

IS THERE A PRODROMAL PHASE TO ALZHEIMER'S DEMENTIA IN ADULTS WITH DOWN SYNDROME?

Introduction

There has been in recent times a proliferation of publications regarding the occurrence of Alzheimer's Disease (AD) in adults with Down Syndrome (DS). Articles have focused on genetic, neuropathological and clinical aspects. Many clinical features of AD seen in the non-learning disability (LD) population have been demonstrated to occur in the DS population (Heston et al., 1981; Dalton and Crapper-McLachlan, 1986). These include an initial phase of mental deterioration, memory impairment, apathy and deterioration in speech (Brugge et al., 1994; Evenhuis, 1990); followed by a period of further decline in skills, behavioural problems, emotional change, incontinence, onset seizures (Oliver and Holland, 1986; Lai and Williams, 1989; Prasher and Filer, 1995). A final phase of double incontinence, hypertonia and individuals requiring total nursing care occurs (Prasher, 1995a; Lai and Williams 1989).

Although cognitive aspects of dementia have often been emphasised (Oliver and Holland 1986, Dalton and Crapper-McLachlan, 1986), significant emotional changes (Prasher, 1995b; Burt et al., 1992), behavioural changes (Prasher and Filer, 1995) and decline in adaptive skills (Minizek, 1993; Prasher et al., 1994) have been reported. The mean age of onset of dementia in adults with DS being in the fifth decade with mean duration of approximately six years (Dalton and

Crapper, 1977; Prasher and Krishnan, 1993).

In the non-LD population it has been demonstrated that a number of prodromal features, for example low mood, can occur before the diagnosis of dementia is made (Burns, 1991). This brief paper investigates the possible presence of prodromal features in adults with DS before a diagnosis of dementia has been made.

Method

As part of the West Midlands Ageing Study, a large sample of adults with DS has been prospectively followed up for several years on a number of cognitive, behavioural and adaptive measures. Many of the subjects are resident in hospital or in the community, from different districts in the region and have a wide age range.

During the 4 year period of the West Midlands Ageing Study, 12 individuals developed 'Dementia in Alzheimer's Disease' according to DCR-10 Criteria (WHO 1993). These individuals had been assessed for a number of years before the onset of dementia and after the diagnosis had been made. Each individual was matched by age (to within 3 years), sex, place of residence and severity of LD to a control subject who was not suffering from any significant medical or psychiatric disorder but who had also been followed up for a number of years.

Information was available from annual semi-structure interviews with primary carers, review of medical records, mental state examinations, physical examinations, haematological, biochemical and thyroid function tests. Cytogenetic studies had been undertaken to confirm the clinical diagnosis of DS. A number of subjects had also undergone EEG and neuro-imaging assessments. All subjects' medication that could influence cognitive functioning was reviewed.

Adaptive functioning was assessed annually using the Adaptive Behaviour Scale (ABS; Nihira, 1974). The main carer who was familiar with the subject was interviewed to complete the scale. Both Part I (Independent functioning) and Part II (Maladaptive Behaviours) were used. For Part II results for medication were excluded. Part I Domain scores and Part I and Part II Total scores were calculated. Severity of LD was assessed by review of previously reported intelligence tests results and from carer and subject interview. Severity of LD was classified using ICD-10 criteria (WHO, 1992).

For the two groups, available data one year before the diagnosis of dementia was made for the dementia group (Year 1) and during the year of the diagnosis of dementia for the dementia group (Year 2) were compared. Non-parametric data analysis was undertaken where necessary.

Results

For the two groups there were 8 females and 4 males with 7 residing in community homes, 3 in their own family homes and 2 in a hospital setting. Ten had moderate LD, 1 mild and 1 severe. For the dementia

group the mean age at time of diagnosis was 51.7 years, standard deviation 8.26 (age range 36-67 years). For the control group, mean age was 51.2 years, standard deviation 8.41 (age range 33-63 years). There was no statistically significant age difference between the two groups.

Findings regarding clinical status for the two study years for both groups are given in TABLE I. These results suggest that for people with DS who develop dementia, there is no significant prodromal phase prior to a diagnosis of dementia being made. Occasional symptoms of slowing and incontinence may be present but overall, there is no associated emotional, behavioural or cognitive change, suggesting the onset of a dementing illness. Such abnormalities only become significantly present after the onset of the dementia illness. For the control group, occasional changes in behaviour, mood and emotion and gait and slight memory impairment can occur with increasing age. However, none of these symptoms in themselves were enough to fulfil DCR-10 criteria (WHO, 1993) for dementia. These symptoms may be associated with the ageing process or associated with age associated functional decline.

Findings for changes in adaptive behaviour are given in TABLE II. These results demonstrate that there is a significant reduction in overall adaptive behaviour skills for the Part I of the ABS for the dementia group once the illness has been diagnosed. A significant fall in scores for the total Part I score and for the domains independent functioning, economic activity, language development, domestic activity, responsibility and socialisation were found. A non-significant increase in Part II maladaptive behaviour

TABLE I
Clinical Features of Demented and Non-demented Group

Feature	Dementia Group		Non-demented Group	
	Yr 1	Yr 2	Yr 1	Yr 2
Mental deterioration	0	12*	0	1
Memory loss	0	12*	0	0
Slowing down	1	9*	2	3
Change in personality	0	7*	0	0
Change in mood	0	4	0	2
Behavioural deterioration	0	3	0	1
Speech deterioration	1	7*	1	3
Gait deterioration	0	6*	0	2
Seizures	1	4	0	0
Incontinence	1	3	2	3
Change in appetite	0	3	0	0
Disturbed sleep	0	0	0	0
Loss of weight	0	3	0	1

* Significant difference between two results at 5% level
(Wilcoxon-parametric test)

score was seen. For the control group there is no significant change in adaptive scores during the study period.

For Year 1 adaptive scores for the dementia group were lower than those for the control group, but no significant difference was found at the 5% significance level. Once a diagnosis of dementia had been made, the dementia group was found to have a significantly lower Part I total score ($z = 2.95$; $P < 0.05$) and a significantly greater Part II total score ($z = 1.7$; $P < 0.05$).

Discussion

This report paper demonstrates that there is no obvious prodromal phase prior to the diagnosis of dementia being made in

adults with DS. However, early signs of dementia were mental deterioration, memory loss, slowing down, change in personality, speech and gait deterioration. Further, a significant decline in adaptive behaviour skills also occurs at this time.

The findings in this report differ from those for the non-LD population where particular features such as low mood, irritability and behavioural changes have been found to occur prior to a research diagnosis of dementia. It cannot be excluded that such changes occur in people with LD but are not readily identified due to the underlying intellectual impairment. Further research is recommended.

TABLE II
Adaptive Behaviour Scale Scores for Demented and Non-demented DS Subjects

Domain	Dementia Group		Control Group		Significance (Wilcoxon test)
	Year 1 Mean (SD)	Year 2 Mean (SD)	Year 1 Mean (SD)	Year 2 Mean (SD)	
Part 1					
Independent functioning	69.00 (14.43)	63.09 (16.69)	73.50 (18.58)	68.33 (24.57)	z=2.01 P<0.05
Physical development	17.00 (4.18)	17.18 (3.60)	19.00 (3.30)	19.42 (3.03)	z=0.59 NS
Economic activity	2.08 (2.64)	1.55 (2.42)	3.50 (4.02)	3.75 (3.89)	z=2.00 P<0.05
Language development	16.33 (7.18)	14.64 (5.63)	18.58 (8.21)	19.75 (8.48)	z=2.56 P<0.01
Numbers and time	3.67 (3.42)	3.18 (3.34)	4.25 (3.62)	5.17 (4.47)	z=1.68 NS
Domestic activity	6.67 (4.12)	5.09 (4.06)	7.67 (5.38)	9.42 (5.99)	z=2.27 P<0.05
Vocational activity	8.25 (1.60)	7.73 (2.80)	9.17 (0.94)	8.83 (1.85)	z=0.00 NS
Self-direction	11.83 (3.07)	10.36 (4.48)	13.58 (4.29)	13.17 (4.47)	z=1.32 NS
Responsibility	2.75 (1.76)	1.82 (1.72)	3.17 (1.85)	3.33 (2.18)	z=2.37 P<0.05
Socialisation	16.33 (5.00)	13.18 (5.31)	16.33 (5.10)	17.83 (4.13)	z=2.93 P<0.01
Part I total score	153.92 (37.89)	127.45 (32.98)	168.75 (50.26)	169.00 (56.02)	z=2.93 P<0.01
Part II total score	15.18 (16.65)	18.18 (19.26)	15.50 (20.50)	9.92 (8.33)	z=0.61 NS

NS = Not Significant

Summary

Little is known about possible prodromal features of dementia in adults with Down Syndrome. This paper reports the findings of investigating clinical and adaptive features in twelve Down Syndrome adults one year prior to a diagnosis of dementia being made and during the first year of diagnosis. Appropriately matched Down Syndrome controls were also assessed. No significant evidence of the presence of a prodromal phase was found. Implications of the findings are discussed.

Dr. V. P. Prasher,
M.Med.Sc., M.R.C.Psych., M.D.
Senior Clinical Lecturer
Department of Psychiatry
University of Birmingham
Queen Elizabeth Hospital
Edgbaston
Birmingham B15 2QZ
U.K.
Tel. 0121 627 2831
Fax 0121 627 2831

References

- Brugge, K. L., Nichols, S. L., Salmon, D. P., Hill, L. R., Delis, D. C., Aaron, L. and Trauner, D. A. (1994) Cognitive impairment in adults with Down Syndrome: Similarities to early cognitive changes in Alzheimer's Disease. *Neurology* 44, 232-238.
- Burns, A. (1991) Affective symptoms in Alzheimer's Disease. *International Journal of Geriatric Psychiatry* 6, 371-376.
- Burt, D. B., Loveland, K. A. and Lewis, K. R. (1992) Depression and the onset of dementia in adults with mental retardation. *American Journal on Mental Retardation*. 96, 502-511.
- Dalton, A. L. and Crapper, D. R. (1977) Down's Syndrome and ageing of the brain. In: P. Mittler (Ed.). *Research to Practice in Mental Retardation*; Vol. 3, Biomedical Aspects pp.391-400, Baltimore: University Park Press.
- Dalton, A. J. and Crapper-McLachlan, D. R. (1986) Clinical expression of Alzheimer's disease in Down's Syndrome. *Psychiatric Perspectives on Mental Retardation* 9, 659-670.
- Evenhuis, H. M. (1990) The natural history of dementia in Down's Syndrome. *Archives of Neurology* 47, 263-267.
- Heston, L. L., Mastri, A. R., Anderson, E. and White, J. (1981) Dementia of the Alzheimer type: clinical genetics, natural history and associated conditions. *Archives of General Psychiatry* 38, 1085-1090.
- Lai, F. and Williams, R. S. (1989) A prospective study of Alzheimer Disease in Down Syndrome. *Archives of Neurology* 46, 849-853.
- Miniszek, N. A. (1983) Development of Alzheimer's disease in Down's Syndrome individuals. *American Journal of Mental Deficiency* 87, 377-385.
- Nihira, K., Foster, R., Shellhaas, M. and Leyland, H. (1974) *AAMD Adaptive Behaviour Scale, 1974 Revision*, Washington, D.C.: American Association on Mental Deficiency.
- Oliver, C. and Holland, A. J. (1986) Down's Syndrome and Alzheimer's disease: a review. *Psychological Medicine* 16, 307-322.
- Prasher, V. P. and Krishnan, V. H. R. ((1993) Age of onset and duration of dementia in people with Down Syndrome. A study of 98 reported cases. *International Journal of Geriatric Psychiatry*. 8, 915-922.
- Prasher, V. P. (1995a) End-stage dementia in adults with Down Syndrome. *International Journal of Geriatric Psychiatry*. 10, 1064-1069.
- Prasher, V. P. (1995b) Age-specific prevalence, thyroid dysfunction and depressive symptomatology in adults with Down Syndrome and dementia. *International Journal of Geriatric Psychiatry* 10, 25-31.
- Prasher, V. P. and Filer, A. (1995) Behavioural disturbance in people with Down syndrome and dementia. *Journal of Intellectual Disability Research*. 39, 432-436.

Prasher, V. P., Krishnan, V. H. R., Clarke, D. J. and Corbett, J. A. (1994) The Assessment of Dementia in people with Down syndrome: Changes in adaptive behaviour. *The British Journal of Developmental Disabilities*. 79, 120-130.

World Health Organisation (1992) The ICD-10 Classification of Mental and Behavioural Disorders. *Clinical Descriptions and Diagnostic Guidelines*. Geneva: WHO

World Health Organisation (1993) The ICD-10 Classification of Mental and Behavioural Disorders. *Diagnostic criteria for research*. Geneva: WHO.