

## Parsing the familiarity of oppositional defiant disorder from that of conduct disorder: A familial risk analysis

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### Abstract

**Background:** Family risk analysis can provide an improved understanding of the association between attention-deficit/hyperactivity disorder (ADHD) and oppositional defiant disorder (ODD), attending to the comorbidity with conduct disorder (CD).

**Methods:** We compared rates of psychiatric disorders in relatives of 78 control probands without ODD and CD (Control,  $N = 265$ ), relatives of 10 control probands with ODD and without CD (ODD,  $N = 37$ ), relatives of 19 ADHD probands without ODD and CD (ADHD,  $N = 71$ ), relatives of 38 ADHD probands with ODD and without CD (ADHD + ODD,  $N = 130$ ), and relatives of 50 ADHD probands with ODD and CD (ADHD + ODD + CD,  $N = 170$ ).

**Results:** Rates of ADHD were significantly higher in all three ADHD groups compared to the Control group, while rates of ODD were significantly higher in all three ODD groups compared to the Control group. Evidence for co-segregation was found in the ADHD + ODD group. Rates of mood disorders, anxiety disorders, and addictions in the relatives were significantly elevated only in the ADHD + ODD + CD group.

**Conclusions:** ADHD and ODD are familial disorders, and ADHD plus ODD outside the context of CD may mark a familial subtype of ADHD. ODD and CD confer different familial risks, providing further support for the hypothesis that ODD and CD are separate disorders.

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### 1. Introduction

Oppositional defiant disorder (ODD) is the most common comorbidity of attention-deficit/hyperactivity disorder (ADHD). Studies have shown that as many as 65% of youth with ADHD have ODD (Biederman et al., 1996b; Kadesjo and Gillberg, 2001; Kadesjo et al., 2003). The behaviors characterizing ODD – temper outbursts, persistent stubbornness, resistance to directions, unwilling-

ness to compromise with adults or peers, deliberate or persistent testing of limits, and verbal (and minor physical) aggression – compound the difficulties of children with ADHD (Biederman et al., 1987, 1991).

Yet, despite the high overlap between these disorders, there has been little investigation of ODD comorbid with ADHD (Loeber et al., 2000). Also, because ODD has been studied largely within the context of conduct disorder (CD), almost nothing is known about ODD proper. This is an important issue considering that a majority of children with ODD do not have CD and may not progress to CD in later years (Hinshaw et al., 1993; Lahey and

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Loeber, 1994; Biederman et al., 1996b). Furthermore, as shown by Greene et al. (2002), ODD is associated with substantial morbidity and significant family and social dysfunction, even when considered outside the context of CD, stressing the importance of disentangling the relationships between ADHD and ODD outside the context of CD. Recent longitudinal studies have shown that ODD is a pivotal developmental disorder that is associated with subsequent mood and behavioral disorders independently of CD (Burke et al., 2005; Biederman et al., in press).

One useful approach to evaluate the association between ADHD and ODD is to examine the familial transmission of these disorders. Familial risk analyses can address whether the aggregation of two disorders through families is compatible with various models of familial transmission as delineated by Pauls et al. (1986b). While disruptive and antisocial behavior has been shown to aggregate in families (Loney et al., 1997; Lahey et al., 1998; Farrington et al., 2001), these models can help in disentangling the patterns of familial transmission of several disorders such as ADHD, ODD, and CD. Although these models have successfully clarified patterns of familial transmission between ADHD and CD (Faraone et al., 1998, 2000), they have not been previously used to examine the association between ADHD and ODD.

An improved understanding of the nature of the association between ADHD and ODD has important scientific and clinical implications. It is possible that the abnormal behavioral and emotional difficulties seen in children with ODD might contribute to such youths being incorrectly classified as ADHD. Conversely, since oppositional behavior is so prevalent in youths with ADHD, such behavior might reflect ADHD and not a separate disorder. Since ADHD and ODD are each morbid psychiatric disorders, clarifying the overlap between them would assist in the development of appropriate interventions to help specifically target the needs of children with these clinical presentations.

The main purpose of this study was to use familial risk analysis to examine the association between ADHD and ODD while addressing the comorbidity with CD. Familial risk analysis examines rates of disorders in the relatives of probands with and without the disorders of interest in order to understand patterns of familial transmission. Co-segregation, the tendency for disorders to be inherited together, identifies the disorders of interest as a family subtype as opposed to independently transmitted. Previously, we have parsed the familial associations of ADHD and CD in a series of papers that suggested ADHD + CD is a distinct familial subtype of ADHD (Faraone et al., 1991, 1997, 2000). The current work extends this line of research by assessing the familial transmission of ODD when it occurs outside the context of CD. We tested three competing hypotheses: (1) ADHD and ODD are independently transmitted in families; (2) ODD plus ADHD represents a distinct subtype of ADHD; and (3) ADHD and ODD represent variable expressions of the same underlying risk factors. In addition, we further examined family risks by comparing the rates of mood, anxiety, and substance

dependence in relatives of probands with and without ADHD, ODD, and CD. To the best of our knowledge this represents the first attempt at elucidating the familial association between ADHD and ODD.

## 2. Methods

### 2.1. Subjects

Subjects were derived from a longitudinal case-control family study of boys with ADHD (Biederman et al., 1992; Biederman et al., 1996a; Biederman et al., 2006). At baseline, we ascertained male Caucasian subjects aged 6–17 years with ( $N = 140$ ) and without ( $N = 120$ ) DSM-III-R ADHD from pediatric and psychiatric clinics. Previously, this sample was followed-up at 1 year and 4 years after baseline. The present study reports on the 10-year follow-up of this sample, where 112 ADHD and 105 control probands were successfully re-ascertained. Details on attrition are provided in a previous publication (Biederman et al., 2006). Briefly, the rate of successful follow-up did not differ between the groups and there were no significant differences between those successfully followed up and those lost to follow-up on age, GAF score, familial intactness, ascertainment source, or psychiatric outcomes. At the 10-year follow-up, probands with ADHD were younger, had lower family socioeconomic status, and had higher lifetime rates of all psychiatric disorders compared to controls (Table 1).

For this analysis, probands were stratified according to ADHD ascertainment status, ODD diagnosis, and CD diagnosis (Table 2). Groups with fewer than 10 probands were dropped from this analysis (nine controls with CD, eight controls with ODD and CD, and five ADHD probands with CD only). Therefore, the final sample consisted of 107 ADHD and 88 control probands and their first-degree relatives ( $N = 371$  and  $N = 302$ , respectively). Parents were assessed at baseline only, while the siblings were assessed at baseline ( $N = 218$ ), 1-year follow-up ( $N = 227$ ), 4-year follow-up ( $N = 247$ ), and 10-year follow-up ( $N = 271$ ). Nearly all siblings were assessed at the 10-year follow-up (96%,  $N = 271$ ), while 4% were not (4-year follow-up,  $N = 9$ ; 1-year follow-up,  $N = 2$ ; baseline,  $N = 1$ ).

As described previously (Biederman et al., 1992, 1996a; Biederman et al., 2006), at baseline, 1-year follow-up, and 4-year follow-up, diagnostic assessments of ADHD were based on the K-SADS-E (Epidemiologic 4th Version) (Orvaschel and Puig-Antich, 1987). 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.

### 2.2. Follow-up assessment procedures

Lifetime psychiatric assessments at the 10-year follow-up relied on the K-SADS-E (Epidemiologic Version)

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