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

Kenneth D. Gadow[a,*] and **Deborah A.G. Drabick**[b]

Kenneth D. Gadow: kenneth.gadow@stonybrook.edu; Deborah A.G. Drabick: ddrabick@temple.edu

[a]Department of Psychiatry and Behavioral Sciences, Putnam Hall, South Campus, Stony Brook University, Stony Brook, NY 11794-8790, USA

[b]Department of Psychology, Temple University, Weiss Hall, 1701 North 13th Street, Philadelphia, PA 19122-6085, USA

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.

Keywords

Oppositional defiant disorder; Autism spectrum disorder; *DSM-5*; Schizophrenia spectrum disorder; Anger; Irritability

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

*Corresponding author. Tel.: +1 631 632 8858; fax: +1 631 632 3703.

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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; Kunihira, Senju, Dairoku, Wakabayashi, & Hasegawa, 2006; Posserud, Lundervold, & Gillberg, 2006; Reiersen, Constantino, Volk, & Todd, 2007; Ronald, Simonoff, Kuntsi, Asherson, & Plomin, 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 includedinthe 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 study these interrelations among youth with ASD, a compelling case also canbe made for such research in general population samples (e.g., Kelleher, Jenner, & Cannon, 2010; Whalley et al., 2011). Youth who met *DSM-IV* symptom criteria for ODD were subdivided into angry/irritable symptom (AIS) or noncompliant symptom (NS) subgroups. Youth with fewer than four ODD symptoms (the number of required symptoms in *DSM-IV*) served as Controls. Despite the relative absence of research in this area, we made the following predictions. We expected (1) more severe ASD symptoms among youth with ODD compared with Controls, with (2) differentially higher levels among youth with AIS versus NS (Drabick & Gadow, 2012). As ASD and SSD symptoms are interrelated (Gadow & DeVincent, 2012), we also expected (3) a similar pattern of relations for SSD symptoms.

There is relatively modest overlap among children that mothers and teachers characterize as ODD in both ASD (Gadow, DeVincent, & Drabick, 2008) and non-ASD (Drabick, Gadow, & Loney, 2007) samples. Thus, two different strategies for defining clinical phenotypes were examined. One set of analyses focused on within-informant group differences in youth classified AIS versus NS defined separately according to mothers' and teachers' ratings (source specificity) (Drabick et al., 2007; Drabick, Bubier, Chen, Price, & Lanza, 2011;

Drabick & Gadow, 2012; Offord et al., 1996). For these source-specific analyses, we expected (4) greater AIS and NS group differences with teachers' than mothers' ratings (e.g., Dirks, Boyle, & Georgiades, 2011; Drabick et al., 2007, 2011). However, one potential limitation of this strategy is that youth with cross-informant AIS are included in both source-specific groups. Therefore, the second set of analyses focused on between-informant differences in youth classified AIS according to mother or teacher report but not both (source-exclusive) versus cross-informant (both mother and teacher) AIS (Drabick, Gadow, & Loney, 2008; Gadow & Drabick, submitted for publication). We expected (5) the source-exclusive (i.e., context bound) AIS groups to differ from each other because the grouping strategy maximizes informant disagreement. If cross-informant AIS represent a differentially more biologically impacted syndrome (see Gadow & Drabick, submitted for publication) or possibly a more homogeneous phenotype, then we would expect (6) the cross-informant group to have more severe co-occurring ASD and SSD symptoms (i.e., less contextually bound) than the source-exclusive groups. Finally, the facts that childhood-onset schizophrenia is rare and the peak ages of onset of psychosis are late adolescence and early adulthood (Paus, Keshavan, & Giedd, 2008) suggest that the severity of at least some SSD symptoms may change over time. Although there are some preliminary data among clinically referred youth to suggest this may not be the case for many SSD symptoms (e.g., Ulloa et al., 2000), we nevertheless expected (7) the pattern of differences in SSD symptom severity would vary for younger versus older ODD groups.

2. Materials and methods

2.1. Participants

Participants were parents (primarily mothers) and teachers of 1160 youth who were consecutive referrals to a university hospital child psychiatry outpatient service that serves an ethnically and economically diverse clientele. Given well-established developmental differences in the emergence of psychiatric symptomatology, we divided the sample into a younger (6–11 year olds; $n = 546$; 73% males) and older (12–18 year olds; $n = 614$; 67% males) cohort (full sample $M = 12.1$, $SD = 3.4$ years; 70% males). Caregiver-identified ethnicity was as follows: European-American ($n = 977$; 84%), African-American ($n = 81$; 7%), Hispanic-American ($n = 127$; 11%), Native-American ($n = 12$; 1%), Asian-American ($n = 30$; 3%), and Other ($n = 11$; 1%). Most (84%) youth lived with their biological mothers and fathers (62%), and in 65% of the cases, parents were married. The two most common clinician-assigned diagnoses were ADHD and ODD, and almost all youth with ODD were also co-morbid for ADHD. This retrospective chart review study was approved by a university Institutional Review Board, and appropriate measures were taken to protect patient (and rater) confidentiality.

2.2. Measures

Mothers and teachers rated youth's symptoms using the *Child and Adolescent Symptom Inventory-4R* (CASI-4R; Gadow & Sprafkin, 2005). The CASI-4R is a parent-(163-item) and teacher-(120-item) completed behavior rating scale for evaluating youth 5–18 years old and combines the symptom modules from the *Child Symptom Inventory-4* (Gadow & Sprafkin, 1986, 2002) and the *Adolescent Symptom Inventory-4* (Gadow & Sprafkin, 1995, 2008). Individual items bear one-to-one correspondence with *DSM-IV* symptoms and are rated on a scale from 0 (*never*) to 3 (*very often*). Item responses were summed to create Symptom Severity scores for ASD and SSD symptoms. Research indicates the ASD subscale has relatively high sensitivity and specificity for identifying children with ASD (DeVincent & Gadow, 2009; Gadow, Schwartz, DeVincent, Strong, & Cuva, 2008). In the present study, Cronbach's alpha was high for both mother- and teacher-completed ASD severity scores (αs = 0.86 and 0.89, respectively). We also examined severity scores for

each of the three core domains of ASD (4 items each) for mothers' and teachers' ratings, respectively: Communication Deficits (αs = 0.70, 0.74), Social Deficits (αs = 0.80, 0.84), and Perseverative Behaviors (αs = 0.68, 0.76). Findings from a number of studies support the divergent validity of the three core ASD domains (e.g., Gadow, DeVincent, & Pomeroy, 2006; Gadow, DeVincent, & Schneider, 2009; Gadow, Guttmann-Steinmetz, Rieffe, & DeVincent, 2011; Guttmann-Steinmetz, Gadow, DeVincent, & Crowell, 2010; Lecavalier, Gadow, DeVincent, Houts, & Edwards, 2009).

The SSD subscale (11 items) of the CASI-4R is comprised of the *DSM-IV*-defined symptoms of schizophrenia and schizoid personality disorder, two disorders that are phenomenologically and genetically related (Faridi, Pawliuk, King, Joober, & Malla, 2009; Mata et al., 2000). The findings from a number of studies indicate CASI-4R SSD component subscales demonstrate satisfactory internal consistency; convergent and discriminant validity with relevant measures; and agreement with structured interview or clinician diagnoses (e.g., Gadow & Sprafkin, 2002, 2008, 2010; Grayson & Carlson, 1991; Mattison, Gadow, Sprafkin, Nolan, & Schneider, 2003; Weisbrot et al., 2005). In the present study the internal reliabilities of the mother/teacher SSD subscale were high (αs = 0.84/0.88).

2.3. Procedure

Prior to scheduling their initial clinic evaluation, parents were mailed a packet of materials including behavior ratings scales for both parent and teacher, background information questionnaire, and permission for release of school, psychoeducational, and special education evaluation records. Teacher ratings were given to the school by parents, completed by teachers (96%), and mailed to the clinic prior to the evaluation. Youth with both parent and teacher reports (n = 1111) and youth with reports from only one informant (n = 49) did not differ on any categorical or dimensional ODD scores, ethnicity, family income, or parental education. However, compared to youth with one informant's report, youth with both informants' reports, respectively, were younger (*Ms* = 13.3 versus 12.0 years), more likely to be male (55% versus 70%), and more likely to have married parents (47% versus 66%).

2.4. Subgrouping

The present study builds on previous research using a priori operationalized criteria for AIS and NS as proposed for *DSM-5*. For both subgrouping strategies, youth with severity ratings of often or very often for “loses temper,” “is angry and resentful,” and “is touchy or easily annoyed by others” were placed in the AIS subgroup. For the source-specific subgrouping strategy, youth were classified as AIS based on mother report (AIS:M) or teacher report (AIS:T). The remaining youth were classified as primarily NS if they met severity criteria for four ODD symptoms, but two or fewer AIS, or Controls (three or fewer ODD symptoms). When mothers' ratings were the basis of group classification, 212 younger (70% male) and 284 older (69% male) youth met symptom criteria for ODD, of whom 53% (n = 112, 63% male) and 64% (n =181, 70% male), respectively, were classified AIS. Remaining youth were Controls (younger cohort: n = 328, 74% male; older cohort: n = 319, 66% male). Using teachers' ratings to construct groups, 204 younger (79% male) and 195 older (77% male) youth were ODD, of whom 61% in each age group (younger cohort: n =125, 82% male; older cohort: n =119, 77% male) were classified AIS. Remaining youth were Controls (younger: n = 333, 69% male; older: n = 396, 63% male).

For the source-exclusive subgrouping strategy, cross-informant youth had to meet criteria for AIS according to both mothers' and teachers' ratings (AIS:M + T; younger cohort: n = 38, 68% male; older cohort: n = 52, 83% male). Informant-exclusive groups were constructed on the basis of one (but not both) informant indicating AIS status: mother only

(AIS:M; younger cohort: *n* = 76, 60% male; older cohort: *n* = 131, 66% male) and teacher only (AIS:T; younger cohort: *n* = 89, 89% male; older cohort: *n* = 68, 74% male). The remaining youth were classified NS (younger cohort: *n* = 21, 81% male; older cohort: *n* = 22, 77% male) if they met severity criteria for four ODD symptoms from either informant, but neither informant endorsed more than two AIS symptoms. Youth were classified Controls (younger cohort: *n* =314, 71% male; older cohort: *n* =316, 65% male) if they were rated as having three or fewer ODD symptoms from each informant.

2.5. Statistical analyses

We conducted one-way ANOVAs with follow-up LSD tests for significant findings (two-tailed) to localize differences among groups. We used a Bonferroni correction within measure. Effect sizes (eta^2) are reported for the main effects and can be interpreted as follows: 0.01 (small), 0.06 (medium), and 0.14 (large; Cohen, 1988).

3. Results

3.1. Source-specific AIS and NS

Mother-defined AIS and NS groups were rated as having more severe ASD and SSD symptoms than Controls (Table 1), with the exception of communication deficits among younger youth (AIS > NS,C). Moreover, younger youth with AIS were rated as having more severe ASD and SSD symptoms than the NS group; however, with two exceptions (ASD social deficits and ASD summary score), this was not the case among older youth.

Teacher-defined AIS and NS groups were rated as having more severe ASD and SSD symptoms than Controls (Table 2). However, unlike mother-defined groups, younger teacher-defined AIS and NS groups evidenced comparable levels of symptom severity, with the exception of SSD (AIS > NS). Among older youth, the AIS and NS groups did not differ from each other for any of the ASD and SSD variables.

3.2. Source-exclusive and cross-informant AIS

Mothers' ratings did not support the notion that cross-informant AIS was associated with more severe ASD and SSD symptoms than source-exclusive AIS:M (Table 3). However, in most instances the two source-exclusive groups were different from each other in a manner consistent with the informant whose ratings were used to define ASD and SSD (AIS:M > AIS:T). Moreover, the AIS:T group was generally comparable to Controls. The NS group was rated as having more severe symptoms than Controls for several variables including SSD symptoms (both younger and older youth). The NS group also differed from AIS groups for perseverative behaviors (AIS:M + T > NS, younger cohort) and SSD symptoms (AIS:M > NS, younger cohort; NS > ASI:T, older cohort).

Teachers' ratings evidenced a generally similar pattern of group differences as mothers' ratings, with the notable exception that younger children in the AIS:T group had more severe communication deficits and ASD summary scores than the cross-informant (AIS:M + T) group (Table 4). However, older AIS:M + T and AIS:T youth were rated similarly. In all but one instance (SSD symptoms, older youth), the two source-exclusive groups were different from each other in a manner consistent with the informant whose ratings were used to define ASD and SSD (AIS:T > AIS:M). Symptom severity scores for the AIS:M group were generally comparable to Controls. Among the younger cohort, the NS group differed from source-exclusive AIS groups for social deficits (AIS:T > NS) and perseverative behaviors (NS > AIS:M).

4. Discussion

Although the ASD literature is replete with research about emotion recognition and findings are mixed (e.g., Jones et al., 2011), relatively less is known about emotion dysregulation with the notable exception of anxiety (reviewed by White, Oswald, Ollendick, & Scahill, 2009). This is curious as many youth with ASD who are referred for clinic or school evaluations experience intense emotional reactions (e.g., anger, irritability), and these reactions play an important role in referral for pharmacotherapy, isolation from peers, parental stress, and family distress. Nevertheless, their co-occurrence raises questions as to whether they are epiphenomena of the ASD clinical phenotype, clinical features of a distinct subtype of ASD, or pathogenically similar to phenomena in non-ASD samples. Evidence of an association between emotion dysregulation and ASD symptomatology in non-ASD referrals suggests shared risk factors, supports dimensional models of symptom behaviors (Barneveld et al., 2011; Drabick, 2009), and underscores the potential value of pursuing similar pathogenic models in youth with ASD. The results of the present study indicate many clinically referred, non-ASD youth with ODD (AIS and NS) exhibit elevated symptoms of ASD and SSD compared with Controls (Prediction 1), and this appears to be the case regardless of age, informant, or source-specific versus source-exclusive comparisons, with one notable exception (i.e., mother-rated communication deficits among younger youth, Table 1). Consistent with the procedure for constructing ODD symptom groups, source-exclusive AIS differed from Controls (who according to both informants had few ODD symptoms) only when the same informant's ratings served as the basis for defining AIS group and ASD and SSD symptom severity (Tables 3 and 4). The extant literature and our reported findings indicate that the emotion dysregulation and interpersonal conflicts that define ODD, to include peer conflicts (Drabick & Gadow, 2012; Gadow & Drabick, submitted for publication), may share similarities with communication and social skills deficits of ASD and SSD; indeed, perhaps the most salient similarity is that social interactions are challenging and thus generate a range of intense emotional reactions. It is also possible that ASD and SSD represent divergent extremes of similar processes (Crespi & Badcock, 2008; Russell-Smith, Maybery, & Bayliss, 2010). Our expectation that source-specific symptom groups based on teachers' (Table 2) versus mothers' (Table 1) ratings would reveal more pronounced group differentiation (AIS, NS, Controls) was not supported (Prediction 4). Indeed, differences between AIS and NS groups were observed more frequently among mother-defined groups (AIS > NS for 7 of 10 comparisons; Table 1) than teacher-defined groups (AIS > NS for 1 of 10 comparisons; Table 2). Consistent with this pattern, there was a slightly greater number of group differences for mothers' (Table 3) versus teachers' (Table 4) ratings of source-exclusive groups compared to cross-informant groups.

4.1. Differential validity of AIS and NS (Prediction 2)

Consistent with our expectation that emotion dysregulation (i.e., anger, irritability) would share more commonality with ASD than NS, within-informant group comparisons indicated youth with source-specific AIS had more severe ASD and SSD symptoms than the source-specific NS groups, but this was the case only for mothers' ratings of younger children, mother's ratings of social deficits in older youth (Table 1), and teachers' ratings of SSD in younger children (Table 2). Nevertheless, these results provide additional support for the notion that AIS and NS represent divergent phenomena in non-ASD clinically referred youth, and extend this observation to ASD and SSD symptoms. Although the AIS and NS dichotomy is sometimes referred to as the affective and behavioral aspects of ODD, respectively (Burke & Loeber, 2010), it is possible that these symptom groups pertain to different types of affect with unique neurobiologic substrates and phylogenetic histories

(e.g., NS may be more associated with novelty-seeking/exploratory behaviors; Alcaro, Huber, & Panksepp, 2007; Drabick & Gadow, 2012).

4.2. Similarities between ASD and SSD (Prediction 3)

In general, both ASD and SSD symptoms evidenced a similar pattern of source-specific (Tables 1 and 2) and source-exclusive group differences (Tables 3 and 4), which was not unexpected as both symptom domains appear to be interrelated (Gadow & DeVincent, 2012). We are mindful of the extraordinary conceptual issues surrounding the differential validity of ASD and SSD symptoms (see Starling & Dossetor, 2009) and would simply add that some questions may not be resolvable with our current nosology. For example, a youth who is cognitively rigid and consequently encounters difficulties complying with authority figures and getting along with peers would exhibit at least one symptom of ASD, but would likely be classified as ODD in everyday clinical settings. Our current categorical nosology may not be well-equipped to address these issues (e.g., Crespi, 2010; Meyer-Lindberg, 2010; Panksepp, 2006), including difficulty with differential diagnosis, informant perceptions, and use of multiple informants (Drabick, 2009; Gadow & DeVincent, 2012).

4.3. Behavioral variation and informant discrepancies (Prediction 5)

For decades, investigators have reported modest levels of agreement between different informants' ratings of child psychopathology, which is illustrated by the findings of an influential meta-analysis conducted by Achenbach, McConaughy, and Howell (1987) who examined inter-rater correlations from 119 studies. They found the *average* correlation between parents' and teachers' ratings of child behavior was low ($r = .27$). Although there has been a long-standing tendency to dismiss the significance of informant differences as being “measurement error” or “methodological nuisances” (see De Los Reyes, 2011), findings of studies conducted in multiple countries have found differences in the environmental, biological, and behavioral concomitants of cross-situational, source-specific, and source-exclusive ODD (e.g., Dirks et al., 2011; Drabick & Gadow, 2012; Drabick et al., 2007, 2008, 2011; Gadow & Nolan, 2002; Gadow, DeVincent, & Drabick, 2008; Gadow, Chernoff, et al., 2010; Munkvold, Lundervold, Lie, & Manger, 2009; Offord et al., 1996; Severa, Lorenzo-Seva, Cardo, Rodríguez-Fornells, & Burns, 2010; Wood, Rijsdijk, Asherson, & Kuntsi, 2009) and between mothers' and teachers' perceptions of therapeutic improvement in ODD symptoms consequent to intervention (e.g., Gadow, Nolan, Sverd, Sprafkin, & Schneider, 2008). As we have discussed elsewhere (Gadow & Drabick, submitted for publication), these source-exclusive groups differ in a wide range of background characteristics and school-functioning variables, some of which (e.g., parental discipline, failure to do school work) are likely behavioral antecedents of or triggers for intense emotional reactions among youth with AIS.

Variation in behavioral, physiological, and morphological characteristics (traits) in response to different environmental variables (*phenotypic plasticity*) is a fundamental concept in evolutionary biology and a pervasive feature of life on this planet (Piersma & van Gils, 2010) and plays an important role in human health and disease (e.g., Hochberg et al., 2011). It can be either reversible or permanent and provides a conceptual model for understanding informant discrepancy. A child can behave very differently in different settings (intra-individual variation), and children vary in their ability to modulate their own behavior according to the demands of the situation (inter-individual variation). Reversible, intra-individual differences in behaviors modulated by environmental variables (*phenotypic flexibility* or *behavioral plasticity*) can be highly stable in specific environments and show little correlation with behaviors in different settings (*context specific*) (e.g., Komers, 1997; Piersma & Drent, 2003; Wilson, 1998). A parallel concept (*developmental plasticity*) applies to irreversible, inter-individual variation in traits resulting from gene × environment

interactions during developmental periods. In other words, developmental plasticity refers to an organism's ability to adjust its developmental trajectory in response to environmental cues. Both phenomena apply to child neurobehavioral syndromes and are probably best illustrated in the case of ADHD (which is highly co-morbid with both ODD and ASD (Gadow et al., 2006; Gadow, DeVincent, & Drabick, 2008)) simply because it is the most common child psychiatric disorder and consequently the most studied.

Many children with ADHD evidence dramatic within-individual changes in behavior depending on contextual features (e.g., task demands, novelty, level of structure, adult presence), illustrated by compliant behavior when in the physician's office (Sleator, 1982). Behavioral plasticity among children with ADHD is also evident in response to different activities within the same school setting (e.g., Whalen et al., 1978; Zentall & Zentall, 1975). Moreover, their reactions to environmental variation evidence between-individual variation compared with typically developing peers without ADHD (e.g., Porrino et al., 1983). Consistent with these observations, there is growing evidence suggesting that common genetic polymorphisms interact with environmental factors to influence within- and between-individual differences in behavioral plasticity (e.g., Bakermans-Kranenburg & vanIJzendoorn, 2007; Belsky et al., 2009; Dmitrieva, Chen, Greenberger, Ogunseitan, & Ding, 2010; Martel et al., 2011; Reiner & Spangler, 2010).

Our research extends this line of inquiry to inter-individual variation within the ODD clinical phenotype by comparing children who were seemingly less behaviorally plastic in terms of emotion regulation (i.e., youth who were rated as having AIS according to both mothers and teachers) with peers who appeared to be more plastic (i.e., exhibited AIS according to only one informant) (Tables 3 and 4). Phenotypic flexibility in youth with ADHD (e.g., Marwit & Stenner, 1972), ODD (e.g., Gadow & Drabick, submitted for publication), or AIS is likely mediated at least in part by cognitive and other child-specific variables (e.g., common gene variants; Belsky et al., 2009) that modulate reactions to task demands and contextual features. In summary, from our perspective, informant discrepancy is not only expected but also clinically relevant, and may be explained in part in terms of mechanisms that underlie behavioral plasticity.

4.4. Cross-informant syndromes (Prediction 6)

Our expectation that cross-informant AIS would be associated with more severe ASD and SSD symptoms than source-exclusive AIS was generally not supported with two notable exceptions: (a) teachers' ratings of communication deficits (but not SSD) symptoms among 6–11 year olds (AIS:T > AIS:M + T), and (b) mothers' ratings of the AIS:T group (Table 3) and teachers' ratings of the ASI:M group (Table 4) (i.e., cross-informant ratings of the source-exclusive groups.) The fact that the younger, teacher-exclusive group had more severe ASD symptoms than the cross-informant group suggests a more environmentally sensitive condition. As previously noted, one plausible explanation for the former seemingly counter-intuitive finding is that different pathogenic processes may be linked to the informant or the environment that serves as the informant's frame of reference (e.g., De Los Reyes & Kazdin, 2005; Drabick et al., 2008). For example, communication and social skills play an important role in successful school functioning, and it is therefore not unexpected that children in the teacher-exclusive AIS group would obtain higher scores for these symptoms than the AIS:M + T group. This is also consistent with our previous findings of a differentially higher rate of early language problems in these same children with AIS:T (see Gadow & Drabick, submitted for publication).

4.5. Age (Prediction 7)

Consistent with our prediction that younger and older youth would exhibit a different pattern of group differences in SSD severity, informants indicated differences between source-specific AIS and NS groups in younger (AIS > NS > C; Table 1) but not older (AIS,NS > C; Table 2) youth. Interestingly, this same pattern of group differences was obtained for both mothers' and teachers' ratings. There were also age-related differences in findings for source-exclusive groups. Unlike source-specific groups, comparisons for each informant and each age cohort resulted in a unique outcome (Tables 3 and 4), though the cross-sectional design precludes our ability to draw conclusions about developmental differences related to age or informant.

4.6. Strengths and limitations

The present study has several strengths, including an operationalized, dimensional approach to parsing ODD symptoms, based on the recommendations for *DSM-5* of an expert consensus panel that reviewed relevant data (Pardini et al., 2010), and assessing ASD and SSD symptoms (Barneveld et al., 2011); a large study sample; consideration of different age groups; and comparison of different informants. Nevertheless, many different biologic, cognitive, and environmental processes can lead to seemingly similar behavioral outcomes (Drabick, 2009), well illustrated by deficits associated with ASD versus SSD (e.g., Crespi & Badcock, 2008; Russell-Smith et al., 2010), and these variables were not considered in the present study. Moreover, although relatively unstudied, it is likely that the social and emotional symptoms that define ODD are pathogenically heterogeneous, and much additional research will be required to understand how they relate to AIS, NS, ASD, and SSD. Given the preponderance of males in the AIS and NS subgroups, we were unable to consider whether patterns of findings differed based on gender. The fact secondary school teachers spend considerably less time with individual students than their colleagues in elementary schools likely impacts opportunities to observe intense emotional reactions by the former.

Information about SSD symptoms (and to some extent ASD symptoms in older youth) are often obtained from self-report (e.g., rating scales, clinical interviews) measures in clinical research, which in the case of SSD may be particularly important for the assessment of positive symptoms such as hallucinations and delusions. Moreover, there is generally poor agreement between parent and youth self-report of psychiatric symptoms (Achenbach et al., 1987; Gadow, Chernoff, et al., 2010). Nevertheless, this does not invalidate mothers' and teachers' ratings of SSD as potentially useful markers of phenotypic heterogeneity or their use in improving understanding of pathogenic processes. For example, poor insight correlates with SSD symptom severity among individuals with adolescent-onset psychosis (Parellada et al., 2009) and ASD is characterized by poor self awareness; therefore, comparisons between younger ASD and non-ASD samples may greatly benefit from the use of caregiver report. Nevertheless, generalization of this study's findings is bounded by assessment and informant considerations.

Age was an important variable in the pattern of diagnostic group differences and though clinically informative, a cross-sectional design cannot address developmental processes. It is reasonable to hypothesize that older youth may represent a somewhat different segment of the clinical population consisting of both early-onset cases with protracted difficulties refractory to caregiver efforts or environmental modifications, as well as youth with recent-onset disturbances modulated in part by different biological process. It would be important to learn whether co-occurring ASD or SSD symptoms in youth with AIS or NS are risk factors for later mental health concerns, and in the case of SSD, whether these relations are similar in ASD and nonASD samples.

Finally, we did not collect information about setting-specific (e.g., individual freedom to chose activity, peer or sibling behaviors, empathy, demands on working memory) or important child-specific (e.g., sensitivity to reward, planning abilities, emotion recognition) variables that may induce or exacerbate intense emotional responses or youth's ability to regulate their reactions. Additional research will be required to determine their role as potential mediators of ODD symptom mechanisms and ASD/SSD processes.

4.7. Clinical and research implications

Owing to the inevitable overlap among youth classified as source-specific versus source-exclusive, it was not possible to test which strategy was superior; however, a more reasonable objective is to determine under what circumstances a particular strategy may be more useful. We illustrate this situation with the following example: in the case of short-acting stimulant medication, it could be argued that if problem behaviors occur primarily in the home (or school), then the evaluation of treatment effects may be better served with parents' (or teachers') assessments, and treatment could be administered in such a way as to address the most problematic setting. Thus, the classification strategy resulting in the greatest degree of phenotypic homogeneity for the purposes of a specific application (e.g., intervention, determination of course) would likely be the most ideal. Unfortunately, in research settings, this may encourage consideration of data from one informant only, which consequently undermines the study of informant discrepancies.

A related issue pertains to qualitative differences in information obtained from different informants. For example, mothers observe child behavior in a much wider range of settings (within-child) than teachers, which is often interpreted to mean their observations are more clinically valid because they capture the youth's “true” behavior. Conversely, a case can be made for the advantages of teachers' ratings as the school provides a standard setting with a restricted range of environmental experiences with many peers and is therefore better able to illuminate individual differences (between child). Moreover, teachers share fewer similarities in genetic background and environmental experiences with their pupils than parents, which is important given the reciprocal nature of social interactions. In view of this complexity, it is truly impressive that any scientific progress is made in understanding emotional responses in children with the aid of conventional assessment instruments.

Proscriptions for action in clinical and research settings are conflicted. In clinical applications, obtaining information from multiple informants, particularly diagnostic evaluations and response to pharmacotherapy, has been advocated for several decades. In clinical research settings, things are a bit muddled. As previously noted, informant discrepancies are often considered a nuisance for many reasons (including an obstacle to publication success; De Los Reyes, 2011). Nevertheless, we would encourage other investigators to examine informant discrepancies with the goal of generating a better understanding of etiology, response to intervention, and predictors of long-term outcome.

As previously discussed (Gadow et al., 2004), informant discrepancy has considerable significance for the interpretation and conduct of clinical research because investigators have generally used the findings of structured interviews with the primary caregiver to construct clinical phenotypes, occasionally conducting similar interviews with the youth. In parallel fashion, many psychologists and school-based investigators have relied heavily on information obtained from the youth's teacher to address inter-individual differences. More recently researchers have incorporated information obtained from multiple informants (i.e., the “or rule”) to define clinical constructs. As the results of the present study indicate, however, these different strategies for defining clinical phenotypes may lead to very different conclusions about similarities and differences between diagnoses and inferences about the magnitude of therapeutic improvement.

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Table 1

Means (SDs) and comparison statistics for mothers' ratings of ASD and SSD symptoms in mother-defined (source-specific) ODD subgroups and clinic controls.

Variable	**Angry/irritable (AIS)**	**Noncompliant (NS)**	**Controls (C)**	***F***	**eta^2**	**Post hoc**
Ages 6–11 years	***n* = 112**	***n* = 100**	***n* = 328**			
ASD						
Communication deficits	2.3 (2.5)	1.7 (2.0)	1.1 (1.8)	14.4***	0.05	AIS > NS,C
Social deficits	4.2 (3.3)	2.7 (2.4)	1.4 (2.0)	61.3***	0.19	AIS > NS > C
Perseverative behaviors	3.4 (2.5)	2.4 (2.6)	1.4 (1.9)	33.6***	0.11	AIS > NS > C
ASD summary score	9.7 (6.6)	6.8 (5.5)	3.9 (4.9)	49.5***	0.16	AIS > NS > C
Schizophrenia spectrum	6.0 (6.1)	3.3 (4.0)	1.9 (2.8)	45.1***	0.15	AIS > NS > C
Variable	Angry/irritable (AIS)	Noncompliant (NS)	Controls (C)	*F*	eta^2	Post hoc
Ages 12–18 years	*n* = 181	*n* = 103	*n* = 319			
ASD						
Communication deficits	1.9 (1.9)	1.4 (1.6)	0.9 (1.6)	21.9***	0.07	AIS,NS > C
Social deficits	3.5 (2.7)	2.7 (2.9)	1.4 (2.0)	46.5***	0.14	AIS > NS > C
Perseverative behaviors	2.3 (2.3)	2.0 (2.2)	0.9 (1.5)	35.0***	0.11	AIS,NS > C
ASD summary score	7.7 (5.4)	6.1 (5.4)	3.2 (4.3)	52.4***	0.15	AIS > NS > C
Schizophrenia spectrum	5.9 (5.3)	4.9 (4.3)	2.5 (3.3)	42.6***	0.13	AIS,NS > C

Note: ASD, autism spectrum disorder; SSD, schizophrenia spectrum disorder; ODD, oppositional defiant disorder; eta^2, effect size.

*** $p < .001$.

Table 2

Means (SDs) and comparison statistics for teachers' ratings of ASD and SSD symptoms in teacher-defined (source-specific) ODD subgroups and clinic controls.

Variable	**Angry/irritable (AIS)**	**Noncompliant (NS)**	**Controls (C)**	***F***	**eta^2**	**Post hoc**
Ages 6–11 years	***n* = 125**	***n* = 79**	***n* = 333**			
ASD						
Communication deficits	3.0 (2.6)	3.1 (2.8)	1.6 (2.4)	20.5***	0.07	AIS,NS > C
Social deficits	6.1 (3.5)	5.8 (3.2)	2.7 (3.1)	65.1***	0.20	AIS,NS > C
Perseverative behaviors	3.6 (3.2)	2.8 (2.6)	1.5 (2.3)	34.3***	0.11	AIS,NS > C
ASD summary score	12.7 (7.5)	11.6 (6.9)	5.7 (6.5)	56.6***	0.18	AIS,NS > C
Schizophrenia spectrum	8.3 (7.9)	6.5 (7.0)	3.6 (5.0)	29.1***	0.10	AIS > NS > C
Variable	Angry/irritable (AIS)	Noncompliant (NS)	Controls (C)	*F*	eta^2	Post hoc
Ages 12–18 years	*n* = 119	*n* = 76	*n* = 396			
ASD						
Communication deficits	2.2 (2.5)	1.9 (2.0)	1.0 (1.7)	20.8***	0.07	AIS,NS > C
Social deficits	5.1 (3.3)	4.3 (3.1)	2.3 (2.8)	49.9***	0.15	AIS,NS > C
Perseverative behaviors	2.7 (2.8)	2.3 (2.4)	0.8 (1.6)	48.4***	0.14	AIS,NS > C
ASD summary score	10.0 (7.6)	8.5 (6.2)	4.1 (5.0)	53.8***	0.16	AIS,NS > C
Schizophrenia spectrum	6.5 (6.7)	5.1 (6.2)	3.3 (4.6)	16.8***	0.06	AIS,NS > C

Note: ASD, autism spectrum disorder; SSD, schizophrenia spectrum disorder; ODD, oppositional defiant disorder; eta^2, effect size.

*** $p < .001$.

Table 3

Means (SDs) and comparison statistics for mothers' ratings of co-occurring ASD and SSD symptoms in mother- and teacher-defined source-exclusive, anger/irritability symptom (AIS) subgroups, cross-informant AIS, children with noncompliant symptoms (NS), and clinic controls.

Variable	**AIS-M**	**AIS-T**	**AIS-M + T**	**NS**	**Controls (C)**	***F***	**eta^2**	**Post hoc**
Ages 6–11 years	***n* = 76**	***n* = 89**	***n* = 38**	***n* = 21**	***n* = 314**			
ASD								
Communication deficits	2.5 (2.6)	1.5 (1.9)	1.8 (2.1)	2.0 (2.4)	1.2 (1.9)	7.0***	0.05	M > T,C
Social deficits	4.3 (3.3)	2.1 (2.3)	4.1 (3.4)	3.2 (2.6)	1.5 (2.1)	27.7***	0.17	M + T,M > T > C; NS > C
Perseverative behaviors	3.1 (2.0)	2.2 (2.4)	3.8 (3.2)	2.5 (2.3)	1.5 (2.0)	16.0***	0.11	M + T,M > T,C; M + T > NS > C
ASD summary score	9.7 (6.3)	5.8 (5.3)	9.7 (7.3)	7.7 (5.7)	4.1 (5.0)	22.0***	0.14	M + T,M > T,C
Schizophrenia spectrum	6.1 (6.1)	2.5 (3.3)	5.7 (6.2)	4.6 (1.0)	2.0 (3.0)	20.7***	0.14	M + T,M > T,C; M > NS > C
Variable	AIS-M	AIS-T	AIS-M + T	NS	Controls (C)	*F*	eta^2	Post hoc
Ages 12–18 years	*n* = 131	*n* = 68	*n* = 52	*n* = 22	*n* = 316			
ASD								
Communication deficits	1.7 (1.8)	1.1 (1.3)	2.5 (2.2)	1.3 (1.4)	1.0 (1.7)	10.7***	0.07	M + T,M > C; M + T > T
Social deficits	3.3 (2.8)	1.8 (2.1)	3.8 (2.7)	2.6 (2.9)	1.7 (2.3)	15.9***	0.10	M + T,M > T,C
Perseverative behaviors	2.1 (2.4)	1.3 (1.6)	3.0 (2.5)	2.3 (2.4)	1.1 (1.6)	14.8***	0.09	M + T,M > C; M + T > T
ASD summary score	7.0 (5.5)	4.0 (4.2)	9.2 (6.1)	6.3 (5.3)	3.7 (4.6)	20.8***	0.13	M + T,M > T,C
Schizophrenia spectrum	5.7 (5.6)	2.6 (3.0)	6.3 (4.9)	5.0 (4.7)	3.0 (3.7)	15.2***	0.10	M + T,M,NS > T,C

Note: ASD, autism spectrum disorder; SSD, schizophrenia spectrum disorder; M, mother; T, teacher; eta^2, effect size.

*** $p < .001$.

Table 4

Means (SDs) and comparison statistics for teachers' ratings of co-occurring ASD and SSD symptoms in mother- and teacher-defined source-exclusive, anger/irritability symptom (AIS) subgroups, cross-informant AIS, children with noncompliant symptoms (NS), and clinic controls.

Variable	**AIS-M**	**AIS-T**	**AIS-M + T**	**NS**	**Controls (C)**	***F***	**eta^2**	**Post hoc**
Ages 6–11 years	***n* = 76**	***n* = 89**	***n* = 38**	***n* = 21**	***n* = 314**			
ASD								
Communication deficits	1.7 (2.2)	3.6 (2.7)	1.6 (1.8)	2.0 (2.0)	2.0 (2.6)	9.2***	0.07	T > M + T,M,C
Social deficits	3.6 (3.3)	6.4 (3.3)	5.4 (3.7)	4.6 (2.9)	3.1 (3.3)	19.0***	0.13	M + T,T > M,C; T > NS
Perseverative behaviors	1.6 (2.2)	3.9 (3.3)	3.0 (2.8)	3.1 (2.8)	1.7 (2.4)	15.0***	0.10	M + T,T,NS > M,C
ASD summary score	6.7 (6.3)	13.9 (7.4)	9.9 (6.1)	9.9 (6.1)	6.7 (7.2)	19.3***	0.13	T > M,C
Schizophrenia spectrum	3.3 (4.4)	8.9 (8.1)	7.0 (7.4)	6.0 (6.3)	4.2 (5.8)	12.1***	0.09	M + T,T > M,C
Variable	AIS-M	AIS-T	AIS-M + T	NS	Controls (C)	*F*	eta^2	Post hoc
Ages 12–18 years	*n* = 131	*n* = 68	*n* = 52	*n* = 22	*n* = 316			
ASD								
Communication deficits	1.1 (1.7)	2.3 (2.6)	2.1 (2.4)	1.5 (1.8)	1.2 (1.9)	7.0***	0.05	M + T,T > M,C
Social deficits	2.7 (3.0)	5.0 (3.0)	5.1 (3.6)	3.8 (2.7)	2.5 (2.9)	16.9***	0.11	M + T,T > M,C
Perseverative behaviors	1.2 (2.1)	2.5 (2.8)	2.7 (2.8)	2.0 (1.8)	1.0 (1.7)	15.2***	0.10	M + T,T > M,C; NS > C
ASD summary score	4.9 (5.6)	9.7 (7.2)	9.9 (8.0)	7.3 (5.6)	4.5 (5.4)	17.3***	0.11	M + T,T > M,C
Schizophrenia spectrum	3.7 (5.0)	6.2 (6.8)	6.6 (6.6)	4.7 (4.8)	3.5 (4.9)	6.5***	0.04	M + T > M,C

Note: ASD, autism spectrum disorder; SSD, schizophrenia spectrum disorder; M, mother; T, teacher; eta^2, effect size.

*** $p < .001$.