White matter abnormalities associated with disruptive behavior disorder in adolescents with and without attention-deficit/hyperactivity disorder

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Abstract

Disruptive behavior disorders (DBD) are among the most commonly diagnosed mental disorders in children and adolescents. Some important characteristics of DBD vary based on the presence or absence of comorbid attention-deficit/hyperactivity disorder (ADHD), which may affect the understanding of and treatment decision-making related to the disorders. Thus, identifying neurobiological characteristics of DBD with comorbid ADHD (DBD+ADHD) can provide a basis to establish a better understanding of the condition. This study aimed to assess abnormal white matter microstructural alterations in DBD+ADHD as compared to DBD alone and healthy controls using diffusion tensor imaging (DTI). Thirty-three DBD (19 with comorbid ADHD) and 46 age-matched healthy adolescents were studied using DTI. Fractional anisotropy (FA), axial diffusivity (AD), radial diffusivity (RD) and mean diffusivity (MD) were analyzed using tract-based spatial statistics (TBSS). Significant lower FA and higher MD, RD and AD in many white matter fibers were found in adolescents with DBD+ADHD compared to controls. Moreover, lower FA and higher RD were also found in the DBD+ADHD versus the DBD alone group. Alterations of white matter integrity found in DBD patients were primarily associated with ADHD, suggesting that ADHD comorbidity in DBD is reflected in greater abnormality of microstructural connections.

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1. Introduction

Oppositional-defiant disorder (ODD) and conduct disorder (CD), collectively referred to as disruptive behavior disorders (DBD), involve persistent symptoms of defiant, disobedient, aggressive and hostile behavior, particularly towards authority figures. This consistent behavior pattern results in problems such as arguing, rule-breaking and, in more extreme forms, aggressive criminal acts (American Psychiatric Association, 1994; Kronenberger and Meyer, 2001; Loeber et al., 2009). The DBD diagnoses are among the most common childhood mental disorders, with CD occurring in 1% to 6% of the population aged 9 to 17 years and ODD occurring in 1% to 6% of the population (Findling, 2008). The difficulty of treating DBD can be compounded by its high comorbidity with attention-deficit/hyperactivity disorder (ADHD) (Loeber et al., 2000; Burke et al., 2002; Ollendick et al., 2008), as well as depression, substance use, and other conditions (Burke et al., 2002). Thus, identifying neurobiological characteristics of DBD with comorbid disorders can help to improve understanding of these conditions and ultimately contribute to the development of more effective treatments.

Depending on the presence or absence of comorbid ADHD, children and adolescents with DBD may differ in behavioral and neuro-psychological characteristics, particularly executive functioning (Oosterlaan et al., 2005; Hummer et al., 2011). Children with ADHD demonstrate inattention, disinorganization, impulsivity and hyperactivity, which disrupt the child's functional and adaptive behaviors (American Psychiatric Association, 1994; Kronenberger and Meyer, 2001; Barkley, 2005). These symptoms can be particularly detrimental when DBD is diagnosed with comorbid ADHD, as impulsivity and poor self-regulation may amplify the defiant behavior that characterizes DBD. Much of the published evidence supporting neurobiological models of DBD comes from behavioral performance measures rather than direct assessments of brain functioning (Loeber et al., 2000; Burke et al., 2002; Loeber et al., 2009). As a result, studies identifying the neural deficits that are uniquely related to the development of DBD in youth are still needed (Loeber et al., 2009). Furthermore, there have been very few studies of the role of comorbid ADHD in the neurobiology of DBD.

Diffusion tensor imaging (DTI) is a magnetic resonance imaging (MRI) technique that provides in vivo information about the direction and integrity of neural fiber tracts (Alexander et al., 2007). Because DTI
is still an emerging technique, only a limited number of DTI studies to date have investigated white matter differences associated with psychiatric disorders of childhood and adolescence. However, there is converging evidence suggesting that white matter abnormalities are associated with ADHD (Ashutari et al., 2005; Casey et al., 2007; Makris et al., 2008; Pavuluri et al., 2009; Silk et al., 2009). These previous DTI studies mainly focused on fractional anisotropy (FA) as a measure of brain tissue integrity, since FA measures the degree to which water molecules diffuse in a given direction, reflecting white matter fiber density (Beaulieu, 2002). Alternatively, overall diffusivity in a tissue can be quantified by mean diffusivity (MD), which is a directionally averaged measure of the apparent diffusion coefficient and may help to better understand white matter structure (Alexander et al., 2007). Some studies also investigated eigenvalues of the diffusion tensor or their related quantities of radial diffusivity (RD) and axial diffusivity (AD) (Schmithorst and Yuan, 2010). RD and AD can provide more specific information about directional changes in white matter integrity (Alexander et al., 2007).

In recent DTI studies, these four DTI parameters, FA, MD, RD and AD, were very useful in characterizing normal regional development in white matter microstructure throughout adolescence (Ashutari et al., 2007; Qiu et al., 2008; Asato et al., 2010; Bava et al., 2010; Schmithorst and Yuan, 2010). Thus far, there are only a very limited number of DTI research studies in DBD samples. Our previously conducted DTI study had assessed structural abnormalities in subjects with DBD compared to healthy controls (Li et al., 2005), where we found significant differences in regions including the anterior region of the corona radiata and bilateral superior longitudinal fasciculus, potentially indicating deficits in connection between frontal and subcortical or parietal regions in DBD. However, it failed to investigate the potential confound of comorbid ADHD among youth with DBD, a limitation that this current study aims to address. The present study is further delineated from prior research by using an automated, unbiased whole-brain analysis method of tract-based spatial statistics (TBSS) (Smith et al., 2006). We examined the microstructural properties of white matter in adolescents with diagnoses of DBD and comorbid ADHD (DBD + ADHD), DBD alone (DBD − ADHD), and controls with no psychiatric diagnosis. To the best of our knowledge, our study is the first to assess DTI characteristics in adolescents with DBD with and without ADHD. As a result, this study offers the potential to contribute important novel information about DBD diagnoses and comorbidities.

2. Methods

2.1. Participants

The study was approved by the local Institutional Review Board, and written informed consent was obtained from subjects and their caregivers prior to any study procedures. Adolescents (13–17 years) with and without DBD diagnoses were recruited via informational flyers posted in community settings. Diagnoses of ODD, CD, and/or ADHD were made based on results of the Schedule for Affective Disorders and Schizophrenia for School-Aged Children, Present and Lifetime Version (K-SADS) (Kaufman et al., 1996). The semistructured Diagnostic Interview (Behavior Disorders Module) was performed. Thirty-three subjects with a DBD diagnosis (ODD: n = 11; CD: n = 22) met criteria for the present study. These criteria included diagnosis of ODD or CD based on the K-SADS, completion of a valid MRI DTI scan, and presence of at least one recurrent Conduct Disorder symptom of aggressive behavior toward people or animals within the past 6 months (as determined with the K-SADS interview). The presence of an aggressive symptom was assessed. Regions of interest (ROIs) were created from clusters showing significant differences in regions including the anterior region of the corona radiata and bilateral superior longitudinal fasciculus, potentially indicating deficits in connection between frontal and subcortical or parietal regions in DBD. However, it failed to investigate the potential confound of comorbid ADHD among youth with DBD, a limitation that this current study aims to address. The present study is further delineated from prior research by using an automated, unbiased whole-brain analysis method of tract-based spatial statistics (TBSS) (Smith et al., 2006). We examined the microstructural properties of white matter in adolescents with diagnoses of DBD and comorbid ADHD (DBD + ADHD), DBD alone (DBD − ADHD), and controls with no psychiatric diagnosis. To the best of our knowledge, our study is the first to assess DTI characteristics in adolescents with DBD with and without ADHD.

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