

The South Korean Twin Registry

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The South Korean Twin Registry (SKTR), previously called the Seoul Twin Family Study, is a nationwide volunteer registry of South Korean twins and their families. Since 2002, the SKTR has been updated in 4 important ways. First, continued sampling led to an increase in the number of twins. Second, the target area, Seoul, was enlarged to include other cities and rural areas in the country. Third, the target population was extended from school-aged twins to preschool and adult twins. Fourth, the research focus was expanded to include psychiatric and physical disease phenotypes. The present article describes a brief history of the SKTR, goals and current research highlights, recent major accomplishments, and future directions.

Brief History

The South Korean Twin Registry (SKTR), previously called the Seoul Twin Family Study (STFS; Hur, 2002), is a nationwide volunteer registry of South Korean twins and their families. In late 2001, the Korea Research Foundation (KRF) provided approximately USD17,000 to the first author (Y. -M. Hur) in support of a twin study of cognitive abilities. South Korea was a new, exciting land for twin research as until then twin studies had been rarely carried out in South Korea. Although the funds provided by KRF were small, the desire of the first author for twin research was not. In an attempt to carry out a large-scale twin study, Y. -M. Hur approached a director of the Seoul Metropolitan Office of Education about the need and importance of twin studies in South Korea, and was able to persuade him to send solicitation letters to all public and private elementary, junior high, and high schools in Seoul to recruit twins for participation in research. As the largest city in South Korea, Seoul has a population of approximately 10 million. Due to this large population, Y. -M. Hur was able to obtain mailing addresses and telephone numbers for over 4500 twin pairs as a result of the solicitation procedure. The SKTR was born from these twins.

In spite of many challenges, the SKTR has continued to grow since its inception. Generous financial

support from various organizations, private donations, self-stimulation, and friendly encouragement were critical to increasing the registry. Media support and counseling services offered to the twins through the SKTR website (www.ktrc.org) and through telephone contact has helped build trust between twins and researchers. The twin participation rate was initially less than 20%. For the past 4 years, the rate has increased steadily, and is often over 50%.

In 2005 we started to expand the SKTR to include preschool twins and school-aged twins residing in various cities and counties in South Korea to obtain a nationally representative sample of South Korean twins and to replenish twins whose contact information had been lost due to moving or other reasons. The number of adult twins in the SKTR has increased as twin participants age, and also as a result of twin volunteers who have contacted us for participation in research.

The research scope of the SKTR has also been broadened during the past 4 years. Initially, the focus of the SKTR was on cognitive abilities; however, over the past 4 years the SKTR has been increasingly involved in a variety of research issues for the South Korean population.

In summary, since the publication of the paper in 2002 (Hur, 2002), the SKTR has been updated in four important ways. First, continued sampling has led to an increase in the number of twins. Second, the target area, Seoul, was enlarged to include other cities and rural areas in the country. Third, the target population was extended from school-aged twins to preschool and adult twins. Fourth, the research focus was expanded to include psychiatric and physical illnesses.

Major Goals and Current Research Highlights

The general goal of the SKTR is to understand the genetic etiologies of various mental and physical illnesses and normal psychological and physical traits. We believe that advances in understanding the genetic etiologies of these diseases and traits will enable us to

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develop optimal prevention, intervention, diagnostic, and therapeutic strategies for various human diseases. The present section provides a brief overview of SKTR current research highlights.

Genetics of Personality, Cognitive Abilities and Psychiatric Disorders

It has been proposed that personality traits and cognitive abilities are endophenotypes of various psychiatric disorders (Gould & Gottesman, 2006; Saperstein et al., 2006). In order to examine the role of personality traits and cognitive abilities in the development of psychopathology, we have collected or are currently collecting normal personality traits (Eysenk Personality Questionnaire; Eysenck & Eysenck, 1975), life satisfaction and happiness, hostility (Koskenvuo et al., 1988), morningness–eveningness (Composite Scale; Smith et al., 1989), life events, puberty as well as depression (Center for Epidemiological Studies — Depression; Radloff, 1977), obsessive-compulsive disorders (Maudsley Obsessive-Compulsive Inventory; Hodgson & Rachman, 1977), substance use and abuse, internalizing and externalizing problem behaviors (Child Behavior Check List; Achenbach, 1992), and other psychiatric data. While we continue to collect phenotype data from twins, we are planning to collect buccal swabs for the collection of DNA in the near future. With these resources, we aim to (1) identify genes for various psychiatric illnesses, personality, and cognitive abilities, (2) determine the role of puberty at the onset of psychiatric diseases, (3) examine gene–environment interactions for the development of psychiatric diseases using both biometric models (Purcell, 2002) and analyses of the candidate genes and measured environments (Moffitt, 2005), and (4) study genetic causation of the comorbidity of psychiatric illnesses using both quantitative modeling (Neale & Cardon, 1992) and multivariate linkage analysis.

Prenatal Influences on Psychological and Physical Health Outcomes

As we explain below, obstetric records of the twins during the prenatal period are available for the majority of the preschool twins. The obstetric records include information on chorion type, birthweight, gestational age, Apgar score, and so forth. Using these data, we plan to investigate (1) the effects of chorion types on physical and mental health outcomes including cognitive abilities and personality by comparing similarities on these variables between mono- and dichorionic monozygotic (MZ) twins, (2) a possible intrauterine hormonal influence on the development of psychological and physical traits by comparing opposite- and same-sex dizygotic (DZ) twins, and (3) the associations between intrainpair differences in fetal growth and differences in later health outcomes using MZ twins discordant for various prenatal variables. To this end, we are currently collecting data on temperaments (Emotionality, Activity, and Sociability; Buss & Plomin, 1984), prosocial activity, body height, weight, asthma, allergic rhinitis, and eczema (International Study of Asthma and Allergies in Childhood; Asher et al., 1995).

Genetic and Environmental Interactions for the Development of Asthma and Allergic Diseases

Asthma is a complex disease in which environmental agents are thought to interact with genetic factors that influence susceptibility (Duffy et al., 1998; Nystad et al., 2005). Over the past two decades, there has been a steady increase in the prevalence of asthma in many developing countries (Asher et al., 2006). To study genetic and environmental causation of asthma and allergic diseases in the South Korean population, we are currently collecting asthma, allergic rhinitis, and the eczema data from the preschool and school-aged twins. We also plan to invite a subset of twins to our laboratory in future for the skin prick, methacholine inhalation, and pulmonary function tests.

Genetic Influences on Ethnic Variations of Physical and Psychological Traits and the Risk and Protective Factors for the Development of Diseases

The causal basis for the ethnic differences in psychological and physical traits and risk and protective factors for the development of various diseases has recently been the focus of heightened discussion (Bonham et al., 2005; Risch, 2006). Many genetic studies of populations have demonstrated allelic frequency variation among ethnic groups (Palmatier et al., 1999). Furthermore, studies have found that some risk alleles are population-specific such that the same allele is associated with different disease outcomes in different populations (Gonzalez et al., 1999). The normal traits and disease data collected through the SKTR are open to studies of genetic and environmental influences on the ethnic variations of psychological and physical traits and risk and protective factors for diseases. We are interested in exploring ethnic differences for these variables at both quantitative and molecular genetic levels.

Recently, in collaboration with twin researchers from several different countries, we explored differences in genetic and environmental variances of the birthweight between Caucasians and East Asians, the results of which are briefly summarized below. As an extension of the birthweight study (Hur et al., 2005), we are currently investigating differences in genetic and environmental variances regarding the body mass index (BMI) between Caucasians and East Asians.

Study Design, Zygosity Determination, and Recruitment

Twins in the SKTR are recruited from a variety of sources including the medical records of maternity hospitals, twin mothers' clubs, media advertisements, and kindergartens and schools throughout South Korea. Thus, twin participants in the SKTR vary from preschool children to adults and include both same- and opposite-sex twins. This recruitment strategy allows researchers to assess same- and opposite-sex twins during childhood, adolescence, and adulthood and examine age-associated genetic and environmental influences on normal behaviors and disease pheno-

types as well as sex-specific genetic and environmental effects on these phenotypes.

During the recruitment, we make efforts to identify high risk twin families where twins and/or biological relatives of the twins have been diagnosed as mentally ill or have developed severe physical illnesses. These resources will be extremely useful not only for gene identification studies but also for gene expression studies that we hope to carry out in future.

As DZ twinning rates are relatively low in South Korea (Hur & Kwon, 2005), whenever possible, the SKTR attempts to include siblings of twins to complement the DZ twins. The recruitment of the SKTR is ongoing in order to include twins broadly representative of the South Korean population as well as to increase sample sizes needed to resolve various important research issues.

Twins' zygosity in the SKTR was determined from the twins' parents' responses to a zygosity questionnaire that contains questions regarding physical similarities and the frequency of confusion by family members, relatives, and friends of the twins and others. When compared to serological tests, the questionnaire method in determining zygosity has yielded over 90% accuracy in Asian twin samples (Ooki et al., 1993).

The twins in the SKTR can broadly be divided into three age groups: preschool twins, school-aged twins, and adult twins. The following section briefly describes major recruitment strategies and the current recruitment status of each age group of the SKTR.

Preschool Twins

The preschool twin group of the SKTR largely consists of those twins aged 6 years or younger. The preschool twins in the SKTR have been identified mainly through the medical records of a maternity hospital located in Seoul, and kindergartens and twin mothers' clubs throughout South Korea. The medical records obtained included contact information for the mothers of twins who were born in the maternity hospital between 1999 and 2005. Recently, due to the efforts of Dr. Shin (second author), another large maternity hospital in Seoul has agreed to provide contact information for twins born in the hospital from 2007. For this reason, we expect that the sample size of the preschool twins registered with the SKTR will grow rapidly in future.

In order to access twins from kindergartens, we are sending solicitation letters to kindergartens whose telephone numbers are registered with the Offices of Education in cities and counties in South Korea. The head of each kindergarten is asked to deliver the solicitation letters to mothers of twins enrolled in his/her kindergarten. When the head of a kindergarten obtains permission from the twin mothers, he/she provides us with the twins' contact information. To access twins from the twin mothers' clubs, we advertised our website information on the websites of the twin mothers' clubs so that mothers of the twins who were

Table 1

Number of Preschool Twin Pairs (age ≤ 6 years) Registered with the SKTR as of July 2006 by Sex and Source of Recruitment^a

Source of the Recruitment	MM	FF	MF	Total
Maternity Hospital	351	366	393	1110 (67%)
Kindergartens and Twin mothers' clubs	328	130	86	544 (33%)
Total	679	496	479	1654 (100%)

Note: MM = male–male twin pairs; FF = female–female twin pairs; MF = male–female twin pairs.

^aAs of July, 2006, zygosity was determined for 741 pairs (44.8%) of the preschool twins.

interested in participating in the research could contact us.

As of July, 2006, 1654 pairs of preschool twins (679 male–male, 496 female–female, and 479 male–female pairs) are registered with the SKTR (Table 1). Of these twins, 1110 pairs (67%) were identified through medical record contact information from the maternity hospital, and the remaining 544 pairs (33%) from kindergartens and twin mothers' clubs throughout South Korea. We are currently conducting initial telephone interviews with mothers of the preschool twins to obtain zygosity and other information on the twins and their families. Opposite-sex twins are classified as DZ twins. As of July 2006, zygosity had been determined for 741 pairs (44.8%) of the 1654 pairs of preschool twins.

School-Aged Twins

The school-aged twin group of the SKTR largely comprises twins aged between 7 and 18 years. Table 2 provides the number of school-aged twins registered with the SKTR as of July 2006, divided by sex and school. In total, 8412 school-aged twin pairs (3327 male–male, 3803 female–female, and 1282 male–female pairs) are currently registered with the SKTR. The school-aged twin group in Table 2 is composed of those twins who were recruited through the Seoul Metropolitan Office of Education in 2001 (Hur, 2002) and are of school age as of July 2006, and twins who had been newly recruited from schools nation-

Table 2

Number of School-Aged Twin Pairs (7 yrs ≤ age ≤ 18 yrs) Registered with the SKTR as of July 2006 by Sex and School^a

School	MM	FF	MF	Total
Elementary	1483	1572	803	3858
Junior High	1050	1239	294	2583
High	794	992	185	1971
Total	3327	3803	1282	8412

Note: MM = male–male twin pairs; FF = female–female twin pairs; MF = male–female twin pairs.

^aAs of July, 2006, zygosity was determined for 3691 pairs (44%) of the school-aged twins.

wide since early 2005. For the recruitment of twins initiated in early 2005 we used a procedure similar to the one described in Hur (2002).

For the purpose of administration, South Korea is divided into seven metropolitan cities (Busan, Daegu, Daejeon, Kwangju, Incheon, Seoul and Ulsan) and nine counties (Kangwon, Kyunggi, Kyungnam, Kyungbuk, Jeonnam, Jeonbuk, Chungnam, Chungbuk, and Jeju). In the new recruitment procedure, we asked Offices of Education in the seven metropolitan cities and nine counties to send letters to elementary, junior high, and high schools in their cities and counties to encourage them to provide us the contact information of the twins enrolled in their schools. Offices of Education from all of the seven metropolitan cities and six of the nine counties (Kangwon, Kyunggi, Kyungnam, Kyungbuk, Jeonnam, & Jeju) agreed to send letters to the schools in their cities and counties to help recruit twins. However, the Office of Education in Incheon city sent letters only to high schools, and Ulsan city only to elementary schools.

On the basis of the Office of Education letter, schoolteachers who had twins in their classroom explained the SKTR research purpose and asked twins to obtain permission from their parents to participate in research. As societal concerns over privacy have increased in recent years, recruitment has moved more slowly than we originally expected. As of July, 2006, contact information for twins from 1202 schools (265 high, 351 junior high, and 586 elementary) had been received. Among those schools that did not return the twin contact information, schools where more than 1000 students were enrolled were selected and asked over the phone to provide contact information of twins if they had twins enrolled in their schools. While making efforts to contact schools to acquire the twin contact information, initial telephone interviews of parents of the newly registered twins were started to obtain information on twin zygosity and other data. As of July 2006, zygosity was determined for 3691 (44%) of the 8412 pairs of the school-age twins.

Adult Twins

The total number of adult twin pairs registered with the SKTR as of July 2006, is 647 pairs. The SKTR adult twin group is made up of twins who are currently between 19 and 26 years. About 92% of these twins were recruited through the Seoul Metropolitan Office of Education in the year 2001, and the remaining twins were volunteer twins who contacted us for participation in the research. The zygosity of the majority of adult twins was already determined: 416 MZ pairs include 176 pairs of male twins and 240 pairs of female twins, and 183 DZ pairs include 50 pairs of male and 58 pairs of female same-sex twins and 75 pairs of opposite-sex twins. Currently, we have 48 pairs of adult twins whose zygosity has not yet been determined. Adult twins clearly show an overrepresentation of MZ twins, which reflected the natural twinning rates in South Korea for these cohorts (Hur & Kwon, 2005).

Major Accomplishments

In an attempt to carry out twin studies systematically, twin birth rates in the South Korean population were examined over the past two decades and it was found that although twin birth rates had been traditionally low in South Korea, twinning rates had recently increased sharply, confirming the feasibility of conducting large-scale twin studies in South Korea (Hur & Kwon, 2005). This investigation also enabled us to examine the selection bias of the twin samples used in subsequent studies in terms of zygosity.

Using parents of twins, we investigated the practice of assortative mating for personality traits, educational level, religious affiliation, height, weight, and BMI in the South Korean population. Degrees of assortative mating for these traits were very similar to those found in Western samples, suggesting that assortative mating may affect heritability estimates in the South Korean population to the similar degree as in Western populations (Hur, 2003).

In addition, we have explored genetic and environmental influences on birthweight (Hur et al., 2005), BMI (Hur, Ando, et al., 2006), coldness of hands (Hur, Kim, et al., 2006), self-concept (Hur, 2005), morningness-eveningness (Hur, 2006b), hostility (Hur, 2006a), and neuroticism and obsessive-compulsive disorders (Hur & Lee, 2006). Overall, we found modest to substantial genetic influences on individual differences in these traits in South Korean twins, suggesting that heritability estimates for various traits found in Caucasian twins may be well generalized to the South Korean population. We also compared various dimensions of self-concept between elementary school twins and singleton children and found that in general, twins had slightly higher self-concepts than singletons during the elementary school period suggesting that the twin situation may have a positive impact on the development of children's self-concept (Yoon & Hur, 2006).

In collaboration with twin researchers in Australia, the Netherlands, Japan, and the United States, we compared genetic and environmental variances in birthweight between Caucasians and East Asians using adolescent twin data. The results showed that the variance of birthweight was larger in Caucasians than in East Asians and that this difference was largely attributable to a greater shared environmental (i.e., intrauterine environmental) variance of birthweight in Caucasians. As female prepregnancy weight has been shown to be a strong predictor of fetal growth, we speculated that differences in frequency of maternal genes between Caucasians and East Asians might be responsible for the difference in shared environmental variance in birthweight found between Caucasians and East Asians (Hur et al., 2005).

Future Directions and Opportunities for Collaboration

Although the SKTR has collected mainly phenotypic data on twins so far, plans are underway for the

establishment of a biobank and extensive genotyping in order to examine polymorphisms that are associated with normal behavioral traits and diseases. Other potential avenues for research include studies of gene expression including epigenetic processes. An important feature of the South Korean population is its ethnic homogeneity, which will undoubtedly facilitate identification of genes for complex phenotypes.

In future, we hope to conduct longitudinal studies on a subset of twins registered with the SKTR from childhood to adulthood to investigate genetic changes and continuity during development from both quantitative and molecular genetic perspectives.

The SKTR is open to students who work in various fields of science, and collaborations with groups worldwide. Although the vast majority of twin studies so far have been carried out in Western countries, the number of twin studies in Asian countries has recently begun to rise. Along with several twin registers in Asia, the SKTR has increased numbers of twin families and has been fruitful for the past 4 years. We hope that the journey of the SKTR, driven by the spirit of science, will continue in the future by accepting new students, creating novel fields of research, and contributing to the well-being of global communities.

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