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Increased clinical and neurocognitive impairment in children with autism spectrum disorders and comorbid bipolar disorder

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ABSTRACT

Bipolar (BD) symptomatology is prevalent in children with autism spectrum disorders (ASD) and may lead to increased impairment. The current study compared clinical and neurocognitive impairment in children (7–13 years) diagnosed with ASD ($n = 55$), BD ($n = 34$), ASD + BD ($n = 23$), and a non-clinical control group ($n = 27$). Relative to the ASD group, the ASD + BD group reported elevated rates of aggression and delinquency, behavioral disorders, depression, obsessive-compulsive disorder, and suicidal ideation, and poorer performance on the Stroop Color-Word Test. Future research might address how best to improve diagnostic assessment and adapt treatment to meet the needs of this uniquely impaired population.

1. Introduction

Accumulating research suggests a high prevalence of bipolar disorder (BD) in children diagnosed with autism spectrum disorders (ASD; Delong, 1994; Frazier, Doyle, Chiu, & Coyle, 2002; Ghaziuddin, 2005). The presence of bipolar symptomatology in ASD youth may lead to increased psychological and psychosocial impairment and higher rates of hospitalization, and may have important implications for behavioral and pharmacological treatment (Frazier et al., 2002; Gillberg, 1985; Lainhart & Folstein, 1994; Wozniak et al., 1997). Yet, few empirical studies have assessed comorbid bipolar symptoms in ASD and directly compared specific areas of clinical and neuropsychological functioning in ASD youth with and without BD. The current study was designed to begin addressing this need by comparing selected cognitive and psychological deficits in ASD children with and without concomitant bipolar symptomatology.

The ASD continuum includes Asperger's and autistic disorders, both of which are characterized by a triad of symptoms: (1) qualitative impairment in communication, (2) naïve and inappropriate social interactions, and (3) restricted, repetitive, and stereotyped patterns of behavior, interests, and activities (American Psychiatric Association, 1994; Damore, Stine, & Brody, 1998; Eisenmajer et al., 1996; Frazier et al., 2002; Verte, Geurts, Roeyers, Oosterlaan, & Sergeant, 2006). Additionally, autistic children, but not those diagnosed with Asperger's disorder, typically show clinically significant delays in language, cognitive development, and adaptive behavior. The prevalence rate for autistic disorder has recently been estimated

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between 10 and 16 in 10,000 children or 0.1–0.16%, while Asperger's disorder is reportedly less common, occurring in approximately 4.3 of 10,000 children or .043% of the population (Fombonne, 2005). Both disorders are substantially more common in males than in females.

Bipolar disorder (BD) is a psychiatric illness associated with high rates of morbidity and mortality (i.e., suicide; Strakowski, DelBello, Adler, Cecil, & Sax, 2000). BD has been estimated to affect up to 1.5% of the US population, with peak onset in mid to late adolescence and males and females equally represented (James & Javaloyes, 2001; Strakowski et al., 2000). BD includes at least one episode of major depression and at least one episode of mania or hypomania (American Psychiatric Association, 1994). By definition, a depressive episode lasts at least 2 weeks and is characterized by sad mood, anhedonia, feelings of guilt or worthlessness, restlessness or irritability, difficulty concentrating or making decisions, anergia and fatigue, changes in patterns of sleep and appetite, and recurrent thoughts of death or suicide. A manic episode lasts at least 1 week (or less if hospitalization is required) and features elevated, expansive, or irritable mood, increased energy, activity, and restlessness, racing thoughts, distractibility, hyposomnia, hypersexuality, and an overall increase in risky behavior and poor decision making. The prevalence of bipolar spectrum disorders (bipolar I, bipolar II, and cyclothymia) in adolescence has been estimated at approximately 1% (Kaufman, Blumberg, & Young, 2004). Although there is little epidemiological research on the rate of BD in prepubertal children, the Great Smoky Mountains study of 4500 youths aged 9–13 years reported no cases of threshold mania, but a 0.1% rate of hypomania (Costello et al., 1996). Additionally, a retrospective study of bipolar adults suggested a childhood-onset rate of 0.4–0.5% (Joyce, 1984).

Several clinical case reports have described comorbidity between affective illness (i.e., bipolar and unipolar depression) and ASD (Frazier et al., 2002; Gillberg, 1985; Komoto, Usui, & Hirata, 1984). Lainhart and Folstein's (1994) review of published case reports of comorbid ASD and affective illness ($n = 17$) found that 35% of patients experienced the onset of a mood disorder in childhood with 50% reporting a positive history of affective illness or suicide. In addition, a handful of clinical research studies have illustrated the prevalence of comorbid affective disorders in ASD. Wing (1981) followed a group of Asperger's children ($n = 18$) into adolescence and found that 23% showed signs of affective illness, 11% had attempted suicide, and 17% manifested some form of psychosis. Wozniak et al. (1997) reported that out of 727 youth evaluated at a pediatric pharmacology clinic, 52 met criteria for ASD or another pervasive developmental disorder (PDD), 114 met criteria for mania, and 14 met criteria for both. Thus, the comorbid group represented 2% of all referrals, 12% of the mania group, and 27% of the PDD group, suggesting a high rate of co-occurrence between these two disorders. A small body of literature has further suggested lower levels of functioning in children with comorbid ASD and BD when compared with single-diagnosis ASD patients. Clinical case reports by Gillberg (1985), Frazier et al. (2002), and Lainhart and Folstein (1994) reported an exacerbation of ASD symptoms and attenuated functioning in the presence of a comorbid mood disorder. These authors proposed that an episode of depression may precipitate an increase in self-injury and an exacerbation of severe autistic features such as echolalia and hand flapping, suggesting the detriment of behavioral symptoms associated with affective illness with respect to the individual's placement and functioning in the home, school, and workplace.

Wozniak et al. (1997) compared a group of comorbid children to two single-diagnosis groups (i.e., PDD and mania) on a number of diagnostic batteries. The study revealed marked impairment in the PDD + mania group specifically with regard to behavior and attention. Children in the comorbid group had higher rates of externalizing disorders (i.e., Attention-Deficit/Hyperactivity Disorder, ADHD; Conduct Disorder, CD; and Oppositional Defiant Disorder, ODD) than PDD youth without mania, as well as more impaired scores on the Delinquent Problems and Aggressive Behavior Child Behavior Checklist (CBCL; Achenbach, 1991) subscales. Children with both PDD and mania also had a higher prevalence of major depression, anxiety disorders, and psychosis than PDD children without mania, and more impaired scores on the Withdrawn, Somatization, and Anxious/Depressed CBCL subscales. With respect to psychosocial functioning, the comorbid group demonstrated more severe impairment than the single-diagnosis PDD group regarding academic and social problems, spare-time activities, spare-time problems, and home problems. Additionally, the comorbid group revealed lower Global Assessment of Functioning (GAF) scores (mean = 38.9) when compared with PDD children (mean = 44.8) and required hospitalization at a rate of 36%, significantly higher than the PDD group without mania. Even when compared with other comorbid psychopathological groups (i.e., PDD + anxiety disorders, mania + anxiety disorders, PDD + disruptive disorders, mania + disruptive disorders, PDD + depression), the functioning of the co-occurring PDD + mania group was extremely poor in terms of their psychosocial functioning, GAF, and CBCL clinical subscale scores. These impaired scores, indicative of attentional, behavioral, and additional psychological deficits, in conjunction with the high rate of hospitalization in this group, suggest that PDD with comorbid mania is a disabling and resource demanding condition warranting further investigation. With the exception of the Wozniak et al. (1997) study, little is known about levels of psychological functioning in ASD children with and without BD symptomatology. Further, we could identify no research comparing neurocognitive impairment between these two groups. This may be an important omission given that numerous studies have documented neuropsychological and neurophysiological deficits in bipolar and ASD populations, independently.

Specifically, both disorders have been shown to feature structural and functional abnormalities in the prefrontal cortex and frontostriatal network, and associated deficits in executive function (Casey & Durston, 2006; Weyandt, 2005), including selective and sustained attention, response inhibition, and cognitive flexibility (Altshuler et al., 2004; Blumberg et al., 2003; Borkowska & Rybakowski, 2001; Dixon, Kravariti, Frith, Murray, & McGuire, 2004; Rinehart, Bradshaw, Tonge, Brereton, & Bellgrove, 2002; Turner, 1997; Verte et al., 2006). In light of the clinical literature reviewed, these neurobiological findings prompt the question: does concomitant bipolar symptomatology in ASD youth further compromise their cognitive abilities as it appears to attenuate their psychological functioning?