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Behaviors related to autism spectrum disorder in children with developmental language disorder and children with 22q11.2 deletion syndrome

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Abstract

Background and Aim.: Children with Developmental Language Disorder (DLD) are at an increased risk to develop behaviors associated with Autism Spectrum Disorder (ASD). The relationship between early language difficulties and the occurrence of ASD-related behaviors in DLD is poorly understood. One factor that may hinder progress in understanding this relationship is the etiological heterogeneity of DLD. We therefore study this relationship in an etiologically homogeneous group of children, who share phenotypic characteristics with children with DLD: children with the 22q11.2 Deletion Syndrome (22q11DS). We compare children with 22q11DS, to children with DLD and age-matched typically developing children (TD).

Method: 44 children with 22q11DS, 65 children with DLD and 81 TD children, between 3.0–6.5 years old, participated in a longitudinal cohort study that included a baseline measure and a follow-up measure with a 1-year interval. A parental questionnaire (SRS-2) was used to measure the incidence of behaviors in two key behavioral domains associated with ASD: *Social Communication and Interaction* and *Restricted Repetitive Behaviors and Interests*. At baseline, we assessed children's expressive and receptive language abilities as well as their intellectual functioning with standardized tests. We compared the distribution of ASD-related behaviors between the three groups. We used regression analyses to investigate whether language abilities at baseline predict ASD-related behavior at follow-up, accounting for ASD-related behavior at baseline, demographic variables and intellectual functioning.

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Results: Both the children with 22q11DS and the children with DLD displayed significantly more ASD-related behaviors than the TD children. Over 30% of children in both clinical groups had scores exceeding the subclinical threshold for ASD in both behavioral domains. Both in 22q11DS and DLD, baseline receptive language scores were negatively correlated with ASD-related behaviors 1 year later, when controlling for baseline SRS-scores. However, this association was statistically significant only in children with 22q11DS, even when controlled for IQ-scores, and it was significantly stronger as than in the TD group. The strength of the association did not differ significantly between 22q11DS and DLD.
Conclusion: Both children with 22q11DS and children with DLD present with elevated rates of ASD-related behaviors at a preschool-age. Only in children with 22q11DS we observed that weaker receptive language skills were related to increased behavioral problems in the domain of social communication and interaction one year later.
Implications: Our findings indicate that relations between early language impairment and other behavioral phenotypes may be more feasible to detect in a subgroup of children with a homogeneous etiology, than in a group of children with a heterogeneous etiology (such as children with DLD). Our results in 22q11DS reveal that receptive language is especially important in predicting the occurrence of ASD-related behaviors. Future research is needed to determine to what extent receptive language predicts the occurrence of ASD-related behaviors in children with DLD, especially among those children with DLD with the weakest receptive language. Clinically, screening for ASD-related behaviors in children with developmental language difficulties is recommended from a young age, especially among children with receptive language difficulties.

Keywords
developmental language disorder, 22q11.2 deletion syndrome, autism spectrum disorder

Introduction

Children with Developmental Language Disorder (DLD) not only present with a variety of language problems, but also display elevated rates of behaviors that are typically observed in children with Autism Spectrum Disorder (ASD). In the present study, we will refer to this with "ASD-related behaviors". However, the extent to which children with DLD develop these ASD-related behaviors varies greatly (e.g., Conti-Ramsden et al., 2006), highlighting the need to understand the mechanisms that contribute to such inter-individual variability in DLD. Previous research suggests that individual differences in the language skills of children with DLD could not explain this variability in the occurrence of ASD behaviors (e.g., Conti-Ramsden et al., 2006; Leyfer et al., 2008). However, it is possible that this research was hindered to detect an association between language and ASD-related behaviors, by the etiological heterogeneity of DLD. That is, a wide range of biological and environmental risk factors, which may vary from child to child, is known to contribute to the development of DLD (Conti-Ramsden & Durkin, 2017). It could be that some of these etiological factors are more strongly associated with the development of ASD-related behaviors than others and that different etiologies may differently impact the association between language skills and the occurrence of ASD-related behaviors in DLD. As a result, wide inter-individual variation in the strength of the relationship between language and ASD may exist among the group of children with DLD, which makes it difficult to elucidate such a relationship. The aim of the present study is, therefore, to investigate if we can more readily detect this relationship within a group of children who all share the same genetic etiology: The 22q11.2 deletion syndrome (22q11DS; McDonald-McGinn et al., 2015). 22q11DS is a relatively frequently occurring genetic disorder that is, like DLD, associated with developmental language difficulties (Solot et al., 2019) and ASD-related behavior (Fiksinski et al., 2018). Here, we report on findings of our comparative study of children with 22q11DS, children with DLD, and typically developing (TD) age-matched peers.

What is developmental language disorder

Developmental Language Disorder (DLD) is a neurodevelopmental condition, with an estimated prevalence of 3%–7% of the children in the general population (Bishop et al., 2017; Norbury et al., 2016). Children with DLD have severely impaired language skills, which negatively affects their functioning in other domains, such as academic and occupational achievement (Bishop et al., 2017). The diagnostic criteria of DLD stipulate that the language difficulties of children with DLD are not explained by a known physical, neurological, intellectual or environmental cause (Bishop et al., 2017). Nevertheless, various biological and environmental risk factors have been associated with DLD that may differ from child to child (Conti-Ramsden & Durkin, 2017; Rudolph, 2017), indicating that the etiology of DLD is highly heterogeneous.

This etiological heterogeneity may be reflected in the phenotypical heterogeneity that characterizes DLD (Bishop, 2006). Children with DLD vary from each other with respect to their level of impairment in the different modalities of language (i.e., receptive and expressive), as well as in the different language domains, including phonology, morphosyntax, semantics and pragmatics (Lancaster & Camarata, 2019; Williams et al., 2008). Furthermore, DLD is not only heterogeneous in terms of its linguistic profile, but also with respect to co-occurring features, including socio-emotional and behavioral difficulties (Chow et al., 2018; Curtis et al., 2018). Of particular relevance to the study presented here is that the prevalence of ASD, and therefore the behavioral symptoms that are associated with ASD, is increased among children with DLD, which appears to be a consistent finding across multiple independent studies (Conti-Ramsden et al., 2006; Leyfer et al., 2008; Loucas et al., 2008; Miniscalco et al., 2018; Mouridsen & Hauschild, 2009).

Autism spectrum disorder in children with DLD

ASD is characterized by impairments in two core behavioral domains, that are described in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013). The first involves difficulties in Social Communication and Interaction (SCI) and the second is related to the presence of Restricted and Repetitive Behaviors and Interests (RRB). In the present study, we use the term ASD-related behaviors to refer to symptoms in these two domains. Experiencing ASD-related behaviors negatively impacts friendship quality, independence, and early work experience in adolescents with DLD, beyond the impact of their language difficulties (Durkin et al., 2011).

Problems with pragmatic language, which refers to the use of language in a social context, are part of the diagnostic criteria for both ASD and DLD. However, behavioral difficulties observed in children with DLD are not limited to pragmatic language problems and overlap with the behavioral characteristics that are commonly seen in children with ASD. These may include weak social competence, difficulties in peer relationships (Howlin et al., 2000; Loucas et al., 2008; McCabe, 2005; Mok et al., 2014) and repetitive behaviors (Honey et al., 2008; Howlin et al., 2000; Ozgyurt & Dinsever Eliküçük, 2018). Previous studies (summarized in Table 1) indicate high variability in the extent to which children with DLD develop ASD-related behaviors. Some children may be meeting full criteria for ASD, whereas others develop subthreshold levels of ASD-related behaviors, while yet another subgroup of children with DLD does not present with any ASD-related behaviors. Overall, previous findings suggest that DLD is associated with an increased probability to develop ASD or ASD-related behaviors, in particular those involving problems in communication and interaction, but to a varying extent. Understanding the factors that impact this variability could enhance our ability to early identify those children with DLD who are most liable to develop ASD behaviors, and ultimately, explore the potential of early interventions (see also Williams et al., 2008).

Relation between language and ASD-related behaviors in DLD

It has been suggested that difficulties in understanding others and expressing oneself may pose a risk for the development of a range of socio-emotional and behavioral difficulties (Bornstein et al., 2013; Salmon et al., 2016). In a meta-analysis of longitudinal studies in TD children, Chow and colleagues (2018) empirically confirmed this suggestion, and even showed that receptive language appeared more important in predicting later behavioral outcomes than expressive language. However, this meta-analysis did not include specific measures of ASD, therefore the observed socio-emotional and behavioral difficulties cannot be considered as equivalent to ASD.

Given that language development is of critical importance for a child's social and behavioral functioning (Conti-Ramsden et al., 2018), one could hypothesize that the variation in language difficulties among children with DLD partly explains the observed variation in the prevalence of ASD and ASD-related behaviors in this population. The existing evidence for this hypothesis is mixed, but appears to tend towards no or at most a weak correlation between language difficulties and ASD-related behaviors in DLD. First, and in contrast to the hypothesis mentioned above, a vast number of studies did not detect a relationship between the language abilities and the development of ASD or subthreshold ASD-symptoms in children with DLD (Conti-Ramsden et al., 2006; Howlin et al., 2000; Leyfer et al., 2008; Mouridsen & Hauschild, 2009), nor between language ability and difficulties with peer relationships (Mok et al., 2014). One study showed that receptive language deficits appeared to be negatively associated with the domain measuring 'communication and language' in the Autism Diagnostic Interview (ADI-R), in children with a mixed receptive/expressive language disorder (Mildenberger et al., 2001). Furthermore, expressive language deficits of children with DLD were shown to be associated with social interaction problems in the school context and weaker receptive language skills in children with DLD were associated with increased repetitive behaviors (Gibson et al., 2013). However, both these latter studies were limited by a small sample size, and one used only cross-sectional data (Gibson et al., 2013).

On the one hand, this evidence may suggest that early language difficulties do not impact the development of ASD-related behaviors in children with DLD. On the other hand, if a relationship between language and

Table 1. Overview of empirical studies that reported prevalence rates of ASD-diagnoses and the incidence of ASD-related behaviors in children that were diagnosed with or referred for DLD, and in whom presence of ASD or suspected ASD was excluded.

Outcome measure of ASD-related behavior	N	Mean Age baseline (years)	Mean Age follow-up	Instrument to assess ASD-related behavior	% of individuals with this behavior at follow-up	Study
Full criteria for ASD on two instruments or diagnostic classification of ASD	76	7	14	ADOS & ADI	4%	Conti-Ramsden et al. (2006)
	108	2.5–3.5	5	Review of clinical records	11%	Miniscalco et al. (2018)
	469	5	35.8	Review of clinical records	2.1%	Mouridsen and Hauschild, 2009
Full criteria for ASD on one instrument only	76	7	14	ADOS or ADI	26%	Conti-Ramsden et al. (2006)
ASD-related behaviors on both SCI and RRBII	108	2.5–3.5	5	Review of clinical records	12%	Miniscalco et al. (2018)
	93	2.5	9 –11	SRS-2	20%	Roy & Chiat (2014)
ASD-related behaviors on SCI only	44	11.1	cross-sectional[a]	ADI or ADOS or Both	41%	Leyfer et al. (2008)
				ADI Social Interaction	*14%*	
				ADI communication	*11%*	
				ADOS Social Interaction	*18%*	
				ADOS communication	*25%*	
ASD-related behaviors on RRBI only	44	11.1	cross-sectional[a]	ADI	25%	Leyfer et al. (2008)
				ADOS	10%	

Abbreviations. ADOS = Autism Diagnostic Observation Schedule . ADI = Autism Diagnostic Interview. SCI = social communication and interaction. RRBI = restricted repetitive behaviors and interests. SRS-2 = Social Responsiveness Scale.
[a]Presence of ASD was explicitly excluded.

ASD-related behaviors exists in some children with DLD, the etiological heterogeneity that characterizes DLD poses a challenge to elucidate this relationship. Given the etiological variability of DLD, it is possible that the co-morbidity of ASD-related behaviors in DLD varies as a function of the specific etiology underpinning DLD. This would also imply that different etiologies of DLD may differently impact the relationship between language abilities and the development of ASD-related behaviors. Against this background, it may therefore be relevant to study the relationship between language and ASD in a group of children who are phenotypically similar to DLD, but who have a more homogeneous etiology.

22q11.2 deletion syndrome

In the present study, we, therefore, compare children with DLD to children with the 22q11.2 deletion syndrome (22q11DS; OMIM #188400, #192430). 22q11DS is a neurodevelopmental condition, that is resulting from a Copy Number Variant (CNV; McDonald-McGinn et al., 2015). A CNV refers to a deletion or duplication of genetic material on a specific region of a child's genome, often encompassing more than one gene (Smajlagić et al., 2021). In this case, 22q11DS is caused by a hemizygous microdeletion of 0.7–3 million base pairs on the long arm of chromosome 22 (McDonald-McGinn et al., 2015). Some of the CNVs, are pathogenic, meaning that they are disease-causing. A subset of these pathogenic CNVs, among others 22q11DS, are associated with a range of neurodevelopmental problems, including both developmental language difficulties and a high incidence of ASD (Barnett & van Bon, 2015; Sønderby et al., 2021).

22q11DS has a prevalence of 1:2000 live births (Blagojevic et al., 2021) and is characterized by a heterogeneous phenotype, including varying physical, cognitive and psychiatric difficulties. The level of intellectual functioning in 22q11DS is variable, and is normally distributed around a full-scale IQ-score of 70 in adulthood (De Smedt et al., 2007). Speech-language difficulties are reported in 95% of children with 22q11DS, making this one of the primary developmental concerns that manifest early in life (Solot et al., 2019). Similar to what is reported in DLD, 22q11DS is associated with impaired language development across modalities and domains (Everaert et al., 2023; Solot et al., 2019; van den Heuvel et al., 2018). Moreover, it has been shown that the language skills of children with 22q11DS are impaired beyond what can be expected given their overall cognitive level, which also corresponds to what is observed in many children with DLD (Goorhuis-Brouwer et al., 2003; Norbury et al.,

2016; Selten et al., 2021; Solot et al., 2001). One previous study investigated neurophysiological functioning during language processing and did not detect differences between children with 22q11DS and children with DLD (VanSteensel et al., 2021). Others concluded that children with 22q11DS have a largely overlapping profile of behavioral difficulties with children with both a language impairment and a learning disability (Swillen et al., 2001). Together this indicates that 22q11DS and DLD share significant overlap. Of note is that the current diagnostic criteria for DLD differentiate children with 22q11DS from children with DLD, based on the presence of a genetic condition (i.e., 22q11DS), which underlies the developmental language difficulties that are observed in virtually all children with 22q11DS.

In addition, 22q11DS is associated with an elevated prevalence of a variety of neurodevelopmental disorders in childhood, as well as schizophrenia in young adulthood. Given differences in assessment tools and age of study populations, prevalence rates are variable across studies. However, the prevalence of ASD in 22q11DS is typically reported between 10% and 40% (Fiksinski et al., 2018; Schneider et al., 2014). It has been observed that early language difficulties are associated with the development of subsequent psychosis in 22q11DS (Solot et al., 2020). However, the relationship between early language difficulties and the development of ASD and ASD-related behaviors has not been studied in 22q11DS.

Aim of the present study

The aim of the present study is to enhance our understanding of the relationship between language difficulties and the occurrence of ASD-related behaviors in children with developmental language difficulties. To this end, we will investigate the relationship between language skills and ASD-related behaviors in children with 22q11DS, and compare these observations to children with DLD and TD children.

Moreover, we use a longitudinal design, which allows us to study the influence of language on the emergence of ASD-related behaviors, while controlling for initial levels of ASD-related behaviors. We use a continuous measure of ASD-related behaviors, which contributes to gaining insight into the severity of both core behavioral symptoms associated with ASD (i.e., problems in social communication and interaction and repetitive restricted behaviors and interests). In addition, we assess the influence of both expressive and receptive language on the occurrence of ASD-related behaviors, as they may be differentially related to behavioral development (Conway et al., 2017). Given that children with 22q11DS on average have a lower level of intellectual functioning than children with DLD, we will account for the potential confounding effect of IQ-scores. We hypothesize that children with 22q11DS and children with DLD present with increased rates of ASD-related behaviors in comparison to TD children, in both domains. Additionally, if a relationship between language and ASD-related behaviors exists, we hypothesize that the etiological homogeneity in the 22q11DS sample will enable us to more readably detect this relationship, while the etiological heterogeneity in DLD hampers our ability to do so.

Method

Participants

The participants were children taking part in the "3T-study", a longitudinal cohort study on the linguistic, cognitive and psycho-social development of children with 22q11DS and children with DLD, in comparison to TD age-matched peers (see also Everaert et al., 2023). Parents or caregivers provided written informed consent, the study was approved by the Ethical Review Board of the University Medical Center Utrecht, The Netherlands, and was performed in accordance with the Declaration of Helsinki (2013). Inclusion criteria were 1). Aged between 3 and 6.5 years old. 2). Being monolingual Dutch and 3). Absence of hearing loss (dB > 35). A child was considered monolingual Dutch if 80% of their life-time daily language input was in the Dutch language. This information was retrieved through a short, standardized phone interview with a child's parents or legal guardians. In the same interview, parents were asked if there had ever been any concerns regarding their child's hearing. In the Netherlands, hearing is assessed during newborn screening and is repeated several times in the first two years of life. We, therefore, included all children whose parents did not indicate any concerns about their child's hearing. In case of hearing concerns, we asked for the results of standardized hearing tests, which allowed us to decide whether a child could participate in the study.

In the 22q11DS group, the genetic deletion was confirmed with a molecular genetic test. Children with DLD met one of the following criteria prior to participation in the study, in accordance with the Dutch criteria for admission to special care or education for children with DLD: a) a standardized global language test score of 2 standard deviations or more below the age-adequate mean, b) two separate standardized test scores of 2 SDs or more below the age-adequate mean for at least one important language domain, c) standardized single test scores of 1.5 SDs or more below the mean for at least *two* of these domains, or d) standardized single test scores of 1.3 SDs or more below the mean for at least *three* of these domains (Stichting Siméa, 2017). Prior to inclusion, children in the TD group were screened for the absence of concerns of developmental language problems or neurodevelopmental disorders. Children with 22q11DS were recruited via the national outpatient clinic for 22q11DS at the University Medical Center Utrecht, or via the national patient

organization. Children with DLD were recruited via national expertise centers for children with severe language problems. TD children were recruited via daycare centers or primary schools for regular education. The final cohort consisted of 44 children with 22q11DS, 65 children with DLD, and 81 TD children.

Measures

ASD-related behaviors. Parents or legal caregivers filled out the second version of the Social Responsiveness Scale (SRS; Roeyers et al., 2011) about their child. The SRS is a questionnaire consisting of 65 items, with each item describing a behavior that is associated with ASD. Each item was scored on a 4-point likert-type scale ranging from 0 (=never) to 3 (=often), indicating whether the child displays that type of ASD-related behavior. Each item belongs to one of two scales that matches with either of the two core domains of ASD as described in the DSM-5, being *difficulties with Social Communication and Interaction (SCI-scale, 53 items)* and *Repetitive and Restricted Behaviors and interests (RRB-scale, 12 items).*

Depending on the age of their child, parents filled out the SRS-version for 2- and 3-year-old children, or 4- to 18-year-old children, which are comparable both in the number and content of items. The SRS is normed on the Dutch population for children aged 2 and 3 years old and children aged 4 to 18 years old, as well as for different sexes. Based on procedures described in the SRS manual, we transformed the raw scores on the SCI-scale and the RRB-scale into age- and sex-corrected normed T-scores for each participant. We used these two T-scores as variables in our analyses (i.e., T-SCI and T-RRB). A T-score lower than 60 indicates behavior in the normal range, a T-score of 60–65 indicates mild to moderate deficiencies in social behavior, T-scores between 66 and 75 indicate moderate social deficits and T-scores >76 indicate severe deficits in social functioning.

Receptive and expressive language. The Dutch version of the Clinical Evaluation of Language Fundamentals – Preschool version (CELF; Wiig et al., 2012) was administered to measure children's language abilities. The CELF consists of different subtests to assess the level of functioning in different language domains. For the present study, we used children's scores on the three subtests that measured receptive language abilities (*sentence comprehension, following directions, and basic concepts or word classes*) and three subtests that measured expressive language abilities (*word structure, expressive vocabulary, and recalling sentences*). The CELF provides normed scores for the Dutch population, which allowed us to transform the raw scores on each subtest into age-corrected normed scores. Subsequently, by taking the sum of these normed scores, we could compute both a Receptive Language Composite score (CELF RLC) and an Expressive Language Composite score (CELF ELC), according to procedures described in the CELF manual (Wiig et al., 2012). These composite scores have a mean score of 100 and a standard deviation of 15.

Intelligence. Results of children's intelligence assessments (i.e., IQ-scores) were collected via medical or school records. If this data were not available, which was the case for all TD participants, we administered a shortened version of the Wechsler Non Verbal (WNV; Wechsler & Naglieri, 2008). We used the full-scale IQ scores (FSIQ) in our analyses. These IQ scores have a mean score of 100 and a standard deviation of 15.

Procedure

Data collection consisted of a baseline measurement and a follow-up measurement after 12 months. The language assessment took place at a child's daycare facility or school by a trained researcher. Parents were asked to fill out online questionnaires regarding the linguistic and behavioral development of their child. Due to the COVID-19 pandemic, follow-up visits at schools and daycares were not possible. Consequently, ASD-related behaviors were measured at both baseline and follow-up, whereas language skills were measured at baseline only. The tasks measuring expressive language were recorded and subsequently scored by the researcher who administered the task and, independently, by a second researcher. In case of discrepancies, a final score was reached by consensus.

Data processing and analyses

All analyses were conducted in RStudio version 4.0.2 (RStudio Team, 2020). We provide a visual overview of the distribution of T-SCI scores and T-RRBI scores for all three participant groups (22q11DS, DLD, TD). In addition, using Analyses of Variance (ANOVA), we compared the distribution of ASD-related behaviors (T-SCI scores or T-RRBI scores) in our three participant groups. We also used Chi-Square tests to compare the proportion of children in each participant group with T-SCI scores or T-RRBI scores in the mildly impaired range or higher ($T > 60$). Overall, we used an alpha-level of .05 to indicate statistically significant main effects. For post-hoc analyses, we applied Bonferroni corrections to correct for multiple comparisons. Given that we compared three groups, and investigated group differences on the two SRS-scales separately, our alpha level indicating statistically significant group differences is $0.05/3 = 0.017$. We report effect sizes and follow Ferguson (2009) for the interpretation.

We took several steps to examine the relationship between early language skills and the occurrence of ASD-related behaviors. First, we conducted, per group,

four sets of partial correlations, each time correlating either scores on the CELF RLC or the CELF ELC with either T-SCI or T-RRB measured at follow-up, controlling for the baseline T-scores on that SRS-scale (e.g., "CELF ELC*T-SCI at follow-up, controlled for baseline T-SCI"). Subsequently, for those partial correlations indicating a significant association, we conducted a multiple regression analysis to investigate to what extent the scores on the relevant language variable predict the scores on the relevant SRS-scale at follow-up, accounting for other relevant variables, including baseline SRS-scale, parental education and intellectual functioning (*e.g., T-SCI at follow-up predicted by parental education + FSIQ + baseline T-SCI + CELF ELC*).

Finally, we conducted a second multiple regression analysis to investigate whether the strength of the association between the relevant language variable and SRS-scale differed between the participant groups, accounting for the effects of demographic variables and FSIQ. Our outcome variable was the relevant measure of ASD-related behavior (T-SCI or T-RRB). Our full model included age, sex, level of parental education, FSIQ, and baseline ASD-related behavior as predictors. In addition, we added the interaction term for group*language (*e.g., group*CELF ELC*) as predictor variable. In all our regression analyses, we centered all continuous variables to avoid multi-collinearity.

Results

Data attrition and sample description

Some parents did not complete the SRS at the follow-up measure, resulting in missing data for children with 22q11DS (n = 2), DLD (n = 8) and TD children (n = 3; see Table 1 in appendix A). In addition, three children from the TD group had a score on the language assessment indicating below average language performance (i.e., CELF core language composite score < −1 SD), and were therefore excluded from further analyses. In comparison to the other two groups, the final sample of children with DLD consisted of more boys than girls ($22q11_{male}$ = 55%, DLD_{male} = 77%, TD_{male} = 44%, [$\chi2(2) = 16.64$, $p < .001$]). In addition, significant group differences were found for level of parental education and IQ scores (see Table 2 for sample descriptives).

ASD-related behaviors at follow-up

T-scores. Figure 1 displays the distribution of T-scores at follow-up on both SRS scales (SRS SCI and SRS RRB). Results of the ANOVA showed a main effect of group for both T-SCI scores [$F(2,171) = 41.45$, $p < .001$, $\eta^2 = .033$] and T-RRB scores [$F(2,171) = 30.31$, $p < .001$, $\eta^2 = 0.26$]. Pairwise comparisons showed that TD children, on average, had lower T-scores on both SRS-scales ($p_{SCI} < .001$; $p_{RRB} < .001$) than the children with 22q11DS or the children with DLD, who did not differ from each other ($p_{SCI} = 1$, $p_{RRB} = .160$). Table 3 shows the proportion of children within each group with a T-score in the mildly impaired range or higher (T > 60). Pairwise comparisons showed that the proportion of children with a mildly impaired score or higher did not differ significantly between the children with 22q11DS and the children with DLD in the SCI-scale [$\chi^2(2) = 0$, $p = >.999$]. The proportion of children with a score in this range on the RRB-scale was significantly larger in the 22q11DS group than in the DLD group (χ^2 (2) = 4.88, $p = .027$), but the effect did not survive Bonferroni correction.

The relation between ASD-related behaviors and language

Missing data. There was missing data in all three participant groups, leaving a subsample of 28 children with 22q11DS (46% male), 52 children with DLD (76% male) and 72 TD children (46% male) who could be

Table 2. Sample characteristics of children with SRS data at follow-up.

	Group												
	22q11DS (n = 42)			DLD (n = 57)			TD (n = 75)			Statistics			
Variable	M	SD	Range	M	SD	Range	M	SD	Range	(df)F	*p*	η^2	post-hoc
Age baseline (months)	58.5	12.2	37–77	57.0	10.2	36–74	55.8	11.0	36–78	F(2,171) = 0.76	.468	.00	-
Age follow-up (months)	71.3	12.2	50–90	70.0	10.2	49–87	68.6	11.0	49–91	F(2,171) = 0.81	.446	.00	-
Parental education[a]	6.44	1.8	2–9	6.5	1.6	3.5–9	7.9	1.2	4–9	F(2,170) = 19.7	<.001	.19	TD > DLD = 22q11
FSIQ[b]	79.6	12.1	50–103	97.0	12.8	69–124	107	13.0	81–139	F(2,166) = 59.5	<.001	.42	TD > DLD > 22q11

[a]Parental education was indexed by the average education level of both parents, ranked on a 9-point scale reflecting the Dutch educational system (ranging from 1 'no education' to 9 'university degree'). This information was missing for 1 TD child.
[b]Full-scale Intelligence Quotient. This information was missing for 2 children with 22q11DS, 2 children with DLD and 1 TD child.

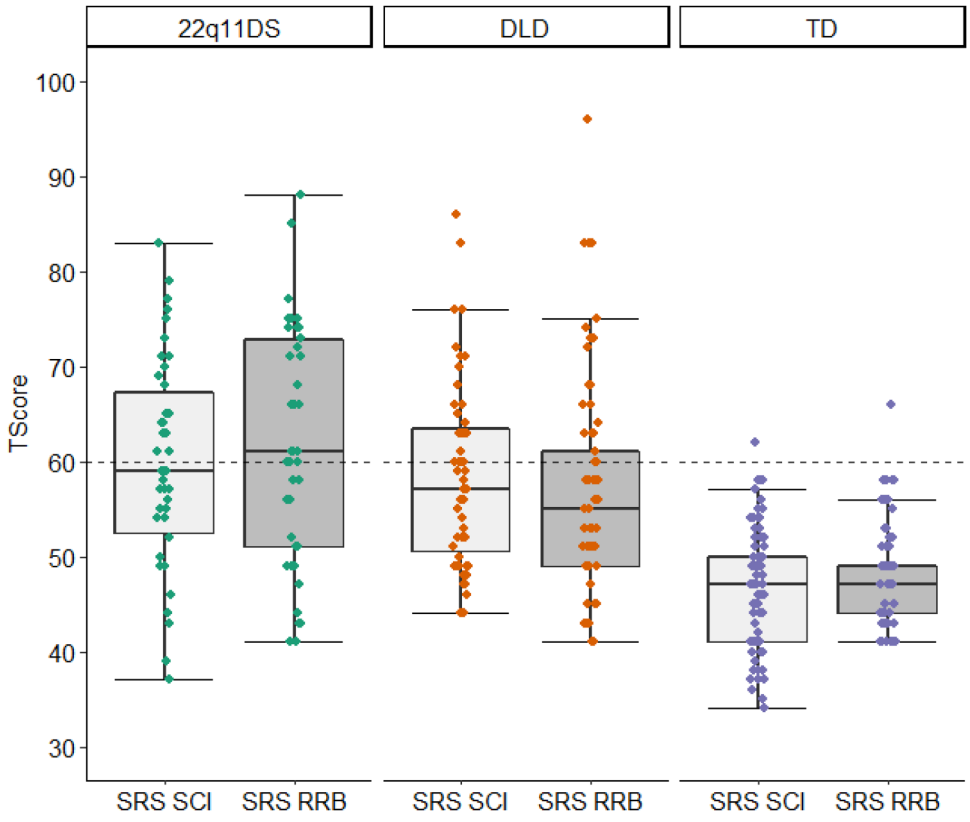

Figure 1. Distribution of T-scores on the two subscales of the SRS (*SRS SCI and SRS RRB*) for children with 22q11DS (n = 42), children with DLD (n = 57), and TD children (n = 75). Each dot indicates the score of an individual participant. Abbreviations. SCI = Social communication and Interaction. RRBI = Restricted Repetitive Behaviors and Interests. Note. A higher T-score on the SRS indicates more ASD-related behaviors. The horizontal dotted line reflects the cut-off score for the subclinical range (T = 60). Each box represents the middle 50% of T-scores ranging from the 25th percentile to the 75th percentile. Black bar in each box represents the median. Whiskers represent the 2,5th percentile and 97,5th percentile.

included in the analyses investigating the relationship between language difficulties and the occurrence of ASD-related behaviors at follow-up. As a substantial number of children with 22q11DS could not be included in the regression analyses, we compared those children to the children with 22q11DS with complete data. The main reason for exclusion in 22q11DS was missing data on the language measures (see appendix A for type of missing data). It appeared that children with and without missing data did not differ significantly in the distributions on age, sex or T-RRB scores (see Appendix A). However, in the group of children with 22q11DS, the comparison of SCI scores between children with and without missing data resulted in a borderline significant difference (p = .052), suggesting that the children with missing data may have had somewhat higher scores on the SCI-scale (indicating more problems) than the children without missing data. Given the small number of children with missing data in both the TD and DLD group, we did not statistically compare the children in these groups to children with complete data.

Final sample description. The descriptive statistics and group comparisons of the subsample that could be included in the regression analyses are reported in Table 4. Again, the gender distribution differed significantly between the three groups [$\chi 2(2) = 15.08$, $p < .001$], as there were more boys in the DLD group (79% male) than in the TD group (46% male) or 22q11DS group (46% male). On all measures of ASD-related behaviors and language, TD children had on average higher scores than children with DLD or children with 22q11DS, who often did not differ. Children with DLD only differed from the children with 22q11DS on their IQ score and score of receptive language, with higher scores of the DLD group.

Partial correlations. Table 5 shows the results of partial correlations for each group. We observed a significant negative correlation with a large effect size between baseline CELF RLC scores and T-SCI scores at follow-up in the 22q11DS group. This indicates that weaker receptive language skills were associated with higher rates of ASD-related behaviors

Table 3. Percentages indicating the proportion of children with 22q11DS, DLD or TD with a T-score >60 on the SRS-scales.

	Group			Statistics		
SRS scale	22q11DS (n = 42)	DLD (n = 57)	TD (n = 75)	χ^2	p	Post-hoc
SCI	45.2%	43.9%	1.33%	41.39	<.001	TD<22q11DS = DLD
RRBI	59.5%	35.0%	1.33%	50.14	<.001	TD<22q11DS = DLD
SCI and RRBI	42.9%	24.6%	0%	36.24	<.001	TD<22q11DS = DLD

Abbreviations. *SCI = T-score on SRS-scale Social Communication and interaction. RRBI = T-score on SRS-scale* Restricted Repetitive Behaviors and Interests.

Table 4. Sample characteristics of the children who were included in the regression analyses.

	Group												
	22q11DS (n = 28)			DLD (n = 52)			TD (n = 72)			Statistics			
Variable	M	SD	Range	M	SD	Range	M	SD	Range	(df)F	p	η^2	post-hoc
Age Follow-up (months)	73.4	12.0	52.1–88.7	70.3	10.3	49.9–87.4	68.9	10.8	48.7–90.9	(2,149) 1.7	.184	.02	-
FSIQ	83.0	10.3	62–103	96.5	12.8	69–124	107.0	13.6	81–139	(2,149) 38.3	<.001	.34	TD > DLD > 22q11
Language *(Baseline)*													
CELF ELC	72.7	11.5	55–100	71.6	9.8	56–98	103.0	13.3	77–132	(2,149) 129.1	<.001	.63	TD > DLD = 22q11
CELF RLC	76.7	14.3	55–112	85.3	13.8	56–115	108.0	12.3	84–139	(2,149) 75.9	<.001	.50	TD > DLD > 22q11
ASD-related behavior													
T-SCI *Baseline*	59.3	12.2	38–83	60.9	10.7	43–85	48.8	7.81	34–79	(2,149) 26.7	<.001	.26	TD < DLD = 22q11
T-RRBI *Baseline*	62.3	13.5	43–99	59.8	11.9	43–91	48.8	7.3	39–72	(2,149) 25.6	<.001	.26	TD < DLD = 22q11
T-SCI *Follow-up*	57.3	11.4	37–77	58.6	8.9	44–83	47.0	6.4	34–62	(2,149) 35,8	<.001	.32	TD < DLD = 22q11
T-RRBI *Follow-up*	60.8	13.1	41–85	58.1	11.5	41–96	48.2	5.3	41–66	(2,149) 25.7	<.001	.26	TD < DLD = 22q11

Abbreviations. FSIQ = full scale Intelligence Quotient. CELF ELC = expressive language composite score. CELF RLC = receptive language composite score. SCI = T-score on SRS-scale Social Communication and interaction. RRBI = T-score on SRS-scale Restricted Repetitive Behaviors and Interests.

in the domain of SCI at follow-up in the children with 22q11DS, while controlling for baseline T-SCI scores.

Regression analysis. We conducted a regression analysis to explore the strength of the association between CELF RLC and T-SCI scores at follow-up in the group of children with 22q11DS. Given that the 22q11DS group is characterized by low FSIQ-scores, we added FSIQ as predictor in this model, together with baseline T-SCI and CELF RLC. The regression model was significant, with a large effect size [$F(3,24) = 22.38$, $p < .001$, R^2-adj = 0.70]. Model estimates showed that CELF RLC scores at baseline significantly predicted T-SCI scores at follow-up, taking into account FSIQ and baseline T-SCI scores (see Table 6).

Subsequently, we investigated if the relationship between CELF RLC and T-SCI differed between the three groups, when accounting for variation in demographic variables and FSIQ. We therefore conducted a final regression model, including age, sex, parental education, FSIQ and baseline T-SCI scores as predictors, as well as adding the interaction term of 'group*CELF RLC'. The full regression model using the TD group as the reference group was significant with a large effect size [$F(10,141) = 41.31$, $p < .001$, R^2-adj = 0.73]. Results showed that receptive language scores at baseline were significantly more strongly associated with T-SCI at follow-up in children with 22q11DS than in TD children, whereas this difference was not significant in the comparison between the TD and DLD groups nor in the comparison between the 22q11DS and DLD groups (see Table 7 and Figure 2).

Discussion

Children with DLD present with varying rates of behaviors that are commonly seen in children with ASD (i.e., ASD-related behaviors). The goal of the present study

was to further our understanding of these inter-individual differences in ASD-related behaviors among children with DLD. To this end, it was investigated to what extent early receptive and expressive language difficulties were related to the occurrence of ASD-related behaviors in preschool-aged children with 22q11DS, children with DLD and TD children. We expected that the more homogeneous etiology of the 22q11DS group would increase the likelihood of detecting such a relationship, if it exists, compared to the etiologically more heterogeneous group of children with DLD.

Prevalence of ASD-related behaviors in 22q11DS and DLD

As expected, we observed that both young children with DLD and children with 22q11DS presented, on average, significantly more ASD-related behaviors than TD children. This was found in both key behavioral domains that are associated with ASD, including the domain of social communication and interaction (SCI) and the domain of Restricted Repetitive patterns of Behaviors and Interests (RRBI). To our knowledge, this is the first study reporting on prevalence rates of ASD-related behaviors in children with DLD in this age-range. Previous studies with older children and adolescents with DLD reported that around 30% of school-aged children with DLD present with ASD or ASD-symptoms, predominantly in the domain of SCI (see Table 1). The results of the present study showed comparable prevalence rates of ASD-related behaviors, as well as a similar pattern of relatively more problems in the domain of SCI than in the domain of RRBI in young children with DLD. Of note, more than half of the sample of children with DLD did not have elevated rates of ASD-related behaviors, indicating that our measures of language and of ASD are not tapping into the same underlying construct. In addition, this highlights the variability in ASD-related behaviors within the group of children with DLD. One previous study has specifically investigated the prevalence of ASD-related behaviors in a sample of young children with 22q11DS (Serur et al., 2019). These authors reported a similar level of problems in both the domain of SCI and RRBI, which is in line with the results of the present study, and which is in accordance with what is reported in school-aged children and adolescents with 22q11DS (Kates et al., 2007; Vorstman et al., 2006).

Relationship between language and ASD-related behaviors

Our analyses revealed that the level of receptive language skills of the children with 22q11DS was negatively associated with the level of ASD-related behaviors in the

Table 5. Results of the partial correlations between the measures of language and ASD-related behaviors at follow-up, while controlling for ASD-related behaviors at baseline.

	Group					
	22q11DS (n = 28)		DLD (n = 52)		TD (n = 72)	
Correlation model	*r*	*p*	*r*	*p*	*r*	*p*
T-SCI – CELF ELC	−0.23	.239	−0.14	.326	−0.09	.460
T-SCI – CELF RLC	−0.59	.001	−0.18	.197	−0.01	.936
T-RRBI – CELF ELC	0.12	.552	−0.08	.594	0.01	.919
T-RRBI – CELF RLC	−0.22	.260	−0.04	.807	−0.04	.767

Abbreviations. T-SCI = T-score on social communication and interaction (SRS-scale SCI). T-RRBI = T-score on Restricted Repetitive Behaviors and Interests. (SRS-scale RRBI). CELF ELC = expressive language composite score (CELF). CELF RLC = receptive language composite score (CELF).

Table 6. Results of the regression analysis for the 22q11DS group (n = 28), predicting t-scores on social communication and interaction at follow-up, using receptive language as predictor, accounting for full scale iq-scores and t-scores on social communication and interaction at baseline.

Variable	Beta	Std-error	t	*p*
Intercept	−0.33	0.22	−1.48	.152
FSIQ	0.06	0.21	0.26	.796
Baseline T-SCI	0.65	0.12	5.55	<.001
CELF RLC	−0.61	0.19	−3.16	.004

Abbreviations. FSIQ = Full Scale Intelligence Quotient. T-SCI = T-score on social communication and interaction (SRS-scale SCI). CELF RLC = receptive language composite score (CELF).

Table 7. Results of the interaction model predicting SRS SCI T-scores at follow-up.

Variable	Beta	Std-error	t	*p*
Intercept	−0.29	0.11	−2.68	.008
Age follow-up	0.15	0.05	2.99	.003
Sex	0.15	0.09	1.57	.119
Parental education	−0.09	0.05	−1.63	.105
FSIQ	−0.06	0.06	−1.09	.280
Baseline T-SCI	0.67	0.06	11.70	<.001
CELF RLC: TD vs. 22q11DS	−0.50	0.17	−2.92	.004
CELF RLC: TD vs. DLD	−0.16	0.14	−1.15	.254
CELF RLC: 22q11DS vs. DLD[a]	−0.34	0.17	−1.97	.051

Abbreviations. FSIQ = full scale IQ score. T-SCI = T-score on social communication and interaction (SRS-scale SCI). CELF RLC = receptive language composite score (measured with CELF).
Note. We did not include main effects for group and RLC in this table as they cannot be interpreted in the presence of a significant interaction effect.
[a]The comparison between the 22q11DS and DLD groups comes from a different model using the 22q11DS group as the reference group. Full model statistics were [$F(10,141) = 41.31$, $p = .<001$, $R^2adj = 0.73$].

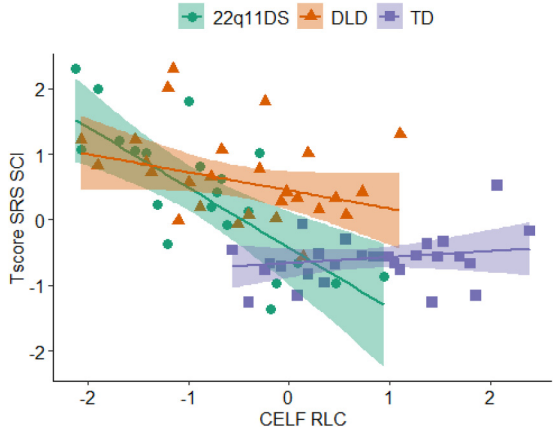

Figure 2. Plot presenting the relationship between receptive language and ASD-related behaviors in the domain of social communication and interaction in children with 22q11DS (n = 28), children with DLD (n = 52) and TD-children (N = 72), using the predicted values resulting from the regression model. Abbreviations. SRS SCI = Social Communication and Interaction (SRS-scale SCI). CELF RLC = Receptive Language Composite score (measured with the CELF). Note. Individual dots represent data points of individual participants. Solid line is predicted mean per group.

SCI-domain 1 year later. In the present study, some children with 22q11DS were excluded from the analyses, because they had missing data on the language tasks. These children had relatively high SCI scores (indicating more problems), and, based on our own observations, had relatively low language levels (resulting in missing data on some of the language tasks). Hence, we expect that the inclusion of these individuals would most likely have strengthened, not weakened, the observed association. The design of the present study did not allow us to investigate the bidirectional relationship between language and ASD. Nevertheless, as we corrected for baseline ASD-related behaviors, the results of this study indicate that receptive language problems contribute to the occurrence of ASD-related behaviors in the domain of social communication and interaction. The present results were based on parent-report of ASD-related behaviors, and additional observational measures of ASD-related behaviors (e.g., using ADOS) would increase the validity of the present results.

Including a global measure of intellectual functioning seemed to demonstrate that variation in the level of intellectual functioning did not contribute to the occurrence of ASD-related behaviors in children with 22q11DS, which is in line with previous observations (van den Heuvel et al., 2018; Vorstman et al., 2006). However, studying the association between intellectual functioning and any co-occurring neuropsychiatric phenotype is challenging in this population, given that discrepant IQ profiles and cognitive decline are commonly observed (Swillen, 2016). As such, follow-up research specifically addressing the association between intellectual functioning and the development of ASD-related behaviors is recommended to draw firm conclusions in this regard.

We observed that the association between receptive language and SCI was stronger in the children with 22q11DS than in the group of TD children. A similar positive association was observed in the DLD children, but weaker and not reaching statistical significance. These observations confirm our hypothesis that such a relationship can be more easily detected in an etiologically homogeneous group (i.e., 22q11DS), than in an etiologically heterogeneous group (i.e., DLD). This supports the possibility that the inconsistent findings in the literature regarding the association between language ability and ASD-related behaviors are due, at least in part, to the etiological heterogeneity of the DLD population.

The strength of the association between receptive language and SCI did not significantly differ between the children with DLD and the children with 22q11DS, when accounting for important demographic variables, such as sex and FSIQ on which the groups differed significantly. The difference in sample sizes between the 22q11DS and DLD groups may have hindered to detect a statistical difference in the strength of the association between language and ASD-related behaviors (Aguinis et al., 2017), although a similar sample size difference existed between the 22q11DS and TD groups, for which our comparison of this relationship did result in a significant difference. Alternatively, our finding leads us to speculate that there may be a subgroup within the larger group of children with DLD, who behaves similarly as children with 22q11DS. The results of the present study seem to indicate

that children with 22q11DS have on average weaker receptive language skills than children with DLD. Although prevalence rates of receptive language problems in DLD have not been frequently reported, also in other samples has been shown that around half of the children perform at an age-expected level (e.g., Boyle et al., 2009). Based on these observations, we may speculate that a relationship between receptive language and SCI may exist only in those children with DLD with receptive language problems. As this has been previously observed in one study (Mildenberger et al., 2001), further research is needed to explore this hypothesis.

We did not observe any relationships between language and ASD-related behaviors in our TD group, which contrasts with research that did demonstrate such relationships (e.g., Larkin et al., 2017). However, other studies suggested that language is only predictive of problem behavior for children with very low language levels (Goh et al., 2021). As our TD children all had language scores in the normal range, this could explain why we did not detect a relationship between language and ASD-related behaviors in this group. In addition, we also did not detect significant associations between expressive language and ASD-related behaviors. This strengthens previous work suggesting that receptive language is more important for socio-emotional and behavioral development (Chow et al., 2018). Alternatively, it has been suggested that the impact of expressive language difficulties increases in a later developmental stage, when these skills are generally more developed (Conway et al., 2017). Future studies using a longer follow-up period or a larger age-range could answer such questions.

Implications

Our results may imply that the degree of receptive language impairment contributes to the occurrence of ASD-type behavior in children with developmental language disorders. It has been suggested that weak receptive language skills may especially be a risk factor for the development of problems in the domain of social interaction and communication, because children with weak receptive language skills may withdraw from their environment due to difficulties understanding parents, peers and teachers, thereby avoiding interactions with others. In turn, this leads to reduced opportunities to practice social skills (Angkustsiri et al., 2014; Bornstein et al., 2013; Salmon et al., 2016). As a next step, it would be interesting to study to what extent therapy targeting receptive language may also influence the development of ASD-related behaviors in children with language difficulties.

Besides ASD-related behaviors, DLD is associated with several other behavioral phenotypes, including Attention Deficit Hyperactivity Disorder (ADHD) and increased levels of anxiety and depressive symptoms. To elucidate to what extent early language difficulties contribute to the emergence of these different developmental phenotypes, future studies may copy the approach of the present study, by investigating these relationships in an etiologically homogeneous group. It has been shown that a small number of children with different CNVs, other than 22q11DS, could be identified in a population of children who were initially diagnosed with DLD (Kalnak et al., 2018; Pettigrew et al., 2015; Plug et al., 2021). This indicates that, besides 22q11DS, there may be several other relevant subgroups with a shared genetic etiology and a phenotype corresponding to DLD. Examining interrelationships between language difficulties and other behavioral phenotypes in 22q11DS and such other subgroups may potentially provide leads for future studies aiming to investigate relationships between different behavioral phenotypes in DLD.

The results presented here likely have implications for clinical practice. The age of the youngest children in this study was three years. This is due to the fact that, in the Netherlands, a diagnosis of (suspected) DLD is often not given before this age. However, we know that ASD-related behaviors may be observed at an earlier age (Zwaigenbaum et al., 2015). Indeed, we found high rates of ASD-related behaviors in both children with 22q11DS and DLD in our sample at the baseline measure, which highlights the need for early awareness and screening of the presence of ASD-related behaviors, both in children with 22q11DS and DLD. It has been reported that receptive language problems tend to increase in children with 22q11DS during school-age (van den Heuvel et al., 2018). These problems may be easily overlooked by caregivers and professionals, particularly in the context of a broad range of physical symptoms that characterizes young children with 22q11DS. However, given the correlation with the occurrence of ASD-related behaviors, careful monitoring of receptive language development in children with 22q11DS is warranted.

Strengths, limitations and future directions

We used composite scores derived from a standardized language assessment, including measures of multiple language domains, which gives a broad indication of both a child's expressive and receptive language skills. A limitation of using such a standardized assessment is that a relatively large proportion of children with 22q11DS did not complete all tasks, and could therefore not be included in the final regression analyses. We therefore recommend future studies to include language measures that are more suitable for children with low language levels or intellectual disability. Such measures, especially spontaneous language

measures, may even more strongly relate to daily life communication problems.

We aimed to test to what extent the homogeneous etiology of 22q11DS, would enable us to detect a stronger relation between language and ASD-related behaviors as compared to children with DLD. It is therefore a strength of this study that we accounted for the effect of the level of intellectual functioning, on which 22q11DS differed from both the DLD and TD children. However, besides weaker intellectual functioning, there are other factors that differ between DLD and 22q11DS. Palatal abnormalities and velopharyngeal insufficiency (VPI) are reported in 67% of children with 22q11DS (Solot et al., 2019), whereas these are not frequently reported in children with DLD. It may be argued that these difficulties impact language development in 22q11DS, and as such contribute to the development of ASD-related behaviors in this population. However, three studies, one using the same sample of children with 22q11DS as the present study (Everaert et al., 2022; Gerdes et al., 1999; Solot et al., 2001), did not provide strong evidence for a direct influence of palatal or speech abnormalities on language development in young children with 22q11DS. Nevertheless, the palatal abnormalities or VPI might require surgical intervention, and besides, 22q11DS is associated with other physical manifestations, including congenital heart defect, for which hospitalizations at an early age may be necessary. This is not the case in DLD. Such hospitalization at an early age may severely influence the early child-caregiver connection and communication (Swillen et al., 2018). As such, in line with our previous reasoning (e.g., Salmon et al., 2016), the physical manifestations of 22q11DS may impact future behavioral outcomes of children with 22q11DS, including the development of ASD-related behaviors. It would therefore be interesting for future studies to include the context of physical symptoms, and their association with the child-caregiver relationship, in models that predict later behavioral outcomes.

To our knowledge, this is the first study directly investigating the relationship between early language difficulties and the occurrence of ASD-related behaviors in children with 22q11DS. We consider it a strength of this study that we used a longitudinal design, including a measure of ASD-related behaviors, that was administered both at baseline and again at the 1-year follow-up assessment. This allowed us to demonstrate the impact of early language difficulties of children with 22q11DS and DLD on the occurrence of ASD-related behaviors one year later, while controlling for the initial level of ASD-related behaviors. To confirm our finding that receptive language difficulties are associated with the occurrence of ASD-related behaviors in children with 22q11DS, replication is necessary.

Such replication studies should take into account that other factors, besides early language difficulties, may influence the development of ASD-related behaviors in children. For instance, it has been suggested that the relationship between language and ASD-related behaviors could be mediated by cognitive factors that were not included in the present study, such as difficulties in emotion-recognition and theory of mind (Vissers & Koolen, 2016). Given that impaired development of these cognitive functions has been reported, both in 22q11DS (Milic et al., 2021) and in DLD (Vissers & Koolen, 2016), it would be interesting to test to what extent these factors play a role in understanding the relationship between receptive language and ASD-related behaviors in these two groups of children. Furthermore, factors such as motor functioning or sensory processing may play a role in explaining the observed variation in the domain of repetitive and restricted behaviors (Berry et al., 2018). Impairments in these domains have been reported in children with DLD (Diepeveen et al., 2017) and in children with 22q11DS (Van Aken et al., 2009). Future studies would need to shed light to what extent the influence of such factors is on the development of ASD-related behaviors, in these groups of children.

Conclusion

We demonstrated that lower receptive language skills of children with 22q11DS, an etiologically homogeneous group with severe language difficulties, were associated with more ASD-related behaviors at a later age, specifically in the domain of social communication and interaction. This association was not significant in children with DLD, which corroborates with our hypothesis that the etiological heterogeneity within the DLD group may hinder our ability to detect such associations. This emphasizes the advantage of studying homogeneous subgroups to increase our understanding of phenotypical variability in DLD. Future research, for instance further comparing 22q11DS and DLD, is necessary to identify for which children with DLD receptive language difficulties play a role in the occurrence of ASD-related behaviors. Clinically, results of our study highlight the importance of screening for ASD-related behaviors in children with DLD and 22q11DS already at a young age, especially in those children with receptive language difficulties.

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All other authors declare that there are no conflicts of interest in relation to the subject of this study.

Data availability statement

The datasets generated and/or analyzed during the current study are not publicly available due to GDPR compliance and legal and ethical limitations, but a subset of the data can be shared by the corresponding author upon reasonable request.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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References

Aguinis, H., Edwards, J. R., & Bradley, K. J. (2017). Improving our understanding of moderation and mediation in strategic management research. *Organizational Research Methods*, *20*(4), 665–685. https://doi.org/10.1177/1094428115627498

American Psychiatric Association (2013). *Diagnostic and statistical manual of mental disorders* (5th ed). https://doi.org/10.1176/appi.books.9780890425596

Angkustsiri, K., Goodlin-Jones, B., Deprey, L., Brahmbhatt, K., Harris, S., & Simon, T. J. (2014). Social impairments in chromosome 22q11.2 deletion syndrome (22q11.2DS): Autism spectrum disorder or a different endophenotype? *Journal of Autism and Developmental Disorders*, *44*(4), 739–746. https://doi.org/10.1007/s10803-013-1920-x

Barnett, C. P., & van Bon, B. W. M. (2015). Monogenic and chromosomal causes of isolated speech and language impairment. *Journal of Medical Genetics*, *52*(11), 719–729. https://doi.org/10.1136/jmedgenet-2015-103161

Berry, K., Russel, K., & Frost, K. (2018). Restricted and repetitive behaviors in autism spectrum disorder: A review of associated features and presentation across clinical populations. *Current Developmental Disorders Reports*, *5*(2), 108–115. https://doi.org/10.1007/s40474-018-0139-0

Bishop, D. V. M. (2006). What causes specific language impairment in children? *Current Directions in Psychological Science*, *15*(5), 217–221. https://doi.org/10.1111/j.1467-8721.2006.00439.x

Bishop, D. V. M., Snowling, M. J., Thompson, P. A., & Greenhalgh, T., & and the CATALISE-2 consortium. (2017). Phase 2 of CATALISE: A multinational and multidisciplinary delphi consensus study of problems with language development: Terminology. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *58*(10), 1068–1080. https://doi.org/10.1111/jcpp.12721

Blagojevic, C., Heung, T., Theriault, M., Tomita-Mitchell, A., Chakraborty, P., Kernohan, K., Bulman, D. E., & Bassett, A. S. (2021). Estimate of the contemporary live-birth prevalence of recurrent 22q11.2 deletions: A cross-sectional analysis from population-based newborn screening. *Canadian Medical Association Open Access Journal*, *9*(3), E802–E809. https://doi.org/10.9778/cmajo.20200294

Bornstein, M. H., Hahn, C., & Suwalsky, J. T. D. (2013). Language and internalizing and externalizing behavioral adjustment: Developmental pathways from childhood to adolescence. *Development and Psychopathology*, *25*, 857–878. https://doi.org/10.1017/S0954579413000217

Boyle, J. M., McCartney, E., O'Hare, A., & Forbes, J. (2009). Direct versus indirect and individual versus group modes of language therapy for children with primary language impairment: Principal outcomes from a randomized controlled trial and economic evaluation. *International Journal of Language & Communication Disorders*, *44*(6), 826–846. https://doi.org/10.1080/13682820802371848

Chow, J. C., Ekholm, E., & Coleman, H. (2018). Does oral language underpin the development of later behavior problems? A longitudinal meta-analysis. *School Psychology Quarterly*, *33*, 337–349. https://doi.org/10.1037/spq0000255

Conti-Ramsden, G., & Durkin, K. (2017). *Developmental Language Disorder*. John Wiley & Sons, Ltd: Child Psychology and Psychiatry: Frameworks for Clinical Training and Practice.

Conti-Ramsden, G., Durkin, K., Toseeb, U., Botting, N., & Pickles, A. (2018). Education and employment outcomes of young adults with a history of developmental language disorder. *International Journal of Language & Communication Disorders*, *53*(2), 237–255. https://doi.org/10.1111/1460-6984.12338

Conti-Ramsden, G., Simkin, Z., & Botting, N. (2006). The prevalence of autistic spectrum disorders in adolescents with a history of specific language impairment (SLI). *Journal of Child Psychology and Psychiatry*, *47*, 621–628. https://doi.org/10.1111/j.1469-7610.2005.01584.x

Conway, L. J., Levickis, P. A., Mensah, F., McKean, C., Smith, K., & Reilly, S. (2017). Associations between expressive and receptive language and internalizing and externalizing behaviours in a community-based prospective study of slow-to-talk toddlers. *International Journal of Language and Communication Disorders*, *52*, 839–853. https://doi.org/10.1111/1460-6984.12320

Curtis, P. R., Frey, J. R., Watson, C. D., Hampton, L. H., & Roberts, M. Y. (2018). Language disorders and problem

behaviors: A meta-analysis. *Pediatrics*, *142*, e:20173551. https://doi.org/10.1542/peds.2017-3551

De Smedt, B., Devriendt, K., Fryns, J. P., Vogels, A., Gewillig, M., & Swillen, A. (2007). Intellectual abilities in a large sample of children with velo–cardio–facial syndrome: An update. *Journal of Intellectual Disability Research*, *51*(9), 666–670. https://doi.org/10.1111/j.1365-2788.2007.00955.x

Diepeveen, F. B., van Dommelen, P., Oudesluys-Murphy, A., & Verkerk, P. H. (2017). Children with specific language impairment are more likely to reach motor milestones late. *Child: Care, Health and Development*, *44*, 857–862. https://doi.org/10.1111/cch.12614

Durkin, K., Conti-Ramsden, G., & Simkin, Z. (2011). Functional outcomes of adolescents with a history of specific language impairment (SLI) with and without autistic symptomatology. *Journal of Autism and Developmental Disorders*, *42*, 123–138. https://doi.org/10.1007/s10803-011-1224-y

Everaert, E*, Selten, I*, Boerma, T., Houben, M., Vorstman, J., de Wilde, H., Derksen, D., Haverkamp, S., Wijnen, F., & Gerrits, E. (2023). The language profile of preschool children with 22q11.2 deletion syndrome and the relationship with speech intelligibility. *The American Journal of Speech and Language Therapy*, *32*, 128–144.

Ferguson, C. J. (2009). An effect size primer: A guide for clinicians and researchers. *Professional Psychology: Research and Practice*, *40*, 532–538. https://doi.org/10.1037/a0015808

Fiksinski, A. M., Schneider, M., Murphy, C. M., Armando, M., Vicari, S., Canyelles, J. M., Gothelf, D., Eliez, S., Breetvelt, E. J., Arango, C., & Vorstman, J. A. S. (2018). Understanding the pediatric psychiatric phenotype of 22q11.2 deletion syndrome. *American Journal of Medical Genetics. Part A*, *176*(10), 2182–2191. https://doi.org/10.1002/ajmg.a.40387

Gerdes, M., Solot, C., Wang, P. P., Moss, E., LaRossa, D., Randall, P., Goldmuntz, E., Clark, B. J., Driscoll, D. A., Jawad, A., Emanuel, B. S., McDonald-McGinn, D. M., Batshaw, M. L., & Zackai, E. H. (1999). Cognitive and behavior profile of preschool children with chromosome 22q11.2 deletion. *American Journal of Medical Genetics*, *85*(2), 127–133. https://doi.org/10.1002/(SICI)1096-8628(19990716)85:2<127::AID-AJMG6>3.0.CO;2-F

Gibson, J., Adams, C., Lockton, E., & Green, J. (2013). Social communication disorder outside autism? A diagnostic classification approach the delineating pragmatic language impairment, high functioning autism and specific language impairments. *Journal of Child Psychology and Psychiatry*, *54*, 1186–1197. https://doi.org/10.1111/jcpp.12079

Goh, S. K. Y., Griffiths, S., & Norbury, C. F., & the SCALES Team. (2021). Sources of variability in the prospective relation of language, emotional and behavior problem symptoms: Implications for developmental language disorder. *Journal of Abnormal Psychology*, *130*, 676–689. https://doi.org/10.1037/abn0000691

Goorhuis-Brouwer, S. M., Dikkers, F. G., Robinson, P. H., & Kerstjens-Frederikse, W. S. (2003). Specific language impairment in children with velocardiofacial syndrome: Four case studies. *The Cleft Palate-Craniofacial Journal: Official Publication of the American Cleft Palate-Craniofacial Association*, *40*(2), 190–195. https://doi.org/10.1597/1545-1569_2003_040_0190_sliicw_2.0.co_2

Honey, E., McConachie, H., Randle, V., Shearer, H., & Le Couteur, A. S. (2008). One-year change in repetitive behaviours in young children with communication disorders including autism. *Journal of Autism and Developmental Disorders*, *38*, 1439–1450. https://doi.org/10.1007/s10803-006-0191-1

Howlin, P., Mawhood, L., & Rutter, M. (2000). Autism and developmental receptive language disorder – a follow-up comparison in early adult life. II: Social, behavioural, and psychiatric outcomes. *Journal of Child Psychology and Psychiatry*, *41*, 561–578. https://doi.org/10.1111/1469-7610.00643

Kalnak, N., Stamouli, S., Peyrard-Janvid, M., Rabkina, I., Becker, M., Klingberg, T., kere, J., Forssberg, H., & Tammimies, K. (2018). Enrichment of rare copy number variation in children with developmental language disorder. *Clinical Genetics*, *94*, 313–320. https://doi.org/10.1111/cge.13389

Kates, W. R., Antshel, K. M., Fremont, W. P., Shprintzen, R. J., Strunge, L. A., Burnette, C. P., & Higgins, A. M. (2007). Comparing phenotypes in patients with idiopathic autism to patients with velocardiofacial syndrome (22q11 DS) with and without autism. *American Journal of Medical Genetics Part A*, *143*, 2642–2650. https://doi.org/10.1002/ajmg.a.32012

Lancaster, H. S., & Camarata, S. (2019). Reconceptualizing developmental language disorder as a spectrum disorder: Issues and evidence. *International Journal of Language and Communication Disorders*, *54*, 79–94. https://doi.org/10.1111/1460-6984.12433

Larkin, F., Meins, E., Centifanti, L. C. M., Fernyhough, C., & Leekam, S. R. (2017). How does restricted and repetitive behavior relate to language and cognition in typical development? *Development and Psychopathology*, *29*, 863–874. https://doi.org/10.1017/S0954579416000535

Leyfer, O. T., Tager-Flusberg, H., Dowd, M., Tomblin, B., & Folstein, S. E. (2008). Overlap between autism and specific language impairment: Comparison of autism diagnostic interview and autism diagnostic observation schedule scores. *Autism Research*, *1*, 284–296. https://doi.org/10.1002/aur.43

Loucas, T., Charman, T., Pickles, A., Simonoff, E., Chandler, S., Meldrum, D., & Baird, G. (2008). Autistic symptomatology and language ability in autism spectrum disorder and specific language impairment. *Journal of Child Psychology and Psychiatry*, *49*, 1184–1192. https://doi.org/10.1111/j.1469-7610.2008.01951.x

McCabe, P. C. (2005). Social and behavioral correlates of preschoolers with specific language impairment. *Psychology in Schools*, *42*, 373–387. https://doi.org/10.1002/pits.20064

McDonald-McGinn, D. M., Sullivan, K. E., Marino, B., Philip, N., Swillen, A. , Vorstman, J. A., … Bassett, A. S. (2015). 22q11.2 deletion syndrome. *Nature Reviews Disease Primers*, *1*(1), 1–19. https://doi.org/10.1038/nrdp.2015.71

Mildenberger, K., Sitter, S., Noterdaeme, M., & Amorosa, H. (2001). The use of the ADI-R as a diagnostic tool in the differential diagnosis of children with infantile autism and children with a receptive language disorder. *European Child & Adolescent Psychiatry*, *10*, 248–255. https://doi.org/10.1007/s007870170014

Milic, B., Feller, C., Schneider, M., Debbané, M., & Loeffler-Stastka, H. (2021). Social cognition in individuals with 22q11.2 deletino syndrome and its link with psychopathology and social outcomes: A review. *BMC Psychiatry*, *21*, 130–148. https://doi.org/10.1186/s12888-020-02975-5

Miniscalco, C., Fernell, E., Thompson, L., Sandberg, E., Kadesjö, B., & Gillberg, C. (2018). Development problems were common five years after positive screening for language disorders and, or, autism at 2.5 years of age. *Acta Paediatrica*, *107*(10), 1739–1749. https://doi.org/10.1111/apa.14358

Mok, P. L. H., Pickles, A., Durkin, K., & Conti-Ramsden, G. (2014). Longitudinal trajectories of peer relation sin children with specific language impairment. *Journal of Child Psychology and Psychiatry*, *55*, 516–527. https://doi.org/10.1111/jcpp.12190

Mouridsen, S. E., & Hauschild, K.-M. (2009). A longitudinal study of autism spectrum disorders in individuals diagnosed with a developmental language disorder as children. *Child: Care, Health and Development*, *35*, 691–697. https://doi.org/10.1111/j.1365-2214.2009.00954.x

Norbury, C. F., Gooch, D., Wray, C., Baird, G., Charman, T., Simonoff, E., Vamvakas, G., & Pickles, A. (2016). The impact of nonverbal ability on prevalence and clinical presentation of language disorder: Evidence from a population study. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *57*(11), 1247–1257. https://doi.org/10.1111/jcpp.12573

Özgyurt, G., & Dinsever Eliküçük, C. (2018). Comparison of language features, autism spectrum symptoms in children diagnosed with autism spectrum disorder, developmental language delay, and healthy controls. *Archives of Neuropsychiatry*, *55*, 205–210.

Pettigrew, K. A., Reeves, E., Leavett, R., Hayiou-thomas, M. E., Sharma, A., Simpson, N. H., Martinelly, A., Thompson, P., Hulme, C., Snowling, M. J., Newbury, D. F., & Paracchini, S. (2015). Copy number variation screen identifies a rare de novo deletion at chromosome 15q13.1-13.3 in a child with language impairment. *PLOS one*, *108*, e0134997.

Plug, M. B., van Wijngaarden, V., de Wilde, H., van Binsbergen, E., Stegeman, I., van den Boogaard, M. H., & Smit, A. L. (2021). Clinical characteristics and genetic etiology of children with developmental language disorder. *Frontiers in Pediatrics*, *9*, 651995. https://doi.org/10.3389/fped.2021.651995

Roeyers, H., Thys, M., Druart, C., De Schryver, M., & Schittekatte, M. (2011). *SRS Screeningslijst voor autismespectrumstoornissen. Nederlandstalige versie*. Hogrefe Uitgevers BV.

Roy, P., & Chiat, S. (2014). Developmental pathways of language and social communication problems in 9–11 year olds: Unpicking the heterogeneity. *Research in Developmental Disabilities*, *35*(10), 2534–2546. https://doi.org/10.1016/j.ridd.2014.06.014

RStudio Team (2020). *RStudio: Integrated Development for R. RStudio, PBC, Boston, MA URL* http://www.rstudio.com/.

Rudolph, J. M. (2017). Case history risk factors for specific language impairment: A systematic review and meta-analysis. *American Journal of Speech-Language Pathology*, *26*, 991–1010. https://doi.org/10.1044/2016_AJSLP-15-0181

Salmon, K., O'Kearney, R., Reese, E., & Fortune, C. (2016). The role of language skill in child psychopathology: Implications for intervention in the early years. *Clinical Child Fam Psychology Review*, *19*, 352–367. https://doi.org/10.1007/s10567-016-0214-1

Schneider, M., Debbané, M. , Bassett, A. S., … the International Consortium on Brain and Behavior in 22q11.2 Deletion Syndrome. (2014). Psychiatric disorders from childhood to adulthood in 22q11.2 deletion syndrome: Results from the international consortium on brain and behavior in 22q11.2 deletion syndrome. *American Journal of Psychiatry*, *171*, 627–639. https://doi.org/10.1176/appi.ajp.2013.13070864

Selten, I., Boerma, T., Everaert, E., VanSteensel, M. J., Vorstman, J., & Wijnen, F. (2021). Narrative comprehension and production abilities of children with 22q11.2 deletion syndrome. *Research in Developmental Disabilities*, *119*, 104109. https://doi.org/10.1016/j.ridd.2021.104109

Serur, Y., Frumer, D. S., Daon, K., Havia, D. S., Weinberger, R., Shulman, C., & Gothelf, D. (2019). Psychiatric disorders and autism in young children with 22q11.2 deletion syndrome compared to children with idiopathic autism. *European Psychiatry*, *55*, 116–121. https://doi.org/10.1016/j.eurpsy.2018.10.007

Simea (2017). *Richtlijn Toelaatbaarheid.* https://simea.nl/media/richtlijnen/simea-brochure-richtlijn-toelaatbaarheid-20170901.pdf.

Smajlagić, D., Lavrichenko, K., Berland, S., Helgeland, Ø, Knudsen, G. P., Vaudel, M., Haavik, J., Knappskog, P. M., Njølstad, P. R., Houge, G., & Johansson, S. (2021). Population prevalence and inheritance pattern of recurrent CNVs associated with neurodevelopmental disorders in 12,252 newborns and their parents. *European Journal of Human Genetics*, *29*, 205–215. https://doi.org/10.1038/s41431-020-00707-7

Søderby, I. E., Ching, C. R. K. , Thomopoulos, S. I., … The ENIGMA 22q11.2 deletion syndrome working group. (2021). Effects of copy number variations on brain structure and risk for psychiatric illness: Large-scale studies from the ENIGMA working groups on CNVs. *Human Brain Mapping*, *43*, 300–328. https://doi.org/10.1002/hbm.25354

Solot, C. B., Gerdes, M., Kirschner, R. E., McDonald-McGinn, D. M., Moss, E., Woodin, M., Aleman, D., Zackai, E. H., & Wang, P. P. (2001). Communication issues in 22q11.2 deletion syndrome: Children at risk. *Genetics in Medicine*, *3*, 67–71. https://doi.org/10.1097/00125817-200101000-00015

Solot, C. B., Moore, T. M., Crowley, T. B., Gerdes, M., Moss, E., McGinn, D. E., Emanuel, B. S., Zackai, E. H., Gallagher, S., Calkins, M. E., Ruparel, K., Gur, R. C., McDonald-McGinn, D. M., & Gur, R. E. (2020). Early language measurers associated with later psychosis features in 22q11.2 deletion syndrome. *American Journal of Medical Genetics Part B*, *183B*, 392–400. https://doi.org/10.1002/ajmg.b.32812

Solot, C. B., Sell, D., Mayne, A., Baylis, A. L., Persson, C., Jackson, O., & McDonald-McGinn, D. M. (2019). Speech-language disorders in 22q11.2 deletion syndrome:

Best practices for diagnosis and management. *American Journal of Speech-Language Pathology*, *28*, 984–999. https://doi.org/10.1044/2019_AJSLP-16-0147

Swillen, A. (2016). The importance of understanding cognitive trajectories: The case of 22q11.2 deletion syndrome. *Current Opinion in Psychiatry*, *2*, 133–137. https://doi.org/10.1097/YCO.0000000000000231

Swillen, A., Devriendt, K., Ghesquière, P., & Fryns, J. P. (2001). Children with a 22q11 deletion versus children with a speech-language impairment and learning disability: Behavior during primary school age. *Genetic Counselling*, *12*, 309–317.

Swillen, A., Moss, E., & Duijff, S. (2018). Neurodevelopmental outcome in 22q11.2 deletion syndrome and management. *American Journal of Medical Genetics. Part A*, *176*(10), 2160–2166. https://doi.org/10.1002/ajmg.a.38709

Van Aken, K., Caeyenberghs, K., Smits-Engelsman, B., & Swillen, A. (2009). The motor profile of primary school-age children with a 22q11.2 deletion syndrome (22q11.2DS) and an age-and IQ-matched control group. *Child Neuropsychology*, *15*, 532–542. https://doi.org/10.1080/09297040902740678

Van Den Heuvel, E., Manders, E., Swillen, A., & Zink, I. (2018). Atypical language characteristics and trajectories in children with 22q11.2 deletion syndrome. *Journal of Communication Disorders*, *75*, 37–56. https://doi.org/10.1016/j.jcomdis.2018.06.001

VanSteensel, M. J., Selten, I., Charbonnier, L., Berezutskaya, J., Raemaekers, M. A. H., Ramsey, N. F., & Wijnen, F. (2021). Reduced brain activation during language processing in children with developmental language disorder and children with 22q11.2 deletion syndrome. *Neuropsychologia*, *158*, 107907. https://doi.org/10.1016/j.neuropsychologia.2021.107907

Vissers, C., & Koolen, S. (2016). Theory of mind deficits and social emotional functioning in preschoolers with specific language impairment. *Frontiers in Psychology*, *7*, 1734. https://doi.org/10.3389/fpsyg.2016.01734

Vorstman, J. A. S., Morcus, M. E. J., Duijff, S. N., Klaassen, P. W. J., Heineman-de boer, J. A., Beemer, F. A., Swaab, H., Kahn, R. S., & van Engeland, H. (2006). The 22q11.2 deletion in children: High rate of autistic disorders and early onset of psychotic symptoms. *Journal of the American Academy of Child & Adolescent Psychiatry*, *45*, 1104–1113. https://doi.org/10.1097/01.chi.0000228131.56956.c1

Wechsler, D., & Naglieri, J. (2008). *Wechsler Nonverbal Scale of Ability (WNV-NL)- Nederlandstalige Bewerking. Afname en Scoringshandleiding (Nederlandse bewerking van Pearson Assessment and Information)*.

Wiig, E. H., Secord, W. A., & Semel, E. (2012). *CELF Preschool-2-NL: Clinical evaluation of language fundamentals: Preschool-Nederlandstalige versie. Handleiding. (J. De Jong, Trans)*. Pearson Benelux BV.

Williams, D., Botting, N., & Boucher, J. (2008). Language in autism and specific language impairment: Where are the links? *Psychological Bulletin*, *134*, 944–963. https://doi.org/10.1037/a0013743

Zwaigenbaum, L., Bauman, M. L., Stone, W. L., Yirmiya, N., Estes, A., Hansen, R. L., McPartland, J. C., Natowicz, M. R., Choueiri, R., Fein, D., Kasari, C., Pierce, K., Buie, T., Carter, A., Davis, P. A., Granpeesheh, D., Mailloux, Z., Newschaffer, C., Robins, D., Roley, S. S., Wagner, S., & Wetherby, A. (2015). Early identification of autism spectrum disorder: Recommendations for clinical practice and research. *Pediatrics*, *136*, S10–S40. https://doi.org/10.1542/peds.2014-3667C

Appendix A

Table 1. Overview indicating the number of children with missing data for each variable, out of all children that were excluded from the regression analyses.

Type of missing data	22q11DS (n = 14)	DLD (n = 5)	TD (n = 3)
CELF ELC	8	2	1
CELF RLC	9	1	0
FSIQ	2	2	1
SRS Baseline	4	1	1

Abbreviatons. CELF ELC = Expressive language composite score. CELF RLC = CELF receptive language composite score. FSIQ = Full Scale IQ score. SRS baseline = baseline score on Social Responsiveness Scale.

Note. Total in 22q11D and DLD some children had missing data on multiple variables (e.g., both CELF ELC and CELF RLC).

[a] Parental education was indexed by the average education level of both parents, ranked on a 9-point scale reflecting the Dutch educational system (ranging from 1 'no education' to 9 'university degree'). This information was missing for 1 TD child.

Table 2. Results of independent t-tests, indicating whether scores on these variables differed between children with 22q11DS who could (n = 28) and could not be (n = 14) included in the regression analyses.

	Statistics	
Variable	t/χ^2	p
Age follow-up	−1.57	.123
Sex	1.45	.228
T-RRB follow-up	0.63	.537
T-SCI follow-up	2.02	.052

Abbreviatons. T-SCI = T-score on social communication and interaction (SRS-scale SCI).

T-RRBI = T-score on Restricted Repetitive Behaviors and Interests. (SRS-scale RRBI).

Note. Significant difference indicated higher rates of T-SCI scores for the children that did not take part in the regression analysis.