
The Osaka University Aged Twin Registry: Epigenetics and Identical Twins Discordant for Aging-Dependent Diseases

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The Osaka University Aged Twin Registry (OUATR) is the largest adult twin registry in Japan. Since its establishment in 1974, the OUATR has conducted a number of studies with particular focus on the environmental contribution to physical–cognitive–mental aging, longevity and aging-dependent diseases in later adulthood. The registry consists of 12,000 pairs of Japanese twins born between 1900 and 1935. Two hundred and fifty pairs of twins have undergone comprehensive medical examination to date. Follow-up questionnaires have been mailed out on a regular basis, for the purpose of checking current vital statuses, health conditions, and so forth. The main objective of this longitudinal twin study is to contribute to the prevention of lifestyle-related diseases and the promotion of successful aging.

Scientific interest in twins started developing in Japan in the 1920s. Since then, participants in twin studies conducted in Japan have been almost exclusively young children. The scarcity of twin studies on adult twins is, as in other countries, due to difficulties in collecting a large number of twins in late adulthood. In this regard, the Osaka University Aged Twin Registry (OUATR) has enjoyed a unique position in that it is the only registry in Japan that contains a large number of aged twins. The twin cohort study has been conducted since 1974, with main interest in the influences of environmental factors on physical–cognitive–mental aging, longevity, and aging-dependent diseases in later adulthood. Recently, epigenetic research is underway for the purpose of preventive medicine and health promotion. This article describes the OUATR and its current research results.

Recruitment of Twins

The OUATR was previously called the Kinki University Adult Twin Registry (Hayakawa & Shimizu, 1987). Twin pairs in this registry were recruited by newspaper advertisements, posters in hospitals, referrals from

nurse midwives, and the follow-up of previous studies conducted by retired twin researchers (Hayakawa & Shimizu, 1982). The OUATR consists of approximately 12,000 pairs of twins born between 1900 and 1935 in Japan. Approximately 2500 twin pairs have been followed up via mailed questionnaires each year since 1974. Zygosity was determined using methods previously reported (Hayakawa et al., 1987).

Focus of the Study

The focus of this study is on the environmental factors affecting the aging process of physical–cognitive–mental functions in later adulthood. We have conducted comprehensive medical examinations for 250 pairs of twins in the register. Items included in the comprehensive medical examinations were as follows:

1. Blood
 - (a) Serum concentration (100 items)
HDL-cholesterol, LDL-cholesterol, protein analysis, IgG, A, D, E, blood sugar, apolipoprotein (AI,II, B, C2, C3, E), electrolytes, HbA1c, phospholipids, and so on.
 - (b) Blood cell
RBC, WBC, PLT, and so on.
2. Psychological Tests
Maudsley Personality Inventory (MPI), Wechsler Adult Intelligence Scale (WAIS), Life Satisfaction Index
3. Other Tests
Hearing ability test, electrocardiogram, tapping, grasping power, anthropological measurement, and so on.

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4. Personal interview

Nutritional intake, smoking habits, alcohol intake, food preference, occupation, family tree, and so on.

We have recently started measuring the telomere length of chromosome in peripheral white blood cells, and epigenetic analysis.

Study Results

Two hundred and fifty twin pairs living apart in the community volunteered to visit the university hospitals for comprehensive medical examinations (Hayakawa & Shimizu, 1987). The heritability estimates of more than 100 health indices have been assessed, such as the serum concentration of various lipids, electrolytes, immunoglobulin (G, A, D, E), apolipoproteins (Allison et al., 1996; Hayakawa, 1988; Hayakawa & Sogi, 2000; Shirakawa et al., 1996). Longevity and the decline of cognitive functions with aging have been analyzed from both genetic and environmental aspects. The results of WAIS scores indicated a relatively strong environmental influence on cognitive decline in later adulthood.

Intrapair analysis of adult twins indicated both genetic and family environmental influences on individual differences in health-related behaviors, food preference, and other lifestyle factors in later adulthood (Kato et al., 2002). The concordance rates of causes of death were generally very low even within monozygotic pairs, except those for death by breast cancer (Hayakawa et al., 1992).

Discussion

The main interest of our study is to investigate the process of human aging phenomenon. We plan to clarify the environmental backgrounds of the decline of psychophysiological functions in later adulthood. In this regard, studying of identical twins discordant for the degree of aging is extremely important. An epigenetic study has recently started on methylation and acetylation of the genomic DNA in identical twins discordant for the length of telomere and for aging-dependent diseases. We plan to start a cross-cultural study with identical twin pairs where one member lives in Japan and the other has emigrated to the United States or Brazil before the age of 20.

Collaborations are welcomed and all requests for collaboration should be directed to the first author, and will be assessed by the study's Steering Committee.

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Table 1

Outline of the Osaka University Aged Twin Registry

Name of register	The Osaka University Aged Twin Registry
Country	Japan
Kind of ascertainment	Volunteers (identified by newspaper advertisement, posters in hospitals, referrals from nurse midwives or retired researchers)
Number of pairs	12,000 pairs (monozygotic and dizygotic pairs)
Age	Born between 1900 and 1935
Primary interest	Aging, dementia, longevity, serum lipids, telomere, ATP, phospholipid, life satisfaction, quality of life, aging-dependent diseases
DNA/blood samples	Blood (250 pairs) stored in deep-freezer
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Major source of funding	Government of Japan

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