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Severity of the Aggression/Anxiety-Depression/Attention (A-A-A) CBCL Profile Discriminates between Different Levels of Deficits in Emotional Regulation in Youth with ADHD

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Conflict of Interests:

Dr. Joseph Biederman is currently receiving research support from the following sources: Elminda, Janssen, McNeil, and Shire. *In 2011, Dr. Joseph Biederman* gave a single unpaid talk for Juste Pharmaceutical Spain, received honoraria from the MGH Psychiatry Academy for a tuition-funded CME course, and received an honorarium for presenting at an international scientific conference on ADHD. He also received an honorarium from Cambridge University Press for a chapter publication. Dr. Biederman received departmental royalties from a copyrighted rating scale used for ADHD diagnoses, paid by Eli Lilly, Shire and AstraZeneca; these royalties are paid to the Department of Psychiatry at MGH. *In 2010, Dr. Joseph Biederman* received a speaker's fee from a single talk given at Fundación Dr.Manuel Camelo A.C. in Monterrey Mexico. Dr. Biederman provided single consultations for Shionogi Pharma Inc. and Cipher Pharmaceuticals Inc.; the honoraria for these consultations were paid to the Department of Psychiatry at the MGH. Dr. Biederman received honoraria from the MGH Psychiatry Academy for a tuition-funded CME course. *In 2009, Dr. Joseph Biederman* received a speaker's fee from the following sources: Fundacion Areces (Spain), Medice Pharmaceuticals (Germany) and the Spanish Child Psychiatry Association.*In previous years, Dr. Joseph Biederman* received research support, consultation fees, or speaker's fees for/from the following additional sources: Abbott, Alza, AstraZeneca, Boston University, Bristol Myers Squibb, Celltech, Cephalon, Eli Lilly and Co., Esai, Forest, Glaxo, Gliatech, Hastings Center, Janssen, McNeil, Merck, MMC Pediatric, NARSAD, NIDA, New River, NICHD, NIMH, Novartis, Noven, Neurosearch, Organon, Otsuka, Pfizer, Pharmacia, Phase V Communications, Physicians Academy, The Prechter Foundation, Quantia Communications, Reed Exhibitions, Shire, The Stanley Foundation, UCB Pharma Inc., Veritas, and Wyeth.

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Abstract

Objective—We examined whether severity scores (1SD vs. 2SDs) of a unique profile of the Child Behavior Checklist (CBCL) consisting of the Anxiety/Depression, Aggression, and Attention (A-A-A) scales would help differentiate levels of deficits in children with ADHD.

Study Design—Subjects were 197 children with and 224 without ADHD. We defined deficient emotional selfregulation (DESR) as an aggregate cut-off score of >180 but <210 (1SD) on the A-A-A scales of the CBCL (CBCL-DESR) and Severe Dysregulation as an aggregate cut-off score of ≥210 on the same scales (CBCL-Severe Dysregulation). All subjects were assessed with structured diagnostic interviews and a range of functional measures.

Results—36% of children with ADHD had a positive CBCL-DESR profile vs. 2% of controls ($p<0.001$) and 19% had a positive CBCL-Severe Dysregulation profile vs. 0% of controls ($p<0.001$). The subjects positive for the CBCL-Severe Dysregulation profile differed selectively from those with the CBCL-DESR profile in having higher rates of unipolar and bipolar mood disorders, oppositional defiant and conduct disorders, psychiatric hospitalization at both baseline and follow up assessments, and a higher rate of the CBCL-Severe Dysregulation in siblings. In contrast, the CBCL-DESR was associated with higher rates of comorbid disruptive behavior, anxiety disorders, and impaired interpersonal functioning compared to other ADHD children.

Conclusion—Severity scores of the A-A-A CBCL profiles can help distinguish two groups of emotional regulation problems in children with ADHD.

Keywords

Affective symptoms; CBCL; bipolar disorder; Severity of illness index

INTRODUCTION

Recent research has begun to recognize that child patients with ADHD manifest deficient emotional self-regulation (DESR). DESR is characterized by poor self-regulation including such symptoms as low frustration tolerance, impatience, quickness to anger, and being easily excited to emotional reactions [1-3].

We recently showed that 44% (vs. 2% of controls, $p<0.001$) of children with ADHD had a profile of moderate (1SD) elevations on specific scales of the Child Behavior Checklist (CBCL) [4].This reflects intense emotions (Anxiety/Depression scale), aggression (Aggression scale) and impulsive behavior (Attention scale) (AAA profile) that we termed the CBCL- DESR profile. Results of this study also showed that ADHD children with the CBCL- DESR profile had elevated rates of anxiety and disruptive behavior disorders and significantly more impairment in emotional and interpersonal functioning when compared with ADHD children without this profile.

Although this profile was selected because of its conceptual congruence with the clinical concept of DESR, a more severe (>2SDs) form of the same profile has been postulated to measure the severe forms of dysregulated mood and behavior associated with pediatric bipolar disorder [5; 6]. This profile has been referred to as the CBCL-pediatric bipolar disorder profile (CBCL-PBD) [5; 6] by us and the CBCL-Dysregulation Profile (CBCL-DP) by others [7-9]. Several groups have shown that children with this profile on the CBCL are more likely than those without this profile to meet diagnostic criteria for DSM-bipolar-I disorder in both epidemiological and clinical samples [10-12]. Although the CBCL-PBD

profile is associated with a wide range of adverse outcomes including a higher risk to develop pediatric bipolar disorder, it is not a substitute for a clinical diagnosis of any specific psychiatric disorder. To avoid any confusion in this matter, we henceforth refer to this profile as the CBCL-Severe Dysregulation profile. Because we previously reported on the correlates of the CBCL-DESR and CBCL-Severe Dysregulation individually, uncertainties remain as to whether these two profiles can be clinically useful in distinguishing between children with varying levels of deficits.

Considering its empirical nature, its excellent psychometric properties and the its ease of use being as a paper and pencil instrument, whether the CBCL can help differentiate children with different levels of deficits is an area of very high clinical importance. Thus, knowledge derived from this work could translate into improved recognition and therapeutics in children at risk for differently compromised courses and outcomes and tailor the intervention strategy toward each condition.

The main aim of the present work was to further investigate if the two CBCL profiles can discriminate between different levels of deficits in emotional regulation in youth with ADHD. To this end, we directly compared the clinical, functional, and familial correlates of the CBCL-DESR and the CBCL-Severe Dysregulation profiles using data from large longitudinal studies of psychiatrically and pediatrically referred children with and without ADHD of both sexes. Based on our previous work, we hypothesized that subjects positive for the CBCL-DESR profile would differ from those positive for the CBCL-Severe Dysregulation profile, both qualitatively and quantitatively in their psychiatric, functional and familial correlates.

METHODS

Subjects

Detailed study methodology has been previously described [13; 14]. Briefly, subjects were derived from two identically designed longitudinal case-control family studies of ADHD. These studies recruited male and female probands aged 6-18 years with (n=140 boys, n=140 girls) and without (n=120 boys, n=122 girls) DSM-III-R ADHD ascertained from pediatric and psychiatric clinics and their first-degree relatives (ADHD families: n=280 mothers, n=274 fathers, n=317 siblings; Control families: n=242 mothers, n=235 fathers, n=260 siblings). Male probands were assessed at baseline and 4-year follow-up while female probands were assessed at baseline and 5-year follow-up. Potential probands were excluded if they had been adopted, or if their nuclear family was not available for study. We also excluded potential probands if they had major sensorimotor handicaps (paralysis, deafness, blindness), psychosis, autism, inadequate command of the English language, or a Full Scale IQ less than 80. Parents and adult offspring provided written informed consent to participate, and parents also provided consent for offspring under the age of 18. Children and adolescents provided written assent to participate. The human research committee at Massachusetts General Hospital approved this study.

Psychiatric assessments of probands younger than 18 years relied on the epidemiologic version of the Schedule for Affective Disorder and Schizophrenia for Children (Kiddie SADSE) [15; 16]. Subjects 18 years of age and older were assessed with the Structured Clinical Interview for DSM (SCID)[17; 18] (supplemented with modules from the K-SADS-E to assess childhood diagnoses). We interviewed the mothers for all subjects and directly interviewed subjects older than 12 years. We combined data from direct and indirect interviews by considering a diagnostic criterion positive if it was endorsed in either interview. Mothers and children were assessed by interviewers blind to all previous information about the child and family.

The interviewers had undergraduate degrees in psychology and were extensively trained. We computed kappa coefficients of agreement by having experienced clinicians diagnose subjects from audio taped interviews made by the psychometricians. Based on 500 tapes from interviews of children and adults, the median kappa coefficient between raters and clinicians was 0.98 for individual diagnoses. Kappa coefficients for individual diagnoses included: ADHD (0.88), CD (1.0), major depression (1.0), mania (0.95), separation anxiety (1.0), agoraphobia (1.0), panic (0.95), and substance use disorder (1.0). We considered a disorder positive if DSM diagnostic criteria were unequivocally met.

A committee of board-certified child and adult psychiatrists and experienced licensed psychologists who were blind to the subject's ADHD status, referral source, and all other data resolved diagnostic uncertainties from notes and information collected by the psychometrician in the structured interview.

Diagnoses presented for review were considered positive only when the committee determined that diagnostic criteria were met to a clinically meaningful degree. We estimated the reliability of the diagnostic review process by computing kappa coefficients of agreement for clinician reviewers. For these diagnoses, the median reliability between individual clinicians and the review committee assigned diagnoses was 0.87. Kappa coefficients for individual diagnoses included: ADHD (1.0), CD (1.0), major depression (1.0), mania (0.78), separation anxiety (0.89), agoraphobia (0.80), panic (.77), and substance use disorder (1.0).

All assessment personnel were blind to proband diagnosis (ADHD or control) and ascertainment site (psychiatric or pediatric). Psychoactive substance use disorder was defined as any alcohol abuse, alcohol dependence, substance abuse, or substance dependence.

Psychosocial functioning was assessed using the Social Adjustment Inventory for Children and Adolescents (SAICA) [19]. The SAICA provides an evaluation of children's functioning in school, in spare time activities, and with peers, siblings, and parents. A SAICA subscale is an average of 3 to 11 Likert items (e.g., 1=Not a Problem, 2=Mild Problem, 3=Moderate Problem, 4=Severe Problem) from an area of social functioning. Family functioning was defined using the Moos Family Environment Scale (FES) [20]. The FES uses standard scores with a mean of 50 and standard deviation of 10. Higher family conflict and lower family cohesion and expressiveness scores indicate poorer family functioning. Socioeconomic status (SES) was measured using the 5-point Hollingshead scale [21].

Child Behavior Checklist

The parent (usually the mother) of each participant completed the 1991 version of the Child Behavior Checklist for ages 4 to 18 years (CBCL/4-18). The CBCL is an affordable pencil and paper test completed by the child's caregiver, requiring no administration by a physician or rater. The CBCL queries the parent about the child's behavior in the past six months and aggregates this data into behavioral problem T-scores [22]. A computer program calculates the T-scores for each scale. Raw scores are converted to gender and age standardized scores (T-scores having a mean = 50 and SD = 10). A minimum T-score of 50 is assigned to scores that fall at midpoint percentiles of ≤50 on the syndrome scales to permit comparison of standardized scores across scales.

CBCL-DESR and CBCL-SEVERE DYSREGULATION Profiles

As described previously, the CBCL-Severe Dysregulation profile [5] was defined as positive by a score of ≥210 (2SDs) on the sum of the Attention, Aggression, and Anxious/Depressed

CBCL scales (AAA profile). The CBCL-DESR was defined as positive by a score of ≥ 180 (≥ 60 on average on each scale) but <210 (average T-score of ≥60 and <70 on AAA scales). For example, a subject with an Attention T-score of 55, an Aggression T-score of 65, and an Anxious/Depressed T-score of 75 would meet criteria for the CBCL-DESR profile (sum of 195 on all three scales).

Statistical Analysis

We compared Controls and ADHD probands with and without CBCL-DESR and CBCL-Severe Dysregulation on baseline demographic characteristics using t-tests, Pearson's chi-squared, or Wilcoxon rank-sum tests. Lifetime prevalence of baseline and one-year prevalence of follow-up psychiatric disorders were compared using logistic regression controlling for demographic confounders. Linear, logistic, or negative binomial regression was used depending on the distribution of other outcome measures. All tests were two-tailed with alpha set at 0.05.

RESULTS

Comparisons were made between ADHD subjects with a positive CBCL-DESR profile (ADHD+CBCL-DESR, N=86), ADHD subjects with a positive CBCL-Severe Dysregulation profile (ADHD+CBCL-Severe Dysregulation, N=45), ADHD subjects with neither (ADHD, N=111) and controls without ADHD or abnormal either CBCL profiles (Controls, N=224). There were no significant differences in sex between the groups (p=0.91, Controls=52% male, ADHD=55%, ADHD+CBCL-DESR=56%, ADHD+CBCL-Severe Dysregulation =53%). There were small but statistically significant differences in age between the groups (Controls: mean=11.9, standard deviation [SD]=3.4; ADHD: mean=11.2, SD=3.2, ADHD+CBCL-DESR: mean=10.7, SD=3.0, ADHD+CBCL-Severe Dysregulation: mean=10.1, SD=3.0), with ADHD+CBCL-DESR and ADHD+CBCL-Severe Dysregulation subjects being younger than Controls (both p<0.01). ADHD+CBCL-Severe Dysregulation subjects also had a significantly lower socioeconomic status (SES) compared to the other groups (all p<0.05, Controls: mean=1.6, SD=0.7; ADHD: mean=1.8, SD=1.0, ADHD+CBCL-DESR: mean=1.8, SD=0.9, ADHD+CBCL-Severe Dysregulation: mean=2.2, SD=1.0). Therefore, all subsequent analyses controlled for age and SES.

Rates of the CBCL-DESR profile and the CBCL-Severe Dysregulation profile were significantly higher in ADHD subjects (35.5% and 18.6%, respectively) compared to Controls (2.2% and 0%, respectively, both p<0.001).

Subjects with the ADHD+CBCL-Severe Dysregulation and ADHD+CBCL-DESR profiles had significantly more impairing ADHD than other ADHD subjects in a dose dependent fashion (ADHD=32% severe impairment, p<0.05 versus both ADHD+CBCL-DESR=50% and ADHD+CBCL-Severe Dysregulation =64%). Subjects with the ADHD+CBCL-Severe Dysregulation profile had a higher rate of psychiatric hospitalization at follow-up than the other ADHD subjects (Controls=0%, p<0.05 versus all 3 ADHD groups; ADHD=6%; ADHD+CBCL-DESR=9%; ADHD+CBCL-Severe Dysregulation =21%, p<0.05 versus other 2 ADHD groups). With one exception, (Difficulty Playing Quietly, ADHD=54% versus ADHD+CBCL-Severe Dysregulation =73%, p=0.01) the symptomatic picture of ADHD was similar in all three ADHD groups.

Patterns of Psychiatric Comorbidity and Dysfunction

As shown in Figure 1A, the baseline risks for ODD, CD, major depression and bipolar disorder were significantly higher among CBCL-Severe Dysregulation probands when compared with CBC-DESR and ADHD and Controls subjects. While the same trend was

observed for anxiety, SUDs and smoking, these differences failed to reach our a priori threshold for statistical significance. The same patterns were observed at follow-up, but the differences did not show the same statistical significance most likely due to lower absolute rates and more limited statistical power (Figure 1B).

Analysis of additional CBCL scales not used in the definitions of DESR and Severe Dysregulation profiles (non A-A-A scales) showed that all non-A-A-A CBCL scales differed significantly between CBCL-Severe Dysregulation and the CBCL-DESR groups at baseline and follow up assessments (Figure 2). Similar patterns were found for the SAICA at both baseline and follow up assessments (Figure 3). Placement in special class (Controls=2%, ADHD=25%, ADHD+CBCL-DESR=22% versus ADHD+CBCL-Severe Dysregulation =47%, all $p<0.05$) and impaired rates of family cohesion (Controls=53.3, ADHD=45.4, ADHD+CBCL-DESR=42.6 versus ADHD+CBCL-Severe Dysregulation =32.9, all $p<0.05$) however, were selectively associated with the ADHD+CBCL-Severe Dysregulation profile. Although ADHD+CBCL-Severe Dysregulation subjects also had worse measures of family conflict (Controls=51.2, ADHD=56.5, ADHD+CBCL-DESR=58.9, ADHD+CBCL-Severe Dysregulation =63.7) and expressiveness (Controls=49.9, ADHD=48.5, ADHD+CBCL-DESR=45.6, ADHD+CBCL-Severe Dysregulation =40.1) on the Family Environment Scale, they were only significantly worse compared to the Controls and ADHD group (all $p<0.05$).

Family Findings

As previously reported [23], all ADHD groups had significantly higher rates of ADHD in relatives than Controls (Figure 4A). A significant linear increase for the CBCL-DESR profile by logistic regression (lowest in Controls to highest in ADHD+CBCL-Severe Dysregulation probands) was found in siblings. In contrast, only siblings of ADHD+CBCL-Severe Dysregulation probands had a significantly higher rate of the CBCL-Severe Dysregulation profile.

DISCUSSION

The CBCL-Severe Dysregulation profile differed from the CBCL-DESR profile in terms of patterns of psychiatric comorbidity with mood and disruptive behavior disorders, more impaired scores on non-A-A-A CBCL scales, more impaired interpersonal (SAICA scores), educational (placement in special classes), and family (lowest cohesion levels) functioning at both baseline and follow-up assessments, higher rates of psychiatric hospitalization, and was selectively associated with the same profile in siblings. In contrast the CBCL-DESR profile was associated with higher rates of disruptive behavior and anxiety disorders and more impaired interpersonal functioning. These results provide evidence that the severity of the scores of the CBCL A-A-A scales (1SD for the CBCL-DESR and 2SDs for the CBCL-Severe Dysregulation) can help distinguish between ADHD children with differing risks for comorbidity and dsyfunction. The CBCL-Severe Dysregulation profile was associated with significantly higher rates of bipolar disorder, than subjects with the CBCL-DESR profile. This finding is consistent with previous work by us and others that documented an association between the CBCL-Severe Dysregulation profile with a diagnosis of bipolar disorder in children both cross-sectionally [6] and longitudinally [5]. Notably, in our study [6], the diagnostic efficiency of CBCL-Severe Dysregulation profile predictions of current (0.97) and lifetime (0.89) diagnosis of BPD as measured by the AUC statistic, were extremely high.

Also consistent with the hypothesis that the CBCL-Severe Dysregulation profile indexes liability for BPD in children with ADHD are the findings that this profile was associated selectively with higher rates of major depression and conduct disorder, very poor

psychosocial outcomes, higher rates of psychiatric hospitalization, and more impaired family cohesion scores than those observed in children with the CBCL-DESR profile. The CBCL-Severe Dysregulation profile was also selectively associated with a significantly higher rate of placement in special classes than those observed in children with the CBCL-DESR profile, reflecting the more severe behavioral, emotional and educational problems associated with bipolar symptomatology. In addition, only the CBCL-Severe Dysregulation profile bred true in siblings; the CBCL-Severe Dysregulation profile in siblings was selectively associated with the CBCL-Severe Dysregulation profile in probands when compared with subjects with the CBCL-DESR profile.

However, three studies [24-26] failed to find an association between the CBCL-Severe Dysregulation profile and a diagnosis of pediatric BPD. While Volk et al. [24] failed to find an association between the CBCL-Severe Dysregulation profile and a diagnoses of pediatric BPD using data from a population-based pediatric twin sample, they did find that children with a positive CBCL-Severe Dysregulation profile had more oppositional defiant disorder (ODD), conduct disorder (CD), ADHD, and suicidal behaviors than other children without it. In addition, the CBCL-Severe Dysregulation profile in Volk et al.'s [24] study was heritable and associated with the number of dopamine transporter (DAT1) 9-repeat 3' untranslated region alleles, a region recently associated with pediatric BPD [27]. Likewise, in the negative study by McGough et al. [25], the CBCL-Severe Dysregulation phenotype was associated with generalized anxiety disorder, ODD, and CD. The negative study by Youngstrom et al. [26] relied on archival data from a large sample from six urban community mental health centers (N=3086) with limited emphasis on operationalized diagnostic algorithms. More work is needed to help reconcile these discrepant findings.

In contrast to the findings associated with the CBCL-Severe Dysregulation profile, the CBCL-DESR profile had a different pattern of associated correlates; it was associated with significantly increased risks for disruptive behavior and anxiety disorders but not with major depression and bipolar disorder when compared with other ADHD subjects, as well as more impaired scores on all non A-A-A- CBCL scores and more impaired interpersonal functioning scores at both baseline and follow up. It also lacked unique patterns of family dysfunction and unique familial associations with the same CBCL-DESR profile in siblings.

These differential findings between the high (2SD) CBCL-A-A-A profile used to define the CBCL-Severe Dysregulation profile and the intermediate (1SD) (used to define DESR) support the hypotheses that different severity levels of the CBCL-A-A-A profile are associated with differing levels of risk, with the severe CBCL-Severe Dysregulation profile associated with the extreme form of mood dysregulation associated with mood disorders, while the intermediate CBCL profile identifies children with ADHD with difficulties in the regulation of strong emotions consistent with the conceptualizations of deficient emotional self-regulation (DESR). While both DESR and mood disorders involve emotional dysregulation, these constructs are substantially different clinically and therapeutically. The cardinal feature of mood disorders is the experience of strong emotions, not their self-regulation [28], which is the hallmark of DESR. Children who fulfilled the CBCL-DESR criteria were ***not*** more likely to have bipolar disorder or major depression than other children with ADHD. In this regard, our data support the utility of the two CBCL profiles in distinguishing children at substantially different levels of risks for adverse outcomes.

However, we emphasize that while the CBCL- Severe Dysregulation profile could be useful to help identify children at risk for BPD, clinicians should not use the CBCL to make a diagnosis of bipolar disorder. Yet, at a very minimum, the CBCL- Severe Dysregulation profile could alert the clinician that the child is at risk for very serious adverse psychopathological and functional outcomes.

Our findings need to be viewed in light of some methodological limitations. Severity scores on the same three CBCL clinical scales (A-A-A) were used to define both profiles. However, it is quite remarkable that marked and syndrome congruent differences were observed between the two profiles: the CBCL-Severe Dysregulation profile was associated with correlates seen in children with BPD and the CBCL-DESR profile (most fully articulated by Barkley) with current conceptualizations of DESR indexing deficits in self-regulating cognition and inhibiting behavior caused by strong emotions. However, others have used this scale without cutoffs to measure dysregulated mood, attention and behavior pathology across DSM-IV diagnoses [8] and we do not know whether our results would be replicated if other methods were used.

Although highly selected, trained and supervised raters administered the structured diagnostic interviews, they were not clinicians. Although our assessment methods may not elicit the same quality of information as clinician interviews, we documented very good kappa coefficients of agreement between lay interviewers and expert clinicians (see Methods). Because our sample had originally been collected for a family study of ADHD, our findings may not generalize to other populations. Because the sample was referred and largely Caucasian, findings may not generalize to community samples and other ethnic groups. While the CBCL remains an attractive tool for identifying children at risk for adverse outcomes due to its ease of administration, brevity, and reliability [22], CBCL scores in our sample are based solely on the mother's scoring. Despite these considerations, our findings indicate that the severity scores on a unique profile of the CBCL consisting of severe (2SDs, CBCL-Severe Dysregulation profile) and intermediate (>1 and <2 SDs; CBCL-DESR) scores on the Anxiety/Depression, Attention and Aggression scales can help identify children with differing levels of risk for morbidity and dysfunction in the primary care setting. Although our proposed classification of two CBCL-A-A-A profiles based on severity could be useful for clinicians for screening children at different level of risk for compromised outcomes, it is important to emphasize that these two profiles lie on a continuum with higher scores predicting greater levels of risk and impairment than the intermediate one. More work is needed to examine the utility of these CBCL profiles outside the context of ADHD.

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Abbreviations

Attention deficit hyperactivity disorder	ADHD
deficient emotional self regulation	DESR
Social Adjustment Inventory for Children and Adolescents	SAICA
Family Environment Scale	FES
Schedule for Affective Disorder and Schizophrenia for Children	Kiddie SADS-E
The Child Behavior Checklist	CBCL
Socioeconomic status	SES

oppositional defiant disorder	ODD
conduct disorder	CD
major depression	MDD
bipolar disorder	BPD
standard deviation	SD).

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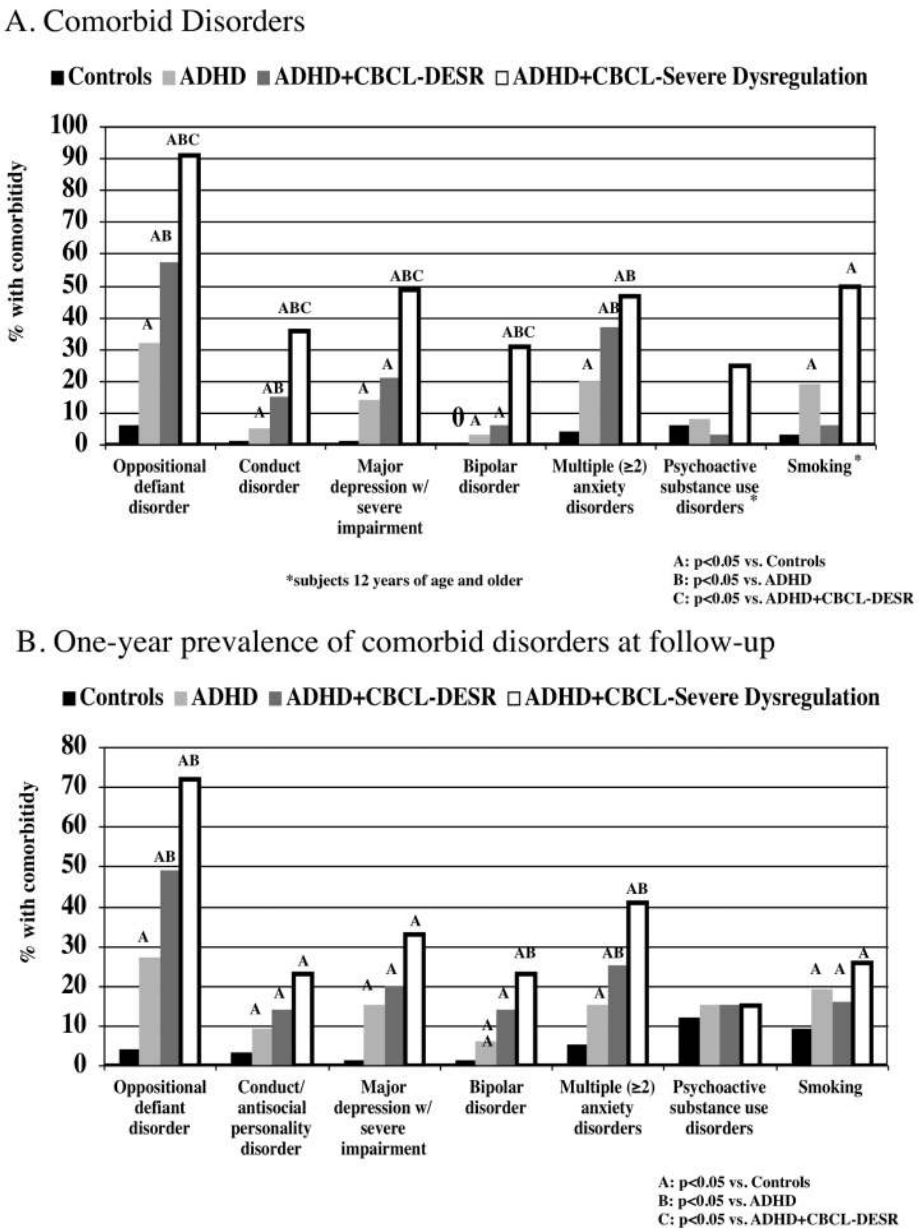


Figure 1.
CBCL-Dysregulation and Psychopathology. A. Comorbid Disorders; B. One-year prevalence of comorbid disorders at follow-up

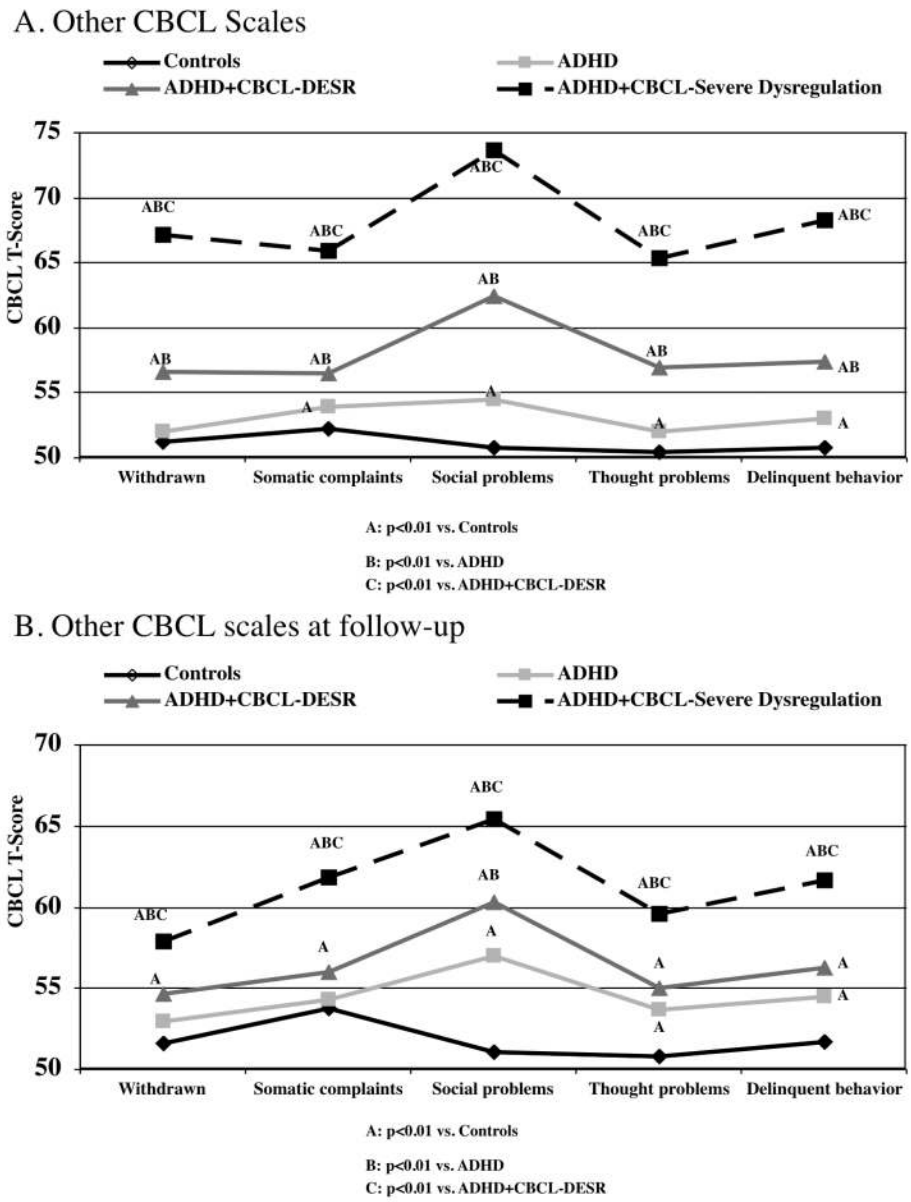
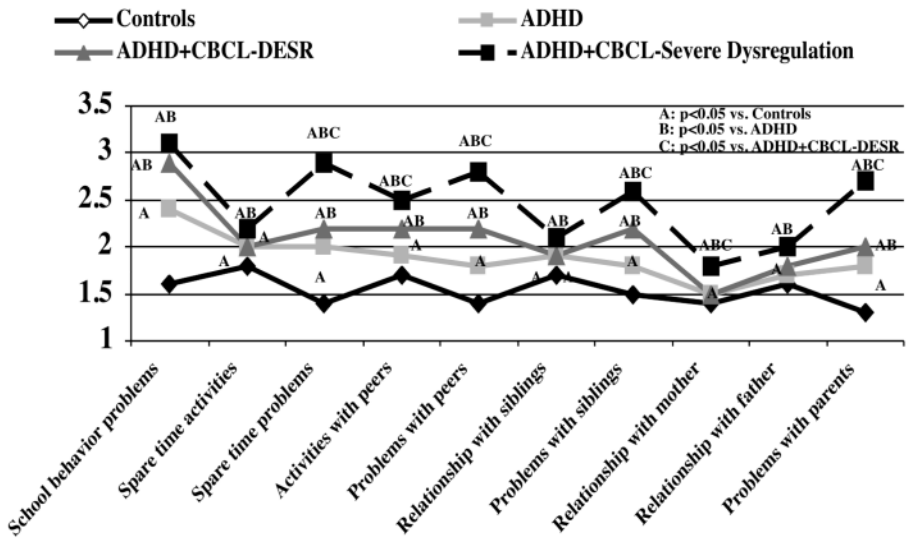


Figure 2.
CBCL-Dysregulation and Psychopathology. A. Other CBCL Scales; B. Other CBCL scales at follow-up

A. SAICA



B. SAICA at follow-up

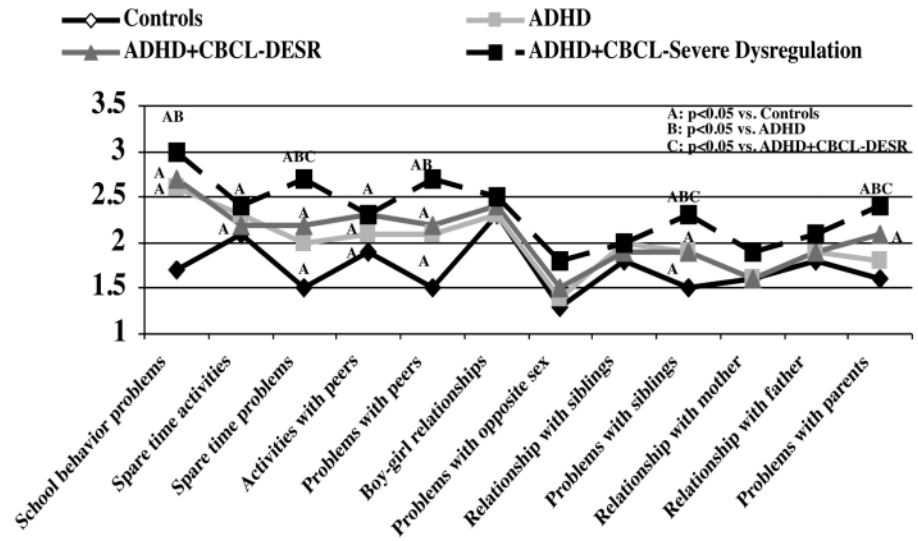


Figure 3.
A. SAICA; B. SAICA at follow-up

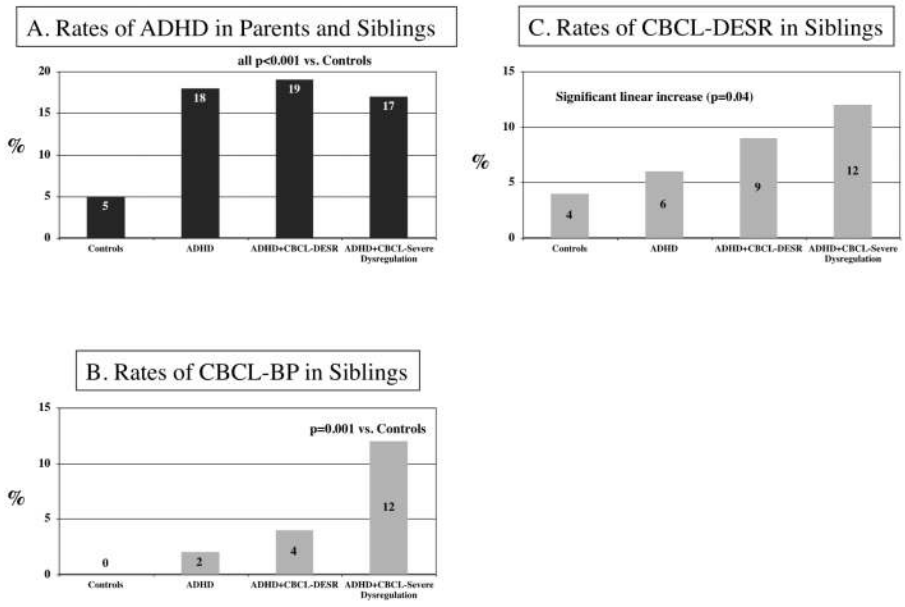


Figure 4.

Familial risk analysis of ADHD and CBCL-AAA Profile. A. Rates of ADHD in Parents and Siblings; B. Rates of CBCL-BP in Siblin; C. Rates of CBCL-DESR in Siblings.