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Childhood Predictors of Written Expression in Late Adolescents with 22q11.2 Deletion Syndrome: A Longitudinal Study

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Abstract

Background—22q11.2 Deletion Syndrome (22q11DS) is the second most prevalent genetic syndrome and has a characteristic academic and behavioural phenotype. The primary objective of the current study was to examine the childhood predictors of written expression achievement in adolescents with 22q11DS. Written expression is an important skill that can impact an individual's overall academic performance, potentially resulting in increased levels of stress and exacerbation of psychiatric symptoms.

Methods—A total of 119 participants were included in this study. Sixty-nine late adolescents with 22q11DS and 50 controls (consisting of a combined sample of 23 unaffected siblings of youth with 22q11DS and 27 community controls) participated in a 6-year longitudinal research project and received neuropsychological test batteries every 3 years. The Written Expression subtest of the Wechsler Individual Achievement Test–2nd edition (WIAT-II) was the primary outcome measure in the current project.

Results—Findings indicated differences in childhood predictors of adolescent written expression between participants in the 22q11DS group and participants in the control group. Whereas childhood verbal IQ scores predicted adolescent written expression for participants in the control group, childhood executive function and language skills were unique predictors of adolescent written expression in individuals with 22q11DS.

Conclusions—Childhood predictors of late adolescent written expression in 22q11DS differ in meaningful ways from predictors in the non-22q11DS population. These results offer some guidance on the underlying factors that may be useful to consider when developing written expression interventions for children with 22q11DS.

Keywords

22q11.2 deletion syndrome; written expression; executive functioning; developmental disorder

Writing is an essential skill for students that can be used to assemble and demonstrate new information and ideas (Graham, Gillespie, & McKeown, 2013). Writing can help improve

critical thinking skills (Quitadamo & Kurtz, 2007) and is a useful modality for students to demonstrate their learning. Individuals with poor writing abilities are at higher risk of grade retention because they are unable to complete assignments that require written work (Abbott, Berninger, & Fayol, 2010). In addition, they may struggle to pass high-stakes tests which are increasingly requiring writing (Jenkins, Johnson, & Hileman, 2004). This puts individuals with poor writing abilities at an increased risk for poor academic performance which can then lead to increased levels of stress (Wenz-Gross, Siperstein, Untch, & Widaman, 1997). Increased stress can potentially exacerbate psychiatric symptoms (Belvederi et al., 2012). Thus, written expression is an important topic to consider in populations with developmental delays and psychiatric diagnoses.

22q11.2 Deletion Syndrome

A population that is commonly diagnosed with both developmental delays and psychiatric diagnoses is 22q11.2 deletion syndrome (22q11DS). Previously known as velo-cardio-facial syndrome (VCFS), 22q11DS is caused by a microdeletion of over 40 genes on chromosome 22 at band q11.2. Estimated at 1:4000 to 1:6000 live births, 22q11DS is one of the most prevalent genetic disorders (Botto et al., 2003). Phenotypic expression of this microdeletion is highly variable (Bassett et al., 2011). Behaviourally, children with 22q11DS are reported to receive comorbid diagnoses of attention deficit/hyperactivity disorder (ADHD; Schneider et al., 2014), autism spectrum disorder (ASD; Fine et al., 2005) and anxiety disorders (Antshel et al., 2006). As adults, psychotic and mood disorders become more prevalent within this population (Murphy, 2002), with over 1/3 of adults with 22q11DS having a psychotic disorder (Schneider et al., 2014).

Cognitively, individuals with 22q11DS may experience intellectual delays with IQ scores primarily falling in the borderline range of intelligence (De Smedt et al., 2007). Furthermore, individuals with 22q11DS often experience an overall cognitive decline of approximately 7 or more full scale IQ points over time (Duijff et al., 2012; Vorstman et al., 2015). In addition, individuals with 22q11DS experience difficulty with attention (Antshel et al., 2008) and working memory (Woodin et al., 2001). Linguistically, language development for individuals with 22q11DS can be delayed (Scherer, D'Antonio, & Kalbfleisch, 1999) and language impairment has been documented in this population (Moss et al., 1999). Academically, individuals with 22q11DS display relative and normative weaknesses in mathematics abilities (e.g., word problem solving; De Smedt et al., 2006) and reading comprehension (Antshel, Hier, Fremont, Faraone, & Kates, 2014). On the other hand, reading decoding, spelling, and phonological processing skills are areas of relative academic strength for individuals with 22q11DS (Antshel, Fremont, & Kates, 2008; Swillen et al., 1999).

Despite knowing about most academic domains, the current 22q11DS literature is lacking both (a) quantitative data on written expression and (b) an understanding of the development of written language and the early predictors of later written expression in children and youth with 22q11DS. Therefore, an objective of this present study is to examine written expression in children and youth with 22q11DS using a longitudinal design. Given the great risk for psychosis in this population (Schneider et al., 2014), as well as the cascade of events noted

above related to written expression vulnerabilities (poor written expression → poor academic performance → stress → exacerbation of psychiatric symptoms), this line of investigation is important and has clinical relevance. Since no previous 22q11DS research has considered written expression, we rely upon the extant, non-22q11DS literature, as described below, for hypotheses.

Written Expression in Typically Developing Populations

A strong association between written expression, attention, and executive functions exists (Hooper et al., 2011; Kent, Wanzek, Petscher, Otaiba, & Kim, 2013). For example, in a study of 55 elementary aged students with and without problems in written expression, the children with writing problems performed worse on tasks involving executive function skills (e.g., initiating behaviour, sustaining behaviour, set shifting, and inhibiting behaviour) than students without writing problems (Hooper, Swartz, Wakely, de Kruif, & Montgomery, 2002). Another executive function, working memory, is also essential to written expression (Swanson & Berninger, 1996) because it allows for the storage of several ideas, retrieval of grammatical rules from long-term memory, and self-monitoring throughout the writing process (Kellogg, 1999). Finally, a relation exists between language skills (e.g., phonological processing, verbal reasoning, expressive language, and receptive language) and written expression abilities (Abbott & Berninger, 1993; Hooper et al., 2011; Kent et al., 2013).

Written Expression in ADHD

As noted above, executive function skills are a predictor of written expression abilities in the typically developing population. A disorder that is often defined by executive dysfunction, ADHD, is highly prevalent in 22q11DS (Hooper et al., 2013; Antshel et al., 2010; Antshel et al., 2006; Vogels et al., 2002). Non-22q11DS ADHD research has indicated that children with ADHD are more likely to display greater problems with written expression when compared to a control sample (Mayes & Calhoun, 2007). Other non-22q11DS ADHD research has indicated that written expression difficulties in adolescents with ADHD may be attributed to executive processing deficits (DeBono et al., 2012).

Current Project

Although research examining the written expression skills of typically developing children is abundant, an understanding of written expression among children with developmental delays is lacking. To our knowledge, no studies have quantitatively investigated childhood predictive variables of written expression skills in children with 22q11DS. An understanding of these predictors may lead to the development of tailored interventions targeted at improving written expression among this population of children. With tailored interventions, students with 22q11DS may be academically more successful which may lead to a lower risk for psychiatric symptom exacerbation. Here, we aim to empirically test whether childhood predictors of adolescent written expression skills in typically developing youth are the same as those with 22q11DS. Consistent with previous research investigating written expression in a typically developing population, we hypothesised that executive functioning

and language skills in children with and without 22q11DS would significantly predict written expression attainment during late adolescence.

Method

Participants

The data from participants enrolled in a longitudinal study investigating risk factors for psychosis in 22q11DS were utilised for this study. Children with 22q11DS were recruited from a large academic medical center. Confirmation of each child's genetic deletion in the q11.2 region of chromosome 22 was obtained for each participant using fluorescent *in situ* hybridisation (FISH). Children with any genetic condition other than 22q11DS and/or children with an identifiable neurological condition (e.g., traumatic brain injury, pre-term birth, etc.) that may affect cognitive or psychiatric functioning were excluded from this study.

In addition to the 22q11DS cohort, siblings of participants with 22q11DS and individuals from the community were combined to form a combined control cohort. Neither control group received a formal molecular genetic screening evaluation. Siblings helped to control for any possible environmental extraneous variables (e.g., socioeconomic status, home environment, etc.) that may affect written expression. The community control sample was not an entirely typically developing sample and included participants with ADHD and/or learning disabilities (recruited to match higher functioning individuals with 22q11DS). The sibling and community control groups were combined into a single group for this study because the two groups did not differ significantly from each other in age ($t_{(48)} = -.413$, $p = .681$), gender ratio ($t_{(48)} = -.797$, $p = .429$), Time 1 Full Scale IQ ($t_{(48)} = -.699$, $p = .488$), Time 1 Performance IQ ($t_{(48)} = -1.23$, $p = .222$), Time 1 Verbal IQ ($t_{(48)} = -.083$, $p = .934$) and Time 3 written expression scores ($t_{(48)} = -.503$, $p = .617$).

Since, for this paper, we were interested in examining predictors to written expression abilities in late adolescence, we only included participants for whom we had longitudinal data through the third timepoint of the study, when the total sample's ($N=119$) mean age was 18.05 (S.D. 1.99) years. Of the 119 participants, ninety-five participants (60 in the 22q11DS group and 35 combined controls [17 community controls, and 18 sibling controls]) were initially recruited at Time 1 of the study. No age differences existed between the study groups ($t_{(117)} = 1.91$, $p = .059$). At Time 2, 24 additional participants (9 in the 22q11DS group, 10 community controls, and 5 sibling controls) were added (see Figure 1) to the original Time 1 sample. Accordingly, the total sample for this study of written expression consisted of 119 participants (69 in the 22q11DS group and 50 in the combined control group).

For participants recruited at Time 2 ($n = 24$), we imputed their Time 1 written expression and neuropsychological test scores for Time 1 from their Time 2 scores. There were no statistically significant differences between participants entering at Time 1 and participants entering at Time 2 in their baseline Verbal IQ, Performance IQ, Full Scale IQ, and Time 3 WIAT-II written expression standard scores across all groups. Sample demographics for all time points are described in Table 1.

Procedures

Informed consent/assent under protocols approved by the institutional review board was obtained from parents and children. A battery of psychological tests was administered to each child enrolled in this study at Time 1, Time 2, and Time 3. An experienced doctoral-level examiner administered the measures in a quiet room. Each participant took approximately three hours to complete the psychological battery and received a 15-minute break halfway through testing. All protocols were double scored by a licensed psychologist or a trained research assistant who was familiar with the measures.

Measures

Executive Function—In the interest of data reduction and embedding psychological tests in a larger model of Executive Functioning as opposed to viewing it as separate tasks, the z-scores of multiple executive function measures were averaged to create a mean executive function score. This omnibus score served as one of our predictor variables. The following measures were included in our Executive Function mean and were selected based upon a well accepted model of executive functioning which includes set shifting, working memory and inhibitory control (Miyake et al., 2000).

Gordon Diagnostic System – Continuous Performance Test (GDS-CPT; Gordon, 1983): The GDS-CPT is a measure of vigilance and inhibitory control. D prime scores were computed according to the method developed by Green and Swets (1966) and represents the ability to correctly respond on targets and inhibit response on non-targets. The GDS-CPT was chosen because previous research demonstrated a relation between attention and written expression (Hooper et al., 2011; Kent et al., 2013).

Wisconsin Card Sorting Test (WCST; Heaton, Chelune, Talley, Kay, & Curtiss, 1993): The WCST was used to measure cognitive flexibility. Perseverative and non-perseverative error standard scores were entered as predictor variables for the WCST. Non-perseverative errors were included because previous research has demonstrated self-monitoring as an important skill in the writing process (Charles, 1990). Perseverative errors were included because previous research has demonstrated set shifting as an important skill in the writing process (Hooper et al., 2002).

Tower of London (TOL; Shallice, 1982): The TOL was included in the executive function mean to measure planning. Our predictor variable for the TOL was the total number of moves. This variable was chosen because planning has been identified as an important basic component within the writing process (Flower & Hayes, 1981). Because standardised scores for the TOL are not provided, the z-score was based on the combined control group mean.

Working Memory Tests: Working memory is a significant contributor to the writing process (Kellogg, 1999, Swanson & Berninger, 1996). Thus, the following tests assessing the working memory of each participant were also included in the executive functioning mean score: the Visual Span Test (Davis, 1998), the Digit Span subtest from the Wechsler Intelligence Scale for Children-third edition (WISC-III; Wechsler, 1991), and the California Verbal Learning Test-Children's version (CVLT-C; Delis et al., 1994). The Visual Span Test

is a computerised adaptation from the Visual memory Span subtest of the Wechsler Memory Scale – Third Edition (Wechsler, 1997), in which participants reproduce patterns of briefly illuminated squares. Z-scores of forward and backward span were used as predictors. Similar to Visual Span, forward and backward Z-scores were calculated for the Digit Span subtest from the WISC-III. The final predictor variable of learning and memory was List A Total of the CVLT-C.

Language—The Clinical Evaluation of Language Fundamentals—fourth edition (CELF-4; Semel, Wiig, & Secord, 2003) was used to assess each participant's receptive and expressive language skills. The CELF-4 was included because previous research has identified language as a critical component to the writing process (Abbott & Berninger, 1993; Hooper et al., 2011; Kent et al., 2013). The CELF-4 Total Language score was used in analyses.

Psychiatric/Behavioural—Given that children with 22q11DS have high incidences of psychiatric disorders (Antshel et al., 2006; Fine et al., 2005; Schneider et al., 2014), the Schedule for Affective Disorders and Schizophrenia for School-Age Children—Present and Lifetime Version (K-SADS-PL; Kaufman et al., 1997) was utilised to assess DSM-IV (APA, 2000) psychiatric diagnoses in all participants. A child and adolescent psychiatrist or a clinical child psychologist administered the K-SADS-PL to the primary caregiver of each participant. Inter-rater reliability was calculated for 10 interviews and determined to have a Kappa coefficient of 0.91. The total number of DSM-IV diagnoses (e.g., anxiety disorder, mood disorder, psychosis, etc.) for which the participant met current diagnostic criteria was included in analyses.

Wechsler Intelligence Scale for Children – Third Edition (WISC-III)—The WISC-III (Wechsler, 1991) was used to measure intellectual functioning in all participants at Time 1. At Times 2 and 3, the WISC-III was administered to all participants who were younger than 16 years, 11 months. For participants at Time 2 ($n = 21$; 14 from the group of individuals with 22q11DS, 1 from the community control group, and 6 from the sibling control group) and Time 3 ($n = 87$; 49 from the 22q11DS-affected group, 18 from the community control group, and 20 from the sibling control group) who were older than 16 years, 11 months, the WAIS-III (Wechsler, 1993) was administered. Performance IQ (PIQ) and Verbal IQ (VIQ) were included as predictors in the model.

Wechsler Individual Achievement Test – Second Edition (WIAT-II)—The WIAT-II (Wechsler, 2001) was administered to participants in order to assess academic achievement. This test was standardised with 4,252 children in grades K-12, and contains nine subtests designed to assess reading, mathematics, oral language, and writing. For the purposes of this study, three WIAT-II written expression subtests were utilised (Word Fluency, Sentences, and Paragraph Composition for participants in 6th grade and younger or Essay Composition for participants in 7th grade and older). The WIAT-II Written Expression composite standard score served as the dependent variable in this study.

Planned Analyses

Using both univariate and repeated measures analyses of variance (ANOVA), descriptive statistics and between group comparisons were computed. Following these descriptive comparisons, one linear regression model was computed for each cohort (22q11DS and combined control) in order to address our research questions. For the regression models in both cohorts, Time 3 WIAT-II written expression composite standard scores were entered as the outcome variable. In both cohorts, gender, age, PIQ, and VIQ were entered in step one of the regression model. Time 1 mean executive function score, presence of any psychiatric disorder, and CELF-4 total was entered into step two of the model.

In order to ensure that our study had adequate statistical power, each cohort consisted of at least 35 individuals in order to establish a power of 90% on a continuous variable with a standard deviation greater than 10.

Results

Descriptive Statistics – Written Expression, Verbal IQ, and Performance IQ

Also shown in Table 1, and entirely consistent with previous research, group differences in intellectual functioning were robust. Group differences in Full Scale IQ existed at all three time periods: Time 1 ($t_{(102)}=12.08$, $p<.001$), Time 2 ($t_{(103)}=12.51$, $p<.001$), and Time 3 ($t_{(91)}=13.06$, $p<.001$). Group differences in Verbal IQ scores were also present at all three time periods: Time 1 ($t_{(108)}=10.41$, $p<.001$), Time 2 ($t_{(102)}=11.05$, $p<.001$), and Time 3 ($t_{(89)}=11.64$, $p<.001$). Finally, group differences in Performance IQ existed at all three time periods: Time 1 ($t_{(90)}=11.90$, $p<.001$), Time 2 ($t_{(97)}=11.93$, $p<.001$), and Time 3 ($t_{(83)}=12.87$, $p<.001$). Please see Table 1 for complete information.

A more novel finding is that group differences in WIAT-II Written Expression scores were also observed at all three time periods: Time 1 ($t_{(74)}=7$, $p<.001$), Time 2 ($t_{(99)}=8.59$, $p<.001$), and Time 3 ($t_{(114)}=9.20$, $p<.001$).

Childhood Predictors of Late Adolescent Written Expression Skills

In the combined control sample, step one of the linear regression (gender, age, PIQ, and VIQ) was statistically significant ($F_{(4,45)}=22.8$, $p<.001$, $R^2=.67$; see Table 2). With gender, age, PIQ and VIQ held constant, the linear regression for the combined control sample indicated that step two of the regression (psychiatric disorder, mean executive function score, and language) was also significant ($F_{(7,42)}=13.31$, $p<.001$, $R^2=.689$). Step two identified the following Time 1 predictor variables as statistically significant predictors of Time 3 WIAT-II Written Expression: gender ($\beta = .23$, $t = 2.64$, $p = .011$) and VIQ ($\beta = .604$, $t = 2.58$, $p = .013$). Females in the combined control group ($M = 103.39$) performed better on Time 3 Written Expression than males in the control group ($M = 97.33$). No other Time 1 predictors were found to be significant after controlling for the effects of gender, age, VIQ and PIQ. The predictors entered into the second step of this model accounted for only an additional 2% of the variance in Time 3 WIAT-II Written Expression scores, suggesting that demographic and IQ variables accounted for the bulk of the variance.

In the 22q11DS sample, the linear regression indicated step one of the regression (age, gender, VIQ, and PIQ) was statistically significant ($F_{(4,61)}=34.79$, $p<.001$, $R^2=.695$; see Table 3). After controlling for the variables entered in step one, step two (psychiatric disorder, mean executive function score, and language) was also statistically significant ($F_{(7,58)}=24.84$, $p<.001$, $R^2=.75$). The final step of the model identified the following Time 1 predictor variables as statistical significant predictors of Time 3 WIAT-II Written Expression scores: gender ($\beta=.149$, $t=2.04$, $p=.045$), PIQ ($\beta=.235$, $t=2.08$, $p=.041$), Executive Function mean ($\beta=.221$, $t=2.86$, $p=.006$), and CELF-4 Total Language composite ($\beta=.313$, $t=2.1$, $p=.04$). Step two of the model accounted for an additional 5.5% of the variance in Time 3 WIAT-II Written Expression scores. Females in the 22q11DS group ($M=81.2$) performed better on Time 3 Written Expression than males in the 22q11DS group ($M=70.3$).

Cognitive Decline

Individuals with 22q11DS often experience a cognitive decline in their verbal IQ scores over time (Duijff et al., 2012; Vorstman et al., 2015). To consider how cognitive decline affected our results, we conducted an analysis to assess the correlation between verbal IQ change and Time 3 WIAT-II Written Expression scores. Results from this analysis indicated that within the 22q11DS sample these two variables (IQ change and Time 3 WIAT-II Written Expression) were not significantly associated with each other ($r(67)=-.08$, $p=.514$).

Discussion

Group differences exist between the 22q11DS group and the combined control group at all three time points in WISC-III FSIQ, VIQ, and PIQ performance. In addition, WIAT-II Written Expression scores also differed between the groups at all three time points. Children and adolescents with 22Q11DS had mean written expression scores on the WIAT-II approximately two standard deviations below the mean, which remained fairly consistent from Time 1 to Time 3. The combined control group written expression attainment was solidly average at all 3 time points. Whereas childhood verbal IQ scores and gender predicted adolescent written expression in both combined controls and youth with 22q11DS, childhood executive function and language skills were additional, unique predictors of adolescent written expression in individuals with 22q11DS.

Predicting Adolescent Written Expression

Executive Function mean score was found to be a significant predictor of adolescent written expression in the 22q11DS group. This finding differed from the control sample. For the 22q11DS sample (but not our control sample), our results are consistent with the extant literature (Hooper et al., 2011; Hooper et al., 2002) and demonstrate a link between executive functioning and written expression.

Exploratory follow-up analyses that separated the executive functioning measures while controlling for age, gender, verbal IQ, and performance IQ scores indicated that working memory and set shifting (as measured by Digit Span Backwards and WCST Perseverative Error) were significant contributors to the writing process for individuals with 22q11DS. These results support Kellogg's model (1999), which emphasises working memory as an

important component in written expression skills of typically developing populations. In addition, these results align well with the findings from Hooper et al. (2002), which identified set shifting as an important skill in the writing process. Further research identifying the components of executive functioning that contributes to the writing process for individuals with 22q11DS is needed in order to understand the best way to address writing difficulties in this population. However, our data suggest that 22q11DS intervention programs in childhood may want to consider targeting working memory and set shifting for improving adolescent written expression abilities.

VIQ was found to be a significant predictor of adolescent written expression for both the 22q11DS sample and the combined control sample. Previous studies have demonstrated that verbal IQ declines during adolescence in individuals with 22q11DS and is predictive of symptoms of psychosis (Vorstman et al., 2015). However, in our study, Verbal IQ decline was not associated with our primary outcome variable (WIAT-II Written Expression). The use of different measures (WISC-III versus WAIS-III) depending on participant age may have also impacted the analyses that included this variable. Nonetheless, these results suggest that despite the predictive importance of decline in IQ in individuals with 22q11DS to outcomes like psychosis, cognitive decline was not a significant factor in predicting written expression skills in this cohort. Verbal abilities in childhood, however, were a significant predictor of late adolescent written expression skills in both groups.

While overall verbal skills appear to be important contributing factors, childhood language skills (as measured by the CELF-4) were also a significant and independent predictor for the 22q11DS sample. These results indicate that performance on written tasks for individuals with 22q11DS relies heavily upon their language ability. Interestingly, this finding did not emerge for the combined control group, in contrast to the cross sectional results from Hooper et al. (2011) and Kent et al. (2013). Our curious combined control group findings may be due to some combination of sampling differences, our longitudinal design as well as our covarying for age, gender and IQ. Future research should continue to explore how best to predict adolescent written expression from childhood variables in both 22q11DS and typically developing populations.

In addition to the cognitive variables described above, gender was also a significant predictor for Time 3 WIAT-II written expression scores. This finding is consistent with the previous literature (Berninger, Whitaker, Feng, Swanson & Abbott, 1996) that has demonstrated gender differences in regards to written expression, such that females generally outperform their same-aged male peers on measures assessing written compositional skills.

Limitations

The results described above must be viewed within the context of several methodological limitations. First, the present study relied upon a single testing episode to characterise the written expression skills of each participant at each time point. Thus, in order to obtain a possibly more accurate depiction of writing, future research should examine written expression skills by using different assessment methods across multiple assessments. Second, the data analysed in the present study was part of a larger study that was not focused

on the examination of predictors of adolescent written expression. Because of this, other measures (e.g., fine motor skills) important in predicting written expression were not included in this study. As a result, the contribution of other skills not examined here within the context of adolescents' written expression development is unknown. Third, the present study included community control participants with ADHD or learning disabilities (recruited to match higher functioning individuals with 22q11DS). This limits the generalisability of the results from our control sample to typically developing populations. Finally, it is unknown whether any of the participants were receiving individualised education plans or intervention services simultaneously with or previous to the study. As such, it is not possible to determine the role that a participant's intervention history may have played in explaining these results.

Conclusions

Results from this study highlight the need for educational interventions to improve written expression skills in children with 22q11DS. In both childhood and adolescence, youth with 22q11DS are approximately 2 standard deviations below the mean in their written expression skills. Our data suggest that males with 22q11DS and those with executive functioning and language deficits represent especially vulnerable subgroups in the 22q11DS population. These findings offer some guidance concerning the underlying factors that can impact written expression in children and adolescents with 22q11DS. Specifically, it is important that interventions initially address the mastery of lower-level processes (e.g., visual perceptual deficits) contributing to the mechanical aspect of written expression in children with 22q11DS before targeting higher-order processes (e.g., attention, set shifting, and working memory). These interventions may help to lessen the gap in writing performance observed between individuals with 22q11DS and individuals who are typically developing. In addition, these interventions may ultimately improve the developmental trajectory of written expression skills in individuals with 22q11DS. By improving written expression trajectories, it is hoped that academic performance can be improved which may have downstream effects on stress and psychiatric symptoms.

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Figure 1.
Flow Diagram of Participant Enrollment in Study at Time 1, Time 2, and Time 3

Table 1**Participant Data**

	22q11DS M (SD)	Control (Sibling and Community) M (SD)
Time 1 – Late Childhood		
<i>N</i>	69	50
Age	12.19 (2.30)	13.02 (2.37)
WISC-III FSIQ	70.16 (14.45) ***	103.46 (15.11)
WISC-III VIQ	73.54 (15.33) ***	102.42 (14.64)
WISC-III PIQ	71.48 (12.75) ***	104.18 (16.11)
WIAT-II Written Expression	73.47 (14.35) ***	94.34 (13.72)
Time 2 – Early Adolescence		
<i>N</i>	68	49
Age	14.98 (2.25)	15.32 (1.56)
WAIS-III/WISC-III FSIQ	69.26 (14.80) ***	104.06 (14.89)
WAIS-III/WISC-III VIQ	72.56 (13.92) ***	101.69 (14.16)
WAIS-III/WISC-III PIQ	70.91 (14.94) ***	106.14 (16.31)
WIAT-II Written Expression	73.43 (14.13) ***	97.14 (15.06)
Time 3 – Late Adolescence		
<i>N</i>	69	50
Age	18.03 (2.23)	18.08 (1.60)
WAIS-III/WISC-III FSIQ	71.46 (13.61) ***	109.28 (16.98)
WAIS-III/WISC-III VIQ	74.90 (12.96) ***	107.52 (16.44)
WAIS-III/WISC-III PIQ	72.22 (12.56) ***	109.60 (17.52)
WIAT-II Written Expression	75.86 (15.68) ***	100.12 (13.01)

Note. The information presented above for Time 1 includes participants whose scores were imputed because they were later recruited at Time 2. WIAT-II Written Expression, Wechsler Individual Achievement Test – second edition (Wechsler, 2001); WISC-III, Wechsler Intelligence Scale for Children – third edition (Wechsler, 1991); WAIS-III, Wechsler Adult Intelligence Scale – third edition (Wechsler, 1993); FSIQ, Full Scale Intelligence Quotient; VIQ, Verbal Intelligence Quotient; PIQ, Performance Intelligence Quotient.

*
 $p < 0.05$,

 $p < 0.001$

Table 2

Predicting Time 3 WIAT-II Written Expression from Time 1 variables in the control sample

Predictor	R ²	β
Step 1	.67***	
Age		.188*
Gender		.229*
Verbal IQ		.720***
Performance IQ		.058
Step 2	.02	
Executive Function Mean		.099
K-SADS-PL		-.102
CELF-4		.071

Note. K-SADS-PL, Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (Kaufman et al., 1997); CELF-4, The Clinical Evaluation of Language Fundamentals – fourth edition (Semel, Wiig, & Secord, 2003)

* $p < 0.05$,

*** $p < 0.001$

Table 3

Predicting Time 3 WIAT-II Written Expression from Time 1 variables in the 22q11DS sample

Predictor	R ²	β
Step 1	.695***	
Age		.064
Gender		.213**
Verbal IQ		.615***
Performance IQ		.206
Step 2	.055**	
Executive Functioning Mean		.221**
K-SADS-PL		-.016
CELF-4		.313*

Note. K-SADS-PL, Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (Kaufman et al., 1997); CELF-4, The Clinical Evaluation of Language Fundamentals – fourth edition (Semel, Wiig, & Secord, 2003)

* $p < 0.05$,

*** $p < 0.001$