD	2.2 ± 0.7	2.8 ± 0.7	$t = 5.44$, $p = <.001$*
Inattentive factor domains			
Attention	2.9 ± 0.8	3.2 ± 0.8	$t = 2.4$, $p = .02$*
Disorganization	2.7 ± 0.8	3.0 ± 0.9	$t = 1.9$, $p = .06$
Emotional dysregulation factor domains			
Hyperactivity/restlessness	2.4 ± 1.1	2.8 ± 1.0	$t = 2.0$, $p = .05$
Temper	1.2 ± 1.0	2.6 ± 1.2	$t = 7.0$, $p < .001$*
Affective lability	2.1 ± 1.0	2.8 ± 0.9	$t = 4.4$, $p < .001$*
Emotional over-reactivity	1.8 ± 1.0	2.8 ± 1.0	$t = 5.5$, $p < .001$*
Other domains			
Impulsivity	2.1 ± 1.0	2.5 ± 1.0	$t = 2.1$, $p = .04$*
Oppositional	1.4 ± 0.8	2.0 ± 0.8	$t = 4.7$, $p < .001$*
Academic	1.9 ± 1.2	2.1 ± 1.1	$t = .67$, $p = .55$
Adult ODD diagnosis present ($n = 67$)	34 % ($n = 19$)	60 % ($n = 48$)	$\chi^2 = 9.4$, $p = .005$*
Personality measures			
WISPI-IV z-scores	−0.3 ± 0.9	0.4 ± 1.0	$t = 3.4$, p .001*
SCID-II items endorsed	31.3 ± 16.6	49.4 ± 17.2	$t = 5.9$, $p < .001$*

Table 2 continued

	ADHD inattentive presentation 41 % ($n = 56$)	ADHD emotional dysregulation presentation 59 % ($n = 80$)	p value[a]
PD-negative %(N)	67 % ($n = 33$)	33 % ($n = 16$)	$\chi^2 = 19.1$, $p < .001$*
PD-positive	22 % ($n = 11$)	41 % ($n = 26$)	
PD plus	12 % ($n = 6$)	33 % ($n = 21$)	
Cluster A	5 % ($n = 2$)	14 % ($n = 10$)	$p = .12$[c]
Cluster B	5 % ($n = 2$)	30 % ($n = 21$)	$p < .001$[c]*
Cluster C	23 % ($n = 10$)	41 % ($n = 29$)	$p = .02$[c]*
Passive aggressive	5 % ($n = 2$)	18 % ($n = 13$)	$p = .03$[c]*
Substance use			
Alcohol misuse ($n = 53$)	38 % ($N = 20$)	62 % ($n = 33$)	$\chi^2 = .45$, $p = .50$
Substance misuse ($n = 30$)	27 % ($n = 8$)	73 % ($n = 22$)	$p = .09$[c]

CGI-S Clinical Global Impressions-Severity, *AISRS* Adult Investigator Symptom Rating Scale, *CAARS* Connor's Adult ADHD Rating Scale, *ODD* oppositional defiant disorder; *WISPI-IV* Wisconsin Personality Inventory-IV, *SCID-II* Structured Clinical Interview for DSM-IV Axis II, *PD* personality disorders, *na* not applicable since these differences were used to define the two diagnoses

* Remains significant using "false discovery rate"

[a] Unless indicated otherwise p values are derived from Student's t

[b] WURS scores of 46 and higher are associated with childhood ADHD

[c] p values are derived using Fisher Exact test

[d] Statistical differences not examined because groups were devised based on these characteristics

We compared the percentage of patients defined by these two proposed types to the percentage defined by customary DSM-IV criteria. The major difference occurs in the increased percentage of patients diagnosed as ADHD inattentive presentation type using our proposed criteria, 41 % versus 15 % defined as inattentive type by DSM-IV criteria. A difference in subtype distribution that is statistically significant ($\chi^2 = 23.7$, $df = 1$, $p = .001$) is seen when those who are inattentive are compared with those not designated inattentive.

We examined the differences in the WRAADDS domains for the two ADHD presentations. The domains reflecting emotional dysregulation were, as expected, more elevated in the ED presentation group, but attentional patients had occasional high scores on these domains.

On all measures of personality pathology, the ADHD emotional dysregulation presentation exceeded the ADHD inattentive presentation subjects. As measured by both the average WISPI-IV z-score and the number of items endorsed on the SCID-II screening questionnaire, the emotional dysregulation presentation group had more overall PD pathology. Additionally, 74 % of the ADHD emotional dysregulation presentation subjects qualified for a PD diagnosis versus 32 % of the ADHD inattentive presentation subjects ($p < .001$). Finally, more subjects in the emotional dysregulation presentation group had cluster B and cluster C diagnoses, as well as passive aggressive PD.

In summary, subjects with ADHD emotional dysregulation presentation show more impairment on measures of childhood ADHD (WURS), adult oppositional symptoms, current ADHD symptoms (CARRS), and PD.

Acute treatment response

Drug versus placebo differences are presented in Table 3. Drug was superior for most measures including: total WRAADDS, both WRAADDS factors, the AISRS/CARRS, the total SR-WRAADS, and the CGI-S.

A repeated-measures ANOVA was used to assess the double-blind treatment response (MPH versus placebo) of the two diagnostic groups using the total WRAADDS as the outcome variable. Medication was superior to placebo at a significant level ($F_{1,89} = 10.1$, $p = .002$). The amount of improvement in the two groups attributable to medication was similar as evidenced by the lack of a significant interaction ($F_{1,89} = 0.37$, $p = .55$) between diagnostic group and medication.

Additionally, two repeated-measures ANOVAs were conducted to compare the double-blind treatment responses (active medication versus placebo) of the two diagnostic groups (inattentive presentation versus emotional dysregulation presentation) using the two WRAADDS factors as the outcome variables. For the inattentive factor score, the interaction between diagnostic group and treatment was not significant ($F_{1.89} = 0.1$, $p = .8$). Similarly, for the emotional dysregulation factor, the interaction between diagnostic group and treatment was not significant ($F_{1,89} = 0.6$, $p = 0.4$).

Table 3 Double-blind treatment response for both diagnostic presentations mean (%) change from baseline values

	ADHD inattentive presentation (n = 33)			ADHD emotional dysregulation presentation (n = 59)		
	MPH	PBO	p value[a]	MPH	PBO	p value[a]
Investigator ratings						
Total WRAADDS	8.5 (46 %)	2.3 (13 %)	.005*	11.4 (47 %)	3.6 (15 %)	<.001*
Inattentive factor	4.0 (48 %)	1.2 (15 %)	.003*	4.3 (44 %)	1.2 (13 %)	<.001*
Attention factor domains						
Attention	1.9 (54 %)	0.5 (14 %)	.001*	1.7 (44 %)	0.5 (12 %)	<.001*
Disorganization	1.6 (46 %)	0.6 (18 %)	.01*	1.5 (43 %)	0.3 (9 %)	<.001*
Emotional dysregulation factor	3.7 (44 %)	0.7 (9 %)	.003*	6.2 (48 %)	2.1 (16 %)	<.001*
Emotional dysregulation factor domains						
Hyperactivity/restlessness	1.0 (42 %)	0.0 (1 %)	<.001*	1.5 (44 %)	0.4 (13 %)	<.001*
Temper	0.3 (25 %)	−0.1 (−8 %)	.18	1.7 (56 %)	0.6 (20 %)	<.001*
Affective lability	1.0 (46 %)	0.2 (9 %)	.02*	1.9 (52 %)	0.7 (19 %)	<.001*
Emotional over-reactivity	1.2 (48 %)	0.4 (16 %)	.03*	1.7 (46 %)	0.6 (15 %)	.001*
Other domains						
Impulsivity	1.3 (46 %)	0.5 (18 %)	.01*	1.5 (44 %)	0.5 (16 %)	<.001*
AISRS/CAARS (% improvement)[b]	45 %	14 %	.007*	43 %	13 %	<.001*
CGI-S [n(%) improved][c]	25 (68 %)	9 (22 %)	<.001*	34 (56 %)	5 (9 %)	<.001*
Self-report measures						
SR-WRAADDS (mean ± SD)						
Total ADHD score	7.6 (49 %)	3.9 (25 %)	.02*	8.8 (45 %)	4.5 (23 %)	.003*
Inattentive factor domains						
Attention	1.5 (50 %)	0.5 (19 %)	.006	1.6 (48 %)	0.6 (19 %)	.001*
Disorganization	1.3 (48 %)	0.6 (22 %)	.03*	1.4 (45 %)	0.7 (22 %)	.004*
Emotional dysregulation factor domains						
Hyperactivity/restlessness	1.1 (47 %)	0.7 (30 %)	.04	1.2 (43 %)	0.5 (17 %)	.002*
Temper	0.8 (57 %)	0.4 (32 %)	.17	1.3 (48 %)	0.9 (32 %)	.06
Affective lability	1.1 (52 %)	0.7 (34 %)	.04	1.3 (48 %)	0.8 (29 %)	.01*
Emotional over-reactivity	0.7 (39 %)	0.4 (21 %)	.13	0.9 (34 %)	0.6 (21 %)	.08
Other domains						
Impulsivity	1.1 (52 %)	0.6 (25 %)	.01*	1.2 (47 %)	0.4 (17 %)	.001*
Oppositional	0.8 (55 %)	0.6 (39 %)	.15	0.9 (44 %)	0.6 (28 %)	.05

AISRS Adult Investigator Symptom Rating Scale, *CAARS* Connor's Adult ADHD Rating Scale, *CGI-S* Clinical Global Impressions-Severity

* Remains significant using "false discovery rate"

[a] Significance calculated based on scores, not percentages

[b] See text re AISRS/CAARS scores

[c] Denotes a score of 3 or less "mildly ill"

Rather consistently the investigators perceived greater drug placebo differences than were suggested by the subjects' self-report. This difference was analyzed by the following procedure. The total WRAADDS and the total ADHD SR-WRAADDS were transformed into standard scores, and standard scores at the end of the drug arm were subtracted from standard scores at the end of the placebo arm. Comparing these change scores for the WRAADDS with the SR-WRAADDS, the greater values for the WRAADDS were indeed significant ($t = 3.2$, $p = .002$). However, both measures successfully documented a treatment effect.

Long-term open-label treatment response

As seen in Figs. 1 and 2, Table 4, while most of the improvement occurred in the double-blind phase, in the open-label phase (end MPH arm to end open label), significant

Table 4 Total symptom reduction to the end of the open-label period and symptom reduction during the open-label period

	ADHD inattention presentation (n = 22)		ADHD emotional dysregulation presentation (n = 48)	
	Baseline to OL[a]	MPH to OL[b]	Baseline to OL[a]	MPH to OL[b]
Total WRAADDS	12.3 (67 %)***	2.1 (12 %)	15.4 (63 %)***	4.1 (17 %)***
Inattentive factor	5.5 (66 %)***	0.9 (11 %)	5.8 (66 %)***	1.6 (17 %)***
Inattentive factor domain scores				
Attention	2.6 (71 %)***	0.3 (8 %)	2.4 (63 %)***	0.8 (21 %)***
Disorganization	2.1 (61 %)***	0.4 (11 %)	1.9 (53 %)***	0.4 (11 %)*
Emotional dysregulation Factor	5.7 (68 %)***	1.1 (13 %)	8.4 (65 %)***	2.2 (17 %)***
Emotional dysregulation factor domains				
Hyperactivity/restlessness	1.6 (68 %)***	0.3 (13 %)	2.1 (60 %)***	0.6 (18 %)**
Temper	0.7 (58 %)***	0.2 (18 %)	2.1 (68 %)***	0.4 (13 %)*
Affective lability	1.7 (71 %)***	0.2 (7 %)	2.3 (66 %)***	0.5 (14 %)*
Emotional over-reactive	1.8 (72 %)***	0.5 (21 %)	2.4 (66 %)***	0.7 (20 %)***
Other domains				
Impulsive	1.8 (66 %)***	0.4 (13 %)	2.2 (64 %)***	0.7 (20 %)***
CGI-S (n(%) improved)	22 (100 %)	22 (100 %)	38 (86 %)	38 (86 %)
Total SR-WRAADDS	9.6 (62 %)***	1.8 (12 %)	10.1 (54 %)***	0.3 (2 %)
Inattentive factor domains				
Attention	1.9 (67 %)***	0.5 (18 %)*	1.5 (54 %)***	0.1 (5 %)
Disorganization	1.8 (64 %)***	0.5 (17 %)	1.4 (50 %)***	0.1 (3 %)
Emotional dysregulation factor domains				
Hyperactivity/restlessness	1.3 (57 %)***	0.2 (9 %)	1.4 (51 %)***	0.0 (−1 %)
Temper	0.7 (56 %)***	0.0 (−2 %)	1.4 (57 %)***	−0.2 (−8 %)
Affective lability	1.2 (60 %)***	0.2 (11 %)	1.4 (53 %)***	−0.1 (−3 %)
Emotional over-reactivity	1.0 (54 %)***	0.3 (14 %)	1.3 (49 %)***	0.2 (8 %)
Other domains				
Impulsive	1.5 (67 %)***	0.2 (8 %)	1.8 (66 %)***	0.2 (7 %)
Oppositional	0.8 (66 %)***	0.1 (11 %)	0.8 (48 %)***	0.1 (4 %)

CGI-S Clinical Global Impressions-Severity

* $p = .05$; ** $p = .005$; *** $p = .001$; not controlled for multiple comparisons

[a] Percentage reflects total change at end of MPH arm divided by initial score

[b] Percentage reflects change (from end of the MPH arm) during the open-label divided by initial score

additional improvement occurred as shown by three repeated-measures ANOVAs [total WRAADDS ($F_{1,64} = 12.6$, $p = .001$); inattentive factor ($F_{1,64} = 12.6$, $p = .001$); and emotional dysregulation factor ($F_{1,64} = 12.9$, $p = .001$)]. Conversely, none of the diagnostic group by treatment interactions was significant (total WRAADDS ($F_{1,64} = 1.2$, $p = .28$,); inattentive factor score ($F_{1,64} = 1.1$, $p = .31$); and emotional dysregulation factor score ($F_{1,64} = 1.1$, $p = .30$)), suggesting that the improvement in the inattentive presentation and the emotional dysregulation subjects was similar.

Symptom measures by self-report (the SR-WRAADDS scores) showed a somewhat different pattern, with a lack of improvement (or perhaps a slight worsening) in emotional symptoms during the open-label for ADHD emotional dysregulation presentation subjects.

For the subsample composed of all open-label participants, the amount of improvement over baseline values was influenced by diagnostic type, with the primary difference in the emotional dysregulation factor scores. A repeated-measures ANOVA examining overall symptom change from baseline to open-label endpoint found that the emotional dysregulation presentation group improved 15.4 points, while the inattentive presentation subjects improved 12.4 points on the total WRAADDS, a difference that was significant ($F_{1,65} = 6.3$, $p = .015$). This difference may be related to greater change on the emotional dysregulation factor experienced by the emotional dysregulation

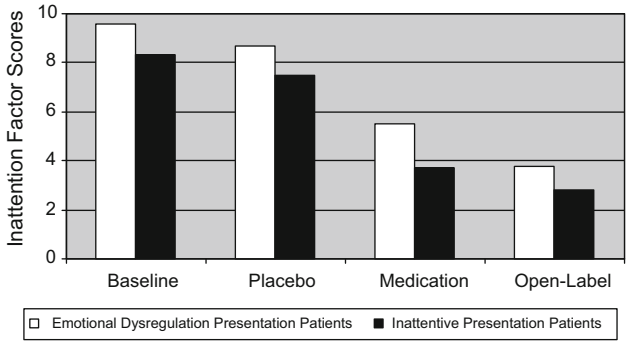

Fig. 1 Inattention factor scores for ADHD inattentive presentation versus emotional dysregulation presentation during each study phase

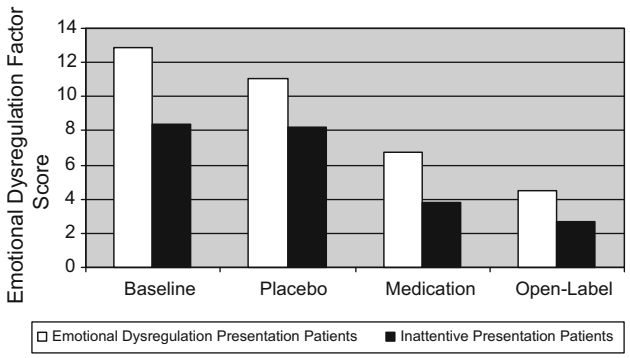

Fig. 2 Emotional dysregulation factor scores for ADHD inattentive versus emotional dysregulation presentation during each study

presentation versus the inattentive presentation subjects [8.4 vs. 5.7 ($F_{1,65} = 15.6$, $p < .001$)]; the inattention factor score changes were similar for both subject groups.

Discussion

These results support the validity of the two diagnostic types in ADHD adults, inattentive presentation and emotional dysregulation presentation. The use of these two categories provides a more complete diagnostic and conceptual picture of adult ADHD than do the DSM types, while the response of all seven WRAADDS symptom domains to a treatment of demonstrated efficacy supports the inclusion of all seven in the diagnostic construct of ADHD. Along with history, symptom assessment by patient interview is at the core of psychiatric evaluation. It is expected that while this process might be supplemented by rating forms, clinicians' face-to-face assessment of problems with affective lability, temper, and emotional over-reactivity, along with the DSM symptoms, will be the critical element.

The presentation of a spectrum of subject characteristics in Table 2 reveals important differences in baseline features between these diagnostic groups. 68 % of emotional dysregulation presentation subjects were considered markedly impaired as opposed to 23 % of the inattention presentation subjects on the Clinician's Global Impression of Severity, meaning that most inattentive presentation subjects were considered moderately ill at baseline. In contrast, most emotional dysregulation presentation subjects were considered more than moderately ill. This increased severity was reflected across a variety of clinical characteristics. While it might be argued that the psychiatrists' global ratings of severity were influenced by their awareness of considerable detail as to the subjects' overall clinical status, the scores on specific instruments measuring symptoms and dysfunction were not known to the psychiatrists at the time they were conducting the baseline assessment of the overall severity of ADHD subjects' illness.

Also, Table 2 compares this classification system to the DSM diagnostic system. Under these proposed criteria, more patients are diagnosed as ADHD inattentive presentation than would be deemed inattentive by the DSM criteria. This is due to demanding a combination of hyperactive restlessness, temper control, mood lability, and emotional over-reactivity for a subject to be diagnosed as ADHD emotional dysregulation presentation. If this relatively high level of emotional symptoms is not present, subjects will be classified inattentive. 41 % of our sample was classified as ADHD inattentive presentation. This figure is higher than the average 30 % incidence of DSM ADHD inattentive presentation reported by a group of recent publications (Conzelmann et al. 2009; Grevet et al. 2006; Rasmussen and Levander 2009; Soendergaard et al. 2014; Wilens et al. 2009).

Additionally, we show a differential association of ADHD type with personality disorder diagnosis. Cluster B, cluster C, and passive aggressive personality disorders occurred more frequently in ADHD emotional dysregulation presentation, although cluster A was independent of ADHD type.

The response to treatment was less marked when measured by the self-ratings of subjects as opposed to investigator ratings. Two considerations might partially account for this difference. First, the investigators were better able than the subjects to focus on problems constituting ADHD and likely to be responsive to medications, while the subjects tended to evaluate their problems and concerns more broadly. Second, the investigators' experience made them better able to ascertain whether the subject was on placebo or medication, and this might have allowed for investigator bias to influence assessment.

In our past studies we have assessed the role of emotional dysregulation as a symptom dimension in adults with ADHD. Those reports showed an association between increased psychosocial impairment and emotional dysregulation (Reimherr et al. 2005, 2010a). We also reported

an association between adult oppositional defiant disorder and emotional dysregulation (Marchant et al. 2011; Reimherr et al. 2010a, 2013). A number of other researchers have found that among adults with ADHD, ongoing emotional symptoms are associated with increased impairment (Barkley and Fischer 2010; Biederman et al. 2012; Bunford et al. 2014; Surman et al. 2013).

It could perhaps be argued that the emotional symptoms of ADHD that we have described in this report could be better understood as "comorbidity" than as an integral element of the illness. The response of these symptoms to MPH, a treatment which is minimally or not at all useful for other psychiatric disorders, argues for these emotion symptoms to be understood as part of ADHD, as does the factor analysis showing an association of emotional symptoms with hyperactivity, a major component of ADHD. By way of contrast, elsewhere we have described the independence of depressive and anxiety symptoms from ADHD symptoms using the methods employed in this report (Reimherr et al. 2005).

We have focused on the question of when symptoms of emotional dysregulation reach a level of severity such that they exceed a diagnostic threshold. As shown in our Table 1, four domains can be used to score subjects on level of emotional dysregulation. As described and shown in Table 2, only when at least three of our domain scores were present at a greater than moderate level did the factor score for emotional dysregulation reach a level of severity similar to the range demonstrated by subjects on the attention factor; this provided a cut-point for distinguishing between subjects low in emotional dysregulation and those high in emotional dysregulation.

However, psychiatry and psychiatric nosology have all but ignored dimensional in favor of categorical diagnosis, the approach taken by the several DSMs, and characteristic of all medical specialties as reflected by the ICD-10. Patients whose blood pressure is too high are assigned to the category of "pre-hypertension" or "hypertension" rather than simply described by their sphygmomanometer reading, and patients who weigh too much are assigned to the category of "overweight" or "obese" rather than simply described by their BMI. This practice, if not bespeaking its utility for physicians, at least reveals a strong preference, and we have followed this approach in examining emotional dysregulation in ADHD and defining it categorically.

As described in the methods, subjects were required to meet the DSM-IV or the Utah Criteria for ADHD, and a brief account of the Utah Criteria is provided above under *Study Population*. When the Utah Criteria were initially formulated in the 1980s, both attentional difficulties and problems with hyperactivity/restlessness were required for the diagnosis of ADHD in adults. As noted above, and as we reported in our recent publication dealing with the psychometrics of the WRAADDS (Marchant et al. 2013), hyperactivity/restlessness was discovered to be one domain of the scale's emotional dysregulation factor. Building on the description reflected in the Utah Criteria of the range of primary symptoms found in ADHD adults, these data support the existence of a general emotionality factor in adults with ADHD, with hyperactivity/restlessness being just one of the domains loading on this factor. It should be acknowledged that some researchers have argued that increased motor activity can be identified even in adult ADHD patients who meet criteria for inattentive type (Teicher et al. 2012). However important this might be in terms of theory, the technology necessary to detect this is available only in research facilities, not in usual clinical settings.

The technique used to construct the inattentive and emotional dysregulation presentations, as described above, will result in the latter group having more of the ADHD symptoms defined by the WRAADDS, and on this basis, it could be argued that identifying a patient as falling into the emotional dysregulation presentation group is simply a statement about severity of illness. This view ignores the information about the character of symptoms that is conveyed by use of the two categories described. An analogous situation might be thought to arise with describing mania; the creators of the ICD-10 chose to distinguish mania without psychotic features from mania with psychotic features, although they could have simply divided patients into "mania" and "severe mania".

That the emotional symptoms loaded on the same factor as hyperactivity/restlessness is not an unprecedented finding. Developers of the CAARS found that the emotional items contained in the CAARS loaded on a factor with hyperactivity (Conners et al. 1999). Barkley (2010) hypothesized that the emotional symptoms of ADHD would load on a factor with hyperactivity and impulsivity. Rösler et al. (2008), using a different scoring technique for the German version of the WRAADDS, reported a two-factor result in which the emotional items loaded on the same factor as hyperactivity. Finally, Karalunas et al. (2014) published a report using a cluster analysis methodology and scores from a temperament scale to arrive at three types of ADHD children. One had prominent anger as a distinguishing feature, while a second evidenced high levels of positive approach motivation. The third was described as normative, resembling non-ADHD children. Overall, these results comport reasonably well with findings described in this paper in that they found that an ADHD individual can be high in negative emotionality, or not. Their finding of three groups is a difference of course, but this can be attributed to their seeking out positive traits and behaviors, something not a salient aspect of clinical psychiatric practice and represented to a very limited degree in psychiatric nosology.

Assessment of these emotional symptoms should aid in the development and assessment of non-pharmaceutical therapies as well as somatic treatment. From a diagnostic perspective, identification of these two presentations of ADHD will decrease the potential for inaccurately assuming that a patient has a mood or anxiety disorder. From a treatment perspective, these emotional symptoms commonly lead to interpersonal conflicts (Wender 1995; Barkley 2010), which may be the reason that many adults seek out mental health professionals. This gives rise to the concern that many adult ADHD patients in such situations may not receive optimal interventions for these difficulties because of the unwarranted assumption that they spring from a different psychiatric diagnosis, such as a personality disorder.

Our experience is that the current child-derived DSM-5 (APA 2013) criteria are used to only a limited degree by psychiatrists in assessing adults who might have ADHD, and this focus on childhood symptoms is even more pronounced in the ICD-10. Indeed, the ICD-10 language implies that an ADHD diagnosis cannot be made in adults.

Limitations

The data used in this study were obtained from two clinical trials as opposed to being an epidemiologic sample. This quite likely led to the inclusion of a more impaired patient population. Patients wanted to be enrolled in the studies, and this might have led to their trying to present themselves so as to meet study inclusion criteria. Similarly, the investigators desired to have patients meeting study inclusion criteria. While these last two concerns are common to clinical trials, issues of sampling are different when the focus is exploring diagnosis and classification—the selectivity in choosing this cohort reduces the stability of conclusions which can be drawn as to the ADHD construct. Results must be understood recognizing that multiple statistical tests were done.

Conclusion

The results presented argue for the validity and utility of dividing adult ADHD into two types: ADHD inattentive presentation and ADHD emotional dysregulation presentation. ADHD emotional dysregulation presentation represents a more impaired group of individuals. Clinically, this group is defined by more than moderate impairment on at least three of four WRAADDS domains: hyperactivity/restlessness, temper, affective lability, and/or emotional over-reactivity. Related to this greater severity, they have more symptoms of oppositional defiant disorder even as adults, more evidence of personality disorder, and a trend toward more substance abuse. At the same time, they are responsive to methylphenidate both acutely and longer term, as are the inattentive presentation patients. Appropriate emphasis on emotional symptoms allows for the definition of a more severe type of adult ADHD, enhances its recognition, and in turn supports both treatment and research.

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