Early Visual Motor Integration Functioning and Subsequent Cognitive Decline in Children and Adolescents with the 22q11.2 Deletion Syndrome: A Longitudinal Study

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Abstract

The 22q11.2 Deletion Syndrome (22q11DS) is a genetic syndrome that is characterized by a deletion at band 11.2 on the long arm of chromosome 22. This study aims to investigate the relationship between the level of visual motor integration (VMI) and cognitive decline in children with 22q11DS. It has been reported that greater cognitive decline occurs in 22q11DS individuals who eventually develop a psychotic disorder and this decline appears to start at the age of approximately eleven years. These results suggest that early cognitive decline could potentially be used as a marker for schizophrenia or other psychotic symptoms. But are there markers that predict cognitive decline? Studies suggest a significant relation between cognitive functioning and VMI. Therefore, we hypothesized that VMI functioning in 22q11DS individuals before the age of eleven is predictive for cognitive decline starting at the age of eleven. Secondly, components of the VMI, visual perception (VP) and motor coordination (MC), are also hypothesized to predict cognitive decline. VMI functioning was measured at T-1 and cognitive functioning at T0 and T1 in a sample of N = 35 (10 males, 25 females; mean age T1 16.8 years, SD = 2.12, age range 14 through 21). Results indicate that VMI skill level does not predict cognitive decline later in life, odds ratio (OR) = 1.05; 95% CI, .930-1.18; $p > .05$. VP and MC neither predict cognitive decline, VP; OR = 1.01; 95% CI, .930-1.09; $p > .05$, MC; OR = 1.09; 95% CI, .916-1.30; $p > .05$. However, we did find that cognitive decline may already have occurred before T0. Therefore, it is important that future studies assess VMI functioning and the change in cognitive functioning earlier in the life of 22q11DS children than was the case in the current study. We must keep on focusing on predictors for cognitive decline, since they may help in diagnosing and treating schizophrenia.
Keywords: 22q11.2 Deletion Syndrome, Cognitive development, Visual Motor Integration, Intelligence Quotient (IQ).

The development of visual motor integration and cognitive functioning in 22q11DS

The 22q11.2 Deletion Syndrome (22q11DS), previously also known as velo-cardio-facial syndrome, DiGeorge syndrome and Shprintzen syndrome, is a genetic syndrome. It is characterized by a deletion at band 11.2 on the long arm of chromosome 22 in the human body (McDonald-McGinn & Sullivan, 2011; Shaikh et al., 2000). The syndrome is estimated to occur at approximately one in 4000 live births (Devriendt, Fryns, Mortier, Van Thienen, & Keymolen, 1998; Oskarsdottir, Vujic, & Fasth, 2004). However, a recent study shows that the prevalence is shifting to 1 in 1000 healthy fetuses (Grati et al., 2015). Cleft palate, heart failures and a typical facial appearance are some of the many common physical anomalies in 22q11DS individuals (Oskarsdóttir, Holmberg, Fasth, & Strömland, 2008; McDonald-McGinn & Sullivan, 2011; Swillen, Vogels, Devriendt, & Fryns, 2000). The Intelligence Quotient (IQ), a measure for cognitive functioning, is significantly lower in 22q11DS (±70-85) compared to the general population (±100) (Swillen, & McDonald-McGinn, 2015). Moreover, psychiatric problems are often present in the 22q11DS population (Monks et al., 2014; Ousley et al., 2013). About 70% of the 22q11DS patients meet DSM-IV criteria for one or more psychiatric disorders (Ousley et al., 2013; Vorstman et al., 2006; Schneider et al., 2014). The syndrome is associated with an increased risk for developing anxiety- and mood disorders, as well as developmental disorders such as autism and attention deficit hyperactivity disorder (ADHD) (Vorstman et al., 2006; Ousley et al., 2013; Swillen et al., 2000). Most importantly, individuals are also at elevated risk for developing schizophrenia (Ousley et al., 2013; Monks et al., 2014; Vorstman et al., 2006). About 25-30% of the 22q11DS individuals develop schizophrenia and approximately 1.5% of schizophrenia patients are diagnosed with 22q11DS (Ousley et al., 2013; Monks et al., 2014; Vorstman et al., 2006; Hoogendoorn et al., 2008). The prevalence of schizophrenia in the general population is about 1% (Arinami et al., 2001). 22q11DS is the largest genetic risk factor for

schizophrenia and a useful model for studies of early predictors for schizophrenia. If it were possible to find early predictive features, it could help in diagnosing and treating schizophrenia in 22q11DS individuals at an early stage. For these reasons, it is important to find early predictive factors for schizophrenia.

Studies show that cognitive functioning (verbal IQ, performance IQ and full scale IQ) declines in individuals with 22q11DS in contrast to non-deleted people (Green et al., 2009; Vorstman et al., 2015; Duijff, Klaassen, Swanenburg de Veye, Beemer, Sinnema, & Vorstman, 2012b). The difference between two or more IQ measurements, in this study called delta IQ, is generally negative in the 22q11DS population. It has been found that greater cognitive decline occurs in 22q11DS individuals suffering from a psychotic disorder (Vorstman et al., 2015). This cognitive decline, which has been associated with psychotic disorders, appears to start at the age of approximately eleven years. In other words, when cognitive decline sets in, 22q11DS individuals are at higher risk of developing a psychotic disorder. Early cognitive decline could potentially be used as a marker for schizophrenia and psychotic symptoms in the 22q11DS population (Reichenberg et al., 2005; Vorstman et al., 2015). As cognitive decline associated with psychotic disorders sets in at approximately the age of eleven, it is possible that an earlier predictor for schizophrenia exists. The cognitive development of some 22q11DS individuals before the age of eleven may be deviant and could eventually result in cognitive deterioration. For this reason it is important to take a closer look at possible predictors for cognitive decline. To our knowledge, this is the first study to investigate a predictor for cognitive decline in 22q11DS individuals.

Research has shown that visual motor integration (VMI) functioning is related to cognitive functioning and therefore could act as a possible predictor for cognitive decline later in life (Duijff, Klaassen, Beemer, Swanenburg de Veye, Vorstman, & Sinnema, 2012a; Van Aken et al., 2009; Niklasson, & Gillberg, 2010). VMI functioning could be defined as the

integration of the visualization of an object and the use of proper movements to copy the object. Problems in VMI functioning are common in the 22q11DS population (Lajiness-O'Neill et al., 2006; Van Aken, Caeyenberghs, Smits-Engelsman, & Swillen al., 2009). Lower VMI skills may affect the academic performances of some 22q11DS individuals, especially on paper and pencil tests (Kulp, 1999; Sortor, & Kulp, 2003). Older children with 22q11DS have more problems with VMI than younger children (Swillen et al., 1999). Studies suggest that VMI functioning is related to cognitive functioning. One study found a negative association between low skills of VMI and cognitive functioning in five-year-old children with 22q11DS (Duijff et al., 2012a). Another study used IQ-matched control groups when researching the VMI of 22q11DS patients, also expecting VMI to be associated with IQ, and this expectation was confirmed (Van Aken et al., 2009). One study found that FSIQ and PIQ significantly explained the variation in VMI by 60% and 50%, also suggesting a relation between VMI and cognitive functioning (Niklasson, & Gillberg, 2010). Moreover, VMI correlates significantly with the Performance IQ (PIQ), which measures visuospatial intellectual abilities (Duijff et al., 2012a).

Besides the association between VMI and IQ, visual perception (VP) and motor coordination (MC) are also related to IQ. VP and MC are components of VMI, and could be possible predictors for cognitive decline as well, since their association between some facets of IQ (Van Aken et al., 2009; Sobin et al., 2005). VP skills seem to be problematic in some 22q11DS individuals (Van Aken et al., 2009; Vicari et al., 2012). Children with 22q11DS are also characterized by their motor difficulties (Boot et al., 2015). Individuals with 22q11DS have difficulties with balance, motor skills (gross and fine) and coordination (Van Aken et al., 2009). Moreover, studies with control groups show that children with 22q11DS score significantly lower on the subtests of the Beery-Buktenica Developmental Test of Visual Motor Integration (VMI), than children with the same IQ, but not suffering from 22q11DS

(Van Aken et al., 2009; Roizen, Higgins, Antshel, Fremont, Shprintzen, & Kates, 2010; Bish, Chiodo, Mattei, & Simon, 2007). The Beery-Buktenica Developmental Test of VMI is a frequently used measure for VMI (Beery, & Beery, 2004). One study found VP to be significantly correlated with Full Scale IQ (FSIQ), which is the total score of the intelligence test (Van Aken et al., 2009). Moreover, VP and MC correlate with PIQ (Van Aken et al., 2009; Sobin et al., 2005). No significant association is found between verbal IQ (VIQ), which measures the verbal skills of a person, and VMI, VP and MC. The significant relationship between VMI functioning and cognitive functioning suggests that problems with VMI before the age of eleven could be predictive for cognitive decline later in adolescence.

To our knowledge, no longitudinal research has been conducted on the relationship between VMI and delta IQ in children and adolescents with 22q11DS. The current study investigates a possible predictor for cognitive decline in children and adolescents with 22q11DS. The research question for this study is: are low scores on VMI functioning in 22q11DS individuals before the age of eleven predictive for cognitive decline later? Secondly, we hypothesized that VP and MC predict cognitive decline, especially the decline in PIQ in 22q11DS individuals. If we were to find low scores on VMI, VP and MC to be associated with a decline in cognitive functioning, we may have identified other early predictors for schizophrenia.

Method

Participants

Participants diagnosed with 22q11DS were included in this study (N = 176). Specialists throughout the country refer their 22q11DS patients to the psychiatric outpatient clinic of the University Medical Centre Utrecht (UMCU). Some participants were also referred by the pediatrician of the national 22q11DS outpatient clinic at the Wilhelmina Children's Hospital (WCH). Informed consent was signed by the participants and their

parents or legal guardians (in case the participant did not reach the age of 18 yet). Here permission for the use of the data of interest was given. The inclusion criteria for participants were a confirmed diagnosis of 22q11DS and a maximum age of 25 years at T0.

The current study is a longitudinal cohort study that follows and observes children and adolescents with 22q11DS and is part of a larger longitudinal and prospective study that was set up in 2002. The original study, which the current study is part of, is approved by the Medical Ethical Committee of the UMCU. For this study, data collected from 2002 to 2015 are used. The current study is carried out in Utrecht, The Netherlands at the University Medical Centre, division Psychiatry. The general set-up of the procedure of the original 22q11DS study is described. The current study specifies on a part of the general set-up.

Materials

To measure VMI skill level, the Beery-Buktenica Developmental Test of Visual Motor Integration (VMI) (Beery, & Beery, 2004) was used. In this paper and pencil task, consisting of 21 items, individuals are asked to copy different kinds of geometric shapes. As the test progresses, the difficulty rate increases. The test is reviewed as valid and reliable, with a Cronbach's alpha of .92. The mean standard score is 100 (SD = 15) (Beery, & Beery, 2004).

The supplemental tests of the VMI, Motor Coordination (MC) and Visual Perception (VP), were also administered. The VMI supplemental test for VP consists of 30 items. During this task, individuals are asked to find the copy of the geometric shape showing at the top. The exact same shape needs to be detected in a row with figures that have subtle differences compared to the correct answer. The task should be completed in three minutes. The test is reviewed as valid and has a Cronbach's alpha of .91. The mean score is 100 (SD = 15) (Beery, & Beery, 2004).

The VMI supplemental test for MC also consists of 30 items. In this test individuals are asked to trace geometric shapes, starting with a vertical and a horizontal line, progressing

to more difficult shapes, such as a cube. Participants are asked to draw within the lines. Participants should finish this task in five minutes. Cronbach's alpha of this test is 0.90. The supplemental test is reviewed as valid and the mean score is 100 (SD = 15) (Beery, & Beery, 2004).

Cognitive functioning in children was measured with the Dutch version of the Wechsler Intelligence Scale for Children (WISC-III-NL) (Wechsler, 1991). The test is used for children aged 6 to 16. The test is reviewed as valid and the reliability of the test is reviewed as sufficient. However, it has been advised not to interpret results on subtest-level, due to low reliability of some subtests (Egberink, Janssen, & Vermeulen, 2005). Performance, verbal and full scale IQ are measured during this test. The mean score is 100 (SD = 15) (Wechsler, 1991). Before the implementation of the WISC-III-NL in 1991, the Dutch version of the Wechsler Intelligence Scale for Children-Revised (WISC-RN) was used (Wechsler, 1974). The WISC-RN is appropriate for children between 6 and 16 years old. The test is reviewed as valid and reliable, with an internal consistency reliability coefficient of .89.

To measure cognitive functioning in adolescents and adults, the Dutch version of the Wechsler Adult Intelligence Scale (WAIS-III-NL, WAIS-IV-NL) was used (Wechsler, 1997; Wechsler, 2008). Both versions of the test are conducted from the ages 17 to 85 years old. The WAIS measures performance, verbal and full scale IQ and the mean score of the WAIS is 100 (SD = 15). The WAIS-III-NL and WAIS-IV-NL are both reviewed as valid and reliable (Wechsler, 1997; Wechsler, 2008).

Procedure

The parent(s) and the child with 22q11DS were seen in the WCH at time point T-1 for psychological evaluation. At this time the child is below the age of eleven. VMI and IQ data were obtained at this assessment. At T0 and T1, the UMCU evaluated patients aged eleven years or older (see Figure 1 for complete study overview). Blood samples of the child with

22q11DS and his/her parents were collected for genetic research and an interview with the parents and the child took place. In this interview, current concerns and problems concerning the child were discussed. The Schedule for Affective Disorders and Schizophrenia (K-SADS), The Autism Diagnostic Interview (ADI-R) and a semi structured interview for DSM-IV criteria were conducted to assess the presence of psychiatric problems, such as schizophrenia, psychotic symptoms, Autism Spectrum Disorders (ASD), ADHD and anxiety disorders. After the interview, the psychiatrist talked alone with the parents, while the child performed the WISC-III-NL to measure cognitive functioning. Behavioral observations were assessed as well. Also the Beery VMI was administered. After these assessments, the child and the parent(s) chose to undergo a MRI scan or not. After 2/3 years a follow up was conducted at time point T1. If at that time children were over the age of 16, the WISC-III-NL was replaced by the WAIS-III/IV.

Statistical analyses

Statistical analyses were conducted with SPSS 21.0 (Statistical Package for Social Sciences version 21, IBM, Chicago, Illinois, USA).

Characteristics of the participants were obtained by descriptive statistics. VMI functioning is the predictive variable and delta IQ is the dependent variable. Both are continuous variables. For this analysis, delta IQ was converted into a dichotomous variable. VMI functioning was assessed at time point T-1. Cognitive functioning (IQ scores) was measured at time points T0 and T1. 22q11DS-based IQ percentile scores were used to identify delta IQ (Vorstman et al., 2015). Longitudinal and 22q11DS-specific IQ data that followed the normative development of 22q11DS individuals made it possible to establish 22q11DS-based IQ percentile scores. IQ development per year was calculated by subtracting the IQ percentile scores of time points T0 and T1 and dividing this number by the difference in of the two time points in years.

The strength of correlation between VMI functioning and delta IQ was determined. To answer the research question, logistic regression analysis was used with VMI functioning as being the predictor and the change in cognitive functioning (delta IQ) as the dependent variable. Moreover, logistic regression analysis was used to test if VP and MC are predictors for cognitive decline. In all analyses, cognitive decline refers to the decline in VIQ, PIQ and FSIQ. Delta IQ was defined as negative when the IQ percentile score of the 22q11DS individuals declined over T0 and T1. A decrease of one IQ percentile point was considered as a decline. Delta IQ was defined as positive when delta IQ did not change or when cognitive functioning improved between time points T0 and T1. Covariates, such as age and gender, were taken into account.

Results

Out of the original group of 176 participants, data of N = 35 was complete for analysis, consisting of 25 females and 10 males (see flowchart of participant selection in Figure 2). Mean (SD) age at the most recent time point is 16.8 (2.12) and an age range from 14 through 21 years. VMI skill levels are shown in Table 1 and cognitive features are presented in Table 2. Out of the 35 participants, n = 21 did not decline in cognitive functioning, and n = 14 did suffer from cognitive decline. Demographic features of these two groups are presented in Table 3. Cognitive functioning is significantly lower in the group of participants without cognitive decline compared to participants with cognitive decline at T0. Moreover, participants without cognitive decline are significantly older than participants with cognitive decline (see Table 3).

VMI correlates with FSIQ, $r(34) = .408$, $p = .015$ and VIQ, $r(34) = .399$, $p = .017$, but not with PIQ, $r(34) = .279$, $p > .05$. VMI standard scores at T-1 do not predict FSIQ decline, odds ratio (OR) = 1.05; 95% CI, .930-1.18; $p > .05$. VIQ decline is not predicted by VMI

standard scores, OR = 1.05; 95% CI, .938-1.17; $p > .05$, neither is PIQ decline, OR = 0.99; 95% CI, .884-1.10; $p > .05$. Mean VMI standard score (SD) in the group of 22q11DS individuals with cognitive decline ($n = 14$) is 85.8 (6.23). The group without cognitive decline ($n = 21$) had a mean visual motor integration standard score (SD) of 81.4 (8.96). The difference between the groups was not significant, $p > .05$ (See table 4).

VP does not correlate significantly with FSIQ, $r(18) = .046$, $p > .05$, VIQ, $r(18) = .031$, $p > .05$ and PIQ, $r(18) = .048$, $p > .05$. FSIQ decline is not predicted by low VP standard scores, OR = 1.01; 95% CI, .930-1.09; $p > .05$. VP standard scores do not predict VIQ decline, OR = .99; 95% CI, .925-1.06; $p > .05$ and PIQ decline, OR = 1.04; 95% CI, .967-1.11; $p > .05$.

A significant correlation was found between MC and FSIQ, $r(18) = .458$, $p = .048$, and PIQ, $r(18) = .541$, $p = .017$, but not with VIQ, $r(18) = .309$, $p > .05$. MC does not predict FSIQ decline, OR = 1.09; 95% CI, .916-1.30; $p > .05$, VIQ decline, OR = 1.08; 95% CI, .925-1.25; $p > .05$. and PIQ decline, OR = 1.06; 95% CI, .925-1.21; $p > .05$.

Discussion

The current study aimed to find an early predictor for cognitive decline in 22q11DS individuals. Many previous studies investigated possible markers for schizophrenia, including cognitive decline, but no previous 22q11DS studies, to our knowledge, have focused on finding potential predictors for cognitive decline related to psychotic disorders. The innovativeness of the study could be considered as a strength. The research question of this study was: are low scores on VMI functioning in 22q11DS individuals before the age of eleven predictive for cognitive decline later? It was also hypothesized that VP and MC predict cognitive decline, especially the decline in PIQ. Results show that low scores on VMI functioning in 22q11DS individuals before the age of eleven do not predict cognitive decline

later. VP and MC neither predict cognitive decline. It was specifically hypothesized that VP and MC would predict PIQ decline. This was not confirmed in the current results. This is not to be expected from the literature, as studies showed a significant relation between VMI and cognitive functioning (Duijff et al., 2012a; Van Aken et al., 2009).

Results of the current study showed a significant correlation between VMI and FSIQ. This is consistent with another study (Duijff et al., 2012a). We also found a significant correlation between VMI and VIQ, however this result is incongruent with other studies (Duijff et al., 2012a; Van Aken et al., 2009). It is notable that we, in contrast to other studies, did not find a significant correlation between VMI and PIQ, as visuospatial intellectual abilities seem necessary to complete the Beery-Buktenica Developmental Test of VMI (Duijff et al., 2012a; Van Aken et al., 2009; Niklasson, & Gillberg, 2009).VP did not correlate significantly with any facet of IQ in the current study. This is in line with the study of Duijff et al. (2012a), but not with the results of Van Aken et al. (2009). MC did significantly correlate with FSIQ and PIQ in the current study, but not with VIQ. In one previous study, MC did also correlate significantly with PIQ, but not with FSIQ and VIQ (Van Aken et al., 2009). In one other study MC did not correlate significantly with any facet of IQ (Duijff et al., 2012a). Differences in correlations could possibly be explained by the difference in sample sizes. Low sample sizes may influence the reliability of the correlation between two variables. In the current study, the group size is 35. In the study of Duijff et al. (2012a), the group size is 65 and in the study of Van Aken et al. (2009) 28 22q11DS participants were included.

As can be seen in Table 4, VMI functioning scores are higher, however not significantly, in the group of 22q11DS with identified cognitive decline in comparison to 22q11DS individuals that are cognitively stable or made cognitive progress. Even with no significant difference between these groups, it is odd to identify that 22q11DS individuals suffering from cognitive decline had a higher VMI skill level at T-1 than 22q11DS

individuals that stayed cognitively stable or cognitively bettered. No previous literature is available to compare these results. No further conclusions should be drawn from this result, since the result is not significant and the sample sizes are small.

In 14 of the 35 participants we could conclude that they have suffered from cognitive decline between time point T0 and T1. However, in 18 participants cognitive functioning bettered over time. In one case the estimated increase in IQ percentile points per year was 11.8. It is unlikely that this many 22q11DS individuals improve their cognitive functioning within one year, since a study suggests that further cognitive decline may set in in 22q11DS adults beyond 25 years (Evers, Amelsvoort, Candel, Boer, Engelen, & Curfs, 2014). An explanation for the annual increase in IQ percentile points may be the change of the WISC-III-NL to the WAIS-III/IV at the age of 16 years. This transition from the WISC-III-NL at T0 to the WAIS-III/IV at T1 may cause different IQ results, because of the different normative groups the IQ scores are based on (Kaufman, & Lichtenberger, 2006). If a person performs equally on the WISC-III-NL and WAIS-III/IV, IQ scores tend to be higher in the WAIS-III/IV than in the WISC-III-NL. Previous research confirmed that versions of the WAIS produced higher IQ scores than versions of the WISC within the population with low mental capabilities (Gordon, Duff, Davidson, & Whitaker, 2010; Spitz, 1988; Nagle, & Lazarus, 1980). In the current dataset, the change from the WISC to the WAIS occurred 17 times. In 12 cases the FSIQ percentile scores were higher at T1 than at T0. The VIQ and PIQ percentile scores were higher at T1 than at T0 in 8 and 10 cases. In 7 participants all facets of the IQ bettered over time. These observations may suggest that the results of the current study were influenced by the use of different Wechsler scales.

Three 22q11DS participants were cognitively stable, meaning their IQ percentiles scores remained exactly the same over the period of T0 and T1. One study observed that some children with 22q11DS between 5.5 and 9.5 years show cognitive decline (Duijff et al.,

2012b). Besides, it is suggested that one-third of the 22q11DS individuals stay stable in their cognitive functioning after 9.5 years when a decline in cognitive functioning has occurred between 7.5 and 9.5 years (Duijff, Klaassen, de Veye, Beemer, Sinnema, & Vorstman, 2013). It could be the case that these three participants may already have suffered from cognitive decline before T0 and at this moment remain cognitively stable. Moreover, in Table 4 it is shown that participants without cognitive decline have a significantly lower IQ (mean FSIQ of 63.5) than participants with cognitive decline (mean FSIQ of 75.4). The participants without cognitive decline are also significantly older at T0 than the 22q11DS individuals with cognitive decline. In the group without cognitive decline it could also be the case that they have already suffered from cognitive decline before the age 5.5 to 9.5. If this is true, it would explain the low FSIQ score and the higher age at T0. This result seems to be in line with the results of the study of Duijff et al. (2013), as it suggests that cognitive decline seems to occur in early childhood as well.

Two limitations of the current study need to be recognized. First, few data were available for analysis. This made it difficult to generate detailed results on the relation between VMI functioning and cognitive decline. Secondly, different IQ measures were used at different ages in the current study. This may have influenced delta IQ scores, specifically when there is a change in IQ measure, for instance a change from the WISC-III-NL to the WAIS-III/IV.

VMI functioning in 22q11DS is not studied extensively yet, as the Beery VMI is not part of the standard assessment protocol. This should be changed in the future, as the Beery VMI is an important tool to identify the strengths and weaknesses of a child (Duijff et al., 2012a). The research question of the current study could not be answered, since the current results suggest that early cognitive decline may already have occurred in the group of participants without cognitive decline in the current study. If we want to answer the current

research question appropriately, future studies should assess VMI functioning and delta IQ earlier than was the case in the current study, as cognitive decline may occur between the age of 5.5 and 9.5 (Duijff et al., 2013). It remains important to study possible predictors for cognitive decline, as cognitive decline is a marker for psychotic disorders. Treatment could start sooner when we are able to detect early psychotic symptoms in individuals with 22q11DS.

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Tables and Figures

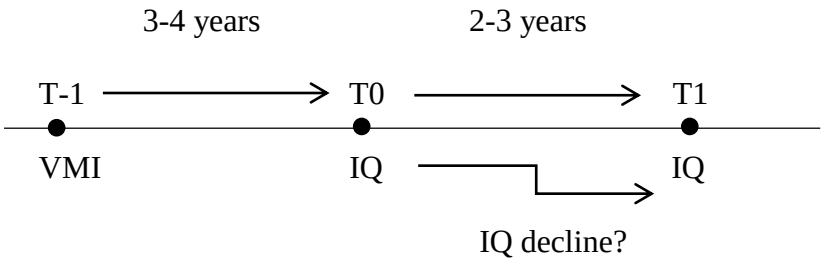

Figure 1. Study overview. Visual motor integration (VMI) was assessed at T-1. After 3-4 years, T0 measurement was performed and IQ data were obtained. Lastly, IQ data were obtained at T1. Delta IQ was determined by the difference in IQ scores at T0 and T1.

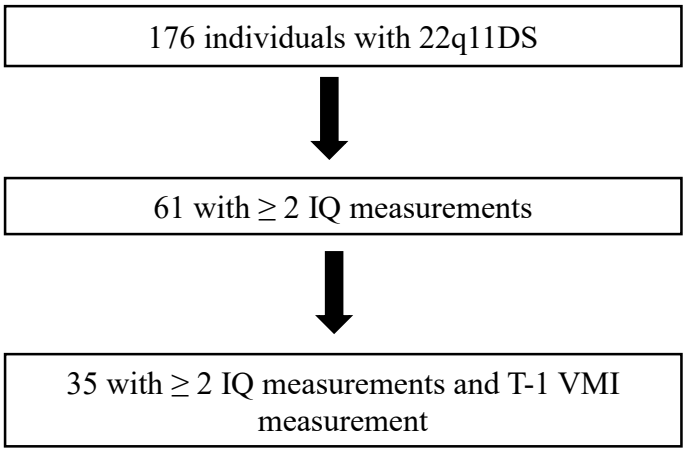

Figure 2. Flowchart of participant selection

Table 1

VMI skill level of the participants at T-1

	T-1		
	M	SD	N
Age in years	9.60	2.10	35
VMI	83.1	8.18	35
Visual perception	90.4	16.1	19
Motor coordination	79.1	8.93	19

Note. M = mean score, SD = standard deviation, VMI = visual motor integration.

Table 2

Cognitive features of the participants at T0 and T1

	T0			T1		
	M	SD	N	M	SD	N
Age in years	13.2	1.70	35	16.8	2.12	35
VIQ	70.7	12.8	35	71.2	13.0	35
PIQ	71.3	12.5	35	71.7	11.0	35
FSIQ	68.3	12.5	35	68.8	10.6	35

Note. M = mean score, SD = standard deviation, VIQ = verbal intelligence quotient, PIQ = performance intelligence quotient, FSIQ = full scale Intelligence Quotient.

Table 3

Differences in features of the participants with and without cognitive decline at T0

Cognitive decline (N = 35)	Yes (*n* = 14)	No (*n* = 21)	*p*
Age in years M (SD)	12.1 (.917)	14.0 (1.67)	< .001*
Males %	28.6 %	28.6 %	
VIQ (SD)	75.9 (13.0)	67.3 (11.7)	.050*
PIQ (SD)	79.5 (12.5)	65.8 (9.17)	.001*
FSIQ (SD)	75.4 (12.4)	63.5 (10.3)	.004*

Note. M = mean score, SD = standard deviation, VIQ = verbal intelligence quotient, PIQ = performance intelligence quotient, FSIQ = full scale Intelligence Quotient.

* Significant at a significance level of .05.

Table 4

Mean VMI standard scores and cognitive decline

Cognitive decline	VMI (SD)
Yes (*n* = 14)	85.8 (6.23)
No (*n* = 21)	81.4 (8.96)*

Note. VMI = visual motor integration, SD = standard deviation. * No significant difference, $p > .05$.