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A longitudinal examination of the psychoeducational, neurocognitive, and psychiatric functioning in children with 22q11.2 deletion syndrome

Stephen R. Hooper [a,b], Kathleen Curtiss [b], Kelly Schoch [b], Matcheri S. Keshavan [c], Andrew Allen [d], Vandana Shashi [b,*]

[a] Department of Psychiatry and The Carolina Institute for Developmental Disabilities, University of North Carolina School of Medicine, CB# 7255, Chapel Hill, NC 27599-7255, USA
[b] Department of Pediatrics, Duke University Medical School, GSRB1 Box 103857, 595 LaSalle St., Durham, NC 27710, USA
[c] Department of Psychiatry, Harvard Medical School, Commonwealth Research Center, 75 Fenwood Rd, 5th Floor, Boston, MA 02115, USA
[d] Department of Biostatistics, Duke University School of Medicine, 7057 North Pavilion, Durham, NC 27710, USA

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ABSTRACT

The present study sought to examine the longitudinal psychoeducational, neurocognitive, and psychiatric outcomes of children and adolescents with chromosome 22q11.2 deletion syndrome (22q11DS), a population with a high incidence of major psychiatric illnesses appearing in late adolescence/early adulthood. Little is known of the developmental changes that occur in the early teen years, prior to the age of highest psychosis risk. Data were collected from 71 participants (42 subjects with 22q11DS and 29 control subjects) at Time 1 (T1) and Time 2 (T2), approximately 3.5 years later. The 22q11DS group was significantly lower functioning than controls on IQ, neurocognition, and academic achievement at both T1 and T2. Children with 22q11DS also showed significantly greater social-behavioral difficulties and psychiatric symptoms, and were more likely to meet criteria for psychiatric disorders at both time points. In evaluating change over time from T1 to T2, the 22q11DS group did not show significant changes in psychoeducational or psychiatric outcomes relative to the controls, however, lack of expected age-related gains in attention regulation were noted. Within the 22q11DS group, an increase in the Attenuated Prodrome for Schizophrenia (number of psychiatric symptoms) was noted from T1 to T2 and four children with 22q11DS met criteria for Psychosis for the first time. Predictors at T1 that uncovered psychopathology symptoms at T2 included full-scale IQ, externalizing symptoms, and problem social behaviors. Overall, younger adolescent and preadolescent children with 22q11DS in this study exhibited slowed growth in attention regulation, with an increase in subclinical symptoms of schizophrenia, suggestive of increasing impairments in domains that are relevant to the high risk of Schizophrenia. Early predictors of later psychopathology included both cognitive and behavioral abnormalities. These findings begin to elucidate the trajectory of changes in psychopathology in children with 22q11DS in the years leading up to the onset of major psychiatric illnesses.

* Corresponding author. Tel.: +1 919 681 2524; fax: +1 919 668 0932.
E-mail addresses: kathleen.curtiss@duke.edu (K. Curtiss), vandana.shashi@duke.edu (V. Shashi).

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1. Introduction

Chromosome 22q11.2 Deletion Syndrome (22q11DS), also known as Velocardiofacial syndrome (VCFS) or DiGeorge Syndrome, is the most common microdeletion syndrome in humans with an incidence of 1:2000 to 1:4000 (Devriendt, Fryns, Mortier, van Thienen, & Keymolen, 1998; Shprintzen, 2000b, 2008; Wilson, Cross, Wren, Scramble, & Burn Goodship, 1994). In addition to multiple medical problems, individuals with 22q11DS experience a wide range of neurocognitive impairments and a high rate of major psychiatric disorders (Robin & Shprintzen, 2005; Shprintzen, 2000a).

Intellectual functioning in children with 22q11DS varies from the borderline to mild intellectual disability range, along with deficits in sustained attention, executive function, and visual spatial functioning, with some reported similarities to a non-verbal learning disability (De Smedt et al., 2007; Jacobson et al., 2010; Lewandowski, Shashi, Berry, & Kwapil, 2007; Moss et al., 1999; Schoch et al., 2012; Swillen et al., 1997; Woodin et al., 2001). Common psychiatric disorders in childhood include Attention-Deficit/Hyperactivity Disorder (ADHD) and anxiety disorders such as Specific Phobias and Obsessive-Compulsive Disorder (OCD; Antshel et al., 2007). In particular, children with 22q11DS evidence a poor repertoire of social skills and high rates of internalizing symptoms (Kiley-Brabeck & Sobin, 2006; Shashi et al., 2011). In a prior study, we found that about 60% of children with 22q11DS met criteria for at least one psychiatric diagnosis, with the most frequent diagnoses including ADHD and various anxiety disorders (Lewandowski et al., 2007; Young, Shashi, Schoch, Kwapil, & Hooper, 2011). In later adolescence or early adulthood, upwards of 25% develop major psychiatric illnesses such as Schizophrenia, Bipolar illness, and Major Depression (Baker & Skuse, 2005; Murphy, Jones, & Owen, 1999; Papolos et al., 1996; Pulver et al., 1994; Usiskin et al., 1999).

1.1. Longitudinal investigations of neurocognitive and psychiatric functioning in children with 22q11DS

In one of the first longitudinal studies of individuals with 22q11DS, Gothelf et al. (2005) reported significant declines in verbal IQ and expressive language scores across two time points separated by approximately five years. Similar findings were identified in subsequent longitudinal examinations by Gothelf and colleagues with an association between changes in various cortical structures, verbal deterioration, and the appearance of severe psychopathology being highlighted (Gothelf et al., 2007; Green et al., 2009). Abnormal developmental trajectories of cortical thickness, with cortical loss during adolescence, has been documented both cross-sectionally and longitudinally, which may affect neurocognitive and psychiatric functioning over time (Schaer et al., 2009). Most recently, Kates and colleagues documented a relationship between changes in brain structure and the emergence of prodromal schizophrenia symptoms at two time points over a three year time period (Kates, Antshel, et al., 2011; Kates, Bansal, et al., 2011). Although the developmental trajectories of most brain structures were similar to their matched controls, volumetric decreases in temporal lobe gray matter and verbal IQ were especially related to positive prodromal psychotic symptoms in their preadolescent sample of children with 22q11DS. Green et al. (2009) noted the need for ongoing prospective longitudinal studies to continue to examine the nature of these changes. Since most of the above studies included children with 22q11DS that were older or included both children and adults and/or examined change over time mainly as related to schizophrenia symptoms, little is known about the longitudinal changes in neurocognition and other psychiatric diagnoses in early adolescence.

1.2. The present study

The primary purpose of the current study was to examine the longitudinal psychoeducational, neurocognitive, and psychiatric functioning of a well characterized group of children and young adolescents with 22q11DS. We had previously reported children with 22q11DS as having an IQ in the borderline range, with deficits in executive function, attention and verbal memory (Lewandowski et al., 2007; Shashi, Berry, & Keshavan, 2009). Our first research objective in this study was to provide a more comprehensive description of the psychoeducational, neurocognitive and psychiatric findings of our sample at T1, and also provide the newest findings of our sample's performance 3.5 years later (T2). A second research question examined change over time for the 22q11DS group in comparison to age and gender matched healthy controls across the psychoeducational, neurocognitive, and psychiatric domains. Finally, a third research question examined specific T1 variables as potential predictors of the emergence of targeted psychopathology at T2, approximately 3.5 years post study entry.

2. Methods

2.1. Participants

Forty-two children with 22q11DS, ages 7.0–15.67 years ($M = 10.05$, $SD = 2.49$), were recruited either at Duke University Medical Center (DUMC) or Wake Forest Baptist Medical Center. All subjects with 22q11DS had a molecularly confirmed deletion of the 22q11.2 region. Twenty-nine healthy control participants were recruited by advertisement in local pediatric practices, schools, and the research study website at DUMC. Control participants ranged in age from 7.92 to 14.33 years ($M = 10.13$, $SD = 1.74$) and were excluded if they had a severe neurodevelopmental disorder (e.g., Autism), or a personal or family history (first-degree relative) of Psychosis, Bipolar Disorder, or Major Depression.