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Predicting reading comprehension academic achievement in late adolescents with velo-cardio-facial (22q11.2 deletion) syndrome (VCFS): A longitudinal study

Kevin M. Antshel, PhD.[1,2], **Bridget O. Hier, M.S.**[1], **Wanda Fremont, M.D.**[2], **Stephen V. Faraone, Ph.D.**[2], and **Wendy R. Kates, Ph.D.**[2]

[1]Syracuse University Department of Psychology

[2]SUNY – Upstate Medical University Department of Psychiatry & Behavioral Sciences

Abstract

Background—The primary objective of the current study was to examine the childhood predictors of adolescent reading comprehension in velo-cardio-facial syndrome (VCFS). Although much research has focused on mathematics skills among individuals with VCFS, no studies have examined predictors of reading comprehension.

Methods—69 late adolescents with VCFS , 23 siblings of youth with VCFS and 30 community controls participated in a longitudinal research project and had repeat neuropsychological test batteries and psychiatric evaluations every 3 years. The Wechsler Individual Achievement Test – 2nd edition (WIAT-II) Reading Comprehension subtest served as our primary outcome variable.

Results—Consistent with previous research, children and adolescents with VCFS had mean reading comprehension scores on the WIAT-II which were approximately two standard deviations below the mean and word reading scores approximately one standard deviation below the mean. A more novel finding is that relative to both control groups, individuals with VCFS demonstrated a longitudinal *decline* in reading comprehension abilities yet a slight *increase* in word reading abilities. In the combined control sample, WISC-III FSIQ, WIAT-II Word Reading, WISC-III Vocabulary and CVLT-C List A Trial 1 accounted for 75% of the variance in Time 3 WIAT-II Reading Comprehension scores. In the VCFS sample, WISC-III FSIQ, BASC-Teacher Aggression, CVLT-C Intrusions, Tower of London, Visual Span Backwards, WCST non-perseverative errors, WIAT-II Word Reading and WISC-III Freedom from Distractibility index accounted for 85% of the variance in Time 3 WIAT-II Reading Comprehension scores. A principal component analysis with promax rotation computed on the statistically significant Time 1 predictor variables in the VCFS sample resulted in three factors: Word reading decoding / Interference control, Self-Control / Self-Monitoring and Working Memory.

Conclusions—Childhood predictors of late adolescent reading comprehension in VCFS differ in some meaningful ways from predictors in the non-VCFS population. These results offer some guidance for how best to consider intervention efforts to improve reading comprehension in the VCFS population.

Correspondence to: Kevin Antshel, Ph.D., Associate Professor of Psychology, Syracuse University, 802 University Avenue, Syracuse, NY 13244; Fax: 315-443-4085, Phone: 315-443-9450, kmantshe@syr.edu.

Keywords

velocardiofacial syndrome (VCFS); 22q11 deletion; reading comprehension; developmental disorder

Velo-cardio-facial syndrome (VCFS), also known as chromosome 22q11.2 deletion syndrome, is a genetic deletion syndrome caused by a deletion of over 40 genes on chromosome 22q11.2. VCFS has a population prevalence of approximately 1:2000–1:4000 live births (Shprintzen, 2008). While there is some degree of variability, VCFS is associated with characteristic physical, behavioural and cognitive phenotypes.

Physically, individuals with VCFS have increased prevalence of congenital heart disease, palatal defects, thymic hypoplasia, and endocrine disorders (Robin & Shprintzen, 2005). Behaviourally, attention deficit / hyperactivity disorder (ADHD), autism spectrum disorders and behavioural inhibition / anxiety disorders are commonly observed during childhood (Antshel et al., 2006; Green et al., 2009) and psychotic and mood disorders are frequently reported in adults (Murphy, 2002). Cognitively, individuals with VCFS often have borderline intellectual functioning, spatial / perceptual vulnerabilities and executive dysfunction (Antshel, Fremont, & Kates, 2008).

Academically, children and adolescents with VCFS struggle most appreciably in math and reading comprehension yet have far stronger reading decoding skills (Antshel et al., 2008). Relative to the math learning disorder literature in VCFS, far less information is presently known about reading comprehension. Moreover, of the few VCFS studies that have reported on reading comprehension skills, all have been descriptive studies using cross-sectional samples (Antshel, AbdulSabur, Roizen, Fremont, & Kates, 2005; Bearden et al., 2001; Lewandowski, Shashi, Berry, & Kwapil, 2007; Moss et al., 1999; Swillen et al., 1999; Woodin et al., 2001). Thus, one aim of the present study is to examine reading comprehension in VCFS using a longitudinal design.

Reading Comprehension

Reading comprehension has traditionally been conceptualized as an end goal of the reading development process (Hock & Mellard, 2005). A simple view of reading is a two-component model in which reading comprehension is the product of decoding and language comprehension (Hoover & Gough, 1990). More complex views propose that reading comprehension is achieved upon mastering less complex skills such as phonological awareness and reading fluency (Johnston & Kirby, 2006).

Comprehension of written text also depends upon higher level processes such as working memory abilities (especially the ability to ignore irrelevant information) (Carretti, Cornoldi, De Beni, & Romano, 2005), inference making, self-monitoring, general semantic knowledge and general linguistic comprehension (Perfetti, Landi, & Oakhill, 2005). Nation (2005) likewise asserts that there are multiple pathways to poor reading comprehension including decoding and/or linguistic comprehension deficits. In general, one single explanation for reading comprehension difficulties is unlikely (Cain & Oakhill, 2006).

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Children who fail to develop adequate reading comprehension skills also experience skills deficits in mathematics (Pimperton & Nation, 2010) and written expression (Cain, 2003). Additionally, reading comprehension skills are predictive of a variety of functional outcomes including the quality of note-taking skills (Peverly & Sumowski, 2012), meaningful causal thinking (Berkant, 2009), high school graduation (McMackin, Tansi, & Hartwell, 2005), and the ability to follow medicine dosage directions (Golbeck, Paschal, Jones, & Hsiao, 2011).

Predicting Reading Comprehension Skill in Typically Developing Populations

In elementary school, early literacy skills (e.g., letter-word identification, decoding, phonological awareness, vocabulary, and oral discourse) are predictive of reading comprehension in 3rd grade (Hemphill & Tivnan, 2008). Nation and Snowling (2004) also discovered that decoding skill, phonological awareness, semantic skills, vocabulary, and listening comprehension at age 8 was predictive of reading comprehension skills 4 years later.

In middle school, intelligence (Kershaw & Schatschneider, 2012; Vaughn et al., 2011), verbal knowledge and oral reading fluency (Denton et al., 2011) as well as phonological processing, syntactic processing, and working memory (Holsgrove & Garton, 2006) have all been reported to be positively associated with reading comprehension. Behaviourally, self- and teacher reports of psychopathy and teacher ratings of callousness are negatively predictive of reading comprehension skills (Vaughn et al., 2011).

In high school students, higher-level cognitive processes such as topic knowledge and participants' value of the reading task (Anmarkrud & Braten, 2009) as well as vocabulary, background knowledge, inference, word reading, and meta-cognitive strategy use (Cromley & Azevedo, 2007) predict reading comprehension. Behaviourally, test anxiety (Minnaert, 1999) has also been demonstrated to negatively affect reading comprehension.

Predicting Reading Comprehension Skill in Developmental Delayed Populations

Despite the abundance of literature that has examined predictors of reading comprehension among typically developing children, much less is known about those variables that predict reading comprehension among children with developmental delays. Although research regarding this topic is sparse, individuals with Down syndrome have received the most attention. For example, Roch and colleagues (Levorato, Roch, & Florit, 2011; Roch, Florit, & Levorato, 2012) have identified verbal memory as a correlate of reading comprehension. Additionally, Laws and Gunn (Laws & Gunn, 2002) followed children and adolescents with Down syndrome over 5 years and discovered that phonological memory and early letter knowledge at baseline predicted reading comprehension.

Current Project

Although individuals with other genetic disorders tend to demonstrate reading comprehension deficits (Mervis, 2009; Temple, 2006), research identifying predictive variables is scarce. There is great value in identifying predictive variables; these predictors can drive intervention efforts aimed at improving reading comprehension. While it is appealing to suggest that those childhood variables that predict late adolescent reading comprehension variables in typical populations will also prove predictive in developmentally delayed populations, this hypothesis needs to be tested empirically. To date, only Down syndrome researchers have researched this topic. While individuals with VCFS and Down syndrome both have developmental delays, individuals with VCFS are less cognitively delayed than individuals with Down syndrome (Levy, 2011), suggesting that results from studies of Down syndrome may not generalize to VCFS.

Similarly, relative to the large literature base examining math abilities in VCFS (Niklasson & Gillberg, 2010; Simon, Bearden, Mc-Ginn, & Zackai, 2005), the extant data that have been published on reading comprehension is scant. This is surprising and represents a clear dearth in the VCFS literature, especially given the importance of reading comprehension to other academic subjects and functional outcomes. The present study attempted to extend beyond descriptive data and predict late adolescent reading comprehension attainment in youth with VCFS from childhood cognitive, academic and behavioural variables.

Identifying predictors is particularly important, as component processes of reading development may be different among individuals with VCFS as compared to children who are typically developing. For example, while reading decoding is mediated by age and positively associated with reading comprehension among typically developing children, children with VCFS experience reading comprehension deficits even though their reading decoding skills remain intact (Antshel et al., 2008; Woodin et al., 2001). Thus, findings from studies that have identified predictors of reading comprehension among typically developing children may not generalize to the VCFS population.

Consistent with reading comprehension research that has examined a typically developing population, we hypothesized that childhood cognitive (IQ, working memory, vocabulary, background knowledge, linguistic comprehension), academic (word reading, reading fluency) and behavioural variables would significantly predict reading comprehension attainment during late adolescence in VCFS.

Methods

Participants

Participants were enrolled in the longitudinal study of risk factors for psychosis in VCFS. In addition to the VCFS cohort, a sibling control and a community control cohort were included. Siblings were included to account for possible environment-specific variables (e.g., socioeconomic status, home environment, etc.). Our recruitment strategy for the community control group was to oversample children with ADHD and learning disabilities given the high prevalence of both conditions in VCFS.

Children with VCFS and their siblings were recruited from a large academic medical centre. Only children with a Fluorescent In Situ Hybridization (FISH) confirmed deletion in the 22q11.2 region of chromosome 22 were included in the sample. Our community control participants were recruited from local public schools. Children with an identifiable genetic disorder (other than VCFS) and/or children with an identifiable neurological condition (e.g., traumatic brain injury, pre-term birth) that is known to affect cognitive or psychiatric function were excluded from participation. Neither group of control participants received formal molecular genetic screening; VCFS is readily identifiable by a facial phenotype and therefore, a higher level of invasiveness (e.g., DNA analysis) was not indicated for our control participants as a measure of screening for VCFS.

Procedure—Informed consent/assent was obtained from parents and children under protocols approved by the institutional review board. Each child enrolled in the study was administered a neuropsychological battery covering intelligence, academic achievement, learning / memory, attention and executive functioning. An experienced doctoral-level examiner conducted the tests in a quiet room in the clinic. The battery took approximately three hours to complete and each participant received a 15-minute break after completing half of the battery. A licensed psychologist or a trained assistant familiar with the measures double scored all protocols. While the children were being assessed, parents completed behaviour rating scales and background information questionnaires.

Measures

Except where noted, all psychological tests and behavioural rating inventories were administered at Times 1, 2 and 3.

Wechsler Intelligence Scale for Children – 3rd edition (WISC-III)—Measures of general intellectual functioning were the Wechsler Intelligence Scale for Children —Third edition (WISC-III) (Wechsler, 1991) or Wechsler Adult Intelligence Scale – Third edition (WAIS-III) (Wechsler, 1993). The WISC-III was administered to all participants at Time 1, and to participants at or under the age of 16 years, 11 months at Times 2 and 3. The WAIS-III was administered to all participants over the age of 16–11 at Time 2. Comparative studies between the Wechsler child and adult intelligence scales suggest that relative to WISC-III scores, WAIS-III scores are inflated between three and seven points (Gold, 1998; Russell, Munro, Jones, Hemsley, & Murray, 1997; Strauss, Sherman, & Spreen, 2006). Accordingly, for our data analyses, we subtracted five points from WAIS-III full-scale, verbal and performance IQ scores.

Wechsler Individual Achievement Test – 2nd edition (WIAT-II)—The WIAT-II (Wechsler, 2001) is an individually administered test of academic achievement, which has been standardized with 4,252 children in Grades K–12. This test contains nine subtests, which are aggregated into four composite scores: reading, mathematics, oral language, and writing (M = 100, SD = 15). For the present study, the three WIAT-II Reading subtests (Word Reading, Reading Comprehension, Pseudoword Decoding) and the two Oral Language subtests (Listening Comprehension, Oral Expression) were utilized.

Attention, Executive Functioning and Learning / Memory Psychological Tests —Attention was assessed using the Gordon Diagnostic System - Continuous Performance Test (CPT) (Gordon, 1983). Errors of omission and commission (z-scores) served as our two predictor variables.

Executive functioning was assessed with the Wisconsin Card Sorting Test (WCST) (Heaton, Chelune, Talley, Kay, & Curtiss, 1993), the Stroop Colour-Word Test (Golden, 1978) and Tower of London (TOL). Perseverative and non-perseverative error standard scores served as our WCST predictor variables. Word, colour, colour-word and interference T-scores comprised our Stroop predictor variables. Total number of moves served as our TOL predictor variable.

Learning and memory was assessed with the California Verbal Learning Test-Children's version (CVLT-C) (Delis, Kramer, Kaplan, & Ober, 1994) or the California Verbal Learning Test (Delis, Kramer, Kaplan, & Ober, 1987) (depending on participant age) and the Visual Span Test (Davis, 1998). CVLT-C List A Total, List A Trial 1, List A Trial 5, List B Total, Short Delay Recall, Long Delay Recall, Intrusions and Perseverations comprised our CVLT-C / CVLT dependent variables. The Visual Span is a computer-presented adaptation of the Visual Memory Span subtest of the Wechsler Memory Scale-Third Edition (Wechsler, 1997), produced on the Colorado Assessment Tests. An irregular array of squares is displayed on the screen, a subset of them is illuminated briefly, and the subject must reproduce these sequences of increasing length. Forward and backward span z-scores were obtained and served as our Visual Span predictor variables.

Psychiatric / Behavioural—The Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL) (Kaufman et al., 1997) was utilized to make DSM-IV (APA, 2000) psychiatric diagnoses at all three time points. The child's primary caregiver (almost always his/her mother) was interviewed with the K-SADS-PL. Every attempt was made to interview the child, but in many cases the child had difficulty responding; in these cases, the K-SADS-PL data was based on the parent's response. A child and adolescent psychiatrist or clinical child psychologist administered the KSADS assessment. Inter-rater reliability, which was calculated for 10 interviews, and assessed with the Kappa coefficient, was .91.

Autism spectrum disorders (ASD) were assessed by the Autism Diagnostic Interview-Revised (ADI-R) (Lord, Rutter, & Le Couteur, 1994), a standardized semi-structured interview conducted with the child's caregiver (usually the mother). The ADI-R provides scores for the three domains in which children with ASD exhibit deficits: Reciprocal Social Interaction, Communication Impairment, and Repetitive Behaviours and Stereotyped Patterns. In order to obtain a diagnosis of an ASD, the child must meet threshold criteria in two of the three domains, and developmental problems must have occurred prior to the age of three years. The ADI-R was telephone administered by a clinician who was trained in the reliable administration of the instrument.

In addition to the K-SADS-PL and ADI-R, both of which record dichotomous outcomes, the Behaviour Assessment Scale for Children (BASC) – Parent and Teacher report versions (Reynolds & Kamphaus, 1992) were administered to provide a continuous measure of behavioural functioning. The Teacher report was only administered at Time 1 and Parent versions were administered at all three time points. Each of the behavioural items of the parent and teacher versions of the BASC are rated on a 4-point frequency scale, ranging from *never* to *almost always*. The child's primary caregiver (almost always his/her mother) and primary teacher completed the BASC. The BASC scales yield composite *T* scores on four dimensions: Externalizing Problems, Internalizing Problems, Behaviour Symptoms, and Adaptive Skills. The teacher rating scale includes an additional School Problem composite. T-scores > 65 indicate clinical significance.

Data Analyses

Descriptive statistics and between group comparisons were computed using chi-square statistics for dichotomous variables and analyses of variance (ANOVA), both univariate and repeated measures, for continuous variables. Holm's (Holm, 1979) sequential Bonferroni procedure to adjust p-values for multiple comparisons was employed for asserting statistical significance for omnibus tests. Eta squared (η^2) is also reported for all analyses. When $\eta^2 > 0.15$, effects are considered "large" in magnitude and when $\eta^2 > 0.06$, effects are viewed as "medium" in magnitude (Cohen, 1988).

Following descriptive comparisons, data analyses were completed in order to best address our *a priori* hypotheses. In a series of two separate linear regressions (one for VCFS, one for sibling/community controls combined), Time 3 (late adolescence) WIAT-II Reading Comprehension standard scores served as our outcome variable. Time 1 (childhood) cognitive, academic and behavioural/psychiatric variables served as our predictor variables. Dichotomous variables (DSM-IV diagnoses) were entered based upon K-SADS-PL and ADI-R results. Based upon empirical evidence suggesting general intelligence best predicts academic achievement (Glutting, Watkins, Konold, & McDermott, 2006), Time 1 WISC-III Full Scale IQ scores were entered into the model in step one. Other variables were entered into the model simultaneously at step two. Finally, to better assimilate and understand the data, two principal component analyses with promax rotations (one for VCFS, one for sibling/community controls combined) were computed on the statistically significant Time 1 predictor variables. Our rationale for using factor analysis was to reduce our data by searching for any underlying latent variables that were reflected in our manifest variables. A promax rotation was selected due to the small to medium correlations among variables.

To detect statistical differences (alpha = 0.05) between the cohorts longitudinally, at least 35 individuals with VCFS, 15 siblings, and 20 community controls are needed to establish a power of 90% on a continuous variable (cognitive function, behavioural ratings) with standard deviations greater than 10. Thus, our study had adequate statistical power.

Results

Descriptive Statistics - Participants

At Time 1, 80 youth with VCFS (Mean age = 11.9 years, SD = 2.2), 33 siblings of youth with VCFS (sibling control; Mean age = 12.2 years, SD = 1.9) and an age and gender matched group of 40 non-VCFS youth (community control; Mean age = 12.0 years, SD = 1.9) participated. No age differences existed between the groups at Time 1, $F(2, 158) = 0.24$, $p = .784$, $\eta^2 = .01$.

At Time 2, 70 youth with VCFS (Mean age = 15.0 years, SD = 2.1), 27 siblings of youth with VCFS (Mean age = 15.0 years, SD = 1.9) and 25 community controls (Mean age = 14.7

years, SD = 1.4) were included in the analyses. At Time 3, 69 youth with VCFS (Mean age = 18.2 years, SD = 2.0), 23 siblings of youth with VCFS (Mean age = 18.0 years, SD = 2.0) and 30 community controls (Mean age = 17.8 years, SD = 1.6) participated in the study. No age, F (2, 120) = 0.44, p = .673, η^2 = .01, or gender differences, χ^2 (df = 2) = 0.91, p = .686, existed between the groups at Time 3. Please see Table 1 for complete participant information.

An independent samples t-test indicated that there were no differences in attrition between our three groups, t (2) = 2.89, p = .307. Furthermore, participants lost to follow-up at Time 3 did not differ from those who did follow-up on any relevant Time 1 sociodemographic measures including participant age, gender, and socioeconomic status. In addition, participants lost to follow-up did not differ from those who did follow-up on any relevant Time 1 psychiatric or cognitive variables. Thus, those participants who completed Time 3 assessments appear representative of the broader Time 1 sample.

Many children and adolescents with VCFS are prescribed a psychotropic medication, especially methylphenidate and selective serotonin reuptake inhibitors (Gothelf, 2007). No attempt was made to control for medication use during the assessment; if a child was prescribed medication, parents were instructed to give the medication as prescribed on the day of the research assessment. At Time 1, significantly more children with VCFS (57%) were prescribed a psychotropic medication than sibling (3%) and community (26%) controls, χ^2 (df = 2) = 7.69, p< .001. At Time 3, this trend continued: significantly more late adolescents with VCFS (63%) were prescribed a psychotropic medication than sibling (6%) and community (13%) controls, χ^2 (df = 2) = 11.06, p< .001. At Time 1, the most commonly prescribed medications for children in all three groups were stimulant medications such as methylphenidate. At Time 3, the most commonly prescribed medications in the sibling and community controls continued to be stimulants yet in the VCFS cohort, atypical antipsychotic medications were the most frequently prescribed medication. Of the 43 late adolescents with VCFS who were prescribed a medication at Time 3, 17 (40%) were prescribed an atypical antipsychotic medication.

Descriptive Statistics – Reading Attainment

As shown in Table 1, WIAT-II Reading Comprehension group differences existed at all three time periods: Time 1, F (2, 147) = 59.86, p < .001, η^2 = .39, Time 2, F (2, 117) = 29.73, p < .001, η^2 = .29 and Time 3 (2, 117) = 35.78, p < .001, η^2 = .33. There was no group x time interaction at Time 2, F (2, 112) = 2.45, p = .091, η^2 = .04. At Time 3, however, a group x time interaction emerged, F (2, 112) = 5.73, p < .001, η^2 = .11. Relative to the control groups, individuals with VCFS demonstrated a decline in reading comprehension scores.

Also shown in Table 1, reading decoding WIAT-II Word Reading group differences existed at all three time periods: Time 1, F (2, 147) = 31.60, p < .001, η^2 = .20, Time 2, F (2, 117) = 23.73, p < .001, η^2 = .17 and Time 3 (2, 117) = 18.49, p < .001, η^2 = .14. There was no group x time interaction at Time 2, F (2, 112) = 2.06, p = .270, η^2 = .03. At Time 3, however, a group x time interaction emerged, F (2, 112) = 6.90, p < .001, η^2 = .12. Relative to the control groups who both had slight decreases in word reading scores, individuals with VCFS demonstrated a slight increase in word reading scores.

Childhood Predictors of Late Adolescent Reading Comprehension

In the combined control sample, the linear regression indicated that step one (WISC-III FSIQ) was significant, F (1, 51) = 7.28, p = .013, R^2 = .259. After controlling for the effect of IQ, step two indicated individual Time 1 predictor variables that were statistically significant predictors of Time 3 WIAT-II Reading Comprehension scores included: WIAT-II Word Reading, WISC-III Vocabulary and CVLT-C List A Trial 1, F (3, 46) = 16.23, p <. 001, R^2 change= .494. No other Time 1 cognitive or psychiatric / behavioural variables were significant predictors after controlling for the effects of IQ. Together, these four predictor variables accounted for 75.3% of the variance in Time 3 WIAT-II Reading Comprehension scores.

In the VCFS sample, the linear regression indicated that step one (WISC-III FSIQ) was significant, F (1, 67) = 8.88, p = .007, R^2 = .297. After controlling for the effect of IQ, step two indicated individual Time 1 predictor variables that were statistically significant predictors of Time 3 WIAT-II Reading Comprehension scores included: BASC-Teacher Aggression, CVLT-C Intrusions, TOL, Visual Span Backwards, WCST non-perseverative errors, WIAT-II Word Reading and WISC-III Freedom from Distractibility index, F (7, 60) = 17.26, p <.001, R^2 change= .559. No other Time 1 cognitive or psychiatric / behavioural variables were significant predictors after controlling for the effects of IQ. Together, these eight predictor variables accounted for 85.6% of the variance in Time 3 WIAT-II Reading Comprehension scores. Please see Table 2 for coefficients of statistically significant Time 1 predictor variables in the VCFS sample.

Data Reduction

Combined Control Sample—As detailed in Table 3, the principal component analysis with promax rotation computed on the statistically significant Time 1 predictor variables resulted in one factor with an eigenvalue above 1.0. Explaining 57.05% of the variance, WISC-III FSIQ, WISC-III Vocabulary subtest and WIAT-II Word Reading subtest all had factor loadings above 0.5. Conceptually, these three variables may be best interpreted as verbal knowledge.

VCFS Sample—As detailed in Table 4, the principal component analysis with promax rotation computed on the statistically significant Time 1 predictor variables resulted in three factors with eigenvalues above 1.0. As noted in Table 4, after the promax rotation, Factor 1 explained the largest proportion of the variance (25.7%) and consisted of three measures (in order of factor loading): CVLT-C Intrusions, WISC-III Freedom from Distractibility IQ and WIAT-II Word Reading. Conceptually, these three variables appear to be best described as Word reading decoding / Interference control. Factor 2 consisted of BASC Teacher Aggression and WCST non-perseverative errors and explained 22% of the variance. Conceptually, these two variables appear to be best described as Self-Control / Self-Monitoring. Finally, Factor 3 consisted of Tower of London and Visual Span Backwards and explained 17.9% of the variance. Conceptually, these two variables appear to be best described as Working Memory.

Discussion

Consistent with previous studies (Antshel et al., 2005; Bearden et al., 2001; Lewandowski et al., 2007; Moss et al., 1999; Swillen et al., 1999; Woodin et al., 2001), children and adolescents with VCFS had mean reading comprehension scores on the WIAT-II which were approximately two standard deviations below the mean and word reading scores approximately one standard deviation below the mean. It is generally considered that word reading is an area of relative strength when considering the VCFS cognitive phenotype (Antshel et al., 2008). A more novel finding is that relative to both control groups, individuals with VCFS demonstrated a longitudinal *decline* in reading comprehension abilities yet stability in word reading abilities.

Childhood Predictors of Late Adolescent Reading Comprehension

Our control sample data are consistent with the extant data on typically developing populations that suggests childhood vocabulary, word reading decoding skills and general knowledge are predictors of adolescent reading comprehension abilities (Hemphill & Tivnan, 2008; Nation & Snowling, 2004; Vaughn et al., 2011).

In our VCFS sample, eight childhood predictors accounted for approximately 85% of the variance in late adolescent reading comprehension performance. A principal components analysis with promax rotation suggested three factors could account for the data reasonably well: 1) Word reading decoding / Interference control, 2) Self-Control / Self-Monitoring and 3) Working Memory. Not unexpectedly, in both our control and VCFS samples, child word reading decoding skills were predictive of late adolescent reading comprehension attainment. However, and unlike the results for our control sample, late adolescent VCFS reading comprehension performance was predicted by several abilities typically subsumed under the umbrella of executive functions. For example, our data suggest that in the VCFS population, word reading and interference control may be latent variables. This is consistent with other child research that has examined reading comprehension in developmentally delayed/LD (Borella, Carretti, & Pelegrina, 2010; Palladino & Ferrari, 2013; Savage, Cornish, Manly, & Hollis, 2006) or psychiatric populations (Miller et al., 2013).

Another executive function, verbal working memory, has been previously reported to predict reading comprehension skills in both typical (Holsgrove & Garton, 2006) and developmentally delayed (Down syndrome) (Laws & Gunn, 2002; Levorato, Roch, & Beltrame, 2009; Roch, Florit, & Levorato, 2013) populations. While verbal working memory is not as consistently reported in the reading comprehension literature as vocabulary, word reading decoding, overall linguistic comprehension, general fund of knowledge or intelligence, multiple studies have reported verbal working memory skills to predict reading comprehension abilities. For example, a meta-analysis (Carretti, Borella, Cornoldi, & De Beni, 2009) found that the working memory involvement in reading comprehension tasks is most robust when measured by experimental tasks that require both the maintenance *and* manipulation of information. To understand written discourse a reader must not only maintain some bit of information but also blend that information with previous knowledge. Visual Span Backwards, a visual working memory task, significantly predicted reading comprehension in our sample of late adolescents with VCFS. While TOL is not considered a working memory task and is generally considered a planning task, the TOL is not a “pure” planning measure and a varied array of cognitive abilities are likely involved in successful task performance (Berg & Byrd, 2002).

Neither childhood ADHD or ASD as categorical diagnoses nor inattentive or hyperactive/impulsive symptoms as continuous variable were predictive of reading comprehension performance in late adolescence. There are a variety of possible explanations for this finding. The prevalence of ADHD (30–40%) in children with VCFS is high (Antshel et al., 2006; Green et al., 2009) and many children with VCFS (regardless of an ADHD diagnosis) have difficulties regulating their attention (Antshel et al., 2008). While not specific to ADHD, childhood self-control and self-monitoring difficulties (and not ADHD) predicted reading comprehension in late adolescents with VCFS.

In addition to childhood ADHD and ASD not predicting late adolescent reading comprehension, linguistic comprehension (as measured by the WIAT-II Language Comprehension task) was also not predictive. Thus, reading comprehension in VCFS may not be predicted by general linguistic competence as is often reported in the typically developing population (Cain & Oakhill, 2006; Nation, 2005; Perfetti et al., 2005).

Study Limitations

These data must be viewed in the context of several methodological limitations. First, rather than using a multi-method assessment design (e.g., curriculum-based measurement conducted in the classroom), our study relied on a single testing episode to generate our primary outcome variable. While the WIAT-II Reading Comprehension has solid predictive validity to classroom performance (Wechsler, 2002), future research should attempt to use multiple different assessment methods to measure reading comprehension. Likewise, the actual WIAT-II stories may not have provided interest in reading (which equates to increased motivation) (Taboada, Tonks, Wigfield, & Guthrie, 2009). Intrinsic motivation may be particularly important for children with low ability (Logan, Medford, & Hughes, 2011), like those with VCFS often demonstrate. Future research should include motivational assessment as a possible independent variable.

In addition, and while K-SADS-PL data were collected from the participants with VCFS themselves at all three time points, at Time 1 (childhood) as a function of the general cognitive delays intrinsic to VCFS, we relied heavily on parent and teacher report of child psychiatric / behavioural functioning. This may have introduced report bias in our data. While psychotic symptoms were rare at Time 1, it is possible that the emergence of psychosis was a factor explaining reading comprehension performance at Time 3. Others (Gothelf et al., 2007; Green et al., 2009) have reported on the decline of verbal IQ as a presage to the onset of psychosis in VCFS. Determining the association between decline in reading comprehension and onset of prodromal symptoms of psychosis is beyond the scope of this investigation; the aim was to predict late adolescence reading comprehension attainment from childhood variables.

Other confounding variables include the limited follow-up period (6 years) that included puberty. Non-linear developmental effects of puberty on cognition have been described previously (Blakemore & Choudhury, 2006). Likewise, the confounding effects of treatment were not considered in our study. Given that nearly all children and adolescents with VCFS has an Individual Education Plan (IEP) and receive intervention services (Cutler-Landsman, 2012), it was not possible to ascertain the role that the child's history of treatment may have in explaining our results. This is a variable that should be considered in future studies (Duff & Clarke, 2011). Finally, given that our community control participants did not exclude participants with ADHD or learning disabilities, these results are not generalisable to typically developing populations.

Clinical / Educational Implications / Future Directions

These methodological limitations notwithstanding, to our knowledge, this is the first study that has examined childhood predictors of late adolescent reading comprehension abilities in adolescents with VCFS. Our results tentatively indicate several clinical/educational implications. First, teachers and parents should continue to stress the importance of acquiring word reading decoding skills and fluency. These are typically noted to be phenotypic areas of strength for children with VCFS (Antshel et al., 2008). Second, efforts to improve working memory abilities via the use of strategies could also be beneficial. Albeit controversial (Melby-Lervag & Hulme, 2012), there is some evidence to suggest that working memory skills can be improved via cognitive remediation/computerized interventions (for a review, see (Diamond, 2012). Future research should consider the extent to which these cognitive remediation interventions improve working memory and reading comprehension as a more distal target.

Third, children with VCFS should be explicitly taught self-monitoring strategies. For example, the multi-component reading comprehension strategy, *TWA (Think Before Reading, Think While Reading, and Think After Reading)* may be worth empirically investigating as a possible educational strategy for improving reading comprehension in VCFS. There is some existing evidence to suggest it is a beneficial strategy in the ADHD population (Rogevich & Perin, 2008). Self-monitoring of academic performance has been demonstrated to be effective in increasing academic productivity (completion and/or rate of completion), accuracy, or use of strategies (Mathes & Bender, 1997; Trammel, Schloss, & Alper, 1994). Fourth, disruptive behaviours and poor self-control negatively affect reading comprehension attainment (Vaughn et al., 2011) and should also be treated with empirically supported interventions such as contingency management, parent management training, etc. (Ollendick & King, 2000).

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Table 1

Participant Data

	VCFS	Sibling Control	Community Control
	Time 1 – Late Childhood		
N	80	33	40
Age	11.9 (2.2)	12.2 (1.9)	12.0 (1.9)
WISC-III FSIQ	71.0 (13.5) *a****, *b****	105.0 (14.5)	97.2 (12.7)
WIAT-II READING COMP.	71.1 (16.2) *a****, *b****	99.6 (17.1)	93.6 (14.1)
WIAT-II WORD READING	85.2 (13.8) *a****, *b***	104.1 (14.7)	98.7 (13.9)
	Time 2 – Early Adolescence		
N	70	27	25
AGE	15.0 (2.1)	15.0 (1.9)	14.7 (1.4)
WISC-III FSIQ	70.4 (14.2) *a****, *b****	103.8 (14.1)	98.5 (13.5)
WIAT-II READING COMP.	70.2 (16.0) *a****, *b****	95.3 (17.6)	85.1 (14.7) *a**
WIAT-II WORD READING	85.9 (13.1) *a****, *b***	103.0 (14.2)	96.2 (13.9)
	Time 3 – Late Adolescence		
N	69	23	30
AGE	18.2 (2.0)	18.0 (2.0)	17.8 (1.6)
WISC-III FSIQ	70.8 (13.2) *a****, *b****	104.9 (14.0)	98.2 (13.0)
WIAT-II READING COMP.	62.7 (13.4) *a****, *b****	96.8 (17.1)	89.8 (15.2) *a**
WIAT-II WORD READING	86.7 (13.4) *a****, *b**	102.1 (14.7)	94.2 (13.8)

Note. WISC-III = Wechsler Intelligence Scale for Children – 3rd edition (Wechsler, 1991). WIAT-II Reading Comp = Wechsler Individual Achievement Test – Second edition (Wechsler, (Wechsler, 2002) – Reading Comprehension subtest.

[a] compared to sibling control participants.

[b] compared to community control participants.

[*] $p < .05$.

[**] $p < .01$.

[***] $p < .001$.

Table 2

Predicting Time 3 WIAT-II Reading Comprehension from Time 1 Variables in the VCFS Sample – Significant Linear Regression Coefficients

	Standardized Beta Coefficient	t	Sig.
	Step One		
WISC-III Full Scale IQ	.436	3.211	.001
	Step Two		
BASC Teacher Aggression	− .284	− 1.357	.016
CVLT-C Intrusions	− .316	− 1.725	.028
Tower of London (# of moves)	− .347	− 1.337	.016
Visual Span Backward	.234	1.297	.037
WCST Non-perseverative errors	.284	1.117	.030
WIAT-II Word Reading	.431	2.881	.001
WISC-III Freedom Distractibility IQ	.338	1.373	.022

Note. WISC-III = Wechsler Intelligence Scale for Children – 3rd edition (Wechsler, 1991). BASC = Behaviour Assessment Scale for Children (Reynolds & Kamphaus, 1992). CVLT-C = California Verbal Learning Test – Children's version (Delis et al., 1994). WCST = Wisconsin Card Sorting Test (Heaton et al., 1993). WIAT-II = Wechsler Individual Achievement Test – Second edition (Wechsler, 2002).

Table 3

Factor Analysis on Significant Time 1 predictors of Time 3 WIAT-II Reading Comprehension Performance – Combined Control Sample

Initial Eigenvalues			
Component	**Total**	**% of variance**	**Cumulative %**
1	2.288	57.051	57.051
2	0.886	21.046	78.097
3	0.673	17.073	95.170
4	0.178	4.458	100.000

Component Matrix – Component 1	
Variable	Factor Loading
WISC-III Full Scale IQ	.904
WISC-III Vocabulary Subtest	.818
WIAT-II Word Reading Subtest	.685
CVLT-C List A Trial 1	.506

Note. WISC-III = Wechsler Intelligence Scale for Children – 3rd edition (Wechsler, 1991). CVLT-C = California Verbal Learning Test – Children's version (Delis et al., 1994). WIAT-II = Wechsler Individual Achievement Test – Second edition (Wechsler, 2002).

Table 4

Factor Analysis on Significant Time 1 predictors of Time 3 WIAT-II Reading Comprehension Performance – VCFS sample

	Initial Eigenvalues			Rotation Sums of Squared Loadings		
Component	**Total**	**% of variance**	**Cumulative**	**% Total**	**% of variance**	**Cumulative %**
1	3.857	38.359	38.359	2.472	25.732	25.732
2	1.512	14.958	53.317	2.267	22.003	47.735
3	1.222	12.363	65.653	1.989	17.918	65.653
4	0.872	8.703	74.356			
5	0.636	6.463	80.819			
6	0.606	6.001	86.820			
7	0.468	4.700	91.520			
8	0.362	3.611	95.131			
9	0.257	2.663	97.794			
10	0.221	2.206	100.000			

Rotated Component Matrix

	Component		
	1	2	3
CVLT-C INTRUSIONS	−**.801**	−.036	.245
WISC-III FDIQ	**.732**	.345	.312
WIAT-II WORD READING	**.702**	.019	.258
BASC-TEACHER AGGRESSION	−.236	−**.884**	.032
WCST NON-PERSEVERATIVE	.328	**.636**	.267
TOWER OF LONDON	−.251	−.036	−**.789**
VISUAL SPAN BACKWARDS	.318	−.025	**.777**

Note. Extraction Method: Principal Component Analysis. Rotation Method: Promax with Kaiser Normalization. WISC-III = Wechsler Intelligence Scale for Children – 3rd edition (Wechsler, 1991). BASC = Behaviour Assessment Scale for Children (Reynolds & Kamphaus, 1992). CVLT-C = California Verbal Learning Test – Children's version (Delis et al., 1994). WCST = Wisconsin Card Sorting Test (Heaton et al., 1993). WIAT-II = Wechsler Individual Achievement Test – Second edition (Wechsler, 2002).