

## PSYCHOTIC FEATURES AND EFFECT OF SEVERITY OF LEARNING DISABILITY ON DEMENTIA IN ADULTS WITH DOWN SYNDROME: REVIEW OF LITERATURE

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### Introduction

During the last decade there has been a dramatic growth of interest in the association between Alzheimer's disease (AD) and Down syndrome (DS). A number of reports demonstrating neuropathological (Mann, 1988), genetic (Goate *et al.*, 1989), psychological (Dalton and Wisniewski, 1990; Devenny *et al.*, 1992) and adaptive behavioural changes (Prasher *et al.*, 1994; Burt *et al.*, 1995; Prasher and Chung, 1996) have been published. Further, in recent years detailed clinical presentation of AD in adults with DS has been evaluated; age of onset and duration of dementia (Prasher and Krishnan, 1993), behavioural changes (Prasher and Filer, 1995) neurological findings (Lai and Williams, 1989) and abnormalities of mood (Prasher, 1995; Burt *et al.*, 1992).

No study to date has been published specifically investigating the occurrence of psychotic features such as delusions and hallucinations in adults with DS who develop dementia. Such phenomenology remains an important area of research.

Are such features part of a dementing process in people with learning disability (LD)? Does underlying intellectual impairment preclude the occurrence and/or presentation of these symptoms? Does the occurrence of such psychotic features affect the prognosis of the dementia process? Such questions remain to be answered.

In a woman without LD, Alzheimer described psychotic symptoms of delusions and hallucinations in his original case report (Alzheimer, 1907). For the non-LD population as a whole the prevalence of delusions has been reported in up to 50% of demented subjects (Cummings *et al.*, 1987). Mendez *et al.* (1990) in a retrospective review of 217 outpatients (mean age 76.2 years) with clinically probable AD found hallucinations in 25.4% of subjects, visual hallucinations in 76.4% and many were mood or theme congruent with a delusion. Cooper *et al.* (1991) reported an overall presence of psychotic symptoms in 677 non-LD adults (mean age 75.0 years) with AD to be 31%. The

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prevalence of hallucinations was 17% and of delusions 26%. Psychotic features were more likely with advanced disease.

The detection of delusions and hallucinations remains an important part of the assessment of dementia in adults with LD. The presence of such features may be an indicator of a sub-type of AD, or be stage-dependent emerging at particular phases of the illness, or be associated with more severe behavioural disturbance (Flynn *et al.*, 1991).

For the non-LD population a number of studies have reported the increased risk of no or low education on the prevalence of dementia (Zhang *et al.*, 1990; Fratiglioni *et al.*, 1991; Sulkava *et al.*, 1985). Stern *et al.* (1994) investigated the influence of education and occupation on the incidence of AD in 593 non-LD adults, of whom 101 developed AD over a 4 year period. The authors found that the risk of dementia was increased in subjects with either low education or low lifetime occupational attainment. The risk was greatest for subjects with both low education and low lifetime occupational attainment. Mortimer (1994) in a review of risk factors for dementia concluded "that the association between education and dementia may represent only one instance of a more general association between education and the rate of biological aging". For people with LD possible effects of the underlying level of intelligence on the onset and duration of dementia remain to be established. No study to date has been published specifically investigating this area of research.

This study reviewed all published reports giving detailed information regarding the clinical presentation of dementia in adults with DS. The occurrence of delusions and hallucinations and the

effect of underlying level of LD on the psychopathology of AD was explored. This approach does have limitations: (i) diagnosis of AD made on clinical grounds but not always confirmed by neuropathological findings, (ii) not epidemiological where a well-defined population is studied to determine the prevalence and/or incidence rates of delusions and hallucinations, (iii) inter-observer bias where particular cases are included and reported, (iv) incomplete descriptions of psychopathology where delusions and hallucinations may not be elicited or if elicited not reported. However, there are several advantages associated with such an approach: (i) a large number of subjects with DS and dementia ( $n = 86$ ), (ii) reports from many independent centres, (iii) high accuracy of clinical diagnosis (cases were often followed up to death), (iv) detailed clinical information available from case reports.

## Methodology

A review of all case reports and studies investigating clinical dementia in adults with DS published principally in the English language in the world literature up to January 1995 was undertaken. Manual and electronic searches were used to ensure a complete review. Studies primarily assessing neuropathological and/or psychological changes were excluded. Of a total of 120 DS cases reported there was sufficient information regarding the presence of clinical dementia and severity of LD on 86 subjects (TABLE I). Thirty-four cases were excluded from the analysis (these are given in TABLE II along with reasons for exclusion). The majority of the 86 cases

**TABLE I**  
**Cases of clinical dementia in people with Down's syndrome - literature review**

Authors (year)	Cases	Sex	Severity of LD	Residence*	Age of onset of dementia	Age at death (Years)	Delusions/ Hallucinations mentioned
Jervis (1948)	1	F	moderate	community unit	42	47	no
	1	F	moderate	community unit	38	42	yes - hallucinations
	1	M	moderate	community unit	31	45	no
Verhaart & Jelgersman 1952	1	F	mild	family home	36	57	no
Haberland (1969)	1	F	severe	community unit	38	56	no
Olson & Shaw (1969)	1	F	moderate	family home	41	51	no
Crapper <i>et al.</i> (1975)	1	M	moderate	family home	44	54	no
Reid <i>et al.</i> (1978)	1	F	moderate	family home	54	59	no
	1	M	moderate	-	50	53	no
Ropper & Williams (1980)	1	F	moderate	community unit	40	49	no
	1	F	severe	community unit	44	49	no
Blumbergs <i>et al.</i> (1981)	1	F	moderate	family home	44	46	no
Pogacar & Rubio (1982)	1	F	severe	-	45	50	no
Wisniewski <i>et al.</i> (1985)	6	5M 1F	severe	-	mean 50.8	mean 56	no
Dalton & Crapper-McLachlan (1986)	1	F	severe	hospital	54	65	no
Lai & Williams (1989)	49	27M 22F	-	-	mean 52.5	mean 57	no
Evenhuis (1990)	15	6M 9F	moderate/ severe/ unknown	hospital	mean 52.1	mean 57	no
Murphy & Ellis (1991)	1	M	severe	-	54	56	no
Rae-Grant <i>et al.</i> (1991)	1	M	moderate	-	-	-	no
<b>TOTAL</b>	<b>86</b>						

\* = majority of life  
 psycho = psychological

included in the final analysis were from different case reports, although 54 subjects were from two recent studies (Lai and Williams, 1989; Evenhuis, 1990). Given information was scrutinised for evidence of delusions and/or hallucina-

tions and for level of underlying LD. Severity of LD from information given was categorised into mild, moderate and severe according to ICD-10 Criteria (WHO 1992).

**TABLE II**  
**Cases excluded from final data analysis**

Report	Cases excluded	Reason for exclusion
Bertrand & Koffas (1946)	1	Inadequate clinical information*
Solitaire & Lamarche (1966)	5	No evidence of clinical dementia**
Olson & Shaw (1969)	3	No evidence of clinical dementia
Schochet <i>et al.</i> (1973)	2	No evidence of clinical dementia
Ellis <i>et al.</i> (1974)	1	Death due to acute medical emergency
Reid & Maloney (1974)	1	No evidence of clinical dementia
Ropper & Williams (1980)	1	Inadequate clinical information
Yates <i>et al.</i> (1983)	5	Inadequate clinical information
Evenhuis (1990)	2	No evidence of clinical dementia
Murphy & Ellis (1991)	2	No evidence of clinical dementia/ death due to acute medical emergency
Prasher & Corbett (1993)	11	Inadequate clinical information
TOTAL	34	

\* Inadequate clinical information to determine presence of dementia and presence of delusions/hallucinations

\*\* Detailed clinical information given but no sufficient evidence for clinical diagnosis of dementia

## Results

The mean age of onset of dementia for the 86 cases was approximately 45.0 years with approximate mean age of death of 52.8 years. Forty-three subjects were female and 43 were male. Five subjects (5.8%) lived in their family home, 6 subjects (7.0%) in community units and 16 subjects (18.6%) in a hospital setting. For 59 subjects (68.6%) information regarding place of residence was not available.

None of the demented cases reviewed referred to the presence of any delusional phenomena. Further, only one case referred to the possible presence of hallucinations (but no details regarding type were given).

For only 18 subjects (Haberland, 1969; Crapper *et al.*, 1975; Pogacar and Rubio, 1982; Evenhuis, 1990) were there valid assessments measuring the level of LD. Sufficient clinical information to estimate the level of LD was available for 36 subjects: 1 person with mild LD, 19 subjects with moderate LD and 16 with severe LD. The mean age of onset for individuals with moderate LD was approximately 46.9 years (SD 6.8) and for subjects with severe LD approximately 50.3 years (SD 6.4). There was no statistically significant difference between age of onset for the two groups (Mann Whitney Test  $z = 1.28$   $p = 0.20$ ). The approximate mean duration of dementia for the moderate LD group was 5.0 years (SD 2.7) and for the severe LD group 6.1 years (SD 4.0). There

was no statistically significant difference (Mann Whitney Test  $z = 0.44$   $p = 0.66$ ).

## Discussion

Although our knowledge and understanding of AD in adults with DS is dramatically increasing (Berg *et al.*, 1993), there remain a number of areas (such as mood changes, psychotic features, degree of insight) that still require further investigation. Such areas may be potentially treatable with medication. The presence of psychotic features (delusions and hallucinations) is a common feature of dementia in the non-LD population (Mendez *et al.*, 1990; Cooper *et al.*, 1991). This paper, although it has a number of limitations, does highlight that such features have generally not been reported to be associated with dementia in the DS population. This is an interesting finding for which there are a number of explanations. Firstly, due to the underlying severity of LD, such symptoms may not occur. Secondly, such features may occur but are not exhibited by patients with LD. Thirdly, although present these symptoms are not elicited/detected/recorded by clinicians or researchers. This latter explanation must be borne in mind in a review of published literature where emphasis of researchers was on cognitive and behavioural changes of dementia. However, it remains interesting to note that of 86 clinically detailed cases of DS adults with AD reviewed, not one remarked on the presence of delusions and only one to the possible presence of hallucinations. This case was reported in 1948 by Jervis, so that it is reasonable to assume that subsequent researchers were aware of the possible occurrence of

hallucinations in adults with DS and dementia.

If psychotic features are absent in dementia in adults with DS, this would be, other than age of onset, one of the main differences between AD in the two populations. It is recommended that, in contrast to published studies to date, future prospective studies specifically question and examine the presence of psychotic pathology in adults with DS who develop dementia. Multi-centre studies are required to reliably investigate this question.

Although still controversial, it is widely reported that for the non-LD population high educational status and subsequent higher IQ may be a protective factor against a dementing process. Extrapolation of such a hypothesis would suggest that as the IQ level falls, the incidence of dementia becomes greater. However, the findings from this study suggest that increasing severity of LD below an IQ of 50 has no significant effect on the prevalence, onset or duration of dementia. Prospective studies specifically investigating the possible effect of severity of LD on dementia are required. In particular, incorporating subjects with mild LD for a greater range of underlying intellectual levels of functioning is recommended.

This initial investigation of a number of important areas of dementia in adults with DS does tentatively suggest that there is a significant absence/reduction of psychotic features. Underlying severity of LD is not a risk factor for onset of dementia and has no significant effect on duration. Although caution should be used in interpreting these findings, it is hoped that this initial paper highlights areas of future research to investigate

these in other more structured longitudinal studies.

## Summary

There remains a paucity of information regarding the assessment of delusions and hallucinations and the effect of severity of learning disability on dementia in adults with learning disability. In this study, all clinical reports of dementia in adults with Down syndrome published up to 1995 were appraised for presence of delusions and hallucinations and references to the underlying level of learning disability. Of 86 cases examined, none referred to the presence of delusions and only one report intimated the possible presence of hallucinations. Severity of learning disability was found not to have a significant effect on onset and duration of dementia. Recommendations for future areas of research are discussed.

## References

- Alzheimer, A. (1907). Über eine eigenartige Erkrankung der Hirnrinde. *Allgemeine Zeitschrift für Psychiatrie und Psychisch-Gerichtliche Medizin*, 64, 146-148.
- Berg, J. M., Karlinsky, H. and Holland, A. J. (1993). *Alzheimer disease, Down syndrome, and their relationship*. New York, USA: Oxford University Press.
- Bertrand, I. and Koffas, D. (1946). Cas d'idiotie mongolienne adulte avec nombreuses plaques seniles et concretion calcaires pallidales. *Revue Neurologique*, 78, 338-345.
- Blumbers, P., Beran, R. and Hicks, P. (1981). Myoclonus in Down's syndrome. Association with Alzheimer's disease. *Archives of Neurology*, 38, 453-454.
- 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.
- Burt, D. B., Loveland, K. A., Chen, Y-W., Chuang, A., Lewis, K. R. and Cherry, L. (1995). Aging in adults with Down syndrome: Report from a longitudinal study. *American Journal on Mental Retardation*, 100, 262-270.
- Cooper, J. K., Mungas, D., Verma, M. and Weiler, P. G. (1991). Psychotic symptoms in Alzheimer's disease. *International Journal of Geriatric Psychiatry*, 6, 721-726.
- Crapper, P. R., Dalton, A. J., Skopitz, Scott, J. W. and Hachinski, V. C. (1975). Alzheimer degeneration in Down Syndrome. *Archives of Neurology*, 32, 618-623.
- Cummings, J. L., Miller, B., Hill, M. A. and Neshkes, R. (1987). Neuropsychiatric aspects of multi-infarct dementia and dementia of the Alzheimer type. *Archives of Neurology*, 44, 389-393.
- Dalton, A. J. and Crapper McLachlan, D. R. (1986). Clinical expression of Alzheimer's disease in Down's syndrome. *Psychiatric Clinics of North America*, 9, 659-670.
- Dalton, A. J. and Wisniewski, H. M. (1990). Down's syndrome and the dementia of Alzheimer's disease. *International Review of Psychiatry*, 2, 43-52.
- Devenny, D. A., Hill, A. L., Patxot, O., Silverman, W. P. and Wisniewski, K. E. (1992). Ageing in higher functioning adults with Down's syndrome: an interim report in a longitudinal study. *Journal of Intellectual Disability Research*, 36, 241-250.
- Ellis, W. G., McCulloch, J. R. and Corley, C. L. (1974). Presenile dementia in Down's Syndrome; ultrastructural identity with Alzheimer's disease. *Neurology*, 24, 101-106.
- Evenhuis, H. M. (1990). The natural history of dementia in Down's Syndrome. *Archives of Neurology*, 47, 263-267.
- Flynn, F. G., Cummings, J. L. and Gornbein, J. (1991). Delusions in dementia syndromes: Investigation of behavioral and neuropsychological correlates. *Journal of Neuropsychiatry and Clinical Neurosciences*, 3, 364-370.

- Fratiglioni, L., Grut, M., Forsell, Y., Viitanen, M., Grafstrom, M., Holmen, K., Ericsson, K., Backman, L., Ahlbom, A. and Winblad, B. (1991). Prevalence of Alzheimer's disease and other dementias in an elderly urban population: relationship with age, sex, and education. *Neurology*, 41, 1886-1892.
- Goate, A. M., Haynes, A. R., Owen, M. J., Farrall, M., James, L. A., Lai, L. Y. C., Mullan, M. J., Roques, P., Rossor, M. N., Williamson, R. and Hardy, J. A. (1989). Predisposing locus for Alzheimer's disease on chromosome 21, *Lancet*, i,352-355.
- Haberland, C. (1969). Alzheimer's disease in Down's syndrome. Clinical-neuropathological observations. *Acta Neurologica Belgica*, 69, 369-380.
- Jervis, G. A. (1948). Early senile dementia mongoloid idiocy. *American Journal of Psychiatry*, 105, 102-106.
- Lai, F. and Williams, R. S. (1989). A prospective study of Alzheimer Disease in Down Syndrome. *Archives of Neurology*, 46, 849-853.
- Mann, D. M. A. (1988). The pathological association between Down Syndrome and Alzheimer disease. *Mechanisms of Aging and Development*, 43, 99-136.
- Mendez, M. F., Martin, R. J., Smyht, K. A. and Whitehouse, P. J. (1990). Psychiatric symptoms associated with Alzheimer's disease. *Journal of Neuropsychiatry and Clinical Neurosciences*, 2, 28-33.
- Mortimer, J. A. (1994). What are the risk factors for dementia? In: Huppert, F. A., Brayne, C. and O'Connor, D. W. (Eds.) *Dementia and normal aging*. Cambridge, UK: Cambridge University Press. 208-229.
- Murphy, G. M. and Ellis, W. G. (1991). The amygdala in Down's syndrome and familial Alzheimer's disease: four clinicopathological case reports. *Biological Psychiatry*, 30, 92-106.
- Olson, M. I. and Shaw, C. (1969). Presenile dementia and Alzheimer's disease in mongolism. *Brain*, 92, 147-156.
- Pogacar, S. and Rubio, A. (1982). Morphological features of Pick's and atypical Alzheimer's disease on Down's syndrome. *Acta Neuropathologica (Berl)*, 58, 249-254.
- 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. and Corbett, J. A. (1993). Onset of seizures as a poor indicator of longevity in people with Down syndrome and dementia. *International Journal of Geriatric Psychiatry*, 8, 923-927.
- 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*, 40, 120-130.
- 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. (1995). 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 Chung, M-C. (1996). Causes of age-related decline in adaptive behaviour in adults with Down syndrome. *American Journal on Mental Retardation*, 101, 175-183.
- Rae-Grant, A. D., Barbour, P. J., Sirota, P. and Gross, P. (1991). Alzheimer's disease in Down's syndrome with SPECT. *Clinical Nuclear Medicine*, 16, 509-510.
- Reid, A. H. and Maloney, A. F. J. (1974). Giant cell arteritis and arteriolitis associated with amyloid angiopathy in an elderly mongol. *Acta neuropathologica*, 27, 131-137.
- Reid, A. H., Maloney, A. F. J. and Aungle, P. G. (1978). Dementia in ageing mental defectives: A clinical and neuropathological study. *Journal of Mental Deficiency Research*, 22, 233-241.
- Ropper, A. H. and Williams, R. S. (1980). Relationship between plaques, tangles and dementia in Down's Syndrome. *Neurology*, 30, 639-644.
- Schochet, S. S., Lampert, P. W. and McCormick, W. F. (1973). Neurofibrillary tangles in patients with Down's syndrome: a light and electron microscopy study. *Acta Neuropathologica (Berl)*, 23, 342-346.
- Solitaire, G. B. and Lamarche, J. B. (1966). Alzheimer's disease and senile dementia as seen in mongoloids: Neuropathological observations. *American Journal of Mental Deficiency*, 70, 840-848.

- Stern, Y., Gurland, B., Tatermichi, T. K., Tang, M. X., Wilder, D. and Mayeux, R. (1994). Influence of Education and Occupation on the Incidence of Alzheimer's disease. *JAMA*, 271, 1004-1010.
- Sulkava, R., Wikstrom, J., Aromaa, A., Raitasalo, R., Lehtinen, V., Lahtela, K. and Palo, J. (1985). Prevalence of severe dementia in Finland. *Neurology*, 35, 1025-1029.
- Verhaart, W. J. C. and Jellgersma, H. C. (1952). Early senile dementia in mongolian idiocy. Description of a case. *Folia Psychiatrica Neerlandica*, 55, 453-459.
- Wisniewski, K. E., Dalton, A. J., Crapper-McLachlan, D. R., Wen G. Y. and Wisniewski, H. M. (1985). Alzheimer's disease in Down's Syndrome: clinicopathological studies. *Neurology*, 35, 957-961.
- World Health Organisation (1992). *The ICD-10 Classification of Mental and Behavioural Disorders. Clinical Descriptions and Diagnostic Guidelines*. Geneva: WHO.
- Yates, C. M., Simpson, J., Gordon, A., Maloney, A. F. J., Allison, Y., Ritchie, I. M. and Urquhart, A. (1983). Catecholamines and cholinergic enzymes in presenile and senile Alzheimer-type dementia and Down's syndrome. *Brain Research*, 280, 119-126.
- Zhang, M., Katzman, R., Jin, H., Cai, G., Wang, Z., Qu, G., Grant, I., Yu, E. and Levy, P. (1990). The prevalence of dementia and Alzheimer's disease (AD) in Shanghai, China: impact of age, gender and education. *Annals of Neurology*, 27, 428-437.