10-2010

22q11.2 Deletion Syndrome: Are Motor Deficits More Than Expected for IQ Level?

Nancy J. Roizen
Anne Marie Higgins
Kevin M. Antshel
Wanda Fremont
Robert J. Shprintzen

Sacred Heart University, shprintzenr@sacredheart.edu

See next page for additional authors

Follow this and additional works at: http://digitalcommons.sacredheart.edu/speech_fac

Part of the Speech Pathology and Audiology Commons

Recommended Citation

This Peer-Reviewed Article is brought to you for free and open access by the Speech-Language Pathology at DigitalCommons@SHU. It has been accepted for inclusion in Speech-Language Pathology Faculty Publications by an authorized administrator of DigitalCommons@SHU. For more information, please contact ferribyp@sacredheart.edu, lysobeyb@sacredheart.edu.
Authors
Nancy J. Roizen, Anne Marie Higgins, Kevin M. Antshel, Wanda Fremont, Robert J. Shprintzen, and Wendy R. Kates

This peer-reviewed article is available at DigitalCommons@SHU: http://digitalcommons.sacredheart.edu/speech_fac/74
22q11.2 Deletion Syndrome: Are Motor Deficits More Than Expected for IQ Level?

Nancy J. Roizen, MD, Anne M. Higgins, RN, FNP, MA, Kevin M. Antshel, PhD, Wanda Fremont, MD, Robert Shprintzen, PhD, and Wendy R. Kates, PhD

1 Department of Psychiatry & Behavioral Sciences, State University of New York-Upstate Medical University
2 Center for the Diagnosis, Treatment, and Study of Velo-Cardio-Facial Syndrome and the Communications Disorder Unit, Department of Otolaryngology, State University of New York-Upstate Medical University
3 Program in Neuroscience, State University of New York-Upstate Medical University
4 Department of Pediatrics, Case Western Reserve School of Medicine
5 Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine

Abstract

Objective—To examine motor function in children with 22q11.2 deletion syndrome (22q11.2) and a Full Scale IQ (FSIQ) comparable control group.

Study design—This study was part of a prospective study of neuropsychological function in children 9–15 years of age with 22q11.2 and community controls and included children from these two populations with comparable FSIQs.

Results—Verbal IQs on the WISC-R for 40 children with 22q11.2 (88.4) and 24 community controls (87.2) were not different (p=.563). However, the Performance IQs were (22q11.2; 81.1 vs community controls; 89.3; p<.001). On the Visual Motor Inventory (VMI), there was no difference between the standard scores of the two groups (22q11.2; 93.0 vs community controls; 98.1; p=.336) but on the motor coordination part of the VMI, the scores of the 22q11.2 deletion syndrome group were lower (77.2 vs 89.3; p=.002). On the general neurological exam (p=.906), the tone exam (p=.705), and the ball skills part of the Motor Battery, (p=.378), there were no differences. However, on the axial stability part of the Motor Battery, the children with 22q11.2 exhibited less good balance (p=.026).

Conclusions—School aged children with 22q11.2 have specific motor deficits in axial stability and graphomotor skills.

Keywords

velo-cardio-facial; syndrome; Shprintzen syndrome; DiGeorge syndrome; 22q11.2 deletion syndrome; conotruncal anomalies face syndrome; motor
22q11.2 deletion syndrome (22q11.2) (also known as velo-cardio-facial syndrome, DiGeorge syndrome, conotruncal anomalies face syndrome, and Shprintzen syndrome) is a complex multiple anomalies syndrome that occurs with a population prevalence of 1:2000–4000 births. The phenotype is highly variable and can include velopharyngeal insufficiency, cleft palate, congenital cardiac defects, characteristic facial appearance, learning disabilities, and cognitive and behavioral abnormalities.

Studies of the developmental profiles of the children with 22q11.2 have noted motor delay, hypotonia, and balance problems. Studies of younger children have reported delayed walking and lower Psychomotor Indexes compared with Mental Developmental Indexes on the Bayley Scales of Infant Development. In school-aged children, reports of lower scores on the Performance IQ (PIQ) on the Wechsler Intelligence Scale for Children-III compared with the Verbal IQ (VIQ) have been inconsistent. On tests of motor function compared with non-IQ matched control groups, children with 22q11.2 generally did less well.

The purpose of this study is to assess the characteristics of the gross and fine motor performance and function of school aged children with 22q11.2 compared with IQ matched controls.

**Methods**

Children with 22q11.2 and community controls were recruited through the Center for the Diagnosis, Treatment, and Study of Velo-Cardio-Facial Syndrome at SUNY-Upstate Medical University as part of a study of psychopathology in 22q11.2. All children in the 22q11.2 group had a FISH-confirmed deletion in the q11.2 locus of chromosome 22. The community control group was recruited from local public schools. Children with an identifiable genetic disorder or an identifiable neurological condition known to affect cognitive or psychiatric function were excluded from participation except for learning disabilities (LD) and attention deficit hyperactivity disorder (ADHD). As the overall goal of the study of neuropsychology in 22q11.2 study was to identify risk factors for schizophrenia and because neither ADHD or LD is associated with a higher incidence of schizophrenia, we reasoned that including controls with these disorders would provide a closer match to participants with 22q11.2 without confounding our ability to predict to severe psychiatric disorder.

Informed consent/assent was obtained from parents and children under protocols approved by the institutional review board. Each child enrolled in the study was administered psychoeducational testing and parents completed behavior rating scales and background information questionnaires. For the current project, only current intellectual and social adaptive functioning, fine and gross motor testing, and neurological examination were included.

In the original data base, some measures were chosen to provide data on the frequently reported findings of motor deficits, hypotonia and balance problems: brief neurological, separate hypotonia measure, motor milestones, and axial stability and ball skills on a motor battery. In this manuscript on the spectrum of motor function, we have analyzed measures chosen from the data base that rely in some degree on fine or gross motor function: Performance IQ on the WISC-III, Ball Skills on the Motor Battery, Visual Motor Inventory (VMI) and subtest on Motor Coordination, and Daily Living Domain on the Vineland Adaptive Behavior Scales. For this manuscript, each child’s current intellectual functioning was determined by the Wechsler Intelligence Scale for Children-Third Edition (WISC) III Full Scale Intelligence Quotient (IQ) was used for identifying children for the IQ-comparable groupings. The Verbal IQ and Performance IQ scores were used to compare with each other.
The brief neurological examination was conducted by a developmental pediatrician (NJR) or a nurse practitioner (AMH) and test-test reliability was established. The exam consisted of two parts: an assessment of tone and an assessment of other neurological findings. Tone assessment was restricted to the upper arms and trunk and included range of motion and shaking of the arms and an attempt to elicit a posterior scarf sign (touching the elbows behind the back). Tone was scored as the following: 0=normal, 1= increased, 2=decreased, 3=very low tone (positive posterior scarf sign). The neurological exam was scored as normal for all or abnormal if one part of the exam was abnormal. The exam consisted of a finger to nose to look for a tremor, keeping arms held horizontally to the side against downward pulling and squeezing examiner’s fingers in a fist to evaluated strength, and deep tendon reflexes at the knees, ankles, elbow, and forearm.

The Motor Battery evaluates motor skills in children 3 to 16 years of age. It consists of four subtests and we choose to include Ball Skills as a measure of play and Axial Stability to measure balance. Ball Skills included: throwing and catching a ball thrown by the examiner; catching a ball in a cup that was thrown by self, and catch a ball thrown against the wall after turning and clapping 3 times. The Axial Stability test included: walking in a tandem gait on a line, standing on preferred foot without holding on for 20 seconds, with eyes closed imitating with the other hand the position the examiner placed the first hand, and persistence of tandem stance with eyes closed for 20 seconds. The Motor Battery norms were based on testing 1200 children ages 36 months to 14 years. At least 50 children were tested at each age intervals of 6 months. They developed mean scores and standard deviations for children on each subtest at each age and also a cumulative mean and standard deviations for each age. Rasch analysis showed good developmental trajectory and reliability for children. The Motor Battery subtests were scored as the following: 0=normal, 1= less than/equal to −1.5 SD, and 2=greater than/equal to +1.5 SD.

Demographic and clinical characteristics were compared using analyses of variance (ANOVA) for continuous variables and chi-square for dichotomous variables. Our analytic strategy was to develop two groups of IQ comparable children from the whole group of children with 22q11.2 and group of control children. To achieve this we performed a median split on IQ and included those children with 22q11.2 whose Full Scale IQ’s were above the 22q11.2 median (74) and those in the community control sample whose Full Scale IQ’s were below the community control median (98).

Results

22q11.2 group (n=40) were younger (10.87 years (SD ±2.49 years) vs 10.45 years (SD ±2.66 years) (two-tailed p = 0.0225) and of higher socioeconomic status (52.83 ± SD 10.16 vs 40.82 ± SD 13.25) (two-tailed p <0.0001). Of the children with 22q11.2, 42.5% had ADHD compared with 35.2% of the controls (p=.347). Using a discrepancy method to identify LD comparing FSIQ and Wechsler Individual Achievement Tests achievement test scores yielded only 3 children with LD. Using FSIQs <85 to compare the 2 groups, 85% of the 22q11.2 group compared with 37.5% of the controls had an IQ of <85 (p=.052).

We compared the Verbal IQs and Performance IQs of the two groups of IQ comparable children (Table I). The mean Verbal IQ’s on the WISC-III for the 40 children with 22q11.2 (88.43± SD 9.40) and 24 community controls (87.08± SD 8.12)) were not different (p=.563). However, the Performance IQs were different (22q11.2 81.76± SD 5.83 vs community controls 89.29± SD 8.51; p<.001). On the Visual Motor Inventory (VMI) there was no difference between groups (22q11.2 93.03± SD 11.58 vs community controls 98.13± SD 13.31; p=.114) but on the Motor Coordination part of the VMI, the 22q11.2 group was lower (22q11.2 77.18± SD 13.46 vs community controls 89.29± SD 13.41; p=.002). On the Daily Living Domain of the Vineland

\[J\text{Pediatr.}\ \text{Author manuscript; available in PMC 2011 October 1.}\]
Adaptive Behavior Scales, there was no difference between the two groups (22q11.2 91.767 ±15.36 SD vs community controls 95.17± SD 10.38; p=.336).

On the Motor Battery Ball Skills test (Table II), there was no difference between the two groups (p=.387) with the majority (67.5%) of the children with 22q11.2 in the normal range. But, on the Axial Stability test (Table II), the children with 22q11.2 did less well (p=.026) with 52.6% functioning at ≤1.5 SD below the mean. The two groups were not different (p=.705) in their tone however the group with 22q11.2 had decreased or very low tone in 37.5% compared with 20.8% in the community controls. On the neurological examination, there were no differences in the two groups (p=.906) with 82.5% of the children with 22q11.2 having a normal neurological examination.

**Discussion**

Our results support some clinical impressions and previous reports and dispute others. This data supports the clinical impression that children with 22q11.2 have axial instability. Although about a third of the children with 22q11.2 have low or very low tone it was not significantly more common than the findings in the IQ-control group. Despite the low tone and axial instability, two thirds of the children with 22q11.2 had ball skills in the normal range.

Several studies of younger children indicate that all but the very earliest motor milestones (e.g. rolling) are later than expected with walking taking place between 16 and 24 months of age and other motor milestones are later than expected suggesting a relative weakness in gross motor skills. Authors have attributed delays to hypotonia which has been observed in up to 70% of infants and/or children with 22q11.2, but perhaps the axial stability is an additional factor or even a more important factor. In a post hoc analysis, we explored the significance of tone and of axial stability in the sample as a whole to have enough statistical power. There were no differences in Visual Motor Integration and Motor Coordination Subscales of the VMI, Vineland Daily Living Skills, total WIAT score, and age of walking related to tone but there was an effect of normal and high axial stability vs low axial stability on the Motor Coordination scale of the VMI (85.6 (SD 15.6) vs 77.4 (SD 14.6); p = .04). On some of the other scales, there were differences in scores that might be considered clinically important: walking at 13.7 months (SD 3.01) vs 15.9 months (SD 4.1) p=.06; Vineland Daily Living Skills SS mean 77.30 (SD 19.8) vs 69.5 (SD 13.6); p =.06. These numbers demonstrate that children with axial instability can have problems in other areas of development that may effect function. In addition, Scherer et al reported in a group of 4 children that their PDI’s (Psychomotor Developmental Index) decreased between 6 months and 30 months. This implies that the discrepancy between motor skills in children with 22q11.2 and typical children widens with time. This speaks to the need for both cross sectional and longitudinal studies.

Two studies using the Movement Assessment Battery for Children (MCAC) have reported deficits in ball skills compared with siblings and to test norms. Another study used the MABC and compared the 22q11.2 group to IQ and age matched controls, and found no difference. In our study, the neurological findings of problems with axial stability and frequent low tone did not predict that the ball skills would be most frequently in the typical range. In fact, ball skills should probably be encouraged with the potential positive social, self-esteem, and physical effects. Graphomotor skill problems were demonstrated on the motor coordination part of the VMI. It is unclear how much the fine motor problem contributed to the lower Performance IQ scores and may have been compensated for in the lack of difference in the Vineland Daily Living Domain. But, the findings of lower motor coordination VMI scores indicates a need to evaluate children with 22q11.2 for graphmotor deficits and initiate...
therapeutic occupational therapy interventions and compensatory strategies including partial scribeying by parents and aids and the development of keyboard competency.

Most studies have not had IQ comparison groups but have reported on differences with the norms on the tests, differences between domains on tests, or used sibling controls. Without controls Oskarsdottir et al. reported in 33 children with a median age of 7 years 6 months delayed walking (mean 18 months), and hypotonia (n=25) and poor balance (n=24) both of which we found in our population. They also reported 2 with spastic hemiplegia which we did not find. Those that have used sibling controls found deficits in motor function in the children with 22q11.2. Swillen et al. studied children with a mean age of 41 months (SD ±9.7 mo) and used controls with the same cardiac lesions to control for congenital heart disease. Using the Peabody Developmental Motor Scales-2, they found that the children with 22q11.2 scored significantly lower on motor performance specifically in locomotion and stationary. Only van Aken et al. controlled for IQ in an article where they reported on motor performance in 28 school-aged children with 22q11.2. Using the Movement Assessment Battery for Children and the Beery-Buctenica test of Visual-Motor Integration, they found deficits in visual motor integration skills and visual-perceptual skills not fully attributed to a general developmental delay but which they thought might be specific to 22q11.2. When comparing their results with ours, they found deficits on the Visual Motor Inventory-Motor Coordination subtest as did we as well as another test of manual dexterity but not deficits in balance skills. They recommended assessment of motor function be included in the study of the neuropsychological profile of this group of children.

Our study has several drawbacks. One problem was the composition and size of the community control group. To identify a 22q11.2 group with IQs high enough to match an IQ comparison community control group without identified genetic disorders or neurological condition limits the 22q11.2 group to those on the higher side of the Verbal IQ spectrum of 22q11.2. Was the community control group the most appropriate comparison group as it included children with LD and ADHD? Did the inclusion in the IQ group-matched control group of children with LD and ADHD compromise the conclusions? Would more differences be identified if the study populations had been larger? Perhaps the inclusion of children with LD and ADHD is a strength of this study as these disorders frequently are associated with minor motor problems such as developmental coordination disorder. Including LD and ADHD in the control group may have better allowed us to specify those deficits associated with 22q11 as opposed to all children with LD and ADHD. On the other hand, in order to match for IQ, our 22q11.2 group included only those on the high side of the verbal IQ spectrum.

By using an IQ-comparable group, we could eliminate IQ as a factor and determined that children with 22q11.2 do have axial instability and graphomotor deficits. We would recommend that an evaluation of graphomotor skills be included in a comprehensive psychoeducational school evaluation.

Acknowledgments

Supported by NIMH (MH64824 and MH65481 to W.K; 5RO1MH064824 to A.H and R.S.), HRSA-T77MC00004 (N.R.), and NHLBI (5RO1HL084410-01 to A.H and R.S.).

References


J Pediatr. Author manuscript; available in PMC 2011 October 1.


Table 1

IQ and fine motor test results

<table>
<thead>
<tr>
<th>TEST</th>
<th>VCFS (n=40)</th>
<th>Controls (n=24)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WISC-Verbal IQ</td>
<td>88.43 ± 9.40</td>
<td>87.08 ± 8.12</td>
<td>.563</td>
</tr>
<tr>
<td>WISC-Performance IQ</td>
<td>81.76 ± 5.83</td>
<td>89.29 ± 8.51</td>
<td><strong>.000</strong></td>
</tr>
<tr>
<td>VMI</td>
<td>93.03 ± 11.58</td>
<td>98.13 ± 13.31</td>
<td>.114</td>
</tr>
<tr>
<td>VMI-Motor Coordination</td>
<td>77.18 ± 14.36</td>
<td>89.29 ± 13.41</td>
<td><strong>.002</strong></td>
</tr>
<tr>
<td>VABS-Daily Living Skills Domain</td>
<td>91.67 ± 15.36</td>
<td>95.17 ± 10.38</td>
<td>.336</td>
</tr>
</tbody>
</table>

WISC – Wechsler Intelligence Scales for Children-III
VABS – Vineland Adaptive Behavior Scales
### Table 2
Results of Ball & Axial Stability Scores and Tone Examination

<table>
<thead>
<tr>
<th>Ball Skills Score *</th>
<th>22 q11.2 (n, %)</th>
<th>Controls (n, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 1.5 SD below mean</td>
<td>11 (27.5%)</td>
<td>4 (16.7%)</td>
</tr>
<tr>
<td>WNL</td>
<td>27 (67.5%)</td>
<td>17 (70.8%)</td>
</tr>
<tr>
<td>≥ 1.5 SD above mean</td>
<td>0 (0%)</td>
<td>1 (4.2%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Axial Stability **</th>
<th>22 q11.2 (n, %)</th>
<th>Control (n, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1.5 SD below mean</td>
<td>20 (52.6%)</td>
<td>4 (18.2%)</td>
</tr>
<tr>
<td>Normal</td>
<td>17 (44.7%)</td>
<td>17 (77.3%)</td>
</tr>
<tr>
<td>≥ 1.5 SD above mean</td>
<td>1 (2.5%)</td>
<td>1 (4.2%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tone Examination ***</th>
<th>22 q11.2 (n, %)</th>
<th>Controls (n, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased</td>
<td>1 (2.5%)</td>
<td>1 (4.2%)</td>
</tr>
<tr>
<td>Normal</td>
<td>23 (57.5%)</td>
<td>17 (70.8%)</td>
</tr>
<tr>
<td>Decreased</td>
<td>10 (25.0%)</td>
<td>3 (12.5%)</td>
</tr>
<tr>
<td>Very low tone †</td>
<td>5 (12.5%)</td>
<td>2 (8.3%)</td>
</tr>
</tbody>
</table>

\* Asymmetric Significance (2-sided) - Likelihood ratio .387
2 not tested from each group

\** Asymmetric Significance (2 sided) - Likelihood ratio .026
2 not tested from each group

\*** Asymmetric significance (2-sided) - Likelihood ratio .705

† positive posterior scarf sign; 1 not tested from each group

---

*J Pediatr.* Author manuscript; available in PMC 2011 October 1.