Neurocognitive profile in 22q11 deletion syndrome and schizophrenia

Eva W. C. Chow^{a,b,*}, Mark Watson^a, Donald A. Young^{a,b}, and Anne S. Bassett^{a,b}

^a Clinical Genetics Research Program, Centre for Addiction and Mental Health, Toronto, Canada

^b Department of Psychiatry, University of Toronto, Toronto, Canada

Abstract

Objective—Schizophrenia is associated with neurocognitive deficits, but its etiologic heterogeneity may complicate the delineation of a neurocognitive profile. Schizophrenia associated with 22q11 Deletion Syndrome (22qDS) represents a more genetically homogeneous subtype for study. We hypothesized that in adults with 22qDS the neurocognitive profiles would differ between those with and without schizophrenia.

Method—Using a comprehensive battery of tests, we compared the neurocognitive performance profiles in those with schizophrenia ($n=27$; 14 M, 13 F; mean age=30.6 years, SD=7.7 years) and those with no history of psychosis ($n=29$; 16 M, 13 F; mean age=25.0 years, SD=9.0 years).

Results—The 22qDS groups with and without schizophrenia had similar mean estimated IQ (71.6, SD=8.2 and 74.8, SD=6.1, respectively) and academic achievement, however the neurocognitive profiles of the two groups differed significantly on multivariate analysis ($F(24,31)=2.25$, $p=0.017$). The group with schizophrenia performed significantly more poorly on tests of motor skills, verbal learning, and social cognition (effect sizes 0.8) after correction for multiple comparisons. Other tests, but not the attentional measures used, showed nominally significant differences.

Conclusions—In adults with 22qDS, the pattern of neurocognitive differences between those with and without schizophrenia appears similar to that between patients with schizophrenia and controls. Attentional dysfunction may be a more general feature of 22qDS. The findings support 22qDS-schizophrenia as a genetic model for neurodevelopmental investigations of schizophrenia.

Keywords

Velo-cardio-facial syndrome; DiGeorge syndrome; Adults; Psychosis; Neurocognition

1. Introduction

Neurocognitive dysfunction has long been considered a core component of schizophrenia.

The presence of cognitive deficits before (Jones et al., 1994; David et al., 1997) and at onset

*Corresponding author. Clinical Genetics Research Program, Centre for Addiction and Mental Health, 1001 Queen Street West, Toronto, Ontario, Canada M6J 1H4. Tel.: +1 416 535 8501x2731; fax: +1 416 535 7199. eva.chow@utoronto.ca (E.W.C. Chow).

None of the authors has financial interests that might present a conflict of interest.

(Saykin et al., 1994; Mohamed et al., 1999) supports a neurodevelopmental hypothesis of pathogenesis (Weinberger, 1987; Bassett et al., 2001), and indicates that chronic illness and/or treatment do not cause these deficits. The majority of patients with schizophrenia have evidence of generalized cognitive deficits (Heinrichs and Zakzanis, 1998; Mohamed et al., 1999), with variability in the magnitude of deficits in individual domains of functioning (Hoff and Kremen, 2003). The level or type of impairments found in different studies were not always the same (Heinrichs and Zakzanis, 1998; Hoff and Kremen, 2003). Material or test specificity, etiologic subtypes, severity of symptoms, and duration of illness are examples of factors reported to contribute to between-subject or between-study heterogeneity in neurocognitive performance in schizophrenia (Heinrichs and Zakzanis, 1998; Kremen et al., 2004; Pelletier et al., 2005). Nonetheless, a meta-analysis found that the largest differences between cases and controls were in verbal memory, motor skills, attention, and executive functions, with effect sizes comparable to those seen in neuroimaging studies (Heinrichs and Zakzanis, 1998). Recent studies have added social cognition as an important domain (Corrigan and Penn, 2001; Frith, 2004). The etiological and clinical heterogeneity of the illness, however, complicate delineation of the pattern and magnitude of neurocognitive dysfunction in schizophrenia (Heinrichs and Zakzanis, 1998; Hoff and Kremen, 2003).

One way to investigate whether clinical heterogeneity of neurocognition is inherent to schizophrenia or related to etiologic heterogeneity is to use more homogeneous samples (Heinrichs and Zakzanis, 1998). Schizophrenia associated with 22q11 deletion syndrome (22qDS) is the only identifiable subtype currently available that is likely to have greater etiologic homogeneity than general population samples of schizophrenia (Bassett et al., 2001; Bassett et al., 2003). 22qDS, also known as velocardiofacial syndrome, is a genetic syndrome associated with detectable microdeletions in chromosome 22q11.2 which affects 1–2% of patients with schizophrenia (Karayiorgou et al., 1995; Wiehahn et al., 2004). Recently, we have demonstrated that the core positive and negative symptoms in 22qDS-schizophrenia are similar to those in other forms of schizophrenia (Bassett et al., 2003). Approximately 25% of individuals with 22qDS develop schizophrenia (Murphy et al., 1999; Bassett et al., 2005), placing individuals with this condition in the highest genetic risk group for schizophrenia next to individuals with an identical co-twin or two parents, with schizophrenia (Bassett et al., 2003). There is potential for a 22qDS subtype of schizophrenia as a genetic high risk group and as a neurodevelopmental model of the illness (Chow et al., 1994; Bassett et al., 2001). Clinical expression in 22qDS, including birth defects and neurobehavioral manifestations, is highly variable (McDonald-McGinn et al., 1999). Most individuals with 22qDS have borderline intellect and about 30 to 40% have mild mental retardation, while more severe levels of mental retardation and average intellect are less common (Moss et al., 1999). Significantly lower performance intelligence quotients (IQ) and visual spatial weaknesses are common in children with 22qDS (Moss et al., 1999). In contrast, 20 to 25% of patients with schizophrenia in the general population may be expected to have IQ<85 (David et al., 1997), and performance IQ is not disproportionately affected (Iverson et al., 2001). To date there is only one study of adults with 22qDS which found that 13 individuals with schizophrenia performed worse than 15 individuals with no psychosis on tests of abstraction, sustained attention, spatial working memory and visual

recognition (van Amelsvoort et al., 2004). The overall profile of neurocognitive performance was not statistically analysed, and many of the tests used were uncommonly used in patients with schizophrenia. Furthermore, even though no exact p -values were provided in that study (i.e. classified as not significant, <0.05 or <0.01 only), the detected differences were unlikely to remain significant after correction for multiple testing given that there were 45 test variables.

In the current study we investigated neurocognition using a comprehensive battery in 56 adults with 22qDS. We hypothesized that in 22qDS the overall neurocognitive profile of subjects with schizophrenia would differ from that of subjects with no history of psychosis.

2. Method

2.1. Subjects

Participating subjects were 56 adults (30 men, 26 women; mean age 27.8 years, $SD=8.8$ years) who met clinical criteria for 22qDS (Bassett and Chow, 1999) and were confirmed to have a chromosome 22q11.2 deletion by standard methods: fluorescence in-situ hybridization (FISH) using a probe from the commonly deleted region (Driscoll et al., 1993). None of the subjects had a significant traumatic head injury or substance abuse at the time of assessment. To minimize possible floor effects on test results, six (three with schizophrenia) 22qDS subjects with moderate or more severe mental retardation (estimated $IQ<54$) were excluded from the study. A research psychiatrist (EWCC or ASB) determined lifetime Axis I diagnoses using the Structured Clinical Interview for DSM-IV (SCID-IV) (First et al., 1995), comprehensive medical records, and collateral information from family members and health care providers.

Twenty-seven subjects meeting DSM-IV criteria for schizophrenia ($n=23$) or schizoaffective disorder ($n=4$) comprised the 22qDS-SZ group. We previously reported on the symptoms of schizophrenia in 21 of these 27 subjects (Bassett et al., 2003) and found a similar (mild) severity of positive, negative, anxiety–depression, and cognitive symptoms compared with another form of schizophrenia, and a slightly higher level of excitement symptoms. The clinical symptom profile of the remaining six 22qDS-SZ subjects was similar to that of previously reported subjects. The comparison (22qDS-NP) group comprised of 29 subjects with no history of psychotic symptoms. In the 22qDS-NP group, there was a lifetime history of an anxiety disorder in six subjects, major depression in four subjects, and childhood attention deficit/hyperactivity disorder (ADHD) in four other subjects (3 persisting into adulthood).

At the time of assessment, twenty-one 22qDS-SZ and one 22qDS-NP subjects were receiving atypical, and four 22qDS-SZ subjects typical, antipsychotics; seven 22qDS-SZ subjects were receiving anticholinergic medications. Twenty-four subjects (three 22qDS-SZ; twenty-one 22qDS-NP;) were recruited from an adult congenital cardiac clinic, twenty 22qDS-SZ from psychiatric sources, ten (four 22qDS-SZ; six 22qDS-NP) were referred by medical geneticists, and two 22qDS-NP subjects were ascertained as transmitting parents.

This research study was approved by the Research Ethics Board of the Centre for Addiction and Mental Health and University of Toronto. After complete description of the study to the subjects, written informed consent was obtained.

2.2. Neurocognitive testing

A trained psychometrist under the supervision of a neuropsychologist (DAY) administered a comprehensive battery of 24 individual neurocognitive tests involving motor, attention, learning and memory, language, visual spatial, and executive (verbal fluency, abstraction and mental flexibility, social cognition) skills (see Table 1). All subjects were assessed during a stable or remitted phase of their psychiatric illness. To minimize subject fatigue, overall IQ was estimated using Silverstein's method (Silverstein, 1982) with scores from the Vocabulary and Block Design subtests of the Wechsler Adult Intelligence Scale-Revised (WAIS-R) (Wechsler, 1981b). We determined the presence or absence of mental retardation based on the estimated IQ and the level of adaptive functioning, as per DSM-IV criteria. We used the Wide Range Achievement Test 3 (WRAT3) (Wilkinson, 1993) to evaluate academic abilities in reading, spelling, and arithmetic.

The ToM test used to evaluate social cognition in this study was developed at our Centre based on another test of mentalizing abilities in the form of social inference by Corcoran and Frith (Corcoran et al., 1995). It aims to evaluate the ability to predict the behavior or thoughts of others within a simple social context. This test was employed because we knew of no published, widely accepted instrument to assess the specific domain of social cognition in schizophrenia. The test is comprised of eight sets of visual stimuli cards and matching verbal scenarios, each with a forced choice of four possible responses. Eight pictures from the Thematic Apperception Test (Murray, 1943) comprise the visual stimuli, and eight corresponding short paragraphs describing the interaction or events in each picture comprise the verbal scenarios. The subject was given a few minutes to examine the picture and read the corresponding paragraph, which was also read aloud to them. The subject was then asked to choose from four possible responses the one that best predicted what the main character in the picture would think or do next, taking into account the context of both the visual stimulus and written scenario. When tested on a group of 30 healthy children and adults, all 15 adults and 13 of 15 seven-year-old children were able to obtain a perfect score of 8 (Russell, 1996). The mean score obtained by a group of 30 random patients with chronic schizophrenia was significantly lower (4.6, $SD=2.2$, $p<0.001$) (Russell, 1996).

2.3. Statistical analyses

The study used a case-control design, with 22qDS-SZ subjects serving as cases and 22qDS-NP subjects as controls. All analyses were conducted using SAS v. 8.2 (SAS Institute, Cary, NC). Two tailed tests with a p -value of <0.05 were used to determine statistical significance. For demographic and clinical variables, chi-square and Fisher's exact tests were used to analyze categorical variables and independent t -tests to compare continuous variables. For the neurocognitive test variables, raw scores were converted to z -scores using available age, sex, and education level adjusted published norms (Wechsler, 1981a, 1987; Heaton et al., 1991; Heaton et al., 1993; Wechsler, 1997; Spreen and Strauss, 1998), and unpublished norms for the ToM test (Russell, 1996). Consistent with the practice of other authors

(Heaton et al., 1991; Lezak, 1995; Townsend et al., 2001), z -scores between -1 and -2 , -2 and -3 and <-3 were considered to indicate mild, moderate and severe impairment respectively. We conducted a one-way multivariate analysis of variance (MANOVA) using diagnostic group as the between-subjects factor and the neurocognitive test z -score as the within-subjects factor to test our main hypothesis of whether neurocognitive profiles differed between the 22qDS-SZ and the 22qDS-NP groups. We chose MANOVA as our method of data analysis because our modest sample sizes and the potential correlation and multicollinearity among the neurocognitive test variables made other statistical methods such as logistic regression less appropriate. All subjects had a complete set of scores for all 24 neurocognitive test variables and all were included in the MANOVA.

In the presence of a significant effect on MANOVA, we then examined the univariate ANOVAs for the individual test variables from the MANOVA for differences between the two 22qDS groups. Since these ANOVAs followed a multivariate analysis for an overall effect and were considered to be exploratory, we maintained $p<0.05$ as our level of significance (Feise, 2002). We provided exact p -values and effect sizes (calculated using Cohen's d (Cohen, 1988)) for individual tests for ease of interpretation of results by readers.

3. Results

3.1. Subject characteristics

The 22qDS-SZ and 22qDS-NP groups were similar on most demographic and clinical variables (Table 2). The median age at onset of psychosis in the 22qDS-SZ group was 22 (range 14 to 32) years. Sixteen (54.1%) 22qDS-NP subjects were under age 22 years. On average, the 22qDS-SZ subjects had been ill for 9.7 (SD 7.8) years. Subjects in the 22qDS-NP group had completed significantly more years of education and, as expected from ascertainment differences, a greater proportion had a history of surgery for congenital cardiac defects than the 22qDS-SZ group (Table 2).

There were no significant differences between the groups in mean estimated IQ, proportion with mental retardation, or academic abilities. The mean estimated IQ for all 56 subjects was 73.2 (SD=7.3; range 59 to 95), in the low end of the borderline intellectual functioning range. Two (3.6%) subjects, one from each group, had estimated IQ in the average range (>84).

3.2. Neurocognitive profiles

Consistent with our main hypothesis, there was a significant multivariate effect for group on z -scores for the 24 neurocognitive tests ($F(24,31)=2.25$, $p=0.017$). A MANCOVA using the only variable showing between-group differences for which z -scores were not adjusted, history of cardiac surgery, showed similar results ($F(24,30)=2.06$; $p=0.031$).

3.3. Individual test results

Table 1 shows the ANOVA results of individual neurocognitive test variables for both groups. The 22qDS-SZ group showed impairment on all test variables: severe in motor skills, verbal learning, and verbal recognition, moderate in social cognition, Comprehension

and Trails B, and mild in the remaining neurocognitive tests. In the 22qDS-NP group, performance was moderately impaired on motor skills and mildly impaired in many of the other tests. Performance on tests of verbal recognition memory, immediate and delayed visual memory, and ToM was relatively intact in the 22qDS-NP group.

Performance was significantly poorer in the 22qDS-SZ than the 22qDS-NP group on motor, verbal learning, verbal recognition, and social cognition tests, but not on tests of attention. The 22qDS-SZ group also showed significantly poorer performance on JLO, immediate and delayed visual memory, Trails B, WCST category, Animal naming, and Vocabulary tests. Performance on WMS-R logical memory tests, WCST perseverative errors, Similarities, FAS, and Block Design, however, was not significantly different between the two groups.

Effect sizes for the individual test variables ranged from 0.07 to 1.18. The test variables showing effect sizes of 0.95 or greater were bilateral and dominant hand Purdue Pegboard, RAVLT-recall and ToM. These four test variables would remain statistically significantly different between the two groups even after Bonferroni correction for multiple testing ($p < 0.002$). RAVLT-recognition, Animal naming test, Picture Arrangement, JLO and nondominant hand Purdue Pegboard had effect sizes between 0.8 and 0.95.

4. Discussion

Using the largest sample of adults with 22qDS yet reported we have shown that neurocognitive profiles differ significantly between those with schizophrenia and those with no history of psychosis. Despite a lower overall intellectual level, the neurocognitive functions showing the greatest differences between the 22qDS groups were among those most consistently reported for general population schizophrenia (Heinrichs and Zakzanis, 1998; Hoff and Kremen, 2003): verbal memory, motor skills, and the executive functioning task social cognition. This provides further support that these neurocognitive functions are most affected in any form of schizophrenia. Interestingly, clinical heterogeneity appears in 22qDS-schizophrenia as it does in schizophrenia in the general population; the central tendency is just shifted. For example, findings from the current study are similar to those from another study of adults with 22qDS-SZ (van Amelsvoort et al., 2004) on only four of the seven shared test variables, despite the same genetic etiology and similar clinical characteristics (duration of illness, age, ascertainment, overall IQ, use of antipsychotic medications). Taken together, these results suggest that heterogeneity in neurocognitive impairments may be a core feature of the schizophrenic illness and not necessarily related to heterogeneity in etiology. Overall, the results support the likelihood that a 22qDS subtype of schizophrenia shares general characteristics of cognitive expression with other forms of schizophrenia, although the effect sizes observed with 56 subjects indicate that the greater etiologic homogeneity of a 22qDS sample provided greater power to detect differences.

The relative pattern of impairment was also similar to that in other studies of schizophrenia. Verbal learning and verbal memory were more impaired than visual memory (Heinrichs and Zakzanis, 1998; Hoff and Kremen, 2003). Category fluency was more impaired than letter fluency (Gourovitch et al., 1996; Bokatz and Goldberg, 2003). Picture Arrangement showed greater impairment than Block Design (Mohamed et al., 1999; Townsend et al., 2001).

Furthermore, ToM, which may be considered to be a purer test of social cognition, was associated with greater impairment than Picture Arrangement or Comprehension. As expected from the literature on executive functioning in schizophrenia (Hoff and Kremen, 2003), the 22qDS-SZ group showed significantly greater deficits in Trails B and WCST categories, with a statistical trend toward a significant difference in Similarities.

No significant differences were detected on the tests of attention used however, indicating a weaker effect than that predicted from the literature on schizophrenia. This may be because attentional dysfunction is a general feature of 22qDS (Woodin et al., 2001) or a feature of a general vulnerability for schizophrenia in the syndrome, and is therefore equally present in all 22qDS subjects, with or without schizophrenia. The presence of three 22qDS-NP subjects with ADHD persisting into adulthood might have obscured the detection of a greater attentional impairment from the schizophrenia illness in the 22qDS-SZ group. However, two of the 22qDS-SZ subjects also had a history of childhood ADHD prior to the onset of their schizophrenia illness. As such, the lack of detectable differences in attention between the two groups is unlikely to be related to the presence of ADHD in the 22qDS-NP group. Other tests, such as a continuous performance test, may be more sensitive measures of attentional deficits in schizophrenia (Heinrichs and Zakzanis, 1998).

Our results are consistent with previous reports of 22qDS showing a mean IQ in the borderline range (Henry et al., 2002; van Amelsvoort et al., 2004), relative preservation of reading and spelling compared with arithmetic skills (Woodin et al., 2001; Bearden et al., 2002), and childhood motor deficits (Golding-Kushner et al., 1985; Maharasingam et al., 2003) which appear to persist into adulthood. The only previous study of neurocognition in adults with 22qDS used different tests and study methods, and did not report *z*-scores, exact *p*-values, nor effect sizes (van Amelsvoort et al., 2004). The visual memory and abstraction deficits and the lack of differences between the 22qDS-SZ and 22qDS-NP groups in block design, stories recall (WMSR Logical Memory I and II) and FAS (van Amelsvoort et al., 2004) however appear in line with our results.

4.1. Advantages and limitations

This study used an extensive neuropsychological battery in a relatively large sample of a relatively rare but more etiologically homogeneous subtype of schizophrenia, and the subgroups studied were comparable on most demographic factors and on IQ and academic achievement. Few subjects were taking anticholinergic medications. These features may be advantageous in studying neurocognition in schizophrenia (Heinrichs and Zakzanis, 1998).

There were several limitations, including the use of multiple tests which may have lead to Type I errors. This is unlikely to account for all 14 variables with $p < 0.05$, particularly the four surviving a conservative Bonferroni correction. On the other hand, sample size restrictions may have limited our ability to detect statistically significant differences in some neuropsychological test variables. Also, some 22qDS-NP subjects may yet develop schizophrenia, and such misclassification could make it more difficult to detect true differences between the two study groups (Chow et al., 2003). There were ascertainment differences between the two 22qDS subtype groups, however surgery for cardiac defects is not associated with cognitive dysfunction (Forbess et al., 2002) and inclusion of this variable

in a MANCOVA did not change results. The 22qDS-SZ group had schizophrenia for nine years on average, however, recent studies show no cognitive decline after onset (Gold et al., 1999; Heaton et al., 2001). Most (69.6%) subjects had estimated IQ>70 and although there was insufficient power for formal subgroup analyses, their neurocognitive profile appeared similar to that for the sample as a whole. This is consistent with findings for other groups of patients with schizophrenia (Minzenberg et al., 2004).

Although not part of our study design, studying a comparison group of subjects with schizophrenia and similar IQ but not 22qDS could have provided direct information on the similarities or differences in the cognitive profiles of 22qDS-SZ and general population schizophrenia. However very large sample sizes would likely be necessary to help determine the specificity of neurocognitive findings to 22qDS, given the high degree of variable expressivity in both 22qDS and schizophrenia.

4.2. 22qDS-schizophrenia as an etiologic subtype of schizophrenia

This study and others (Gothelf et al., 1999; Murphy et al., 1999; Bassett et al., 2003) support 22qDS as a genetic subtype of schizophrenia, identifiable by its associated physical features, chromosomal abnormality and lower IQ. As for core clinical symptoms (Bassett et al., 2003), 22qDS-schizophrenia does not appear to represent a distinct clinical subtype of the illness with respect to its neurocognitive profile. The genetic homogeneity of 22qDS-SZ makes this subtype a potentially powerful model to elucidate the other genetic, genomic, or non-genetic etiopathogenetic factors and neurodevelopmental expression of the schizophrenic illness. Reduced genetic heterogeneity has already allowed the identification of core neurocognitive deficits in schizophrenia using only samples of modest size in the current study, and of pregnancy and birth complications associated with schizophrenia using smaller samples in a previous study (Chow et al., 2003).

A 22q11.2 deletion is likely to be one of multiple possible genetic predispositions to the neurodevelopmental changes that could lead through a general pathogenetic pathway to expression of schizophrenia (Bassett et al., 2001). Future studies, including comparisons of 22qDS-schizophrenia with IQ-matched schizophrenia from the general population, and using advanced molecular genetic approaches, will be needed to investigate how well this genetic subtype can assist in understanding schizophrenia.

Acknowledgments

Funded in part by the Canadian Institutes of Health Research (grant no. MOP-38099), W. Garfield Weston Foundation, Ontario Mental Health Foundation, Scottish Rite Schizophrenia Research Program, Canada Research Chair in Schizophrenia Genetics (ASB) and a National Alliance for Research on Schizophrenia and Depression Young Investigator Award (EWC). The authors thank the subjects and their families for their participation, and Ed Janiszewski, genetic counselors Heather Dorman, Linda Chiu, and Sheri O'Neill, and Dr. Nighat Parveen and Dr. Oana Caluseriu for their assistance in the collection of data.

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Comparison of individual neurocognitive test z-scores in 27 subjects with 22qDS-schizophrenia and 29 subjects with 22qDS and no history of psychosis

Table 1

	Subject groups				Analyses		
	22qDS-SZ		22qDS-NP		F(1,51)	p	Effect size
	Mean	SD	Mean	SD			
Motor							
Bilateral ^a	-4.05	1.22	-2.58	1.27	19.32	<0.0001	1.18
Dominant ^a	-3.38	1.07	-2.17	1.21	15.68	0.0002	1.06
Non-dominant ^a	-3.47	1.02	-2.56	1.24	8.81	0.005	0.80
Attention							
Stroop interference ^b	-1.74	0.81	-1.24	1.06	3.76	0.06	0.53
Trail's A ^c	-1.98	1.07	-1.68	1.16	0.96	0.33	0.27
Digit span ^b	-1.02	0.95	-1.16	0.65	0.40	0.53	-0.17
Learning and memory							
RAVLT — recall ^a	-3.06	1.19	-1.56	1.68	14.46	0.0004	1.02
RAVLT — recognition ^a	-0.97	1.74	0.17	0.91	9.49	0.003	0.83
WMS-R logical memory I ^b	-1.76	0.68	-1.43	0.87	2.37	0.13	0.42
WMS-R logical memory II ^b	-1.61	0.89	-1.29	0.93	1.71	0.20	0.35
WMS-R visual reproduction I ^b	-1.28	0.95	-0.60	1.02	6.64	0.01	0.69
WMS-R visual reproduction II ^b	-1.48	0.98	-0.73	1.20	6.58	0.01	0.68
Language							
Vocabulary ^b	-1.94	0.54	-1.54	0.62	6.71	0.01	0.69
Visual spatial skills							
JLO ^a	-1.93	0.62	-1.33	0.84	9.19	0.004	0.81
Block design ^b	-1.54	0.51	-1.32	0.57	2.24	0.14	0.34
Verbal fluency							
Animals ^d	-1.81	1.06	-1.03	0.85	9.12	0.004	0.81
FAS ^d	-1.55	0.81	-1.49	0.90	0.08	0.78	0.07

	Subject groups				Analyses		
	22qDS-SZ		22qDS-NP		F(1,51)	p	Effect size
	Mean	SD	Mean	SD			
<i>Abstraction and mental flexibility</i>							
Trails B ^c	-2.28	1.04	-1.68	0.85	5.76	0.02	0.63
Similarities ^b	-1.68	0.81	-1.26	0.78	3.85	0.06	0.53
WCST — categories ^d	-1.90	0.93	-1.35	1.03	4.30	0.04	0.56
WCST — perseverative errors ^d	-1.19	1.46	-1.30	0.91	0.11	0.74	-0.09
<i>Social cognition</i>							
ToM	-2.52	2.39	-0.53	1.80	12.57	0.0008	0.95
Picture arrangement ^b	-1.81	0.59	-1.34	0.57	9.29	0.004	0.81
Comprehension ^b	-2.26	0.60	-1.95	0.58	4.01	0.05	0.52

Animals and FAS tests (Spreen and Benton, 1969); Block Design, Vocabulary = same name subtests of WAIS-R (Wechsler, 1981b); Comprehension, Digit Span, Similarities, Picture Arrangement = same name subtests of WAIS-R (Wechsler, 1981b) ($n=45$) and WAIS-III (Wechsler, 1997) ($n=11$); JLO = Judgment of Line Orientation (Benton et al., 1994); Motor = Purdue Pegboard (Tiffin, 1968); RAVLT = Rey Auditory Verbal Learning Test 5-trial recall and recognition (Rey, 1958); Stroop Interference = Stroop Color-Word Test (Golden, 1976); ToM = Theory of Mind test (Russell, 1996); Trails A and B (Reitan and Wolfson, 1985); WCST = Wisconsin Card Sorting Test (Heaton et al., 1993); WMS-R = Wechsler Memory Scale-Revised (Wechsler, 1987).

^aCorrected for age and sex.
^bCorrected for age.
^cCorrected for age, sex and education level.
^dCorrected for age and education level.

Table 2

Demographic and clinical features of 56 subjects with 22qDS

	Subject groups				Statistics		
	22qDS-SZ (n=27)		22qDS-NP (n=29)		χ^2	df	p
	n	%	n	%			
Sex (% male)	14	51.9	16	55.2	0.06	1	0.80
Left-handedness	6	22.2	5	17.2	0.22	1	0.64
Mental retardation	10	37.0	7	24.1	1.10	1	0.29
CHD requiring surgery	9	3.33	20	69.0	7.11	1	0.008
	Mean	SD	Mean	SD	T	df	p
Age (y)	30.6	7.7	25.0	9.0	2.48	54	0.02
Education (y)	10.7	2.0	12.1	1.5	-3.04	54	0.004
Estimated IQ	71.6	8.2	74.8	6.1	-1.65	54	0.10
Reading (grade level)	6.9	4.0	7.2	4.0	-0.36	54	0.72
Spelling (grade level)	5.8	3.6	6.8	4.2	-1.01	54	0.32
Arithmetic (grade level)	3.9	2.0	4.1	2.6	-0.40	54	0.69