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The Beijing Twin Study (BeTwiSt): A Longitudinal Study of Child and Adolescent Development

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Rates of emotional and behavioral problems among children and adolescents in China are increasing and represent a major public health concern. To investigate the etiology of such problems, including the effects and interplay of genes and environment, the Beijing Twin Study (BeTwiSt) was established. A representative sample of adolescent twins in Beijing ($N = 1{,}387$ pairs of adolescent twins, mostly between the ages of 10 and 18 years) was recruited and assessed longitudinally. Data collection included the following: emotional and behavioral problems (e.g., depressive symptoms, anxiety, delinquency, drinking, and smoking); family, peer, and school environments; stress; social and academic competence; cognitive traits (e.g., emotion suppression, rumination, and effortful control); and saliva samples for DNA genotyping and sequencing. The combination of quantitative and molecular genetic approaches and the timeliness of the project, with the sample residing in a region with a rapidly changing economic and cultural climate, are particular strengths of this study. Findings from this study are expected to help understanding of the etiological mechanisms underlying child and adolescent normal and abnormal development in regions undergoing substantial social, cultural, and economic changes.

■ **Keywords:** BeTwiSt, twin study, Beijing, adolescent, psychopathology

Child and adolescent psychopathology in China has received increasing attention from academic, social, clinical, and policy communities. The prevalence data suggest that more than 30 million Chinese children and adolescents under age 17 are affected by emotional and behavioral problems (Fourth International Conference on Child and Adolescent Psychopathology, 2009), which is about three times greater than the same population in the United States (Merikangas et al., 2010). Child and adolescent psychopathology has both short- and long-term deleterious impacts (Merikangas et al., 2009), and youth mental health has become a topic of major public health concern in China. An improved understanding of the etiological mechanisms underlying child and adolescent psychopathology — especially how these mechanisms function in the context of China's rapid economic growth and social changes — may contribute to the development of empirically based prevention and intervention programs in China. Given that psychopathology is likely to be a developmental product of the complex interplay of genes and environment, a longitudinal study enriched by behavioral, genetic, and environmental measurement can help further the understanding of the etiology of child and adolescent mental health problems.

As an 'experiment of nature', twin studies have been a valuable tool for investigating the genetic and environmental origins of human behavior (Boomsma et al., 2002; Rutter et al., 1993). Over the past few decades, a number of well-designed twin studies have been conducted on child and adolescent psychopathology (see Table 1), mainly in the United States and Europe (Bartels et al., 2007; Eaves et al., 1997; Hewitt et al., 1997; Iacono et al., 2006; Kaprio, 2006; Lemery-Chalfant et al., 2006; Lichtenstein et al., 2007; Neiderhiser et al., 2007; Trouton et al., 2002; van den Bree et al., 2007), with a few studies in Asia and Australia (Ando et al., 2006; Bennett et al., 2006; Huang et al., 2009; Hur

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TABLE 1

Twin Studies on Child and Adolescent Psychopathology Across the World

Registry	Primary interests	Sample	Country
Australian Twin ADHD Project (ATAP)	Attention Deficit Hyperactivity Disorder (ADHD), Conduct Disorder (CD), Obsessive Compulsive Disorder (OCD),Generalized Anxiety Disorder(GAD)	Child and adolescent twins	Australia
Cardiff study of All Wales and North West of England Twins (CaStANET)	Depression, anxiety, ADHD, CD, substance abuse	Child and adolescent twins	UK
Colorado Twin Registry (CTR)	Early cognition, executive function, antisocial behaviors	Infant, child, and adolescent twins	USA
FinnTwin12 and FinnTwin 16	Substance abuse, mental health	Two cohorts (12 and 16 years old)	Finland
Minnesota Twin Family Study (MTFS)	Psychopathology, psyshophysiological endophenotypes	11-, 17-year-old twins and parent	USA
Nonshared Environment in Adolescent Development (NEAD) project	Family relationships, adolescent adjustment, and competence	10–18 years old siblings varied in degree of genetic relatedness	USA
Quebec Newborn Twin Study (QNTS)	Emotional and behavioral development	Infant twins	Canada
South Korean Twin Registry (SKTR)	Personality, cognitive abilities, psychiatric disorders	Child, adolescent, and adult twins	South Korea
Swedish Twin Study of Child and Adolescent Development	Health and behavioral problems from childhood to adulthood	Twin pairs from childhood (age 8–9)	Sweden
Taipei Adolescent Twin/Sibling Family Study	Behavioral problems, personality and emotion problems	Twin pairs (12–16 years old)	Taiwan
Tokyo Twin Cohort Project	Behavioral, neurological, physical development	Infant twins	Japan
Twin's Early Development Study (TEDS)	Language, cognitive and academic abilities, and behavior problems	Child twins from 2 years old	UK
Twin Registry in Southwestern China (TRiSC)	Behavioral development and cognitive abilities	Child and adolescent twins (0–16 years old)	Mainland China
Virginia Twin Study of Adolescent Behavioral Development (VTSABD)	Childhood and adolescent psychiatric disorders, such as Major Depressive Disorder (MDD), Separation Anxiety Disorder (SAD), ADHD, and CD	8–16 years old twin pairs	USA
Wisconsin Twin Project (WTP)	Psychopathology and emotional development	Child and adolescent twins	USA
Young Netherlands Twin Register (Y-NTR)	Internalizing and externalizing behaviors	Child twins from 2 years old	Netherland

Note: The twin studies are listed alphabetically.

et al., 2006; Kuo et al., 2006). These studies have contributed significantly to the field by disentangling the intertwined roles of genetic and environmental factors in complex human traits, as well as by providing new information about the complex interplay between genes and the environment.

In contrast to the proliferation of twin studies in Western countries, the twin study approach to understanding the etiology of psychopathology has only recently been adopted in China. Findings from Western twin studies may not be readily translated to the Chinese context for several reasons. Most importantly, the context surrounding twins and their families in China is culturally unique. As a result of China's strict one-child policy, the majority of Chinese families (especially those in urban areas) have only one child, with the exception of families with twin children (Falbo & Poston, 1993). Therefore, knowledge of family environments, particularly sibling interactions, cannot be readily introduced from Western countries to China; the knowledge must originate directly from a Chinese context. Second, the prevalence of certain alleles has been shown to differ between China and Western countries. For example, population frequency data has shown that the ALDH2*487Lys allele, which is related to protection against alcohol dependence, is extremely rare in Europeans but is widely prevalent among East Asians (Goedde et al., 1992). The BDNF Met66 allele, which is related to depression, has also shown higher prevalence in East Asians than in Europeans (Petryshen et al., 2009). Finally, and perhaps most obviously, developmental contexts, such as cultural norms and values, differ between China and Western countries (Chen & French, 2008), which may have differing effects on the development of psychopathology. Hence, studies based on a genetically informative design, such as twin studies, are needed to clarify how genes, environment, and their interplay influence the development of psychopathology in children and youth in Chinese population.

Despite their importance, twin studies on psychopathology and psychological development of Chinese youth, especially studies with a longitudinal component that incorporate a molecular genetic approach, are lacking. To fill this gap, a longitudinal twin project, the Beijing Twin Study (BeTwiSt), was launched in 2005. The overarching goal of the BeTwiSt is to prospectively investigate genetic and environmental influences on developmental psychopathology among Chinese youth between the ages of 10 and 18 years old. To our knowledge, the Twin Registry in Southwestern China (TRiSC; Huang et al., 2009), which mainly focuses on child cognitive ability and behavioral development, and the BeTwiSt are the only projects that investigate child and adolescent psychopathology in Mainland China. Each study focuses on different aspects of development, with the BeTwiSt specializing in emotional and behavioral problems and their correlates.

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The conceptual model for the BeTwiSt is based on the following hypotheses: (a) most types of psychopathology are influenced by genes (G), environment (E), and their interplay (G × E interaction and GE correlation); (b) change and continuity in psychopathology are influenced by both genes and environment; and (c) regulatory processes (e.g., emotional suppression and effortful control) may mediate or moderate the influence of genes, environment, and their interplay on psychopathology. We focus on two major developmental pathways: internalizing and externalizing problems. Other related problems, such as substance use, Internet use, and sleeping disorders, are also of interest.

Research Aims

The BeTwiSt is guided by three primary aims. The first aim is to understand how genes, environment, and their interplay affect adolescent psychopathology (Aim 1). There is a great consensus that most psychopathologies result from genetic and environmental influences and their interplay. However, the specific genetic and environmental factors that play these key roles in the development of psychopathology and how they do so continue to be poorly understood. The BeTwiSt examines the effect of specific genetic and environmental factors. Moreover, this study examines the genetic homogeneity between different types of psychopathology to suggest possible avenues for molecular genetic research, given the evidence of multi-finality (i.e., different outcomes from a single etiology) in the development of psychopathology.

The second aim is to investigate the effects of genes, environment, and their interplay, as identified in Aim 1, in a longitudinal framework (Aim 2). A growing body of evidence suggests that the heritability of psychopathology, including anxiety, depression, and externalizing behaviors, increases during the transitional period from adolescence to adulthood (Bartels et al., 2007; Rice et al., 2003; Van Beijsterveldt et al., 2003). Furthermore, the development of psychopathology during the transition from childhood to adolescence seems to be affected by both age-stable and age-specific genetic effects (Kendler et al., 2008; Lichtenstein et al., 2007). However, the mechanisms that are responsible for this changing heritability during developmental transitions remain unclear. The longitudinal design of the study will permit an examination of developmental changes and stability of genetic and environmental influences on psychopathology from adolescence to adulthood in China.

The third aim is to examine the role of regulatory processes in mediating the effects of genes, environment, and their interplay on psychopathology (Aim 3). Before any palpable symptoms are manifested, compromised development of emotional, cognitive, and behavioral regulatory processes may occur, presaging the subsequent psychopathology (Cicchetti & Toth, 2009). In fact, empirical studies have shown that several maladaptive processes, such as emotional suppression, rumination, dysfunctional attitude, and low effortful control, are associated with adolescent internalizing and externalizing psychopathologies (Aldao et al., 2010; Eisenberg et al., 2009; Hilt et al., 2010). Examining the genetic and environmental origins of these hypothesized regulatory processes will advance our understanding of the developmental pathways of psychopathology and may contribute to the development of prevention and intervention strategies to reduce rates of psychopathology in China.

Design and Methods of the BeTwiSt

The BeTwiSt is founded on four methodologically unique features. First, this study is based on a large, representative twin sample from Beijing, China. To ensure representativeness, over 600 public schools were randomly selected from all 18 districts and counties in Beijing municipality. All twins aged 10–18 years old in these schools were invited to participate in the study. The representativeness of the sample was ensured via the comparison of this sample to a population-based school student sample in Beijing (see below). Second, the BeTwiSt utilizes a longitudinal design. Currently, the twins have been assessed twice (the T0 [pilot] and T1 assessments) within a 1.5-year interval. We are in the process of collecting the T2 data that focuses on young adulthood, which will allow for an investigation of developmental stability and change in genetic and environmental effects on emotion and behaviors across adolescence and adulthood. Third, the BeTwiSt includes both quantitative and molecular genetic approaches. Quantitative genetic analyses are useful in defining heritable phenotypes and selecting appropriate sub-samples for molecular genetic studies (Wood & Neale, 2010). Molecular genetic analyses allow for an investigation of interactions between specific genes and measured environment (Caspi & Moffitt, 2006; Dodge, 2009; Moffitt, 2005). The combination of the two approaches will provide more information than the use of a single approach. Fourth, multiple informants, including parents, twins, and teachers, participated in the study. The use of multiple reporters partially resolves rater bias in assessment and captures a more comprehensive view of children's emotion and behaviors in different contexts (e.g., home, school, and society; Achenbach, 2006; De Los Reyes, 2011).

Recruitment

A pilot survey (the T0 assessment) was conducted during the 2006–2007 school year, followed by a comprehensive survey (the T1 assessment) during the 2008–2009 school year. The purpose of the T0 assessment was to establish a feasible and efficient recruitment procedure and to obtain basic demographic information about adolescent twins in Beijing. In the T0 data collection, 620 elementary and secondary schools were randomly selected from all 18 districts

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and counties in Beijing municipality, and 1,675 pairs of twins enrolled in these schools were identified and recruited as the T0 sample. All 1,675 pairs of twins at T0 completed a brief self-report questionnaire.

In the T1 assessment, we contacted the families from the T0 sample by mail or telephone and invited them to participate in the longitudinal part of the project. Of the 1,675 pairs from the T0 sample, 806 pairs and their parents agreed to participate, representing a 48.1% participation rate. The remaining 869 pairs in the T0 sample refused to participate in the study, either because they were reluctant to provide saliva samples or they decided not to commit to a longitudinal study. To supplement the attrition rate, 581 additional pairs of twins were recruited through a procedure similar to the T0 recruitment methods. Therefore, the full T1 sample (the core BeTwiSt sample) consists of 1,387 families, each of which has one participating twin pair. Both twins and at least one parent participated in the T1 assessment. The BeTwiSt is now in the process of following the core sample in a new wave of assessment (T2) during the transition to young adulthood.

Assessment Procedures

For the T0 assessment, we obtained informed consents from the twins and the school administrators. Then twins completed a brief questionnaire after school. For the T1 assessment, after obtaining written informed consents from the twins and their parents, arrangements were made for the twins to stay in their classrooms after school. After describing the purpose and procedures of the study, trained research staff distributed the questionnaires to the twin participants and instructed them to complete the questionnaires independently. Research staff members were present to answer any questions that the students might have about the questionnaires. After the twins completed the questionnaires, they were asked to provide saliva samples using the Oragene DNA self-collection kit (DNA Genotek Inc., Ontario, Canada). Questionnaires for parents were taken home by the twins and were mailed back to our laboratory. The T2 assessment, which is currently ongoing, takes place in the twins' homes. Two research staff members visited each family in their home to administer the assessment. The confidentiality and anonymity of the participants' genetic information and their responses to the questionnaires are ensured. The Institutional Review Board has approved all research protocols for BeTwiSt.

Overview of Measures

Despite the ongoing debate over the dimensional or categorical view of psychopathology, scholars have accepted the notion that normal and abnormal trait variation can be treated within a single, unified structural framework and that abnormal traits can be modeled as extremes of normal trait variation (Hudziak et al., 2007; Krueger et al., 2005). In fact, a growing body of evidence suggests continuous liability between normal and abnormal traits, which may be subject to the influence of similar genes and environmental factors (Rutter, 2011). Hence, the BeTwiSt adopts a dimensional view of psychopathology when assessing children's emotion and behaviors. Table 2 summarizes the variables of interest.

When applicable, multiple informants provided information. The twins, parents, and teachers rated the twins' emotional and behavioral outcomes, which included both internalizing (depression and anxiety) and externalizing problems (aggression, delinquency, and attention problems). The participation rates of parents and teachers were 99% and 64%, respectively. Children also reported their smoking and drinking behaviors, sleep problems, and Internet use. Environmental factors, such as stressful life events, parenting practices, deviant peer affiliation, and sibling interactions, were reported by both children and parents. Children reported cognitive and emotional factors (e.g., emotional regulation strategies, rumination, dysfunctional attitudes, and effortful control) that putatively link genes and environment to psychopathology. Fathers and mothers also reported their own emotional and behavioral problems, such as depression, anxiety, hostility, smoking, and drinking behavior. Finally, information about the children's height, weight, and pubertal status were collected to reflect their physical development. Genomic DNA was extracted from the participants' saliva samples, and genetic polymorphisms, located in 5-HTT, 5-HT1AR, BDNF, COMT, and MAOA genes, were assayed.

Zygosity Determination

Among 1,387 pairs of twins (T1 sample), 262 pairs are opposite-sex dizygotic (DZ) twins. The zygosity of the remaining 1,125 pairs of same-sex twins was determined by DNA analyses and the questionnaire method (Chen et al., 2010). Among the 1,125 pairs of same-sex twins, 990 pairs were determined by DNA analyses, and 116 pairs, whose saliva samples yielded insufficient DNA, were determined by the questionnaire method. Zygosity of 19 pairs was unable to be identified because of missing responses to the zygosity questionnaire and insufficient DNA. For the DNA analyses, nine short tandem repeat loci, which are highly heterogeneous in the Chinese population, were used. Same-sex twins with at least one different genetic marker were classified as DZ twins; otherwise, the twins were classified as monozygotic (MZ) twins. The posterior probability of being MZ for same-sex twins with the same genotype in all nine loci was estimated to be 99.99%. The validity of the questionnaire method was examined through the comparison with the results of DNA analyses. The predictive accuracy of the questionnaire method used in this study reached 91% (Chen et al., 2010).

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TABLE 2

The Variables of Interest in this Study

	T0 wave	T1 wave		T2 wave	
	Child report	Child report	Parent report	Child report	Parent report
Demographic variables	Age, sex, race Parent education	Age, sex, race Parent education	Age, sex, race Parent education	Age, sex, race Parent education	Age, sex, race Parent education
Biological variables	Puberty Height, weight	Puberty Height, weight Saliva sample	Birth weight	Puberty Height, weight	Birth weight
Adolescent psychopathology	Depression Anxiety Problem behaviors	Depression Anxiety Problem behaviors	Depression Anxiety Problem behaviors	Depression Anxiety Problem behaviors Sleep quality	Depression Anxiety Problem behaviors
Psychological processes		Emotion regulation Effortful control	Effortful control	Rumination Effortful control Dysfunctional attitude	Effortful control
Social variables	Life stress Parenting	Life stress Parenting Peer affiliation	Life stress Parenting Peer affiliation Sibling interaction	Life stress Parenting Peer affiliation Sibling interaction	Life stress Parenting Peer affiliation Sibling interaction
Parents' psychopathology			Depression Anxiety Drinking, smoking		Depression Anxiety Drinking, smoking Hostile personality

TABLE 3

T1 Sample Composition by Sex, Age, and Zygosity

	MZ		DZ			Unknown	Total
Age (years)	Male	Female	Male	Female	OST	zygosity	(pairs)
10–	50	59	26	19	47	1	202
11	36	47	17	16	28	2	146
12	63	38	22	21	37	0	181
13	50	52	20	32	28	2	184
14	56	60	22	23	40	4	205
15	37	49	10	13	28	0	137
16	36	33	12	12	26	4	123
17	22	30	4	8	14	3	81
18+	30	47	13	21	14	3	128
Total (pairs)	380	415	146	165	262	19	1,387

Note: OST = opposite sex twins; MZ = monozygotic twins; DZ = dizygotic twins.

Sample Description

Sample Size by Age, Gender, and Zygosity

Table 3 shows the sample size by age, gender, and zygosity group of the BeTwiSt core sample ($N = 1{,}387$ pairs of adolescent twins). For the 1,368 pairs of twins with known zygosity, 795 pairs were MZ twins (380 male pairs, 415 female pairs), 311 pairs were same-sex DZ twins (146 male pairs, 165 female pairs), and 262 pairs were opposite-sex twins. The MZ to DZ ratio in our sample was 1.39, consistent with that found in most Asian twin samples (Ando et al., 2006; Hur et al., 2006). The mean age of the T1 sample at the time of the assessment was 13.52 ($SD = 2.67$) years.

Sample Representativeness

To assess the representativeness of the core sample (i.e., the T1 sample), we compared the basic demographic characteristics of the T1 twin sample to a general youth population in Beijing. We randomly selected one twin from each pair between the ages of 12 and 18 ($N = 973$). Using a frequency matching method, an age- and gender-matched sub-sample ($N = 969$) was randomly selected from a large population-based representative youth sample in Beijing (Chen et al., 2009). Comparisons were conducted between the two

TABLE 4

Comparison of Socio-Demographic Characteristics Between Twin Sample and General Youth Sample in Beijing, China

Characteristics	Twin sample ($N = 973$)	General sample ($N = 969$)	Statistics	p
Age (mean, *SD*)	14.34 (1.80)	14.33 (1.80)	$t = -0.12$	.90
Child gender			$\chi^2 = 0.13$	.72
Male (*N*, %)	477 (49.0%)	467 (48.2%)		
Female (*N*, %)	496 (51.0%)	502 (51.8%		
Parent education level				
Father (mean, *SD*)	2.84 (.99)	2.77 (.96)	$t = -1.65$	.10
Mother (mean, *SD*)	2.81 (.95)	2.71 (.95)	$t = -2.29$	.02
Perceived SES (mean, *SD*)	2.22 (.68)	2.17 (.67)	$t = -1.71$	.09
Parental marital quality (mean, *SD*)	1.71 (.91)	1.75 (.93)	$t = -0.99$	.33
Marital status of birth parents			$\chi^2 = 1.71$	.43
Living together (*N*, %)	873 (92.3%)	860 (90.7%)		
Separated (*N*, %)	24 (2.5%)	32 (3.4%)		
Divorced (*N*, %)	49 (5.2%)	56 (5.9%)		

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samples in terms of basic demographic information. The results are presented in Table 4. No significant differences were detected in terms of perceived family social economic status, fathers' educational attainment, or parents' marital status or marital quality, with one exception: mothers' educational level was significantly higher in the twin sample than in the general youth sample, $t(1,898) = -2.29$, $p < .05$. Overall, these comparisons suggest that the representativeness of the BeTwiSt twin sample was acceptable.

Future Plans

The BeTwiSt is a prospective longitudinal twin study that aims to unravel the intricate interplay between genes and environment in the development of psychopathology. After the completion of the T2 assessment, we will continue to conduct follow-up studies until the participating adolescent twins enter adulthood. A long-term longitudinal investigation, such as the current study, enables us to examine our research aims across different stages of the life span, and to advance our understanding of how adult psychopathology is linked to earlier experience during adolescence. Future work will be funded by National Natural Science Foundation of China.

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