Acta Genet Med Gemellol 41: 187-195 (1992)

Seventh International Congress
on Twin Studies

Risk Factors for Cognitive Aging in Adult Twins

K. Hayakawa[1], T. Shimizu[1], Y. Ohba[2], S. Tomioka[3]

Departments of[1] Public Health, [2]Clinical Pathology, [3]Central Clinical Laboratory, Kinki University School of Medicine, Osaka, Japan

Abstract. Monozygotic (MZ) and dizygotic (DZ) twins in later adulthood were studied in order to examine genetic and environmental contributions to the decline of cognitive performance. In this study, 118 twin pairs took a comprehensive medical examination at a university hospital. Cognitive function was measured by the Wechsler Adult Intelligence Scale (WAIS). The intraclass correlation coefficients on Digit Span (D) and Digit Symbol (DS) subtests of the WAIS did not show any significant difference between MZ and DZ twins although Block Design (BD) showed a significant difference. The values of the intraclass correlation coefficients were mostly around 0.5 and showed significant within-pair similarity of test scores. The mean score of D, DS and BD declined with advancing age. The intraclass correlation coefficients for D, DS and BD were around 0.2 in the MZ twins reared apart, and around 0.6 in the MZ twins reared together. These results indicated a significant environmental influence on cognitive aging in later adulthood.

Key words: Twins, Cognitive Aging, Environments, Risk Factors

INTRODUCTION

The genetic and environmental contributions to the decline of cognitive performance and senile dementia are unknown. Monozygotic (MZ) and dizygotic (DZ) twins in later adulthood provide an outstanding opportunity to examine the influence of genetic and environmental factors on cognitive aging and senile dementia.

The literature on cognitive aging, provides several twin studies conducted from the genetic viewpoint [16,17,23,24], but few [2] from the environmental viewpoint. MZ twins in later adulthood, as special siblings, gentically identical, and almost always living in different environments, can be the most indicative subjects for detecting the risk factors for cognitive aging. In this study, MZ and DZ twins were compared to detect the relative involvement of genetic and environmental influences on the decline of cognitive ability in later adulthood. MZ twins, whose lifestyles differed were also compared in order to detect the influence of each lifestyle on cognitive aging.

METHODS

The subjects were 118 pairs of adult twins aged 50 to 78 years old, recruited from the Kinki University Adult Twin Registry [8-10]. The total Kinki University panel consists of 1982 pairs collected from all over Japan by several means, such as referrals from nurse-midwives, poster advertisements in hospitals, newspaper advertisements, and follow-ups of twin subjects previously studied in collaboration with the retired researchers. These twins have been periodically surveyed on their health condition through mailed questionnaires over twelve years.

From the Kinki University panel, these 118 twin pairs volunteered to undergo comprehensive medical examinations including cognitive ability tests. Cognitive function was measured on three subtests of the Wechsler Adult Intelligence Scale (WAIS) [26]. These were the Digit Span (D), Digit Symbol (DS) and Block Design (BD) tests. The Digit Span test requires the subject to verbally repeat numerical figures, forward or backward, after the examiner. The Digit Symbol test requires the subject to write certain symbols in a given form within 90 seconds and the Block Design test requires the subject to make certain designs with blocks. These cognitive ability tests were conducted by single examiners in order to avoid the influence of examiner differences. The Digit Symbol test which measures psychomotor speed is generally considered the test most sensitive to normal aging. Due to time limits, the Block Design test was conducted on 42 pairs only.

In addition to the cognitive tests, personal interviews were conducted as a general health enquiry into lifestyle factors, family history, medical history, and nutritional intake. Comprehensive medical examinations, including the analysis of blood chemicals, were conducted simultaneously.

The ages of twin subjects varied from 50 to 78 years, with most in their 50s and 60s. Twin zygosity was established from the results of PTC (phenylthiocarbamide) and 9 blood system analysis ABO, Rh (C, c, D, E, e), MN (M,N), Lewis (Le^a, Le^b), P (P_1), Duffy (Fy^a, Fy^b), Kidd (Jk^a, Jk^b), Kell (k) and Diego (Di^a). There were 76 monozygotic pairs (46 male and 30 female) and 21 like-sexed dizygotic pairs (18 male and 3 female). A further 21 unlike-sexed dizygotic pairs were excluded from the data analysis in this study.

The analysis of variance performed according to Snedecor et al [10] produced intraclass correlation coefficients. Skewness and kurtosis of the data distribution were tested by Fisher's cumulative method [14]. The raw data were $\log_{10}$ transformed for the analysis of variance when the distribution of values deviated significantly from the normal standards.

RESULTS

The mean values of the test scores in three age groups were calculated for each of the WAIS subtests. Figure 1 shows the mean values of the three age groups, 50 to 59, 60

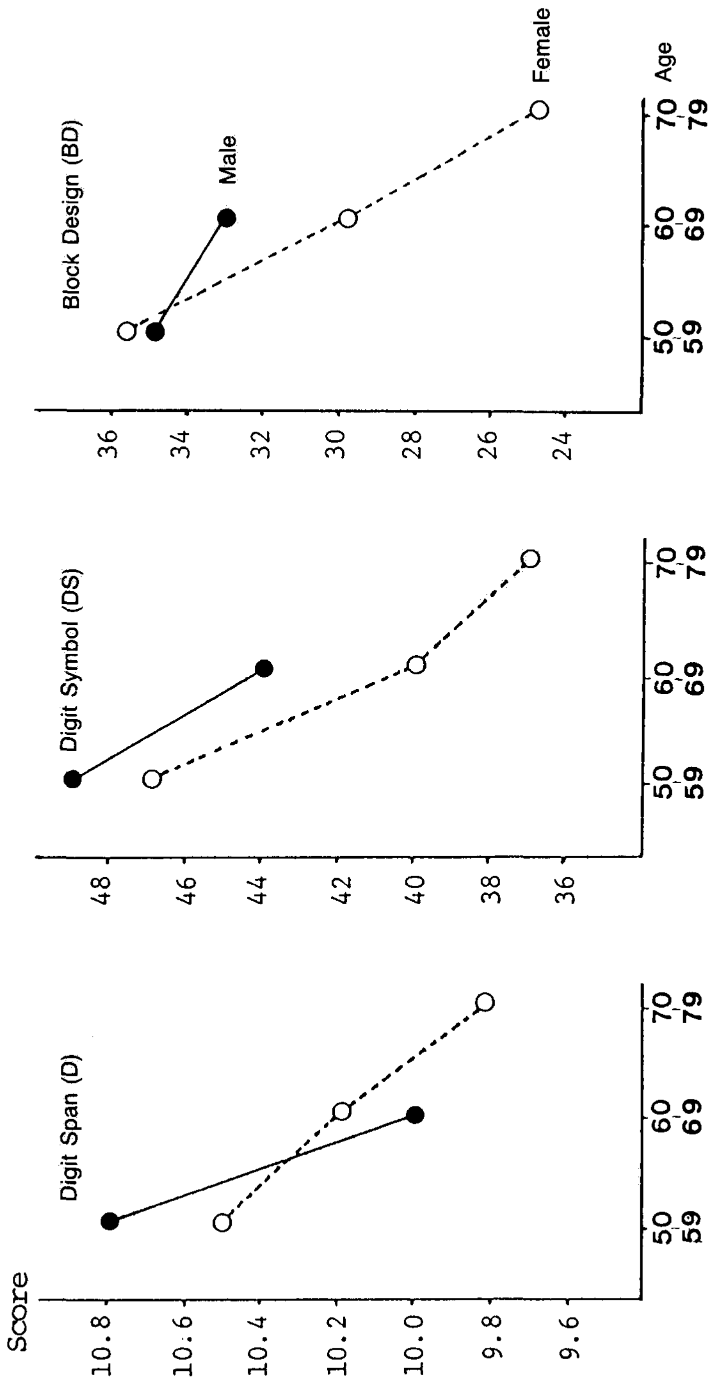

Fig. 1 - Mean values of test scores by age groups in WAIS subtests

to 69 and 70 to 78 years old, respectively. The mean value of D scores dropped from 10.8 ± 1.79 to 10.01 ± 1.59 for the males; and from 10.51 ± 1.55 to 9.83 ± 1.34 for the females. The mean value of DS scores dropped from 48.68 ± 11.29 to 44.01 ± 10.36 for the males, and from 46.86 ± 9.35 to 37.00 ± 7.04 for the females. The mean value of BD scores dropped from 35.02 ± 7.83 to 32.56 ± 7.55 for the males and from 35.88 ± 7.34 to 25.33 ± 3.30 for the females. Each of the three subtests showed a significant ($p < 0.05$) decline of mean values with advancing age.

Intraclass correlation coefficients of test scores were calcualted and compared beteween the MZ and DZ twins. Table 1 shows the intraclass correlation coefficients in D, DS and BD. D did not show any significant difference between MZ (male 0.352; female 0.670) and DZ (male 0.498) twins. Neither did DS show any significant difference between the MZ (male 0.669; female 0.683) and DZ (male 0.559) twins. However, BD showed a significant difference between MZ (male 0.559; female 0.573) and DZ (male 0.165) twins.

Although there was no significant difference between the monozygotic and dizygotic twins in D and DS, the values of the intraclass correlation coefficients were relatively high in all three subtests. There was a significant tendency of intrapair similarity in test scores in all three subtests for the monozygotic twins and in two subtests for the dizygotic twins.

Fig. 2 shows the intraclass correlation coefficients in the test scores by age at separation in the MZ twins. Age at separation means the age when the twin pair separated and began to live apart. The twin subjects whose age at separation was indicated as 0 to 5 years were mostly those who were reared apart from early infancy. Comparing the intrapair similarity by age at separation is an effective method for detecting the degree of influence rearing environments have on childhood.

In this study, the intraclass correlation coefficients tended to rise sharply as the age at separation advanced. This tendency was observed in all three subtests for both the male and female twins with the exception of the BD test for the females. The intraclass correlation coefficient for the male MZ twins rose from 0.009 to 0.575 in D; from 0.05 to 0.781 in DS; and from 0.35 to 0.803 in BD. For the female MZ twins, the intraclass correlation coefficient rose from 0.397 to 0.684 in D and from 0.093 to 0.795 in DS. The intrapair similarity in the MZ twins changed significantly ($p < 0.01$) as age at separation advanced.

Fig. 3 shows the mean values of DS scores in the MZ twins who were discordant on occupation, alcohol consumption and school career. Digit Symbol (DS) scores were compared within the MZ pairs in this study as this test was considered to be the most sensitive index to detect the influence of environmental factors. For the occupation-discordant pairs, the subjects were 11 male MZ twin pairs. Of these pairs, one twin had been engaged in heavy work, such as agricultural or production labour, and the other had been engaged in light work, such as clerical or professional work. The MZ twins engaged in light work showed a higher average score (52.8 ± 10.1) than the MZ twins engaged in heavy work (46.0 ± 6.0). As regards alcohol consumption, the subjects were 24 male MZ pairs. In these pairs, one twin hardly drank at all while the other one drank between 40 and 100 ml of pure ethylalcohol per day. The average score was 53.8 ± 7.4 for the twins of higher alcohol consumption and 49.9 ± 8.6 for the twins of little or no alcohol consumption. The twins of higher alcohol consumption showed a higher average

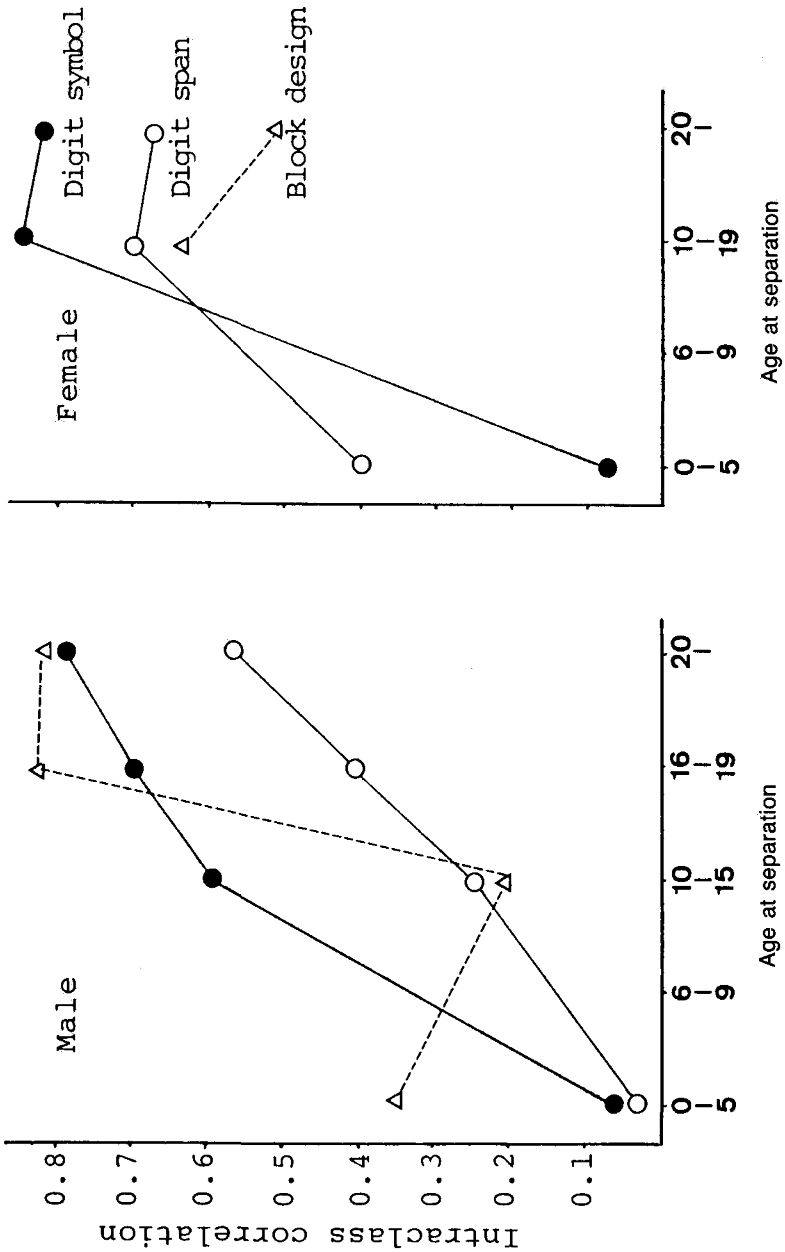

Fig. 2 - Intraclass correlation coefficients of test scores by age at separation in MZ twins

score. In comparing school career, the subjects were 7 male MZ pairs. The length of formal education differed by more than five years within each pair. The average score was 47.2 ± 7.3 in the twins of lower school career and 53.6 ± 13.3 in those of higher school career. Although the difference in mean values of DS was only statistically significant as regards occupation and not so as regards alcohol consumption and school career, a certain degree of environmental influence was recognized in these results.

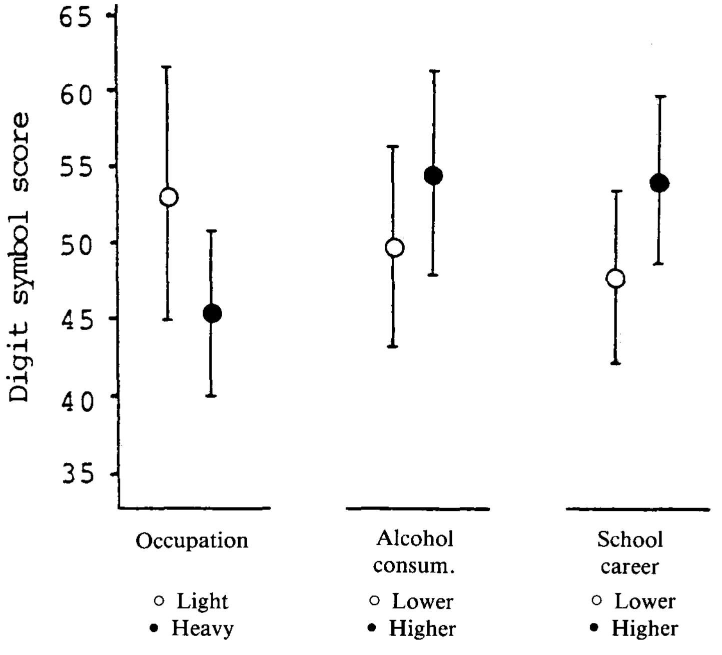

Fig. 3 - Intrapair difference of Digit Symbol scores in the MZ twins discordant on occupation, alcohol consumption, and school career

DISCUSSION

The decline of cognitive ability and the onset of senile dementia is becoming one of the major social issues of today. While genetic research on senile dementia at molecular level has been actively conducted on chromosome 19 and 21 in recent years [6,22], it has become clear that difficulty still remains in identifying the major gene loci responsible for the Alzheimer type of senile dementia. A recent study [19] also indicated the difficulty to clearly differentiate between normal cognitive aging and cognitive disorders in the elderly. In this study, the decline of cognitive ability with aging was studied from the environmental viewpoint. Twin research on MZ pairs has become noted as a very important method in the detection of heredity risk factors and the role of enviromental influence [21].

Three subtests of the Wechsler Adult Intelligence Scale were used to measure the levels of cognitive ability of these three subtests, the results of Digit Symbol are perhaps the most noteworthy, since DS is an index of psychomotor speed and considered to be a sensitive barometer in indicating the decline of cognitive ability in later adulthood [24]. As shown in Fig. 1, all three subtests showed a significant decline in scores as age advanced. The influence of aging was clearly indicated in both the male and female subjects.

Concerning the within-pair similarity of test scores, the intraclass correlation coefficients on D and DS showed a tendency of possible interest to epidemiologists. The results in Table 1 indicated environmental factors, rather than genetic factors, as having a significant influence on the scores of these two subtests. In previous studies on WAIS scores among young twins [1,3,5], the DS tended to show a significantly higher within-pair similarity in MZ than in DZ twins, which would indicate a strong genetic influence. This discrepancy between high similarity in young twins and low similarity in older twins may be the result of the significant decline of cognitive ability which was probably strongly influenced by environmental factors, in the older twins.

Table 1 - Intraclass correlation coefficients of test scores in WAIS subtests on MZ and DZ twins

	Digit Span (D)		Digit Symbol (DS)		Block Design (BD)	
	Male	Female	Male	Female	Male	Female
MZ	0.352	0.670	0.669	0.683	0.599	0.573
DZ	0.498	—	0.559	—	0.165	—

This assumption would seem to find support in the results shown in Fig. 2 which indicated highly similar within-pair test scores in the MZ pairs reared together, while the MZ twins reared apart tended to show quite different scores within the pair. These results strongly indicated that the intrapair similarity of test scores was affected by environmental or lifestyle factors relating to age at separation. Taking the intrapair similarity of lifestyle factors in identical twins, we have reported previously [7,11] that the intrapair concordance rates on occupation, sports activities and food preference tended to rise sharply as the age on separation advanced. These results can be considered as indicating the influence of lifestyle factors on the DS test scores.

Twin researchers might note that it was not rare for Japanese twins born before the Second World War to be reared apart from very early childhood. In my estimation, approximately 10-15% of Japanese twins were reared apart in the era before the Second World War.

As a further examination of the influence of lifestyle factors, the results in Fig. 3 showed an interesting trend among the identical twins discordant on occupation, alcohol consumption and school career. On alcohol consumption, it is well known that heavy drinkers have a tendency to develop brain atrophy with severe cognitive disfunction [13,15], while the effects of mild alcohol intake are not clear. Occupational work load and the levels of school career can be considered as social factors. The influence of these factors on cognitive ability may be interrelated to each other. Some previous studies [18,25] indicated that school career affected cognitive function in later adulthood, while others [4,12] denied the influence of school career.

The number of pairs discordant on each factor was limited in this study, especially on school career. Although a slight tendency of each factor to influence aging cognitive function was seen, more detailed study on each factor could be further explored. The results of this study may be used as the guiding base for future investigation since it is possibly one of the first twin studies on cognitive decline in later adulthood from the environmental viewpoint.

REFERENCES

1. Bouchard JJ, McGue M (1981): Familial studies of intelligence. Science 212: 1055-1059.
2. Breitner JCS, Murphy E, Woodbury MA (1991): Case-control studies of environmental influences in diseases with genetic determinants with an application to Alzheimer's disease Am J Epidemiol 133: 246-256.
3. De Fries JC, Fuker DW, La Buda MC (1987): Evidence for a genetic aetiology in reading disability of twins. Nature 329: 537-539.
4. Fillenbaum GC, Hughes DC, et al (1988): Relationship of health and demographic characteristics to Mini-Mental State Examination score among community residents. Psychol Med 18: 719-726.
5. Fischbein S (1979): Intra-pair similarity in IQ of monozygotic and dizygotic male twins at 12 and 18 of age. Ann. Hum. Biol. 6: 495-504.
6. Goate A, Chartier-Hartin MC, Mullan M, et al (1991): Segregation of a missense mutation in the amyloid precursor protein gene with familiar Alzheimer's disease. Nature 349: 704-706.
7. Hayakawa K and Shimizu T (1987): Blood pressure discordance and lifestyle: Japanese identical twins reared apart and together Acta Genet Med Gemellol 36: 485-491.
8. Hayakawa K (1987): Smoking and drinking discordance and health conditions: Japanese identical twins reared apart and together Acta Genet Med Gemellol 36: 493-501.
9. Hayakawa K, Shimizu T, Ohba Y, Tomioka S (1987): Lifestyle factors affecting intrapair differences of serum apoproteins and cholesterol concentrations in adult twins. Atherosclerosis 66: 1-9.
10. Hayakawa K (1988): Gemellological study on genetic and environmental factors affecting serum concentrations of lipids and electrolytes in adult twins. Jpn J Hygien 43: 763-777.
11. Hayakawa K and Shimizu T (1991): Genetics and environments in twin studies. In Morimoto K (ed.). Lifestyle and Health. Tokyo: Igakushoin pp. 247-257.
12. Holzer CF, Tischer GL, et al (1984): An epidemiologic assessment of cognitive impairment in a community population. In Research in Community and Mental Health (vol. 4), Greenwich: JAI Press.
13. Ishii T (1983): Alzheimer's disease Tokyo: Seiwa Shoten Pub. pp. 32-39.
14. Ishikawa E (1979): New statistics. Tokyo: Maki Publishing.
15. Jorm AF (1991): The epidemiology of Alzheimer's disease and related disorders. Melbourne: Chapman & Hall p. 144.
16. Kallman FJ, Sounder G (1949): Twin studies on senescence. Am J Psychiatry 106:29-36.
17. Kallman FJ, Feingold L, Bondy E (1951): Comparative adaptational, social and psychometric data on the life histories of senescent twin pairs. Am J Hum Genet 3:65-73.
18. Kramer M, German PS, et al (1985): Patterns of mental disorders among the elderly residents of eastern Baltimore. J Am Geriatr Soc 33: 236-245.

19. Rjandal T (1991): Alzheimer's disease: a disease of the elderly or simply aging phenomena (in Japanese) JAMA 3:14.
20. Snedecor GW, Cochran W (1967): Statistical methods (6th ed). Iowa State Univ Press.
21. Stern C (1973): Principles of human genetics (3rd ed.). San Francisco: WH Freeman and Co. pp. 635-684.
22. St. George-Hyslop PH, Tanzi R, Polinsky RJ, et al (1987): The genetic defect causing familial Alzheimer maps on chromosome 21 Science 235: 855-890.
23. St. George-Hyslop PH, Myers RH, et al (1989): Familial Alzheimer's disease; progress and problems. Neurology of Aging 10: 417-425.
24. Swan GE, Carmelli D, et al (1990): Heredity of cognitive performance in aging twins. Arch Neurol 47: 259-262.
25. Yu ESH, Lie WT, et al (1989): Cognitive impairment among elderly adults in Shanghai, China.J Gerontol Soc. Sci. 44: 97-106.
26. Zimmerman IL, Woo-Sam JM (1973): Clinical interpretation of the Wechsler Adult Intelligence Scale. New York: Grune & Stratton.

Correspondence: Prof. K. Hayakawa, Department of Public Health, Kinki University, School of Medicine, 377-Ohno-Higashi, Osaka-Sayama, Osaka 589, Japan.