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Deficient Emotional Self-Regulation in Children and Adults With Attention-Deficit/Hyperactivity Disorder

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Deficient Emotional Self-Regulation in Adults With Attention-Deficit/Hyperactivity Disorder (ADHD): The Relative Contributions of Emotional Impulsiveness and ADHD Symptoms to Adaptive Impairments in Major Life Activities

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ABSTRACT

Background: Recent reviews have argued that emotional impulsiveness (EI) and deficient emotional self-regulation are central components in attention-deficit/hyperactivity disorder (ADHD), not merely associated features or the consequence of comorbidity.

Objectives: Our study has 2 aims: (1) to determine the frequency/severity of EI in adults with ADHD relative to these control groups; and (2) to evaluate the degree to which EI contributed to impairment in various domains of major life activities beyond that made by severity of the traditional 2 dimensions of ADHD (inattention, hyperactivity-impulsivity).

Methods: We examined the frequency and severity of problems with EI in 3 groups: adults with ADHD (n = 146), clinical-control adults not diagnosed with ADHD (n = 97), and a community-control group (n = 109). Self- and other ratings of EI were utilized.

Results: Results indicated that adults with ADHD had significantly more EI than either clinical or community controls, whether by self- or other reports, and whether symptoms were studied individually or in total. We also evaluated the extent to which EI contributed to the prediction of global ratings of self- and other rated impairments in 10 different domains beyond the contribution made by the traditional 2 dimensions of ADHD symptoms. EI uniquely contributed to 6 of 10 domains and overall impairment. We then evaluated this issue using more detailed measures of occupational impairment, educational history, criminal history, adverse driving outcomes, marital satisfaction, parenting stress, and offspring severity of ADHD, oppositional defiant disorder, and conduct disorder. Severity of EI independently contributed to most measures of impairment beyond severity of the 2 ADHD symptom dimensions and, in many cases, was the only predictor of some impairments.

Conclusions: Our results indicate that EI is as central a component of ADHD as are its 2 traditional symptom dimensions. EI severity is not merely redundant with the other ADHD symptom dimensions, but adds additional explanatory and predictive power to understanding various forms of adult impairment. (*J ADHD Relat Disord.* 2010;1[4]:5–28) © 2010 Excerpta Medica.

Key words: emotional impulsiveness, attention-deficit/hyperactivity disorder, ADHD, adults, adaptive impairment.

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INTRODUCTION

Attention-deficit/hyperactivity disorder (ADHD) is traditionally characterized as representing developmentally inappropriate levels of symptoms in 2 dimensions of neuropsychological functioning: inattention and hyperactivity-impulsivity.[1] Recent reviews of the scientific literature, however, have challenged this conceptualization of ADHD on the basis that it excludes an equally central feature that involves emotional impulsivity and deficient emotional self-regulation.[2–4] Emotional self-control is believed to comprise a 2-stage process that includes: (1) the inhibition of strong emotional reactions to events, and (2) the subsequent engagement of self-regulatory actions that include self-soothing, refocusing attention away from the provocative event, reducing and moderating the initial emotion, and organizing the eventual emotional expression so that it is more consistent with and supportive of individual goals and long-term welfare.[2,3,5–7] It is argued that deficits in both of these components of emotional self-control lead to impulsive emotional expression and the subsequent deficient self-regulation of those emotions. Both problems can be mapped directly onto the 2-dimensional structure of ADHD and explain the existence of emotional impulsiveness (EI) and its subsequent poor self-regulation as additional core features of the disorder. Deficits in behavioral inhibition (hyperactivity-impulsivity) in ADHD result in the expression of raw, unmoderated, and strong initial emotional reactions (both positive and negative). Deficits in executive functioning (inattention) interfere with the subsequent effortful actions needed to downregulate and moderate the subsequent emotional state of the individual to make it more age-appropriate, socially acceptable, and consistent with the individual's longer-term welfare.[3,8,9]

The specific impulsive emotions evident in ADHD are impatience, low frustration tolerance, hot-temperedness, quickness to anger or volatility, irritability, and a general propensity for being easily emotionally excitable.[2,4] The lines of argument supporting the central placement of EI in the conceptualization of ADHD have been reviewed recently[2] and include the long history of inclusion of EI in conceptualizations of ADHD and its precursor disorders, dating back to the first medical descriptions in 1798 by Crichton and later by Still (1902) up to 1976 (see Barkley 2010[2] for a review); current neuropsychological models of ADHD (combined type) that include poor emotional self-regulation as a key component[8–12]; current evidence from neuroimaging studies that the prefrontal brain networks likely involved in ADHD[13–17] also include those that serve to self-regulate emotions in the service of larger, longer-term goals (especially the linkage of the lateral prefrontal cortex to the anterior cingulate cortex and subsequently the amygdala/limbic system)[18–21]; and the small but growing body of evidence that symptoms of EI are frequently observed in association with ADHD, whether on rating scales or direct behavioral observations.[2–4]

Barkley[2] has argued that there is great value in the explicit inclusion of EI and subsequent deficits in emotional self-regulation in the conceptualization of ADHD beyond the arguments made previously. That is because it better explains the high comorbidity of ADHD with oppositional defiant disorder (ODD) and possibly other related disorders. It also may better account for certain impairments evident in ADHD not as readily apparent or easily explained by the traditional 2-symptom dimensions now included in ADHD (inattention and hyperactivity-impulsivity). Such impairments may include problems with peer relationships and social rejection, parent–child interaction conflicts and associated parenting stress, driving anger and aggression, a greater risk of employment problems, marital conflict and dissatisfaction, and offspring behavioral problems, among others. All of these problems occur with greater frequency in ADHD than in control groups. Some evidence implies that they may be related to the degree of poor emotional regulation evident in the disorder and not just the inattention and hyperactivity-impulsivity.[2,22] Yet the body of evidence that bears on this issue is small, limited primarily to children with ADHD, largely studied in research on peer relationships, and nearly absent in research on adults with the disorder. Also, prior research typically did not intentionally examine the relative contribution of EI symptoms beyond the severity of ADHD symptoms alone to explaining variance in the domain of adap-

tive functioning under study. It is quite possible that EI symptoms do not explain any further variance in impairments in major life activities than those already accounted for by ADHD severity. After all, if the 2 components of EI and emotional self-control map onto the 2-dimensional structure of ADHD, then the contributions of the former may already be included in measures of ADHD symptom severity. The former EI would therefore add little or no additional utility to explaining or predicting variance in adaptive impairments beyond the traditional 2 dimensions now included in ADHD.

We do not believe this is the case, however, and we hypothesize that, given the limited available evidence, symptoms of EI make separate, additional contributions to impairment in various major life activities beyond just the 2 recognized dimensions of ADHD symptoms. The present study therefore sought to examine this issue more thoroughly, using not only large samples of both adults with ADHD and a general community of adults traditionally included in typical research, but also a clinical-control group of adults not diagnosed with ADHD but having other psychiatric disorders. The latter group was self-referred to the same adult ADHD clinic as that used to recruit the ADHD sample and believed they may have had ADHD, but this group did not receive a subsequent clinical diagnosis of such. Thus, they comprise a better control group than just a general community sample in helping to control for referral biases that may have affected the nature of the adult ADHD sample. Such a clinical group also permits a better determination of the degree of specificity of EI symptoms associated with ADHD beyond that seen in other clinical outpatient disorders. Our study, therefore, had 2 aims: (1) to determine the frequency/severity of EI in adults with ADHD relative to these control groups; and (2) to evaluate the degree to which EI contributed to impairment in various domains of major life activities beyond that made by severity of the traditional 2 dimensions of ADHD (inattention, hyperactivity-impulsivity). Having previously conducted an extensive evaluation of the impairments associated with ADHD across many major life activities such as education, occupation, driving, money management, crime, marriage and dating, and parenting, among others,[22] we have a unique opportunity in the present study to evaluate the contribution of EI symptoms to impairment in these domains. We did not have measures of the deficient emotional self-regulation component and so this must be left to future research to investigate.

METHODS

Participants

Three groups of participants were used: (1) ADHD: 146 adults clinically diagnosed with ADHD; (2) clinical controls: 97 adults evaluated at the same clinic but not diagnosed with ADHD; and (3) community controls: 109 adult volunteers from the local community. Both the ADHD and clinical-control groups were obtained from consecutive referrals to the Adult ADHD Clinic in the Department of Psychiatry at the University of Massachusetts Medical School, Worcester, Massachusetts. The community-control group was recruited from advertisements posted throughout the medical school lobbies and from periodic advertisement in the regional newspaper. The project was reviewed and approved by the University of Massachusetts Institutional Review Board for Research on Human Participants, and all participants signed statements of informed consent.

To be eligible, all subjects were required to have an IQ of 80 or higher. They also had to have no evidence of deafness, blindness, or other significant sensory impairment; significant and obvious brain damage or neurological injury, or epilepsy; significant language disorders that would interfere with comprehension of verbal instructions in the protocol; a chronic and serious medical condition such as diabetes, thyroid disease, cancer, heart disease, etc; or a childhood history of mental retardation, autism, or psychosis. To be placed in the ADHD group, clinic-referred participants had to meet the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (*DSM-IV*) criteria for ADHD,[1] excepting the age of onset criterion, as judged by an experienced clinical psychologist using a structured interview for ADHD created by the authors. For more information on the process used in making these clinical judgments, see Barkley et al.[22] Participants in the clinical-control group were evalu-

ated at this same clinic but did not receive a clinical diagnosis of ADHD.

No precise age of symptom onset producing impairment was required for placement within the ADHD group, as one purpose of this study, reported elsewhere,[22] was to examine the value of specifying various age ranges of onset for the diagnosis of ADHD in adults. Also, the results of prior studies do not support the validity of the age of onset of 7 years currently included in the *DSM-IV* diagnostic criteria for ADHD.[22,23] All had the onset of their symptoms prior to age 21 years; mean age of onset was 7 years. Of the 146 adults assigned to the ADHD group, 30 were inattentive types (21%), 6 were residual (4%), and 110 were combined types (75%) according to clinician diagnosis.

The clinical-control group comprised patients not clinically diagnosed as having ADHD. The primary diagnoses given by the clinician to members of this group were varied, but comprised the following: anxiety disorders (43%), drug use disorders (15%), mood disorders (12%), learning disorders (4%), partner relationship problems (4%), adjustment disorders (4%), personality disorders (1%), and ODD (1%); 17% of these subjects received no diagnosis.

The community-control group consisted of relatively normal adults drawn from the local central Massachusetts region via advertisements. To be eligible for this group, subjects must have met the criteria noted earlier for all participants. In addition, they had to have a score on the Adult ADHD Rating Scale (see *Measures—Interviews and Rating Scales*) based on current symptoms (by self-report) *below* the 84th percentile (within +1 SD of mean) for their age (using norms reported in Barkley and Murphy[24]). Community controls also had to be free of any ongoing medication for treatment of a medical condition or psychiatric disorder that could be judged to interfere with the measures to be collected here.

The demographic characteristics of our 3 groups have been previously reported.[22] Participants in the ADHD group were significantly younger (mean age, 32 years) than that of the other 2 groups (clinical = 37 years; community = 36 years). Therefore, in all of the analyses of continuous measures conducted on these groups, we correlated age with the measure and, if significant, used it as a covariate. The ADHD group had significantly less education (14 years) than the 2 control groups (clinical = 16 years; community = 15 years), a finding consistent with prior research on the impact of ADHD on the educational outcomes of children followed to adulthood.[22] The groups did not differ in their IQ scores, but the clinical group had a significantly higher occupational index than the other 2 groups on the Hollingshead Index of Social Position (unpublished data, A.B. Hollingshead, 1975). The groups did not differ significantly in the percentage who were currently employed (ADHD, 73%; clinical, 71%; community, 77%). The groups differed significantly in gender composition (C^2 = 11.60; P = 0.003), with the ADHD group having a significantly higher composition of males than the 2 control groups (ADHD, 68% male and 32% female; clinical, 56% male and 44% female; community, 47% male and 53% female). This finding is similar to many studies of adults with ADHD,[24,25] where the ratio of males:females is 2:1. As a result, in any group comparisons conducted here, sex is used as a second factor after that of the group in the statistical analyses. As for the ethnic composition of the groups, 94% of each group identified themselves as European-American (Caucasian) descent.

Upon enrollment, 17% of the ADHD group, 30% of the clinical group, and none of the community group were treated with psychiatric medication. To evaluate the potential effect that medication status may have had on our results, we compared those ADHD cases that were on medication with those not on medication in the following measures: frequency of their ADHD symptoms from the interview, age of onset, number of domains of impairment from the interview, number of childhood ADHD symptoms (interview), total score for ADHD symptoms from self-ratings in adulthood and in childhood, self-rated impairment total scores on these same scales, total score for ADHD symptoms from ratings provided by others for both current and childhood behavior, and total impairment scores provided by others for both current and childhood functioning. None of these comparisons were significant. We conducted the same analyses for the subjects in the clinical-control group who

were and were not currently on medication. Again, no differences were significant. Thus, we felt reasonably confident that the small proportion of patients in these 2 groups currently taking medication would not bias our results by significantly reducing the severity of their ADHD-related symptoms. If bias were to occur, however, it would likely make the study a more conservative one by reducing the differences between the 2 clinical groups and the community-control group. We therefore combined the medicated and nonmedicated patients in each group for all subsequent analyses.

Procedures

After contacting a project staff member, all participants were scheduled for their initial diagnostic interview with the second author and an IQ screening test to be administered by a Master's-level psychology assistant. The initial interview was a structured interview to evaluate ADHD diagnostic criteria, including symptoms, onset, and impairment, that was designed for our research projects on adult ADHD. These steps were taken to determine eligibility for participation in any of the 3 groups. Participants also completed a structured interview to determine impairments in multiple domains of major life activities, including demographic information, educational and work history, current and prior psychiatric treatment, driving history, and money management. Official driving records were obtained from the state Department of Motor Vehicles (DMV), with the subjects' permission. Several behavior rating scales, as well as academic achievement and neuropsychological testing, were also completed by the subjects. The vast majority of the results concerning the comparisons of these groups on the various measures collected have been previously reported in the textbook by Barkley et al.[22] The present paper focuses on the symptoms of EI and their relationship to various measures of impairment collected in the project—this information has not been previously published. The complete details of this entire evaluation can be found in the text by Barkley et al. Following the evaluation, all participants were paid US $100 for their participation. Significant others were paid $20 each for the forms we requested that they complete.

Measures—Interviews and Rating Scales

Structured Clinical Interview for ADHD

A paper-and-pencil interview was created that consisted of the criteria from the *DSM-IV* for ADHD. An experienced clinician used this interview during the initial visit as part of the selection criteria for identifying those with ADHD. Symptoms were reviewed twice; once for current functioning (within the past 6 months), and a second time for the childhood ages of 5 to 12 years. A symptom was endorsed only if it occurred often or more frequently. The onset of symptoms was also reviewed, along with 6 domains of impairment: occupational, home, social, participation in community activities, education, and dating/marriage. In addition, subjects indicated approximately at what age each domain became impaired. This interview was used to create the groups. Interjudge reliability (agreement) was established by audiotaping this interview. Approximately 11% (41) of these tapes were randomly sampled and received a blinded independent review by another expert to determine if the responses met *DSM-IV* criteria for ADHD (as amended for onset, see previous). Agreement between the 2 judges on whether or not the *DSM-IV* criteria for ADHD were met was 85.3% ($\kappa = 0.712$; approx. $T^b = 4.76$; $P < 0.001$). If the tapes involving the potential subjects of the community-control group were excluded, agreement would have been 91.2%.

Adult ADHD Symptoms Scale

Apart from reporting on their symptoms in the clinical interview, subjects completed a rating scale containing the ADHD items from the *DSM-IV*.[24] Each item was answered on a 4-point scale (0–3), using the responses "not at all," "sometimes," "often," and "very often." Subjects completed the scale twice; once with reference to current symptoms and a second time to retrospectively recalled childhood (ages 5–12 years) symptoms of ADHD. Respondents also rated the degree to which their ADHD symptoms produced impairment in 10 different major life activities: home life, work, social interactions, community activities, educational activities, dating or marriage, money management, driving, leisure activities, and handling daily responsibilities.

Each domain was rated on the same 0 to 3 Likert scale as the ADHD symptoms mentioned previously. These specific impairment ratings were summarized to create an overall adaptive impairment index. In the present study, we used both the impairment ratings for each specific domain and the overall adaptive impairment index in our analyses. We also obtained the same ADHD rating scale from someone who knew the participant well, such as a parent (or sibling, should parents be deceased or unavailable) or current spouse or cohabiting partner. The validity of the scale has been demonstrated through past findings of significant group differences between ADHD and adult controls.[26,27] An earlier *DSM-III-R* version (Third Edition, Revised) of the current symptoms scale also correlated significantly with the same scale completed by a parent ($r = 0.75$) and by a spouse or intimate partner of the adult with ADHD ($r = 0.64$).[28] Agreement in this project between participants and others who knew them well on this scale was 0.70 ($P < 0.001$) for the total ADHD symptoms score, comparing favorably with other research ($r = 0.69$).[29]

Structured Clinical Interview of Impairments

For this project, we created an interview consisting of highly specific questions on various domains of major life activities, including educational history, occupational history, antisocial activities, drug use, driving, money management, and dating and marital history. This interview was administered by a psychological technician holding a Master's degree in psychology and trained in the evaluation of clinic-referred adults. The questions dealing with driving and occupational history are the focus of this paper.

Emotional Impulsiveness Scale

An aim of the larger, grant-funded project was the examination of poor executive functioning symptoms in adults with ADHD. With this in mind, we created a large rating scale consisting of 99 items, with each item being answered on a 0 to 3 Likert scale (0 = rarely or not at all; 1 = sometimes; 2 = often; and 3 = very often). Two versions of this scale were created; one to be completed by the subjects, and the second by someone who knew them well ("other" ratings), typically a parent or cohabiting partner, as previously mentioned. We had other ratings on 129 (88%) of the ADHD group, 88 (91%) of the clinical group, and 92 (84%) of the community group. These differences were not significant. Examination of the pattern of relationships of these other people to the participants across the groups also revealed no significant differences.

The item pool was initially created by the first author, based largely on his theory of executive function and ADHD,[8,9] but also on other conceptualizations of the construct.[30–32] Items were developed that assessed the 5 major constructs in this theory: inhibition, nonverbal working memory (self-directed sensing, especially visual imagery), verbal working memory (self-directed private speech), emotional–motivational self-regulation, and reconstitution (generativity, problem-solving, and goal-directed inventiveness). Additional items concerning problems with executive function in daily life were generated from an examination of the charts of at least 200 previous patients diagnosed with ADHD seen at this same clinic. For purposes of the present paper, we chose the 7 items that represented the symptoms of EI thought to be involved in ADHD as described previously and in recent reviews.[2–4] These 7 items were: (1) find it difficult to tolerate waiting–impatient; (2) quick to get angry or become upset; (3) easily frustrated; (4) overreact emotionally; (5) easily excited by activities going on around me; (6) lose my temper; and (7) am touchy or easily annoyed by others. We used these items to create the Emotional Impulsiveness Scale (EIS), which assessed the construct of EI for this project. The score consisted of the total created by summing the individual item scores. Both self- and other ratings of these items were used in our subsequent analyses.

Employer ADHD Rating Scale

We also obtained the ADHD rating scale mentioned in the previous section from the employers of our subjects, with their permission.[24] Employers were blinded to the diagnosis of the subjects. Questions on impairment in 10 domains of work activities were included: relations with coworkers, relations with supervisors, relations with clients or

customers, completing assigned work, educational activities, punctuality, meeting deadlines, operating equipment, operating vehicles, and managing daily responsibilities. ADHD symptom scores and these impairment ratings were devised using a Likert scale of 0 to 3 (rare to very often). The employer also provided an overall work performance rating using a 1 to 5 Likert scale (1 = excellent; 5 = poor). Four scores were obtained: inattention symptom score, hyperactive-impulsive symptom score, a rating of impairment (the sum across all the impairment items), and an overall work performance rating.

Social and Occupational Functioning Assessment Scale (SOFAS)

The SOFAS[33] provides the clinician a means to rate functioning on a scale from 1 (grossly impaired) to 100 (superior or excellent functioning), based on the individual's social, occupational, and educational functioning. Impairment must be a direct consequence of the mental and physical health problems of the individual and not a result of lack of opportunity or other environmental limitations. Descriptors are provided at each 10-point marker on the scale to guide clinicians in their ratings. For example, a score of 10 is indicated if the patient has a "persistent inability to maintain minimal personal hygiene, or unable to function without harming self or others or without considerable external support (eg, nursing care and supervision)." In contrast, a score of 70 would be given if there is "some difficulty in social, occupational, or school functioning but generally functioning well, has some meaningful interpersonal relations."

Department of Motor Vehicle Records

With permission from the subjects, we applied for each of their official driving records from the current state DMV. From these records, we coded the frequency of license suspensions or revocations, speeding citations, vehicular crashes, and the total number of citations. Official driving records are not necessarily more accurate than self-reports and should not be viewed as a gold standard in driving research. The 2 sources are certainly correlated significantly, but share <36% of their variance. For instance, in a prior study of adults with ADHD and driving,[34] the correlation between self-reported accidents and those on the DMV record was $r = 0.41$ ($P < 0.001$), with self-reports yielding higher accident frequencies than the DMV record. The same was true for self-reported traffic citations; correlation in that study was $r = 0.39$ ($P < 0.001$), and self-reports once again gave higher citation frequencies than did DMV records. Arthur et al[35] also found only moderate correlation between self-reported information and DMV records ($r = 0.48$ for crashes and $r = 0.59$ for citations). Numerous limitations plague state DMV record keeping that often result in higher frequencies of events being self-reported than are found in archival data, with the higher self-reported events likely reflecting adverse events never reported to or recorded by DMV officials. There is also a stronger relationship of self-report information to other predictors known to be related to driving risks.[35] Thus, both sources of information need to be included in driving studies, even though archival data are not necessarily superior to or more accurate than self-reported data in reflecting participant histories of adverse driving outcomes.

The Locke-Wallace Marital Adjustment Test

This widely used rating scale[36] evaluates marital satisfaction using 15 multiple-choice items. These items include an initial overall happiness in the marriage, followed by 14 items that examine the degree of agreement on specific issues such as finances, recreation, affection, friends, sexual relations, conduct, life philosophy, dealing with in-laws, and mutual problem-solving, among others. The Locke-Wallace Marital Adjustment Test (LW-MAT) was used here to evaluate the quality of the relationship between the currently cohabiting adult partners, whether married or not. Numerous studies attest to its validity and utility in distinguishing distressed from nondistressed couples.[37] A single raw score was employed here to assess relationship satisfaction among the subjects and their cohabiting partners. The developers recommend that scores <100 signify maladjustment.

Parenting Stress Index (PSI)

The PSI[38] is a multiple-choice parent self-report form. We utilized the PSI-Short Form (PSI-SF),

which consists of 36 items from the PSI that comprise 3 scales: Parental Distress, Difficult Child Characteristics, and Dysfunctional Parent-Child Interaction. Reitman et al[39] examined the psychometric characteristics of the PSI-SF in a low-income, predominantly minority population. Internal consistencies for the PSI-SF were very good to excellent. Parents completed this scale based on their relationship to just one of their children (ages 3 years and older).

Disruptive Behavior Disorders Rating Scale (DBDRS)

Participants who were also biological parents of children currently in their custody were asked to complete a rating scale of their child's disruptive behavior disorder symptoms using the DBDRS. This scale[24] contains the symptoms for ADHD, ODD, and conduct disorder (CD) as they appear in the *DSM-IV*.[1] The ADHD and ODD items are rated on a 4-point Likert scale (0–3; 0 = not at all or rarely, 1 = sometimes, 2 = often, and 3 = very often). The ADHD and ODD scores were obtained by summing all of the item scores for those item lists. The score for CD is simply a count of the number of items answered "yes." Parents completed this scale for all of their children aged ≥3 years.

RESULTS

The initial group comparisons on the measures of impairment noted above, as well as many others, have been previously reported.[22] Here we focus specifically on the group differences in EI and their utility in predicting impairment beyond just the traditional symptom dimensions of ADHD. We initially submitted the 7 self-rated items on emotion comprising the EIS to a factor analysis with varimax rotation using the entire sample to determine if they comprised a unitary dimension. A single factor emerged accounting for 72% of the variance in the ratings, with individual item loadings ranging from 0.746 to 0.908. We did the same for the same 7 items from the other ratings with similar results (74% of variance; item loadings ranged from 0.730–0.934). EI as measured here can be considered a single, unitary construct. The self- and other ratings on this scale correlated highly with each other ($r = 0.71$; $P < 0.001$), providing evidence of good external validity (interjudge agreement). The EIS self-ratings correlated highly with the ADHD symptom ratings ($r = 0.81$ for inattention, $r = 0.81$ for hyperactivity-impulsivity; $P < 0.001$ for both), approaching colinearity with them and supporting our point that those emotional symptoms are as central to ADHD as the traditional symptoms.

Because the groups differed in age, we examined the relationship of age to the EIS scores. We found it did not correlate significantly with self-ratings, but did so for other ratings, albeit to a low degree ($r = -0.12$; $P = 0.036$). We therefore used age as a covariate in the group comparison below for the other ratings on the EIS.

Group Differences in EI

We first examined the frequency with which the 7 EIS symptoms were endorsed by participants as occurring at least "often" or more frequently, given that this is the descriptor used in the *DSM-IV* criteria for ADHD to identify a clinically significant symptom of the disorder. The results for the self-ratings are shown in **Figure 1**. We subjected these results to χ^2 analyses and found that the EIS symptoms each occurred significantly more often in the ADHD group than in the clinical or community groups.* The clinical group displayed these symptoms more often than the community group as well. Within the ADHD group, the EIS symptoms occurred in 53% to 86% of the participants, which was nearly as frequent as the symptoms of ADHD inattention (73%–97%) and more frequent than the symptoms of ADHD hyperactivity-impulsivity (30%–79%). This supports our position that symptoms of EI are as much a problem for adults with ADHD as are the traditional symptoms of the disorder.

We conducted the same analyses for the EIS symptoms based on other ratings (**Figure 2**). χ^2 Analyses indicated that more members of the ADHD group displayed each of these symptoms

*Specific detailed analyses are available upon request from the first author.

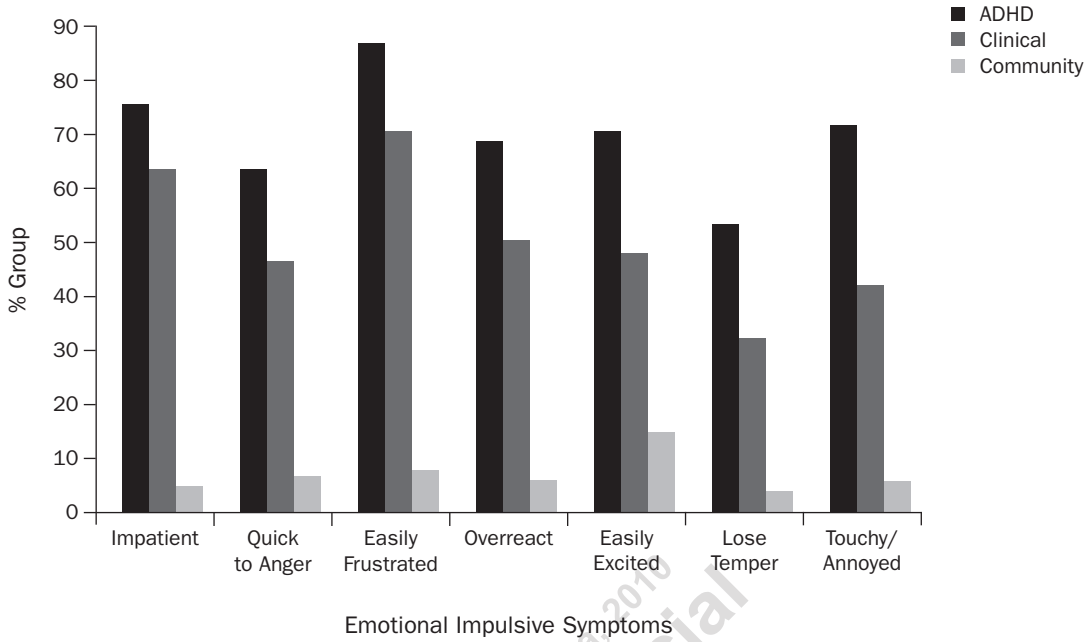

Figure 1. Percentage of each group manifesting each self-reported symptom of emotional impulsiveness that occurred at least "often" or more frequently. ADHD = attention-deficit/hyperactivity disorder; clinical = clinical-control group; community = community-control group. For all symptoms, the ADHD group > clinical group > community group with all pairwise statistical comparisons being significant ($P < 0.05$).

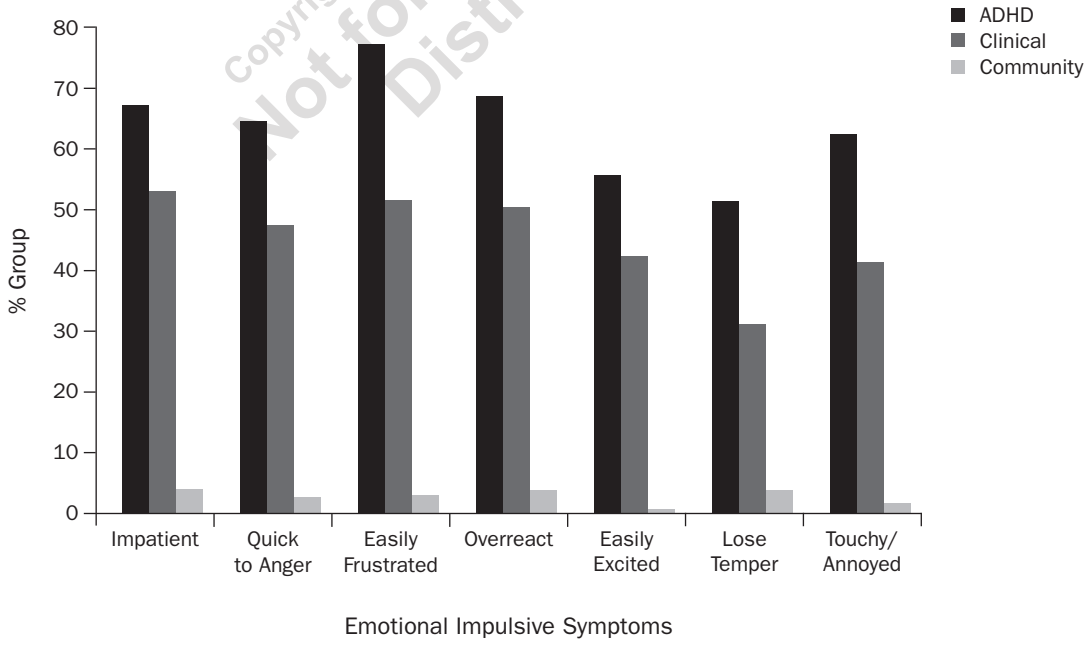

Figure 2. Percentage of each group manifesting each self-reported symptom of emotional impulsiveness that occurred at least "often" or more frequently. ADHD = attention-deficit/hyperactivity disorder; clinical = clinical-control group; community = community-control group. For all symptoms, the ADHD group > clinical group > community group with all pairwise statistical comparisons being significant ($P < 0.05$).

than those in the community group for all 7 symptoms.* The ADHD group differed from the clinical group in 6 of the 7 symptoms, the exception being the item "easily excited" (P = 0.057). The frequency of the items in the ADHD group ranged from 51% to 76%. These symptoms occurred as commonly as those for inattention (45%–76%) and more so than those for hyperactive-impulsive symptoms (28%–56%) as rated by others. While lower than the self-reported frequencies, the majority of adults with ADHD displayed these symptoms as reported by others and did so as often as or more than the traditional ADHD symptoms.

We then compared the groups on their self-rated EIS total scores and found that the analysis of variance was significant (F = 215.20; df = 2/328; P < 0.001). Pairwise comparisons showed that the ADHD group had a higher mean (SD) score (13.7 [5.1]) than both the clinical (11.6 [4.7]) and community groups (2.4 [2.7]). The clinical group also had a higher score than the community group. The same was the case for the other ratings on the EIS total scores where age served as a covariate (F = 123.93; df = 2/290; P < 0.001). Pairwise comparisons again showed that the ADHD group had a higher mean score (13.4 [5.8]) than both the clinical (9.9 [5.7]) and community groups (2.4 [SD] = 2.9). The clinical group also had a higher score than the community group.

Predicting Global Impairment Ratings

Based on the entire sample of participants, multiple linear regression analyses with stepwise entry were used to determine the relative contributions of ADHD symptom ratings and EIS symptom ratings to self-rated impairment in the 10 domains of major life activities from the Adult ADHD Rating Scale. We were particularly interested here, as noted earlier, in whether EIS symptoms make any additional contributions to predicting impairment beyond that contributed by ADHD symptoms (**Table I**). The largest contributor by far to self-rated impairments was the inattention dimension of ADHD symptoms, contributing significantly to 9 of the 10 specific domains and, in particular, the overall adaptive impairment rating. EIS ratings, however, contributed significant additional variance to impairment in 6 of the 10 specific domains: occupational functioning, social interactions with others, educational settings, money management, driving, and leisure/recreational activities. In the driving domain, EIS ratings made the largest contribution (30% of variance) to self-rated impairment. In the remaining 5 domains to which EIS ratings contributed, the additional explained variance ranged from <1% to nearly 5%. In 5 of these 6 domains, EIS ratings contributed more explained variance than did the hyperactive-impulsive dimension of ADHD. For the prediction of overall adaptive impairment, the greatest contribution was made by symptoms of inattention (78%), followed by emotionally impulsive (4%) and hyperactive-impulsive symptoms (<1%).

We conducted this same set of analyses for the other ratings of impairment using the other ratings of ADHD and EIS symptoms. Once again, symptoms of inattention contributed the largest share of variance to most of these domains, and contributed significantly to 9 of 10 specific domains. EIS symptoms again contributed to 6 of the 10 specific domains; however, these were not identical to those domains to which they contributed for the self-ratings mentioned earlier. These specific domains included home life, occupational functioning, social interactions with others, community activities, managing money, and leisure/recreational activities. EIS ratings did not contribute to other rated driving impairment or impairment in educational settings as in the self-rated impairments mentioned previously. EIS ratings did, however, contribute to impairment in home life and community activities in these other rated domains, whereas they did not for the self-ratings. In general, the pattern was relatively similar to what was found for self-ratings when we examined the overall adaptive impairment scores, where once again symptoms of inattention contributed most of the variance (77%), followed by emotional (3.8%) and hyperactive-impulsive symptoms (<1%). In summary, symptoms of EI do appear to make additional contributions to impair-

*Specific detailed analyses are available upon request from the first author.

TABLE I. PREDICTION OF THE GLOBAL SELF-RATINGS OF IMPAIRMENT IN 10 LIFE ACTIVITY DOMAINS USING SELF-RATED ADHD SYMPTOMS AND SYMPTOMS OF EMOTIONAL IMPULSIVENESS.

Domain of Impairment/Predictors	β	*R*	R^2	$R^2\Delta$	*F*	*P*
Home life with immediate family						
Inattention	0.531	0.724	0.525	0.525	314.53	<0.001
Hyperactive-impulsive	0.239	0.738	0.545	0.020	12.51	<0.001
Occupational functioning						
Inattention	0.682	0.774	0.598	0.598	426.01	<0.001
Emotionally impulsive	0.120	0.777	0.604	0.006	4.43	0.036
Social interactions with others						
Inattention	0.431	0.721	0.519	0.519	311.14	<0.001
Emotionally impulsive	0.191	0.742	0.551	0.031	20.08	<0.001
Hyperactive-impulsive	0.180	0.748	0.559	0.009	5.60	0.019
Activities or dealings in the community						
Inattention	0.486	0.669	0.448	0.448	226.96	<0.001
Hyperactive-impulsive	0.226	0.682	0.465	0.018	9.18	0.003
Educational settings						
Inattention	0.608	0.739	0.546	0.546	339.96	<0.001
Emotionally impulsive	0.354	0.761	0.579	0.033	22.28	<0.001
Hyperactive-impulsive	−0.171	0.766	0.587	0.008	5.12	0.024
Dating or marital relationship						
Inattentions	0.463	0.679	0.460	0.460	239.81	<0.001
Hyperactive-impulsive	0.267	0.697	0.485	0.025	13.44	<0.001
Managing money						
Inattention	0.470	0.679	0.461	0.461	245.00	<0.001
Emotionally impulsive	0.276	0.702	0.493	0.033	18.45	<0.001
Driving a motor vehicle						
Emotionally impulsive	0.308	0.544	0.296	0.296	120.11	<0.001
Hyperactive-impulsive	0.295	0.572	0.327	0.032	13.40	<0.001
Leisure/recreational activities						
Hyperactive-impulsive	0.286	0.677	0.459	0.459	242.16	<0.001
Emotionally impulsive	0.308	0.711	0.506	0.048	27.54	<0.001
Inattention symptoms	0.180	0.719	0.516	0.010	5.99	0.015
Managing daily responsibilities						
Inattention	0.839	0.839	0.703	0.703	678.19	<0.001
Total overall adaptive impairment						
Inattention	0.583	0.880	0.775	0.775	905.63	<0.001
Emotionally impulsive	0.262	0.903	0.815	0.040	56.11	<0.001
Hyperactive-impulsive	0.117	0.905	0.818	0.003	5.01	0.026

ADHD = attention-deficit/hyperactivity disorder; β = standardized β coefficient from the final model; *R* = regression coefficient; R^2 = percent of explained variance accounted for by all variables at this step; $R^2\Delta$ (change) = percent of explained variance accounted for by this variable added at this step; *F* = F to change results.

Analyses are for linear multiple regression with stepwise entry. Domains of impairment are from the Adult ADHD Rating Scale (rated 0–3). Predictors were inattention symptoms and hyperactive-impulsive symptoms from the Adult ADHD Rating Scale and emotionally impulsive symptoms from the Emotional Impulsiveness Scale.

TABLE II. PREDICTION OF THE GLOBAL OTHER RATINGS OF IMPAIRMENT IN 10 LIFE ACTIVITY DOMAINS USING OTHER-RATED ADHD SYMPTOMS AND SYMPTOMS OF EMOTIONAL IMPULSIVENESS.

Domain of Impairment/Predictors	β	*R*	R^2	$R^2\Delta$	*F*	*P*
Home life with immediate family						
Inattention	0.669	0.766	0.586	0.586	321.42	<0.001
Emotionally impulsive	0.148	0.774	0.599	0.013	7.06	0.008
Occupational functioning						
Inattention	0.642	0.752	0.586	0.586	285.57	<0.001
Emotionally impulsive	0.170	0.763	0.583	0.017	8.78	0.003
Social interactions with others						
Hyperactive-impulsive	0.263	0.677	0.459	0.459	191.66	<0.001
Inattention	0.316	0.733	0.537	0.079	38.18	<0.001
Emotionally impulsive	0.264	0.752	0.566	0.028	14.52	<0.001
Activities or dealings in the community						
Inattention	0.312	0.599	0.358	0.358	119.57	<0.001
Emotionally impulsive	0.219	0.648	0.420	0.062	22.63	<0.001
Hyperactive-impulsive	0.208	0.660	0.436	0.016	5.93	0.016
Educational settings						
Inattention	0.793	0.793	0.629	0.629	365.77	<0.001
Dating or marital relationship						
Inattention	0.517	0.689	0.474	0.474	193.81	<0.001
Hyperactive-impulsive	0.239	0.708	0.502	0.028	11.82	0.001
Managing money						
Inattention	0.615	0.646	0.417	0.417	160.97	<0.001
Emotionally impulsive	0.277	0.658	0.432	0.015	6.08	0.014
Hyperactive-impulsive	−0.219	0.671	0.450	0.018	7.30	0.007
Driving a motor vehicle						
Hyperactive-impulsive	0.432	0.609	0.371	0.371	133.61	<0.001
Inattention	0.259	0.637	0.406	0.036	13.62	<0.001
Leisure/recreational activities						
Hyperactive-impulsive	0.479	0.660	0.436	0.436	174.59	<0.001
Emotionally impulsive	0.241	0.679	0.462	0.026	10.73	0.001
Managing daily responsibilities						
Inattention	0.831	0.831	0.691	0.691	509.12	<0.001
Total overall adaptive impairment						
Inattention	0.647	0.878	0.772	0.772	641.53	<0.001
Emotionally impulsive	0.207	0.900	0.809	0.038	37.61	<0.001
Hyperactive-impulsive	0.124	0.903	0.815	0.006	5.81	0.017

ADHD = attention-deficit/hyperactivity disorder; β = standardized β coefficient from the final model; *R* = regression coefficient; R^2 = percent of explained variance accounted for by all variables at this step; $R^2\Delta$ (change) = percent of explained variance accounted for by this variable added at this step; *F* = F to change results.

Analyses are for linear multiple regression with stepwise entry. Domains of impairment are from the Adult ADHD Rating Scale (rated 0–3). Predictors were inattention symptoms and hyperactive-impulsive symptoms from the Adult ADHD Rating Scale and emotionally impulsive symptoms from the Emotional Impulsiveness Scale.

ment beyond those made by traditional ADHD symptom dimensions, and likely do so to a greater degree than symptoms of hyperactivity-impulsivity.

Predicting Specific Measures of Occupational Functioning and Impairment

Employer ratings of work performance and self-reports of work history and performance were obtained, in addition to self-reported information on the number of jobs in which the subjects had various workplace problems. Using multiple linear regression and the entire sample of participants, we examined the extent to which ADHD symptoms and those of EI contributed to these various measures (**Table III**). Problems with EI contributed significantly to more occupational measures than did either of the traditional ADHD symptom dimensions. Symptoms of EI contributed to 6 of the 11 employment measures beyond any contribution made by ADHD symptoms, including the number of jobs in which subjects had problems with their own behavior and work performance, had problems getting along with others, had quit over hostility with their employers, and had quit out of boredom, as well as the number of times they had been unemployed for 1 month or longer and clinician ratings of social and occupational functioning. For 4 of the outcomes, symptoms of EI were the only significant predictors. Symptoms of inattention contributed to 5 of the 11 measures, while hyperactive-impulsive symptoms contributed to just 2. Thus, symptoms of EI seem to contribute to various problems in the workplace and with employment history beyond any contribution made by ADHD symptoms.

Predicting Educational History and Impairments

In the impairment interview, subjects were asked specific questions about their education and various problems they may have had, as well as types of special educational services they may have received. We once more evaluated the extent to which current symptoms of EI may have contributed to these educational measures apart from any contribution made by current ADHD symptom dimensions. Technically, this is a form of postdiction rather than concurrent prediction, because the symptom scores are for current functioning, while the educational measures are historical, dating back to childhood and adolescence. Nevertheless, such analyses can still be informative of the *relative* contributions of ADHD and emotion to these historical measures. We used multiple linear regression to evaluate the number of years of education participants had received. Only symptoms of EI contributed significantly to this outcome, with higher EIS scores predicting less education ($R = 0.122$; $R^2 = 0.015$; $F = 4.66$; $P < 0.032$). Only hyperactivity-impulsivity symptoms predicted the number of times subjects reported having been suspended from school ($R = 0.164$; $R^2 = 0.0275$; $F = 8.43$; $P = 0.004$). Rates of truancy from school were predicted only by symptoms of EI ($R = 0.166$; $R^2 = 0.027$; $F = 8.71$; $P = 0.003$). The remaining educational measures were binary in nature (typically yes/no questions), and these were evaluated using logistic regression (**Table IV**). Graduation from high school was not related to either current ADHD or symptoms of EI in adulthood. However, graduation from college was significantly related only to the level of EI, as was risk for grade retention, risk for having had formal special education, and risk for having received any extra assistance at school. Hyperactive-impulsive symptoms were related to the risk for receiving learning disability services in school, having had behavior problems in school, and whether or not they believed they had been punished more than others at school. Current inattention was also related to the latter risk and for having had problems getting along with others. Current symptoms of EI also predicted the latter risk, but to a greater extent than inattention.

Predicting Driving Problems and Criminal History

Our self-reported and DMV measures of adverse driving outcomes were evaluated using multiple linear regression analyses with stepwise entry and, again, ADHD symptoms and symptoms of EI served as predictors (**Table V**). Only hyperactive-impulsive symptoms contributed significantly to self-reported frequencies of license suspensions, driving before having received a valid license, vehicular crashes, and speeding citations. However, only emotionally

TABLE III. PREDICTION OF OCCUPATIONAL IMPAIRMENTS USING SELF-RATED ADHD SYMPTOMS AND SYMPTOMS OF EMOTIONAL IMPULSIVENESS.

Domain of Impairment/Predictors	β	*R*	R^2	$R^2\Delta$	*F*	*P*
Employer-rated work performance						
Inattention	0.361	0.361	0.130	0.130	14.80	<0.001
Employer-rated overall impairment						
Inattention	0.521	0.223	0.050	0.050	4.48	0.037
Emotionally impulsive	−0.377	0.320	0.102	0.053	5.02	0.028
Self-rated work quality						
Inattention	0.342	0.342	0.117	0.117	30.28	<0.001
# Jobs held since completing school						
Hyperactive-impulsive	0.188	0.188	0.035	0.035	10.61	0.001
# Jobs: problems with own behavior and work performance						
Inattention	0.220	0.392	0.154	0.154	54.60	<0.001
Emotionally impulsive	0.219	0.415	0.172	0.019	6.79	0.010
# Jobs: problems getting along with others						
Emotionally impulsive	0.321	0.321	0.103	0.103	34.80	<0.001
# Jobs: fired						
Hyperactive-impulsive	0.197	0.197	0.039	0.039	12.24	0.001
# Jobs: quit over hostility with employer						
Emotionally impulsive	0.214	0.214	0.046	0.046	14.56	<0.001
# Jobs: quit due to boredom						
Emotionally impulsive	0.317	0.317	0.100	0.100	33.73	<0.001
# Jobs: were formally disciplined for substandard work						
Inattention	0.119	0.119	0.014	0.014	4.37	0.037
# Times unemployed for 1+ months						
Emotionally impulsive	0.187	0.187	0.035	0.035	10.33	0.001
Clinician rating of social and occupational functioning						
Inattention	−0.523	0.751	0.564	0.564	382.99	<0.001
Emotionally impulsive	−0.291	0.773	0.597	0.033	24.28	<0.001

ADHD = attention-deficit/hyperactivity disorder; β = standardized β coefficient from the final model; *R* = regression coefficient; R^2 = percent of explained variance accounted for by all variables at this step; $R^2\Delta$ (change) = percent of explained variance accounted for by this variable added at this step; *F* = F to change results.

Analyses are for linear multiple regression with stepwise entry. Domains of impairment are from the Adult ADHD Rating Scale (rated 0–3). Predictors were inattention symptoms and hyperactive-impulsive symptoms from the Adult ADHD Rating Scale and emotionally impulsive symptoms from the Emotional Impulsiveness Scale.

TABLE IV. PREDICTING EDUCATIONAL HISTORY AND IMPAIRMENT USING CURRENT ADHD SYMPTOM DIMENSIONS AND SYMPTOMS OF EMOTIONAL IMPULSIVENESS.

Outcome/Predictors (block entered)	β	SE	Wald	*P*	Odds Ratio	95% CI
Graduated high school						
No significant predictors						
Graduated college						
Emotionally impulsive	−0.040	0.017	5.72	0.016	0.96	0.93–0.99
Retained in grade						
Emotionally impulsive	0.086	0.025	12.20	<0.001	1.09	1.04–1.14
Received special education						
Emotionally impulsive	0.065	0.021	9.62	0.002	1.07	1.02–1.11
Received extra assistance at school						
Emotionally impulsive	0.090	0.019	23.27	<0.001	1.09	1.05–1.13
Received learning disability services						
Hyperactive-impulsive	0.069	0.022	10.19	0.001	1.07	1.03–1.12
Had behavior problems at school						
Hyperactive-impulsive	0.144	0.022	42.59	<0.001	1.15	1.11–1.21
Punished more than others						
Inattention	0.068	0.034	4.04	0.044	1.07	1.00–1.14
Hyperactive-impulsive	0.108	0.034	10.04	0.002	1.11	1.04–1.19
Problems getting along with others						
Inattention	0.056	0.028	3.86	0.049	1.06	1.00–1.12
Emotionally impulsive	0.149	0.032	21.47	<0.001	1.16	1.09–1.24

ADHD = attention-deficit/hyperactivity disorder; β = standardized β coefficient from the final model.
Analyses were binary logistic regression using stepwise forward conditional entry and entire sample.

impulsive symptoms contributed significantly to self-reported frequencies of crashes in which the participant was held to be at fault and citations were received for driving under the influence of alcohol (DUI). Current level of inattention was unrelated to these adverse self-reported driving outcomes. When we examined some of these same measures from official DMV records, we found that only current symptoms of EI were related to frequency of speeding citations, DUI citations, vehicular crashes, and total citations recorded. None of the symptom scores predicted frequency of license suspensions. Current severity of inattention symptoms was again not related to outcomes reflected on the DMV record.

The impairment interview also included several questions concerning whether or not the subjects had ever been arrested or jailed. The number of self-reported CD symptoms for the subjects' childhood and adolescent years on the Adult ADHD Rating Scale–Childhood Recall form was also utilized. We examined the extent to which ADHD symptoms and symptoms of EI predicted these outcomes (**Table V**). Only current symptoms of EI were significantly associated with these measures of antisocial conduct and criminal outcomes.

Predicting Marital Satisfaction, Parenting Stress, and Offspring Disruptive Behavior Problems

If our subjects were cohabiting with a spouse or partner, we had them both complete the LW-MAT (**Table VI**). Again, only the current symptoms of EI

TABLE V. PREDICTION OF DRIVING AND CRIME MEASURES FROM DMV RECORDS AND SELF-RATED CURRENT ADHD SYMPTOMS AND SYMPTOMS OF EMOTIONAL IMPULSIVENESS.

Domain of Impairment/Predictors	β	*R*	R^2	$R^2\Delta$	*F*	*P*
Self: # license suspensions/revocations						
Hyperactive-impulse	0.250	0.250	0.063	0.063	20.28	<0.001
Self: # times drove before licensed to do so						
Hyperactive-impulsive	0.222	0.222	0.049	0.049	15.71	<0.001
Self: # vehicular crashes						
Hyperactive-impulsive	0.197	0.197	0.039	0.039	12.30	0.001
Self: # crashes held to be at fault						
Emotionally impulsive	0.292	0.292	0.085	0.085	28.45	<0.001
Self: # speeding citations						
Hyperactive-impulsive	0.227	0.227	0.052	0.052	16.59	<0.001
Self: # citations for reckless driving						
Emotionally impulsive	0.256	0.256	0.066	0.066	21.48	<0.001
Self: # DUI citations						
Emotionally impulsive	0.201	0.201	0.040	0.040	12.85	<0.001
DMV record: # speeding citations						
Emotionally impulsive	0.154	0.154	0.024	0.024	6.44	0.012
DMV record: # DUI citations						
Emotionally impulsive	0.129	0.129	0.017	0.017	4.51	0.035
DMV record: # license suspensions						
No significant predictors						
DMV record: # vehicular crashes						
Emotionally impulsive	0.130	0.130	0.017	0.017	4.57	0.033
DMV record: total citations on record						
Emotionally impulsive	0.191	0.191	0.037	0.037	10.10	0.002
Self: # times arrested						
Emotionally impulsive	0.229	0.229	0.053	0.053	17.06	<0.001
Self: # times jailed						
Emotionally impulsive	0.258	0.258	0.066	0.066	21.80	<0.001
Self: # childhood CD symptoms						
Emotionally impulsive	0.332	0.332	0.104	0.104	34.90	<0.001

ADHD = attention-deficit/hyperactivity disorder; β = standardized β coefficient from the final model; *R* = regression coefficient; R^2 = percent of explained variance accounted for by all variables at this step; $R^2\Delta$ (change) = percent of explained variance accounted for by this variable added at this step; *F* = F to change results; DUI = driving under the influence of alcohol; DMV = Department of Motor Vehicles; CD = conduct disorder.

Analyses are for linear multiple regression with stepwise entry.

score were a predictor of the current level of marital quality and self-rated marital satisfaction on the LW-MAT. For the other ratings, we entered not only self-ratings of ADHD symptoms and symptoms of EI, but also other ratings of EI symptoms. Once more, only symptoms of EI (other rated) were associated with the spouse–partner level of marital satisfaction on the LW-MAT.

Enough of our subjects had biological children to permit us to collect measures of parenting stress and child behavioral problems on all children aged ≥3 years. The average number of children the subjects had per group was 0.8 (SD = 1.2) for the ADHD group, 1.0 (1.3) for the clinical-control group, and 1.0 (1.2) for community controls. This difference was not significant, nor was there a main effect for sex or an interaction of group with sex. The sample sizes for the offspring on which we collected data were ADHD = 56, clinical = 34, and community = 26. There were no group differences in gender representation of the offspring (percent males by group: ADHD = 52%, clinical = 51%; community = 49%).

TABLE VI. PREDICTION OF MARITAL SATISFACTION, PARENTING STRESS, AND OFFSPRING DISRUPTIVE BEHAVIOR SYMPTOMS FROM SELF-RATED CURRENT ADHD SYMPTOMS AND SYMPTOMS OF EMOTIONAL IMPULSIVENESS.

Domain of Impairment/Predictors	β	*R*	R^2	$R^2\Delta$	*F*	*P*
Self: current quality of marriage (interview)						
Emotionally impulsive	0.283	0.283	0.080	0.080	10.31	0.002
Self: LW-MAT marital satisfaction						
Emotionally impulsive	0.344	0.344	0.118	0.118	15.28	<0.001
Partner: LW-MAT marital satisfaction						
Emotionally impulsive (other rated)	–0.405	0.405	0.164	0.164	21.13	<0.001
PSI: parent domain						
Parent emotionally impulsive	0.630	0.630	0.397	0.397	30.98	<0.001
PSI: parent–child interaction domain						
Parent inattention	0.474	0.474	0.225	0.225	13.62	0.001
PSI: child domain						
Parent emotionally impulsive	0.483	0.483	0.233	0.233	14.29	<0.001
Child ADHD inattention symptoms						
Parent inattention	0.560	0.560	0.313	0.313	27.81	<0.001
Child ADHD hyperactive-impulsive symptoms						
Parent emotionally impulsive	0.457	0.457	0.209	0.209	16.10	<0.001
Child ODD symptoms						
Parent emotionally impulsive	0.487	0.487	0.237	0.237	18.98	<0.001
Child CD symptoms						
Parent emotionally impulsive	0.715	0.412	0.170	0.170	12.47	0.001
Parent inattention	–0.380	0.222	0.196	0.053	4.05	0.049

ADHD = attention-deficit/hyperactivity disorder; β = standardized β coefficient from the final model; *R* = regression coefficient; R^2 = percent of explained variance accounted for by all variables at this step; $R^2\Delta$ (change) = percent of explained variance accounted for by this variable added at this step; *F* = F to change results; LW-MAT = Locke-Wallace Marital Adjustment Test; PSI = Parenting Stress Index; ODD = oppositional defiant disorder; CD = conduct disorder.

Analyses are for linear multiple regression with stepwise entry.

The mean ages of the parents and offspring did not differ among the groups.

We used multiple linear regression with stepwise entry again to evaluate the contributions of ADHD symptoms and symptoms of EI to these measures (**Table VI**). Concerning parenting stress ratings on the PSI, only current symptoms of EI predicted current stress in the parent and child domains, while only current ADHD inattention predicted stress in the domain of parent–child interactions. ADHD is known to be a hereditary disorder. It is therefore not surprising that we found that the current severity of ADHD inattention in subjects' offspring was predicted only by the current severity of parent ADHD inattention, sharing a remarkable 31% of their variance. In contrast, the severity of child ADHD hyperactivity-impulsivity was predicted only by parent symptoms of EI, sharing nearly 21% of their variance. This was not surprising in view of our earlier discussion that symptoms of EI are likely to be part of the larger dimension of inhibitory problems associated with ADHD and its hyperactive-impulsive symptoms. Both symptoms of EI and ADHD hyperactive-impulsive symptoms reflect this larger domain of inhibitory problems and, therefore, such problems in parents would be predictive of similar problems in their children. Finally, the number of CD symptoms reported in the children was predicted significantly by both parent symptoms of EI and parental inattention. That higher levels of parental expressed emotion would be related to more child CD symptoms was also not surprising. Once parental symptoms of EI were entered, however, the contribution of parental inattention was *opposite* of that which one might initially have expected, with higher levels of parental inattention predicting lower levels of child CD symptoms.

DISCUSSION

One major purpose of this trial was to examine the frequency of symptoms of EI in adults with ADHD relative to a control group and the relationship of such symptoms to severity of the disorder. We hypothesized that EI is an inherent component of ADHD. Thus, it would be present in a substantial proportion of adults with the disorder and would otherwise correlate highly with ADHD severity in all of our adults. Our results were quite consistent with this hypothesis. We found that the 7 symptoms of EI, including impatience, low frustration tolerance, quickness to anger, hot-temperedness, and being more irritable and generally emotionally excitable, were present in a majority of the adults with ADHD, with a significantly greater frequency than that evident in both of our control groups (**Figures** 1 and 2). This was true whether these symptoms were rated on the EIS by the subjects or by others who knew them well. We found that these symptoms constituted a single construct which was as highly correlated with the 2 traditional ADHD symptom dimensions (inattention, hyperactivity-impulsivity; r = 0.81 for each) as they were with each other. The total severity of symptoms of EI was found to be significantly greater in the adult ADHD group than in the clinical- and community-control groups, whether on self- or other ratings. This current trial provides further evidence that EI is a significant area of symptom expression in ADHD and extends the initial findings of such linkage in children to that of adults. It also corroborates the conclusion of recent reviews that these symptoms are a major part of the nature of ADHD.[2–4,8,23]

The second but larger aim of this trial was to evaluate the extent to which symptoms of EI make additional contributions to impairment in various major life activities beyond those explained merely by the traditional 2-dimensional structure of ADHD. That EI may be associated with an even map directly onto the 2-dimensional structure does not necessarily mean it provides any additional predictive utility concerning impairment beyond that already contributed by the traditional ADHD symptom dimensions. We hypothesized otherwise, given the limited evidence available, arguing that the emotional symptoms would provide additional utility in contributing to impairment. We found substantial evidence supporting this hypothesis across numerous, though by no means all, domains of major life activities studied here. For instance, we found that ratings on the EIS contributed additional variance to self-ratings of impairment in 6 of 10 different major life domains (occupational functioning, social interactions with others, educational settings, money management, driving, and leisure/

recreational activities). These ratings also contributed to an omnibus adaptive impairment score. Typically, symptoms of inattention contributed the most variance to self-rated global impairment, followed by symptoms of EI and those of hyperactivity-impulsivity. A similar pattern was found for EI and impairment ratings obtained from others who knew the participants well. Such findings indicated that EI symptoms are not merely redundant with the traditional 2 dimensions of ADHD symptoms, but provide additional explanatory power.

We further examined the predictive utility of EI symptoms beyond just those of ADHD symptoms in more detail using more specific measures of impairment. For occupational functioning, we found that symptoms of EI contributed to 6 of the 11 employment measures beyond any contribution made by ADHD symptoms: the number of jobs in which they had (1) problems with their own behavior or work performance; (2) problems getting along with others; (3) quit over hostility with their employer; (4) quit out of boredom; (5) the number of times participants had been unemployed for 1 month or longer; and (6) the clinician ratings on the SOFAS. For 3 of these outcomes, symptoms of EI were the only significant predictor. This suggests that symptoms of EI provide important additional information on the risk of impairment in the workplace for adults with ADHD than just those risks resulting from inattention and hyperactive-impulsive behavior.

In the analysis of educational impairment, we found that the current severity of symptoms of EI contributed significantly to the amount of education participants had received, whereas current ADHD severity showed no additional explanatory power. This does not mean that ADHD is unrelated to level of education. We have previously shown in these samples that degree of childhood ADHD symptoms is a predictor of educational attainment.[22] In the current trial, we could only examine current ADHD severity in adulthood given that we only had EI ratings for current functioning. Nevertheless, our results showed that current EI severity is associated with a history of more limited educational attainment. While the current hyperactive-impulsive symptoms were associated with the frequency of school suspensions in the educational histories of our participants, only the severity of EI symptoms was related to the history of truancy from school. We also found that EI ratings were significantly associated with whether or not subjects had graduated from college, the risk for grade retention, the risk for having had formal special education, the risk for having received any extra assistance at school, and the risk of problems in getting along with others in school. As in occupational functioning, EI symptoms provided unique additional explanatory power in accounting for the impairments in educational history of these participants beyond simply those explained by ADHD symptom severity alone. To our knowledge, this is the first trial to show such a unique contribution for problems in EI to both workplace and educational maladjustment in adults with ADHD beyond any contribution made by ADHD symptoms alone.

Our project had access to specific information from both the subjects' self-reports and their official DMV records on vehicular crashes and frequency of citations for various driving infractions. Driving is one of the best-studied impairments associated with ADHD in adults.[22,40] There is substantial evidence that ADHD is associated with a variety of adverse driving outcomes, including crash risk, severity of crashes, frequency of speeding citations, etc. Our analyses demonstrated that symptoms of EI contributed significantly to self-reported frequencies of such adversities, including crashes in which the subject was held to be at fault and DUI citations. The severity of hyperactive-impulsive symptoms also contributed to additional self-reported driving problems such as frequency of speeding citations and license suspensions. When we examined the official DMV records, however, we noted that only current symptoms of EI were related to frequency of speeding citations, DUI citations, vehicular crashes, and total citations recorded. ADHD inattention symptoms were not associated with any of these adverse driving outcomes by either self-report or DMV records. Thus, in the domain of driving, both the severity of hyperactive-impulsive behavior and of EI made significant and separate contributions to various driving risks. Prior research had shown that adults with high levels of ADHD symptoms have higher levels of driving-related anger and aggression (road rage).[41] While

we did not include measures of road rage in this project, our findings on EI would be consistent with these results and provide a likely explanation for them.

We selected several measures from our project concerning criminal history for further examination of the relative roles of EI and ADHD symptoms in contributing to such a history. We found that only severity of EI contributed to the frequency of our subjects having been arrested and jailed, with ADHD symptoms making no additional contributions to variance in these outcomes. We also found that only symptoms of EI were related to the severity of symptoms of CD in the childhood and adolescent histories of our subjects, with no additional variance explained by ADHD severity. To our knowledge, this is the first trial to show such a significant role for EI symptoms in explaining variance in the criminal histories of adults with ADHD. Once more, as in the other domains discussed in the previous section, EI severity is not just redundant with ADHD symptom severity in explaining or predicting the risk of impairment, but has its own unique role in such impairments.

Another novel feature of this trial was its ability to examine the relative roles of EI and ADHD symptom dimensions in the maladjustment of family functioning; we believe this may be the first trial to do so. We found that only self-rated EI severity contributed to the degree of self-rated marital quality and marital dissatisfaction. We found this to be true for the ratings of marital dissatisfaction from the spouses/partners of our subjects, where the severity of EI ratings (rated by others) was the only predictor of marital dissatisfaction. This appears to be the first trial to show that the EI element of adult ADHD is more predictive of marital disharmony than are inattention or hyperactivity-impulsivity.

Subjects provided us with ratings of their parenting stress, which we could in turn break down into separate domains of parent stress, child-related stress, and stress specifically arising from parent–child interactions. Our results showed that only current symptoms of EI predicted current stress in the parent and child domains, while only current ADHD inattention predicted stress in the domain of parent–child interactions. Thus, different components of parental ADHD are related to different aspects of parenting stress. Our findings of high EI in conjunction with both adult ADHD and parenting stress are certainly consistent with research showing that parental ADHD is associated with more parental negative expressed emotion in parent–child interactions.[42] It is likely that the EI aspect of adult ADHD accounts for such negative expressed emotion.

Substantial evidence exists showing that ADHD is among the most genetically influenced psychiatric disorders, having heritability estimates that average 0.78 and range as high as 0.94.[43] Research suggests that 43% to 57% of the offspring of adults with ADHD will have ADHD as well.[44,45] While the same genes appear to contribute to the severity of expression on both dimensions of ADHD symptoms, evidence suggests some small yet significant unique genetic contributions to each dimension as well.[46] This may help to explain some of our findings regarding the relationship of parental ADHD dimensions and EI symptoms to child ADHD symptoms. We found that only severity of parental ADHD inattention predicted parent-rated severity of that same dimension in their offspring, accounting for 31% of the variance in offspring inattention. Interestingly, we found that severity of parental EI was the only predictor of offspring hyperactivity-impulsivity, while parent hyperactivity-impulsivity did not contribute to that dimension in their offspring. This makes sense, however, if one considers that EI symptoms are part of the same larger, more global impairment in behavioral inhibition that likely accounts for the specific problems with hyperactivity-impulsivity in ADHD. This may illustrate that symptoms of poor inhibition in parents, as indexed by EI, are predictive of severity of inhibition problems in offspring, as indexed here by hyperactivity-impulsivity. Thus, while both dimensions of ADHD have shared genetics, there may be specific contributions of each parental dimension to those same dimensions in their offspring.

While we did not have precisely the same ratings of EI in the offspring as we did in the parents, we had a very good proxy for them in our offspring ratings of ODD symptoms. Given that 4 of the 8 symptoms of ODD consist of the same 4 symptoms of EI seen in our adult participants, one should not

be surprised to learn that only parental EI severity predicted the severity of ODD symptoms in their offspring, explaining nearly 25% of the variance in offspring ODD. Moreover, given the strong linkage of ODD to CD demonstrated in prior research,[47] it is understandable why we also found a significant contribution of parental EI severity to offspring CD symptoms. However, it could also be that parental EI contributes significantly to the level of expressed emotion in families. High negative expressed emotion in parent–child interactions has been shown to be a correlate of childhood CD symptoms. Our results may have unearthed a significant contributor to such expressed emotion: parental ADHD severity and, in particular, severity of the associated EI symptoms. It is possible that the influence of parental attributes on offspring risk for CD symptoms may well be one of family environment (high expressed emotion), although this linkage may simply reflect the shared genetic overlap of ADHD with ODD/CD.[48,49] Thus, parents with more severe ADHD and EI not only have offspring with higher levels of these same symptoms (ADHD, ODD), but the latter symptoms account for the later risk of CD in these offspring. Family environment may be largely serving as a marker for shared genetic effects among the 3 disorders.[48,49]

Our trial is subject to several limitations worth considering in interpreting our results. Our ratings of EI were obtained by the same method and source as some of the measures of impairment (rating scales, self-reports) that may have inflated the relationships found here. Even so, we also collected information on these constructs from others who knew the participants well and found the same pattern of relationships as in the self-reports, suggesting some validity to our findings beyond shared source and measurement. We also found significant relationships between self-ratings of EI and those domains of impairment in which we had obtained information from independent sources, such as employer ratings, official DMV records, and spousal/partner ratings. Even here, we found a significant association of self-rated EI with various measures from these independent sources, again supporting the validity of our findings and the pervasive impact of EI on impairment. Nevertheless, it will be important in future studies to examine the role of EI in impairment associated with ADHD using independent sources and measures of impairment from those utilized to establish the severity of EI and ADHD.

Another limitation may have been in the recruiting of ADHD and clinical-control adults from the same adult ADHD clinic. Despite not meeting all diagnostic criteria for ADHD according to the *DSM-IV* and clinician judgment, it is quite possible that some members of the clinical-control group had some degree of ADHD and indeed might have been diagnosed as such by others. This could explain the high level of EI symptoms we found in that group. Even so, such cross-contamination of these 2 groups provided a more conservative test for our group comparisons. However, we still found the ADHD group to have more severe EI symptoms than the clinical group, whether by self- or other reports. A further limitation may have been in the potential for bias to enter the evaluations of offspring behavioral problems, especially ADHD, as a consequence of parental ADHD. Two previous studies, however, have not found this to be a problem.[45,50] In view of no evidence of such bias, we believe we can place some integrity within the reports of parents with ADHD concerning their child's ADHD and psychological adjustment.

CONCLUSIONS

The present trial found that the symptoms of EI are highly associated with the severity of ADHD in adults and occur in the majority of those having a clinical diagnosis of the disorder. Such findings provide further evidence that EI is a component of ADHD, occurring as frequently as inattention and hyperactivity-impulsivity, the 2-symptom dimensions traditionally associated with ADHD. This trial also found substantial evidence that the symptoms of EI are not merely redundant with those traditional symptom dimensions of ADHD in predicting impairment in major life activities. EI makes significant and unique contributions to impairment in most of the domains of major life activities examined here, including social functioning, occupational functioning, educational history, driving risks, criminal history, marital satisfaction, parenting stress, and severity of offspring disruptive

behavior disorders. Our findings indicate that the long-overlooked EI component of ADHD deserves more respect and consideration in future research on ADHD and its comorbid disorders and impairments than has generally been the case.

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The Use of Emotional Dysregulation as an Endophenotype for Genetic Studies in Adults With Attention-Deficit/ Hyperactivity Disorder

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ABSTRACT

Background: Attention-deficit/hyperactivity disorder (ADHD) is a common multigenetic disorder that is phenotypically heterogeneous. Genetic studies have provided inconsistent results. Individuals with ADHD often have symptoms of emotional dysregulation. Since more homogeneous patient samples may improve the results, this study used emotional dysregulation in ADHD as an additional endophenotype to create a more homogeneous sample.

Methods: Eighty adults were recruited from 2 ADHD clinical trials. The Wender-Reimherr Adult Attention Deficit Disorder Scale (WRAADDS) was used to assess ADHD, including emotional dysregulation (based on the symptoms temper, emotional overreactivity, and affective lability). Genotyping was conducted using TaqMan®, with predesigned single nucleotide polymorphism (SNP) assays from Applied Biosystems for the SNPs in the following genes: *DAT1 (SLC6A3)*, *5-HT1B (HTR1B)*, *BDNF*, *TPH2*, *HTR2A*, *SNAP25*, *COMT*, and *MAOA*. Data analysis was conducted using PLINK to compare allele frequencies between adults with ADHD (non-ED) and adults with ADHD and emotional dysregulation (ADHD + ED).

Results: Eight SNPs were genotyped using TaqMan assays (rs40184, rs6296, rs6265, rs1843809, rs6314, rs362987, rs4680, and rs909525). Before correcting for multiple testing, 1 SNP (rs6296 in the *5-HT1B* gene) was significantly associated with emotional dysregulation ($\chi^2 = 4.68$; $df = 1$, $P = 0.03$). This SNP was not associated with higher scores on the total WRAADDS.

Conclusions: While none of the SNPs tested remained significant after Bonferroni correction, rs6296 (*5-HT1B*) showed a trend toward significance when using ED as an ADHD subtype. This suggests that the different symptoms of ADHD might be selectively associated with specific genetic variants. The use of endophenotypes, such as emotional symptoms in ADHD, may be effective in clarifying the genetics underlying the disorder. (*J ADHD Relat Disord*. 2010;1[4]:29–38) © 2010 Excerpta Medica Inc.

Key words: adult ADHD, genetics, emotional dysregulation, endophenotype.

INTRODUCTION

Attention-deficit/hyperactivity disorder (ADHD) is a common neurobehavioral disorder affecting up to 1 in 20 children in the United States, with as much as 50% of the affected population remaining symptomatic into adulthood.[1] Twin and family-based studies have shown that genetic factors likely play a substantial role in the etiology of ADHD, with heritability estimates of 60% to 90%.[2,3] As a result, a variety of genetic linkage, candidate gene, and genome-wide association studies have been conducted. These studies have not led to conclusive findings. Further, the results of these studies have shown that "…there are no

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genes of large effect contributing to the ADHD phenotype."[4]

Individuals with ADHD are likely genetically heterogeneous, which complicates the search for genes involved in the etiology of the disorder. One potential solution is to study individuals who have higher symptom loads, hoping that these subjects will also have higher genetic loads. A higher genetic load in the sample might make identification of these genes more likely. In addition, ADHD is phenotypically heterogeneous.[5] This additional source of heterogeneity in sample populations may contribute to inconsistent results in genetic studies.[6] Consequently, another solution is to use subjects with homogeneous signs and symptoms, hoping that these subjects will have more homogeneous genetics, making identification of these genes more likely. This approach has been done with several distinct groups within the ADHD population, including those with conduct disorder,[7] impulsivity,[8] cognitive dysfunction,[9] disruptive behavior disorder,[10] and depression.[11]

We have reported that adult ADHD samples can be subdivided on the basis of emotional symptoms (temper, emotional overreactivity, and affective lability), which we have labeled ADHD-related emotional dysregulation.[12] These symptoms are distinct from the symptoms of mood disorders.[13] Temper symptoms are usually short-lived and reactive to environmental stimuli. ADHD-type affective lability often dates back to childhood. The mood shifts are usually short (minutes to hours, not days) and occur both in response to and separate from environmental stimuli. In contrast with depressed patients, the ADHD patient remains responsive to environmental stimuli. Further, the "ups" of the adult ADHD patient resemble the excitement of an overstimulated child rather than the elation of the hypomanic, while the "lows" present more like boredom, and the vegetative symptoms of depression are seldom present. Emotional overreactivity in ADHD patients is commonly described as an inability to handle stress effectively. This can result in cycles in which the patient reacts inappropriately to stress, which leads to more stress. However, when the situation is resolved, the patient rebounds emotionally. Others have noted this distinction.[14] Also, in the Multimodal Treatment Study of Children With ADHD (MTA), sponsored by the National Institute of Mental Health (NIMH) and one of the most complete descriptions of childhood ADHD, 39% of the subjects had significant anxiety and/or mood-related symptoms.[15] This frequency is similar to what we noted in our initial publication,[12] but lower than we noted in later reports.[5,16] It is unknown how similar the patients in these studies are in terms of emotional symptoms because they were assessed with different measures.

We also explored the importance of emotional dysregulation in a methylphenidate clinical trial.[5] In this study, adults with ADHD were categorized based on emotional and oppositional symptoms. Personality disorder and problems in social adjustment were found to be more frequent in ADHD patients who had additional emotional or oppositional symptoms.[17] Our adult studies[5,12,18,19] confirm that these symptoms are associated with a more complex and impaired ADHD presentation, and symptoms of emotional dysregulation respond to treatment in a manner supportive of their presence as a dimension of symptoms in ADHD patients. Further, emotional dysregulation occurs in the absence of major anxiety or mood disorders.

We recently completed 2 clinical trials assessing the use of methylphenidate in long-acting preparations (B.K.M., unpublished data, 2009).[5,16] Both trials used similar measures and, in both, samples of DNA were collected. We planned to analyze the genetic material in these studies based on specific symptom dimensions to generate distinct patient groups with more homogeneous symptoms and potentially less genetic heterogeneity. Therefore, as part of a genetic analysis of adult ADHD, we used emotional dysregulation to categorize subjects and compared the resulting groups for each candidate gene.

As a preliminary exploration of this sample, we decided to examine a small number of candidate genes. The following genes were selected on the basis of a recent meta-analysis of genes implicated in ADHD[6]: dopamine transporter gene (*DAT1*), *5-HT1B*, brain-derived neurotrophic factor gene (*BDNF*), *TPH2*, serotonin 2A receptor (*HTR2A*),

synaptosomal-associated protein 25 gene (*SNAP25*), Catechol-*O*-methyl transferase (*COMT*), and *MAOA*.

DAT1 (also known as *SLC6A3*), was one of the first candidate genes studied in ADHD.[20] Using a sample of 57 children with ADHD, the investigators found that a 10-repeat allele in the *DAT1* 3' untranslated region (UTR) was overrepresented in ADHD subjects. Subsequent studies have yielded mixed results.[21–25] A recent meta-analysis of more than 100 studies examining *DAT1* and ADHD concluded that multiple variants within *DAT1* may confer risk for ADHD.[6] A recent study also looked at the connection between emotionality and treatment response and polymorphisms in the *DAT1* gene in children with ADHD. Gruber et al[26] reported that children with the homozygous 9/9-repeat allele of *DAT1* had higher emotionality scores compared with those who had the 9/10-repeat allele when taking a placebo. When treated with methylphenidate, their emotionality scores improved.

The serotonergic system is thought to play a role in ADHD due to the interaction between the dopaminergic and serotonergic neurotransmitter systems. In a study by Zouk et al,[27] the *5-HT1B* gene was found to be correlated with impulsive and aggressive behavior. Several independent studies have suggested that there is a significant association between *5-HT1B* and ADHD.[28,29] Another study conducted in the Chinese Han population found no association between ADHD and the *5-HT1B* gene, but found a preferential transmission of the 861G allele in offspring with the inattentive subtype of ADHD.[30]

BDNF is involved in neurogenesis and synaptic plasticity[31] and has been shown to enhance the effects of stimulant medications on dopaminergic pathways in the brain.[32] One polymorphism of interest, a valine-to-methionine substitution at codon 66 (Val66Met; rs6265), has been shown to influence *BDNF* secretion in the brain.[33] Initial studies found an association between this polymorphism and ADHD, but only when paternally inherited.[34] Subsequent studies,[34–36] including a recent meta-analysis,[6] failed to replicate this association.

Tryptophan hydroxylase is considered the rate-limiting enzyme in the synthesis of serotonin. Single nucleotide polymorphism (SNP) rs1843809 of gene *TPH2* was significantly associated with ADHD in 179 Irish families.[37] However, a second study by the same group in a sample of 108 English families found no association.[38]

Another serotonergic gene implicated in ADHD is *HTR2A*. *HTR2A* inhibition dampens amphetamine-induced increases in dopamine activity and hyperlocomotion.[39] Additionally, antipsychotic medications such as clozapine show similar results.[40] Multiple polymorphisms in *HTR2A* have been linked to a number of neuropsychiatric conditions.[41]

The *SNAP25* codes for a protein involved in axon growth, neurotransmitter release, and synaptic plasticity.[42] An animal model bred with only 1 copy of the gene displays hyperactive behavior.[43] The first study showing a significant association between a variant in the *SNAP25* gene and ADHD was published in 2005.[44] A subsequent meta-analysis that included this and 4 other studies did not support an association between this SNP and ADHD.[6]

COMT is one of several enzymes that degrade catecholamines such as dopamine, epinephrine, and norepinephrine. The most well-studied SNP (rs4680) in the *COMT* gene is the Val158Met polymorphism. A polymorphism at this site alters valine 158 to methionine, and reduces enzyme activity threefold.[45] One study found that Val/Val is more common in ADHD patients and predicts response to treatment.[46] Another recent study found that the Val allele was more common in children with ADHD and is associated with methylphenidate response.[47] A third study of 188 children with ADHD concluded that the *COMT* Val158Met polymorphism modulates task-oriented behavior, but had no effect on methylphenidate treatment response.[48]

Evidence for genetic linkage near the *MAOA* gene with impulsive and aggressive behaviors has been reported in a large Dutch family.[49] This finding is supported by an *MAOA* knockout mouse that displays increased aggression.[50] Further evidence supporting *MAOA* in ADHD stems from treatment studies showing that *MAOA* inhibitors can reduce ADHD symptoms.[51] A number of studies have evaluated *MAOA* polymorphisms in ADHD, with evidence supporting the 30-bp VNTR 1.2kb upstream of the *MAOA* gene.[52–54]

METHODS

Subjects

Eighty adults who met the criteria for ADHD in the *Diagnostic and Statistical Manual of Mental Disorders,* Fourth Edition, Text Revision (*DSM-IV-TR*) and/or the Wender Utah Rating Scale (Utah criteria) participated in 1 of 2 clinical trials (osmotic-release oral system [OROS] methylphenidate [MPH] and MTS [methylphenidate transdermal system]) of methylphenidate-based products. The University of Utah Institutional Review Board reviewed and approved both studies, including the genetic component discussed here.

Inclusion and exclusion criteria were very similar for the 2 trials. Subjects were required to have a current diagnosis of adult ADHD using *DSM-IV-TR* criteria based on the Conners' Adult ADHD Diagnostic Interview for *DSM-IV-TR* and/or the Utah criteria. All subjects from the OROS-MPH trial met both Utah and *DSM-IV-TR* ADHD criteria. Most subjects in the MTS trial met both criteria. Two failed to meet the Utah criteria, but met *DSM-IV-TR* criteria for ADHD inattentive type. Another 3 subjects failed to meet *DSM-IV-TR* criteria, but met the Utah criteria. Although these 3 subjects were experiencing significant impairment due to inattention and/or hyperactivity-impulsivity, these symptoms were poorly covered using the *DSM-IV-TR* terminology. *Moderate impairment* was defined as a score of 4 or greater on the Clinical Global Impression–Severity (CGI-S) scale for ADHD at both screening and baseline visits. Subjects were between 18 and 65 years of age. Female subjects were eligible if they were of nonchild-bearing potential or agreed to use an approved form of contraception. A psychiatric review of systems was performed on each patient and the following *DSM-IV-TR* Axis I current diagnoses were exclusionary: major depressive disorder, panic disorder, obsessive-compulsive disorder, posttraumatic stress disorder, bipolar disorder, schizophrenia, and other psychotic disorders. Subjects with a seizure disorder, hyperthyroidism, or hypothyroidism were excluded. While some patients met criteria for generalized anxiety disorder (GAD), the primary condition contributing to the patients' symptoms and impairment was ADHD. Subjects with significant medical conditions who were likely to become unstable during the trial or likely to be destabilized by treatment with methylphenidate (eg, those with cardiovascular disease) were excluded. The current sample is a subset of the subjects in these 2 primary trials who agreed to participate in the genetic add-on segment reported here. Consent for participation in this genetic analysis was obtained separately from the primary trials and was not a requirement of participation in the primary trials.

The Wender-Reimherr Adult Attention Deficit Disorder Scale (WRAADDS) was used to assess 7 core symptoms of ADHD: hyperactivity, inattention, disorganization, overreactivity, impulsivity, affective lability, and temper (each scored from 0–4, with 4 being most severe) at baseline and throughout the study. The emotional dysregulation score was based on the emotional overreactivity, temper, and affective lability scores, as described in a previous publication.[12] Subjects with a total score of 7 or higher (at least moderate impairment) on these 3 subscales were categorized as having emotional dysregulation. We are testing an additional section of the WRAADDS that assesses oppositional defiant disorder (ODD) symptoms in adults based on the *DSM-IV-TR* ODD symptoms.

Blood samples were collected, and DNA was extracted by a core laboratory. Genotyping was conducted using TaqMan® (PREMIER Biosoft International, Palo Alto, California),[55] with predesigned SNP assays from Applied Biosystems (**Table I**).

Data Analysis and Statistical Procedures

Data analysis was conducted using PLINK[56] to compare allele frequencies and generate a χ^2 statistic, odds ratio (OR), and corresponding *P* value for each SNP. Baseline characteristics of the ADHD patients with and without emotional dysregulation were compared using χ^2 for categorical variables, *t* test for continuous variables, and Mann-Whitney *U* test for the individual WRAADDS items. A Bonferroni correction was applied to $P = 0.05$ (α) to account for the 8 multiple tests (κ) that were performed. This resulted in a new threshold for significance of $P = 0.00625$, though this adjustment may be somewhat conservative because the genes being analyzed are in associated pathways, and, therefore,

TABLE I. SNPS SELECTED AND CORRESPONDING ABI ASSAY ID.

rs#	Genes	TaqMan® Assay ID*
rs40184	*DAT1* (*SLC6A3*)	C___2960969_10
rs6296	*5-HT1B* (*HTR1B*)	C___2523534_20
rs6265	*BDNF*	C__11592758_10
rs1843809	*TPH2*	C__11479729_10
rs6314	*HTR2A*	C__11696920_20
rs362987	*SNAP25*	C_____15041_20
rs4680	*COMT*	C__25746809_50
rs909525	*MAOA*	C___8817688_10

OR = odds ratio; SNPs = single nucleotide polymorphisms; ABI = Applied Biosystems Inc.; ID = identification; rs = refSNP.

*Manufactured by PREMIER Biosoft International, Palo Alto, California.

the tests may be correlated. While our sample has reasonable power to detect a moderate effect size with a single test,[57] it is underpowered for multiple testing; a sample size close to 170 would be required to detect a moderate effect with this adjusted significance threshold. However, as a pilot study, our sample provides information that might direct future studies. Furthermore, the effect size of serotonergic genes with regard to emotional dysregulation in ADHD is not yet known.

RESULTS

Ninety adults with ADHD gave written informed consent and furnished blood samples for genetic analysis. Ten samples were not genotyped due to poor DNA quality, leaving 80 subjects for the analysis. As indicated in **Table II**, 58 (73%) of the subjects met criteria for emotional dysregulation (ADHD + ED). Compared with subjects who did not meet criteria for emotional dysregulation (non-ED), ADHD + ED subjects were more likely to have combined type ADHD (χ^2 = 36.45, *df* = 2, *P* < 0.001) and were more likely to meet criteria for ODD (χ^2 = 3.87, *df* = 1, *P* = 0.05). ADHD + ED subjects also had more symptoms on the WRAADDS hyperactivity/impulsivity subscale (*t* = 3.58, *df* = 78, *P* = 0.001).

PLINK association studies were performed using a χ^2 test to compare minor allele frequencies for the emotional dysregulation phenotype. As seen in **Table III**, rs6296 in the *5-HT1B* gene was significantly associated with emotional dysregulation (χ^2= 4.68, *df* = 1, *P* = 0.03) before correcting for multiple testing. This SNP was not associated with higher scores on the total WRAADDS (*t* = 1.65, *df* = 1, *P* = 0.29), nor were the other 7 SNPs associated with emotional dysregulation. In addition, this SNP was not associated with higher scores on the ODD section of the WRAADDS (χ^2 = 1.327, *df* = 1, *P* = 0.2441), nor were the other 7 SNPs associated with ODD symptoms.

DISCUSSION

Genetic analyses were performed for 8 candidate loci using subjects recruited from clinical trials of 2 different forms of methylphenidate. The subjects were experiencing ADHD of at least moderate severity, and both clinical trials produced very positive results. Methylphenidate produced significant improvement in the *DSM-IV-TR* symptoms of inattention and hyperactivity/impulsivity and the Utah criteria symptoms of emotional dysregulation.

In their meta-analysis, Gizer et al[6] suggested that future genetic studies should explore potential moderators. The genetic results reported here suggest the potential utility of using emotional dysregulation as an additional phenotype to increase the sensitivity of genetic studies in ADHD. Though none of the 8 candidate genes analyzed were associated with the emotional dysregulation phenotype at a significant level (*P* = 0.00625), these results support further evaluation of rs6296 in *5-HT1B*. Before correcting for multiple testing, rs6296 in the *5-HT1B* gene showed significance for association with emotional dysregulation (*P* = 0.0305), but not with total WRAADDS score. The *5-HT1B* gene is part of the serotonergic system. Zouk et al[27] found that this gene was correlated with impulsive and aggressive behavior, which is at least modestly similar to the symptoms of ADHD + ED patients. (ADHD + ED subjects had relatively higher levels of impulsivity and temper at baseline.) Further, knockout mice show increased aggression and im-

TABLE II. BASELINE DEMOGRAPHICS AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) SYMPTOM ASSESSMENTS.

	Non-ED (n = 22)	ADHD + ED (n = 58)	*P*
Distribution, % (n)*	28 (22)	73 (58)	
Male, % (n)	33 (18)	67 (37)	0.12
Female, % (n)	16 (4)	84 (21)	
Age, mean (SD)	33.9 (11.8)	33.9 (11.1)	0.99
ADHD diagnostic group, % (n)			
Combined type	32 (7)	91 (53)	<0.001
Attentional type	68 (15)	5 (3)	
Hyperactive/impulsive	0 (0)	3 (2)	
Emotional dysregulation	0 (0)	0 (0)	NA
Oppositional defiant disorder	23 (5)	47 (27)	0.05
Total WRAADDS, mean (SD)	17.2 (2.6)	23.7 (2.6)	<0.001
Attention + disorganization	7.0 (0.8)	7.3 (1.2)	0.36
Attention	3.5 (0.5)	3.7 (0.9)	0.033
Disorganization	3.5 (0.5)	3.6 (0.8)	0.35
Hyperactivity + impulsivity, mean (SD)	5.3 (1.5)	6.5 (1.2)	0.001
Hyperactivity	2.5 (1.0)	3.1 (0.9)	0.011
Impulsivity	2.9 (3.3)	3.3 (0.7)	0.05
Emotional dysregulation, mean (SD)	4.8 (1.1)	9.8 (1.7)	<0.001
Temper	0.9 (0.8)	2.7 (1.1)	<0.001
Affective lability	2.0 (0.7)	3.5 (0.6)	<0.001
Emotional overreactivity, mean (SD)	1.9 (0.9)	3.6 (0.7)	<0.001
Childhood measures			
WURS	44.3 (18.9)	56.2 (15.6)	0.007
PRS	18.6 (5.6)	18.3 (7.0)	0.86

Non-ED = subjects not meeting criteria for emotional dysregulation; ADHD + ED = subjects meeting criteria for emotional dysregulation; NA = not applicable; WRAADDS = Wender-Reimherr Adult Attention Deficit Disorder Scale; WURS = Wender Utah Rating Scale; PRS = Parent Rating Scale.

*Totals do not equal 100% due to rounding of numbers.

pulsivity[58,59] and increased response to novel stimuli.[60] In contrast, the meta-analysis of rs6296 by Gizer et al[6] involved 9 studies and concluded that rs6296 was associated with childhood ADHD (mixed effects: OR = 1.11; 95% CI, 1.02–1.20; (χ^2 = 5.45; *df* = 1, *P* = 0.010).

LIMITATIONS

This study has several limitations worth addressing. First, this analysis was an add-on study to 2 clinical trials, rather than a genetic study designed a priori to detect genetic markers associated with emotional symptoms in adult ADHD. As such, this study was potentially underpowered to detect genetic associations. Similarly, the small sample size of this study is a significant limitation. Additionally, this was not a genome-wide scan and, therefore, the analysis was biased toward the candidate genes we selected based on our review of the literature.

Potential confounding variables in this analysis include ethnicity and demographics. While all sub-

TABLE III. CANDIDATE GENE ANALYSIS OF EMOTIONAL DYSREGULATION IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Gene	CHR	SNP	BP	A1	MAF	A2	χ^2	*P**
SLC6A3	5	rs40184	1395077	A	0.431, 0.500	G	0.61	0.43
5-HT1B	6	rs6296	78172260	C	0.181, 0.341	G	4.68	0.03
BDNF	11	rs6265	27679916	A	0.181, 0.119	G	0.86	0.35
TPH2	12	rs1843809	72348698	G	0.181, 0.136	T	0.45	0.50
HTR2A	13	rs6314	47409034	T	0.138, 0.114	C	0.17	0.68
SNAP25	20	rs362987	10277452	C	0.395, 0.523	A	2.12	0.15
COMT	22	rs4680	19951271	G	0.434, 0.524	A	0.88	0.35
MAOA	23	rs909525	43553202	G	0.311, 0.320	A	0.01	0.93

CHR = chromosome; SNP = single nucleotide polymorphism; BP = base position; A1 = allele 1; MAF = minor allele frequencies; A2 = allele 2.

**P* values listed are uncorrected. Significance threshold after Bonferroni correction is 0.00625.

jects in this analysis were white, we were not able to further refine the sample using ethnic markers due to the lack of genome-wide SNP data. Age and gender did not significantly differ at baseline; however, we did not collect data regarding socioeconomic status, life stressors, or other potential confounding demographic features.

While the sample size in this study was small and the *P* value modest, these results support the idea of selecting subjects with more homogeneous symptoms/signs in genetic analyses, such as in the case of emotional dysregulation. While the subjects in this analysis were highly impaired and probably carry a high genetic load, our results with rs6296 (*5-HT1B*) approached significance only when a more homogeneous subgroup was created using emotional dysregulation as a potential endophenotype of ADHD.

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A Pilot Study of Ecological Momentary Assessment of Emotion Dysregulation in Children

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ABSTRACT

Background: Emotion dysregulation (EDr) in children is linked to a wide variety of maladaptive outcomes, including externalizing and internalizing behaviors, irritability and aggression, emotional outbursts, and social dysfunction.

Objective: This pilot study examined the feasibility and utility of ecological momentary assessment (EMA) to differentiate patterns of EDr in children with attention-deficit/hyperactivity disorder (ADHD) versus pediatric-onset bipolar disorder (PBD).

Methods: Two elementary school–aged children were assessed to allow for a comparison between a child with ADHD with significant EDr (ADHD-EDr) and a child with PBD. The children's mothers completed ratings of their children's mood, irritability, and affect 3 times per day for 28 days (82 ratings total) using a personal digital assistant. Recurrence Quantification Analysis was used to assess the variability, predictability, stability, and episodic versus chronic nature of the children's mood, irritability, and affect over the study period.

Results: The child with PBD demonstrated more variability and stability and less predictability across all ratings than the child with ADHD-EDr. Further, the child with ADHD-EDr demonstrated a chronic pattern of dysregulation across all ratings, while the child with PBD demonstrated episodic variation in dysregulation.

Conclusions: The study provides encouraging evidence for the feasibility and utility of using EMA to assist in further defining and differentiating patterns of EDr across PBD and ADHD. (*J ADHD Relat Disord.* 2010;1[4]:39–52) © 2010 Excerpta Medica Inc.

Key words: ADHD, bipolar disorder, emotion dysregulation, ecological momentary assessment.

INTRODUCTION

Emotion regulation is the fundamental process by which individuals modulate their internal emotional states to meet internal and external demands.[1] Emotion regulation requires the continual and simultaneous activation of physiological, neurological, cognitive, and behavioral systems to maintain adaptive emotional states and ameliorate maladaptive emotional states.[2] Emotion dysregulation (EDr) occurs when individuals are unable to successfully modulate their emotional states to fit their internal or environmental needs. Children who are unable to effectively regulate emotions are at risk for a broad range of emotional, behavioral, social, and adaptive impairments.[3] Dickstein and Leibenluft[4] describe EDr as a "primary contributor" towards emotional and behavioral impairment in children.

EDr in children is linked to a wide variety of maladaptive outcomes, including externalizing and internalizing behaviors, irritability and aggression,[5] emotional outbursts,[6] and social dysfunction.[7] Children with EDr are more emotionally labile than well-regulated children, as they demonstrate more

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emotional distress, lower thresholds for distress, more intense and longer-lasting reactions to distress, and greater difficulty reducing distress.[3] EDr has increasingly been recognized as either a core feature or associated contributor to several disorders, including internalizing disorders (eg, mood disorders, certain anxiety disorders) and externalizing disorders (eg, attention-deficit/hyperactivity disorder [ADHD], disruptive behavior disorders).

EDr and ADHD

EDr has been identified as a "core component" of ADHD.[8] Barkley[8] and Skirrow et al[9] reviewed studies demonstrating evidence of physiological, neurological, cognitive, and behavioral markers of EDr in children with ADHD. Geller et al[10] reported that irritable mood was present in 71.6% of a sample of children diagnosed with ADHD, while Skirrow et al[9] indicated that children with ADHD experienced more emotional instability, were less able to regulate emotions, and demonstrated greater irritability and emotional explosiveness than typically functioning children. Barkley[8] and Carlson[11] both noted that EDr-based symptoms such as irritability, explosive behavior, and emotional lability were actually listed as criteria in early formulations of ADHD.

While Barkley[8] and others have identified EDr as a core component of ADHD, studies have also noted substantial variability in EDr among children with ADHD.[12] Notably, studies have identified a subset of children with ADHD who experience significantly severe EDr.[5] Children with ADHD who are more severely emotionally dysregulated demonstrate greater emotional, behavioral, and social difficulties than their more well-regulated counterparts,[6,12] including irritability, aggression, emotional distress, and more severe ADHD symptomatology (particularly hyperactive/impulsive symptoms).[6,9,12,13] EDr in children with ADHD has been linked with significantly increased rates of comorbid internalizing and externalizing diagnoses, including disruptive behavior disorders and depression,[13] and some have posited EDr as a common factor underlying ADHD and comorbid internalizing/externalizing pathology.[14] However, EDr remains inconsistently defined and classified among children with ADHD,[4,11] in part because current diagnostic classification systems do not comprehensively account for the difficulties seen in children with severe EDr (ie, chronic irritability, mood instability, and emotional intensity). As a result, the ADHD-EDr subgroup has been inconsistently identified and labeled in both research literature and clinical practice[15] (ie, "Severe Mood Dysregulation," "Broadband pediatric-onset bipolar disorder [PBD]," "comorbid ADHD").

EDr in ADHD Versus Pediatric Bipolar Disorder

There has been an increasing tendency in recent years among both clinicians and researchers to classify children with severe and chronic EDr according to the PBD criteria (particularly as bipolar not otherwise specified [NOS][15,16]). PBD is by definition a disorder of EDr,[5] and studies have noted that children with PBD demonstrate impaired physiological, neuropsychological, affective, and behavioral regulation of positive and negative emotions.[15] Accordingly, rates of PBD diagnoses have skyrocketed in recent years, with increases of 200% to 400% over the past decade across outpatient and inpatient settings.[15] There has been considerable controversy regarding this extension of PBD to account for children with the chronic patterns of EDr seen among children with ADHD.[4,11] Much of this debate concerns whether children with ADHD-EDr are being misclassified as PBD. Carlson and Meyer[17] noted that "EDr is central to the debate regarding PBD." Many investigators believe that the EDr observed in children with ADHD-EDr is structurally different from the EDr observed in PBD,[5] and studies have demonstrated etiological, neurological, and symptomological distinctions between children who meet *Diagnostic and Statistical Manual of Mental Disorders,* Fourth Edition (*DSM-IV*) criteria for PBD and children who demonstrate severe EDr in the context of ADHD.[15] Accordingly, it has been proposed that a distinct diagnostic category ("Temper Dysregulation Disorder"[18]) be created to account for children with severe but nonepisodic EDr.

Patterns of EDr

EDr encompasses several temporal facets of emotional experience, including variability, instability, predictability, and episodicity (ie, episodic versus

chronic) of emotional arousal.[1,4,19] The facets describe interrelated yet distinct dynamic features of the temporal structure of emotional variability.[19,20] Eaton and Funder[21] demonstrated that different facets of EDr were associated with distinct forms of psychological dysfunction. The following facets have been identified.[19,20]

(1) **Variability**: the degree to which children's emotional states vary around a set point (**Figure 1a**). The set point reflects the child's typical (trait level) emotional state, whether positively or negatively valenced.[22] Children with PBD have been described as more emotionally variable than children with ADHD-EDr.[10]

(2) **Stability/Instability**: the extent that children maintain consistent emotional states over time, whether aroused or at set point (ie, a depressed child may demonstrate stable but intensely negative emotional states[22]; **Figure 1b**). Emotional instability over time is a hallmark feature of PBD,[10] and is also common to a lesser extent in ADHD-EDr.[8]

(3) **Chronicity/Episodicity**: the patterned rate of change of a child's emotional state.[22] Children with chronic patterns of arousal demonstrate arousal around a fixed emotional set point, while children with episodic patterns of arousal demonstrate changes in the set point itself[4] (**Figure 1c**). Episodicity has been described as a "cardinal symptom" of PBD[10] and the primary differential feature of PBD versus ADHD-EDr.[5] Episodicity is rarely seen in ADHD-EDr regardless of the severity of other facets of EDr.[10]

(4) **Predictability/Unpredictability**: the degree of patterned structure within the child's emotional arousals over time (ie, in fairly predictable sequences or as unpredictable "affective storms"; **Figure 1d**).[16,19] Unpredictability of emotions has not been thoroughly studied in children.

Assessment of EDr

Limitations of Current Measures of EDr

To date, most studies of EDr have used retrospective report instruments (eg, Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children [KSADS], Emotion Regulation Checklist) or laboratory-based physiological evaluation to assess EDr in children. Retrospective report interviews and rating scales provide useful information regarding overall EDr, but typically collapse across time points (and facets) to provide a single rating of EDr.[3,23] These measures also rely on retrospective reports, which are susceptible to cognitive biases, such as recency effects, emotional salience, summing across events, and recall deficiencies,[24] and often do not accurately or fully capture the temporal structure of emotional fluctuations. Of note, while some measures (eg, KSADS) provide information regarding diagnosis of disorders with EDr components, no measure to date has provided clinical norms or cutoffs regarding severity of EDr. Conversely, physiological assessment of EDr traditionally measures physiological markers of emotional arousal in response to single time-point laboratory-based experimental stimuli,[2] which does not provide information regarding long-term fluctuation. Although rating scales and physiological assessment both provide considerable information regarding EDr, neither method is able to capture the dynamic temporal structure of EDr.

Ecological Momentary Assessment of EDr

Ecological momentary assessment (EMA) provides an ideal methodology to assess the temporal patterns of EDr in children. EMA describes methodologies developed to collect real-time data from participants within the context of their typical daily lives.[24] Rating scales are completed by participants (or their parents) directly on personal digital assistants (PDAs) several times during the day.[24] EMA provides substantially more accurate response data than retrospective or summary reports, even when compared with end-of-day recall.[24] EMA-based data collection allows for control of the times at which rating scales may be completed and is substantially less susceptible to cognitive biases, increasing the reliability of time-linked reporting.[24] EMA holds substantial promise for the assessment of patterns of EDr over time. Two studies in particular have demonstrated the potential utility of EMA in examining the temporal structure of EDr. Axelson et al[25] reported that more than 80% of study participants (affectively disordered adolescents) were able to complete an 8-week EMA protocol, and case studies demonstrated clear differentiation in the patterns of

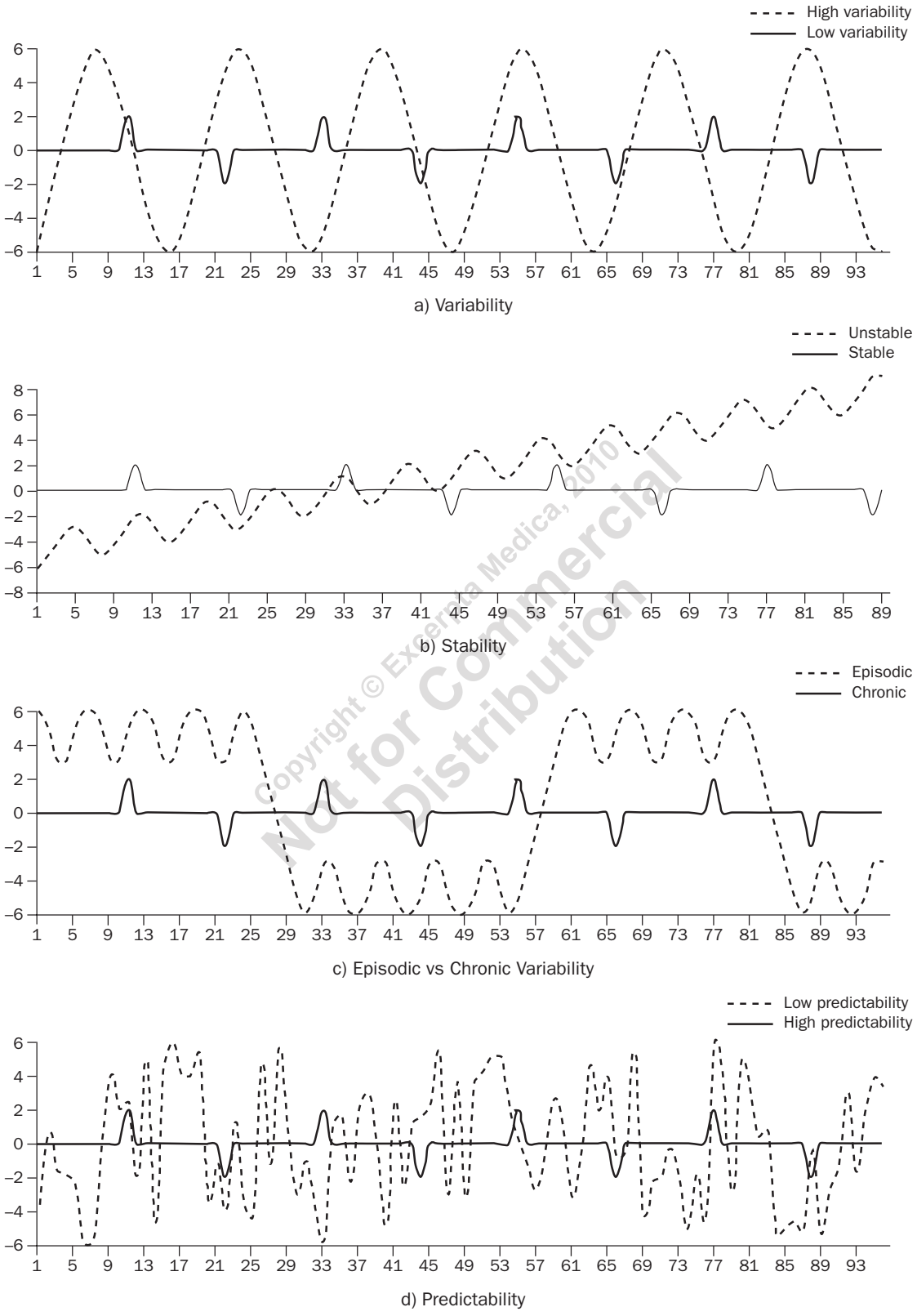

Figure 1. Examples of the facets of EDr. Each graph represents 2 extremes of the dimensions of interest. The dimensions of interest have been exaggerated. The same comparison line is used for all 4 graphs. EDr = emotion dysregulation.

emotional fluctuation exhibited by children across differing mood disorder conditions. Chow et al[19] were able to determine the temporal structure of the emotional fluctuations of college students who completed ratings once per day for a 52-day period. EMA represents a substantial advance on retrospective reports and laboratory-based physiological observation of EDr.

Current Pilot Study

The purpose of the present study was to examine the feasibility and utility of using EMA technology using case studies to assess differential patterns of emotion regulation among clinic-referred children with ADHD-EDr versus PBD. It was hypothesized that parents would be able to complete at least 80% of all assessment points across the study period. It was hypothesized that ratings of the mood, irritability, and affect of a child with ADHD-EDr would demonstrate a pattern of lower variability, higher predictability, and higher stability compared with that of a child with PBD. It was further hypothesized that the ratings of a child with ADHD-EDr would be characterized by a pattern of chronic but consistent dysregulation, while those of a child with PBD would reflect a pattern of EDr.

METHODS

Screening/Participants

Parents of children referred to an ADHD clinic and a pediatric mood disorders clinic were contacted to determine interest in participating in the present study. To ensure that their children met criteria either for ADHD-EDr or PBD, parents completed (1) the *Vanderbilt ADHD Parent Rating Scales*[26] (VADPRS), a *DSM*-based symptom inventory of ADHD; (2) the *Child Behavior Checklist*[27] (CBCL), a broadband measure of internalizing and externalizing behaviors; and (3) the *General Behavior Inventory – Parent Version, Short Form*[28] (PGBI), a 10-item screener of mania symptoms. Parents also completed the *Diagnostic Interview Schedule for Children-Parent Version 4.0* (DISC-P). The following criteria were specified for participation in this study:

– *ADHD-EDr:* ≥6 symptoms on VADPRS Inattention *and* Hyperactive/Impulsive scales; AND T ≥65 on CBCL-Internalizing *and* CBCL-Externalizing; AND PGBI <14.

– *PBD:* T ≥65 on CBCL-Internalizing *and* CBCL-Externalizing; AND PGBI ≥14.

Thresholds on the CBCL were determined according to Youngstrom et al's[28] recommendations. Thresholds on the PGBI were determined according to the cutoff identified by Youngstrom et al.[28] The first children to meet criteria for 1 of the 2 categories were enrolled in the study. The following 2 children were enrolled in the study.

ADHD-EDr

Dylan was a 9-year-old white male entering fourth grade. At the time of assessment, Dylan lived in a single-parent household. All ratings were completed by his mother. Dylan had received a primary diagnosis of ADHD-combined type prior to his participation in the study, and was on a consistent dose of stimulant medication (27 mg methylphenidate) throughout the study. Dylan's mother's rating scale results indicated significant symptoms of inattention (VADPRS = 9 of 9 symptoms) and hyperactivity/impulsivity (VADPRS = 6 of 9 symptoms), as well as broad-spectrum internalizing (CBCL-Internalizing = 65T, 93rd percentile) and externalizing (CBCL-Externalizing = 71T, 98th percentile) behavior. His mother did *not* indicate significant symptoms of mania (PGBI Total = 4). On the DISC-P, Dylan met criteria for ADHD-combined type and oppositional defiant disorder (ODD).

PBD

David was an 8-year-old white male entering third grade. At the time of assessment, David lived in a single-parent household. All ratings were completed by his mother. David had been diagnosed with ADHD-combined type and ODD prior to his participation in the study, but was concurrently being evaluated for a primary diagnosis of bipolar disorder I. David was on a consistent dose of stimulant medication (20 mg mixed amphetamine salts) throughout the study. David's mother's rating scale results indicated significant symptoms of inattention (VADPRS = 8 of 9 symptoms) and hyperactivity/impulsivity (VADPRS = 9 of 9 symptoms), as well as broad-spectrum internalizing

(CBCL-Internalizing = 71T, 98th percentile) and externalizing (CBCL-Externalizing = 72T, 99th percentile) behavior. Her results *did* indicate significant symptoms of mania (PGBI Total = 22). On the DISC-P, David met criteria for ADHD-combined type, ODD, and mania (mother endorsed 9 of 13 symptoms, but denied impairment from his mania symptoms).

EMA Procedures

Parents were provided with a preprogrammed Palm® Z22 PDA (Palm, Inc., Sunnyvale, California), which had been programmed using Purdue Momentary Assessment Tool software (PMAT) (Purdue University, West Lafayette, Indiana).[29] The PDA was programmed to set off alerts at 3 specific predetermined intervals (before school, after school, and evening) requested by parents to be compatible with the family's schedule. Prior to initiating EMA, parents completed a 15-minute training and practice session regarding use of the PDA. Parents were prompted to complete ratings at each time point in the presence of their child. At each time point, parents were asked to report on their child's current mood, irritability, and affect. Parents completed ratings with the PDA 3 times daily for a period of 28 days to ensure that assessments captured a full range of temporal emotional variation, as well as to ensure an adequate number of rating points to complete analyses. Children were not asked to complete ratings for this study given the concerns regarding their ability to accurately complete ratings (particularly while dysregulated), as well as their capacity to safely and responsibly operate the PDA.

To enhance compliance with EMA procedures, parents were asked to return to the laboratory each week to allow data to be uploaded from the PDA. At each visit the parent was provided with a "score card" regarding their adherence to the procedures over the previous week. Parents received monetary compensation for their participation, with compensation prorated to reflect the percentage of completed intervals and weekly "adherence bonuses" available to parents who completed >80% of intervals over the previous week. To further enhance compliance, parents were also provided opportunities to modify the schedule of PDA alerts and receive technical support regarding the PDA performance at each of these visits. Parents were also allowed to contact investigators during the week regarding technical support.

EMA Ratings

Mood Rating

Parents were asked to rate their child's mood *at the time of the assessment* using a visual analog scale (VAS) at each assessment interval. Parents completed a VAS stating, "What is your child's mood *right now?*" directly on the PDA. As mood is widely considered to be homeostatic,[22] parents rated their child's mood on an 11-point scale ranging from –5 to +5, whereby –5 = "much worse mood than usual," 0 = "typical mood for my child," and +5 = "much better mood than usual."

Irritability Rating

Parents were also asked to rate their child's irritability level *at the time of the assessment* using a VAS at each assessment interval. Parents completed a VAS stating, "How irritable is your child *right now?*" directly on the PDA. Parents rated their child's irritability on a scale of 1 to 10, with greater numbers reflecting greater irritability.

The Positive and Negative Affective Scale – Parent Report[30] (PANAS-PR)

Parents were asked to complete a parent-report form of the PANAS directly on the PDA at each assessment interval. The PANAS-PR is a 27-item measure that was developed as a parent-report analogue of the child-report PANAS. Parents were presented with adjectives describing positive (eg, *excited, proud*) or negative (eg, *upset, irritable*) mood states, and asked to rate the presence or absence of that mood state in their child on a 5-point Likert scale ("not at all" to "extremely"). The measure yields 2 subscales, Positive Affect (PA) and Negative Affect (NA). Parents were explicitly instructed to report on their child's *current* emotions at each assessment time point.

Recurrence Quantification Analysis

EDr is by definition a nonlinear and temporal phenomenon that presents variably across individuals. Studies of EDr have typically relied on aggregate data

and linear measures of variance (eg, standard deviations) to assess intraindividual emotional variability. However, aggregate measures of emotional variability "fail to acknowledge sequential dependence"[31] and do not provide any information about the *patterns* of variability.[20] Studies using conventional linear analysis may thus account for one facet of EDr (eg, variability or intensity), but do not accurately capture the full dynamic pattern of emotional fluctuation over time. Conventional linear methods of time series analyses (eg, ARMA [Auto Regressive Moving Average] models, autocorrelation) are similarly limited in their ability to examine fluctuations in emotional state,[31] as the basic assumptions of these methods are violated by time or data series where the mean is nonstationary (as would be seen in episodic patterns of emotional fluctuation).

By contrast, nonlinear methodologies such as Recurrence Quantification Analysis (RQA) have been developed to capture the dynamic structure of an individual temporally dependent data series.[32] RQA derives recurrence plots by computing the distances between all possible data points in the multidimensional "phase space." RQA uses "pattern recognition algorithms" to assess the manner in which values repeat within this "phase space" to detect subtle and intrinsic structural dynamics of the time series.[32] RQA is conducted on an individual temporal data series, and yields several statistics of specific facets of the fluctuation patterns of a temporal data series that cannot be obtained through linear analysis. Specifically, RQA yields the following statistics: (1) percentage recurrence (%REC): the extent to which values repeat in a temporal data series. Lower %REC is indicative of more *variability*, as it reflects mood differing from a "set point"; (2) percentage determinism (%DET): the extent to which specific sequences of data reappear within a data series. Lower %DET is indicative of *unpredictability*; (3) mean line (MnL): the average length of repeating sequences within the temporal series. Lower MnL indicates more *instability*, as it indicates that the average repeating sequence (ie, period of stable mood) is of shorter duration; and (4) trend (TND): measure of how stationary is the mean of the data series. Higher absolute TND indicates *nonstationary mean*, as in random, stochastic, or episodic data series. RQA is already used widely in the physical and biological sciences but has only recently been applied to the behavioral sciences.[32] RQA is a powerful and innovative methodology for identifying disparate patterns of EDr among children with ADHD-EDr versus PBD. The data were analyzed using customized programming[31] within MatLab (The MathWorks, Inc., Natick, Massachusetts).

RESULTS

Feasibility

Participants completed 79/82 (96.3%; ADHD-EDr child) and 71/82 (86.6%; PBD child) of the assessment intervals, respectively. Neither participant missed 2 or more consecutive assessment intervals.

EMA Analyses

Mood

The mood variability ratings of the child with PBD suggest a pattern of episodic mood variability, with notably more variable and elevated mood over the initial portion of the assessment period and more consistent mood over the latter portion of the period. By contrast, the mood ratings of the child with ADHD-EDr appear to be consistent with a pattern of typically consistent mood interspersed with chronically appearing discrete single instances of negative mood (**Figure 2**).

Quantitative analyses of the EMA mood ratings indicated several differences in the pattern of variability demonstrated by children with ADHD-EDr versus PBD. Notably, while the child with PBD demonstrated a more positive overall mood than the child with EDr (**Table**), RQA suggested that his mood was also markedly more dysregulated. Specifically, analyses indicated that the child with PBD demonstrated more variability (%REC = 15.01% vs 27.45%), less predictability (%DET = 33.70% vs 50.33%), and more episodic (TND = 265.28 vs 54.22) mood than did the child with ADHD-EDr (**Table**). No noticeable differences were noted in mood stability.

Irritability

The irritability ratings suggest a pattern of discrete episodes of varying irritability in the child

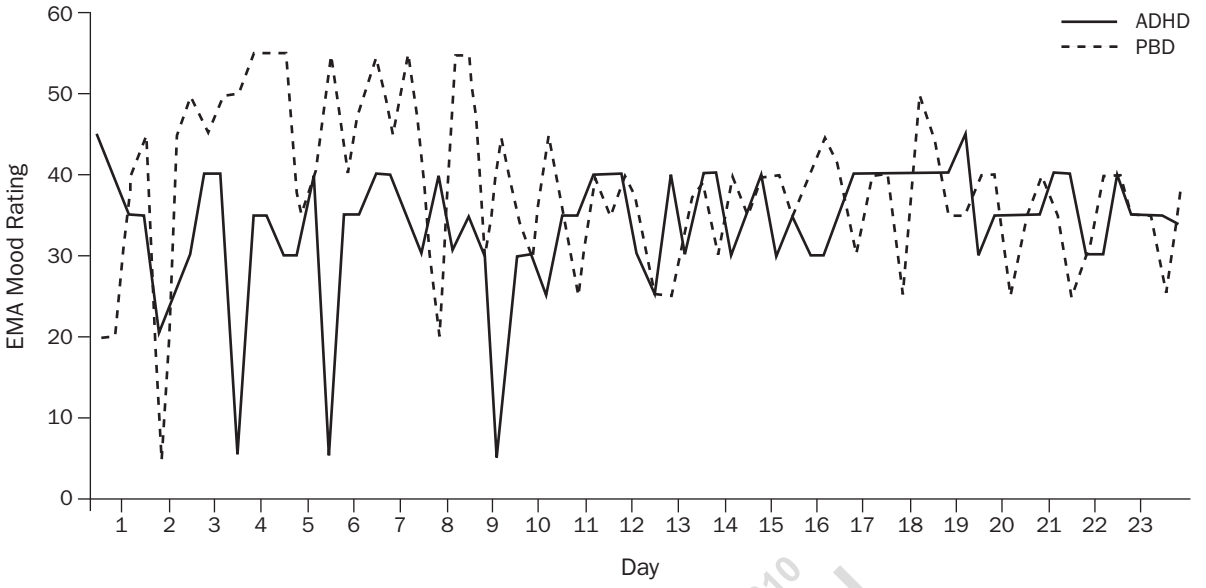

Figure 2. EMA ratings of mood. EMA = ecological momentary assessment; ADHD-EDr = attention-deficit/hyperactivity disorder-emotion dysregulation; PBD = pediatric-onset bipolar disorder.

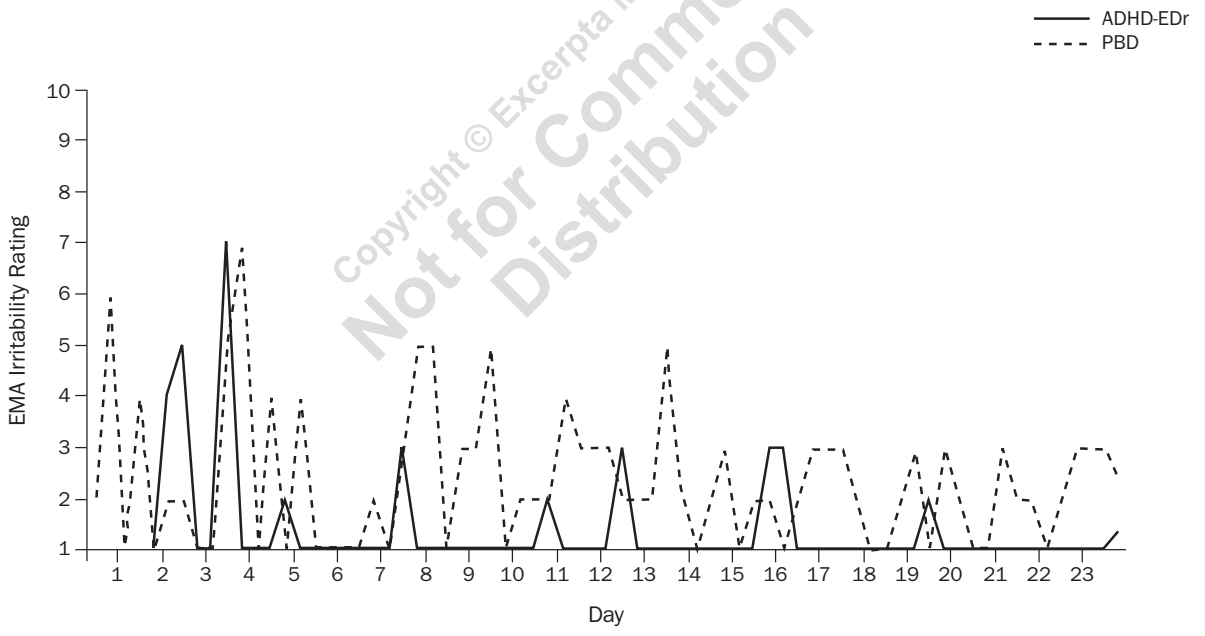

Figure 3. EMA ratings of irritability. EMA = ecological momentary assessment; ADHD-EDr = attention-deficit/hyperactivity disorder-emotion dysregulation; PBD = pediatric-onset bipolar disorder.

with PBD, with more variable and greater irritability at the start of the assessment period and more consistent low-level irritability over the latter portion of the assessment period. By contrast, ratings of the child with ADHD-EDr appear consistent with a pattern of chronic low-level irritable arousals (**Figure 3**). Qualitative analyses of the EMA irritability ratings indicated several differences in the pattern of variability demonstrated by the children with ADHD-EDr versus PBD. The child with PBD demonstrated much more overall irritability than the child with EDr, although RQA also suggested notable differences in the pattern of irritability. Specifically, analyses indicated that the

TABLE. EMA RATING AND RQA RESULTS.

	Mood		Irritability		PANAS-PA		PANAS-NA	
	ADHD-EDr	PBD	ADHD-EDr	PBD	ADHD-EDr	PBD	ADHD-EDr	PBD
Mean	0.77	1.68	1.34	2.37	1.43	4.13	1.06	2.48
%REC	27.45	15.01	79.96	23.89	35.75	35.24	67.39	42.48
%DET	50.33	33.70	97.65	40.38	73.75	76.62	91.59	77.39
MnL	2.33	2.21	5.45	2.33	2.95	2.00	4.22	3.08
Trend	54.22	265.28	82.12	141.45	312.07	1103.01	52.07	826.12

EMA = ecological momentary assessment; RQA = Recurrence Quantification Analysis; PANAS-PA = Positive and Negative Affective Scale-Positive Affect; PANAS-NA = Positive and Negative Affective Scale-Negative Affect; ADHD = attention-deficit/hyperactivity disorder; EDr = emotion dysregulation; PBD = pediatric-onset bipolar disorder; %REC = percentage recurrence; %DET = percentage determinism; MnL = mean line.

Notes regarding RQA statistics:

1. %REC used as an indicator of variability. Lower %REC indicates greater variability.
2. %DET used as an indicator of unpredictability. Lower %DET indicates greater unpredictability.
3. MeanLine used as an indicator of instability. Lower MeanLine indicates greater instability.
4. Trend used as an indicator of episodicity. Higher trend indicates greater instability.

child with PBD demonstrated more variable (%REC = 23.89% vs 79.96%), more unpredictable (%DET = 40.38% vs 97.65%), more unstable (MnL = 2.33 vs 5.45), and more episodic (TND = 141.45 vs 82.12) irritability than did the child with ADHD-EDr (**Table**).

PANAS-PA

The PANAS-PA ratings are consistent with the proposed pattern of chronic versus episodic EDr, with the child with ADHD-EDr demonstrating chronically low positive affect and the child with PBD demonstrating evidence of episodic variation in positive affect (**Figure 4**). Qualitative analyses of the EMA PANAS-PA ratings indicated several differences in the pattern of variability demonstrated by the child with ADHD-EDr versus the child with PBD. Notably, while the child with PBD demonstrated a markedly greater overall positive affect than the child with EDr (**Table**), RQA suggested that his mood was also markedly more dysregulated. Specifically, analyses indicated that the child with PBD demonstrated positive affect that was noticeably more unstable (MnL = 2.00 vs 2.95) and episodic (TND = 1103.01 vs 312.07) than the child with ADHD-EDr. No differences were noted in variability or predictability.

PANAS

Irritability ratings suggest a pattern of discrete episodes of negative affect among the child with PBD, with lower negative affect at the start of the assessment period and higher negative affect over the latter portion of the assessment period. By contrast, ratings of the child with ADHD-EDr appear to be consistent with a pattern of chronic low-level arousals of negative affect (**Figure 5**). Qualitative analyses of the EMA PANAS-NA ratings indicated several differences in the pattern of variability demonstrated by the child with ADHD-EDr versus the child with PBD. The child with PBD demonstrated much more overall negative affect than the child with EDr (**Table**). RQA suggested notable differences in the pattern of variation of negative affect as well. Specifically, analyses indicated that the child with PBD demonstrated more variable (%REC = 42.48% vs 67.39%), more unpredictable (%DET = 77.39% vs 91.59%), more unstable (MnL = 3.08 vs 4.22), and more episodic (TND = 826.12 vs 52.07) negative affect than did the child with ADHD-EDr (**Table**).

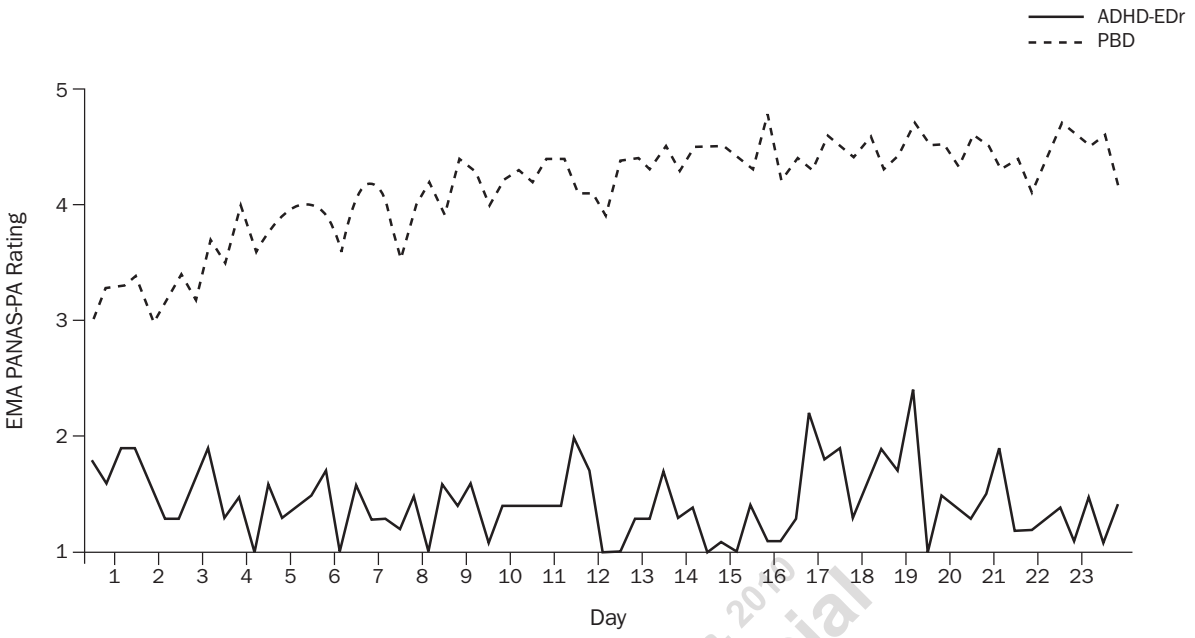

Figure 4. EMA ratings of PANAS-PA. EMA = ecological momentary assessment; PANAS-PA = Positive and Negative Affective Scale-Positive Affect; ADHD-EDr = attention-deficit/hyperactivity disorder-emotion dysregulation; PBD = pediatric-onset bipolar disorder.

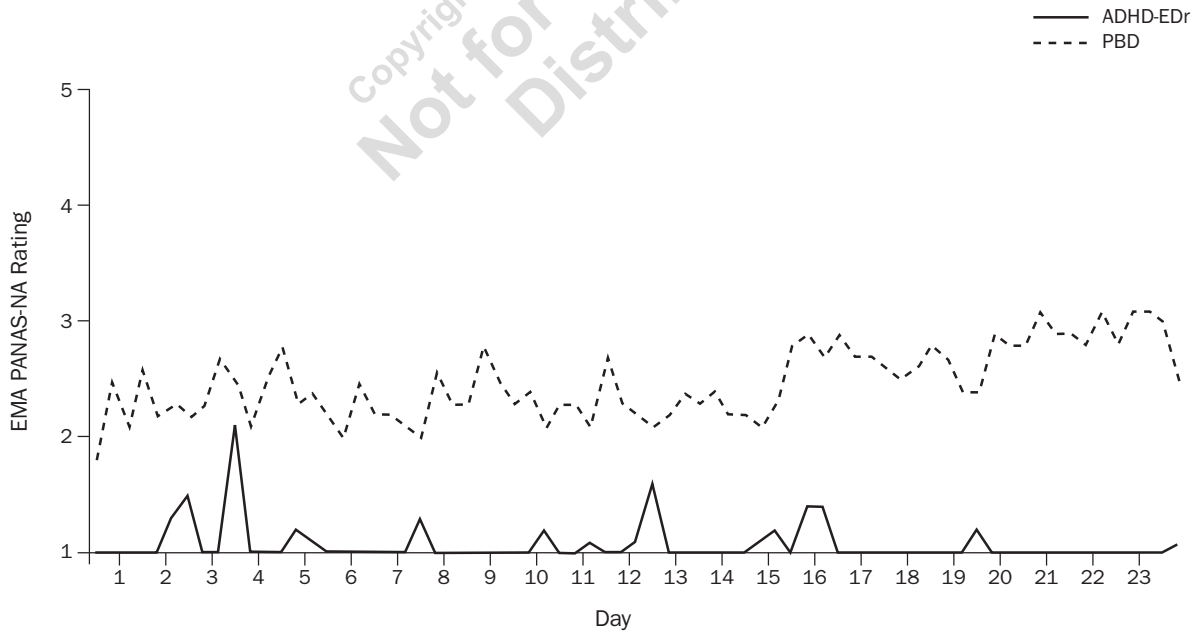

Figure 5. EMA ratings of PANAS-NA. EMA = ecological momentary assessment; PANAS-NA = Positive and Negative Affective Scale-Negative Affect; ADHD-EDr = attention-deficit/hyperactivity disorder-emotion dysregulation; PBD = pediatric-onset bipolar disorder.

DISCUSSION

The present case studies demonstrated the feasibility and utility of using EMA-based methodologies to assess differential patterns of EDr in children with ADHD-EDr versus PBD. Parents of each of the children in the study were able to rate their child's mood, irritability, and affect during at least 85% of the 82 rating points over the 28-day study assessment period (3 ratings per day/28 days). Notably, differential patterns of dysregulation of mood, affect, and irritability emerged among the 2 children. Consistent with the study's hypothesis, the child with ADHD-EDr demonstrated a pattern of chronic but consistent dysregulation, while the child with PBD demonstrated a considerably more episodic pattern of dysregulation.

The child with ADHD-EDr demonstrated a pattern of consistently low positive affect and generally stable mood, with chronic "outbursts" throughout the 28-day period of negative affect, poorer mood, and greater irritability. Notably, RQA results suggested low episodicity, as the child's mean level of mood, irritability, and positive and negative affect remained generally consistent across the study period, despite variability in the actual ratings. This pattern of dysregulation is consistent with Dickstein and Leibenluft's[4] hypothesized description of a "Severe Mood Dysregulation" subset of children with ADHD. Specifically, Dickstein and Leibenluft[4] noted that children within this group demonstrate "chronic, nonepisodic irritability that is operationalized by having a baseline negative mood… and markedly increased reactivity to negative emotional stimuli manifesting verbally or behaviorally." In essence, the ADHD-EDr pattern is characterized by "baseline" and "irritated" states. During the baseline state, the child demonstrates low positive affect with or without accompanying negative affect. The child remains in the baseline state unless aroused by a stimulus that provokes a negative emotion, at which point the child becomes irritable and distressed. Following resolution of the incident, the child's mood returns to the baseline state. This pattern is consistent with the pattern of dysregulation demonstrated by the ADHD-EDr child in the present study, as he demonstrated generally low positive affect along with 10 single time-point ratings of mild to moderate irritability over the 4 weeks.

By contrast, the pattern of dysregulation demonstrated by the child with PBD was considerably more variable over the course of the study. Specifically, ratings for the child with PBD can best be characterized as episodic, with 2 discrete phases evident in the ratings. An initial phase lasting for the first 23 to 26 rating points (8–9 days) was evident in the ratings whereby the child demonstrated substantially elevated mood *and* irritability along with generally lower positive *and* negative affect. Of note, the child's mood and irritability were also notably variable during this initial phase around this elevated mean. By contrast, the child's ratings shifted dramatically over the following 50 to 60 rating points (17–20 days), with a pattern of more euthymic (ie, centered around the "typical" rating) mood, decreased irritability, and increased positive *and* negative affect emerging. Notably, the variability of the child's mood and irritability appeared to decrease noticeably during this phase as well. RQA results were consistent with this interpretation of the child's results, as the higher TND statistics indicated that the mean of the child's ratings shifted over the course of the assessment period, suggesting episodic rather than chronic variability.

This study represents an initial attempt to address substantial gaps in the assessment and classification of EDr in childhood. EDr has emerged as a construct of substantial clinical and theoretical importance in recent years, yet there continues to be debate regarding both its definition and most valid means of assessment.[1] Nowhere has this been more apparent than in the efforts to delineate and differentiate patterns of EDr among children with ADHD-EDr versus PBD.[4] EDr is a core component of both areas of difficulty; however, evidence increasingly supports the conceptualization of children within these groups as experiencing distinct *patterns* of EDr rather than as subgroups of a single disorder (eg, PBD). The present pilot study provides very encouraging initial evidence of the feasibility and usefulness of the EMA-based methodology in demonstrating critical differences in EDr patterns of children with ADHD-EDr and PBD.

Clinically speaking, children within both subgroups demonstrate considerable irritability, negative mood, and emotional and behavioral distress; however, the *patterns* of disruption distinguish the 2 disorders.[5] It can be very difficult for parents to accurately observe and report the temporal sequences of EDr experienced by their children. EMA offers considerable utility above and beyond conventional methods of assessing EDr by allowing the real-time sequences of EDr to be mapped and compared. EMA allows for assessment not just of the variability of the construct of interest, but of *changes in the variability* at different time points. A larger-scale study using the described methodology has the potential to provide information regarding the different types of mood patterns across disorders. Such understanding may eventually aid in defining diagnostic mood symptoms, which should help in the differential diagnosis of a variety of pediatric conditions (eg, ADHD-EDr, ODD, PBD).

Limitations

The present study has several limitations that need to be acknowledged. First and foremost, this was an N = 2 case study. The present study demonstrated differences in the patterns of EDr among the 2 subjects that were prescreened to ensure that they met "prototypic" criteria for the 2 subgroups of interest. Thus, the generalizability of the results is limited. Further, the N = 2 design did not allow for significance testing of any of the differences between the 2 subjects. This is particularly limiting when examining the EMA ratings and RQA results, as there are no clinical norms or comparison groups by which the meaningfulness of the differences can be assessed. Additionally, both children met criteria for ODD on the DISC-P, which has often been associated with EDr.[4] However, behavior difficulties in general and ODD specifically are more commonly conceptualized as an outcome of EDr rather than a cause.[14] Moreover, the 2 children demonstrated substantially divergent patterns of EDr despite the shared diagnosis. Another limitation concerns the assessment methodology. The PDA-based ratings allow for multiple assessments of mood, behavior, and irritability, but do not provide information about the context of the ratings. There are multiple internal and environmental factors that can impact mood, behavior, and irritability, and it was not possible to determine why a child's ratings were elevated or decreased at any time point. The 28-day assessment period also provided a limitation to this study, particularly given the episodic nature of the child with PBD ratings. Finally, it must be acknowledged that the PDA-based assessment methodology has several costs, including both the material cost of the PDAs and the time cost to the participants. However, both parents were able to complete greater than 85% of assessments, and both indicated in informal feedback that completing ratings did not represent a major inconvenience in their daily routines.

CONCLUSIONS

With the recent sharp increase in new diagnoses of PBD,[15] it has become increasingly important to improve the ability of clinicians and researchers to differentiate between "true" PBD and other patterns of EDr. EDr in children can take many forms, and differentiating patterns of EDr can be very challenging. The present study provided encouraging evidence for the feasibility and utility of EMA as a tool to assist in further defining and differentiating patterns of EDr across PBD and ADHD, which may substantially improve our ability to understand, conceptualize, and provide services to these vulnerable groups of children.

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Emotional Dysregulation as a Core Feature of Adult ADHD: Its Relationship With Clinical Variables and Treatment Response in Two Methylphenidate Trials

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ABSTRACT

Background: Previous studies have suggested that many patients with attention-deficit/hyperactivity disorder (ADHD) have significant emotional symptoms. This observation raises the question whether there are core emotional features of more severe ADHD in adults.

Objective: We combined data from 2 adult ADHD trials to compare the clinical presentation and treatment response of patients with and without emotional dysregulation.

Methods: Data from 2 placebo-controlled, crossover studies examining methylphenidate were combined (N = 136). Using previously published criteria, scores showing an average of moderate impairment or worse on the Wender-Reimherr Adult Attention Deficit Disorder Scale items assessing temper, mood lability, and emotional overreactivity were used to categorize patients with emotional dysregulation. Both studies were highly positive and used many of the same measures assessing ADHD symptoms, childhood symptoms, social adjustment, substance abuse, and personality.

Results: Patients were 71% male and a mean of 33.7 years old. Those with emotional dysregulation (72%) more frequently had combined-type ADHD, more oppositional defiant symptoms, higher ADHD ratings, worse social adjustment, higher personality disorder ratings, and a trend toward more substance abuse. Both groups responded to methylphenidate. Emotional symptoms in subjects with emotional dysregulation also showed a very significant response (effect size = 0.83).

Conclusion: A large portion (72%) of adults with ADHD showed symptoms of emotional dysregulation. These patients have more severe, complex symptoms and their emotional symptoms were highly responsive to methylphenidate. These results support including emotional dysregulation as a core feature of more severe adult ADHD. Adults with ADHD and emotional dysregulation should be viewed as a distinct subgroup. (*J ADHD Relat Disord*. 2010;1[4]:53–64) © 2010 Excerpta Medica Inc.

Key words: adult, ADHD, treatment response, emotional dysregulation, impairment, personality disorder.

INTRODUCTION

Historical descriptions of illnesses connected with attention-deficit/hyperactivity disorder (ADHD) by Still,[1] Hohman,[2] and Bradley,[3] and descriptions of minimal brain dysfunction by Wender[4] and Anderson,[5] have presented a complex, multifaceted illness producing significant personal distress and potentially contributing to a variety of far-reaching social problems. In 1980, the *Diagnostic and Statistical Manual of Mental Disorders, Third Edition* (*DSM-III*) defined the disease as ADD with a narrow set of childhood criteria. Two conditions frequently occurring with ADHD, oppositional defiant disorder (ODD) and conduct disorder (CD), were also presented in the *DSM-III*. Since then, many ADHD studies, both clinical and descriptive, have de-

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scribed their populations as meeting *DSM-III* or *DSM-IV* criteria without providing sufficient attention to the tremendous heterogeneity concealed within their patient populations.

In 1985, we published one of the first adult ADHD trials[6] using a set of criteria that we later labeled as the "Utah criteria." Since our initial studies preceded the publication of *DSM-III*, we developed our own diagnostic criteria for ADHD by examining adults who had both a history of ADHD as children as reported by their parents and current symptoms of ADHD as reported by both the patients and their significant others. We attempted to define a more severely impacted group of ADHD patients and present a description of the more complex symptoms found in adults with severe ADHD. Besides the *DSM-IV* symptoms of inattentiveness, hyperactivity, and impulsivity, our patients commonly experienced 4 additional sets of symptoms which responded to treatment: disorganization, temper, affective lability, and emotional overreactivity. Our description of adult ADHD symptoms evolved into a set of research criteria. The Wender-Reimherr Adult Attention Deficit Disorder Scale (WRAADDS) was developed to assess these symptoms and treatment response.

The emotional symptoms associated with adult ADHD are distinct from mood disorder symptoms. Two publications by Wender[7] and Williams et al[8] give a qualitative view of the symptoms. In a more quantitative analysis, Rosler et al[9] documented that the emotional symptoms defined by the WRAADDS show a treatment response to methylphenidate in adults with ADHD, while the depression and anxiety measured by the Symptom Checklist-90 does not. The ADHD patient's temper is usually shorter lived and reactive to something in the environment. When adults with ADHD report current affective lability, they often report that it dates back to childhood. The mood shifts are usually temporally short (minutes to hours, not days) and are both in response to and separate from environmental stimuli. In contrast with depressed patients, the patient with ADHD remains responsive to environmental stimuli. The highs of the adult resemble the excitement of an overstimulated child rather than the elation of the hypomanic. The lows present as boredom or a lack of contentment, and the vegetative symptoms of depression are seldom present. When emotional overreactivity is present, it is commonly expressed through an inability to handle stress effectively. Patients may respond inappropriately to ordinary demands, possibly leading to a cycle where they are under stress and act inappropriately, leading to more stress. However, when the situation is resolved, the patient rebounds emotionally.

Since development of the Utah criteria, one of the most complete descriptions of childhood ADHD was presented in the National Institute of Mental Health–sponsored Multimodal Treatment Study of Children With ADHD (MTA). Most patients had significant anxiety, ODD, and/or CD symptoms and could be subtyped based on the presence of these dimensions. Only 30% had ADHD alone.[10]

In 2005, we published a reanalysis on the 2 key studies that produced the Food and Drug Administration (FDA) approval of atomoxetine for adult ADHD.[11] In this paper, the WRAADDS symptoms of temper, affective lability, and emotional overreactivity were combined into a factor that we called "emotional dysregulation." Using the WRAADDS to assess symptoms in these trials, 35% of the patients had significant symptoms in this dimension. These trials excluded patients with affective disorders, and used the Hamilton Rating Scale for Depression (HAM-D) and Hamilton Anxiety Rating Scale (HAM-A) to further control for affective disorders. The patients in this trial had very low HAM-D and HAM-A scores at baseline, which did not improve with treatment. In 2007, we assessed the females in this set of studies.[12] We found women had the largest treatment effect and a higher level of emotional dysregulation. While only limited formal factor analysis has been published verifying these items as a separate ADHD dimension, there is substantial face validity differing these from the traditional *DSM-IV* factors of inattention and hyperactivity/impulsivity.

Subsequently, in 2007,[13] we presented the results of a methylphenidate clinical trial. Similar to the childhood MTA study, adults with ADHD could be separated based on the presence of emotional and oppositional symptoms. Only 20% had ADHD alone. Both social adjustment and personality disor-

der were assessed in this study and we found that problems in these areas were concentrated in these more complex patients.[14]

Based on these data, we believe that this cluster of emotional symptoms frequently occurs as part of adult ADHD and contributes to the patient's psychosocial impairment. The symptoms of emotional dysregulation respond to standard ADHD medications in parallel with the *DSM* symptoms. To explore these hypotheses, we combined data from 2 trials of methylphenidate. One trial, noted above, used osmotic-release oral system methylphenidate (OROS-MPH)[13] and the other used methylphenidate transdermal system (MTS).[15] This paper addresses the following questions:

1. What percentage of ADHD patients have emotional dysregulation?
2. Are there differences between ADHD patients who experience emotional dysregulation and other adults with ADHD?
3. Do the symptoms of emotional dysregulation respond to treatment?
4. If emotional dysregulation responds to treatment, does it do so parallel with traditional ADHD symptoms?

METHODS

The impact of emotional dysregulation was evaluated using data from 2 similar studies conducted at the University of Utah. The University of Utah Institutional Review Board reviewed and approved both studies, which were similar in design and used sustained-release formulations of methylphenidate. One trial assessed OROS-MPH[13] and the other assessed MTS.[15] Data from the 2 studies have been combined and will be presented as one data set in this reexamination. Both trials were double-blind, placebo-controlled, crossover designs containing a screening/baseline phase followed by a double-blind crossover phase with two 4-week arms. During the double-blind crossover phase, patients were randomly assigned to 1 of 2 groups in a double-blind manner: placebo or active treatment. Patients were seen weekly, and at the end of 4 weeks, patients were crossed to the other treatment arm for an additional 4 weeks.

Study Population

In both trials, patients were required to have a current diagnosis of adult ADHD using *DSM-IV, Text Revision* (*DSM-IV-TR*) criteria for ADHD and/or the Utah criteria for ADHD in adults. This included the requirement for clear evidence of clinically significant impairment caused by ADHD. Patients were between 18 and 65 years of age. Female patients were eligible if they were of nonchildbearing potential or agreed to use an approved form of contraception. The following *DSM-IV* Axis I diagnoses were exclusionary: current diagnosis of major depressive disorder, panic disorder, obsessive-compulsive disorder, posttraumatic stress disorder, bipolar disorder, schizophrenia, or other psychotic disorder. Patients with a seizure disorder, untreated hyperthyroidism or hypothyroidism, or significant medical conditions likely to become unstable during the trial or likely to be destabilized by treatment with methylphenidate (eg, cardiovascular disease) were also excluded.

Measures

The WRAADDS and the Clinical Global Impressions–Severity (CGI-S) scale were used to assess the severity of ADHD symptoms in both trials at baseline and to define treatment responders. The CGI-S scale ranges from no symptoms (1) to very severely impaired (7). *Responders* were defined as having a score of 3 (mildly ill) or better. ADHD symptoms were also assessed by the ADHD Rating Scale (ADHD-RS) in the OROS-MPH trial and by the Conners Adult ADHD Rating Scale (CAARS) in the MTS trial. Emotional dysregulation is used as a dimensional measure using the sum of the 3 WRAADDS scales. It is also used to categorize patients based on the severity of emotional dysregulation at baseline using previously published criteria[11] of scores ≥7 on the 3 WRAADDS scales. Scores ≥7 indicate at least moderate impairment. Not only is there face validity in distinguishing these symptoms from the *DSM* factors of inattention and hyperactivity/impulsivity, but prior analysis found that: (1) the 3 items made a factor separate from the *DSM* items; (2) the 7 items of the WRAADDS had high internal consistency with a Cronbach's $\alpha > 0.80$; and (3) a strong treatment effect was evident for the

WRAADDS using the 7 individual items or combining them into 3 factors.[16]

The self-report ADHD (SR-WRAADDS) scale mirrors items from both the WRAADDS and the Wender Utah Rating Scale (WURS). It is being developed as an adult-oriented questionnaire that assesses the 7 symptom areas of the WRAADDS as well as symptoms in 4 other areas: oppositional defiant symptoms, academic impairment, symptoms not otherwise specified (NOS), and social functioning. It uses a 5-point scale ranging from 0 = none to 4 = very much. Copies of this scale are available from the corresponding author. The determination of having significant ODD symptoms was based on having a moderate impairment on the ODD items in this scale.

The Parent Rating Scale (PRS) and the WURS were used to help verify childhood symptoms of ADHD in the patients before randomization. Both scales have published cutoff scores which indicate that childhood ADHD was present.[7] Not all patients completed both scales; 124 patients completed the WURS and 104 patients had parents who completed the PRS.

In both studies, the Wisconsin Personality Disorders Inventory (WISPI-IV)[17,18] and the Structured Clinical Interview for *DSM-IV-TR* Personality Disorder (SCID-II)[19,20] were used to measure personality. In a previous study,[21] we showed that both scales produced an acceptable estimate of personality disorder in adult patients with ADHD. In this study, we showed that the average number of items endorsed on the SCID-II screening questionnaire and the average *z* score on the WISPI-IV both provided an estimate of the severity of personality disorder.

Finally, the presence of substance abuse was assessed during the study intake process in each study.

Data Analysis and Statistical Procedures

Baseline differences between patients who did or did not exhibit emotional dysregulation were assessed using the Student *t* test for continuous variables, the χ^2 test for dichotomous variables, and the Mann-Whitney *U* test for ordinal variables.

Treatment effects were assessed using repeated-measures ANOVA including sex, study (OROS-MPH vs MTS), and emotional dysregulation status (ADHD + ED [patients with emotional dysregulation scores of 7 or greater] or non-ED [patients with emotional dysregulation scores below 7]) as variables. Improvement for the CGI-S was assessed using both the McNemar test and the Fisher exact test.

Pearson correlation coefficients were used to assess the relationships between the 3 WRAADDS factors at baseline and to document whether they improved in parallel.

All analyses were done using the SPSS 13.0 statistical package (SPSS Inc., Chicago, Illinois). All statistics were 2-tailed with $P < 0.05$.

RESULTS

Baseline

At baseline, 136 patients signed consent forms to start the screening process, and completed sufficient intake evaluations to be assessed for ADHD and emotional dysregulation in these 2 trials. As seen in **Table I**, 72% of the sample were categorized ADHD + ED. Of the females, 83% were categorized ADHD + ED compared with 68% of males. This difference did not meet statistical significance ($\chi^2 = 2.8$, $df = 1$, $P = 0.09$).

There were significant differences in the ADHD subtypes. As seen in **Table I**, non-ED patients were more likely to be attentional type only while ADHD + ED patients were more likely to be combined type. Additionally, ADHD + ED patients had higher ODD symptom levels.

Emotional dysregulation was associated with higher symptom levels on most clinical scales. On the investigator-rated WRAADDS, ADHD + ED patients had significantly higher scores in the symptom area of hyperactivity + impulsivity ($t = 8.9$, $df = 133$, $P < 0.001$). The investigators also rated these patients as more impaired in the CGI-S scale ($z = 5.0$, $P < 0.001$). On the SR-WRAADDS, ADHD + ED patients had higher symptom loads in attention + disorganization ($t = 2.7$, $df = 130$, $P = 0.007$), hyperactivity + impulsivity ($t = 2.2$, $df = 130$, $P = 0.03$), and oppositional defiant symptoms ($t = 5.1$, $df = 129$, $P < 0.001$), and poorer social adjustment ($t = 4.3$, $df = 110$, $P < 0.001$).

There was a significant positive relationship between the 3 primary WRAADDS factors at base-

TABLE 1. BASELINE DEMOGRAPHICS FOR PATIENTS.

	All Patients	Non-ED	ADHD + ED	*P*
Distribution, N (%)	136 (100)	38 (28)	98 (72)	
Male, N (%)	96 (71)	31 (32)	65 (68)	$\chi^2 = 2.8$, $df = 1$, $P = 0.09$
Female, N (%)	40 (29)	7 (18)	33 (83)	
Age, mean (SD)	33.7 (11.7)	34.6 (12.3)	33.4 (11.5)	$t = 0.5$, $df = 130$, $P = 0.62$
BMI, mean (SD)	28.8 (6.4)	28.4 (6.3)	29.0 (6.4)	$t = 0.3$, $df = 112$, $P = 0.76$
ADHD Diagnostic Group, N (%)				
Combined type	105 (77)	14 (37)	91 (93)	
Attentional type	28 (21)	23 (61)	5 (5)	
Hyperactive/impulsive	3 (2)	1 (3)	2 (2)	$\chi^2 = 51.5$, $df = 2$, $P < 0.001$
ODD	59 (43)	7 (18)	52 (53)	$\chi^2 = 13.4$, $df = 1$, $P = 0.001$
WRAADDS, mean (SD)				
Total	21.5 (4.1)	16.7 (2.8)	23.4 (2.7)	$t = 12.7$, $df = 133$, $P < 0.001$
Attention + disorganization*	3.6 (0.5)	3.4 (0.6)	3.6 (0.5)	$t = 1.96$, $df = 133$, $P = 0.052$
Hyperactivity + impulsivity*	3.0 (0.8)	2.3 (0.7)	3.3 (0.6)	$t = 8.9$, $df = 133$, $P < 0.001$
Emotional dysregulation*	3.1 (0.7)	2.4 (0.7)	3.4 (0.5)	$t = 8.9$, $df = 133$, $P < 0.001$
CGI-S, mean (SD)	4.7 (0.7)	4.2 (0.4)	4.9 (0.7)	$z = 5.0$, $P < 0.001$
SR-WRAADDS, mean (SD)				
Attention + disorganization*	3.0 (0.7)	2.7 (0.6)	3.1 (0.7)	$t = 2.7$, $df = 130$, $P = 0.007$
Hyperactivity + impulsivity*	2.5 (0.9)	2.2 (0.9)	2.6 (0.9)	$t = 2.2$, $df = 130$, $P = 0.03$
Emotional dysregulation*	2.3 (1.0)	1.5 (0.8)	2.6 (0.8)	$t = 7.6$, $df = 130$, $P < 0.001$
ODD	1.8 (0.8)	1.2 (0.8)	2.0 (0.8)	$t = 5.1$, $df = 129$, $P < 0.001$
Academic impairment	2.0 (1.2)	1.9 (1.2)	2.1 (1.1)	$t = 0.9$, $df = 109$, $P = 0.39$
NOS	1.8 (0.8)	1.7 (0.9)	1.9 (0.8)	$t = 1.4$, $df = 130$, $P = 0.16$
Social adjustment	1.8 (0.9)	1.2 (0.7)	2.0 (0.8)	$t = 4.3$, $df = 110$, $P < 0.001$
Childhood measures, mean (SD)				
WURS (n = 124)	53.6 (16.7)	42.5 (16.5)	57.7 (14.9)	$t = 4.9$, $df = 123$, $P = 0.001$
PRS (n = 104)	18.1 (6.7)	16.4 (6.7)	18.9 (6.6)	$t = 1.8$, $df = 103$, $P = 0.07$

(continued)

TABLE 1 (CONTINUED). BASELINE DEMOGRAPHICS FOR PATIENTS.

	All Patients	Non-ED	ADHD + ED	*P*
Personality disorder, mean (SD)				
Average WISPI-IV *z* score	0.13 (1.0)	–0.3 (0.8)	0.3 (1.1)	$t = 3.0$, $df = 113$, $P = 0.004$
SCID-II items endorsed	32.4 (18.4)	25.4 (16.2)	35.6 (18.5)	$t = 2.9$, $df = 127$, $P = 0.004$
SCID-II PD – Average number of personality disorders per patient	1.4 (1.7)	0.9 (1.2)	1.6 (1.8)	$t = 2.1$, $df = 114$, $P = 0.04$
Substance abuse,† N (%)				
Alcohol problems	13 (10)	3 (8)	10 (10)	$z = 0.5$, $P = 0.65$
Drug use problems	27 (20)	5 (13)	22 (22)	$z = 1.3$, $P = 0.19$
Substance use problems	35 (26)	7 (18)	28 (29)	$z = 1.3$, $P = 0.19$

Non-ED = patients with emotional dysregulation scores below 7; ADHD + ED = patients with emotional dysregulation scores of 7 or greater; BMI = body mass index; ADHD = attention-deficit/hyperactivity disorder; ODD = oppositional defiant disorder; WRAADDS = Wender-Reimherr Adult Attention Deficit Disorder Scale; CGI-S = Clinical Global Impressions–Severity scale; SR-WRAADDS = Self-Report Wender-Reimherr Adult Attention Deficit Disorder Scale; NOS = symptoms not otherwise specified; WURS = Wender Utah Rating Scale; PRS = Parent Rating Scale; WISPI-IV = Wisconsin Personality Disorders Inventory IV; SCID-II = Structured Clinical Interview for *DSM-IV-TR*; PD = personality disorder.

*Item averages reported.

†Alcohol problems were more than mild. Drug use problems were any illegal drug use. Substance use problems were alcohol more than mild and/or any drug use problems documented.

line. Emotional dysregulation correlated with attention + disorganization (r = 0.379, n = 136, P < 0.001) and hyperactivity + impulsivity (r = 0.459, n = 136, P < 0.001). In comparison, attention + disorganization correlated with hyperactivity + impulsivity (r = 0.276, n = 136, P = 0.001). Similarly, in the SR-WRAADDS, the symptoms of emotional dysregulation correlated with attention + disorganization (r = 0.465, n = 133, P < 0.001) and hyperactivity + impulsivity (r = 0.573, n = 133, P < 0.001), while attention + disorganization correlated with hyperactivity + impulsivity (r = 0.485, n = 133, P < 0.001). Consequently, emotional dysregulation correlated at least as closely with each of the other 2 ADHD symptom dimensions as they did with each other.

Patients with emotional dysregulation had higher ADHD pathology in both assessments of childhood ADHD. On the patient-rated WURS, the mean (SD) of patients with emotional dysregulation was 57.7 (14.9) while the mean of patients without emotional dysregulation was 42.5 (16.5). This difference was significant (t = 4.9, df = 123, P = 0.001). On the PRS, the mean of patients with emotional dysregulation was 18.9 (6.6) while the mean of patients without emotional dysregulation was 16.4 (6.7). This difference approached significance (t = 1.8, df = 103, P = 0.07).

All 3 measures of personality disorder showed an increased level of personality disorder in ADHD patients with emotional dysregulation. This distinction was greater on the dimensional measures than on the categorical measure. Finally, there was a trend for emotional dysregulation patients to have higher levels of substance abuse.

EFFICACY

A total of 99 patients furnished outcome data from these 2 trials.

Patients with and without emotional dysregulation experienced significant treatment effects (**Table II**). For the total WRAADDS, treatment was significant ($F_{1,84}$ = 17.6, P < 0.001) with a Cohen's effect size of d = 0.90. However, the interaction between treatment and emotional dysregulation status was not significant (ADHD + ED vs non-ED) ($F_{1,84}$ = 0.032, P = 0.857); the study (OROS-MPH vs MTS) did not interact with treatment ($F_{1,84}$ = 3.0, P = 0.09); and sex (male vs female) was not significant ($F_{1,84}$ = 0.2, P = 0.66). The similar treatment effects experienced by the 2 groups were evidenced by comparing their individual Cohen's d scores. For ADHD + ED patients, it was d = 0.88 and for non-ED patients, it was d = 1.25. While all 3 dimensions of the WRAADDS had significant treatment effects, emotional dysregulation status was not associated with a higher or lower treatment response for the total WRAADDS. The factor attention + disorganization had a significant treatment effect ($F_{1,67}$ = 21.5, d = 0.94, P < 0.001) but the interaction of treatment and emotional dysregulation status was not significant ($F_{1,67}$ = 0.52, P = 0.47). Similarly, hyperactivity + impulsivity had a significant treatment effect ($F_{1,67}$ = 22.7, d = 0.84, P < 0.001) but the interaction between treatment and emotional dysregulation status was not significant ($F_{1,67}$ = 0.70, P = 0.407). Finally, the symptoms of emotional dysregulation had a significant treatment effect ($F_{1,67}$ = 10.9, d = 0.74, P < 0.001) but the interaction between emotional dysregulation status and improvement in these symptoms was not significant ($F_{1,67}$ = 0.27, P < 0.605).

When assessed separately, ADHD + ED patients improved in the total WRAADDS ($F_{1,67}$ = 22.1, P < 0.001) and in all 3 subscales: attention + disorganization ($F_{1,67}$ = 23.5, P < 0.001), hyperactivity + impulsivity ($F_{1,67}$ = 21.6, P < 0.001), and emotional dysregulation ($F_{1,67}$ = 19.2, P < 0.001). More patients met CGI-S criteria for improvement in the active treatment arm (χ^2 = 10.3, P = 0.001). In comparison, the small sample of non-ED patients improved in the total WRAADDS ($F_{1,17}$ = 7.3, P = 0.015) and 2 of the 3 subscales: attention + disorganization ($F_{1,17}$ = 7.1, P = 0.017) and hyperactivity + impulsivity ($F_{1,17}$ = 11.0, P = 0.004), but only approached significance for emotional dysregulation ($F_{1,17}$ = 3.8, P = 0.067). This lack of significance reflects the limited room for improvement on this measure in the non-ED group. Treatment effects using the SR-WRAADDS were significant for all but the social adjustment scale for the ADHD + ED patients: attention + disorganization ($F_{1,58}$ = 15.2, P < 0.001); hyperactivity + impulsivity ($F_{1,58}$ = 18.9, P < 0.001); emotional dysregulation

TABLE II. OUTCOME FOR ADHD CLINICAL SCALES AS A FUNCTION OF TREATMENT (ACTIVE TREATMENT OR PLACEBO).

	Non-ED (N = 28)				ADHD + ED (N = 71)			
	Placebo	Active Tx	*P**	Cohen's *d*	Placebo	Active Tx	*P**	Cohen's *d*
WRAADDS total, mean (SD)	15.5 (6.2)	8.1 (5.6)	0.015	1.25	19.9 (7.0)	13.2 (8.2)	0.000	0.88
Attention + disorganization	6.2 (2.5)	3.0 (2.2)	0.017	1.36	6.4 (2.2)	4.3 (2.7)	0.000	0.86
Hyperactivity + impulsivity	4.8 (2.3)	2.7 (1.8)	0.004	1.02	5.5 (2.0)	3.8 (2.2)	0.000	0.81
Emotional dysregulation	4.6 (2.6)	2.5 (2.5)	–0.067	–0.82	8.0 (3.3)	5.1 (3.7)	0.000	0.83
CGI-S, n (%) improved	4 (17)	18 (75)	0.004	NA	16 (23)	41 (56)	0.001	NA
Self-Report WRAADDS, mean (SD)								
Attention + disorganization	2.3 (0.9)	1.3 (0.8)	0.003	1.18	2.5 (1.1)	1.7 (1.1)	0.000	0.73
Hyperactive + impulsive	1.7 (1.1)	1.2 (0.8)	0.014	0.57	2.1 (1.1)	1.4 (1.0)	0.000	0.67
Emotional dysregulation	1.1 (0.8)	0.7 (0.6)	0.09	0.41	2.0 (1.0)	1.5 (1.0)	0.004	0.50
Oppositional defiant	0.7 (0.7)	0.6 (0.4)	0.75	0.18	1.4 (0.9)	1.1 (0.9)	0.018	0.33
Academic impairment	1.9 (1.1)	1.3 (1.1)	0.25	0.54	2.1 (1.2)	1.6 (1.0)	0.005	0.45
NOS	1.0 (0.7)	0.7 (0.6)	0.12	0.46	1.4 (0.8)	1.1 (0.8)	0.023	0.38
Social adjustment	0.8 (0.5)	0.5 (0.5)	0.12	0.60	1.7 (1.0)	1.6 (1.0)	0.26	0.10

ADHD = attention-deficit/hyperactivity disorder; Non-ED = patients with emotional dysregulation scores below 7; ADHD + ED = patients with emotional dysregulation scores of 7 or greater; Active Tx = medication arm (osmotic-release oral system methylphenidate or methylphenidate transdermal system); WRAADDS = Wender-Reimherr Adult Attention Deficit Disorder Scale; CGI-S = Clinical Global Impressions–Severity scale; NOS = not otherwise specified.

**P* results from repeated-measures ANOVA (controlling for sex and study) except CGI-S which resulted from χ^2.

($F_{1,58}$ = 9.1, P = 0.004); oppositional defiant symptoms ($F_{1,58}$ = 5.9, P = 0.018); academic impairment ($F_{1,51}$ = 8.8, P= 0.005); NOS ($F_{1,58}$ = 5.5, P = 0.023); and social adjustment ($F_{1,51}$ = 1.3, P = 0.26). Treatment effects for the smaller sample of non-ED patients were significant for only 2 of the SR-WRAADDS scales: attention + disorganization ($F_{1,15}$ = 8.3, P = 0.015); hyperactivity + impulsivity ($F_{1,15}$ = 5.2, P = 0.037); emotional dysregulation ($F_{1,15}$ = 2.0, P = 0.71); oppositional defiant symptoms ($F_{1,15}$ = 0.1, P = 0.75); academic impairment ($F_{1,10}$ = 1.5, P = 0.25); NOS ($F_{1,15}$ = 2.8, P = 0.12); and social adjustment ($F_{1,10}$ = 3.0, P = 0.12).

There was a significant positive correlation between *change scores,* defined as the difference between active treatment and placebo conditions, for the 3 primary WRAADDS factors. Change scores for emotional dysregulation correlated with attention + disorganization (r = 0.896, n = 92, P < 0.001) and hyperactivity + impulsivity (r = 0.886, n = 92, P < 0.001). In comparison, attention + disorganization correlated with hyperactivity + impulsivity (r = 0.874, n = 92, P < 0.001). Similarly, in the SR-WRAAADDS, change scores for the symptoms of emotional dysregulation were correlated with attention + disorganization (r = 0.875, n = 81, P < 0.001) and hyperactivity + impulsivity (r = 0.898, n = 81, P < 0.001), while attention + disorganization correlated with hyperactivity + impulsivity (r = 0.866, n = 81, P < 0.001).

DISCUSSION

The earliest reports on ADHD-like conditions noted that many patients showed a combination of attentional, emotional, and conduct symptoms.[1–3] Since the initial adult trials in 1976, we have examined the symptoms of adults with ADHD using interviews with their parents, significant others, and themselves. These reports have consistently included 3 emotional symptoms, temper, affective lability, and emotional overreactivity, that Wender included in the Utah criteria.[7] While these symptoms were developed pragmatically, theories underlying ADHD give increasing support for their inclusion as basic components of ADHD. Barkley and Murphy[22] suggested that ADHD represents a developmental delay in response inhibition processes including self-regulation of affect/motivation/arousal. Symptoms of emotional dysregulation appear to fit within this concept as a part of ADHD, not a comorbid condition.

Our first question was: "What percent of ADHD patients have emotional dysregulation?" We found that 70% had at least moderate levels of emotional dysregulation symptoms at baseline. Emotional dysregulation constituted 79% of the sample in the OROS-MPH trial and 67% in the MTS trial. Since other Axis I disorders were exclusionary, there is little reason to believe that these symptoms resulted from comorbid mood or anxiety disorders.

The second question was: "Are there differences between ADHD patients who experience emotional dysregulation and other adults with ADHD?" We found multiple differences. In general, ADHD + ED patients were more impaired in several areas compared with non-ED patients. They were more likely to have combined-type ADHD, and had higher childhood and adult ADHD symptom loads. In a previous trial of atomoxetine,[13] we found that women had a higher symptom load, primarily explained by a higher frequency of emotional dysregulation and hyperactivity + impulsivity symptoms. They were more likely to be diagnosed with combined-type ADHD. That observation was replicated in this trial; compared with the non-ED group, a greater percentage of the ADHD + ED group were women and had combined-type ADHD.

In a previous analysis of the OROS-MPH trial,[14] we reported that the WRAADDS scores for hyperactivity + impulsivity (P = 0.024) and emotional dysregulation (P < 0.001) were significantly higher for patients who had one or more personality disorders. We also found that a personality disorder was associated with the presence of emotional dysregulation. In this analysis, ADHD + ED patients had higher baseline values on the personality disorder measures.

Our third question was: "Do the symptoms of emotional dysregulation respond to treatment?" ADHD + ED patients demonstrated a treatment response that was at least as good as the non-ED patients. Attention + disorganization, hyperactivity +

impulsivity, and emotional dysregulation improved for these patients. In the ADHD + ED patients, the effect size for the symptoms of emotional dysregulation was large. Surprisingly, non-ED patients experienced benefits for these symptoms that approached significance, suggesting that treatment may be beneficial even if the level of emotional dysregulation is mild.

The OROS-MPH trial used the ADHD Rating Scale (ADHD-RS) and the MTS trial used the Conners Adult ADHD Rating Scale (CAARS). While the psychometric properties of the 2 scales preclude combining them for analysis in this trial, they are worth reporting. Within the OROS-MPH trial, ADHD + ED patients demonstrated a significant treatment response using the Adult ADHD Investigator Symptom Report Scale (AISRS) as the outcome measure ($F_{1,31} = 11.7$, $P < 0.002$). Within the MTS trial, ADHD + ED patients demonstrated a significant treatment response using the CAARS as the outcome measure ($F_{1,34} = 13.2$, $P = 0.001$).

Finally, our fourth question was: "If emotional dysregulation responds to treatment, does it do so parallel with traditional ADHD symptoms?" The symptoms of emotional dysregulation responded to treatment in parallel with the *DSM* symptoms of attention + disorganization and hyperactivity + impulsivity. When we correlated the change scores in either the active treatment group or the placebo group for these 3 symptom groups, we found that when patients improved in one area, they almost always experienced improvement in the other symptoms at the same time. Change scores between the 3 factors were highly correlated and all 3 correlations were above $r = 0.8$.

Very few other studies of ADHD have assessed emotional symptoms in ADHD in this manner. Oddly, symptoms described as emotional dysregulation have been addressed perhaps more frequently in disorders other than ADHD, including anxiety disorder,[23] major depression,[24] and bipolar disorder.[25,26] Two sets of studies have addressed emotional dysregulation in patients with conditions that might be considered ADHD-spectrum conditions or closely related conditions. First, in 2006, Brotman et al[27] reported on children with severe mood dysregulation that he defined as similar to child bipolar disorder, but lacking the key definitional criteria of mania. Many of these children had ADHD, ODD, and/or CD. Second, in adult personality disorder in general[28–30] and in borderline personality in particular,[31,32] emotional dysregulation has been considered a critical dimension. The relationship between emotional dysregulation as described in these disorders and the version of emotional dysregulation used in these trials remains unexplored.

At this time, we still believe that the diagnosis of ADHD should be based on presence of sufficient attentional and/or hyperactivity/impulsivity symptoms. We view this set of emotional symptoms as being descriptive of more severely impaired adults with ADHD. Consequently, we would then advocate that patients with high levels of emotions be viewed as a distinct subgroup of adults with ADHD. In our studies, approximately 70% of the adults with ADHD have this set of symptoms. We suspect that the presence of emotional symptoms leads many clinicians to miss the diagnoses of ADHD. We also believe that such patients frequently end up on other psychotropic medications instead of those indicated for the treatment of ADHD.

This study had several limitations. First, the data were taken from 2 clinical trials as opposed to being an epidemiologic sample or using a random sample of psychiatric patients. Next, although both studies were positive, the MTS trial had a higher level of efficacy. The trials included different *DSM*-based ADHD scales. One study used the ADHD-RS and the other study used the CAARS, which differ enough that they could not be combined for this analysis. We are preparing to publish standardization data for the WRAADDS, but it has yet to go through the process of peer review. Finally, this study contains data from a self-report version of the WRAADDS and standardization data for this scale are being collected.

CONCLUSION

Data from 2 clinical trials of methylphenidate were combined for this report. Together they support including the 3 symptoms in emotional dysregulation as core symptoms of adult ADHD. In

the absence of other Axis I disorders, many of the patients were experiencing at least moderate impairment in emotional dysregulation. These symptoms help to define more complex and impaired patients with ADHD. The symptoms of emotional dysregulation responded to treatment in parallel with the 2 traditional *DSM* symptoms.

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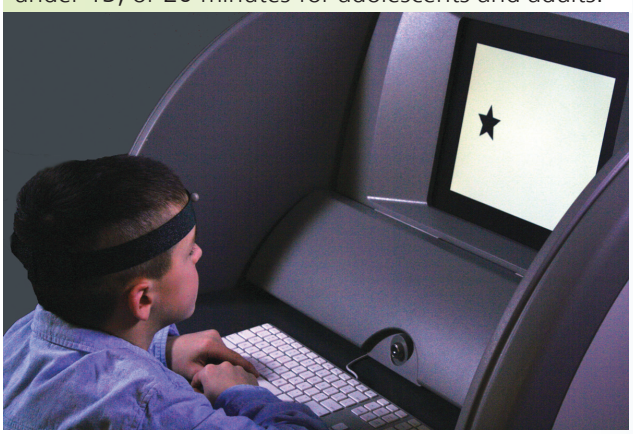

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