Premorbid personality characteristics in Alzheimer's disease: an exploratory case-control study

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Linking data from a case-control study of Alzheimer's disease with data from a Minnesota Multiphasic Personality Inventory (MMPI) outpatient study, we identified 13 Alzheimer's disease cases and 16 controls for case-control comparison. The mean time between personality testing and onset of Alzheimer's disease (or corresponding age for controls) was 13 years in cases and 14 years in controls. Alzheimer's disease cases, but not the controls, had scores significantly greater than the normative reference on MMPI scales measuring Social Introversion ($p = 0.05$), and Pessimism ($p = 0.01$). When compared to controls, Alzheimer's disease cases had significantly greater scores on the Social Introversion scale ($p = 0.03$). Despite the small sample size and some design limitations of this exploratory study, our findings may suggest that subjects who score higher on these personality scales have a greater risk of Alzheimer's disease.

Keywords: Alzheimer's disease – Case-control study – Minnesota Multiphasic Personality Inventory (MMPI) – Pessimism – Premorbid personality – Social Introversion

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INTRODUCTION

Patients with Alzheimer's disease (AD) experience symptoms of depression (Baker *et al.*, 1991; Migliorelli *et al.*, 1995) and a history of depression was found to increase the risk of AD (Jorm *et al.*, 1991; Speck *et al.*, 1995). Personality changes are observed in the progression of dementia in AD (Petry *et al.*, 1989; Siegler *et al.*, 1991; Bózzola *et al.*, 1992; Chatterjee *et al.*, 1992; Strauss *et al.*, 1993; Siegler *et al.*, 1994; Wild *et al.*, 1994); however, whether certain personality characteristics precede the onset of AD has not been established. One study suggested that a history of social and interpersonal inactivity increases the risk of developing AD (Kondo and Yamashita, 1990). Another study suggested that high scores on a personality dimension pertaining to a need to keep other people at a distance, and low scores on a dimension pertaining to mental energy, predicted the development of dementia in women (Persson *et al.*, 1991).

We conducted a case-control study to preliminarily

investigate the association between premorbid personality and AD using two existing data sources available at the Mayo Clinic. The advantage of our study was that personality was measured substantially before AD onset, thus avoiding the possible recall bias and the confusion between premorbid personality and personality changes due to AD.

METHODS

This investigation was based on linking data from two unrelated studies (Swenson *et al.*, 1973; Kokmen *et al.*, 1993). The first study involved 50,000 Mayo Clinic outpatients who were administered the Minnesota Multiphasic Personality Inventory (MMPI) for research purposes between 1962 and 1965 (Swenson *et al.*, 1973). Patients were included in the study from anywhere in the US if they came to the Mayo Clinic for any medical reason other than an acute illness, a

surgical procedure, or hospitalization. Patients referred primarily for evaluation or treatment of any psychiatric disorder were also excluded (Swenson *et al.*, 1973).

The second study involved the 959 patients who developed AD between 1960 and 1984 while residents of Rochester, MN (incident cases). The cases were identified through a review of medical records in the Rochester Epidemiology Project records-linkage system, as described elsewhere (Kokmen *et al.*, 1993). The study also involved 959 subjects free of dementia (controls), each matched to a case by age (± 3 years) and sex, and identified from the same Rochester population through the records-linkage system.

Using the Mayo Clinic identification number, we identified those cases and controls who participated in the MMPI study. However, we excluded cases whose AD onset occurred within 5 years of completing the MMPI. As a result of the linkage, we found 13 cases and 16 controls eligible for the case-control comparison reported in the present study. The original matching of cases and controls was ignored in these analyses.

We analyzed 12 of the 13 basic MMPI scales (excluding the Masculinity-Femininity scale) and the newly-derived Optimism-Pessimism scale (Peterson *et al.*, 1988; Colligan *et al.*, 1994). This last scale was selected because of the hypothesis that pessimism may

be a risk factor for physical illness (Peterson *et al.*, 1988). Raw scores on each scale were transformed into T-scores to adjust for age and sex and to obtain comparability across scales (standardization and normalization of scores) (Colligan *et al.*, 1989). Mean T-scores in cases and controls were independently compared to the normative reference mean of 50 (Colligan *et al.*, 1989). In addition, mean T-scores in cases were directly compared to mean T-scores in controls. Statistical testing was based on two-tailed *t*-tests at the conventional α level of 0.05.

RESULTS

Table I shows that AD cases were similar to controls in age, sex and chronology of testing. The average interval between MMPI administration and onset of AD was 13 years. Table II shows that AD cases had mean scores significantly greater than the reference mean on the scales measuring social introversion-extroversion ($p = 0.05$) and optimism-pessimism ($p = 0.01$), while controls had no significantly elevated mean scores. Consistently, AD cases had a mean score significantly greater than controls on social introversion-extroversion ($p = 0.03$); however, the case-control comparison for optimism-pessimism did not reach statistical significance ($p = 0.19$).

TABLE I. Characteristics of Alzheimer's disease cases and controls

Characteristic	Alzheimer's disease cases (<i>n</i> = 13)	Controls (<i>n</i> = 16)	<i>p</i> ¹
Date of MMPI administration			
Earliest	11/28/62	1/15/63	—
Latest	2/18/65	6/1/65	—
Median	1/24/63	12/16/63	—
Sex			
Women no. (%)	8 (61.6)	9 (56.3)	0.93
Men no. (%)	5 (38.5)	7 (43.8)	—
Age at MMPI administration, mean $\pm$ S.D. Range	64.5 $\pm$ 9.2 (46.9–75.2)	64.3 $\pm$ 10.0 (48.3–80.0)	0.95
Age at AD onset (or index age) ²			
Mean $\pm$ S.D. Range	77.5 $\pm$ 7.1 (63.5–87.2)	78.6 $\pm$ 11.2 (52.0–91.9)	0.76
Years between MMPI and onset of AD (or index age) ²			
Mean $\pm$ S.D. Range	13.0 $\pm$ 4.6 (5.4–20.8)	14.3 $\pm$ 4.7 (3.7–19.5)	0.45

¹ Two-tailed *p* value testing whether the AD cases differ from the controls.

² Index age for a control is the age at which the matched case experienced the onset of AD.

MMPI = Minnesota Multiphasic Personality Inventory.

AD = Alzheimer's disease.

TABLE II. Mean scores of Alzheimer's diseases cases and controls on the scales of the Minnesota Multiphasic Personality Inventory (MMPI)¹

MMPI Scale ²	Alzheimer's disease cases (n = 13)		Controls (n = 16)		Case-control comparison
	Mean T-score* ± S.D.	p ³	Mean T-score* ± S.D.	p ³	p ⁴
L (Lie)	49.0 ± 12.0	0.77	50.2 ± 8.0	0.93	0.75
I (Infrequency)	51.8 ± 9.8	0.51	49.4 ± 6.3	0.73	0.43
K (Correction)	47.1 ± 10.1	0.31	52.9 ± 12.1	0.36	0.18
1 (Hs, Hypochondriasis)	52.3 ± 6.3	0.21	53.3 ± 12.7	0.32	0.80
2 (D, Depression)	55.3 ± 9.9	0.08	51.7 ± 10.0	0.50	0.34
3 (Hy, Hysteria)	49.5 ± 10.5	0.87	53.5 ± 13.4	0.31	0.39
4 (Pd, Psychopathic Deviate)	48.6 ± 15.0	0.74	52.7 ± 8.9	0.24	0.36
6 (Pa, Paranoia)	52.5 ± 10.1	0.39	46.2 ± 10.6	0.17	0.12
7 (Pt, Psychasthenia)	54.2 ± 9.4	0.14	48.9 ± 9.2	0.65	0.14
8 (Sc, Schizophrenia)	51.8 ± 9.1	0.48	47.8 ± 9.8	0.38	0.26
9 (Ma, Hypomania)	43.1 ± 14.3	0.11	47.2 ± 13.4	0.42	0.44
9 (Si, Social Introversion-Extroversion)	54.6 ± 7.7	0.05	47.5 ± 8.5	0.25	0.03
(PSM, Optimism-Pessimism) ⁵	55.7 ± 6.8	0.01	51.5 ± 9.5	0.53	0.19

¹ Raw scores on MMPI scales were transformed in T-scores to adjust for age and sex and to obtain comparability across scales (standardization and normalization of scores) (Colligan *et al.*, 1989). A T-score is a transformation of the raw score that expresses the individual's performance relative to a normative reference group of the same age and sex; SD = standard deviation.

² Scores for the masculinity-femininity scale were not calculated since we combined men and women in our samples.

³ One sample two-tailed *t*-test *p* value comparing mean T-score to the normative reference (mean = 50).

⁴ Two sample two-tailed *t*-test *p* value testing whether AD cases differ from controls.

⁵ The newly developed optimism-pessimism scale is based on 298 MMPI items. The scores on this scale were not age-adjusted.

DISCUSSION

Understanding the personality characteristics that precede the onset of AD may lead to new hypotheses on the etiology of the disease and may influence the management of dementia. In our study, the personality scales were administered long before a diagnosis of AD was suspected (mean 13 years); therefore, our measures genuinely reflect the premorbid status of AD patients. We found that patients who later developed AD had elevated scores, compared to the reference mean, on the MMPI scales measuring social introversion and pessimism. When directly comparing cases to controls, cases scored significantly higher on the Social Introversion scale. The pessimism scores were significantly different at case-reference comparison but only suggestively different at case-control analysis. Our results support the findings that social inactivity or a pessimistic view of life years before the onset of symptoms of dementia increases the risk of developing AD (Kondo and Yamashita, 1990; Persson *et al.*, 1991).

Our study has several methodological limitations and should be considered a preliminary exploration of a hypothesis rather than a hypothesis testing study. First, because subjects in the MMPI study did not undergo a structured psychiatric interview, we cannot

exclude the possibility that the higher scores on the Social Introversion and the Pessimism scale were a reflection of depression rather than of a premorbid personality. However, an effort was made to reduce this problem by excluding from the study patients referred primarily for a psychiatric disease. Secondly, because the overlap between the MMPI study and the AD study was very limited (13 cases and 16 controls), we cannot exclude the effect of an important selection bias. Inclusion in the study required residency of a subject in Rochester at the onset of AD (or equivalent year for controls) between 1960 and 1984. However, residency in Rochester was not required for the MMPI study and it occurred in only 24% of subjects. This geographic mismatch explains, in part, the minimal population overlap of the two studies. Thirdly, 39 hypothesis tests were conducted at the 0.05 α level and three statistically significant results were found; two significant results would have been expected by chance alone. Nevertheless, the consistency of our findings (only the AD patients had significantly elevated mean scores; the social introversion findings were significant both at case-reference and at case-control comparison) encourages us to believe that our results are not statistical artifacts. Finally, due to the small sample sizes, we

had low statistical power to detect other important differences. However, the independent comparison of cases and controls with the normative reference maximized our power.

In summary, our exploratory study adds to the evidence that pessimism and social introversion are risk factors that may precede the onset of AD by many years. This leads to several as yet unanswered questions: are the observed associations due to an unknown bias? Are these personality traits the earliest signs of an evolving AD? Are they a surrogate for an as yet undetermined genetic or environmental risk factor? Further studies are needed to answer these provocative questions.

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