The severity of vestibular dysfunction in deafness as a determinant of comorbid hyperactivity or anxiety.

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Abstract

Attention-deficit/hyperactivity disorder (ADHD) and anxiety-related disorders occur at rates 2-3 times higher in deaf compared with hearing children. Potential explanations for these elevated rates and the heterogeneity of behavioral disorders associated with deafness have usually focused on socio-environmental rather than biological effects. Children with the 22q11.2 deletion or duplication syndromes often display hearing loss and behavioral disorders including ADHD and anxiety-related disorders. Here, we show that mouse mutants with either a gain- or loss-of-function of the T-Box transcription factor gene, Tbx1, which lies within the 22q11.2 regions and is responsible for most of the syndromic defects, exhibit inner ear defects and hyperactivity. Furthermore, we show 1) that inner ear dysfunction due to the tissue-specific loss of Tbx1 or Slc12a2, which encodes a sodium-potassium-chloride cotransporter and is also necessary for inner ear function, causes hyperactivity, 2) that vestibular rather than auditory failure causes hyperactivity, and 3) that the severity rather than the age of onset of vestibular dysfunction differentiates whether hyperactivity or anxiety co-occur with inner ear dysfunction. Altogether, these findings highlight a biological link between inner ear dysfunction and behavioral disorders and how sensory abnormalities can contribute to the etiology of disorders traditionally considered of cerebral origin.

SIGNIFICANCE STATEMENT

This study examines the biological rather than socio-environmental reasons why hyperactivity and anxiety disorders occur at higher rates in deaf individuals. Using conditional genetic approaches in mice, the authors show 1) that inner ear dysfunction due to either Tbx1 or Slc12a2 mutations cause hyperactivity, 2) that it is vestibular dysfunction, which frequently co-occurs with deafness but often remains undiagnosed, rather than auditory dysfunction that causes hyperactivity and anxiety-related symptoms, and 3) that the severity of vestibular dysfunction can predict whether hyperactivity or anxiety co-exist with inner ear dysfunction. These findings suggest a need to evaluate vestibular function in hearing impaired individuals, especially those who exhibit hyperactive and anxiety-related symptoms.