Comparison of physical and psychiatric status in individuals with translocation and trisomy 21 Down syndrome

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No study to date has investigated clinical differences between adults with translocated Down syndrome and those with trisomy 21. Nine translocated Down syndrome individuals were matched to 9 trisomy 21 controls and assessed for medical differences. Significant findings included the translocated group having less severe learning disability according to ICD 10 criteria, less obesity and increased frequency of psychiatric disorders (in particular dementia and depression). However, on the Adaptive Behaviour Scale, the translocated group have significantly poorer independent functioning skills and more maladaptive behaviour, possibly as a consequence of the higher incidence of dementia and depression. Further studies investigating differences between the differing cytogenetic forms of Down syndrome is recommended.

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Introduction

Lejeune et al, in 1959 were the first to demonstrate that Down syndrome was due to an abnormality of an extra chromosome in the G group. This was subsequently confirmed to be chromosome 21. Other studies followed demonstrating that the characteristic appearance of Down syndrome could also be due to other aberrations involving chromosome 21. These included Robertsonian translocations, usually 14/21 and 21/21 (Polani et al, 1960; Penrose et al, 1960), mosaicism (Clarke et al, 1961) and other mixoploids (Smith and Berg, 1976).

The phenotypic expression is determined by the type of underlying cytogenetic abnormality (Smith and Berg, 1976). In particular, individuals with mosaicism have been demonstrated to function at a higher intellectual level and have less characteristic features of Down syndrome than those with complete trisomy 21 (Verresen et al, 1964; Ridler et al, 1965; Fischler et al, 1976). It is, therefore, apparent that people with Down syndrome are a heterogeneous group and the type of underlying chromosomal abnormality is an important factor in subsequent development.

Previous studies of people with Down syndrome have often reported findings on individuals with Down syndrome without specifying cytogenetic origin or where the vast majority of individuals had complete trisomy 21. Studies investigated differences between individuals with mosaic and trisomy 21 have been described (Rosecrans, 1968; Fischler et al, 1976). Although Down syndrome has been reported to result from a Robertsonian translocation in 3-5% of cases (Hamerton, 1971; Cortes et al, 1990), studies investigating differences between translocated Down syndrome and trisomy 21 Down syndrome individuals have not been reported.

Case reports focusing on the genetic and physical status of individuals with translocations involving chromosome 21 have been described (22/21, Jackson & Ashford, 1967; 1/21, Sayee & Thomas, 1993; 21/21, Shaffer et al, 1993; 12/21, Koskinen et al, 1993). Details regarding psychiatric status were often omitted. This article reports on medical findings between individuals with Robertsonian translocated Down's syndrome and individuals with complete trisomy 21 DS.

Materials and Methods

Two hundred and one adults with Down syndrome were assessed for physical and psychiatric morbidity (Prasher, 1994a and Prasher, 1995). One-hundred and seventy-two individuals underwent cytogenetic studies, of which, 161 (93.6%) had complete trisomy 21 and 9 (5.2%) individuals were found to have a Robertsonian translocated form of Down syndrome. All 9 individuals with translocated Down syndrome were randomly matched by age, sex and place of residence to a known Down syndrome individual with trisomy 21. Age matching was to within two years. A physical examination was undertaken with particular emphasis given to those medical disorders associated with Down syndrome, e.g. obesity, ophthalmologic and audiological problems. Visual acuity was assessed using Kay's graded picture test (Kay, 1983). An external examination of the eyes and ophthalmoscopy was undertaken to assess for cataracts, strabismus, keratoconus and nystagmus. Hearing acuity was assessed using whisper speech and distraction tests.

Table 1. Information for translocated and trisomy 21 groups.

Findings		Translocated Down syndrome group	Trisomy 21 Down syndrome Group
Age	Mean	37.0 Years	36.9 Years
	SD	13.7	13.5
	Range	18-53 Years	18-55 Years
Sex	Males	5	5
	Females	4	4
Residence	Hospital	2	2
	Group Home	2	2
	Family Home	5	5
Severity Of LD	Mild	4	2
	Moderate	5	2
	Severe		5
Cytogenetic Findings	14/21 Translocation	5	
	21/21 Translocation	4	

Presence of cerumen was assessed by otoscopic examination. Screening for haematological, biochemical and thyroid function abnormalities was also performed. The normal range for free thyroxine (T4) was 11-24 pmol/l and for thyroid stimulating hormone (TSH) 0.3-4.5 microIU/ml. Values outside these ranges were considered to be abnormal.

Carers were interviewed to elicit evidence of a past or ongoing psychiatric disorder. All available medical records were reviewed for evidence of a psychiatric illness. Individuals were interviewed and a mental state examination performed. Psychotropic medication administered was recorded.

Psychiatric diagnoses were made according to Diagnostic Research Criteria (DCR-10; WHO, 1993). Severity of learning disability was assessed by review of previously reported intelligence tests' results and from carer and subject interview. Severity of learning disability was classified using ICD-10 criteria (WHO, 1992). Comparative statistical analysis was undertaken for the two groups.

Adaptive functioning was assessed using the Adaptive Behaviour Scale (ABS; Nihira, 1974). The main carer who was familiar with the participant was interviewed to complete the scale. Both Part I (Independent functioning) and Part II (Maladaptive Behaviours) were used. Part II results for medication were excluded. Mean scores for the domains and for overall Part I and Part II scores were determined.

Results

Information for the two groups is given in Table 1. Although the two groups were matched for age, sex and place of residence, severity of learning disability was greater for the trisomy 21 group than the translocated group. Findings for relevant medical conditions are given in Table 2 (page 11) and show that there was no significant difference in stature for the two groups, although the trisomy 21 group had more severe obesity. Ophthalmologic, audiological and thyroid dysfunction were equally present in both groups. Findings for both groups for mean cell volume were in the upper normal range and for the neutrophil count and calcium levels in the low normal range. No significant differences in results were found.

Assessment for psychiatric disorders (Table 3 - page 11) found that 7 (77.7%) of the translocated group compared to 2 (22.2%) of the trisomy 21 group had a lifetime history of a recognisable psychiatric disorder. Dementia and depression in particular were associated with the translocation group.

Findings for adaptive functioning are given in Table 4 (page 12). The trisomy 21 group scored significantly higher in the overall Part I ABS score and for all the domains except physical development, numbers and time, domestic activity and vocational activity. The translocated group scored higher in the Overall Part II score (but not significantly).

Discussion

Due to recent advances in molecular genetics, genetic makeup is beginning to play an important role in many clinical aspects of learning disability; no more so than in people with Down syndrome. It is important, however, that people with Down syndrome are assessed as a heterogeneous group and further research undertaken to investigate possible differences between the different cytogenetic types. It must be remembered that trisomy 21 and mosaic Down syndrome is a disorder of the number of chromosomes

Table 2. Medical findings for translocated and trisomy 21 groups.

Finding		Translocated Group	Trisomy 21 Group
Height-mean (SD)*		149.7 cms (6.3)	146.9 cms (9.4)
Weight-mean (SD)**		64.2 Kgs (11.2)	75.2 Kgs (17.7)
Body Mass Index	Desirable Weight (21-24)	2	
	Overweight (25-29)	3	3
	Obesity (>30)	4	6
Eyes	Significantly Impaired Vision	3	2
	Cataracts	2	4
	Keratoconus	1	1
	Nystagmus	1	0
Ears	Significantly Impaired Hearing	3	2
	Excess Cerumen	4	1
Thyroid Status (T4 and TSH)	Normal levels	6	6
	Abnormal Levels	2	1
	Unknown	1	2
	Perscribed Thyroxine Replacement	1	2
Blood Results	Mean Cell Volume (normal range - 90-98fl)*	96.36 fl (90-98)	97.82 fl (90-98)
	Neutrophil Count (normal range - 2.0-7.5x10 /l)*	2.87 x 10 /l	3.16 x 10 /l
	Calcium (normal range - 2.20 - 2.65 mmol/l)*	2.22 mmol/l	2.24 mmol/l

* No significant difference at 5% level (independent t test analysis).
** Significant difference at 5% level (independent t test analysis).

Table 3. Psychiatric Disorders found for translocated and trisomy 21 groups.

Psychiatric Disorder		Translocated Group (N=9)	Trisomy 21 Group (N=9)
Dementia		2	1
Depressive Episode	Present	2	0
	Past	1	0
Conduct Disorder		2	1
Total with Lifetime History of Disorder		7	2

Table 4. Adaptive behaviour scale scores for translocated and trisomy 21 groups.

Domain		Translocated Group Mean (S)	Trisomy 21 Group Mean (S)	Significance*
Part I	Independent Functioning	53.56 (16.40)	70.44 (14.32)	p<0.05
	Physical Development	16.00 (5.89)	20.11 (2.85)	NS
	Economic Activity	0.89 (1.27)	5.33 (4.02)	p<0.05
	Language Development	12.22 (6.96)	21.11 (5.95)	p<0.05
	Numbers and Time	2.11 (2.71)	3.89 (2.52)	NS
	Domestic Activity	4.22 (3.80)	7.33 (3.39)	NS
	Vocational Activity	1.11 (3.33)	2.33 (4.64)	NS
	Self-direction	8.00 (3.67)	12.58 (4.03)	p<0.05
	Responsibility	1.22 (1.09)	3.33 (1.73)	p<0.05
	Socialization	12.11 (5.21)	17.11 (4.37)	p<0.05
Part I Overall Score		111.44 (35.97)	163.56 (42.48)	p<0.05
Part II Overall Score		21.11 (16.47)	8.44 (11.67)	NS

* Mann-Whitney analysis
NS=not significant

present whereas translocated Down syndrome is a disorder of structure. Such cytogenetic differences may prove important.

Findings in this study suggest that translocated and trisomy 21 Down syndrome individuals are similar in respect to stature, ophthalmologic and audiological disorders and to increased risk of thyroid dysfunction. Significant differences may be present for risk of obesity and severity of learning disability. Translocated Down syndrome individuals may have less severity of learning difficulty as compared to trisomy 21 individuals according to IQ and ICD 10 rating. Particular interest may lie in the increased risk of psychiatric morbidity for translocated Down syndrome individuals. Dementia, although primarily associated with trisomy 21, has been demonstrated to occur in Down syndrome individuals with Robertsonian translocations (Prasher, 1993). Further research is needed to confirm or refute these provisional findings.

Adaptive functioning was found to be greater for the trisomy 21 group than the translocated group. However, as previously demonstrated (Miniszek, 1983; Collacott and Cooper, 1992) dementia and depression can have a detrimental effect on ABS scores. The presence of such disorders most probably account for the above scores.

This study highlights the need as previously demonstrated, (Prasher, 1994b) for the underlying cytogenetic make-up to be investigated and reported in studies of people with Down syndrome. Cytogenetics, in particular molecular mapping of the Down syndrome phenotype (Korenberg et al, 1990), may identify which genes are responsible for particular clinical features. Several cases of partial trisomy 21 have been reported and reviewed, demonstrating that particular areas of chromosome 21 are involved with specific clinical signs (Delabar et al, 1993; Korenberg et al, 1994). Such findings will have prognostic implications for the differing forms of Down syndrome.

The sample size investigated was small and caution must be applied in interpreting these results. However, this is the first study to compare translocated Down syndrome individuals with trisomy 21 controls. The findings of this study although requiring repetition with a larger sample, do nevertheless highlight an important area of further research. Collaborative studies involving different centres are recommended so as to increase the sample of translocated individuals with Down syndrome assessed.

Glossary

Cerumen: Ear wax.
Cytogenetic: Related to genetic structure of the cell.
Keratoconus: Abnormal conical shape of the cornea of the eye.
Mixoploids: Where the chromosome number or arrangement is not normal.
Neutrophil: A form of white cell which kills bacteria.
Nystagmus: Rapid short movements of the eye.
Otoscopic: To do with the ear.
Phenotypic: The observable characteristics which result from the interaction between gene and the environment.
Psychotropic: Drugs used in mental illness.
Strabismus: Squint.
Thyroxine: Thyroid hormone.

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