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Reading related white matter structures in adolescents are influenced more by dysregulation of emotion than behavior

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ABSTRACT

Mood disorders and behavioral are broad psychiatric diagnostic categories that have different symptoms and neurobiological mechanisms, but share some neurocognitive similarities, one of which is an elevated risk for reading deficit. Our aim was to determine the influence of mood versus behavioral dysregulation on reading ability and neural correlates supporting these skills in youth, using diffusion tensor imaging in 11- to 17-year-old children and youths with mood disorders or behavioral disorders and age-matched healthy controls. The three groups differed only in phonological processing and passage comprehension. Youth with mood disorders scored higher on the phonological test but had lower comprehension scores than children with behavioral disorders and controls; control participants scored the highest. Correlations between fractional anisotropy and phonological processing in the left Arcuate Fasciculus showed a significant difference between groups and were strongest in behavioral disorders, intermediate in mood disorders, and lowest in controls. Correlations between these measures in the left Inferior Longitudinal Fasciculus were significantly greater than in controls for mood but not for behavioral disorders. Youth with mood disorders share a deficit in the executive-limbic pathway (Arcuate Fasciculus) with behavioral-disordered youth, suggesting reduced capacity for engaging frontal regions for phonological processing or passage comprehension tasks and increased reliance on the ventral tract (e.g., the Inferior Longitudinal Fasciculus). The low passage comprehension scores in mood disorder may result from engaging the left hemisphere. Neural pathways for reading differ mainly in executive-limbic circuitry. This new insight may aid clinicians in providing appropriate intervention for each disorder.

1. Introduction

1.1. Reading difficulties in youth with mood or behavioral disorders

Of U.S. 4th graders, 27%–58% do not achieve basic levels of reading proficiency (The Nation's Report Card, National Center for Education Statistics, see (Donahue et al., 1999)). For approximately 10% of these children, the cause is primarily a deficit in reading mechanisms (i.e., dyslexia (O'Hare, 2010)). For the other 90% (24%–52% of all 4th graders), reading difficulties are secondary to another primary diagnosis. Approximately 30%–40% of youth with either mood or behavioral disorders have comorbid reading difficulties Behavioral disorders include attention deficit hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), and conduct disorder (CD) while mood

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disorders include depressive, bipolar, and anxiety disorders.

Although both mood- and behavioral-disordered youth suffer from severe learning difficulties (Forness and Knitzer, 1992), the neuroimaging literature describes different neural circuits contributing to the difficulties manifested within each group. Mood disorders are thought to be accompanied by neural abnormalities related to the limbic system (greater activation of the amygdala (Davidson et al., 1999; Donegan et al., 2003) and frontal lobe (frontal asymmetries; see Coan and Allen, 2004 for review, Davidson et al., 1999), abnormalities in functional connectivity between the frontal lobe and amygdala (Banks et al., 2007), decreased activation in temporo-parietal (Halari et al., 2009) and parietal regions (Fitzgerald et al., 2008), and decreased functional connectivity in the fronto-parietal and cingulo-opercular networks (Sylvester et al., 2012). In contrast, individuals with behavioral disorders share abnormalities, mainly in neural circuits related to either decreased or altered frontal lobe activation (Spalletta et al., 2001; Brower and Price, 2001, respectively).

Several neuroimaging studies have attempted to characterize neural correlates that can differentiate individuals with mood disorders from those with behavioral disorders, especially using structural-connectivity tools. Fractional anisotropy (FA), a measure related to the diffusivity of white matter water molecules measured by diffusion tensor imaging (DTI), reflects the ratio of axial versus radial diffusivity. Researchers have demonstrated reduced FA values in individuals with mood disorders in white matter tracts in temporal and frontal brain regions (Frazier et al., 2007; Abler et al., 2008), whereas individuals with behavioral disorders had reduced FA values in different tracts, including limbic white matter tracts (van Ewijk et al., 2012; Makris et al., 2008; Konrad et al., 2010; Sarkar et al., 2013). Versace and colleagues recently examined relationships between mood or behavioral dysregulation and white matter structure in three major mood regulation tracts in adolescents (forceps minor, uncinate fasciculus, cingulum). They found that youth with mood dysregulation showed lower FA in these tracts when compared to youth with behavioral dysregulation and with typically developing youth (Versace et al., 2015). They suggested that lower FA in these tracts is associated with altered structural connectivity between the anterior temporal lobe and prefrontal cortex and between the left and right prefrontal cortex, which may represent a neural mechanism of mood dysregulation in youth (Versace et al., 2015). These regions, as well as the parietal regions, which are highly involved in the reading process, are often reported to be abnormal in youth with both mood and behavioral disorders (Horowitz-Kraus et al., 2014a). Because reading relies on most of these anatomical regions, the existence of reading difficulties in youth with mood and behavioral disorders is not surprising.

1.2. Neural circuits related to reading (phonological processing, orthographical processing and reading comprehension)

Reading is one of the most complex cognitive human abilities; it generally engages orthographic, phonological, and semantic processors simultaneously (Parallel Distributed Processing model; Seidenberg and McClelland, 1989). The most traditional neuroimaging model for reading suggests that neural circuits related to reading include the Occipito-temporal Ventral Stream, Angular Gyrus, and Inferior Parietal Lobule (in proximity to Wernicke's area), as well as the Inferior Frontal Gyrus (including Broca's Area) corresponding to these three processors, especially in the left hemisphere (Shaywitz, 2003). Whereas the left hemisphere has been primarily related to phonological and orthographic processing at the word level, the right hemisphere has been related to reading comprehension (Horowitz-Kraus et al., 2014b). The Arcuate Fasciculus (AF) and the Superior Longitudinal Fasciculus (SLF) connect the frontal and the temporo-parietal regions (Makris et al., 2005), whereas the Inferior Longitudinal Fasciculus (ILF) connect the temporal and occipital regions (Uddin et al., 2010), and the inferior fronto-occipital fasciculus (IFOF) connect the frontal-occipital regions (Makris et al., 2009). Interestingly, greater FA values in the right AF and a greater functional connectivity between regions generated in the sentence comprehension task in 17-year-old typical readers have been correlated with higher passage comprehension scores from the Woodcock-Johnson III battery (WJ-III) (Horowitz-Kraus et al., 2014b). This correlation was evident primarily in the anterior part of the AF, emphasizing right hemispheric contributions to reading-comprehension performance. An association of higher reading-comprehension scores with greater functional and structural connectivity in the right hemisphere was also evident in 7- to 9-year-old typical readers (Horowitz-Kraus et al., 2015b).

The advancing field of neuroimaging has revealed that the reading process involves more than the classical phonological, orthographic, and semantic regions. Additional processors include the engagement of executive functions and control networks, such as the fronto-parietal and cingulo-opercular networks (Horowitz-Kraus et al., 2015a; Horowitz-Kraus et al., 2014a; Horowitz-Kraus et al., 2014c; Vogel et al., 2014). The involvement of regions related to error monitoring (Anterior Cingulate Cortex; Horowitz-Kraus et al., 2014a; Horowitz-Kraus and Breznitz, 2014), executive functions (Dorsolateral Prefrontal Cortex; Horowitz-Kraus et al., 2014a), and visual attention (Precuneus; Vogel et al., 2014; Vogel et al., 2013) are all part of a dual cognitive control network (Dosenbach et al., 2008), indicating these regions are critical for intact reading.

Literature points at behavioral evidence of reading impairments and general differences in FA values in different white matter tracts in individuals with mood or behavioral disorders (Pavuluri et al., 2006). However, there is still a gap in knowledge on differences in sub-domains of reading (i.e., phonology vs orthography vs reading comprehension) and neural circuits related to these reading components between the two groups. Recruiting from a multisite longitudinal study of youth with mood or behavioral dysregulation, the Longitudinal Assessment of Manic Symptoms (LAMS) study (Horwitz et al., 2010), the current exploratory study investigated different effects of mood and behavioral disorders on reading ability. According to Frith's model for reading development and for an intact reading comprehension, phonology and orthography should be mastered (Frith, 1985). Therefore in the current study, ewe focused on phonemic awareness (i.e., phonological processing), orthographical processing (i.e., word recognition), and reading comprehension (i.e., passage comprehension) to identify differences between mood and behavioral disorders in FA values that correlate with these abilities in white matter tracts known to be involved in reading ability. Based on studies described above, this study examined several bilateral white matter tracts as regions of interest (ROIs): AF, ILF, SLF, and IFOF We hypothesized that, due to evidence of lower activation and structural connectivity in these neural circuits related to reading as well as impairments in the limbic circuitry (involving the frontal regions) in youth with mood disorders, greater reading difficulties would be observed in mood disorders than in behavioral disorders. We also postulated that youth with mood disorders would exhibit lower FA values in frontal portions of reading-related tracts compared to youth with behavioral disorders.

2. Results

2.1. Behavioral data

Differences in IQ between the groups were not significant [full scale IQ for mood disorders $M = 114.57$, $SD = 17.06$; for behavioral disorders $M = 105.59$, $SD = 12.34$; for controls $M = 110.85$, $SD = 12.77$ [$F(2,36) = 1.25$, $p = 0.3$].

ANOVAs for the three groups (mood disorders, behavioral disorders, and controls) and three reading measures (phonemic awareness, orthographical ability, and reading comprehension) indicated significant differences between the groups for phonological awareness and reading comprehension. Post-hoc independent *t*-tests revealed that youth with