



Symptoms of autism and schizophrenia spectrum disorders in clinically referred youth with oppositional defiant disorder

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ABSTRACT

Examined autism spectrum disorder (ASD) and schizophrenia spectrum disorder (SSD) symptoms in a clinically referred, non-ASD sample ($N = 1160$; ages 6–18) with and without oppositional defiant disorder (ODD). Mothers and teachers completed *DSM-IV*-referenced symptom checklists. Youth with ODD were subdivided into angry/irritable symptom (AIS) or noncompliant symptom (NS) subtypes. Two different classification strategies were used: within-informant (source-specific) and between-informant (source-exclusive). For the source-specific strategy, youth were classified AIS, NS, or Control (C) according to mothers' and teachers' ratings separately. A second set of analyses focused on youth classified AIS according to mother or teacher report but not both (source-exclusive) versus both mother and teacher (cross-informant) AIS. Results indicated the mother-defined source-specific AIS groups generally evidenced the most severe ASD and SSD symptoms ($AIS > NS > C$), but this was more pronounced among younger youth. Teacher-defined source-specific ODD groups exhibited comparable levels of symptom severity ($AIS, NS > C$) with the exception of SSD ($AIS > NS > C$; younger youth). Source-exclusive AIS groups were clearly differentiated from each other, but there was little evidence of differential symptom severity in cross-informant versus source-exclusive AIS. These findings were largely dependent on the informant used to define the source-exclusive groups. AIS and NS groups differed in their associations with ASD and SSD symptoms. Informant discrepancy provides valuable information that can inform nosological and clinical concerns and has important implications for studies that use different strategies to configure clinical phenotypes.

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1. Introduction

During the past decade, much progress has been made in conceptualizing emotional, behavioral, and cognitive disturbances among children with autism spectrum disorder (ASD) as co-occurring syndromes, many of which appear to share similarities in clinical features with psychiatric disorders defined in the *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV; American Psychiatric Association, 1994)*, though they are not necessarily clinically equivalent in terms of phenomenology, response to intervention, or natural history. This effort has been matched by an equally ambitious endeavor to examine ASD symptoms in nonASD, clinically referred, and population-based samples (e.g., Constantino & Todd, 2003; Gadow, DeVincent, Pomeroy, & Azizian, 2005; Kunihiro, Senju, Dairoku, Wakabayashi, & Hasegawa, 2006; Posserud, Lundervold, & Gillberg, 2006; Reiersen, Constantino, Volk, & Todd, 2007; Ronald, Simonoff, Kuntsi, Asherson, & Plomin,

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2008). The collective results of these and related efforts indicate that the phenotypic characteristics of psychiatric disorders are widely distributed in the general population and commonly co-occur in neurodevelopmental syndromes, which poses enormous challenges to the pursuit of more compelling models of nosology and pathogenesis.

One psychiatric syndrome of particular relevance for ASD is oppositional defiant disorder (ODD), which is characterized by angry and irritable affect and noncompliant behaviors. Collectively, the symptoms of ODD are (a) common reasons for clinical referral and personal and family distress for individuals with ASD, (b) the focus of much interest in pharmacotherapy (reviewed by Stigler & McDougle, 2008), and (c) the only Food and Drug Administration-approved indications for psychotropic medication among ASD individuals in the United States. Although figures vary, a substantial percentage of children with ASD meet *DSM-IV* diagnostic or symptom criteria for ODD (e.g., de Bruin, Ferdinand, Meester, de Nijs, & Verheij, 2007; Gadow et al., 2005; Simonoff et al., 2008; Witwer & Lecavalier, 2010) or evidence marked problems with specific symptoms such as irritability (Lecavalier, 2006; Mayes, Calhoun, Murray, Ahuja, & Smith, 2011). Some of these studies involve hundreds of youth with ASD, something almost unheard of just a decade ago.

Although research is limited, children with ASD plus ODD appear to differ in clinically important ways from youth with ASD who do not meet symptom criteria for ODD (Gadow, DeVincent, & Drabick, 2008). Moreover, there are similarities in associated clinical features of ODD among children with and without ASD, including (a) differentially more severe co-occurring psychiatric symptoms (Gadow, DeVincent, & Drabick, 2008) and sleep problems (DeVincent, Gadow, Delosh, & Geller, 2007) compared with peers without ODD; (b) informant discrepancies (mother versus teacher) in perceived symptom severity (Gadow, DeVincent, & Drabick, 2008); and (c) association with similar psychosocial and biological risk factors (e.g., Dean et al., 2010; Gadow, DeVincent, Olvet, Pisarevskaya, & Hatchwell, 2010; Gadow, DeVincent, & Schneider, 2008; Kirley et al., 2004). Although these consistencies support a “co-morbidity” interpretation, there are inconsistencies in the literature as well, and it is fair to say that the issue is far from being (if ever) resolved.

As for typically developing youth, a community-based study of preschoolers (Gadow & Nolan, 2002) found higher levels of ASD symptom severity among children who met symptom criteria for ODD versus peers who did not, and this was true for both mothers’ and teachers’ ratings. Similarly, Mulligan et al. (2009) examined a sample of 821 youth with attention-deficit/hyperactivity disorder (ADHD), their siblings, and controls, and found elevated levels of ASD severity in probands, with differentially higher levels in probands with ADHD plus ODD. Importantly, they also suggested that assessment of ASD symptoms at intake may be a useful indicator of risk for developing ODD or conduct disorder.

1.1. ODD and DSM-5

As with most psychiatric disorders, only a subset of symptoms is required for a diagnosis (*polythetic criteria*), and this inevitably results in phenotypic heterogeneity (Drabick, 2009; Sanislow et al., 2010). Given that angry/irritable symptoms (AIS) of ODD may contribute uniquely to the development of anxiety and mood disorders (Burke & Loeber, 2010; Burke, Hipwell, & Loeber, 2010; Leibenluft, Cohen, Gorrindo, Brook, & Pine, 2006; Rowe, Costello, Angold, Copeland, & Maughan, 2010; Stringaris & Goodman, 2009a, 2009b), the ADHD and Disruptive Behavior Disorders Workgroups for *DSM-5* recommended organizing ODD symptoms within the *DSM* to distinguish between AIS and noncompliant symptoms (NS) (reviewed by Pardini, Frick, & Moffitt, 2010; www.dsm5.org). This is also relevant for the National Institute of Mental Health’s (NIMH) recent Research Domain Criteria (RDoC) initiative, which identifies negative affect as one of its recognized domains (Sanislow et al., 2010). Our own prior research (Drabick & Gadow, 2012; Gadow & Drabick, submitted for publication) with the same large sample of clinically referred youth examined in the present study indicates that (a) individuals with ODD and more severe AIS differ in a number of ways from youth with primarily NS (Drabick & Gadow, 2012), and (b) youth whose AIS are essentially a problem at home but not school and vice versa are unique in a number of ways that suggest possible differences in pathogenesis (Gadow & Drabick, submitted for publication).

1.2. Schizophrenia spectrum disorder

Although child-onset schizophrenia is uncommon in ASD (reviewed by Starling & Dossetor, 2009), the symptoms of ASD and schizophrenia spectrum disorder (SSD) often co-occur (e.g., Sporn et al., 2004; Weisbrot, Gadow, DeVincent, & Pomeroy, 2005), are moderately to highly inter-correlated (e.g., Barneveld et al., 2011), and share pathogenic mechanisms (Cheung et al., 2010; Guilmatre et al., 2009; Kirov et al., 2008; Mikhail et al., 2011; Sahoo et al., 2011; Sebat, Levy, & McCarthy, 2009; Sugranyes, Kyriakopoulos, Corrigall, Taylor, & Frangou, 2011; Walsh et al., 2008). Thus, further study of their interrelation is warranted (Gadow & DeVincent, 2012). SSD symptoms are included in the present study given that both ASD and SSD are (a) characterized by social interaction deficits and (b) associated with emotion dysregulation (Gadow & DeVincent, 2012; Weisbrot et al., 2005).

1.3. Objectives

In spite of an intuitive overlap among disorders characterized by deficits in social interactions and emotion dysregulation, relatively little is known about ASD or SSD symptoms among youth with ODD, and more specifically, whether there is a differentially greater association with AIS or NS. The present study examined ASD and SSD symptom severity in a large sample ($N = 1160$) of clinically referred, non-ASD youth between 6 and 18 years of age. Although an alternative approach is to

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