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Research Report

Attention deficit hyperactivity disorder characteristics: II. Clinical correlates of irritable mood

Paul J. Ambrosini [a,*], David S. Bennett [a], Josephine Elia [b]

[a] Division of Child & Adolescent Psychiatry, Drexel University College of Medicine, Philadelphia, PA, USA
[b] Department of Child & Adolescent Psychiatry, The Children's Hospital of Philadelphia and Department of Psychiatry, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA

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ABSTRACT

Background: This study describes the relationship of irritable mood (IRR) with affective disorders in youths with attention deficit hyperactivity disorder (ADHD).
Methods: Five hundred ADHD subjects were assessed with the childhood version of the Schedule for Affective Disorder & Schizophrenia. Subjects were in a genetic ADHD protocol and limited to those of Caucasian/European descent.
Results: The most prevalent concurrent diagnoses were oppositional defiant disorder (ODD) (43.6%), minor depression/dysthymic disorder (MDDD) (18.8%), and generalized anxiety (13.2%)/overanxious disorder (12.4%). IRR subjects (21.0%) compared to the non-IRR (NIRR) group had higher rates of all affective disorders (76.2% vs. 9.6%) and ODD (83.8% vs. 32.9%) but lower rates of hyperactive ADHD (1.9% vs. 8.9%). Among those without comorbidities, 98.3% were NIRR. Logistic regression found IRR mood significantly associated with major depressive disorder (odds ratio [OR]: 33.4), MDDD (OR: 11.2), ODD (OR: 11.6), and combined ADHD (OR: 1.7) but not with anxiety disorders. Among symptoms, it associated IRR mood with a pattern of dysthymic and ODD symptoms but with fewer separation anxiety symptoms. Diagnostic and symptomatic parameters were unaffected by demographic variables.
Limitations: Potential confounders influencing these results include patient recruitment from only one clinical service; a cohort specific sample effect because some presumed affective disorders and non-Caucasians were excluded; and the young mean age (10.2 years) limiting comorbid patterns.
Conclusions: The prominence of an MDDD pattern suggests this IRR group is appropriate in the DSM V's proposed chronic depressive disorder, possibly with or without temper dysregulation. A new diagnosis of disruptive mood dysregulation disorder may be unwarranted.
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1. Introduction

Irritable mood (IRR) has taken center stage in the diagnosis of childhood-onset bipolar disorder. Numerous reports suggest that, in contrast to the "classical" distinct and time-limited periods of irritability and dysphoria, chronic, nonepisodic irritability is characteristic of pediatric bipolar disorder (Kowatch et al., 2005). This conceptualization of pediatric bipolarity emerged from Biederman's work, which first identified the association of nonepisodic irritability with bipolar symptoms in children with attention deficit hyperactivity disorder (ADHD) (Wozniak et al., 1995). As this theme entered the clinical practice of child psychiatry, reports of pediatric bipolarity greatly increased (Blader and Carlson, 2007; Moreno et al., 2007), although some questioned this interpretation of the clinical data (Biederman et al., 1998a; Brotman et al., 2006; Carlson, 1998; McClellan, 2005). This diagnostic issue was further complicated by the fact that irritability is associated not only with bipolar disorder but also with oppositional defiant disorder (ODD), major depressive disorder (MDD), and dysthymic disorder (DD) in youths (Mick et al., 2005). The diagnostic meaning of "rage attacks" or anger episodes in youths also remains unsettled (Carlson, 2007). Both clinical and physiological data regarding IRR are sparse (Leibenluft et al., 2003a).

Liebenluft has suggested interpreting this IRR phenotype as a manifestation of severe mood dysregulation (SMD) (Brotman et al., 2006; Leibenluft et al., 2003b, 2006; Stringaris et al., 2009). Although ongoing research is attempting to clarify the diagnostic parameters of early-onset bipolarity and severe mood disturbances, it is unclear how the symptom of irritability segregates within ADHD samples, how it influences the clinical presentation of ADHD, and whether there is a continuum between more severe rage and

* Corresponding author at: Drexel University College of Medicine Division of Child & Adolescent Psychiatryb P.O. Box 45358 Philadelphia, PA 19124, USA. Tel.: +1 215 831 6962; fax: +1 215 831 7830.
E-mail address: paul.ambrosini@drexelmed.edu (P.J. Ambrosini).

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less intense IRR. The *Diagnostic and Statistical Manual of Mental Disorders V* (DSM V) working committee is addressing this issue and has proposed a diagnostic category within the mood disorder section labeled disruptive mood dysregulation disorder (DMDD), based predominately on Liebenluft's work with SMD. This new classification attempts to more clearly differentiate the phenotype of SMD for both treatment and research purposes. The aim of this study was to identify the demographic and clinical characteristics of IRR in youths with ADHD and its relationship with comorbid disorders. Classification issues related to the IRR child are discussed.

2. Method

2.1. Procedures

This study used a cross-sectional design incorporating 500 parent-child triads with one or more ADHD probands. Subjects were recruited from local pediatric and behavioral health clinics for an ADHD genetic study. Patient recruitment was completed over a 55-month period and this sample represented consecutive admissions to the study. All subjects were Caucasian of European descent. Other ethnicities were excluded to maximize the power to detect genetic associations because haplotype frequencies can vary substantially across major world populations (Chang et al., 1996). Approximately 10% of the sample (52/500) were sibling pairs or triads. The initial inclusion/exclusion criteria were verified by phone screenings: age range, 6–18 years; presence of ADHD symptoms; European descent; and availability and willingness of both biological parents to participate in a genetic study. Exclusionary criteria were premature birth (at $<$ 36 weeks) and major medical, neurological, or neuropsychiatric problems including pervasive developmental disorder, mental retardation, psychoses, bipolar disorder, and MDD with symptoms starting prior to ADHD or with ADHD symptoms that occurred primarily during depressed episodes. Children with documented IQ scores $<$ 75 were excluded as were children unable to comprehend or complete the Schedule of Affective Disorders & Schizophrenia-Present State Version (K-SADS-P IVR).

A child psychiatrist trained to reliability with the K-SADS-P IVR completed the diagnostic assessments. This K-SADS is keyed to DSM IVR criteria, but where there is overlap with research diagnostic criteria (RDC), RDC take precedence (Spitzer et al., 1978). The K-SADS-P IVR records irritability as a symptom independent of depressed mood. Irritability/anger (subjective) was added as a third primary symptom of major depression to verify whether it was synonymous with depressed mood. K-SADS defined irritability/anger as a subjective feeling of bad temper, short temper, crankiness, or annoyance within the context of a mood disorder. This change permitted diagnosing an "irritable affective disorder," which is a depressive disorder in which irritability replaces depressed mood or pervasive anhedonia as the cardinal symptom. This approach implies that those with IRR affective disorders met standard diagnostic criteria but had IRR mood only, not depressed mood or pervasive anhedonia. The symptoms (being easily angered and easily annoyed) are within the domain of ODD. These are overt symptoms related to being easily bothered by or resentful of others. This is ODD-type irritability as described by Biederman's group (Mick et al.,2005). All ADHD and concurrent comorbid diagnoses analyzed were active at the time of the evaluation; furthermore, subjects were not in treatment by the research team when assessed.

For this study, several diagnostic groupings were calculated: MDDD (minor depression [MD] or dysthymic disorder [DD]); any anxiety disorder (AnyAD); and any depressive disorder (AnyDD). Minor depression is an RDC category that includes the criteria of major depression plus 8 additional symptoms (Table 1). The four ADHD subtypes are labeled inattentive ADHD (ADDI), hyperactive ADHD (ADDH), combined ADHD (ADDC), and ADHD not otherwise specified (ADDN). A detailed list of the diagnoses available with the K-SADS-P IVR is available (Elia et al., 2008). This protocol was approved by the institutional review boards of the participating institutions.

2.2. Statistical analysis

All K-SADS score sheets were scanned into an SPSS (version 18) database for analyses. Descriptive statistics, including examination of sex differences in demographic variables and comorbidity rates, are presented using *t* tests and chi-square tests. Chi-square analyses were used to examine comorbidity differences between the IRR and NIRR

Table 1
Criteria of minor depression.

Criterion	Minor depression (RDC)	Dysthymic disorder (DSM IVTR)	Overanxious disorder (DSM III/IIIR)
Dysphoric mood	+	+	
Two or more of the following:	+	+	na
Decrease/increase appetite or weight loss/gain	+	+	
Sleep difficulty or excess sleep	+	+	
Loss of energy/fatigue	+	+	
Psychomotor agitation/retardation	+		
Loss of interest/pleasure	+		
Self-reproach/excessive guilt	+		
Difficulty concentrating /indecisive	+	+	
Suicidal ideation/behavior	+		
Tearfulness or sad facies	+		
Pessimistic attitude (hopeless/helpless)	+	+	
Brooding	+		+
Feeling inadequate (negative self-image)	+	+	+
Resentful, irritable, angry, complaining	+		
Demanding/clinging (excessive reassurance)	+		+
Self-pity	+		
Excessive somatization (aches and pains)	+		+
Duration	1 wk for probable; 2 wk for definite	1 y, child; 2 y, adult	6 months
Not meet criteria for other mood disorders	+	variable	na
May be superimposed on other nonaffective disorders	+	+	na
Impairment at home, work or in social situations	+	+	+

DSM III/IIIR = *Diagnostic and Statistical Manual of Mental Disorders,* 3rd Edition Revised; DSM IVTR = *Diagnostic and Statistical Manual of Mental Disorders*, 4th Edition, Text Revision; na = not applicable; RDC = research diagnostic criteria.

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