

Emotional Dysregulation in Adult ADHD and Response to Atomoxetine

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ABSTRACT

Objective: Agreement on the symptoms of adult ADHD remains problematic. The Wender-Reimherr Adult Attention Deficit Disorder Scale (WRAADDS) contains three items which could be considered signs of emotional dysregulation: temper, affective lability and emotional over-reactivity. Previously published data were reexamined to assess: 1) the pervasiveness of these symptoms; 2) if their presence predicted a favorable response to atomoxetine; and 3) was their response to atomoxetine similar to other ADHD symptoms.

Method: This placebo-controlled, double-blind study was conducted concurrently at 31 outpatient sites. Patients met DSM-IV criteria for ADHD, confirmed using the Conners' Adult ADHD Diagnostic Interview. Outcome was assessed using the Conners' Adult ADHD Rating Scale (CAARS) and the WRAADDS. Emotional dysregulation was operationally defined as scores of 7 or more on the three scales.

Results: Emotional dysregulation affected 31% of the population. There was a significant interaction between treatment and emotional dysregulation on improvement of the CAARS (p=.031). These emotional factors displayed a treatment effect (p<.001) similar to the CAARS.

Conclusions: Patient outcome was related to emotional dysregulation as defined using the WRAADDS. These emotional symptoms showed treatment effects that were statistically significant and similar in size to the traditional signs of hyperactivity/impulsivity and inattention.

INTRODUCTION

In the past, ADHD was known as MBD and included emotional and personality dimensions. It is uncertain whether these dimensions should be viewed as part of an ADHD spectrum or independent comorbid diagnoses. Recent studies with atomoxetine in adults were carefully designed to exclude other comorbid adult psychiatric diagnoses and used both the CAARS and WRAADDS to assess outcome. Three factors on the WRAADDS appear to measure emotional dysregulation while the other four factors measure DSM-IV criteria. These factors were used to assess the frequency of emotional dysregulation in adult ADHD. We then examined the attributes of these patients and effects of atomoxetine in these patients both on emotional dysregulation and DSM-IV criteria symptoms of ADHD.

METHODS

The impact of emotional dysregulation was evaluated using data from two identical studies conducted concurrently at 31 outpatient sites with 451 patients providing outcome data. Patients met DSM-IV criteria for ADHD assessed by clinical interview and confirmed by the Conners' Adult ADHD Diagnostic Interview. The CAARS, CGI-S and the WRAADDS were collected at baseline and study termination to assess outcome. Patients meeting DSM-IV criteria for current major depression, anxiety disorder, current or past bipolar disorder, psychotic disorders, any other current Axis I or alcohol dependence were excluded. Additionally, symptoms of depression and anxiety were evaluated using the HAMD-17 and HAM-A. The study consisted of a 3-week, pre-randomization phase followed by a 10-week, placebo-controlled, double-blind trial of atomoxetine.

The score separating patients who did or did not show emotional dysregulation on the three emotional factors of the WRAADDS was chosen by regressing the post-treatment on the pre-treatment scores of the two therapy groups.

RESULTS

At baseline, one-third of patients were experiencing emotional dysregulation. Prior analyses substantiate that atomoxetine was effective in the treatment of Adult ADHD using the WRAADDS, CAARS or CGI-Severity as the outcome measure.² When improvement on the CAARS was reanalyzed with treatment (placebo vs. atomoxetine) and emotional dysregulation (the sum of the 3 WRAADDS emotional factors) as between subject variables the interaction of these two variables was significant (p=.031). Patients experiencing emotional dysregulation displayed the greater treatment effect. Under placebo conditions, emotionally dysregulated patients showed less improvement (20%) than the others (28%). Under atomoxetine conditions the emotionally dysregulated patients showed more improvement (37%) than did the others (33%), but neither difference was statistically significant by itself. Patients experiencing emotional dysregulation displayed similar treatment effects across all measures of ADHD. For the CAARS (which does not include measures of emotional dysregulation) the treatment effect was p=.002; for the CGI-severity, p=.008; for the total WRAADDS, p=.001; and for Emotional Dysregulation, p=.001. Symptoms of emotional dysregulation improved 42% under atomoxetine and 19% under placebo conditions. Emotional dysregulation was not accounted for by changes in depression or anxiety. Although baseline measures of anxiety and depression were higher for the emotionally dysregulated patients, they were never-the-less low by clinical standards, and subsequently showed no treatment effect.

Table 1: Baseline Patient Characteristics of All Enrolled Patients and the Cohort Used in this Reanalysis.

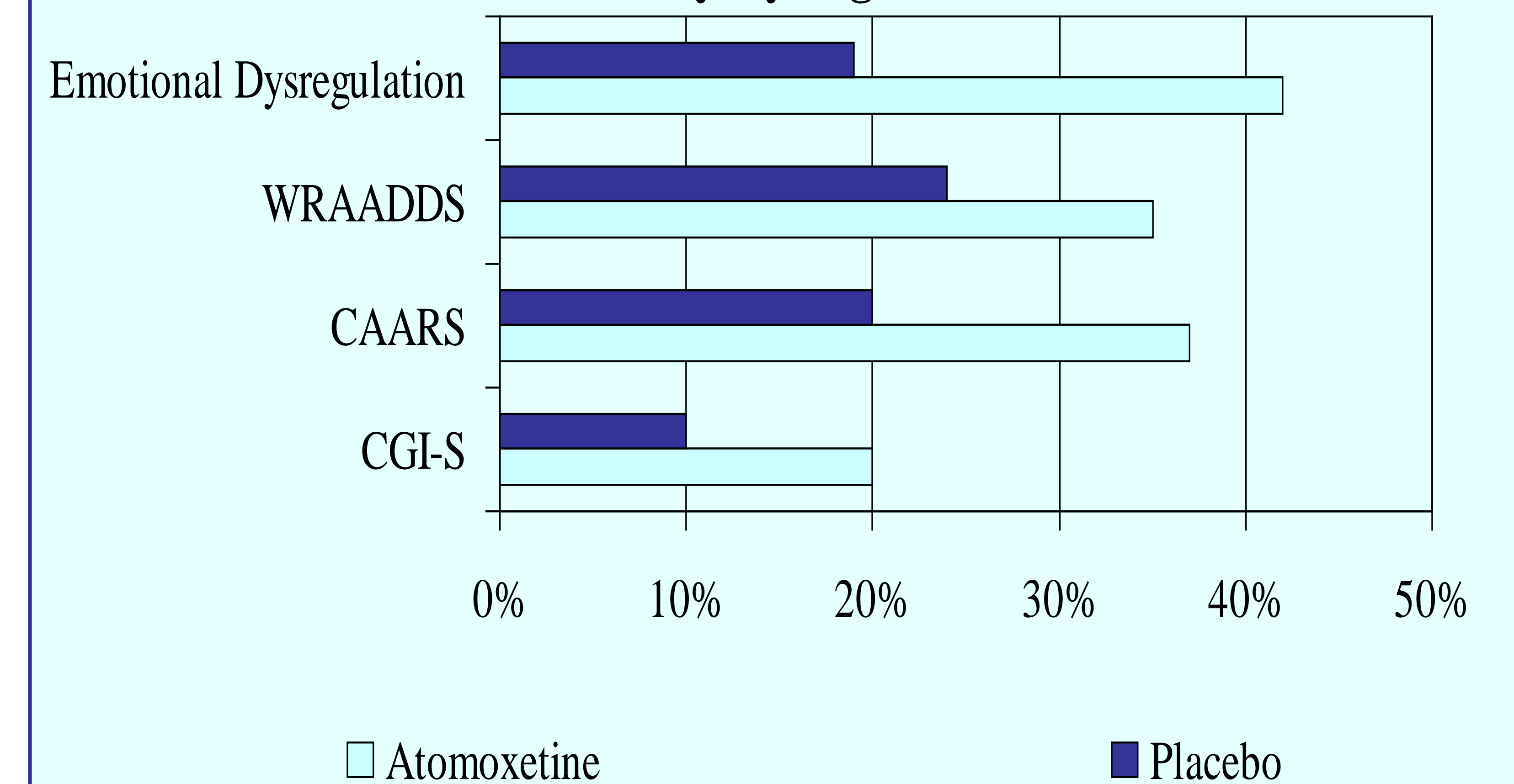
	All Randomized Patients	Emotional Dysregulated	Not Emotional Dysregulated	p-value ¹
N	536	142	302	
Male - n %	348 (65%)	84 (59%)	206 (68%)	ns
Age - mean (SD)	41.2 ± 11.2	40.4 ± 10.2	42.0 ± 11.6	ns
ADHD SubType - n(%)				
Combined	356 (66%)	117 (82%)	184 (61%)	
Inattention	167 (31%)	24 (17%)	110 (36%)	.001
Hyperactive/Impulsive	13 (2%)	2 (1%)	9 (3%)	
Previous Stimulant Exposure	43 (8%)	6 (4%)	27 (9%)	ns
HAMD-17	5.1 ± 3.6	6.0 ± 4.1	4.8 ± 3.4	.001
HAM-A	7.0 ± 4.9	9.2 ± 5.6	6.1 ± 4.4	.001
Baseline CAARS (total)	34.0 ± 7.4	38.9 ± 6.7	34.9 ± 7.4	.001
Baseline WRAADDS (total)	17.0 ± 4.9	22.2 ± 2.6	14.6 ± 0.7	.001
Baseline CGI-S	4.7 ± 0.7	4.9 ± 0.7	4.6 ± 0.7	.001

1) p-values compare the two emotional dysregulation groups.

Table 2: Efficacy Outcome for Both the WRAADDS and CAARS Factors for Patients Experiencing Emotional Dysregulation: Mean ± SD change from baseline to endpoint.

	Placebo	Atomoxetine	F	p-value
TOTAL WRAADDS	-3.7 ± 5.6	-7.5 ± 7.0	12.53	.001
Emotional Factors	-1.7 ± 2.8	-3.7 ± 3.3	15.10	.000
Inattention Factors	-.9 ± 1.9	-2.0 ± 2.4	8.59	.004
Hyperactivity Factors	-1.1 ± 1.8	-1.9 ± 2.2	5.03	.026
CAARS TOTAL-ADHD	-7.7 ± 9.4	-14.3 ± 13.5	10.24	.002
Inattentive	-3.6 ± 5.0	-7.4 ± 7.4	12.47	.001
Hyperactivity/Impulsivity	-4.1 ± 5.3	-6.6 ± 6.7	5.78	.018
CGI-S	-.5 ± 1.0	-1.0 ± 1.3	7.22	.008

Percent of Improvement as a Function of Treatment for the Emotionally Dysregulated Patients



CONCLUSIONS

- One third of patients in this study had substantial elevations on the three WRAADDS factors that appear to measure emotional dysregulation.
- Atomoxetine was superior to placebo in treating the symptoms of emotional dysregulation.
- Patients exhibiting emotional dysregulation displayed as much or more medication effect than the rest of the population.
- The increased medication effect was due to both a decrease in the placebo response rate and an increase in the atomoxetine response rate.
- Emotional dysregulation was not connected to symptoms of depression or anxiety in a clinically important manner.

REFERENCES

- 1) Wender, PH. Attention-Deficit Hyperactivity Disorder in Adults. (1995). Oxford University Press: New York.
- 2) Michelson D, Adler L, Spencer T, Reimherr FW, et al. Atomoxetine in Adults with ADHD: Two Randomized, Placebo-Controlled Studies. Accepted for publication by Biological Psychiatry.

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