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SLEEP–WAKE PATTERNS OF TWINS AND THEIR MOTHERS IN THE POSTPARTUM PERIOD

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The purpose of this study is to observe the sleep–wake behaviors of twin infants and their mothers in the postpartum period. This longitudinal study examined the development of the circadian sleep–wake rhythm of twin infants and their mothers simultaneously during the first 8 months after birth. Data were obtained from 3 healthy identical twins and their mothers in domestic settings for 6 continuous 14-day periods, at 1st, 6th, 11th, 16th, 21st and 32nd week, using actigraph monitoring. Small actigraph units were mounted on the mothers' nondominant wrist and the infants' ankles. We examined the development of circadian rhythm by autocorrelograms for each observed periods. The infants' autocorrelograms clearly indicated 24-hour peak of correlation coefficient from 11th to 16th week age. The mothers' autocorrelograms also clearly indicated 24-hour peak of correlation coefficient from 2nd to 6th postpartum week. In the 17th week, synchronization of the infants' circadian rhythm and the mothers' circadian rhythm appeared, and the synchronization was increasingly observed subsequently. The process of the development of circadian sleep–wake rhythm of twin infants did not show much difference from that of nontwin infants. These results may explain the reasons why mothers of twins suffer from the strong sense of fatigue caused by childrearing such as the lack of sleep until the circadian sleep–wake rhythm of the twin infants was stabilized along the development. The result suggests that it is quite important for healthcare providers to provide mothers with intervention to reduce the child-rearing burden during the postpartum period.

THE HERITABILITY OF SOMATIC SYMPTOMS IN A SRI LANKAN TWIN SAMPLE

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Few twin studies have examined large representative samples in nonwestern, developing countries. This is important to address because the relative magnitude of environmental influences on common mental disorders may differ in populations experiencing qualitatively and quantitatively different environmental risk factors to those commonly experienced in more developed countries. It has been suggested that depressed people in nonwestern populations often present with a high rate of somatic symptoms. We measured somatic symptoms that are cross-nationally associated with depression and anxiety, using the Bradford Somatic Inventory (BSI), on our population-based twin sample (N = 930 adult pairs). We ran variance components models in Mx to assess the relative contribution of genetic (A), shared environmental (C) and nonshared environmental (E) factors to the variance in BSI scores. The shared environmental factor accounted for 20% of the variance in BSI scores for females, but none for males. The rest of the variance was accounted for by genetic and nonshared environmental factors in approximately equal proportions. Environmental as well as genetic factors are important in explaining somatic symptoms in Sri Lanka, and the environmental influences differ in men and women. These results are a good indicator of the relative importance of genetic and environmental factors on anxious and depressive disorders in this population.

THE ASSOCIATION BETWEEN PRENATAL MATERNAL EXPECTATIONS AND ADJUSTMENT TO THE MATERNAL ROLE AMONG MOTHERS OF TWINS: COMPARISON BETWEEN IVF AND SPONTANEOUSLY CONCEIVED MOTHERS

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Over the last few years, the number of twin births in Israel and abroad has risen significantly as a result of the extended use of fertility technologies. This research joins a broad spectrum of research attempting to determine whether the use of these fertility technologies change various aspects of the transition to parenthood. This research examined the relations among prenatal maternal expectations, parenting stress, and coping resources (sense of coherence, maternal efficacy, perceived social support and perceived marital quality) 6 months after birth, among first time mothers of twins conceived through assisted reproductive technologies — in vitro fertilization (IVF), in comparison to first-time mothers of twins conceived spontaneously. Ninety-eight conceived-spontaneously mothers of twins and 88 conceived through IVF were recruited from 28 maternity clinics during the years 2003 to 2005. Main results show that IVF mothers had higher maternal expectations and experienced higher levels of parental stress than spontaneously conceived mothers. There was no association between maternal expectations and parental stress in both groups. Moreover, IVF mothers' coping resources were depleted in comparison to those of the comparison group of spontaneously conceived twins. It can be concluded that first-time IVF mothers, especially mothers of premature babies, should be considered as a high-risk population. Ongoing consultation is needed to assist these mothers in decreasing the stress they experience, which might adversely effect their children's development and wellbeing.

CONSIDERATIONS IN THE ANALYSIS OF RESEARCH STUDIES USING SIBLING DATA

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The past 2 decades have witnessed tremendous growth in the number of methods available for analyzing cluster-correlated data with continuous and discrete outcomes. These methods have been applied to a wide range of studies using clustered designs, due to widespread appreciation of the fact that clustered data cannot be analyzed using 'ordinary' methods for independent data. But there remains a question as to whether common analytic practices make the best use of the richness of correlated data. For example, public health researchers rely on family (or sibling or twin) studies to evaluate the impact of a host of factors on health in infancy, childhood, and even adulthood. These study designs permit us to discriminate between factors operating at the family level and those operating at the level of the individual within a family. This 'sifting' of effects might allow for better control of confounding factors, separation of environmental and genetic influences, and causal interpretation of effects. These advantages, however, may not always be realized. We will review strategies for model specification and their implications for inference in the analysis of family studies using regression models for clustered data.

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EXTENDING THE TWIN DESIGN: EXTRAFAMILIAL INFLUENCES ON EARLY ADOLESCENT ALCOHOL USE AND RELATED BEHAVIOR PROBLEMS

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A limitation of the traditional twin design is its inability to distinguish between familial and extrafamilial environmental influences, which are both encompassed in the shared/common environmental component. In the Finnish Twin Study, FinnTwin12, we collected data on gender- and age-matched classmate-controls, in addition to twins, allowing us to disentangle familial and extrafamilial environmental influences. By grouping each twin pair and their classmate controls into double dyads, we can compare correlations between twins and controls in order to identify genetic, familial and extrafamilial environmental influences on these outcomes. Classmate control dyads share neither genes nor family environments, suggesting correlation between them is attributable to extrafamilial environmental influences (e.g., neighborhood, school, peers). Here, we report analyses of alcohol outcomes, measured by self-report, and behavioral outcomes (such as aggression, hyperactivity-impulsivity, and inattention), measured by teacher report, both at age 12. Control dyads were significantly correlated for each of the alcohol and related behavior variables, suggesting that extrafamilial environments do influence alcohol use and related behavioral outcomes among adolescents. Monozygotic (MZ) correlations exceeded dizygotic (DZ) correlations for 4 of the 5 alcohol outcomes and each of the behavior outcomes, suggesting genetic influence for these 4 alcohol outcomes and each of the behavior outcomes. Comparing MZ–DZ differences in correlation revealed much greater evidence for genetic influence on the behavior outcomes than the alcohol outcomes. These results are consistent with prior analyses (Rose et al., 2003), suggesting that the neighborhoods in which adolescents live do influence their behaviors.

ANALYSIS OF LIPID FRACTIONS IN DUTCH TWIN FAMILIES

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In the past 2 years we have collected fasting blood samples in Dutch families consisting of adult twins, their parents, spouses and siblings. Blood sampling was highly standardized and occurred during a home visit between 7 a.m. and 10 a.m. In the blood we assessed lipid fractions (total cholesterol [TC], high-density lipoproteins [HDL], low-density lipoproteins [LDL] and triglycerides [TG]). Up until now, around 7000 family members have taken part in the study. Familial correlations (corrected for sex, age, medication, OC) are significant and suggest that familial resemblance is mainly attributable to genetic factors. Correlations between spouses living together are zero or very low. In 2 subsamples, we also have earlier lipid assessments available, obtained 10 to 20 years ago. In participants who were adolescents at the time of the first measurement temporal stability was lower than in participants who were adults at the time of the first measurement. However, longitudinal HDL correlations were high in both samples.

TWIN PREVALENCE IN PARENTS AND GRANDPARENTS OF ITALIAN TWIN AND SINGLE NEWBORNS

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It is widely accepted that twinning, especially of dizygotic (DZ) pairs, is a familial trait. Different transmission patterns for DZ twinning have been proposed, and the role of both parental lineages for monozygotic (MZ) and DZ twinning is controversial. Since most studies simply compare twinning prevalence among relatives of MZ and DZ twins, we adopted a case-control approach to estimate the relative risk of being a MZ or DZ twin given that a parent or grandparent is a twin. Participants in this study were all members of the Mercurio Project that enrolled consecutive singleton and twin births in 40 Italian hospitals during 1993–1995. Twins were recontacted 10 years later by the Italian Twin Registry to better ascertain their zygosity. Data on twin parents and grandparents were collected 3 months after birth for 552 spontaneously conceived twin pairs (229 MZ, 323 DZ), and 1162 singletons. Twin prevalence is not significantly different between twins' and singletons' parents. Instead, the odds ratio (OR) of being a twin, given that at least one grandparent is a twin is 1.6 (95% CI: 1.1–2.3). This OR rises to 1.9 (95% CI: 1.2–3.0) if at least one maternal grandparent is a twin, but is not significant for paternal side. Having one maternal or paternal twin grandparent confers a higher risk of DZ twinning (OR = 1.8, 95% CI: 1.0–3.1 and OR = 1.7, 95% CI: 1.0–3.1). The risk of being a MZ twin is increased when the maternal grandmother is a twin (OR = 2.7, 95% CI: 1.3–5.6). In our sample MZ twinning seems to be transmitted by maternal grandmother, while both lineages contribute to DZ twinning.

HERITABILITY OF SLEEPING BEHAVIOR IN 18-MONTH ITALIAN TWINS

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Self-organization of sleep and waking in infants represents a significant milestone of early child development. Sleep problems are experienced by 25% to 30% of children and adolescents, regardless of age. Twin studies might bring useful information about etiopathology of these disorders, and might help to determine the relative contribution of genetic and environmental factors to a given sleep phenotype. Participants in this study were all members of the Italian Multiple Pregnancies Registry that started in April 1993 (Mercurio Project). They were all recontacted 10 years later by the Italian Twin Registry to better ascertain their zygosity. Data on sleep habits were available on 314 pairs, 127 monozygotic and 187 dizygotic. A questionnaire concerning sleep-related problems was developed. The sleep measures probe about: (i) co-sleeping defined as the sharing of room and/or bed; (ii) sleep–wake organization (time spent in nocturnal sleep; time spent in diurnal sleep; presence and weekly frequency of awakening during the nocturnal sleep). Twin correlations for the various sleep dimensions were estimated by zygosity and gender, and genetic and environmental effects were estimated using structural equation models. Shared environment accounted for at least 60% for co-sleeping and time spent in nocturnal and diurnal sleep. Heritability was higher (49% males, 54% females) for weekly frequency of awakening during the night. For each item, gender differences in genetic and environmental variance components were detected. Even though heritability estimate for frequency of awakening is around 50%, pediatricians should first educate parents to improve sleep hygiene before prescribing any kind of drugs.

FACTORS AFFECTING CHILD NONVERBAL REASONING ABILITIES IN 5- TO 11-YEAR-OLD TWINS

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Data from this study was used to examine the association between nonverbal reasoning abilities and sex, priority of birth, birthweight, hand dominance, parent's education, similarity of task performance in twin pairs, in monozygotic (MZ) and dizygotic (DZ) twins. Participants were 22 pairs of twins (7 pairs MZ and 15 DZ) aged 5- to 11-years-old, and their parents. Raven's Coloured Progressive Matrices (CPM) was administered for the measurement of nonverbal reasoning abilities. Parents completed the Strength and Difficulties Questionnaire (SDQ) and environmental questionnaire. Similarity between twins in task performance was investigated by way of control group. Twin CPM results were more similar than between 2 randomly paired children. Statistically significant differences were found between the CPM performance and priority of birth, hand dominance and parents' education. No statistically significant difference was found between boys and girls and hand dominance, except that children who equally used both hands received higher SDQ score results. A variety of environmental and genetically determined factors influence a child's nonverbal reasoning abilities. Those factors have different effects, but all of them are important and meaningful.

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SMOKING, TWINS AND HERITABILITY

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Long-term tobacco use is a major public issue. If uptake and persistence of smoking are mediated by both social factors and individual biology, then epidemiological studies of twin pairs have an important role to play in helping to reduce this health burden. It has become conventional to estimate 'heritability' of smoking by assuming 2 untested models. First, that monozygotic (MZ) and dizygotic (DZ) twin pairs share those environment factors relevant to the trait of interest to an equal extent (equal environment assumption). Second, that binary traits are adequately explained by probit, or liability, models in which the explanatory factor is a weighted count of genetic variants. If this second assumption does not hold, genetic correlations cannot be inferred from relatedness. This methodology has produced contradictory, even paradoxical estimates. In a study of twins reared apart and together, Kendler et al. (2000) estimated that 'In women born before 1925 … resemblance was environmental in origin … . For women born after 1940, heritability of [regular tobacco use] was similar to that seen in men (63%)'. Such a mutable form of genetic contribution should not inspire us to seek specific genetic variants associated with smoking. Yet Vink et al. (2006) have suggested a genome-wide scan is justified, while Tyndale (2003) claims 'a role for genetics … to identify novel targets for treatment'. To examine the relative importance of directly acting genetic factors and the shared and individual specific environment in regular smoking, we examined data from a longitudinal cohort of twins, followed from adolescence to young adulthood over 4 survey waves. Rather than attempt to estimate heritability, we developed a method of estimating the odds of greater than expected (excess) concordance of smoking behavior associated with various covariates. These included zygosity (MZ vs. DZ twins), frequency of contact, age and similarity of smoking behavior of friends. We also examined how these estimates varied as the twins moved out of home and began living apart as young adults. Zygosity was found to be a significant predictor of excess concordance only while the twins were living together at home, whereas similar smoking behavior of friends was persistently the strongest predictor. It was notable that the marginal probability of smoking was lower in MZ twins, which inflated the role of zygosity in concordance if not adjusted for.

GENETIC AND ENVIRONMENTAL FACTORS AFFECTING THE LIFE SATISFACTION LEVELS IN LATER ADULTHOOD: A TWIN STUDY IN JAPAN

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This study aims to clarify the factors affecting life satisfaction levels in later adulthood. Life Satisfaction Index-A (LSI-A) of the 18-item version was employed as the measurement of life satisfaction in elderly twins. The subjects of this study were 1008 twins. These participants include 699 male and 309 female, as well as 719 monozygotic (MZ) and 289 dizygotic (DZ), whose mean age was 70.6 (±11.9). Intraclass correlation coefficient (ICC) and the intrapair difference of LSI-A in MZ were calculated to estimate the intrapair similarity of life-satisfaction levels. Logistic analysis was conducted to analyzed the environmental factors affecting the levels of life satisfaction. Concerning the factors affecting life satisfaction, 13 candidates were selected, which were age, gender, living with spouse, social activity, balanced nutrition, breakfast, sports activity, sleep-time, job, subjective stress, smoking, alcohol drinking and suffering from disease. There were 6 factors, which were obviously distinguished from others that are 'stress, social activity, nutrition, age, sport activity and smoking'. The study results showed that genetic factors had very limited influence on life satisfaction levels in later adulthood. Life satisfaction highly correlated with mood, communication with other persons, nutrition, and sport. These results suggested that those with a healthy lifestyle have better life satisfaction.

TWINS, TELOMERES AND AGING

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Telomeres are the protective tips of chromosomes, and decrease in length with age. However, it is unknown if shortened telomeres decrease longevity or whether telomere length is merely a marker of aging. Twin research is a valuable tool to assess the heritability of telomere length, and the factors that are associated with telomere attrition. Cross-sectional study design, validated where possible by discordant twin analysis, was used to assess the relationship between telomere length and multiple phenotypes including anthropomorphic, demographic, radiographic and biochemical measures, collected over 10 years. Subjects comprised monozygotic and dizygotic volunteer twin pairs, mainly female, over the age of 18,unselected for any particular trait. 36% of variation in telomere length is attributable to genetic factors with significant linkage on chromosome 14q23.2. Shortened telomeres were found to be associated with cigarette smoking, obesity, osteoarthritis, osteoporosis, insulin resistance, poor cognitive function, low levels of vitamin D, low socioeconomic status, and lack of exercise. Discordant twin analysis, in the exercise and socioeconomic studies, further validated the telomere findings. No association between telomere length and blood pressure, total cholesterol, birthweight, age at menopause, or parity, was found. Oxidative stress and chronic inflammation are factors that can explain most of the observed associations. However, it is still unclear whether telomeres are merely a useful marker of this process, or play a protective role in the aging process.

DETECTING BONE SIZE QUANTITATIVE TRAIT LOCI USING DXA IMAGING

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Human height is a highly heritable and complex trait. Studies have shown demi-span and lower limb length as useful surrogates for height in individuals with vertebral or hip fractures. The aim of this study was to conduct a genome-wide linkage scan to identify quantitative trait loci (QTL) for height-estimator body segments in a large, population–based twin sample. 2725 normal Caucasian females, 18–80 years old, with whole body DXA data were used. A novel and reproducible method, linear pixel count (LPC) was used to measure skeletal sizes on DXA images. Intraclass correlations were calculated using STATA for height, trunk, femoral, tibial, humeral and radial length on monozygotic (MZ; $n = 431$) and dizygotic (DZ; $n = 2294$) twin individuals. Estimates for heritability were calculated using Mx. A genome-wide scan using 737 micosatellite markers spaced every 10 cM was performed on 1958 DZ twin subjects using robust regression analysis. All sites were highly correlated with height. Intraclass correlations showed results for MZ twins to be significantly higher than DZ twins. Heritability for total height was 81%, trunk length was 74%, femoral length was 72%, humeral length was 74% and radial length was 67%. A genome-wide scan produced reliable evidence of significant linkage on chromosome 5 for height (LOD score = 5.8) and femur (LOD score = 2.03) at the same region of 150–155 cM. This is the first bone size linkage study and provides clear evidence for linkage to chromosome 5 in the region of 150–155 cM. The fine mapping of this region is needed to determine potential genes influencing diseases affecting bone size.

ASSOCIATION OF VMAT2 GENE POLYMORPHISMS WITH DEPRESSION SYMPOMATOLOGY IN ELDERLY TWINS

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Several twin studies have demonstrated that genetic factors contribute considerably to both clinical depression and subsyndromal depressive symptoms and variations in genes within the serotonin system has long been considered candidates as possible genetic risk factors. Using a sample of 684 elderly Danish twins we have previously shown that a polymorphism in the gene encoding the vesicular monoamine transporter VMAT2 is associated to mean level of depression symptomatology assessed over several years and thus reflecting each individual's underlying mood level. In the present study we used a haplotype tagging approach to further investigate the association of VMAT2 to depression symptomatology, thereby covering the main part of the genetic variation within this gene. We tested a total of 12 tagging SNPs in a sample of 42 dizygotic (DZ) twin pairs which were either concordant or discordant for depression symptomatology. We applied the sibship disequilibrium test (SDT) to assess the association between depression phenotypes and SNP genotypes while adjusting for age and sex using the PBAT software package. The mean level of depression symptomatology was highly significantly ($p < .005$) associated with SNP marker rs363393 and significantly ($p < .03$) associated with SNP marker rs363226. Haplotype-based analysis further confirms the associations in the regions

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with high significance for a 2-SNP haplotype of rs363393 and rs363399 ($p < .009$) and of rs363226 and rs363227 ($p < .03$). Highly significant ($p = .01$) associations were also observed for a 3-SNP haplotype covering rs363226, rs363227 and rs363275. Our analysis using DZ twins reconfirms the association between VMAT2 gene and depression phenotypes in the Danish population.

THE FEASIBILITY OF CREATING A POPULATION-BASED NATIONAL TWIN REGISTRY IN THE UNITED STATES

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Between 4 to 6 million twins exist in the United States (US) today who offer scientists a valuable resource for conducting behavioral and biomedical research. However, unlike many other countries, there is no national system in the US for identifying twins and eliciting their participation in these important research programs. Therefore, a study was conducted to determine the feasibility of creating a national, population-based twin registry in the US. Major goals of the study were to estimate the potential size and characteristics of a national twin registry based on the current US twin population, our ability to ascertain and enroll them, and their willingness to participate. Existing US twin cohorts were also examined as well as alternatives for improving US twin resources should a national twin registry be deemed infeasible. The various options are compared in terms of possible source populations, generalizability and adequacy for statistically powering etiological studies. Having a national population-based twin registry in the US would be advantageous to US scientists and those worldwide. It would provide ample numbers of twin pairs to conduct various types of environmental genomic studies currently not possible with existing US twin resources. It would also allow US scientists to select for characteristics (race, ethnicity, environments, etc.) inherent in our own population. Finally and foremost, it would help to meet the worldwide demand for twin resources which is expected to increase over time, as new genomic and analytical tools become available and new hypotheses emerge concerning the complex interplay between genes, lifestyles and environment.

VIDEO ANALYSIS OF SIBLINGS AT PLAY: TWINS AND NONTWINS AND THEIR COOPERATIVE BEHAVIOR

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It is not unusual that self-descriptions do not correspond with the actual observed behavior. This study compares questionnaire data with data derived from video analyses. Pairs of siblings ($n = 104$), aged 10 to 12, played the game 'Jenga' with a slightly changed instruction to gather information about their cooperation with each other (solving the task together in agreement). With the help of 7 subscenes (intercoder reliability .62 to .86), a total score for cooperative behavior was derived for each pair. Not the specific kind of sibling relationship (monozygotic twins, dizygotic twins of the same and opposite sex, siblings of the same and opposite sex) had a significant influence on cooperation, but the degree to which siblings evaluated their relationships in a similar way (assessed with the Brunswick Dyadic Identity Scale for Siblings, BDISS). The more they agreed, the higher was their cooperation. Furthermore, we analyzed the influence of the children's personalities (PFK9-14) on the observed cooperation. Not the personality of one child was crucial, but the combination of both the children's personalities. The higher the product of the siblings' values on the scale 'obedience to adults', the lower was the observed cooperation between the children. First longitudinal results from our study will also be presented.

VARIANCE COMPONENTS FOR EXHALED NITRIC OXIDE IN TWIN FAMILIES

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Exhaled nitric oxide (eNO) has strong associations with many asthma-associated phenotypes and may represent another distinct pathogenic pathway leading to asthma. This study aimed to investigate genetic and environmental components of variance of eNO, and interrelationships between genetic determinants of eNO and known asthma associated phenotypes. Variance components models were used to estimate the genetic and environmental components of variance of eNO, and to investigate the sharing of genetic effects between eNO and other asthma associated phenotypes. A population-based sample of 155 multiple birth (twin and triplet) families (572 individuals) in Western Australia were investigated. Questionnaire data, eNO, atopic status, spirometry, airway hyperresponsiveness and eosinophils were measured on each family member. Increased eNO levels were associated with 'ever asthma', 'current wheeze', and atopy. Atopy was an important modifier of the relationship between eNO and eosinophils, and eNO and airway hyper-responsiveness. eNO had a broad sense heritability estimate of 51% ($SE = 14\%$) in children and 80% ($SE = 39\%$) in adults. The dominance variance component was greater than zero in both children and adults. Adjustment for total immunoglobulin E and airway hyperresponsiveness individually did not provide strong evidence for a sharing of genetic determinants between eNO and these traits. This is the first study to estimate the heritability of eNO in a twin-family setting with children. Our results suggest that eNO is strongly heritable and are consistent with the existence of multiple genetic determinants of the pathophysiological traits associated with asthma.

GENOTYPE BY ENVIRONMENT INTERACTIONS IN BMI: A PRELIMINARY INVESTIGATION OF THE EFFECTS OF CHILDBIRTH ON POST-PREGNANCY WEIGHT RETENTION IN AN AUSTRALIAN FEMALE TWIN SAMPLE

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Genetic effects explain 50–90% of the variation in weight. However, recent increases in the prevalence of obesity are likely to have been caused by changes in the environment rather than changes in genetic background given the short period over which this increase has occurred. Environmental conditions such as lifestyle and eating habits that promote excessive caloric intake and sedentary patterns are in direct contrast to our hunter-gatherer past and thus, genotypic interaction with the current environment may explain interindividual differences in weight. Additionally, over the last 5 years, studies have shown that post-pregnancy weight retention (Gutersohn et al., 2000) is a possible cause in the development of obesity in women after child bearing years. Women who are homozygous for the 825T allele (825T/C is a polymorphism in exon 10 of the GNβ gene) retain more weight after delivery compared with women with at least one 825C allele. Furthermore, the 825T homozygous genotype has been associated with increased BMI. The moderator model (Purcell, 2002) was used in a sample of ~10,000 Australian twin families to investigate the changes in genetic and environmental estimates over time due to the influence of childbirth in women. Moreover, the moderator model was incorporated into the Quantitative Trait Locus (QTL) Linkage Analysis (Purcell & Sham, 2002) to examine the influence of childbirth in QTL estimates of BMI. These results may give some indication of the impact that childbirth has on genetic, environmental, and QTL factors relating to obesity in an Australian adult population.

USING TWINS TO STUDY IMMUNE-RELATED RISK FACTORS

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It is known that severe inherited or acquired immunodeficiency is associated with a much higher risk of certain diseases. However, subtle, subclinical variations in immune response may play an etiologic role as well. There are a variety of ways to study immune-related risk factors. Epidemiologic surrogates such as indicators of childhood crowding,

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atopic conditions and 'marker' diseases such as infectious mononucleosis can be informative. Immune response biomarkers are also useful but have limitations in case-control studies because the biomarkers may be affected by the diseaese process. Twins as subjects offer unique opportunities to study these hard-to-measure immune related risk factors. Various twin study designs using both surrogate and direct markers of immune response to identify etiologic pathways of lymphoma, atopic disease and other chronic disease conditions, will be discussed.

MATERNAL OBESITY AT DELIVERY AND BIRTHWEIGHTS IN TWINS

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Obesity is a pervasive public health epidemic among women in United States. Maternal obesity is a significant risk factor for macrosomia and cesarean delivery in singleton pregnancies. The objective was to determine if there is any difference in the birthweights and discordancy rate between obese and non-obese women who delivered twins. A search of all women's records that delivered twins at Mount Sinai hospital (Chicago Illinois) between 1/1/1997 and 12/31/2006 was done from the perinatal computerized database. Records with missing data and birth weight < 500 grams, were excluded. The body mass index (BMI, kg/m^2) at delivery was calculated for each mother. The women were classified in 2 groups: non-obese (BMI < 30 kg/m^2) and obese (BMI ≥ 30 kg/m2). Variables like: birthweights of the first, the second, the larger twin of each set, and the discordancy rate (used the birthweight of the larger twin as index), were determined and compared for each group. A total of 355 women met the criteria. Of these 38.6% (n = 137) were non-obese and 61.4% (n = 218) were obese. Further sub classification of the obese group revealed that: 25% (n = 91) of all women were Class I (BMI = 30.0-34.9 kg/m2), 18.6% (n = 66) were Class II (BMI 35.0-39.9 kg/m2), 17.2% (n = 61) were Class III (BMI 40 kg/m2) and 3.1% (n = 11) were Super-obese (BMI ≥ 50 kg/m2). There were statistical differences in the mean birthweight of the first twin: 2.147 ± 687 grams non-obese group versus 2.369 ± 633 grams obese group (z test, p = .002); the second twin: 2.105 ± 664 grams non-obese versus 2.314 ± 624 grams obese (z test, p = .003); and the larger twin of each set: 2.249 ± 695 grams non-obese versus 2.487 ± 625 grams obese group (z test p = .001). There was no statistical difference between the birthweight discordancy rate of 18.2% (n = 25) in the non-obese group and the rate of 16.1% (n = 35) in the obese group (Odd ratio = 0.86; 95% CI: 0.47–1.57; p = .59]). Obese women delivered twins with higher birthweights than non-obese women. The birthweight discordancy rate was similar in both groups.

TWIN RELATIONSHIP, PEER RELATIONSHIP: A CASE STUDY OF A FEMALE MZ TWIN PAIR IN A PRESCHOOL SETTING

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Children's friendship is a powerful predictor of social success. The paper presented derives from a large study investigating the impact of the twin situation of friendships and social competencies. The focus of this paper is an investigation of the social interactions of 1 pair of female, monozygotic (MZ) twins aged 4 years. This pair was chosen for case study because reports from parents, teachers, peers and the twins themselves indicate that they had a close relationship with each other (including a shared imaginary friend) and a limited social connection with their peers. We video recorded the social interactions of this pair in their preschool setting. Recordings were micro-analyzed to determine the social strategies used by each child as they interacted with each other and with their peers. The analyses indicated that the children's relationship and social behaviors were not conducive to positive peer interactions and were associated with social isolation. Discussion examines the association of twin relationship on those with peers.

SAME AND DIFFERENT/FAIR AND BALANCED: AN ANTHROPOLOGICAL ANALYSIS OF IDENTICAL TWINS AND THE EMBODIMENT OF CORE CULTURAL VALUES IN NORTH AMERICA

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The popular science literature depicts identical twins as impaired individuals or a kind of deviant cultural persona that challenge core values of competitive individualism characteristic of North American conceptualizations of person or self. Identical twins as topics of research raise questions about identity, individuality, and uniqueness as well as mutuality and attachment. Typically for purposes of cultural analysis and discussion these issues of same and different and of independence and interdependence are subsumed under prototypes of a valued egocentric versus a devalued sociocentric construction of self and personhood. Analysis of data collected during interviews with 22 sets of identical twins, ages 22 to 77, during the 2003 Twinsburg Twins Festival shows that when pairs of twins talk about their lifetime experiences of being twins, a second important theme for cultural analysis emerges. This is the problematical ideal that Americans are born equal and as co-equals will have equal opportunities in life. Informed by the methods and perspectives of cultural psychology, the study emphasizes language and interaction, features self in practice, recognizes the existence of multiple self ways within a culture, and views self and culture as mutually constructing each other. Analysis of narrative data show how this sample of adult, American twins reflect, and reflect upon, the wider egalitarian values of their society as they voice their concerns with, and strategies for, balancing their experiences of being same and different with an overriding ideal of fairness or balance. Analysis demonstrates the situated and positioned co-existence of positive and negative features of deviance.

GENERALIST GENES, SPECIALIST ENVIRONMENTS AND THE INTERNET GENERATION: ETIOLOGY OF LEARNING ABILITIES USING WEB-BASED TESTING AT 10 YEARS

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The Generalist Genes hypothesis states that genes contributing to individual differences in abilities such as reading and math are largely shared. However, this hypothesis is yet to be proven using direct tests administered on large samples. We assessed 2541 pairs of 10-year-old twins for reading, math, and general cognitive ability, using an innovative web-based test battery that allowed us to gather the largest ever sample of this kind. Genetic analyses were carried out using maximum-likelihood structural equation modeling in Mx. Phenotypic analysis gave correlations of .51 between reading and mathematics, .54 between reading and g, and .63 between math and g. Univariate genetic analyses gave heritabilities of .38, .49, and .44 for reading, maths and g, respectively. Family-wide environmental influences (shared environment) accounted for .25, .23, and .27, while environmental influences affecting twins differentially (nonshared environment) accounted for .37, .29, and .28. Multivariate genetic analysis revealed substantial genetic correlations between learning abilities (r = .57–.75), demonstrating considerable genetic overlap. Likewise, shared environmental influences correlated highly between abilities (r = .89–.94). Overall, genetic factors accounted for 50% of the correlation between abilities, with shared environment accounting for 40%. By contrast, nonshared environmental influences correlated only .15–.22 between abilities and mediated only 10% of the phenotypic correlation. These results provide support for the Generalist Genes hypothesis, and they also imply that nonshared environmental influences tend to be unique not only to one twin, but also to each ability: a Specialist Environments hypothesis.

PERINATAL OUTCOME OF SINGLETONS AFTER SET

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The first studies assessing perinatal outcome of children after assisted reproductive technologies (ART) did not differentiate their results between singletons and twins. These studies were thus suspected to be biased because of the large amount multiple pregnancies in the ART group. Later studies adjusted for number of children expected per pregnancy and confirmed pregnancy outcome to be less advantageous in

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nonspontaneously conceived singletons. These findings were less explicit n twin pregnancies; however multiple pregnancies are anyhow in disfavor in terms of pregnancy outcome. Single embryo transfer in twin-prone patients is the only effective answer to the twin epidemic as a result of ART. Since professionals involved in ART are concerned to provide the best possible quality especially in terms of health outcomes, we wanted to test which consequences the introduction of elective SET (eSET) has on pregnancy outcome. As such, we compared gestational age and birthweight between 404 eSET singletons and 431 singletons resulting from double embryo transfer (DET). Our analysis demonstrated that singleton birth after SET is advantageous compared with DET: birthweight was significantly lower in DET singletons (3204.3 g vs. 3324.6 g, $p < .01$). Furthermore, preterm birth (OR 1.77, 95% CI: 1.06–2.94) and low birthweight (OR 3.38, 95% CI: 1.86–6.12) occurred significantly more often in DET-singletons. These findings are illustrations of additional advantages of SET beyond its initial purpose and shed new light on the reasons why singletons after ART are in disadvantage compared with spontaneously conceived children.

GENOME-WIDE LINKAGE SCAN FOR EXERCISE PARTICIPATION ACROSS SEVEN COUNTRIES PARTICIPATING IN THE GENOMEUTWIN PROJECT

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It is well-known that exercise behavior is a heritable trait. A previous study using samples from 7 countries participating in the GenomEUtwin project has shown that there are no cross-cultural differences inheritability of exercise participation (Stubbe et al. 2006). Not much is known yet about the actual genetic variants that influence exercise participation. Aim of the present analysis is to identify the genomic regions that are involved in exercise participation in the 7 GenomEUtwin countries and to investigate whether the identified regions in these samples overlap. In each country we selected siblings aged 18-50 years for which both exercise and genotypic data were available. The exercise data from each country were recoded into exercise participation (yes/no), in order to create a comparable measure across countries. Further, the genetic markers used in each country were placed on the interpolated Duffy map. IBD probabilities were estimated in Merlin using the Lander-Green algorithm and a 1 cM grid, and pi hat was estimated for each sibling pair. The linkage scan was carried out in Mx using a variance components threshold model in each country separately. It was next tested whether the QTL effects could be equated across countries. The results from the Dutch sample show suggestive linkage in females on chromosome 19p13.3 (LOD = 2.87). This region harbors a number of genes related to muscle performance and muscle blood flow. Linkage scans in the 6 other countries will be carried out to investigate whether the results from the Dutch sample are replicated.

VANISHING TWIN SYNDROME AND DEVELOPMENT OF THE SURVIVED TWIN

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The study aimed at exploring certain aspects of the development of children born from pregnancies affected by the Vanishing Twin Syndrome, a specific kind of early spontaneous pregnancy reduction. Specifically, the children's motory activity and the parent-child relationship, with particular attention to parental perception, were investigated. The sample consisted of 53 children, aged between 1 and 11 years, encountered at the Centre for Sterility of the Arcispedale Santa Maria Nuova in Reggio Emilia. Through telephone interviews, information was gathered on the socioanagraphical data, the pregnancy, the development of the children and the quality of their school experiences. Furthermore, the motory scale of QUIT (Italian Questionnaires of Temperament, Axia, 2002) was administered, to measure the children's motory activity along with the Vulnerable Child Scale (Forsyth et al., 1996) to measure parental perception of the children's vulnerability. The data show that the 'survived' children have a significantly lower motory activity compared to the Italian population, they have a high incidence of scholastic initial problems, problems predominantly connected to separation from parents. The parents, moreover, show an extremely low perception of vulnerability in the 'survived' child, in contrast with literature, according to which a higher perception would be expected. This perception of 'invulnerability' in the 'survived' children, we hypothesize, could be a defence against the cumulative traumas of infertility and the co-twin's death; associated to the difficulties in separation found within the parent-child relationship, it could favor an ambiguity which thwarts the development of independence, the processes of individuation and of learning.

SET AND THE BELGIAN MODEL

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At inception of assisted reproduction, multiple embryos were transferred in order to increase pregnancy rates. This procedure not only resulted in an acceptable pregnancy rate, also an epidemic of multiple pregnancies emerged. In the beginning of the 1990s, double embryo transfer (DET) was introduced in order to cease the exponential rise in multiple pregnancies. This approach resulted in a successful reduction of triplets; however without engendering any changes in twin rates. The move from DET towards single embryo transfer (SET) was more complicated in that initial studies assessing pregnancy rates after SET were disappointing. However, these early studies were biased because the study group consisted of SET-patients with only one embryo available for transfer after ovarian stimulation and pick-up protocols. Since the availability of several good-quality embryos is predictive for success, remarkable better results were observed in patients who underwent DET.

UNDERSTANDING ENVIRONMENTAL INFLUENCES ON ADOLESCENT SUBSTANCE USE: DATA FROM THE FINNISH TWIN STUDIES

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Twin studies provide compelling evidence of the importance of the environment in adolescent substance use. Accordingly, we have been conducting analyses aimed at identifying the specific environments important for adolescent substance use. Using data from the population-based Finnish twin studies, we have been studying several aspects of the environment, including parenting, peer, and neighborhood characteristics. We will present analyses exploring main and moderating effects associated with parenting characteristics, on adolescent smoking and drinking, measured at ages 14 and 17. We find significant evidence of moderating effects associated with 2 dimensions of parenting (parental monitoring and time spent in activities with parents) on adolescent smoking, measured at 2 time points across development. Genetic influences on smoking increased, and common environmental effects decreased, as adolescents reported less parental monitoring and spending more time with their parents. However, there were no significant moderating effects associated with parenting and adolescent drinking. There were main effects of parenting on adolescent alcohol use, and evidence that parenting characteristics mediate, in part, the relationship between parental and adolescent alcohol use. Furthermore, peer influences appeared to be particularly influential on adolescent alcohol use. There was evidence that genetic influences were more pronounced among adolescents with drinking peers. These analyses illustrate the importance of incorporating measured aspects of the environment into genetically informative twin models to begin to understand how specific environments are related to various outcomes.

DEVELOPMENT AND CHARACTERISTICS OF TRIPLETS

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Triplets are often treated in the same way as twins, and are frequently looked upon as 'twins plus one'. But since twins grow up in a paired relationship, as a couple, and triplets find themselves in a group or more precisely in a triangular relationship, one can presume that triplets should show their own specific characteristics. Going along with this thesis, a study was carried out in which 276 triplet families from Germany, Austria and Switzerland took part. The main issues concentrated on were: (1) How do important stages of development take place for triplets? Do special problems arise for parents and children? (2) Are there different types of triplets that can be distinguished? (3) Does the genetic composition of the triplet set show a special effect? Results allow explicit conclusions concerning the social and emotional development of the triplets, their development of speech, their dealing with physical likeness and the advantages and disadvantages of co-education or separated educa-

tion in kindergarten or at school. The results of the study show that the genetic composition and the personality of each individual child play a very important role in the triplet set. It depends on this and the behavior of those in their environment as to how the triplets cope with the conflicting situation of the positive feeling they get from their sibling companionship, and their striving for individuality, and whether they have a sense of security and stability with their siblings or whether it is constant competition.

ITALIAN TWIN REGISTRY: WEB-BASED RECRUITMENT

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Traditionally, twin data for the Italian Twin Registry (ITR) are collected either by mail questionnaires or personal interviews. A web-based enrolment has been recently implemented through ITR web site (www.gemelli.iss.it). The web registration is based on a standard MySQL suite of scripts and tables. In order to preserve twins' privacy, the MySQL database keeps personal and scientific data in separate autonomous tables. The front-end access system is based on the Php sessions/cookies architecture, and is designed to allow registered twins the possibility to view and modify only their data. An advertisement campaign was launched soon after the on-line twin enrolment started, in order to promote the registry activity, its scientific value, and the twin recruitment itself. Leaflets and posters aimed at the better dissemination of information concerning twin study's value in genetic epidemiology were sent to general practitioners, schools, sport centers; a number of brief articles are programmed to appear in general magazines and newspapers, as well as in radio and TV programs, with local and national audience. Accesses to the website and the number of twins enrolled to the ITR has been monitored over time in order to discover the most effective way of advertisement for on-line recruitment.

INFLUENCE OF UNIQUE ENVIRONMENTAL FACTORS ON PHYSICAL ACTIVITY PARTICIPATION: ROLE OF THE BUILT ENVIRONMENT

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The health benefits of physical activity are well established. However, the relative contribution of heritable and environmental factors to participation in physical activity remains controversial. Using a cut-point of 60 minutes/week of moderate-intensity activity, data from the GenomEUtwin project revealed consistent genetic influence on physical activity participation in twin pairs from 7 countries. We hypothesized that the heritability of physical activity participation would be attenuated using the CDC recommended cut-point of 150 minutes/week of moderate-to-vigorous-intensity activity. Data were obtained from 1389 twin pairs from the University of Washington Twin Registry. Tetrachoric correlations in same-sex pairs were higher in monozygotic (MZ; .43, 95% CI: 0.33-0.54) than dizygotic (DZ) pairs (.30, 95% CI: 0.12-0.47) using the 60 minute cut-point. However, the differences were attenuated using the 150 minute cut-point (rMZ = .30, 95% CI: 0.20-0.40; rDZ = .25, 95% CI: 0.07-0.42). Using the lower cut-point, the best fitting model only included additive genetics and unique environment with a heritability of 45%. In contrast, using the higher cut-point, the best fitting model included the common and unique environment with the unique environment contributing 72% of the variance. We are exploring objective measures of the unique environment by geocoding twin addresses to assign a 'walkability index' to each location. Preliminary analysis in 176 twins revealed a nonsignificant trend (p = .17) in moderate-to-vigorous activity across tertiles of walkability (103, 115, and 122 minutes/week, respectively). We will extend this analysis by geocoding addresses of over 2000 twin pairs residing in Washington State.

THE IMPACT OF FAMILY STRUCTURE ON INTRAPAIR SIMILARITY OF TWINS IN ACADEMIC ACHIEVEMENT

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This study is a part of comparative research of academic achievement in school-age twins and singletons, which was supported by a grant from the Russian Humanitarian Scientific Fund. The aim of this part of the study was to evaluate the impact of family structure on educational achievement. The sample consisted of 2325 pairs of monozygotic (MZ) and dizygotic (DZ) twins aged 7-19. We analyzed the scholastic measures of Reading, Literature, Foreign Language, Mathematics, History, Science, several other school subjects and generalized (total) measures. Results were as follows: twins with no sibs have more similar scholastic measures, than twins with sibs; significant differences in the intrapair similarity of twins for academic achievement appears between 2-children and 3-children families; in families with more than 3 children, the intrapair similarity of twins is lower than in 3-children families, these differences were not statistically significant, but interesting from a psychological point of view; and the impact of family structure on intrapair similarity of twins in academic achievement is more evident for MZ and opposite-sex DZ twins than for same-sex DZ twins. These results are influenced by the impact of factors which vary in different families: the socioeconomic status of the family, time which the parents are able to devote to their children, the direction of attention (orientation) of parents either towards the similarity of twins or the individual differences of twins.

ACADEMIC ACHIEVEMENT OF TEENAGERS — TWINS AND SINGLETONS

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The study investigates the academic achievement of twins and their single-born classmates (grades 7 through 11). About 2300 pairs of twins and 4000 singletons were the subjects of our analysis. We compared the levels of academic achievement of twins and singletons. The list of subjects included 12 subjects, which are obligatory for all Russian pupils in grades 7 – 11.We did not find many differences between the levels of academic achievement in twins versus singletons. Their average marks in all school subjects were very close to each other. Singletons were only more successful in one subject - Russian language (p = .028). Teenage twins appear to be more successful in gymnastics (p = .008). The average indexes of school achievement, including all subjects studied, for twins and singletons do not differ. Consequently, we can conclude that twins and singletons in grades 7-11 study almost equally. But it is possible to assume that the deficit of twins in the sphere of speech development remains until the end of school education. Obviously, the feature of twins' developmental conditions includes the negative factors influencing their language fluency.

REPRODUCTIVE SUCCESS IN SIBSHIPS WITH RECURRENT MULTIPLE MATERNITIES

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Is the phenomenon of multiple maternities (twinning) an atavism or a new mutation? The majority of apes and monkeys have lower twinning rates than man. Is the twinning a cost intensive error in an adaptive brood reduction system? In parish archives we have studied the incidence of twinning among about 10,000 relatives of triplets born in Finland 1905-59. Of the 627 mothers of triplets, 94 (15.0%) had a recurrent multiple maternity. In the 594 investigated sibships of mothers of triplets 81 (13.6%) contained multiple maternities. In the 572 sibships of fathers 52 (9.1%) contained multiple gestations. In the sibships of the triplets the chance to reach the age of 7 days was about 98% among singletons, 95% among twins but only 77% among triplets. The chance of triplets reaching adolescence rose considerably during the observation period from about 25% of the triplets born round 1910 to 47% for triplets born round 1950. Corresponding percentages for twins were 60 and 74 and for singletons 80 and 89. In spite of better prenatal maternal care, better treatment of prematures and lower perinatal and infant mortality, the mechanism of multifetal pregnancies seems not to have been of selective advantage, because the average number of survivors per pregnancy with multiple births was not higher than with singleton births. Furthermore, the maternal risk attendant on multiple gestations were in the past considerably higher than on singleton ones. The loss of maternal care for all children in the family seems to have exerted a severe selective pressure.

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MULTIVARIATE GENETIC ANALYSIS OF ANXIETY DIMENSIONS IN YOUNG ITALIAN TWINS

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Although anxiety dimensions in children have been widely investigated, to our knowledge no previous studies have aimed at exploring, in a population-based twin sample, the intraindividual covariation of these dimensions and its genetic and environmental basis. We used the twin design to estimate the genetic and environmental correlations between Generalized Anxiety(GAD), Panic (PD), Social Phobia (SP) and Separation Anxiety (SAD) disorder. Three hundred and seventy-eight twin pairs (135 monozygotic, MZ; and 243 dizygotic, DZ) from the Italian Twin Registry, aged 8-17 years and resident in the Northern Provinces of Milano and Lecco, filled in the Italian version of the 41-item SCARED questionnaire through a mail survey. We estimated twin correlations in MZ and DZ pairs for the various anxiety dimensions, and performed a multivariate genetic analysis comparing models that implied different parameterizations of the observed variance/covariance structure, namely Cholesky, Independent and Common pathway model. Cross-twin within-trait correlations ranged from .49 (SAD) to .57 (SP) in MZ pairs, and were all around .30 in DZ pairs. Individual phenotypic correlations ranged from .34 (SAD-SP) to .47 (GAD-PD). Cross-twin cross-trait correlations were moderate and generally higher in MZ than in DZ pairs. Model comparison showed that the data were best explained by the AE Cholesky decomposition, which provided estimates for genetic correlations from .40 (GAD-SAD) to .61 (PD-SP), and for environmental correlations from .01 (PD-SP) to .34 (GAD-PD). Our results indicated that the intraindividual covariation of the explored anxiety dimensions was substantially accounted for by genetic effects common to these dimensions.

CONCORDANCE, HERITABILITY AND SHARED GENETIC EFFECTS OF ASTHMA AND HAY FEVER IN 8- TO 17-YEAR-OLD ITALIAN TWINS

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Allergic diseases such as asthma (AS) and hay fever (HF) in childhood and adolescence are among the most common chronic diseases worldwide. Previous studies have showed a substantial familial resemblance for each of AS and HF, and have detected a close relationship between the 2 conditions at individual level. We used the twin design to unravel the genetic and environmental components of AS and HF, and asses the magnitude of shared genetic cause. The study sample was derived from the Italian Twin Registry, and consisted of 392 twin pairs aged 8-17 and resident in the Northern Provinces of Milano and Lecco. Information on AS and HF in twins was elicited through a parent-administered questionnaire following the structure adopted in the Italian SIDRIA study within the ISAAC project. We estimated: (i) twin concordances and tetrachoric correlations for AS and HF in monozygotic (MZ) and dizygotic (DZ) pairs; (ii) heritabilities of AS and HF, and their genetic correlation under a bivariate structural equation approach. Probandwise concordances were 67% (MZ) and 35% (DZ) for AS, and 65% (MZ) and 31% (DZ) for HF. The individual association of AS and HF was sizeable, and cross-twin cross-trait correlations by zygosity pointed to pleiotropic genetic effects. A Cholesky decomposition provided heritabilities of around 90% for AS and 80% for HF, and a substantial genetic correlation (~60%) between them. Our results showed strong genetic influences on child and adolescent AS and HF, and indicated that shared genetic factors are important in explaining the co-morbidity of the 2 conditions.

RECENT INCREASES IN THE RATES OF MULTIPLE MATERNITIES

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After a long continuous decrease, the twinning and other multifetal rates in many developed countries have increased during the last 2 to 3 decades. This change has been attributed to delayed childbearing and to increased use of subfertility treatments particularly in women over 35 years old. We applied indirect standardization techniques and analyzed how these new trends depend on changes in the effect of maternal age on the rates of multiple maternities. In order to simplify the comparisons, we have transformed the triplet and quadruplet rates according to Hellin´s law. Our study is based mainly on data for England and Wales for the period 1938-2003, Denmark, 1901-2000, Finland, 1901-2003, Norway, 1901-2003 and Sweden, 1901-2000. For all populations studied the temporal variations showed during the second half of the 20th century a decreasing trend to a trough and after that a steady increase. For England and Wales this increase was more marked among higher multifetal rates and particularly high among quadruplets. For triplet and quadruplet rates we noted after 1985 peaks followed by decreases caused mainly by new improved subfertility treatment strategies. Furthermore, we identified changes in the age-specific rates resulting in increased levels for older mothers. The only discrepancies between the different countries are the time for and the depth of the trough.

BIOMETRIC ANALYSIS OF DYNAMIC RELATIONSHIP BETWEEN PROCESSING SPEED AND COGNITIVE AGING

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Biometric dynamic change score models were applied to longitudinal data from the Swedish Adoption/Twin Study of Aging to compare the dynamic predictions of two-component theories of intelligence and the processing speed theory of cognitive aging. Data from up to 5 measurement occasions covering a 16-year period were available from 806 participants ranging in age from 50 to 88 years at the first measurement wave. Factors were generated to tap 4 general cognitive domains: verbal ability, spatial ability, memory, and processing speed. Model fitting indicated no dynamic relationship between verbal and spatial factors, providing no support for the hypothesis that age changes in fluid abilities drive age changes in crystallized abilities. The results suggest that, as predicted by the processing speed theory of cognitive aging, processing speed is a leading indicator of age changes in memory and spatial ability, but not verbal ability. Biometric analyses indicated that genes influencing processing speed also impact changes in memory and spatial ability.

MANAGING ON-LINE COMMUNICATION WITH PARENTS OF MULTIPLES

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Tamba, in line with so many voluntary and commercial organizations in recent years, has seen a huge shift in the focus of its image and communication with members and supporters, from printed literature to the world-wide web. www.tamba.org.uk was launched in 2003 and has recently undergone further improvements and investments but the challenge to keep up with technology and the expectations of our users is growing almost daily. This presentation will give a brief overview of the issues facing Tamba, both in terms of providing and updating free on-line information while also balancing the books, and as importantly managing communications between the virtual on-line community of multiple birth parents which exists on the message boards. Issues arising include confidentiality, appropriate topics, child protection and harassment. To minimize risks in these areas the Tamba message boards are now only open to members to post and reply to topics, attach photographs and contact one another. Nonmembers are free to read the wealth of advice and information that has been posted. It is envisaged that the session will give COMBO members the opportunity to have a facilitated discussion and share ideas and best practice in this key area of communication.

TAMBA CHALLENGES, PROGRESS AND ACHIEVEMENTS

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This presentation to COMBO colleagues will give an overview of new services, successes and challenges faced by Tamba, the UK Twins and Multiple Births Association, in the 3-year period since the 11th International Congress of the International Society for Twin Studies. In that period Tamba has developed a new 3-year Strategic Plan which is two-thirds complete. In 2005 the organization was awarded the Investors in People standard, the international standard in recognition of effective commitment to supporting and training staff and volunteers. Tamba has seen a shift in statutory funding opportunities in the United Kingdom (UK), with the organization's work now being more closely aligned with the Department for Education and Skills and its focus on child welfare

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and parenting support, as opposed to our historic links with the Department of Health. This new funding stream has enabled us to develop an entirely new service, the Parenting with Multiples in Mind parenting course, a 7-week parenting course with associated support materials. The last 3 years has also seen a huge growth in the number of visits to the Tamba website and in particular the message boards, where a vibrant online community of parents and expectant parents now exists. All this activity has taken place against a backdrop of increasingly hard work to recruit and retain members and attract sustainable ongoing funding for Tamba's services. As we mark the successes and challenges of the last 3 years Tamba is also looking forward to celebrating its 30th anniversary of supporting multiple birth families in 2008.

MULTIPLE BIRTH DATA COLLECTION

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Twin registries and databases are useful tools for collecting up to date information about multiples and multiple births. This information can be used for noting trends in prenatal care, birthweights, medical conditions, etc. NOMOTC has developed a new database collection that could use its 25,000+ members for data collection, as well as the general public who accesses our web site. We average 11,600 visitors generating over 300,000 hits per month. Data can be submitted online. Questions consist of a combination of demographics, ethnicity, frequency of multiple births in the family tree, assisted reproductive technology, low birthweight, handedness, and special needs of both parents and multiples. Results are currently housed in a Microsoft Access Database designed by a volunteer. A total of 1720 surveys have been completed: 1614 sets of twins, 79 triplet sets, 5 quadruplet sets, and 1 set of quintuplets. NOMOTC feels that this could result in one of the largest data bases of parents of multiples and will be useful for numerous epidemiological and medical studies in the future. Current access can be found on the Research section of our website, www.nomotc.org.

SET: FROM CONCEPT TO PRACTICE

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Multiple pregnancies resulting from IVF/ICSI treatment are recognized as an adverse outcome and are responsible for morbidity and mortality related to prematurity and very low birthweight. Due to the increase in iatrogenic multiple births, the incidence of maternal, perinatal and childhood morbidity and mortality has increased. This results in a hidden healthcare cost of infertility therapy and may also lead to social and political concern. Reducing the number of embryos transferred and the use of natural cycle IVF will obviously decrease the number of multiple gestations. The Belgian project, in which reimbursement of assisted reproduction technology-related laboratory activities is linked to a transfer policy aiming at substantial multiple pregnancy reduction, is a good example of cost-efficient health care through responsible, well-considered clinical practice. In the discussion with the health authorities, data from clinical research and health-economic studies were useful in showing that a reduction in multiple pregnancy rates following IVF could save enough money to reimburse IVF. On July 1, 2003, the Belgian government started with the reimbursement of IVF/ICSI laboratory costs of couples with female age less than 43 years for a maximum of 6 treatment cycles in a lifetime. This strategy was coupled with a reduction in the number of embryos transferred in twin-prone patients, subsequently leading to a considerable decrease in multiple pregnancies and their associated perinatal costs.

MODELING GENETIC AND ENVIRONMENTAL FACTORS TO INCREASE HERITABILITY AND EASE THE IDENTIFICATION OF CANDIDATE GENES FOR BIRTHWEIGHT: A TWIN STUDY

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Heritability estimates of birthweight have been inconsistent. Possible explanations are heritability changes during gestational age or the influence of covariates (e.g., chorionicity). The aim of this study was to model birthweight of twins across gestational age and to quantify the genetic and environmental components. We intended to reduce environmental variance to increase heritability and thereby the chance of identifying candidate genes that influence the genetic variance of birthweight. Perinatal data were obtained from 4232 live-born twin pairs from the East Flanders Prospective Twin Survey, Belgium. Heritability of birthweights across gestational ages was estimated using a nonlinear multivariate Gaussian regression with covariates in the mean model and in the covariance structure. Maternal, twin-specific, and placental factors were considered as covariates. Heritability of birthweight decreased during gestation from 25 to 42 weeks. However, adjusting for covariates increased the heritability over this time period. First-born twins without neonatal death of multipara with separate placentas had the highest heritability (from 52% at 25 weeks to 30% at 42 weeks). Twin-specific factors revealed latent genetic components, whereas placental factors explained common and unique environmental factors. The effect of chorionicity was masked by the number of placentas and site of the insertion of the umbilical cord. Modeling genetic and environmental factors leads to a better estimate of their role in growth during gestation. For birthweight, addition of covariates to the model explained a great part of environmental factors, resulting in an increase of the heritability estimates and thereby the chance of finding genes influencing birthweight in linkage and association studies.

NONSHARED ENVIRONMENT AND GENETIC INFLUENCES ON EXPERIENCE IN RUSSIAN ADOLESCENT TWINS

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There exists well-documented evidence of genetic influence on measures of family environment (Plomin & Bergeman, 1991), as well as of importance of nonshared environment in development (Plomin & Daniels, 1987). However, no research of this kind was previously reported for Russian sample. We have collected scores on the Russian version of the Sibling Inventory of Differential Experience (SIDE: Daniels & Plomin, 1985) from Russian 11- to 17-year-old monozygotic and dyzygotic (of same-sex and of different-sex) twin pairs, 225 pairs in overall. Model fitting was used to investigate genetic, shared environmental and nonshared environmental effects on SIDE factors.

MODELING MULTIPLE SOURCE RISK FACTOR DATA AND HEALTH OUTCOMES IN TWINS

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The objective was to incorporate multiple-source risk-factor data in regression modeling for twin pairs. Twin researchers often have measures of the same risk factor from 2 different data sources. For instance, in the Vietnam Era Twin (VET) Registry, military service in Vietnam is available by both self-report and military records. The simultaneous use of multiple source risk factors in a regression modeling framework offers advantages for interpretation and precision. We propose a GEE regression model that builds on previous work for multiple-source risk-factor data. We extend the method to account for the dual clustering of multiple source data and twin pairs. We conduct simulations to estimate efficiency gains resulting from combining information from multiple sources and examine efficiency gains for within and between pair effects. The method is illustrated using data on Vietnam service and post-traumatic stress disorder (PTSD) symptoms. Simulations show that combining multiple

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source data reduces parameter variance estimates by 5-10%. With VET Registry data, the PTSD log odds ratio estimate was 0.97 (SE = 0.045) for self-reported Vietnam service and 0.83 (SE = 0.046) from the military record. The log odds ratio for the combined report was 0.90 (SE = 0.044), representing a 7.3% reduction in variance. The within-pair combined data source effect showed a slightly better gain in efficiency (8.3%). The GEE regression framework for multiple source risk factor data using twins is a highly flexible methodology and can be used for assessing source effects as well achieve potential gains in statistical efficiency.

LONG-TERM EFFECTS OF PRETERM MULTIPLE BIRTH

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The National Organization of Mothers of Twins Clubs, Inc. (NOMOTC) initiated this study in 2004 to assess the types and duration of effects caused by preterm birth of multiples. A questionnaire was presented in NOMOTC's 'Notebook' and it was also sent out in an NOMOTC national mailing. The survey was to be completed by a parent of preterm multiples who were at least 5 years old when the survey was completed. A total of 92 surveys were completed. Eights sets of twins, 11 sets of triplets, and 1 set of quadruplets were represented in the study. The total number of children was 197. The gestation of the multiples ranged from 25-37 weeks, but most were born between 32-36 weeks' gestation. Three of the families experienced a death of one of the multiples — all 3 were in a higher-order multiple pregnancy. Most of the preterm multiples experienced mild, but also some severe, complications of prematurity, especially respiratory difficulties and feeding problems. Less commonly, some of the children had more severe problems including cerebral palsy, epilepsy, necrotizing enterocolitis, and intraventricular hemorrhage. By the time these preterm multiples became school-age children, many of them had special schooling needs, most commonly, speech therapy. The majority of the children did well once they were treated for the immediate types of complications that occurred soon after birth. Some had medical problems that continued to require treatment, however. This study demonstrates the dangers of preterm birth in a multiple pregnancy.

RECURRENCE RISK AMONG OFFSPRING OF TWINS DISCORDANT FOR ORAL CLEFT

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Oral cleft (OC) is one of the most common congenital malformations (1:500 newborns). Previous twin and family studies have suggested that the etiology is multifactorial with genes playing a major role. The aim was too estimate the heritability as well as the recurrence risk for the offspring of both the healthy and the affected twin discordant for OC. The studies are based upon 3 registries: The Danish Facial Cleft Register, The Danish Twin Registry, and The Danish Central Person Registry. A total of 188 twin pairs with OC were born in 1936-2001 in Denmark. The proband-wise concordance rates were 50% (95% CI: 27 - 71) for monozygotic twins and 7.6% (95% CI: 3 -16) for dizygotic twins, corresponding to a heritability of 92% (95% CI: 83 - 97). Two hundred and twenty-seven offspring were born of the 167 twin pairs discordant for OC. The recurrence risk for the offspring of the affected twins was 1.9% while it was 1.6% for the offspring of the healthy twins, that is, we found no difference in the relative risk for OC between offspring of the twins with OC compared to the offspring of the healthy co-twins (RR = 1.16; 95% CI: 0.17 - 8.11). For both groups the risk is increased compared to the background population. Despite the fact that the study premise is population-based and estimated for a period of 65 years the power is small, but the estimates indicate that the healthy co-twins are passing on the risk to their offspring as if they had the OC themselves. This study supports the strong genetic component to the etiology of OC.

A TWIN STUDY OF THE GENETIC CONTRIBUTION TO AGE-RELATED FUNCTIONAL DECLINE

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Quality of life in the elderly includes age-related functional decline as a key element. The extent of genetic influence on functional decline is thus a question of some practical importance because it can help inform discussions about the potential impact of interventions. To study this question, we did a health survey of more than 7000 twins in the NAS-NRC Twin Registry, consisting of male-male twin pairs who were born in the years 1917-1927 and who served in the US military; these twins were 70-80 years old at the time of survey. The response rate was 79%, yielding 2721 twin pairs, 1384 monozygotic and 1337 dizygotic. There were 10 indicators of functional decline, such as health limitations on heavy chores and social activities, or blocks walked without having to rest. Mx analyses found that additive genetics accounted for 19 to 33% of variability in 8 of the 10 items, with 3 of the 8 being statistically significant. Common environment was non-zero in only 2 of the models (walking 10 or more blocks and needing regular assistance). We also analyzed a summary score of the 10 indicators. With age as a covariate, additive genes accounted for 22% of covariance in liability for a higher summary score, unique environment accounted for almost all the remaining variance, and age was a minor factor. We found that genetics effects play a modest but also important role in age-related functional decline. Plans are underway to examine additional data on healthy and successful aging.

INTERPRETING BETWEEN- AND WITHIN-PAIR REGRESSION COEFFICIENTS IN MODELS FOR TWIN DATA

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The regression analysis of twin data should allow for the possibility of distinct between- and within-pair exposure effects on the outcome measure, represented respectively by coefficients for the pair mean and the deviation of the individual-level exposure value from this mean. The within-pair regression effect is conditional on exposure effects shared within-pairs, including any common genetic or environmental influences. There are several ways to specify an appropriate regression model to capture between- and within-pair exposure effects, and the interpretation of the resulting regression coefficients remains controversial. One fact that is underappreciated is that the model specifying between- and within-pair exposure effects is identical to the model that regresses the outcome on the exposure values of the both the twin and their co-twin. If the regression coefficient for the co-twin exposure is zero then the within- and between-pair regression coefficients are equal and vice versa. It may be reasonable to conclude that a marginal association between a twin's outcome and their co-twin's exposure is due solely to separate non-zero correlations between the twin's exposure and each of these other 2 factors. We have shown that comparing within-pair regression coefficients between dizygous and monozygous twin pairs cannot be used to determine if there is a genetic basis for an exposure-outcome association. One should exercise similar caution when comparing between- and within-pair regression coefficients; they may be equivalent even when there are factors shared by a twin's outcome and their co-twin's exposure that are not shared with the twin's exposure.

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ASSOCIATION BETWEEN URINARY COTININE AND BIOMARKERS FOR OXIDATIVE STRESS IN MONOZYGOTIC TWINS OF KOREA: HEALTHY TWIN STUDY

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The association between cigarette smoking and oxidative stress might be modified by genetic influences. We aimed to examine the relationship between urinary cotinine and oxidative stress biomarkers, malondialdehyde (MDA) and 8-hydroxydeoxyguanosine (8-OHdG), independently of genetic influences. Two hundred sixty-one monozygotic twin pairs (age 37.7 ± 7 years, 96 male pairs, 165 female pairs), who participated in Korea Healthy Twin study, were studied. Zygosity of twin pairs was determined using a self-administered questionnaire. The levels of cotinine, MDA and 8-OHdG were measured by high performance liquid chromatography in 12-hour urine. All biomarkers were adjusted by the concentration of urinary creatinine. In the 82 male and female pairs who were discordant by 100 (ug/g creatinine) or more cotinine (mean, 253.5), the difference of urinary MDA (uM/g creatinine) within pair (mean, 0.76) was significantly increased according to increasing the difference of urinary cotinine (ß = 0.0011, p = .002), while the difference of urinary 8-OHdG was not (ß = 0.0009, p = .52). In female twins, the difference of MDA within pair (mean, 0.87) was significantly associated with the increasing the difference of cotinine in all 163 pairs (p = .005) and in 48 pairs discordant by 100 or more cotinine (p = .01). The levels of MDA and 8-OHdG suggested the effects of gene environmental interaction in simple plots with logarithmic difference within pairs by logarithmic mean within pairs of MDA and 8-OHdG (p < .0001, both). Cigarette smoking measured by urinary cotinine is associated with the level of MDA, an oxidative stress biomarker, independent of genetic influences, particularly in women.

GENETIC INFLUENCE ON EEG POWER ASSOCIATED WITH WORKING MEMORY

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Our aim was to examine genetic influence on EEG power bands recorded at rest and during a working memory task. Analyses focussed on alpha and theta power because they have both previously been associated with cognitive function. EEG data were collected from 548 adolescent twin pairs (252 monozygotic and 296 dizygotic). Preliminary work suggests (a) variation in magnitude of genetic influence dependent upon brain region (EEG recorded over prefrontal and parietal brain regions was examined), and (b) an independent source of genetic influence associated with working memory.

THE WESTERN AUSTRALIAN TWIN REGISTER (WATR)

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The WATR is a population-based register of all multiples born in Western Australia since 1980. Eligible families were contacted to participate in the WA Twin Child Health (WATCH) study. The aims were to (1) to establish the WATR and (2) to determine whether it was representative of the WA population. Records of all multiple births to have occurred in Western Australia (WA) between 1980 and 1997 were obtained from the Maternal and Child Health Research database (MCHRDB) using the code for plurality and confirmed by probabilistic record linkage. The Australian Bureau of Statistics (ABS) socioeconomic indexes for areas (SEIFA) codes were used to assess the representativeness of the Register. A total of 11,189 multiple birth children from 5456 families were identified, comprising 5340 twin pairs and 166 sets of higher order multiples. The multiple birth rate rose from 2.0% of all births in WA in 1980 to 3.1% in 1997. Seven hundred and thirty-seven children from 500 families were known to have died. The perinatal death (PND) rate was 54/1000 births for twins and 114/1000 births for higher order multiples. The PND rate was higher in male twins than in female twins (58/1000 births vs.50/1000 births), but was lower in male twins with a female co-twin than those with a male co-twin (62/1000 births vs. 46/1000 births). Same-sex twin pairs comprised 64.5% of all twins, which declined from 73% in 1980 to 56% in 1997. Examination of the SEIFA codes showed no difference between the WATR and the WA population with respect to social disadvantage, economic resources and education and occupation. The WATR is a population-based register of multiple births which is representative of the population from which it is drawn.

THE NATURE AND NURTURE OF OBESITY IN CHILDREN: THE ABNORMAL IS NORMAL

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The objective was to understand the overlap between the etiology of obesity and normal variation in body mass index (BMI) in children. Data were obtained from a large UK representative sample of twins: 2342 same-sex pairs at 7 years and 3526 same-sex pairs at 10 years. The twin method and model-fitting techniques were used to estimate genetic and environmental contributions to BMI. DeFries-Fulker (DF) extremes analyses were used to investigate genetic and environmental influences on the mean difference between obese children and the children of normal weight. Obesity was classified using the International Obesity Task Force criteria. At both ages, BMI and obesity were highly heritable (.60-.74) and only modestly influenced by shared environmental factors (.12-.22). Extremes analyses indicated that genetic and environmental influences on obesity are quantitatively and qualitatively similar to those operating across the normal range of BMI. Obesity is the extreme of the same genetic and environmental factors responsible for variation throughout the distribution of adiposity. This finding implies that genes that influence obesity will also be associated with adiposity in the normal range, and similar environmental influences will affect adiposity in the clinical and normal range. These findings have implications for investigating the mechanisms for weight gain and developing interventions for weight control. Finally, knowing that obesity is strongly influenced by genetic factors will help clinicians to respond to patients and carers appropriately - awareness that genes are important in determining weight can reduce the burden of blame on the parents and the child.

RELATIONSHIP BETWEEN TWIN LANGUAGE, TWINS' BOND, AND SOCIAL COMPETENCE

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This study investigated the relationship among twin language, the twins' bond, and social competence in a prospective longitudinal study. We hypothesize that twins whose bond is close would be more likely to have a twin language, and twins who have a twin language would be less likely to develop social competence. In addition, we hypothesize that some environmental factors such as having an older sibling, preschool attendance and biological factors are also related to twin language, the twins' bond and social competence. A mailed questionnaire survey was conducted in 958 mothers from a study in 1999, as a follow-up study. As a result, 516 respondents returned the questionnaire (53.9%). In this study, we used only 216 twins aged 6-12 years old (school-age children) for analysis, excluding those with missing values. In the present study, we found that biological factors such as whether the twins were exactly alike or not and sex were associated with the twins' bond. On the other hand, having an older sibling and preschool attendance did not affect the twins' bond, twin language or social competence. One of the most important findings was that the twins' bond affected social competence not directly but through twin language.

PSYCHOLOGICAL CHARACTERISTICS OF SURVIVORS OF 'VANISHING TWIN' PHENOMENON

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I have made a 5-year study of the psychological characteristics of the surviving twin when the death of a twin occurs in the first or second trimester. As a surviving twin myself, I have corresponded with over 100 sole survivors of a twin or multiple pregnancy, learned about their attitudes and feelings towards their twin and created a long list of 54 possible

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psychological indicators of the loss of a twin in the womb. In the 2006 cohort of 104 questionnaires, the statements most commonly marked as 'true' were:

I feel different from other people (90%)

I tend to hold on to things (89.4%)

All my life I have felt in some way 'incomplete' (88.4%)

I fear abandonment or rejection (87%)

I feel the pain of others as if it were my own (87%)

I know I am not realising my true potential (87%)

I grieve deeply and for a very long time after someone close to me, or a beloved pet, has died (86.5%)

I find disappointment very painful (86.5%)

There are 2 very different sides to my character (85.5%)

All my life I have felt restless and unsettled (84.6%)

I have been searching for something all my life but I don't know what it is (83.6%)

I am editor of U*ntwinned: Perspectives on the death of a twin before birth*, with a foreword by Dr Louis G. Keith, published January 2007 which is an anthology of papers about this.

CAN WE PREDICT THE EVOLUTION OF THE TWIN BIRTH RATE IN BELGIUM?

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The increment of the twin birth rate has major repercussions on preterm delivery rate. One Belgian neonatal intensive-care bed out of 4 is occupied by a multiple birth infant, mainly a twin. Since July 2003, in the so-called SET Royal Decree (Single Embryo Transfer), the INAMI — the Belgian national health insurance — introduced the reimbursement of laboratory fees accompanying in vitro fertilization (IVF). This provided Belgian couples with better financial access to IVF. However reimbursement was conditioned to the strict reduction in the number of embryos transferred; in most circumstances it was one (elective SET). Doing so it was hoped to finance indirectly the expenses for IVF reimbursement by reducing the costs of these high-risk pregnancies and ensuing neonatal intensive care hospitalizations. Since then, has the SET Decree modified the incidence of twin births? In our hospital, the decree seemed to be first followed by a decrease from 6.5% in 2002 to 4.9% in 2004 (*ns*). But in 2006, this trend reversed to 5.7% (*ns*).At the Belgian Neonatal Intensive Care Units (NICU) level, we compared the percentage of newborns with a birth-weight of less than 1500 g due to multiple pregnancies. All (19/19) Belgian NICUs participated in that audit in 2001 and 17 out of 19 in 2004 and 2005. The percentage of multiple birth VLBW-babies was 29.1% (287/985) in 2001 before the SET Decree, 30.1% (277/918) in 2004 and 34% (339/996) in 2005, showing a significant proportional increase of VLBW infants due to multiple birth in 2005 compared to 2001 (p = .02). Data from the ONE database (Oeuvre de la Naissance et de l'Enfance), show the same percentage of twin pregnancies in 2002 and 2005 (1.65%) in the French speaking Belgian population. We can conclude that up to now there is no consequential decrease of high risk twin birth incidence after the implementation of the SET decree. One explanation could be, among others, that even if the relative risk of multiple pregnancy after IVF has diminished from around 25 % to less than 10 % thanks to the SET policy, this good result could be counterbalanced by the twofold increase in the number of IVF requests after not even one year since the enforcement of the SET decree.

ASSOCIATION JUMEAUX

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Association Jumeaux provides help and information concerning twins, multiples and multiple births. Created by parents in 1987, it continues its activities in the French-speaking part of Switzerland, with a small bulletin, meetings, a telephone hotline for information and psychological help and website : www.jumeaux.com. Other activities include the loan of strollers, small clothing for babies, production of specific documentations, and so forth. In January 2006, one of our members had the occasion to write some lines for a new book intended for general public *Le Guide des Jumeaux*, published by authors Jean-Claude Pons, Christiane Charlemaine, and Emile Papiernik in partnership with the federation of *Jumeaux et plus*, France, and edited by Odile Jacob.

GENETIC INFLUENCE ON HUMAN LIFESPAN AND LONGEVITY

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There is an intense search for longevity genes in both animal models and humans. Human family studies have indicated that a modest amount of the overall variation in adult lifespan is accounted for by genetic factors. But it is not known if genetic factors become increasingly important for survival at the oldest ages. Using the Danish, Finnish and Swedish twins born between 1870 and 1910 comprising 20,502 individuals we first estimate mean lifespan of twins by lifespan of co-twin and then turn to the relative recurrence risk of surviving to a given age. Mean lifespan for male monozygotic (MZ) twins increases 0.39 (95% CI: 0.28–0.50) years for every year his co-twin survives past age 60 years. This rate is significantly greater than the rate of 0.21 (0.11, 0.30) for dizygotic (DZ) males. Females and males have similar rates and these are negligible before age 60 for both MZ and DZ pairs. We, moreover, find that having a co-twin surviving to old age substantially and significantly increases the chance of reaching the same old age, and this chance is higher for MZ than for DZ twins. The patterns for females and males are very similar, but with a shift of the female pattern with age that corresponds to the better female survival. The present large population-based study shows that genetic influences on lifespan are minimal prior to age 60 but increase thereafter. These findings provide support for the search for genes affecting longevity in humans, especially at advanced ages.

ON THE CHARACTERIZATION OF ADVANCED AGE MORTALITY

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We aim at characterizing the upper tail of the human lifespan distribution by applying extreme value theory models to advanced age mortality data of twins. The extreme value theory models of late life mortality exhibit properties as the notion of a potential lifespan and 'force of mortality' (hazard function) that allows for modeling mortality rate plateaus and decline. We seek to investigate if such mortality patterns appear among long-livers in population-based cohorts and how it depends on various background variables as gender and birth cohort. We describe the extension of the models to allow for within twin pair dependency and for studying genetic influences at advanced ages.

BODY COMPOSITION, SMOKING AND DIZYGOTIC TWINNING

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With the increasing prevalence in twinning, interest into the association of twinning with fertility related factors has also increased. This study examined differences between mothers of monozygotic (MZ) and dizygotic (DZ) twins in risk factors for DZ twinning. All twin mothers (N = 33,330) registered with the Netherlands Twin Register (Boomsma et al., 2006) received a questionnaire in which they were asked to report on familial twinning, parity, use of artificial fertility techniques, medication, height, weight, smoking behavior prior to the twin pregnancy and age at time of the twin pregnancy. Information on the father of the twins was also collected. Completed questionnaires were received from 19,313 twin mothers, including 19,020 mothers of one twin pair, 147 mothers of 2 sets of twins and 146 mothers of triplets. In total 982 mothers said they had a sister with a twin. As a first analysis we selected data from mothers with natural MZ (N = 2865) and natural DZ twins (N = 6444). We used stepwise binary logistic regression with known risk factors for DZ twinning (parity and maternal age) in the first step and (height, body mass index [BMI], smoking) in the second step and the zygosity of the twins as the outcome variable. Results indicated that height, a BMI of 25 or higher and maternal smoking prior to the twin pregnancy are significantly associated with natural dizygotic twinning.

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CAN TWIN STUDIES BE USED TO INFER CAUSATION?

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Consider pairs of traits X and Y measured for twin pairs. If X causes Y, and if X is correlated in twin pairs, there will be a marginal correlation between Y in one twin and X in the co-twin (cross-trait cross-twin correlation) that will reduce or disappear once allowance is made for (i.e., we condition on) the X value of the twin. If Y and X are correlated due only to familial factors for Y and for X that overlap, then the cross-trait cross-twin association may be altered by conditioning on the X value of the twin, but probably to a lesser extent than in the first scenario. If the relationship between X and Y is due to within-person confounding alone, there will be no marginal cross-trait cross-twin association. By analyzing relationships between Y and X using data from twins or relatives it might be possible to distinguish situations in which a relationship between the 2 variables is more or less likely to be causal. Note that the X variable could represent a measured genotype. We present a general regression framework to analyze these scenarios, and a series of examples with continuous outcomes variables (Y = blood pressure, X = body mass index; Y = bone area, X = muscle area; Y = mammographic density, X = number of live births, age at menarche, and height) that illustrate the different results from application of the regression model. We also discuss the plausibility of the competing models. Twin studies may therefore be important to help identify associations that may have a causal component and therefore be worthy of investigation by intervention studies, and help rule out associations most likely and/or mostly due to confounding. It could also help identify genetic associations in which the measured variant is of functional significance. Care needs to be taken in making these judgements and ancillary information would help in any decision making. This paradigm could help relaunch twin studies as a tool for medical and scientific research.

A SUCCESSFUL MODEL OF A NORTH–SOUTH COLLABORATION

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This presentation will describe the process of setting up a population-based twin study in Sri Lanka, funded by Wellcome Trust, and representing a collaboration between the Sri Lankan Twin Registry and the Institute of Psychiatry, King's College London. This study has recruited nearly 2000 twin pairs, and 2000 singletons sampled from an identical sampling frame, and has collected data on common mental disorders, substance misuse, post-traumatic stress disorder and somatic symptoms. The main issues in developing such a collaboration will be described and include: (a) gaining funding; (b) developing relations of trust; (c) developing research which is culturally appropriate; (d) learning to communicate from a distance; (e) having robust research governance; and (f) ensuring the project adds value for both parties.

EMERGENCE OF PRIMARY INCISORS IN AUSTRALIAN TWINS

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The biological basis of human tooth eruption is still not completely understood and very few studies have explored how genetic factors contribute to this process. Model-fitting methods were applied to tooth emergence data for 98 twin pairs aged between 1 and 3 years who are enrolled in a continuing longitudinal study of Australian twins. The contributions of genetic and environmental factors to variation in timing of emergence of human primary incisors were quantified. Comparisons of means and variances for timing of tooth emergence did not reveal any systematic differences between zygosity groups or between sexes. Emergence times of maxillary centrals and mandibular laterals were less variable than those of maxillary laterals and mandibular centrals. The only antimeric pair to display significant directional asymmetry was the maxillary laterals, with the left side tending to emerge earlier than the right. Estimates of narrow-sense heritability were high, ranging from 82 to 94% in males and 71 to 96% in females. Variation in timing of emergence of the primary incisors in this twin cohort was under strong genetic control, with a small but significant contribution from the external environment.

TWIN REGISTERS IN ASIA AND AFRICA

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Recently, the number of twin registries has increased sharply in Asian countries. To foster collaborations among twin researchers in Asia and other countries in the world, the Asian Society for Twin Studies (ASTS) was developed. This paper presents an overview of existing twin registers in Asia and recent activities of the ASTS. Additionally, a plan on the development of a population-based twin registry in South Africa will be discussed.

INFLUENCE OF CHORIONICITY ON HERITABILITY ESTIMATES OF HEIGHT, WEIGHT, AND BODY MASS INDEX IN SOUTH KOREAN TWIN CHILDREN

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The aim of the present study was to assess whether the heritability of body size (height, weight, and body mass index) among preschoolers, measured from maternal reports, differs according to the chorionicity of the monozygotic (MZ) twins. The twin sample was drawn from the South Korean Twin Registry, in which chorionicity data were collected at birth. Twin correlations were calculated and model-fitting analyses were carried out. Heritability estimates of body size do not differ significantly according to the chorionicity of the MZ twins.

EFFECTS OF CHORION TYPE ON PERSONALITY IN SOUTH KOREAN PRESCHOOL TWINS

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Prenatal influences on children's personality development are still largely unknown. The present study investigated effects of chorionicity, and genetic and environmental factors on personality in preschool twins. The sample included 64 pairs of monochorionic (MC) and 37 pairs of dichorionic (DC) monozygotic (MZ) and 376 dizygotic (DZ) twins. Parents (mostly mothers) rated emotionality, activity, and sociability of these twins. Twin correlations were computed and model-fitting analyses were carried out. Chorionicity effects were significant and substantial only for emotionality. These findings were contrasted to results from the Riese study (1999) where chorion type was not related to co-twin similarity on any of the personality traits.

GENETIC SUSCEPTIBILITY TO HERPES VIRUS INFECTION: TWIN CONCORDANCE OF INFECTIOUS MONONUCLEOSIS AND HERPES ZOSTER

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Herpes viruses typically cause a more severe infection when acquired relatively late in life (adolescence or adulthood). For example, primary infection with Epstein-Bar virus during early childhood is generally asymptomatic but delayed primary infection during adolescence/adulthood results in clinical syndrome of infectious mononucleosis (IM). The viruses in the Herpes family also share the characteristic of reactivation after primary infection. Herpes zoster (shingles) is the reactivated infection associated with varicella zoster virus after a primary chickenpox infection. Higher concordance rate of disease among monozygotic (MZ) compared to dizygotic (DZ) twins suggest that genetic and/or early childhood risk factors may play an etiological role. We used twins registered in California Twin Program at University of Southern California, a twin registry of native Californians composed of 51,609 who have completed a 16-page questionnaire to examine whether genetic factors may be involved in susceptibility of IM and shingles. We used self-reported information from double-responding twins of whom at least one twin reported history of IM (699 pairs) and shingles (357 pairs) to calculate pair-wise concordance. Our analysis showed that concordance rate for IM was higher in MZ (12.11%) than DZ (6.07%). The concordance rate for shingles did not differ between MZ and DZ twins (MZ = 4.38, DZ = 4.48).

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These concordance patterns generally persisted across gender. We will analyze hazard ratio to examine the risk for each of these diseases in the co-twins by duration of onset after the diagnosis in the proband.

RECENT PROBLEMS FOR INCREASED MULTIPLE BIRTHS IN JAPAN FROM THE VIEWPOINT OF STATISTICAL ANALYSIS USING VITAL STATISTICS

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Yearly changes in twinning, triplet, and quadruplet rates were analyzed using vital statistics for the period from 1951 to 2005 in Japan. The dizygotic twinning rate remained nearly constant from 1955 (1.86 per1000 births) to 1987 (2.29), and gradually increased to 1998 (4.64). Triplet rates gradually increased from 58 per million births in 1974 to 109 in 1988 and rapidly increased to 275 in 1994 and remained constant thereafter. The quadruplet rate was 3.3 per million births in 1974 and increased to 26.7 in 1994 and decreased thereafter. The rising twinning, triplet, and quadruplet rates have been attributed to the higher proportion of mothers treated with ovulation inducing hormones and IVF. The proportion of low birthweight (under 2500 g) was 8.1 % for single births in 2005; whereas it was 72.9 % for multiple births. Among low birthweight children, proportion of multiple children was 9.4 % in 1969 and increased to 17.4 % in 2005. Geographical variations of multiple birth rates depend on the number of hospitals for IVF in each prefecture. It seems that number of neonatal intensive care units (NICU) are insufficient in many prefectures. According to Yokoyama et al. (1995), multiple births had a higher rate of cerebral palsy (CP) than singletons. Then, raising multiple babies will bring a slightly higher number of CP in future in Japan. The cooperative relationship that exceeds the academic society is necessary to prevent a rising multiple birth rate.

STRESS-RELATED NEGATIVE AFFECTIVITY AND GENETICALLY ALTERED SEROTONIN TRANSPORTER FUNCTION: EVIDENCE OF SYNERGISMIN SHAPING RISK OF DEPRESSION

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Genetic moderation of the depression-inducing effects of stressful life events (SLEs) has been reported, but findings suggest that genes may not moderate the effects of SLEs per se but instead may moderate the risk of depression associated with the stable tendency to develop negative emotions in response to minor environmental experiences. This study was conducted to examine whether a functional polymorphism of the serotonin transporter gene (5-HTTLPR) moderates the association between negative affectivity (neuroticism) and depression and to what degree this can explain previous findings involving SLEs. A population-based sample of 374 ethnically homogeneous young adult female twins from the East Flanders Prospective twin Survey (EFPTS) was included in this longitudinal study. Results of this study showed that the depressogenic effect of SLEs in the 3 months before interview was significantly greater in women with 2 short (S) alleles compared with women with 1 or none. However, this effect disappeared after accounting for the effect of SLEs conditional on neuroticism. Similarly, the depressogenic effect of neuroticism was progressively greater with number of S alleles, and this was unchanged after accounting for the effect of neuroticism conditional on SLEs. Genotype x environment interactions in depression may be more productively interpreted by involving mechanisms more proximal to psychological experience itself. The probability that stress-related vulnerabilities for depression result in symptom formation may be moderated by a neurobiologic phenotype characterized by altered processing of negative emotions associated with variation in 5-HTTLPR.

EVIDENCE-BASED PRENATAL FOLLOW-UP OF TWIN PREGNANCIES

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In the case of a multiple pregnancy, complications both for mother and children are higher during pregnancy. In this review evidence-based guidelines on the prenatal care of multiple pregnancy are proposed. A literature review was performed including articles based on meta-analysis, systematic review and original research published between January 2000 and January 2007. There is no consensus on the ideal frequency of prenatal visits in multiple pregnancy, no RCT has provided data on possible advantages of specialized multiple pregnancy clinics. Blood pressure should be taken at every consultation, there are no data on screening for gestational diabetes in multiples. Chorionicity should be determined as early as possible, although no prospective trials have indicated that changing clinical care improves pregnancy outcome. Nuchal translucency measurement is the method of choice to screen for aneuploidy, maternal serum methods should not be used. At 18–20 weeks, a fetal anomaly scan should be performed. Transvaginal measurement of cervical length is a strong predictor of preterm delivery, but no useful interventions have been proven, actually cerclage of a short cervix in case of twins is assoicated with a higher risk of preterm delivery. Preventive tocolytics are of no use, routine hospitalization and bed rest should be avoided as these increase the likelihood of preterm birth. Home uterine activity monitoring and daily nursing contact in twins increase the use of tocolytic therapy without any benefit. In case of threatening preterm delivery corticosteroids should be administered, there are no arguments to change the dose as compared to singletons. Associating umbilical artery Doppler to biometry reduces perinatal mortality. Although perinatal mortality and morbidity are lowest between 36 and 38 weeks, no benefit of systematic induction of labour from 37 weeks has been demonstrated in twins. Studies on the management of prenatal care in twins are hampered by low numbers and low quality in general making the management based on authority and/or consensus more than really evidence based. For most interventions we still are in the era of no proof of effect but also no evidence for no effect.

TWO PEAS OR NOT TWO PEAS? TWIN RELATIONSHIPS AND THE ASSOCIATED PERSONALITY SIMILARITIES AND DIFFERENCES

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David Lykken was very aware that being a twin is a different experience of living in the world than being a singleton. However cherished, the singleton initially experiences the bright buzz of the new world alone, but the twin has a similarly dependent partner right to hand, sometimes jabbing an elbow in her face, others cuddling against his back. David introduced the idea of measuring twin closeness as a variable that might impact our understanding of genetic and environmental influences on personality and other forms of individual differences in the Minnesota Twin Registry. Here I follow in that tradition by presenting some data on the twin relationship and its associations with the twins' similarities and differences in personality from the twin sample from the Midlife Development in the United States survey.

FACTORS AFFECTING THE INTRAPAIR DIFFERENCES OF TELOMERE LENGTH IN AGED IDENTICAL TWINS

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The Osaka University Aged Twin Registry was established 1974. Presently, we have been conducting laboratory experiments, focusing on ageing and environmental factors, in relation to epigenetics. This study aims to clarify the relationship between telomere length and lifestyle factors. Comprehensive medical examinations were conducted for 250 pairs of adult twins. Their age ranged from 34 to 71 years-old. Telomere length of peripheral leukocytes was measured for 13 pairs, out of the 250 pairs. Personal interviews on lifestyle factors, such as alcohol drinking, cigarette smoking, food intake, and so forth, were also conducted as a part of the comprehensive medical examinations. Blood chemical analysis was conducted on 100 items, including 9 blood types. Length of DNA telomere was measured by the southern blotting method. There was no difference within the pair in 5 monozygotic (MZ) pairs (1 male, 4 females). The intrapair difference of 0.1–0.4kb was shown in one male MZ pair. The intrapair difference over 0.5kb was shown in 3 MZ pairs (2 males, 1 female). The twins who had a longer telomere within the pair showed a higher level of serum concentration of phospholipids in those 3 MZ pairs who showed a large intrapair difference over 5kb.

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MULTIPLES AND FAMILIES COPING WITH ADOLESCENCE AND SUBSTANCE ABUSE

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Parenting has its challenges at every stage of the child's development. With adolescence comes the increase of hormones, the need to find independence and to prove themselves with their peers. Parents often ask 'where has my wonderful child gone?' When multiples are added to the equation the impact on the parents, the families and the co-multiples themselves are increased. Labels such as 'good twin – bad twin' are used more often. The differences between parenting same-sex multiples and mixed-sex multiples become more pronounced, especially when the varying rates of maturity come into play particularly with the boy/girl multiples. Parents are finding there is little or no help to cover multiples during this transition from child to young adult. With society so willing to place the blame on parents for teenagers 'gone wrong' many families close ranks and suffer in silence, unable to find a peer support network to assist them in this parenting nightmare. How do you talk about one or both of your multiples in prison? How difficult is it for a teenager to stand beside their co-multiple in court to support them whilst being judged for an offence? As a twin how do you watch your co-twin travel the road of substance abuse and not know how best to help? Where are those books on multiples now?

COMBINED LINKAGE SCAN OF BODY MASS INDEX IN EUROPEAN-ORIGINATED TWIN COHORTS

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The GenomEUtwin consists of twin cohorts from 8 countries (Australia, Denmark, Netherlands, Finland, Italy, Norway, Sweden and UK) with a total data collection of hundreds of thousands twin pairs. Variance due to early life events and environment is reduced in twin pairs which makes them highly beneficial for studies of genetic factors in complex traits. We combined genome-wide scans of 8 cohorts to identify common loci and potential genetic variants affecting BMI in the European study populations. We performed quantitative linkage analysis of body mass index (BMI) using genome-wide scans performed in 4409 twin families (10,928 individuals) derived from twin cohorts from Australia, Denmark, Finland, the Netherlands, Sweden and United Kingdom with an approximate 10 cM microsatellite marker map. Variance component linkage analysis was performed with age, sex and country-of-origin as covariates. The covariate adjusted heritability was 54% for BMI in the pooled data set. We found suggestive evidence for a quantitative trait locus (QTL) on 3q29 and 7q36.3 in this combined sample of DZ-twins (MLOD 2.6 and 2.4 respectively). Two cohorts showed significant evidence independently: 16q23.2 area (MLOD 3.7) in the Dutch cohort, 2p24.1 (MLOD 3.4) in the Dutch cohort and in 20q13.2 (MLOD 3.2) in the Finnish. Combined analysis of this large twin cohort study thus provided only suggestive evidence of linkage to BMI although 2 cohorts independently provided significant evidence of linkage. This supports the concept of locus heterogeneity behind the trait and also indicates the lack of major common QTL variants affecting BMI in European populations.

THE ASSOCIATION BETWEEN BIRTH WEIGHT AND ADULT BODY MASS INDEX AND LIPID PROFILES IN A TWIN STUDY IN KOREA — HEALTHY TWIN

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It is suggested in utero environment influences serum lipid levels. Comparing twins can contribute to distinguish the genetic influences and the nongenetic environmental impacts. It is not unclear whether this influence persists in adults. We investigated the relationship between birthweight and serum lipid profiles in adult. Study participants were recruited through mailing from existing registry, and through media campaigns. Twins and their families visited the hospital to complete a questionnaire and joined the clinical examinations. Zygosity of twin pair was determined using a self-administered questionnaire. After excluding twin pairs who had missing information or same birthweight between twins, 92 monozygotic (MZ) and 27 dizygotic (DZ) adult twin pairs were included in the analysis. The birthweight differences between discordant co-twins were 0.31 (kg) in both MZs and DZs. Intrapair differences in birthweight were associated with differences in body mass index only in DZs (beta = 2.07, 95% CI: 0.60-3.54). The associations between birthweight difference and total cholesterol, high-density lipoproteins and triglyceride differences did not show statistically significant associations. It is not unclear whether the intrauterine environmental effects in childhood are attenuated in adult life or whether the relatively small difference in the birthweight together with insufficient number of discordant twin pairs caused the lack of association. Because the Healthy Twin is collecting adult twin pairs (supposed to collect more than 550 pairs at the end of 2007), it may be able to give better evidence about the birthweight effects on adult health. This study was supported by the Center for Genome Science, Korea, National Institute of Health research contract, budgets 2005-347-2400-2440-215, 2006-347-2400-2440-215, 2007-090-091-4854-300.

HERITABILITY OF PHYSICAL ACTIVITY MEASURED BY INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE (IPAQ) IN A KOREAN FAMILY STUDY

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Physical activity is increasingly recognized as an important factor associated with a range of diseases. The levels of physical activity may be determined by genetic and environmental factors, which may vary depending on the context. We assessed the heritability of physical activity in different domains such as work, transportation, domestic, and leisure domains. IPAQ measures physical activity levels in 4 separate domains: work, transportation, domestic, and leisure domains. The reliability and validity of IPAQ have been shown in previous international studies. We used IPAQ to compute domain-specific as well as total physical activity score (MET-minutes/week). Our study was conducted on 372 families with at least 1 twin pair including 284 monozygotic and 67 dizygotic twins. Heritability was estimated using Merlin adjusting for age. The physical activity score was highest for work domain, and lowest for transportation domain in general. The heritability of physical activity was highest (30.66%) in transportation domain, however, total physical activity score did not show significant heritability. Although the physical activity in transportation domain showed significant heritability, this part contributed little to the entire activities so that total physical activity failed to demonstrate significant genetic components. This study was supported by the Center for Genome Science, Korea, National Institute of Health research contract, budgets 2005-347-2400-2440-215, 2006-347-2400-2440-215, 2007-090-091-4854-300. The views in this article are not necessarily those of the funding body.

SEX DIFFERENCES IN RELATIONS BETWEEN BODY COMPOSITION AND BONE MINERAL DENSITY IN KOREAN ADULT TWINS — HEALTHY TWIN

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Previous studies show that bone mineral density (BMD) is closely associated with body mass. However, it is not still clear whether the association differs by the body composition, or sex and age. The objective of this study was to assess if there were any differences in the relations between body composition and BMD by the type of body composition, sex and age using the co-twin control design. We measured body composition and BMD by dual energy X-ray absorptiometry in 217 monozygotic twin pairs (female and male twin pairs). To examine the effect of age, they were divided into 2 age groups: under 50 years old (196 pairs) and over 50

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years old (21 pairs). Lean body mass showed more evident positive relations with total body BMD than fat mass did in women under age 50. Fat mass was inversely associated with total body BMD in women under age 50 (0.006 [0.007–0.004] mg/dl decrease per 1% increase of fat mass). Moreover, men under 50 showed negative relation between fat mass and total body BMD (0.007 [0.009–0.005] mg/dl decrease per 1% increase of fat mass). Fat mass and Lean mass show different relationships with total body BMD in both men and women. This study was supported by the Center for Genome Science, Korea, National Institute of Health research contract, budgets 2005-347-2400-2440-215, 2006-347-2400-2440-215, 2007-090-091-4854-300. The views in this article are not necessarily those of the funding body.

LEUKOCYTE TELOMERES AND MORTALITY: A STUDY IN ELDERLY DANISH TWINS

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Leukocyte (lymphocyte) telomere length (LTL) is inversely correlated with age. It is shorter in men than women and in individuals who display a host of aging-related diseases relative to their peers. As the lifespan of men is shorter than that of women and aging-related diseases may lead to premature death, it seems that LTL might be a bio-indicator of human aging. Yet, conflicting findings have been reported about the connection between LTL and mortality in the elderly. We explored the association between leukocyte telomere parameters and mortality in 548 (274 pairs) Danish twins (aged 73–94 years), of whom 255 twins died during a 8–9 year follow-up. Comparison within 185 twin pairs of the same sex (either male or female) eliminated confounding due to age and gender as well as genetic factors (100% for monozygotic and 50% for dizygotic). From the terminal restriction fragments (TRF) distribution of each leukocyte DNA sample we obtained the mean length (mTRFL), the means of the lowest 50% (mTRFL50) and 25% (mTRFL25) and computed the mode (MTRFL). Intrapair comparisons in same-sex twins showed that the twin with the shorter telomere length died first in the majority of the twin pairs (proportion, 95% confidence intervals; mTRFL 0.59, 0.51-0.66; mTRFL50 0.61, 0.53-0.68; mTRFL25 0.61, 0.53-0.68; MTRFL 0.62, 0.54-0.69). Individual level analyses using the full sample with a total of 3674 follow-up years confirmed the association between telomere length and mortality. In the elderly, the risk for death increases with shortened LTL.

PREDICTORS OF CANNABIS USE AMONG FINNISH ADOLESCENT TWINS

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Although there is evidence for modest heritability of cannabis use, the influence of shared and unique environmental factors predominate among adolescents. The aim of this study was to explore predictive factors of cannabis use in a Finnish adolescent twin population. We used the longitudinal data of the FinnTwin12 study with baseline at age 12 and 2 follow-ups at ages of 14 and 17, including 4138 individuals. The outcome variable was self-reported ever use of cannabis or other similar drugs at age 17 follow-up. The potential predictors were chosen based on literature and were self-reported measures at age 12, 14 or 17. As individual factors we tested smoking behavior and alcohol use as well as behavioral and emotional problems. As peer factors, we considered number of smoking friends and acquaintances with drug experience. As family factors we analyzed parental drinking and smoking as well as parental education. Prenatal exposure to nicotine was considered as an environmental exposure factor. We used logistic regression models controlling for twinship. First, adjusting for sex and age, we analyzed the Odds Ratios (OR) of each potential predictor of cannabis use. Second, to test causality of each predictor, conditional logistic regression analysis was conducted among twin pairs discordant for cannabis use (n = 246). Only those showing significant associations within families were taken into further consideration. Among our sample 13.5% of adolescents had ever used cannabis or similar drugs. In addition to sex and age, the final model included early onset of cigarette smoking (OR = 25.7; $p < .001$), binge drinking (OR = 2.6; $p < .001$), number of smoking friends (OR = 1.3; $p = .001$) and knowing others who have experimented with drugs (OR = 1.5; $p < .001$), as well as father's weekly binge drinking (OR = 3.5; $p < .001$). Aggressive behavior showed a sex interaction ($p = .03$), indicating that this behavioral problem predicted cannabis use among boys only (OR = 1.7; $p = .01$). Early exposure to tobacco seems to have a strong causal effect on cannabis use during adolescence.

GENETICS OF NORMAL AND ABNORMAL BEHAVIOR IN CHILDHOOD. THE ABNORMAL IS NORMAL: THE SAME GENETIC AND ENVIRONMENTAL FACTORS AFFECT NORMAL VARIATION IN MATHEMATICAL ABILITY AND COMMON MATHEMATICAL DISABILITY

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Quantitative genetic research has moved beyond merely demonstrating the wide-spread importance of genetic influence to ask more interesting questions, including questions about etiological overlap between ability and disability. In this study the genetic and environmental etiologies of 3 aspects of low mathematical performance (disability) and the full range of variability (ability) were compared for boys and girls in a UK sample of 2674 pairs of same-sex and opposite-sex 10-year-old twins. The measures, which we developed for web-based testing, included problems from 3 domains of mathematics taught as part of the UK National Curriculum. Using quantitative genetic model-fitting analyses, similar results were found for disabilities and abilities for all 3 measures: moderate genetic influence and environmental influence mainly due to nonshared environmental factors that are unique to the individual, with little influence from shared environment. Group heritabilities from DF extremes analyses were substantial, which also suggests strong links between genetic etiologies of mathematical difficulties and variation in mathematical ability in the normal range. There is some suggestion that genetic factors may be more important at the very low end of performance. This might mean that beyond a certain threshold of accumulated genetic risk factors, the influence of some otherwise relevant environmental factors is suppressed. We found no sex differences in the etiologies of mathematical abilities and disabilities. We conclude that low mathematical performance is the quantitative extreme of the same genetic and environmental factors responsible for variation throughout the distribution in both boys and girls.

FREEMARTINS: HISTORY, BIOLOGY AND POSSIBLE CLINICAL RELEVANCE

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The freemartin syndrome represents one of the most frequently occurring forms of intersex in cattle and was described for the first time in 1779 by the Scottish surgeon John Hunter. Their outer phenotype is female. But inner genitals are aberrant. Mullerian duct derivatives as uterus and upper third of the vagina are absent and ovaries are small and contain testicular structures. Sometimes Wolffian duct derivatives such as seminal vesicles are found. They are obviously infertile whereas the male co twin is not. Frank Lilly established in 1910 that the freemartin is genetically female and described for the first time vascular anatomises between the placenta's of the heterosexual bovine twin and assumed male hormonal influence as cause for the typical appearance. Testosterone from the male cannot be held responsible since the placenta's massive aromatase capacity converts virtually all androgens into estrogens. In 1947, Jost showed that a testicular derived substance known now as Anti Mullerian Hormone (AMH) suppresses mullerian duct derivatives and today the freemartin syndrome is understood to be the final result of intrauterine exposure of the female to AMH from the male co twin and local overproduction of testosterone by the ovaries cause the development of some of the male Wolffian structures. In primates freemartins do not seem to occur. For completely unknown reasons this is also the case in the marmoset monkey that always delivers dizygotic twins and always have vascular placental anatomises. In humans only in case of monochorionicity vascular anatomises are possible which is highly unusual in DZ twinning. However, over the past 4 years 13 cases of monochorionic DZ twins were reported in the literature. In all cases the offspring was chimerical and in one case a girl with aberrant sexual development was described. Remarkably all cases except for one were pregnancies that occurred after assisted reproduction or ovulation induction. Possibly multiple ovulation induction techniques and/or simultaneous implantation of multiple embryos in close vicinity play a role.

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MULTIPLE IMPLANTATION IS NOT HEREDITARY

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Familial basis for dizygotic twinning is known for multiple ovulation. But does multiple implantation also have a familial basis? In IVF/ICSI there is artificial 'multiple ovulation'. If multiple implantation is not hereditary, we expect comparable incidences of (any type of) twins in families of A) patients with single implantation and B) patients with multiple implantation after IVF/ICSI with double embryo transfer. All patients with an intrauterine pregnancy at 6 weeks of gestation, after IVF/ICSI treatment at our hospital between 2000 and 2004 with double embryo transfer 3 days after oocyte retrieval, received a questionnaire containing questions regarding family history of twinning. Data of patients with single implantation (group A) and patients with multiple implantation (group B) were analyzed using *t* test and multivariate regression analysis. Fifteen hundred and ninety-three questionnaires were sent, 933 patients (58.7%) gave their informed consent (group A: 659 patients (57.4%), group B: 274 patients (61.4%)). Baseline characteristics were not different. Incidences of one and of multiple twins among the whole family were 27.3% and 15% (group A) and 31% and 15.9% (group B), $p = .439$. Incidences of one and of multiple twins among first degree relatives were 9.5% and 1.1% (group A) and 7% and 1.6% (group B), $p = .427$. Multivariate regression analysis for multiple implantation at 6 weeks did also not reveal 'twins in family' or 'twins in first degree' as an associated variable. Incidences of twins in families of patients with single and patients with multiple implantation after IVF/ICSI are comparable. Our data do not support that multiple implantation is hereditary.

TRIPLETS AND HIGHER ORDER MULTIPLE BIRTHS IN AUSTRALIA

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The increasing trend in multiple births in many countries is attributable to a higher proportion of older mothers, greater use of fertility drugs, and the widespread use of in-vitro fertilization (IVF) and other types of assisted conception. National data from birth registrations and, more recently, perinatal data systems in each Australian State and Territory have enabled analysis of trends and various factors influencing multiple births, including maternal age, type of conception, sometimes the fertility drugs used, and the number of embryos transferred. The minimum criteria for reporting live births and fetal deaths are a gestational age of 20 weeks or birthweight of 400 g. Triplet rates in Australia gradually doubled from 1 to 2 per 10,000 confinements between the late 1960s and mid-1980s, then increased rapidly to 4 per 10,000 by the early 1990s. By 2004, triplet births had declined slightly to 3 per 10,000. Higher order multiple births, including 1 nonuplet pregnancy in 1971, peaked in the1980s, usually accounting for fewer than 5 among 250,000 confinements each year. Since the early 1980s, variations in the number of embryos transferred in IVF pregnancies have been the main influence on changing trends in triplet and higher order multiple births. International comparison of multiple births is frequently affected adversely by the different criteria of gestational age and birthweight used for registering these births. This often results in understating the extent of clinical problems and the population impact of multiple births.

PERCEPTIONS OF PARENTING AND ADOLESCENT ALCOHOL USE: PREDICTIVE UTILITY, DISPARITY, AND TWIN CONCORDANCE

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Adolescence is an important period in the initiation and development of alcohol use behaviors. Additionally, many parenting behaviors have been correlated with adolescent drinking. As levels of influence are apt to vary with measurement, researchers have called for methods that coincide with the dynamic nature of parenting. Furthermore, recent studies suggest significant discrepancies in parents' and adolescents' perceptions of parenting and in their associations with adolescent use. Using data from the population-based Finnish Twin Studies, we conducted latent profile analyses (with parent and adolescent reported parenting dimensions) to derive 2 independent sets of underlying parenting configurations, which were then examined in relation to adolescents' alcohol use behaviors at age 14 and 17. Multiple regression analyses indicated that parent- and adolescent-derived profiles accounted for little shared variance, with those based on adolescents' reports being stronger predictors of adolescent drinking. Moreover, the magnitude of these effects decreased across time. In addition, within-informant ANOVAs demonstrated significant between-profile-discrimination in levels of adolescent drinking, and pointed to multiple parenting strategies that may effectively reduce adolescent alcohol experimentation. Finally, comparisons of profile concordance were made across 5 twin types (monozygotic [MZ] females/males, dizygotic [DZ] females/males and opposite-sex pairs) to determine whether adolescents' perceptions were genetically informed. Overall, girls had greater concordance, and among both males and females, MZ twins were more concordant than DZ twins. Together, these results illustrate the distinct predictive utility of 2 largely independent perspectives, and indicate some measure of heritability in adolescents' perceptions of parenting.

HERITABILITY OF ALCOHOL DEPENDENCE IN KOREAN ADULT TWINS — THE HEALTHY TWIN STUDY

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Alcohol dependence is a chronic disease, which is often progressive, which may be influenced by genetic and/or environmental factors. Previous studies reported that the Alcohol Use Disorder Identification Test (AUDIT) is an efficient screening instrument to identify alcohol dependence. Our study aimed to examine the genetic influence on alcohol dependence applying the AUDIT questionnaire in adult Korean twins (532 monozygotic, MZ, twins and 128 dizygotic twins, DZ). Twin zygosity was determined by a standardized questionnaire. Pairwise resemblance was assessed for MZ and DZ separately by the intraclass correlation coefficient. The AUDIT score was calculated for 393 MZ and 99 DZ twins. The AUDIT score was adjusted by multiple regression for age, sex, income level, duration of education and marital status, and the residuals were used for heritability estimation. The mean AUDIT score was higher in men than in women. A higher AUDIT score was associated with lower education and a lower income level in both types of twins among men and women. For the AUDIT score the MZ intraclass correlation (= .347) was greater than the DZ intraclass correlation (= .116). Heritability of alcohol dependence was estimated to be .46. Our results suggest that genetic factors play a significant role in determining alcohol dependence. This study was supported by the Center for Genome Science, Korea, National Institute ofHealth research contract, budgets 2005-347-2400-2440-215, 2006-347-2400-2440-215, 2007-090-091-4854-300.

FETAL PROGRAMMING AND FUTURE MENTAL HEALTH

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Obstetrical complications, above all, low birthweight and reduced fetal growth, have been associated with a range of mental health problems and psychiatric diseases (e.g., attention-deficit/hyperactivity disorder, depression, schizophrenia). These associations have generally been interpreted in the context of the fetal programming hypothesis, that is, that there is a causal effect of complications around birth and later development of mental health problems. However, different obstetrical complications as well as mental health problems are to a considerable degree heritable. Thus, it is possible that the observed associations are confounded by genetic effects, that is, that a common set of genes are important for obstetrical complications and mental health problems. In this presentation we will review previous and new twin studies that address this issue.

THE HISTORIMETRIC DATABASE: A PLATFORM FOR QUANTIFYING HISTORICAL INFORMATION FOR TWIN RESEARCH

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We have observed that there is a wealth of underused quantitative data available in the public historical record. Census records, vital statistics, and other archival sources offer a number of unexplored avenues for research. For example, from birth and death records of twins identified in census records, it may be possible to estimate the heritability of longevity. Additionally, this wealth of data would open up the possibility of assessing change in heritability across historical periods. This paper discusses a design for a platform which will enable researchers to collect and access such records in a systematized, rigorous fashion. We discuss potential sources of data, as well as the available approaches for analyzing such data with uncertain zygosity information. We propose a database which is accessible to the public, and accepts input of all types of systematized biographical data from researchers and third parties, inspired by the successful developmental models of Wikipedia and the Free (libre) Software community. In order to maintain the quality of data and the academic rigor of the project given this openness, we outline a stringent requirement of citing primary sources for all data, based on established standards of historical research.

THE FETAL ORIGINS OF ADULT DISEASE: A TWIN APPROACH

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A large number of epidemiological studies have shown that low birthweight is associated with an increased risk of cardiovascular and metabolic disease in adult life. We have studied body composition and glucose-insulin metabolism in 424 twin pairs aged 18 to 34 years, from the East Flanders Prospective Twin Survey. Twin members share the same maternal environment. Nevertheless, each fetus has its own feto-placental environment, which may differ substantially from that of the co-twin. Because of their genetic identity, differences between monozygotic (MZ) twins at birth can be attributed to the feto-placental environment. Pairwise analysis showed that the lighter twin at birth was significantly smaller and lighter as an adult, but had a higher waist-to-hip-ratio, more subcutaneous fat, and less lean body mass, compared to the heavier co-twin. These intrapair differences increased with increasing intrapair birthweight differences, in MZ as well as in dizygotic twins. Despite the large intrapair birthweight difference, both MZ twins had similar fasting insulin and glucose concentrations. We also found that low maternal BMI before pregnancy and high maternal age at delivery were significantly associated with increased adult fasting insulin concentrations in the twin offspring. These studies suggest that maternal as well as feto-placental influences contribute to an adverse body composition and to an abnormal glucose-insulin metabolism in adults. Studies of twins may shed light on the relative contribution of maternal and feto-placental influences to the programming of adult diseases.

'NO THANKS, IT KEEPS ME AWAKE': THE GENETICS OF COFFEE-ATTRIBUTED SLEEP DISTURBANCE.

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Previous genetic investigations of sleep disturbance have shown various measures of sleep quality and sleep pattern to be heritable. But none of these studies have investigated the genetic predisposition to sleep disturbance attributed to caffeine. In this study, the heritability of coffee-attributed sleep disturbance and its relationship with other sleep measures were estimated and chromosomal regions influencing this trait were identified. A classical twin design was used to estimate the heritability of coffee-attributed sleep disturbance and its genetic covariance with other measures of sleep disturbance (e.g., due to anxiety, depression) and sleep quality (e.g., variability in sleep quality). To locate quantitative trait loci influencing coffee-attributed sleep disturbance a genome-wide linkage screen of 1395 microsatellite markers was performed. Participants included 3808 Australian adult twin pairs (N = 1799 monozygous pairs; N = 2009 dizygous pairs). A subsample of 1989 individuals from 1175 families was used for the linkage analysis. The heritability of coffee-attributed sleep disturbance (measured by self-report) was approximately .40, with 3/4 of this genetic variance explained by genes unrelated to the general sleep disturbance factor. One region of significant linkage to coffee-attributed sleep disturbance was identified on chromosome 2q (LOD score of 2.9). While no candidate genes known to be related to caffeine metabolism or sleep disorder were identified in the significant linkage region, 2 candidates were found under a smaller peak on chromosome17q.

ACCOUNTING FOR CONFOUNDING IN THE CO-TWIN CASE CONTROL DESIGN

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The inherently matched nature of twin data lends itself to case-control studies that have the potential to separate main effects from confounding that arises from the shared family environment and shared genetic pathways. This is of particular relevance to the study of the association between birthweight and adult phenotypes where confounding factors in the maternal and intrauterine environment and in the shared upbringing of twins during growth and development all have a potentially important influence. However, analysis of these designs is complex. Interpretation needs combinations of parameters to be taken into account derived from sets of models that include individual-specific, within-pair and between-pair effects in both zygosities together with measures of growth. To date, we have examined a series of datasets from the TwinsUK Registry relating birthweight to a range of variables measured in adult twins including systolic and diastolic blood pressure, serum lipid levels, measures of insulin resistance, and measures of body composition. In each analysis, the extent to which confounding influences the overall interpretation of the analysis differed, producing a range of patterns of results with subtle differences in interpretation. Our analysis confirms the pervasive influence of confounding in case-control data and the power of fully parameterized co-twin models to take its influence into account.

LONGITUDINAL GENETIC ANALYSIS OF TOBACCO USE IN ADOLESCENT VTSAB TWINS

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Evidence from several cross-sectional twin studies suggests the importance of shared environmental contributions in the initiation of tobacco use, whereas the role of genetic factors tends to increase towards young adulthood. Studies of lifetime tobacco use in adult samples consistently report heritabilities over 50% with a significant contribution of shared environmental factors. We tested whether the trend of increasing genetic and decreasing shared environmental influence is significant using longitudinal prospective data. We report the prevalence of lifetime tobacco use in adolescents and estimate the contribution of genetic, shared and unique environmental influences on tobacco use. Tobacco use data were collected using the Child and Adolescent Psychiatric Assessment on a population sample of 1412 male and female monozygotic (MZ) and dizygotic (DZ) twin pairs, ages 8 through 16 from the Virginia Twin Study of Adolescent Behavioral Development (VTSABD), measured up to 4 times. The prevalence of tobacco use rose steadily from about 5% at age 12 to about 40% at age 17. While MZ correlations increased moderately from .63 to .84, DZ correlations decreased from .76 and stabilized around .50 over this age range. This corresponds to shared environmental factors explaining family resemblance in early adolescence and genetic influences accounting for the majority of the resemblance in later adolescence. Multivariate longitudinal genetic analyses showed that the loadings on the genetic common factor increased while those of the shared environmental common factor decreased with increasing age. Genetic and shared environmental factors both explained variation in lifetime tobacco use in 12- to 17-year-old adolescents. The shared environment appears to play a predominant role in starting to smoke at a younger age, while genetic factors contribute more in late adolescence.

LONGITUDINAL GENETIC ANALYSIS OF TOBACCO USE IN ADOLESCENT LLTS TWINS

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Cross-sectional twin studies suggest that shared environmental factors contribute to the initiation of tobacco use, whereas the role of genetic factors tends to increase towards young adulthood. We report the prevalence estimates of lifetime tobacco use in adolescents and estimate the contribution of genetic, shared and unique environmental influences on tobacco use using longitudinal prospective data and test whether the results are similar to those obtained from a population based US sample. Tobacco use data were collected by questionnaire on a population sample of 105 male and female monozygotic and dizygotic twin pairs and their parents from the Leuven Longitudinal Twin Study (LLTS). The twins, all part of the East Flanders Prospective Twin Study (EFPTS), were measured annually up to 8 times, between the ages of 10 and 18 years. The prevalence of tobacco use rose steadily from about 5% at age 15 to about 30% at age 18. Genetic factors increased moderately explaining 59% to 85% of the variance over this age range. Shared environmental factors contributed moderately at age15 but not at all at age 18. Multivariate longitudinal genetic analyses showed increasing loadings with age on the genetic common factor increased while those of the shared environmental common factor decreased. Furthermore, estimates of the genetic and environmental parameters could be equated between the Belgian sample and the Virginia adolescent sample for the overlapping age range (15-17 years), but the prevalence estimates could not. Smoking initiation appears to occur about 2 years later in the Belgian sample. Both genetic and shared environmental factors explained a proportion of the variation in lifetime tobacco use in adolescence, but they appear to influence different stages.

GENOME-WIDE LINKAGE ANALYSES OF LIPIDPROFILE BIOMARKERS IN THE GENOMEUTWIN COHORT: RESULTS FROM POOLED DATA AND META-ANALYSIS

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Disturbances in lipid and cholesterol metabolism as routinely measured clinically are known to be strongly linked with atherosclerosis and subsequent development of life threatening diseases such as coronary heart disease and ischemic stroke. Identification of genetic factors underlying variation in lipid and cholesterol levels are therefore of paramount importance for the understanding of development of CVD. Studying dizygotic twins as opposed to ordinary siblings offers the potential to increase power in genetic linkage studies. We here report on results obtained from genome-wide linkage analysis of quantitative trait loci for total cholesterol, HLD, LDL, Triglycerides, Apolipoprotein A1 and Apolipoprotein B in joint analyses of 6 populations of European origin.

ARE SYMPTOMS OF POST-TRAUMATIC STRESS DISORDER INVERSELY ASSOCIATED WITH GOOD HEALTH? A REPORT FROM THE VIETNAM ERA TWIN (VET) REGISTRY

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There are few studies of the long-term impact of symptoms of post-traumatic stress disorder (PTSD) on physical health. The purpose of the current investigation is to examine this association. The analyses follow up on previous work by Eisen et al. (1991) which evaluated the relationship between combat (without PTSD) and physical health. The sample consists of a cohort of 4303 US male twin pairs who served in the military during the Vietnam era. Data were collected by survey in 1987 (at which time the twins' average age was 38.1 years) and included measures of zygosity, symptoms of PTSD, combat exposure, and 15 health conditions. Twins who did not endorse any of the 15 health conditions were considered in good health. Twins were grouped into quartile son the basis of a PTSD symptom score. Unadjusted analysis revealed an inverse association between PTSD symptoms and good health ($p$trend < .0001). Compared to those in the lowest PTSD symptom quartile, twins in the highest quartile were 0.25 times less likely to report good health (95% CI: 0.20-0.32). The inverse association between PTSD symptoms and good health persisted and was nearly identical after adjusting for combat exposure. Within-pair analysis found similar significant relationships for both monozygotic and dizygotic (DZ) pairs ($p$trend < .0001 for both); however, the relationship was only significant for DZ pairs in the 2 highest quartiles. These findings demonstrate that PTSD symptoms are strongly related to health problems in Vietnam era veterans. It remains unknown if the adverse influence of PTSD symptoms continues as veterans age.

GENETIC ASPECTS OF PHYSICAL ACTIVITY, HEALTH-RELATED PHYSICAL FITNESS, OVERWEIGHT, AND OBESITY: A STUDY IN PORTUGUESE TWINS AGED 6 TO 20 YEARS

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We aim to present a research project with twins being conducted in Portugal. Its general purposes are as follows: (1) estimate genetic and environmental factors in physical activity levels, health-related physical fitness, overweight and obesity; (2) to explore possible correlations among mtDNA (particularly its haplotypes) polymorphisms and physical activity, and health-related physical fitness; (3) to cross-validate an indirect method of zygosity determination against DNA information; (4) describe the possible influences of low levels of physical activity in obesity and their genetic influences; (5) determine the genetic effects of variable patterns of physical activity. The sample comprises 400 twin pairs aged 6 to 20 years from different regions of Portugal (north, center, Azores and Madeira islands). Physical activity was assessed with 2 different questionnaires, a Yamax pedometer and a tri-axial accelerometer. With these 2 electronic devices we monitored 5 full days of physical activity (this provides a lot of information concerning levels and patterns of physical activity). Zygosity was evaluated with an indirect method provided by Peeters et al. (1998), and it will be cross-validated against DNA information (using highly polymorphic loci — 17 STRs). Health-related physical fitness was evaluated with the Fitnessgram test battery (assessing flexibility, aerobic performance, strength, and BMI). Body composition was use to measure different compartments of the body mass, using bio-impedance Tanita equipment, providing information about fat mass and free-fat mass of right and left arm, right and left leg, trunk, as well as an overall estimate of body fat, and fat-free mass. We shall provide exploratory information regarding body composition, patterns of physical activity, as well as concordant and discordant behaviors in physical activity, and running the mile (monitored for time, energy expenditure using a tri-axial accelerometer [Tritrac R3D], and heart rate [using a POLAR monitor]). This is the first twin study conducted in Portugal using multifaceted data concerning relevant aspects of healthy living. They may be very useful in providing information concerning the implementation of healthy lifestyles dealing with physical activity and

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sport programs at the population level. This study was support by a grant from the Portuguese Foundation for Science and Technology (POCTI/DES/62499/2004).

SOMATOTYPE AND BODY COMPOSITION. A STUDY IN PORTUGUESE SIBLINGS

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The purposes of this study were to estimate the influence of genetic and environmental factors in several measures of body composition and somatotype in Portuguese siblings. Two hundred and sixty-two sibling pairs (75 female pairs, 59 male pairs, and 128 opposite-sex pairs) were sampled from Bragança county, a northeast region of Portugal. Somatotype, an overall impression of physique, was compute according to the Heath-Carter method that allows the estimation of endomorphy (relative fat component), mesomorphy (muscular component) and ectomorphy (linear component). Body composition was estimate with a two-compartment model (body fat, and lean body mass) using equations derived for children and adolescents; we computed also a sum of several skinfolds to have a rough estimate of overall body fat. Correlations within sibships (i.e., brother-brother, sister-sister, brother-sister) and univariate heritability estimates were calculated with S.A.G.E. version 5.1, and genetic correlations were computed with SOLAR version 4.02. All estimates were adjusted for sex, age, age × sex, and age squared. The anthropometric measures used in the computation of somatotype and body composition showed a very low measurement error (< 2%). Individual estimates of heritability, adjusted for significant covariates were: endomorphy, $h2 = .33 \pm .04$, mesomorphy, $h2 = .19 \pm .12$, ectomorphy, $h2 = .31 \pm .12$, body fat, $h2 = .57 \pm 0.09$, fat-free mass, $h2 = .55 \pm .09$, and sum of skinfolds, $h2 = .49 \pm .09$. Multivariate estimates of genetic correlations adjusted for significant covariates were:endo-meso, $r = .73 \pm .07$; endo-ecto, $r = -.87 \pm .09$; meso-ecto, $r = .94 \pm .03$. In conclusion, these results showed a low-to-moderate influence of genetic factors in physique and body composition. This reveals, also, the potential of environmental factors in changing somatotype components, as well as reducing levels of body fat. It is important to keep in mind that change due to exercise, diet, a combination of these and any other external agents are limited to some extent to the genetic make-up of each individual, leading to persons with high response to changes, and others that show a very low response. This call for specific physical activity and exercise intervention programs if relevant changes are to be induced in people leading them to healthy and active lifestyles. This study was support by a grant from the Portuguese Foundation for Science and Technology (POCTI/DES/62499/2004).

TWIN-FAMILY STUDIES OF MOLINESS AND OTHER MELANOMA RISK FACTORS

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Melanoma risk is influenced by the number of nevi (moles) on the skin, and by pigmentary characteristics including skin, hair and eye color and the degree of freckling. We have been studying these characteristics in twins and their siblings for 15 years and now have data on over 1000 families. We have found a number of highly replicable linkage peaks for moliness, and are close for identifying the variants responsible for blue eye color, which independently appear to affect melanoma risk. Latest results will be presented.

SCHOOL PLACEMENT AND SOCIAL ISSUES OF TWINS AND MULTIPLES

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The social and educational issues facing twins and multiples as learners are discussed in school and educational settings. Recent survey data will be presented on the knowledge, views, and attitudes of experienced and novice (pre-service) teachers. Specific questions to be discussed include:

- Do teachers view the learning styles of twins and multiples as unique?
- Do peers or teachers encourage competition to the point that it interferes with learning?
- Do teachers encourage sibling-sibling learning?
- Do teachers offer and advocate nonformal and informal learning experiences for twins/multiples?

Part of this presentation will also discuss recent school placement litigation occurring in the United States with many states enacting a parental bill of rights enabling parents of twins/multiples to make the ultimate decision on whether their children are placed into the same or separate classrooms.

FAMILY AND SIBLING RELATIONSHIPS WHEN TWINS ARE DISCORDANT FOR ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER

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Attention-deficit/hyperactivity disorder (ADHD) is a common childhood disorder which occurs more often in twins than singletons. Despite the extensive research of twins with ADHD, few studies have focused on the psychosocial consequences of having a twin with the disorder. The present study examines the relationship of dizygotic twins discordant for ADHD between the ages of 12 and 18. Parental report data were used to identify twins as discordant for ADHD-PI, ADHD-C, or concordant controls. The first phase of the study was quantitative and involved parents and twins completing questionnaires measuring the perceptions of twin experiences within the family (Sibling Inventory of Differential Experience, SIDE), and overall family functioning (Family Assessment Device, FAD). Twins also completed the Behavior Assessment System for Children —second edition (BASC-2) which provided self-perceptions of internalizing behaviors, externalizing behaviors, and adaptive functioning. The qualitative phase of the study captured pertinent themes of the twin relationship by asking twins to discuss their relationships in a 5-minute telephone interview. Progressive findings are suggestive of greater levels of disruption in families with an ADHD twin and that ADHD is a significant factor in determining co-twin report of caretaking roles and internalizing disorder symptomatology. Given the high rates of ADHD diagnosis in Australia, this study emphasizes the priority for more research on the impact on non-ADHD twins and siblings.

THE MINNESOTA TWIN FAMILY STUDY: DAVID LYKKEN'S LASTING LEGACY TO DEVELOPMENTAL BEHAVIORAL GENETICS

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David Lykken was known to have famously said, 'any research one might think of doing with human subjects is likely to be more interesting if you do it with twins.' A man of great convictions, Lykken clearly followed this advice throughout his professional career. He is the 'father' of twin research at the University of Minnesota. He started the Minnesota Twin Study in the 1960s and the Minnesota Twin Registry in the 1980s and played a principal role in Thomas Bouchard's Minnesota Study of Twins Reared Apart. In 1988 with a grant from the NIH, Lykken also initiated the Minnesota Twin Family Study (MTFS), a longitudinal study of approximately 1400 pairs of like-sex twins and their parents. Nearly 20 years after its inception, the MTFS is still going strong. Lykken saw the MTFS as an opportunity to test one of his many original ideas, namely that genetic influences on complex behavioral traits are largely mediated by environmental processes (he liked to say that the proper phrase was 'Nature via rather than nature versus nurture'). Findings from the MTFS have supported Lykken's radical hypothesis: when given the opportunity, genetically similar individuals tend to construct similar environments, which in turn help to reinforce their behavioral similarity. Rather than simply being a vehicle for estimating heritability, Lykken saw twin studies as a way for psychologists to gain unique insights into the origins of human behavior. The MTFS continues to show that, like with so many of his ideas, Lykken was right.

WHY DO WE NEED DEVELOPING COUNTRIES TO HELP SOLVE THE PUZZLES OFBEHAVIORAL GENETICS?

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Both normal and abnormal behavioral traits have been studied extensively using twins but this has largely been confined to western, industrialized countries. Estimates of parameters such heritability, or proportion of variance explained by additive genetic effects, are only strictly applicable to the populations from which they are derived. Therefore, statements such as 'severe unipolar depressive disorder is 70% heritable' need to be qualified by a statement of where this was estimated (in this case the UK). The overall variance in liability to a disorder may differ from country to country as may the exposure to environmental risk factors. Further, different types of environmental risk factors are likely to exist in different societies. Therefore a full and comprehensive understanding of etiology,

including gene-environmental interplay, can only be obtained by strategies that include parallel designs in developed and developing countries.

HERITABILITY OF NEUROCOGNITIVE FUNCTIONING IN THE ELDERLY: EVIDENCE FROM AN ITALIAN TWIN STUDY

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The progressive reduction of cognitive ability that emerges with aging is a result of complex interactions of genetic and environmental factors, whose nature and mechanisms still remain largely unknown. The main purpose of this study is to explore the relative contributions of genetic and environmental factors in determining interindividual variation of neurocognitive abilities as evaluated by a series of neuropsychological tests. A sample of 62- to 80-year-old twins, belonging to the population-based Italian Twin Registry, underwent a battery of neuropsychological tests providing information about different areas of cognition. The contributions of genetic and environmental effects were assessed using standard univariate twin modeling based on linear structural equations. The study population included 93 twin pairs; 35 pairs were monozygotic (12 males, 23 females) and 58 were dizygotic (11 males, 20 females, 27 opposite-sex). The best fitting model incorporated additive genetic (A) and unique environmental (E) sources of variance for the following tests: Mini-Mental State Examination (A = 55%), Raven (A = 56%), Attentional Matrices (A = 79%), Copying Drawings (A = 69%) and Story Recall (A = 54%). For Phonological and Semantic Verbal Fluency, the best explanation of the data was obtained under nonadditive (D) and unique environmental influences (D = 62% and 54%, respectively). For Token test, the interindividual variance was entirely due to environmental factors not shared by the twins. The results suggest that individual differences in specific cognitive abilities in the elderly are explained by moderate to high genetic contribution, and that the environmental factors of relevance for these abilities are those causing within-family differences.

MODELING PARENT OF ORIGIN LINKAGE EFFECTS USING THE IBD MIXTURE DISTRIBUTION APPROACH

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Parent of origin linkage effects (POE) have previously been observed for phenotypes in which the maternal and paternal evolutionary interests differ. The genetic conflict theory predicts that given the possibility of multiple paternity among siblings, paternal interests are best served by maximizing fetal growth, while maternal interests are best served by preventing the over-draining of resources to ensure the mother can care for other offspring and is able to reproduce again. However, it is not necessary for all the genes in a given pathway to be subject to imprinted regulation for POE to arise, and is possible that the maternal and paternal genomes may target different genes within the pathway. Differential modeling of maternal and paternal IBD allows the detection of POE effects. To this end we implemented a POE linkage model using the full IBD mixture distribution approach to increase the power to detect POE effects. We demonstrate this model using birthweight data from 2 samples of Australian dizygotic twins. We identified significant maternal linkage on 20p12 in a region previously reported as maternally linked to childhood BMI (Gorlova et al., 2003). This finding suggests the presence of one or more maternally expressed genes that influence pre- and postnatal growth and body mass index. In addition we found suggestive non-imprinted linkage to chromosome 6q22 a region that has been recently identified and replicated by Ayra et al. (2006).

GENETIC MARKER ANALYSIS IN COMMON AND RARE CASES OF TWINNING

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Twins generally fall into 2 classes of dizygotic (DZ) and monozygotic (MZ) twins arising through very different mechanisms. Rare twinning events occur and alternative twinning mechanisms have been proposed. Recent availability of genome-wide marker data in twins and twin families allows us to directly test relationships between twins at different chromosomal regions in both common and rare cases of twinning. DZ twin pairs are a special case of the simultaneous survival of 2 genotypes, and there have been reports of DZ pairs with excess allele sharing around the HLA locus, a candidate locus for embryo survival. Analysis of allele sharing in 1592 DZ twin pairs from 2 independent Australian cohorts and 336 DZ twin pairs from the Netherlands found no evidence of excess allele sharing, either at the HLA locus or in the rest of the genome. The distribution of allele sharing was similar to sibs and there was no evidence for outliers that might represent alternative mechanisms of twinning. Rare cases of twins do occur. A recent case of 46,XX/46,XY twins where Twin A presented with ambiguous genitalia and Twin B was a phenotypically normal male demonstrate a rare mechanism for twinning. Cytogenetic, histological and genetic marker analyses were performed on peripheral blood cells and skin fibroblasts. Twin A was determined to be a true hermaphrodite and Twin B an apparently normal male. Both twins had a 46,XX/46,XY chromosome complement in peripheral lymphocytes, skin fibroblasts, and gonadal biopsies. The proportion of XX to XY cells varied between the twins and the tissues evaluated. Most significantly the twins shared 100% of maternal alleles and approximately 50% of paternal alleles in DNA analysis of skin fibroblasts. The twins are chimeric and share a single genetic contribution from their mother, but have 2 genetic contributions from their father thus supporting the existence of a rare and unusual mechanism of twinning.

DIZYGOTIC TWINNING IS ASSOCIATED WITH VARIATION IN OOCYTE GROWTH FACTOR GENES

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Genetic factors contribute to an increased chance of having dizygotic (DZ) twins. The ovarian bonemorphogenetic signalling pathway genes (GDF9 and BMP15) are critical for normal human fertility and implicated in twinning variation. We analyzed common variants in both GDF9 and BMP15 in families with a history of DZ twinning and also screened for rare variants in GDF9 and BMP15 in 279 unrelated mothers of DZ twins. Rare variants identified by denaturing high performance liquid chromatography (DHPLC) were confirmed by DNA sequencing and rare and common variants were typed by MALDI-TOF mass spectrometry in our DZ twinning families. Common variants in GDF9 were not associated with DZ twinning. We found 2 novel insertion/deletions (c.392-393insT, c.1268-1269delAA) and 4 missense alterations (p.Pro103Ser, p.Thr121Leuin the pro-region and p.Pro374Leu and p.Arg454Cys in the mature protein region) in the GDF9 sequence in mothers of DZ twins. The frequency of all GDF9 variants was significantly higher ($p < .0001$) in mothers of twins (4.12%) compared with controls (2.29%). In contrast, we identified 4 missense variants (p.Pro174Ser, p.Phe194Ser, p.Ala311Thr, pArg391Thr) in BMP15 in mothers of DZ twins, but there was no evidence for an increased frequency of these rare variants in mothers of twins. We conclude that rare variants in GDF9, but not BMP15 are associated with DZ twinning. However, these variants account for only a small part of twinning variation.

CREATING AWARENESS OF MULTIPLE-BIRTH ISSUES AND CHALLENGES

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As the incidence of multiple-birth pregnancies increases, so too does the need to educate the public of the risks involved in carrying twins, triplets, quadruplets and more. In 2005, Multiple Births Canada (MBC) launched National Multiple Births Awareness Day. With the blessing of the remaining Dionne Quintuplets, (Canada's first surviving monozygotic quintuplets, born May 28th, 1934), MBC chose their birth date as the annual day of celebration and education. National Multiple Births Awareness Day encourages a better understanding of the individuality and complexity of the multiple-birth relationship as well as the challenges faced by the multiple-birth community. Each year, the day focuses on a single theme to educate those who are not familiar with the multiple-birth experience. MBC believes that creating awareness and helping others to understand the journeys multiple-birth families travel will lead to opportunities to advance change on behalf of the entire multiple-birth community within Canada.

Themes to date:

- 2005: A Call to Dialogue regarding current provisions for maternity, parental and compassionate care leave under the Canadian federal Employment Insurance Program

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- 2006: Raising awareness of the unique risks of multiple-birth pregnancies and the postnatal issues faced by parents and multiples
- 2007: Raising awareness of the need to recognize and encourage the individuality of multiple-birth individuals, while respecting the uniqueness of their multiple-birth relationship.

Using a Power Point presentation, Gail Moore, Director of Communications, MBC, and lead organizer of National Multiple Births Awareness Day, will share Canada's successes and invite participants to consider launching an International Multiple Births Awareness Day.

PHYSICAL GROWTH CURVES AND FEATURES OF TWINS' GROWTH

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It is well known that there are 4 types of growth curves. Physical growth does not start suddenly from birth but continuously from the conception. The standard physical growth curves are constructed based on the birth age and can not diagnose the growth features correctly in some cases. We are developing analysis for the physical growth curves based on the conceptional age instead of the birth age. In previous work, one author (YM) has proposed the analysis and has suggested that it is useful for grasping the original features of twins' growth appropriately. On the other hand, the physical growth data used consisted of several twins and the statistical problem remained. In this paper, we apply the analysis to a large number of physical growth data. The database, which an author (SO) has collated, consists of 1748 twins born between 1986 and 2001 in Japan and is expected to be almost population-based. We point out that the new analysis is valuable except just after the birth and that we are able to grasp correctly the catch-up phenomena.

CAN WE GENERALIZE FROM FINDINGS IN TWINS?

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Twins provide a unique opportunity to shed light on causal pathways relating to the developmental origins of health and disease, but there is debate as to whether we can generalize from findings in twins. Issues that have been raised and need to be addressed, include: Twins have a shorter gestation length than singletons. Twins have lower birthweight than singletons. Despite themselves being lighter at birth, twin women do not have lighter babies, suggesting low birthweight in twins has different implications. Volunteer twin cohorts are biased groups. Studies of twin cohorts often use recalled birthweights, likely to be inaccurate. Some twins share a placenta and there are likely to be connections between their circulations, which could affect later health. Some twins are exposed to an opposite-sex twin in utero and this may affect their later health. Twins are more likely to have parents with a fertility problem who have needed medical intervention to conceive. Twins are more prone to some cardiovascular risk factors than singletons. Researchers don't get the same results within twin pairs as they do in numerous studies of singletons, so there must be something different about twins. Some of these issues cannot be fully addressed until we have better data, particularly with respect to chorionicity (for which in general we have poor data) and infertility and its treatment.

MATCH (MOTHERS AND TWIN CHILDREN): A PRENATALLY RECRUITED VOLUNTEER REGISTER OF TWINS

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There is increasing interest in the role of prenatal factors as determinants of later health and well-being. Twins provide unique opportunities to investigate the role of genetics, twin specific and shared intrauterine environmental factors exposures. Most twin registers do not have access to good prenatal data or biological samples. MATCH, part of the Australia Twin Registry, aims to recruit twins prenatally and collect prospective data and samples. Recruitment and data and sample collection will depend on women with twin pregnancies across Australia choosing to join and contribute. Logistic challenges have included: ethical and legal issues, getting information about MATCH to all women with a pregnancy, obtaining fully informed consent, getting data sent to MATCH, optimizing chorionicity determination, and optimizing collection and processing of samples, and transfer to the bio-repository. We have designed an attractive folder as a resource for women expecting twins, in collaboration with obstetricians, neonatologists, nutritionists and parents of twins. It will be available in all antenatal clinics and contains information booklets about twinning and twin pregnancy, information about MATCH, a consent form, self-duplicating data collection forms (so parents can keep the record) and request forms for sample collection. We have also designed educational material for midwives, ultrasonologists and laboratories. After a 30-month gestation, MATCH will be launched in the 3 largest maternity units in Melbourne in March / April 2007. It will not be a population-based cohort but will provide unique opportunities to test etiological hypotheses.

AN EXTENDED MODEL FOR GXE INTERACTIONS IN TWIN DATA

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The traditional model for genotype × environment interaction, described by Purcell (2002) specifies that the genetic factors that contribute to variation are also the factors whose effects are moderated by covariates, such as environmental factors. This model allows for changes in the magnitude of variance components as a function of the value of the covariate, but it has several limitations. Of note here is that it is possible that different environments switch on or off different sets of genetic factors. Modeling this situation, of which nonscalar sex-limitation (where the genetic correlation between unlike sexed pairs of twins is less than between like-sexed pairs) is one example, is relatively straightforward. Therefore, 2 sets of genetic factors are modeled. One represents those that contribute to a constant (level) heritability, while the second changes linearly with the effect of the moderator. These 2 components are allowed to correlate freely. In the event that they correlate perfectly, the model reduces to the conventional single variance component case. Otherwise, the correlation between twins may decrease as a function of the difference in their moderator variable values. With a moderator such as age, this extended model makes good intuitive sense and may be more consistent with patterns of resemblance between twins measured at different ages.

FAMILY ENVIRONMENT, PARENTING ANXIETY AND CHILDHOOD DEVELOPMENT OF TWINS AS COMPARED TO SINGLETONS

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Compared to mothers of singletons, it is reported that mothers of twins experience a greater physical and mental burden of parenting. This study aims to describe the difference of parenting anxiety by age, and to investigate whether parenting anxiety affects child's mental development in both twin and singleton groups. Questionnaires were mailed or handed out to 218 mothers of 0- to 2-year-old twins and 348 mothers of 0- to 2-year-old singletons, from March to May 2005. In all, 124 mothers of twins (56.9%) and 101 mothers (28.1%) of singletons returned the questionnaires. The questionnaire included parents' employment, pregnancy complications, labor complications, gestational age, infertility treatment, Child Rearing Support Questionnaire, and Tsumori-Inage infant developmental Scale. Compared to their counterparts with singletons, mothers of twins showed significantly higher rate of unemployed status, maternal complication, and parenting anxiety. On multiple logistic regression analysis, high parenting anxiety in mothers of 2-year-old twins, especially negative feelings, were related to delay in the children's mental development. However, there was no significant relationship with twins aged 0 or 1 year and with singletons of 0 to 2 years of age. The results suggest that negative feelings toward children influence mother-child interactions and complicate relationships. Parenting anxiety is a severe problem in mothers of twins not only because it causes mental problems in mothers but also because it has an impact on child mental development.

SHOULDER CUFF TENDONS IN MONOZYGOTIC AND DIZYGOTIC ITALIAN TWINS

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Most research regarding the etiology of shoulder rotator cuff disease has investigated factors responsible for tendon tear such as acromial shape,

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occupational and daily activity, and tendon blood supply. Very few studies have explored the genetic contribution. Thus, we started clinical and MR Imaging assessment of shoulder cuff in elderly asymptomatic twins to evaluate if also heritability may play a role in rotator cuff tear. In the Italian Twin Registry (ITR), we identified 83 twin pairs aged 60–72 and resident in Rome. Of these, 50 have so far been contacted by telephone, and 36 agreed to participate in the study. Agreeing pairs are invited to the Department of Orthopaedic and Traumatology Surgery of our University in order to: (a) undergo standard clinical and morphological assessment by Constant Score and Simple Shoulder Test on both shoulders, and MR evaluation on right shoulder; (b) give, after signing a specific informed consent, saliva specimen for zygosity ascertainment by DNA and for ITR bio-bank implementation. To date, we studied 11 pairs of right-handed twins (3 monozygotic and 8 dizygotic, 4 male-male and 7 female-female). Mean Constant scores were 78.5 (range: 50–87) and 82.4 (range: 72–87) on the right and left shoulder, respectively. Mean value for the Simple Shoulder Test was 10.6 (range: 6–12). On average, females performed slightly worse than males. At the end of the study, we will estimate zygosity-specific twin correlations for shoulder clinical and morphological parameters such as pain, range of movement, power and tendon thickness, and will infer their heritabilities.

ETHNIC DIFFERENCES IN THE ASSOCIATION OF BIRTHWEIGHT AND BLOOD PRESSURE IN ADOLESCENTS — THE GEORGIA CARDIOVASCULAR TWIN STUDY

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African Americans (AA) not only have higher blood pressure levels, but also an increased risk of low weight at birth, compared to European Americans (EA). In light of fetal programming theories it has been suggested that ethnic differences in blood pressure originate in utero. However, most previous bi-ethnic studies in children and adolescents have not found any significant inverse association between birthweight and blood pressure in AAs. In 361 EA and 274 AA adolescent twin pairs of the Georgia Cardiovascular Twin Study we investigated potential ethnic differences in the blood-pressure–birthweight association. Potential confounding by socioeconomic status and maternal factors was taken into account and paired twin analysis was conducted to control for confounding by familial factors. Blood pressure levels were significantly higher in AAs compared to EAs, independent of birthweight. An inverse association between birthweight and systolic blood pressure was found in all, and appearing to be more pronounced in AAs than in EAs (in which estimates did not reach significance). In addition a significant ethnic interaction was revealed in paired analysis, where the inverse association remained in AAs but not EAs. The associations with diastolic blood pressure were generally weaker and non significant. We could show that low birthweight was associated with an elevated systolic blood pressure in AAs, independent of familial factors. The results also suggest that the association between birthweight and blood pressure may be more pronounced in AAs in adolescence.

LIFESTYLE FACTORS AFFECTING THE INTRAPAIR DIFFERENCES OF COGNITIVE DECLINE IN AGED IDENTICAL TWINS

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The purpose of this study is to analyze the relationship between lifestyle factors (alcohol drinking, cigarette smoking, foods intake, etc.) and cognitive abilities, and to clarify the environmental factors affecting intrapair differences of the decline of cognitive functions in aged identical twins. The subjects in this study were 206 pairs of aged twins living in Japan. Comprehensive medical examinations were conducted for the twins. The Wechsler Adult Intelligence Scale (WAIS) and personal interviews on their lifestyle were conducted for the twin pairs (monozygotic, MZ, 156; dizygotic, DZ, 50). The higher consumers of alcohol within the MZ pairs tended to show a higher score than the lower consumers in the subtest of digit symbol ($p < .05$). Concerning food intake, the subtest of digit span tended to show a higher score in twins who had more vegetables, milk, beans and bean products than the twins who had less of those foods within the MZ pair ($p < .05$). There was not any significant difference between MZ and DZ in the average scores of intrapair difference in 4 subtests of WAIS.

POPULATION-BASED DATABASE OF MULTIPLES IN CHILDHOOD OF ISHIKAWA PREFECTURE, JAPAN

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A new type of population-based database of multiples in childhood at the prefecture level was initiated in 2004 in Ishikawa Prefecture, Japan. The population of Ishikawa Prefecture is small compared to that of other major prefectures. Recently, the number of multiple maternities in Ishikawa Prefecture has been approximately 100 to 150 every year. We conducted an exhaustive search for demographic information concerning families with multiples, family support provided by governmental and medical institutions by mailed questionnaire, and at the same time tried to organize a human network to support such families. This registry aims not only to aid research on human genetics and maternal and child health, but also to contribute to the development of welfare programs for families with multiples. This strategy is welcomed by the many participants and other involved parties, and seems to be highly cost-effective. The project has only just begun; we hope it will become fruitful, allowing our approach to be applied to other small prefectures in Japan. The author gratefully acknowledges the assistance of the members of the 'Ishikawa network of support for families with multiples,' especially that of Dr. Megumi Shimura, the director of the network. The author is also grateful for the help of Kaoru Tachibana, the president of Kazekko Kids, an association for the parents of multiples, and other party organizers of this network. This work was supported in part by a Grant-in-Aid from the Ministry of Health, Labor and Welfare of Japan.

THE MURCIA TWIN REGISTRY: A POPULATION-BASED REGISTRY OF ADULT FEMALES IN SPAIN

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The Murcia Twin Registry is an initiative to develop a population-based register of twins in Spain. The main short term objective is the analyses of genetic and environmental factors influencing behaviors related to women's health. We describe the methods and progress in locating and contacting all female twin pairs resident in the Region of Murcia (southeast of Spain; 1.3 million inhabitants) and born between 1940 and 1965. A brief telephone interview is carried out after introducing the initiative. The questionnaire includes questions relative to: zygosity, demographic and anthropometric data, perception of health status and quality of life, preventive attitude and behaviors, lifestyle, reproductive history, medical record, and use of health services. Three hundred and thirty-five possible female twin pairs, born between 1945 and 1955, were initially identified using the computerized databases of the Regional Health System. A pair was selected if they matched on both surnames and birth date. 40.6% of the selected pairs were removed for not being twins. 68.1% out of 398 identified twins have been interviewed with a participation rate of 97.8%. At the moment, the data collection on the pilot and first phase samples is completed. The methodology used is being useful to the implementation of the Murcia Twin Registry and high rates of twin contact and response are being achieved.

HERITABILITY OF CIGARETTE SMOKING HABITS IN KOREAN FEMALE TWINS — HEALTHY TWIN

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Many twin studies have reported that cigarette smoking is affected by genetic factors. And that the influence of genetic factors on smoking habits differs by the sex. But the role of genetic factors on women's smoking habit is not clear yet. Thus, this study attempted to investigate the role of genetic factors in smoking habits among Korean adult twins participating in the Healthy Twin study.

The sample was 235 female twin pairs (187 monozygotic, MZ; 48 dizygotic, DZ pairs) by questionnaire-based classification. Four hundred and sixty-six individuals were analyzed (all except 4 who lacked information on their smoking status). Smoking status was classified into 2 categories; current- and nonsmoker including past smoker. We calculated probandwise concordance rate, tetrachoric correlation and heritability. The mean age of study participants was 37.7 and the smoking rate was 8.15%. The probandwise concordance rate was 62.06% for MZ pairs and 22.22% for DZ pairs. Tetrachoric correlation for MZ, DZ and estimated heritability were .87, .37 and .99, respectively. This result shows strong genetic influence, with possible epistasis, because MZ correlation exceeds twice that of DZ. This study was supported by the Center for Genome Science, Korea, National Institute of Health research contract, budgets 2005-347-2400-2440-215, 2006-347-2400-2440-215, 2007-090-091-4854-300.

TWIN'S INTRAPAIR RELATIONSHIPS, FAMILY STRUCTURE AND ACADEMIC ACHIEVEMENT

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This study is a part of comparative research of academic achievement of school-age twins and singletons, which was supported by grant from the Russian Humanitarian Scientific Fund. The aims of this part of the study were (1) to describe family structure in families where twins have different Intrapair relationships; (2) to compare academic achievement of twins according to their position in the twin pair (leader or not). The sample consisted of 1395 pairs of twins aged 9-20 (352 pairs – preadolescent and 1043 pairs –adolescent). The results were: 61% of preadolescent twin pairs and 55% of adolescent twin pairs has a leader; the presence of a leader in the twin pair correlates with the number of siblings and parents' age: leaders on average have more siblings and older parents; the number of siblings and the difference between twins and the nearest siblings' age have no effect on the intrapair relationships; adolescent twin pairs who have no leader have higher school achievement, and leaders have higher academic achievement than co-twins.

A POTPOURRI OF MULTIPLE-BIRTH LOSS

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Fetal, perinatal and childhood losses are significant complications of multiple pregnancy and parenting. With the increase in multiple births, losses correspondingly increased, with absolute numbers of affected children sometimes constant despite lower mortality rates. Selected topics in multiple-birth loss are presented from an international perspective. The methods used were literature review, and empirical experience of support facilitators, and materials used were medical and support-organization literature and writings, mementos, and photographs from bereaved parents. Successful implementation of bereavement protocols is reported by families who were offered adequate time, mementos and photographs with deceased and/or living multiples together. Moreover, internet resources and literature in many languages make loss support widely available. Adult surviving multiples urge bereaved parents to discuss losses with surviving children, and many support groups assist bereaved parents, children and adults. Challenges include better dissemination of optimal multiple-birth bereavement protocols, cultural sensitivity, ethics, and difficult scenarios. Further research is needed among families who lose an entire set of multiples, parents who lose some high-order multiples, parents experiencing multifetal pregnancy following prior multiple-birth loss, and families affected by early loss in multifetal gestation. Research would be welcome on the efficacy of support groups and of interventions offered to survivors of vanishing-twin phenomenon. Similarly, late follow-up studies of families who elected multifetal pregnancy reduction (MPR) are needed, including sound guidelines for families who plan to discuss MPR or selective termination with living children. Although good support exists for bereaved multiple-birth families, many research and support opportunities remain. Peer-support experience and future research may enhance current resources.

GENETIC AND ENVIRONMENTAL DETERMINATION OF TRACKING IN SUBCUTANEOUS FAT DISTRIBUTION DURING ADOLESCENCE

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The distribution of fat and adipose tissue is an important predictor of disease risk. Variation in fat distribution (FD) during adolescence is correlated with FD in adulthood. The objective is to gain insight into the relative contribution of genes and environment to the stability of subcutaneous FD from early adolescence into young adulthood. Trunk-extremity skinfold ratio (TER) data from the Leuven Longitudinal Twin Study, (n = 105 Belgian twin pairs followed from 10 to 18 years of age), was entered into a longitudinal path analysis. The best fitting model included additive genetic sources of variance and nonshared environment. Heritabilities range between 84.3% (CI: 63.9%–92.3%) and 88.6% (CI: 76.5%–94.1%) in boys and between 78.4% (CI: 59.3%–88.3%) and 88.3% (CI: 77.0%–93.8%) in girls. The majority of the phenotypic tracking (boys: .40–.78; girls: .38–.72) could be attributed to the moderate to high genetic correlations (rG; between .27–.84 and .38–.80 for the various age-intervals in boys and girls respectively). This rG could be attributed to both genetic sources of variance which are the same throughout adolescence as well as genetic sources of variance that are 'switched-on' at a certain age, the effect of which is then transmitted to subsequent observations. Environmental correlations (rE) in boys ranged between .51 and .70 but contributed relatively little to phenotypic tracking as the amount of variance explained by the environment was low (11.4–15.7%). In girls rE was low to moderate at best (.09–.48). Phenotypic tracking in subcutaneous FD during adolescence is predominantly explained by additive genetic sources of variance.

COMBINED GENOME SCANS FOR BODY STATURE IN 6602 EUROPEAN TWINS: EVIDENCE FOR COMMON CAUCASIAN LOCI

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The GenomEUtwin consortium consists of 8 twin cohorts (Australian, Danish, Dutch, Finnish, Italian, Norwegian, Swedish and UK) with the total resource of hundreds of thousands of twin pairs. We performed QTL analysis of one of the most heritable human complex traits, adult stature (body height) using genome-wide scans performed for 3817 families derived from twin cohorts from Australia, Denmark, Finland, Netherlands, Sweden and United Kingdom with an approximate 10 cM microsatellite marker map. Variance component linkage analysis was performed with age, sex and country-of-origin as covariates. The covariate adjusted heritability was 81% for stature in the pooled data set. We found evidence for a major QTL for human stature on 8q21.3 (MLOD 3.28), and suggestive evidence for loci on chromosomes X, 7 and 20. Some evidence of sex heterogeneity was found however, no obvious female-specific QTLs emerged. Several cohorts contributed to the identified loci, suggesting an evolutionally old genetic variant having effects on stature in European-based populations. In a separate, family-based cohort we have identified a male-specific linkage and association to a SNP on COL11A1–gene on chromosome 1p21 (lod score 4.25, p for association = .0004). Some evidence for linkage was shown in the sample restricted to male dizygotic twins for this locus as well. To facilitate the research in the field we have also set up a website which lists all stature genome scans published and their most significant loci (www.genomeutwin.org/height-genetics/index.html).

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THE CO-OCCURRENCE BETWEEN INTERNALIZING AND EXTERNALIZING BEHAVIORS: EVIDENCE FROM A GENERAL POPULATION ITALIAN TWIN STUDY

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Although internalized and externalized problem behaviors are well separated at the psychometric and clinical-descriptive levels, they frequently co-occur in individuals. Very few studies, however, have aimed at investigating the causes of such co-morbidity. We analyzed parent-rated CBCL/6-18 Internalization and Externalization scores in a sample of twins to investigate the genetic and environmental basis of the within-individual association between these 2 dimensions. The study sample consisted of 398 twin pairs (144 monozygotic and 254 dizygotic) drawn from the general population-based Italian Twin Registry, aged 8-17 years and resident in the Northern Provinces of Milano and Lecco. We estimated twin correlations for the Internalizing and Externalizing continuous scales, and also calculated within-individual and within-pair odds ratios after dividing subjects into 'non problematic' and 'borderline/problematic' by means of Italian norm values for the CBCL/6-18 scores. Furthermore, we fitted bivariate genetic models to Internalization and Externalization scores using the software Mx. Model fitting showed that the covariation of Internalizing and Externalizing dimensions was best explained by additive genetic and common environmental latent sources, each accounting for about 50% of total covariance. Odds ratio estimates indicated that a borderline/clinical level of Internalization predicted a sizeable risk of co-existing Externalizing problems both in the same child and within a sibship. Our findings may help to approximate individual risks (e.g., in clinical practice, predicting the presence of Externalization in an internalizing child, and vice-versa), and to recognize that several shared environmental and genetic factors can affect a child's proneness to suffer from both types of problem behaviors.

SELECTION BIAS IN POPULATION-BASED STUDIES AMONG ADOLESCENT TWINS

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We have shown that in recent Danish birth cohorts there is no difference in academic performance between twins and singletons. The zygosity of Danish twins is based on a mail-back questionnaire on similarities. We investigate the influence of nonresponse on studies of academic performance of students in 9th grade. All twins of the birth cohorts 1986-1988 have been linked to Statistics Denmark. The Danish Twin Registry has provided information on zygosity, and Statistics Denmark on birthweight, gestational age, test scores at 9th grade, age at test, data on hospital admissions as well as parental age and education. The study base comprised 1171 same-sexed intact twin pairs living in Denmark until January 2003. Intact same-sexed nonresponding twin pairs had a significantly lower test score than responders (difference = 0.43; 95% CI: 0.31-0.56). The nonresponding twins were on average 38 g (95% CI: -23-101 g) lighter at birth, and their parents were about half a year younger than the parents of the responders. Among nonresponders 40% of the mothers had no education compared to 27% for responders; 31% of the fathers had no education compared to 24% for responders. The difference in mean test score was attenuated, but still significant (0.30; 95% CI: 0.19-0.42), when controlling for birthweight, gestational age, age, sex, parental age and education. Adolescent twins responding to the zygosity questionnaire had significantly higher test scores in the 9th grade than nonresponders, and the parents of responding twins are older and have higher education.

A SINGLETON OR A TWIN BORN AT THE SAME GESTATIONAL AGE: IS THERE A DIFFERENCE?

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The objective was to determine whether, for the same gestational age, twins and singletons have a comparable obstetrical and neonatal outcome. The study was a case (= twins) – controlled (singletons) study in all 70 labor wards in Flanders (Northern Belgium). From 1/1/1999 to 31/12/2005, 13847 twins and 13847 singletons were selected according to the following criteria: same gestational age, same sex of the offspring, same age, parity and level of education of the mother. Cases and controls were compared with respect to the incidence of induced labor, epidural analgesia, Cesarean section, transfer of the baby to the neonatal ward and fetal/neonatal death. Induction of labour occurred more frequently in twin than in singleton pregnancies (25% vs. 19%). Mothers, pregnant with twins, made more use of epidural analgesia (77% vs. 62%) and delivered more frequently by means of a cesarean section (48% vs. 30%). All these differences were highly significant. Twin babies had a mean birthweight that was lower than that of singletons (2415 g vs. 2743 g) and twins were more frequently transferred to the neonatal ward (66% vs. 48%). More importantly, fetal death was significantly lower in twins than in singletons (0.90% vs. 1.73%). Once born alive, no significant differences in neonatal or in infantile death were encountered. Fetal death occurs more often in singletons than in twins of a comparable gestational age. As soon as they are born alive, twins and singletons have a comparable neonatal outcome. A mother, pregnant with twins, will more frequently undergo medical acts.

CHRONIC ANTI-EPILEPTIC DRUG (AED) TREATMENT IS ASSOCIATED WITH INFERIOR BALANCE FUNCTION IN AED-DISCORDANT TWIN AND MATCHED SIBLING PAIRS

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Anti-epileptic drug (AED) users suffer fractures, potentially due to bone disease and falls. Therefore we assessed the effect of chronic AED use on falls risk in AED-discordant twin and matched-sibling pairs. Twenty pairs discordant for AED use (13 female, 7 male; 3 monozygous, 5 dizygous, 12 sib pairs within 3 years of age), mean (SD) age 47.0 (16.9) years were assessed. Duration of AED use was 22.6 (16.9) years. Tests of static and dynamic balance (clinical and force platform tests), lower limb strength and gait, all of which are falls predictors, were performed. Serum AED levels were measured. Results were adjusted for height and weight as required. There was no significant within-pair difference in age, height, weight, muscle strength, gait (velocity, double support duration) or maximum activity level. Significant mean within-pair differences (AED-user vs. nonuser) were seen with adjusted activity score (–7 points, $p = .012$) and balance measures including: Chattecx Balance System (positive score indicating greater unsteadiness) — stable platform with distraction task (serial 3s): left-right sway (LR) cm/height +0.468, $p = .022$; AP moving platform LR cm/height +0.509, $p = .016$; medial-lateral (ML) moving platform cm/height +0.231, $p = .037$, with distraction LR cm/height +0.831, $p = .030$; single leg stance: stable platform LR cm/height +0.748, $p = .025$, with distraction LR cm/height +0.395, $p = .051$. Lord's clinical balance test — eyes closed +41 mm, $p = .045$, coordinated stability track ($n = 14$) +4.4 points, $p = .045$. There were multiple significant within-pair differences in balance measures in chronic AED users compared with matched twin/sibling controls. Impairment of balance function may have important implications for AED users re increased falls risk, contributing to the increased fracture risk seen in this population.

SUDDEN INFANT DEATH SYNDROME IN TWINS AND SINGLETONS

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Twins compared with singletons and monozygous (MZ) compared with dizygous (DZ) twins are at increased risk of fetal and infant death, cerebral palsy and many congenital anomalies. The aim was to test the hypothesis that zygosity is a risk factor for the sudden infant death syndrome (SIDS). Birth registration data and draft infant death certificates for all multiple births in England and Wales 1993 to 2003 were provided by the Office for National Statistics. As a partial proxy for zygosity, same-sex was compared with opposite-sex twins for SIDS birthweight specific mortality. Data on singleton infants was obtained by subtraction of multiple births from routinely published population births and infant deaths. SIDS mortality among low birthweight infants was significantly less in twins than singletons. This twin-singleton relative risk was reversed in infants of normal birthweight. Among infants of normal birthweight, neonatal SIDS was significantly more common in same- compared with opposite-sex pairs. Among infants of low birthweight, postneonatal SIDS was significantly more common in same- compared with opposite-sex pairs. Zygosity is a risk factor for SIDS in twins. As congenital cerebral anomalies are a feature of many MZ twin conceptions, a detailed macro- and microscopical examination of the brain in twin SIDS may indicate an otherwise unrecognized pathology.

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TWINS: CONGENITAL ANOMALIES AND CEREBRAL PALSY HAVE A COMMON PATHOGENESIS

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Many congenital anomalies (CA) and cerebral palsy (CP) have a common pathogenesis associated with very early episodes of feto-fetal transfusion. Singletons with these anomalies are surviving co-twins of a 'vanished' twin. If CA and CP have a common pathogenesis, co-existence of CA and CP will be observed more commonly than expected by chance. The objective was to compare the prevalence of CA in children with CP with that in all children. Medical records of all children on a CP register were abstracted for coincident CA. These were coded using the International Classification of Disease 10th edition (ICD 10). For comparison, data from the 8 United Kingdom (UK) CA registers contributing to EUROCAT were used. There were 5- to 33-fold increased prevalence ratios for the cardiac anomalies (Q20 Malformations of the cardiac chambers and connections; Q22 and Q23 Malformations of the pulmonary, tricuspid, aortic and mitral valves, Q25 and Q26 Malformations of the great arteries and veins). The population prevalence ratio for anomalies of the eye (Q11-Q14) was 8.8, for cleft lip and palate (Q35-Q37) was 4.0 and formal formations of the oesophagus, small and large intestine (Q39, Q41 and Q42) was 6.4. Microcephaly (Q02) and Hydrocephaly (Q03), diagnosed antenatally or at birth, had population prevalence ratios greater than 50. Children with CP, compared with all births, have about a 10-fold increase in the prevalence of major CA. It supports the hypothesis that CA and CP have a common pathogenesis of feto-fetal transfusion in a monochorionic twin gestation.

LOST IN TRANSLATION: HOW BEHAVIORAL GENETIC FINDINGS REGARDING 'SHARED ENVIRONMENT' ARE MISUNDERSTOOD

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Since its inception, the field of human behavioral genetics has received a lot of attention from the public, and, as many behavioral geneticists have pointed out, some of the findings from twin studies have had important social implications that have been subject to public uptake. However, behavioral genetic findings have been occasionally misinterpreted, typically by those without formal training in psychology, but also by reputable psychologists themselves. Such has been the case with findings related to the concepts of shared environment and nonshared environment. As Turkheimer and Waldron (2000) have pointed out, the term shared environment is often mistakenly thought to refer the objective family environment rather than to the phenotypic similarities among children reared in the same home that cannot be attributed to shared genes. As a result, findings which suggest that the influence of shared environment tends to be insignificant for certain traits and populations have been interpreted by some to mean that 'parents don't matter' when it comes to 'who children turn out to be' (e.g., Harris, 1998). Careful analysis of the concepts of shared and nonshared environment suggest, however, that such a conclusion is not substantiated solely by the aforementioned findings. From this, certain questions follow: What can behavioral geneticists do to minimize the possibility of their work being misunderstood? In cases where their work is misunderstood, and especially when such misunderstandings might lead to negative social consequences, how should behavioral geneticists respond?

FETAL PROGRAMMING AND IMPLICATIONS OF INTRAUTERINE GROWTH FOR THE DEVELOPMENT OF TYPE 2 DIABETES

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The relationship between low birthweight and the development of Type 2 diabetes (T2D) and associated defects of glucose metabolism is well established. Whether this association is of genetic or nongenetic origin is under debate. Studies have suggested that a common genotype may result in both low birthweight and T2D. We have previously demonstrated lower birthweights in twins with T2D than in their genetically identical nondiabetic co-twins, suggesting that the association between T2D and low birthweight is not merely a coincidence involving the putative T2D susceptibility genotype and a genetically determined low birthweight. The finding of significant intrapair correlations between birthweight and key metabolic components underlying the development of T2D (i.e., impaired insulin secretion and sensitivity) in monozygotic (MZ) twins, eliminates the influence of genotype and provides further evidence for a nongenetic origin. MZ twins have a different and potentially more adverse fetal environment compared to dizygotic (DZ) twins, and may therefore be more prone to develop various metabolic abnormalities. Furthermore, twins all together may have an increased risk of metabolic impairments compared to singletons. Accordingly, we have reported that elderly MZ twins are more insulin resistant than DZ twins, consistent with, and providing a mechanistic explanation for our previous findings of elevated glucose and insulin profiles after oral glucose ingestion in MZ compared with DZ twins. In addition, twin status per se was associated with elevated hepatic glucose production. The effect of fetal programming (i.e. birthweight, twin- and zygosity-status) on glucose metabolism was only apparent in elderly subjects, hence suggesting an important role of age in unmasking the impact of an adverse intrauterine environment on the development of T2D and insulin resistance.

PUBLIC ATTITUDES TO ASSISTED REPRODUCTION, GENE SELECTION, AND HUMAN REPRODUCTIVE CLONING: IMPORTANT LESSONS FROM TWO TWIN STUDIES

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Surveys have shown strong opposition to human reproductive cloning (HRC) in many countries. Views of identical (monozygotic, MZ) twins are of particular interest, as they naturally share 100% of their genes. We investigated the attitudes of 4651 MZ and nonidentical (dizygotic, DZ) British twins towards HRC in the context of assisted reproduction technologies (ART) and gene selection in a self-completion questionnaire. Most subjects (77%) did not regard the use of medical technologies to treat infertility as interfering with nature, or with God's will, despite believing that infertility is not a disease. Attitudes to gene selection and HRC were context dependent, with favorable views towards treating a medical condition being more common than towards enhancing traits. 44% supported a permanent ban of HRC. Notably, MZ twins were significantly more likely to agree that HRC should be allowed for medical purposes than were DZ twins. Religiosity correlated with more negative attitudes towards both ART and HRC. Data from a second (small-scale and qualitative) study involving in-depth interviews with MZ and DZ twins as well as nontwin siblings (Prainsack & Spector, 2006) support these conclusions. Furthermore, they show that twins do generally not employ genetic determinism and understand very well that genes are only partly responsible for what makes a person. Both qualitative and quantitative findings suggest that the experience of identical twinship, which arguably has a strong social component, is likely to affect the attitudes of MZ twins towards HRC. They also lead to a better understanding of the ongoing debate on human reproductive cloning.

READY, STEADY, GO! DEVELOPING LEARNING THROUGH MOVEMENT

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The movements of babies and young children up to about 14 months of age are dominated by primitive reflexes located in the brain stem (base of the brain). These are essential for survival but should be inhibited (put to sleep) by movements such as crawling by about 14 months of age. Postural reflexes located in the cerebellum (mid brain) should then take over. These enable the child to have automatic control of his or her body for both gross and fine movements. It may be the case that greater numbers of multiple birth children are impacted by the retention of primitive reflexes. This presentation describes how providing daily opportunities for physical movement helps children to develop: body awareness and control; muscle tone; balance; grip and finger movements; hand–eye coordination; the sensory systems (especially sight, hearing and touch). The birth process can be particularly traumatic for multiple birth children and combined with the lack of opportunities for movement that some multiples experience, may impact on their learning. The presentation includes a practical demonstration of *Ready, Steady. Go!* a daily 5- to 10-minute program of movements for babies and young children based upon traditional music and rhymes. It is proposed to conduct a research project investigating this area from a multiple birth perspective — suggestions for this research would be greatly appreciated following the presentation.

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ASSISTED CONCEPTION: ARE PARENTS OF TWINS WILLING TO TELL RESEARCHERS?

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To our knowledge there are no published data on whether parents are prepared to fully disclose the mode of conception of their twins, especially if assisted reproductive techniques were used. The aim was to ascertain the views of parents of twins about disclosure of mode of conception to researchers and to their children. Questionnaires were mailed by the Victorian branch of the Australian Multiple Birth Association to 1600 members, to be returned to us anonymously. We asked whether parents needed medical help to conceive, if yes the mode of conception, and whether they were prepared to disclose that information to researchers or their children. Altogether 938 (59%) responded, and 372 (40%) of them had conceived after some form of assisted conception. Among these 372 respondents, 17 (5%) said they would not or may not disclose the method by which they conceived their twins to researchers studying assisted conception, 22 (6%) to researchers studying twin pregnancies and 26 (7%) to researchers studying twin children. Further, 23 (6%) indicated that they would not or may not tell their children. Altogether 362 respondents added a comment and it was clear that there was sensitivity about gratuitous questions regarding conception, even among those who conceived spontaneously … 'essentially you're asking about my sex life'. Researchers need to restrict questions about mode of conception to information needed for their study, and ask questions sensitively. They also need to recognise that some parents may not disclose mode of conception and their offspring may never know.

THE IMPORTANCE OF GENES AND ENVIRONMENTAL FACTORS FOR SYMPTOMS OF NIGHT EATING AMONG 4964 PAIRS OF TWINS FROM SWEDEN

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The Night Eating Syndrome is characterized by disordered eating with large food intake after supper time or awakenings during late evening/night with food intake. The aim of the study was to investigate the relative importance of genes and environmental factors for symptoms of night eating in a large population-based study of Swedish twins. The twins responded to a web-questionnaire or a telephone interview during 2005/2006. The dataset, including 1171 pairs of monozygotic male twin pairs, 824 dizygotic male twin pairs, 1753 monozygotic female twin pairs and 1216 dizygotic female twin pairs, were analyzed by structural equation modeling. Mean age (*SD*) of male and female twins was 33.9 years (7.6) and 33.8 years (7.6). With night eating symptoms defined as 25% of the daily food intake after supper time or awakenings at least once per week with food ingestions, heritability was found to be 43% for men and 22% for women. Unique environmental factors were responsible for 57% and 71% of the variance of the phenotype in men and women. Common environmental factors explained 7% of the variance among women and 0% among men. When more strict criteria were applied, for example, at least 50% of daily food intake after supper time, heritability was estimated to 62% among men and 34% among women. These early findings from the first twin study in the world on night eating symptoms clearly indicate that not only additive genetic factors but also unique environmental factors are important in this condition.

THE ASSOCIATIONS OF GESTATIONAL AGE AND INTRAUTERINE GROWTH WITH SYSTOLIC BLOOD PRESSURE IN A FAMILY BASED STUDY OF 386,485 MEN FROM 331,089 SWEDISH FAMILIES

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We conducted a population-based family study to explore mechanisms underlying the associations of birthweight *z*-scores and gestational age with systolic blood pressure measured at age 17-19 years. A record linkage study of 386,485 singleton-born men from 331,089 families was undertaken. To compare the within sibling and between nonsibling associations we used random effects linear regression models that take account of clustering within families. The random effects regression coefficients were obtained as the weighted average of the within sibling and between nonsibling effects. Birthweight was inversely associated with systolic blood pressure within siblings with a mean difference (adjusted for age at examination, examination centre and year of examination) within siblings per 1standard deviation difference in birthweight of -0.21 mmHg (95% CI: –0.33 – –0.08) and between nonsiblings of –0.12 (95% CI: –0.16 – –0.08). Gestational age was inversely associated with systolic blood pressure within siblings (–0.18 mmHg; 95% CI: –0.25 – –0.11, per week of gestational age) and between nonsiblings (–0.26 mmHg; 95% CI: –0.29 – –0.24). Adjustment for socioeconomic position and maternal characteristics did not alter these within or between family associations. Further, the associations were not affected by adjustment for paternal height, body mass index or systolic blood pressure. Our findings suggest that the inverse associations of birthweight and gestational age with systolic blood pressure are not explained by confounding due to family socioeconomic position or other factors that are shared by siblings. Variations in maternal metabolic or vascular health during pregnancy or placental implantation and function may explain these associations.

TWIN PAIR CONTACT AND SIMILARITY IN PERSONALITY: AN 11-YEAR LONGITUDINAL STUDY

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Most studies show that monozygotic (MZ) twins have closer relationships than dizygotic (DZ) twins and it has been suggested that this may violate the Equal Environments Assumption (EAA). However, 2 arguments could stand in defence of the EEA: (1) It is the greater similarity in their genetic tendencies that leads MZ twins to develop closer relationships; and (2) greater social interaction between twins is unrelated to greater twin similarity. In this study we looked at the relationship between frequency of twin pair contact and twin similarity in personality across a time period of 11 years. The twins were part of the ongoing longitudinal study carried out in the Netherlands Twin Register. The sample consisted of 1185 and 1293 same-sex twin pairs, respectively, in 1991 and 2002 (64% MZ and 35% DZ in 1991, and 68% MZ and 32% DZ in 2002). The mean age was 17.70 in 1991 and 33.46 in 2002. Contact was measured with the question 'we do a lot together' in 1991 and 'how often do you contact your siblings?' in 2002. Both in 1991 and 2002, MZ twins interacted significantly more with each other than DZ twins. In 1991, twin correlations for personality are higher among the twin pairs who do a lot together. DZ correlations increase relatively more than MZ correlations. In 2002, twins who contact each other more often are not more similar in personality. Twins who did a lot together in 1991 do not resemble each other more in personality in 2002. Multivariate ANOVA shows that twin pair contact does not predict personality differences either cross-sectionally or longitudinally, once the effects of zygosity are controlled for. Results are in line with previous studies that suggest that zygosity differences in frequency of contact reflect the process of gene-environment correlation. Like the effects of shared environment, the adolescent effects of frequency of contact fade in adulthood.

TWIN ASSOCIATION ANALYSES OF GROWTH CURVES USING SAS PROC MIXED

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The SAS Proc Mixed program is commonly used to fit latent growth curves to longitudinal data and has recently been extended to estimate genetic and environmental variance components of growth features. We extend the model to simultaneously consider candidate gene association. We present simulation analyses varying allele frequencies and QTL effect sizes. Simulation analyses demonstrated recovery of population parameters, though as expected standard errors varied dependent on sample size. We implement the model for the APOE candidate and memory performance measured longitudinally across 16 years in Swedish twins.

TAMBA'S MULTIPLE SPECIFIC PARENTING COURSE: PARENTING WITH MULTIPLES IN MIND

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Following on from our poster presentation at ICTS in 2004 proposing a multiple specific parenting course — we would like to report on the success of 'Parenting with multiples in mind' which is now an integral part of Tamba's parenting services. The course has been devised with the National Occupational Standards for the sector and is a recognized course on Parenting UK's commissioning toolkit. It is delivered by experienced freelance facilitators that are either parents of multiples themselves, or

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have demonstrated an understanding of parenting issues for families of multiples. All facilitators receive a day's training by Tamba's Parenting Team. Central to the philosophy of the course is the concept of 'good enough' parenting and the enhancement of individuality; it takes a parent-centered approach with the aim of facilitating parents and carers to develop their own style of parenting. This is done through discussion, exercises and by sharing experiences. The course is organized into the following sessions: Being a parent of multiples, family relationships, enhancing individuality, managing behaviour 1, managing behaviour 2, play and development, and focusing on the future. This presentation will outline the activities that make up the course and describe the positive evaluations received from the participants and by facilitators.

GENETIC INFLUENCE ON DYNAMICS OF COGNITIVE DECLINE IN LATE AGE

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Cognitive abilities were studied using a series of tests in Swedish twin pairs who were over 50 years at the beginning of the study. Up to 5 repeats of cognitive tests were taken over a period of 16 years. The longitudinal test results were analyzed using random change point models, which identified individual specific turning points leading to terminal drop of the cognitive abilities. These turning points estimated to appear on average almost a decade earlier for speed of processing than for other abilities. Resemblance in ages of turning points as well as in rates of the terminal drop after the turning points for 167 identical twin pairs exceeded resemblance for 278 fraternal twin pairs, particularly for verbal and spatial abilities. Estimates of heritability for age at turning point from random change point models were highest for verbal ability measure and lowest for speed of processing. Similarly, heritability estimates for rate of decline after turning point were high for verbal ability, spatial ability and for speed of processing and low for memory.

PARENTING WITH MULTIPLES IN MIND: TAMBA'S NEW DVD

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Tamba has produced a DVD that features mothers and fathers of preschool twins and triplets talking about their parenting experiences and the strategies they use when they find themselves in challenging situations. The film is divided into 6 key themes: being a parent of multiples, family relationships, enhancing individuality, managing behavior, play and development, and focusing on the future. Each section is summarized by Dr Carol Cooper who also adds further information and advice from her broad experience as a mother of twins and as a GP supporting families with multiples. This resource is designed for anyone parenting or caring for twins or triplets, and for practitioners supporting families with twins or more. It can also be used in conjunction with Tamba's successful 7-week parenting course of the same name. Evaluations have shown that this film provides a vital resource for parents who are reassured that they are 'not alone' and that having multiples can be a thoroughly enjoyable experience, without ignoring the challenges. This poster presentation will display images from the film, outline its content and include comments from parents who have seen the DVD and practitioners who have used it with groups.

TAMBA'S RELATIONSHIP SURVEY

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Having been made aware of parents' concerns during the 'Family Relationships' session of our parenting courses, Tamba carried out a survey to discover more about the stresses couples find themselves under when there are multiples in the family. The survey was devised in light of our own experiences and by drawing on the expertise of other organizations concerned with supporting relationships. It was designed to be easy to access and easy to complete and was available on-line and by post. It was open from May to August 2006. Responses were received by 1113 parents of multiples. 26% identified couple relationship difficulties and of these 73% said they did not have opportunities to spend quality time as a couple. Parents of twins identified the first year as the most challenging time for them as a couple, whilst parents of triplets identified the preschool years as the most challenging time. The financial demands of having multiples were identified as putting stress on relationships, particularly by those with older multiples. Our survey also showed that as children got older the principal stress factors changed. The survey has enabled Tamba to review some of its parenting services and to develop information and resources that acknowledge the importance of nurturing the couple relationships. In particular plans are in place to extend services for those with older multiples.

HUMAN RESEARCH IS MORE INTERESTING, AND MORE INFORMATIVE, IF DONE WITH TWINS: RESULTS FROM FINNTWIN STUDIES

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I was David Lykken's first doctoral student, and in remembering him, I find his influence reflected throughout my career. David sought to address socially important questions; he was a critical and demanding methodologist; and he appreciated efforts to circumvent the inherent limitations of nonmanipulative correlational data. This symposium affords me a brief opportunity to reflect on Lykken's lasting influence with an illustration from analyses of drinking data assessed across 4 waves of FinnTwin16-25. Five consecutive cohorts of Finnish twins, born 1975–1979, were sequentially enrolled into study as they reached age 16. Follow-up assessments were conducted at ages 17, 18 and 25. Frequency, quantity, and density of drinking were assessed at each wave, drinking-related problems at ages 18 and 25, and diverse behavioural outcome measures were followed to age 25. Epidemiological studies of twins as individuals confirm strong associations of adolescent alcohol exposure with negative adult outcomes. Adolescents reporting drinking-related problems at age 18 have escalated alcohol-related problems at age 25, along with blunted educational trajectories, unfulfilling social relationships, unstable employment, sexual difficulties, poor general health, and other adjustment difficulties. But such between-family associations may be artifactual, mediated by unmeasured third-variable confounds, a problem Lykken appreciated. To address that, we sought to confirm the between-family associations in within-family comparisons of adult outcomes among co-twins discordant for adolescent alcohol exposure. The within-family replications offer more convincing evidence that the associations are causal, and illustrate David's contention that 'human research is more informative if done with twins'.

RELATIONSHIPS BETWEEN OBESITY, HYPERTENSION, TAPPING SPEED AND THE DECLINE OF COGNITIVE ABILITIES IN AGED TWINS

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This study aims to clarify the relationship between obesity, hypertension, tapping speed and cognitive abilities in aged twins. The subjects are 155 pairs of aged twins (118 pairs of monozygotic, MZ; 37 pairs of dizygotic, DZ). The analysis was conducted on body mass index (BMI), skin fold thickness (SFT), blood pressure (BP), tapping speed and the scores of Wechsler Adult Intelligence Scale (WAIS). Intraclass correlation coefficients and one-way analysis of variance were used on each analysis. Intraclass correlation coefficients of SFT were as follows; MZ (male: .492, female .779), DZ (male: .409, female: .217). When analyzed, there were negative relationships between BMI and digit span, digit symbol ($p < .05$) in females. In one-way ANOVA on BP, the F value on digit symbol was 5.438 ($p < .01$), F value on digit span (backward) was 3.035 ($p < .05$) in MZ. Intraclass correlation coefficients on tapping test were as follows; MZ (male .406, female .375), DZ (male .565, female .441). Conclusions drawn are: (1) the influence of environmental factors was stronger than genetic factors on SFT in male twins, but not in female twins; (2) the influence of environmental factors was stronger than genetic factors on the score of tapping test in both male and female twins; (3) it was suggested that obesity was a risk factor for the decline of cognitive abilities in females, but this tendency was not found in males; (4) it was also suggested that there were relationships between hypertension, lower score of tapping test and the decline of cognitive abilities.

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CHINESE TWIN CHILDREN REARED APART AND SAME-AGE UNRELATED CHILDREN REARED TOGETHER: MIRROR-IMAGE LOOK AT BEHAVIORAL DEVELOPMENT

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David Lykken is famous for saying that research is generally 'more interesting if you do it with twins.' Findings from studies of 2 novel pairs — Chinese Twins Reared Apart (CTAs) and Virtual Twins (same-age unrelated siblings reared together; VTs) — will be described. CTAs are an unintended consequence of China's One-Child Policy, in place since 1979. The policy led to the abandonment and adoption of thousands of infants, mostly female. Included among these children were twins, some adopted by separate families in the United States. VTs result when families adopt 2 near-in-age children at the same time, or adopt a child just before, or just after, the birth of a biological child. These 'mirror-image' kinships (shared genes vs. shared environments) offer new insights into genetic and environmental influences on behavioral and physical traits. A pilot study comparing co-twins' health-related characteristics (illnesses, allergies, height, weight) and behavioral measures (general intelligence; psychological adjustment) was conducted using 7 CTA pairs (3 monozygotic and 4 dizygotic). Developmental similarities and differences between the co-twins will be described. The sample size is quite small, but viewed with reference to findings on young twins reared together and adult twins reared apart, preliminary findings can suggest new hypotheses. Complementing that work is a follow-up study of general intelligence in 43 VT pairs which found a decrease in the VT IQ correlation, and an increase in the within-pair difference. These results indicate increasing genetic and/or nonshared environmental influences and decreasing shared environmental influence on general intellectual development during childhood.

HERITABILITY OF FEMALE ADULT ANTHROPOMETRIC MEASUREMENTS AND BONE DENSITY IN KOREA: HEALTHY TWIN STUDY

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A genetic factor are an important component determining individual variability in anthropometric measurements, but the proportion attributed by genetic factors in body size and bone density is known to be different according to body sites and types of measurement. In this study we aimed to analyze the heritability ($h2$) of these various measurements. We conducted a study of 227 nuclear families including 181 monozygotic and 46 dizygotic female twin pairs aged 29-54 years and their parents from the nationwide twin registry. Total body and pelvic bone mineral density (BMD), and total body fat percent were measured using dual energy X-ray absorptiometry (DXA). We used a self-administered questionnaire-based algorithm to determine zygosity, and estimated $h2$ and variance components of anthropometric values adjusted by age and body size using Merlin program and SAS 9.2. For height, sitting height and sitting height to height ratio, the $h2$ were 95.6%, 87.7% and 70.0%, individually. The $h2$ of weight, BMI and waist to hip ratio were lower than height-related measurement (78.5%, 74.1% and 56.9%). For the measurements from DXA (Total body BMD adjusted by height, pelvic BMD and fat per cent of total body) were 81.7%, 85.7% and 78.0%. In conclusion, we confirmed that the heritabilities of body size and composition are relative high to make these phenotypes to be good targets for further genetic studies. This study was supported by the Center for Genome Science, Korea, National Institute of Health research contract, budgets 2005-347-2400-2440-215, 2006-347-2400-2440-215, 2007-090-091-4854-300.

GENETIC REGULATION OF GROWTH FROM BIRTH TO 18 YEARS OF AGE: THE SWEDISH YOUNG MALE TWINS STUDY

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Growth is a complex process, and only little is known on the genetic regulation of it. In this study, we aim to analyze the genetic regulation of growth in a population-based sample of Swedish male twins. The data were analyzed by 2 different multivariate variance component models (Cholesky decomposition and Simplex model) for twin data using the Mx statistical package. A longitudinal Swedish cohort of 231 monozygotic and 144 dizygotic twin pairs born 1973–1979 with height or length measured annually from birth to age 18 was used. After 2 years of age, 91 to 97% of the variation of height could be explained by genetic differences; at birth and 1 year of age common environmental factors had a substantial effect on length. The genetic correlation between heights at ages 2 and 18 was .73 (95% CI: 0.68–0.77); with increasing age the correlation with genetic effects at age 18 become subsequently stronger. Especially in mid-childhood, growth was largely regulated by the same genetic factors. During puberty new genetic factors started to affect height, but also genetic variation affecting at previous ages remained. These results suggest that genetic regulation of growth is rather uniform throughout most of childhood and adolescence, which is encouraging for further efforts to identify genes affecting growth.

BETA-CELL FUNCTION IN TWINS AND SIBLINGS

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In Type 2 diabetes mellitus 2 pathogenic factors play a crucial role in the development of hyperglycaemia: impaired insulin secretion and insulin resistance. Remarkably, only a few studies have addressed the heritability of beta-cell function. We have recruited twin families from the Netherlands Twin Register to participate in a study of different aspects of beta-cell function. Recruitment is targeted at healthy monozygotic and dizygotic twins, aged 20 to 41 years with additional siblings of the same sex. The protocol involves a home visit for an Oral Glucose Tolerance Test (OGTT) including the completion of questionnaires about health and food intake and 2 visits to the clinic. The first clinic visit involves a physiological meal test and during the second visit participants undergo a combined standardized euglycaemic- and hyperglycaemic-clamp test modified with GLP-1 and Arginine administration, allowing the accurate assessment of several aspects of beta-cell function in relation to the ambient insulin sensitivity. So far, 70 twin families have taken part (including 46 MZ pairs, 19 DZ pairs, 5 twins from incomplete pairs and 39 additional sibs) and another 5 families have agreed to take part. There are 80 male and 105 female participants, with a mean age of 31.1 years ± 5.7. We will present the first results of the fasting and 2 hours post challenge blood glucose (OGTT, meal test) and body mass index, waist/hip ratio, HbA1c and cholesterol distribution.

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HERITABILITY OF QT INTERVAL. HOW MUCH IS EXPLAINED BY GENES FOR RESTING HEART RATE?

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The rate-corrected QT interval (QTc) is known to be influenced by genetic factors. However, it is unknown to what extent the uncorrected QT interval and resting heart rate are influenced by the same genes and whether different formulae to correct QT for heart rate (e.g., Bazett, Framingham) influence QTc heritability estimates. Subjects in this classic twin study were 105 monozygotic and 256 dizygotic female twin pairs (mean age: 49.9 ± 11.5). ECG parameters were measured electronically using the Cardiofax ECG-9320K. Quantitative genetic modeling was performed with Mx software. Best fitting univariate models showed significant heritabilities for heart rate (.55, 95% CI: .44–.65), uncorrected QT interval (.60, 95% CI: .49–.69) and the Framingham QTc interval (.50, 95% CI: .39–.60). Familial resemblance of Bazett's QTc was best explained by shared environmental factors (.34, 95% CI: .24–.43) rather than genes. Heart rate and uncorrected QT interval showed an inverse linear relation (r = –.83). The best fitting bivariate model that simultaneously modeled heart rate and the uncorrected QT interval mirrored the univariate results, that is, both heart rate ($h2$ = 56%) and QT interval ($h2$ = 60%) showed considerable heritabilities. The genetic correlation between the 2 phenotypes was -.86 (95% CI: –.90 – –.80), indicating important overlap between the genetic effects on both phenotypes. Forty-four per cent of the variance in QT interval was due to genes in common with heart rate, whereas 16% was due to genes specific to QT interval. The heritability of QT interval after the removal of effects shared with heart rate within the bivariate model (cf. QTc) was .51 (95% CI: .40–.61). Correction with Bazett's formula may not be optimal for gene finding studies of QT interval. About a quarter of the QT interval heritability is due to genes specific for QT interval, while the remainder is shared with genes for heart rate. Importantly, these results will guide the analytic strategy of our ongoing whole genome association scan of QT interval in 2650 subjects from the TwinsUK registry.

ROLE OF GENETIC AND ENVIRONMENTAL INFLUENCES IN A RELATION BETWEEN HEIGHT AND INSULIN RESISTANCE IN KOREAN ADULT TWINS — HEALTHY TWIN

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Previous studies reporting the increased risk of cancer (i.e., breast, colon) with increasing height suggested that height was a surrogate marker reflecting genetic predisposition or environmental exposure in fetal or early childhood. To examine the factors influencing insulin sensitivity, the relation between height and homeostasis model assessment (HOMA) index calculated from the fasting insulin and glucose concentration lipid level was investigated. Study participants were 361 Korean adult twin pairs who did not take lipid lowering agents. They were recruited through media campaigns and individualized mailing based on a previously constructed nationwide twin registry regardless of health status. Zygosity of the twin pair was determined using a self-administered questionnaire. Age and body mass index adjusted regression analysis at individual level indicated that a 1 cm increase in the height was associated with 0.17 (0.03, 0.31) increase in HOMA. In a regression analysis including both the mean height of the twin pair and individual difference from the pair mean, significant association between height and HOMA was found only between pairs. When we did the analysis according to the zygosity of twin pairs, the same association was observed only in monozygotic pairs. Height was associated with insulin sensitivity and genetic factors might have greater influence on the association between height and insulin than other factors. This study was supported by the Center for Genome Science, Korea, National Institute of Health research contract, budgets 2005-347-2400-2440-215, 2006-347-2400-2440-215, 2007-090-091-4854-300.The views in this article are not necessarily those of the funding body.

ASSOCIATION BETWEEN VARIANTS IN THE LEP GENE AND ITS RECEPTOR (LEPR) WITH BIRTHWEIGHT AND PRE-DIABETIC PHENOTYPES IN YOUNG HEALTHY TWINS

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Leptin acts as a satiety signal regulating food intake and energy expenditure. The relation between variants in the leptin (LEP; 19 G > A) gene and its receptor (LEPR; Q223R and K109R) with obesity and Type 2 diabetes has been studied extensively, but results are inconclusive. In a population-based association study, we examined the effect of these variants on pre-diabetic phenotypes measured in young healthy twins. In this study, 396 monozygotic and 230 dizygotic twins (mean age 25 years) were recruited from the East Flanders Prospective Twin Survey. Several diabetes related traits were measured, including birthweight, adult body composition, fasting concentrations of cholesterol, triglycerides, free fatty acids, leptin, insulin and glucose. Genotyping was performed using Pyrosequencing. Linear mixed models, including a random effect term for twin pair membership, were used to evaluate associations between the variants and the phenotypes. Subjects carrying the 19 G allele of LEP had higher high-density lipoproteins-cholesterol levels compared to 19 A homozygotes (GX vs. AA [95% CI]: 1.62 [1.58–1.66] vs. 1.49 [1.40–1.58] mmol/l; p = .008). The K109R variant in the LEPR was associated with birthweight (KK, KR and RR [95% CI]: 2507 [2462-2553], 2577 [2519–2536] and 2762 [2643–2882] gram; p = .0002). Also the Q223R variant in the LEPR showed association with birthweight (QQ, QR and RR [95% CI]: 2493 [2431–2554], 2541 [2492–2591] and 2670 [2583–2756] gram; p = .002). These results indicate that genetic variation in the LEP gene affects high-density lipoprotein-cholesterol levels. Furthermore, this study suggests a possible role for the LEPR in explaining the inverse relationship between birthweight and the development of metabolic diseases in adult life.

HERITABILITY OF AGE-RELATED CATARACT: AN ITALIAN TWIN STUDY

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Most epidemiologic research into nuclear and cortical cataract has concentrated on environmental risk factors such as diet and UV light exposure. Very few studies have explored the role of genetic susceptibility, and to our knowledge only 2 have estimated the heritability of cataract in twins. A twin study of age-related cataract is underway in Italy. Through the Italian Twin Registry, twins resident in the Province of Parma, aged more than 49 years, have been identified and are asked to participate in the study. Agreeing twins are invited to the Eye Clinic of the University of Parma where they are administered a questionnaire regarding known environmental risk factors for cataract, undergo an ocular examination and lens photographs, and donate, after signing a specific consent form, a blood sample for DNA extraction. Lens status is assessed by grading slit-lamp and retro-illumination lens photographs according to a modification of the Age-Related Eye Disease Study (AREDS) lens opacities grading system. To date, 109 intact and 38 broken twin pairs have been enrolled (50 monozygotic, 95 dizygotic [52 same-sex, 43 opposite-sex], 2 with unknown zygosity). Lens photographs have been taken for 228 subjects (89%) in both eyes. Blood samples are available for 243 individuals (95%). Photographic grading scores of nuclear, cortical, and PSC opaci-

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ties have so far been assigned for 80 twins (35%) in both eyes. Once the grading procedure is completed, twin correlations for the different scales will be investigated, and heritabilities will be estimated by univariate genetic models including age among variance components.

PATERNAL INHERITANCE OF MONOZYGOTIC TWINNING IN ANGLO-NORMAN SCOTTISH FAMILIES

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A direct paternal genetic effect in human twinning has been documented (St Clair & Golubovsky, 2002). This has important genetic/medical implications and may challenge the basis of twins studies (Golubovsky, 2002). A study of paternal inheritance patterns in Scottish Anglo-Norman families of Norse extraction further demonstrates the inheritance pattern through statistical analysis and its association with monozygotic twins. One birth in 81.60 was the general Scottish twinning rate (1856–1961) extracted from published data on approximately 12 million live-births. However, the twinning rate was significantly higher than the average where the father of twins bore the particular Anglo-Norman patronymics Sinclair (28,210 live-births) and Bruce (21,370 live-births), with the twinning rate 1856-1961 respectively 1 in 68 and 1 in 73.69. In similar studies of 2 indigenous Scottish patronymics (18,184 live-births) the twinning rates were lower than average, 1 in 91.5 and 1 in 84.12. The general monozygotic twinning rate for the period 1856-1961 based on Weinburg's differential calculus was projected from available data as one monozygotic set per 337 births. In the case of the Sinclair and Bruce patronymics there were 64 more monozygotic sets of twins than projected (212 instead of 147.2), whereas in the indigenous names, the number of monozygotic twins was slightly less than projected. This uplift in the monozygotic twinning rate would account for the higher than average twinning rate in the Anglo-Norman families.

BIRTH ORDER: A NEW VARIABLE?

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The perception and importance of birth order in the social processing of twins are neglected areas. Questions about birth order in general have been examined and studied by psychologists and sociologists, resulting in 2 opposing camps: those who conclude that birth order is important in shaping personality and predicting values and interests of individuals, and those who take the opposite view. After critically reviewing birth order research, this study examines the assumptions that there is no significance in birth order for twins and that birth order is not important outside the familial home. It is argued that birth order as applied to twinship is a social anomaly. The cultural significance of birth order for twins and the normalizing strategies different societies adopt are explored. The study analyses questionnaires obtained from parents of twins, twins themselves and sometimes their respective mothers, inquiring into what difference(s) birth order made to them, respectively, at what age parents informed their children or when the twins themselves learned about their birth order, and what the ensuing consequences were, if any. Finally, it is suggested that birth order may pose alternative questions for twins, critical questions of identity that singletons do not have to consider.

SRI LANKAN TWIN REGISTRY: CHALLENGES, BARRIERS AND LESSONS LEARNED

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As with any new initiatives, we faced many obstacles. Determination, commitment and team work were our strengths. Acquisition of basic knowledge was vital. This demanded networking with experienced international twin researchers. Collaboration was based on mutual benefits and scientific merit, but not on economically cheap and easy research in the developing world. As twin research unites diverse disciplines, forming a multidisciplinary team was essential, but for most local colleagues the concept was new. However, enlisting support was not difficult but consolidating what was achieved was challenging. Funding was the most difficult, as it so competitive and is usually available for people with credentials. Local ethical framework was inadequate. Ethical guidelines had to be developed for informed consent processes, data collection, storage and access to the database and collection, storage and access to the human biological material including genetic material, funding, commercial exploitation, international collaboration, and dissemination of results and authorship. This was to safeguard the Sri Lankan interests as the moral 'rights' and 'wrongs' are not absolute but vary with the culture. We initiated a volunteer register and worked towards a population-based register. Local capacity building for twin research was one of the main objectives of the project. We have not only managed to achieve this goal of 20,000 population-based twins in one district (25 of such in Sri Lanka) but also gained a wealth of experience through the whole process. These include how to face challenges, barriers and hurdles in establishing an ethical research culture especially in the developing world.

DETERMINING ADULT TWIN ZYGOSITY BY QUESTIONNAIRE, CLINICAL MEASUREMENTS AND GENOTYPING IN KOREA — HEALTHY TWIN

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Determining zygosity is a basic requirement for twin studies. However, discrimination by genotypes is not always available in some cases, and reasonable tools to classify monozygotic (MZ) and dizygotic (DZ) are necessary. We attempted to determine the zygosity of 720 adult Korean twin individuals in the Healthy Twin study by simple zygosity questionnaire. Comparing the genotypes (standard forensic markers) of 282 individuals, we examined the validity of the questionnaire-based algorithm classifying zygosity. We also explored whether some clinical measurements such as physical characteristics and blood tests, if added, can improve or complement the zygosity estimation algorithm. Matching more than 15 markers (out of 16) between pairs were determined as true MZs (= 121 pairs) and others as DZs (= 20 pairs). The algorithm-based method showed 254 MZ, 66 DZ and 34 of undetermined zygosity (XZ) where co-twins' zygosity conflicted. The algorithm demonstrated good predictive power for MZ (97.1 %), however less accuracy for DZ (86.4%), and most of XZ were MZ (10 out of 11 pairs). Most clinical tests, such as high-density lipoprotein cholesterol, QT interval (ECG), FEV1 (PFT), and DEXA fat measurements, did not improve the discrimination power, while certain physical measurements, especially sitting height, correctly predicted the zygosity for XZ, but not for DZ. We concluded that adding clinical measurements may not significantly enhance the zygosity assessment, especially for those confused DZ twins who might share similar physical characteristics. This study was supported by the Center for Genome Science, Korea National Institute of Health budgets (2005-347-2400-2440-215, 2006-347-2400-2440-215 and 2007-090-091-4854-300).

THE EFFECT OF BIRTHWEIGHT FOR THE DEVELOPMENT OF RHEUMATOID ARTHRITIS

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The objective is to study the influence of birthweight for the development of rheumatoid arthritis using a case-control study of twins discordant for rheumatoid arthritis in the Danish population. Subjects were 8 monozygotic and 19 dizygotic twin pairs discordant for rheumatoid arthritis. Main outcome measures were the difference in birthweight between twin pairs discordant for rheumatoid arthritis. Valid information on birthweight was obtained for 27 twin pairs discordant for rheumatoid arthritis. Eight pairs were monozygotic and 19 pairs were dizygotic. There was no significant difference in birthweight between monozygotic and dizygotic twins with rheumatoid arthritis (2441 g vs. 2660 g, difference –219 g, 95% CI: –694–256). There was no significant difference in birthweight between twins with rheumatoid arthritis and the healthy co-twins; in monozygotic twin pairs (difference –143 g, 95% CI: –557–271); in dizygotic twin pairs (difference –19 g, 95% CI: –214–176) or combined (difference –56 g, 95% CI: –225–113). It is concluded that birthweight is not a risk factor for the development of rheumatoid arthritis.

GENETIC AND ENVIRONMENTAL INFLUENCES ON SLEEPING BEHAVIORS (FALLING ASLEEP AND REGULARITY)

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Individual sleeping behaviors from infancy to early childhood are considered to be complex compounds by genetic and environmental factors. To clarify the genetic and environmental influences on sleeping behaviors (falling asleep and regularity), the extent to which these individual differences are influenced by genetic and environmental factors was examined in a large Japanese infant twin sample (497 monozygotic, 1071 dizygotic pairs; 2-35 months). The infant twin sample was drawn from the population-based registry of Tokyo Twin Cohort Project (ToTCoP). More information on the ToTCoP can be found elsewhere (Ando et al., 2006). Univariate genetic analyses revealed shared environmental influences on both falling asleep ($a2 = .34$, $c2 = .57$, $e2 = .08$) and regularity ($a2 = .23$, $c2 = .72$, $e2 = .05$). By multivariate analysis, significant genetic and environmental positive correlations were showed between falling asleep and regularity, but nonshared environmental influences on them were largely independent ($rA = .20$, $rC = .30$, $rE = .09$). The findings suggest that time to fall asleep has a relatively large influence by additive genetic factor, because it might be related to neurophysiological conditions. In contrast, regularity has a relatively large influence by shared environmental factor, because the parental control might be greatly related on it.

ASSESSING GENETIC REGULATION ON GENE EXPRESSION USING RELATED INDIVIDUALS

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Our previous study has reported a modest correlation on the transcriptional profiles of functionally active genes observed in our elderly female Danish twins. We now perform a confirmatory study using published microarray gene expression data in the CEPH Utah families provided by the 15th Genetic Analysis Workshop (GAW15) to further investigate the genetic regulation on gene expression of active and functionally differentially expressed genes advantaged by the multiple sibs (7 to 8 sibs in each family) available for correlation estimation and who, similar to dizygotic twins, share half of their genetic materials. The studied samples contain 110 sibs from 14 families together with their grandparents (56 individuals). RNA extracted from lymphoblastoid cells for each individual was hybridized to one Affymetrix Focus Array containing about 8500 genes. Intrasibship correlation coefficient (ICC) was estimated for each of the 3554 genes selected in Morley et al. (2004). Significance of the ICCs was assessed by permuting a random ICC distribution across sibships. Among the 3554 genes, 1006 showed significantly ($p < .001$) high correlation (ICC > .408). It is interesting to see that genes showing high ICC are also functionally active genes. Among the 157 genes identified by GEE model as differentially expressed across the old and young generations, 56 are highly significantly correlated (ICC > 0.29, $p < .001$) indicating a remarkable functional remodeling of transcriptional profiles during aging of which activities of many of these genes are under modest genetic control.

CONTRIBUTORS TO MATERNAL MENTAL HEALTH AND MARITAL ADAPTATION ONE YEAR AFTER THE BIRTH OF TWINS: COMPARISON OF MOTHERS OF PRETERM AND FULL TERM TWINS

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Parenting twins is considered more stressful than parenting singletons. Moreover, twins born prematurely place additional stress, which may affect the mothers' mental health and marital adaptation. The current longitudinal study aimed to examine the contribution of infants' temperament, mother's internal resource of attachment style, and external resource of perceived grandmother's support following delivery, to the mental health and marital adaptation of first-time and non-first-time mothers of preterm and full-term twins, a year later. Mothers of twins (70 of preterm, 78 of full term) participated in the study twice: about a month after birth and one year later. Participants were asked to complete the Infant Characteristics Questionnaire, the Experiences in Close Relationships Scale, the Support Functions Scale, the Family Inventory of Life Events and Changes, the Evaluating and Nurturing Relationship Issues Communication and Happiness Scale, and the Mental Health Inventory. The level of stress and the internal stress-resistance resource of attachment style played a crucial role in the mother's personal and interpersonal adaptation. The external resource of grandmother's support contributed directly only to the mothers' marital adaptation, whereas it contributed to their mental health upon infant's difficult temperament. In spite of the growing numbers of twins born prematurely, little attention has been paid to the examination of the multiple stress of giving birth for the first time to preterm twins. Interestingly, whereas the circumstances (being first time mother or mothering preterm twins) seem to contribute to mental health, they appear to have no effect on marital adaptation.

EMBRYOLOGICAL TIMING IN MIRROR-IMAGING TWINNING

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Despite being a well known phenomenon (Google search: about 1,400,000!) no systematic study of the phenomenon has ever been performed. Two of us (DT & KP) have developed a reliable method to diagnose mirror imaging based on standardized photography of the face followed by analysis with digital overlay. The current explanation for this phenomenon relates to zygotic splitting at a relatively advanced stage, usually at day 7 or beyond. We have studied a small series of cases in which the time of splitting of the zygote was established, on the basis of the structure of the placental membranes: dichorionic means early (up to day 3) and monochorionic means late (days 4–7) division. Four of the 9 pairs were dichorionic (early), 5 monochorionic (late). All pairs but one were discordant for handedness. There was no correlation between chorionicity and the mirror phenomenon. The current hypothesis of late origin may therefore be abandoned. Mirror imaging originates early, either immediately after fertilization or even before. It is well known that most probably the structure of the cytoskeleton of the oocyte determines the lateralization of some organs and may influence the antero–posterior development of some organs. The opposite handedness of mirror-image pairs suggest that the brain hemispheres deal in the process. Clearly, the study of brain lateralization could benefit from our findings.

THE LEUVEN GENES FOR MUSCULAR STRENGTH STUDY: GENOME-WIDE SNP LINKAGE SCAN FOR MAXIMAL ISOMETRIC KNEE STRENGTH

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Lower limb muscular strength is an important protective factor for falls-related injury in elderly. Instrength and power-related sports it is a major contributing factor to success. Heritability estimates for muscle-cross sectional area and maximal isometric force vary between 44-78% in adults. Within a subset of the Leuven Genes for Muscular Strength Study, we performed genome-wide multipoint linkage analyses to identify chromosomal regions harboring genes influencing maximal isometric muscle contraction torques of the knee flexors and extensors in young adult male sibs ($n = 283$) using Illumina's SNP based Linkage IV Panel (6008 markers). Maximal isometric knee strength was measured using a Cybex dynamometer at a 30° knee angle. Linkage was tested using the revised regression and variance components analysis using Merlin and QTDT. A LOD score of 3.06 was found at chromosome 7 q31.1 for maximal knee extension torque. Also chromosomal regions 8q12.3 and 22 q12.3 show suggestive linkage signals (LOD 2.04-2.86). For knee flexor torques, LOD values at 2p24.1 range between 2.38 and 2.59. A LOD score of 2.01 was found for rs3935212 (at12q13.2), which replicates earlier findings using STR markers in the vicinity of the CDK2 gene in that chromosomal region. Several genomic regions were identified to harbor QTLs for maximal isometric knee strength in this first genome-wide SNP linkage scan for muscular strength related phenotypes. Supported by Fund for Scientific Research Flanders (FWO) G.0496.05 and FWO G.0567.07.

COMPROMISED OR COMPETENT? TWIN CHILDREN'S SOCIAL DEVELOPMENT

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Research examining the social interactions of twin children has largely focused on those within the family and on the first years of life. These studies indicate that twin children have reduced quality of social interaction in the early years. The direct effect of having to divide time between 2 children of the same age and indirect negative effects of care demand on parental emotional wellbeing combine to reduce the average quality of adult interaction received by twins compared with single-born children. This effect is evident even in comparison with close-spaced single born children (Thorpe et al., 2003). Less is known about the experiences of twin children outside the home environment and of the competence of twin children in peer interaction. This paper will report on the study of twin children's social competencies and social interactions in their preschool environments. This study of 200 twin pairs and a comparison group of singletons utilizes evidence from reports of parents, teachers, twin children and their peers. Additionally, researcher observation of twin children and singleton controls in play settings within their preschool classrooms was undertaken. The analyses presented in this paper focus on twin-singleton differences in measures of social competency.

BEHAVIORAL DIFFICULTIES IN EARLY CHILDHOOD: TWIN-SINGLETON AND TWIN TYPE COMPARISONS

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The question of whether the twin situation constitutes a risk for children's healthy social-emotional development is an important question because twinning brings with it both additional biological and social risk which may predispose to higher rates of psychopathology. Reposts of increased rates of language delay (a factor associated with psychopathology) and moderately raised rates of attention-deficit/hyperactivity disorder are among the findings suggesting twin children may be at higher risk of psychopathology. However not all studies indicate raised risk. The current study compared parent- and teacher-reported behavioral difficulties in a sample of 200 preschool-aged twins and a comparison group of singletons drawn randomly from the same preschool class. A standard measure of behavioral difficulty was completed by parents (SDQ) and teachers (TRSSA) on each of the children studied. Data presented examine total difficulties and behavioral subtypes (peer problems, conduct problems, emotional problems and hyperactivity) to assess whether twin children have higher rates of behavioral difficulty at 4 years.

EXPLAINING THE CAUSES OF PHENOTYPIC VARIATION IN THE TEETH OF TWINS

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For 25 years we have studied teeth of Australian twins to clarify how genetic and environmental factors influence dental variation, including the occurrence and expression of individual cusps, the overall size of dental crowns, the arrangement of teeth in dental arches, and the relationships between opposing teeth. Dental casts from over 600 pairs of twins have been collected and analyses performed using the traditional monozygotic (MZ)/dizygotic (DZ) model, opposite-sex DZ model, and MZ co-twin model. Phenotypic variation has been partitioned into genetic and environmental components and findings interpreted in the light of knowledge about evolution of the human dentition and our understanding of molecular events occurring during odontogenesis. We have found significant contributions of additive genetic variance to overall crown dimensions, a significant common environmental effect on permanent first molars, and significant levels of nonadditive genetic variation on canines, consistent with selective pressures acting on these teeth at some stage in human development. We have also found high phenotypic variation in intercuspal distances with only moderate genetic influence, suggesting substantial epigenetic influence on the process of crown formation. Differences in the expression of missing and extra teeth have been noted often between MZ co-twins and we propose that minor variations in developmental processes can lead to these distinct differences. The dentition provides an excellent model system for exploring ontogenetic and phylogenetic processes. Our next challenge is to identify key genes influencing variation at all levels from individual cusps to complete dentitions. Supported by the NHMRC of Australia.

CONCORDANCE IN OBSTETRIC FACTORS EXPERIENCED BY AUSTRALIAN MZ AND DZ TWINS IN THEIR FIRST DELIVERIES

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The etiology of maternal factors in obstetric and perinatal health can be usefully identified via twin studies. In an Australian Twin Registry cohort first contacted in 1980–1982 we collected retrospective questionnaire data from 906 parous female twin pairs (580 monozygotic, MZ; 326 dizygotic, DZ) from the Australian Twin Registry. Questions on the twin mothers' first deliveries included length of labour, difficulty of labour, prematurity, induction, mode of delivery (e.g., caesarean section, forceps), epidural anaesthesia, episiotomy and stillbirth. In addition, we asked about birthweight of the baby, length of breast-feeding and age when solids were introduced. The twin pair correlations for length of labour (rMZ = .30, rDZ = –.04), perceived difficulty of labour (rMZ = .28, rDZ = .12) and length of breastfeeding (rMZ = .42, rDZ = .23) suggested that genetic influences contributed to variation. For all binary obstetric factors except for stillbirth, where numbers were low, MZ odds ratios were around twice the magnitude of DZ pair odds ratios. Odds ratios were for prematurity (MZ 2.1, 95% CI: 1.0–4.7; DZ 0.9, 95% CI: 0.3–2.4), epidural (MZ 3.4, 95% CI: 2.0–5.7; DZ 1.7, 95% CI: 0.9-3.3), forceps (MZ 2.4, 95% CI: 1.6–3.5; DZ 1.2, 95% CI: 0.7–2.0), episiotomy (MZ 2.2, 95% CI: 1.5–3.1; DZ 1.2, 95% CI: 0.7–2.1), and for induction (MZ 2.3, 95% CI: 1.6-3.4; DZ1.2, 95% CI: 0.7–1.9). The most notable difference between MZ and DZ pairs was for cesarean section (MZ OR 8.6, 95% CI: 4.6-16.1; DZ OR 2.0, 95% CI: 0.7-5.6). This finding suggests strong genetic influence on clinical indications for needing surgical delivery. Without taking account of the gender of the offspring, the MZ twin pair correlation for birthweight of first baby was r = .29 while the DZ correlation was r = .19, suggesting maternal genetic as well as environmental influence on offspring birthweight.

RESEARCH PARTICIPATION OF TWINS ENROLLED WITH THE NATIONAL, VOLUNTEER AUSTRALIAN TWIN REGISTRY

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Over 34,270 twin pairs have been enrolled, either by their parents or themselves as adults, with the national Australian Twin Registry (ATR) since its inception in the late 1970s. Of these pairs, 27,308 are still both active, 1067 pairs have withdrawn, in 526 pairs one twin has died, and in 829 pairs either one or both have lost contact with the Registry, there are also 1172 pairs where one or both twins require tracing to update contact details. The ATR does not conduct research, but approaches twins with information about a forthcoming approved study and requests the twins' consent for the ATR to pass their contact details to the researcher so they may approach the twin with more detailed information about the study. We have analyzed the number of approaches to twins and the participation of ATR twins in studies in which they have been invited to participate over the past 10 years. The 4661 youngest (aged under 10 years) and oldest twins (1194 aged 75 years and older) have been approached less frequently for studies than the other age groups; in the latter group over 50% had not been approached at all in the past 10 years. In the other age groups, the great majority had received at least one approach regarding a study, although there were still twins who had never been approached. We analyzed positive and negative response according to the number of approaches made, and by age group. Apart from the very elderly, the lowest positive response rate is observed in the 25- to 29-year-old age group and the highest by 5- to 19-year-olds and 55- to 79-year-olds. For all age groups, positive response declines with number of approaches after a threshold of 3 to 4 approaches is reached. Results suggest that new recruitment to the ATR may be best directed towards the specific age groups relevant to study needs and that, in order to maximize response, twins who have been approached less than 3 times over the past 10 years should be given priority in selection for study approaches.

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PREVALENCE OF PREMATURE OVARIAN FAILURE IN AUSTRALIAN TWINS

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Premature ovarian failure (POF) before 40 years of age from natural causes affects approximately 1% of adult women, with minor variations between ethnic groups. A recent case of ovarian transplantation between young monozygotic (MZ) twins in which one had undergone unexplained POF at 14 years old prompted a study of the prevalence of POF in twins. Menopausal ages of 428 female twin pairs from the Australian Twin Registry were analyzed and compared with 404 twin pairs from the St. Thomas' Hospital Twin Registry UK and the large European EPIC female data set. The prevalence of POF in MZ as well as dizygotic (DZ) twins was higher than in the comparison group. The proportion of Australian MZ twins who had reached menopause before 40 years was 0.046 ($SE = 0.006$), which is 3-fold higher and significantly different from 0.014 (0.002) for the same age threshold from the EPIC data set ($p < .001$). If a MZ twin experienced menopause before 40 years then her co-twin was 6.9 times as likely to do so. The proportion of Australian DZ twins who reached menopause before 40 years was 0.038 (0.011), significantly higher than the proportion of women in the EPIC data set (0.013). The proportion of UK twins reaching menopause by 40 years was identical to the Australian data but higher for DZs. Data were based on self-reported age menses ceased, with limited detail or explanation. Further investigation including family data and clinical characterization of twins reporting POF are needed to unravel fundamental insights regarding ovarian biology, ovarian reserve, fertility and menopause. Female twins and clinicians need correct information about the increased risk for POF that may come with being a twin in order to avoid infertility problems.

INTER-TWIN AND PARENT–TWIN RELATIONSHIPS AND MENTAL HEALTH

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We evaluated inter-twin and parent-twin relationships in relation to mental health in young adult twins. The sample consisted of 419 twins, born 1965-1973, from Northern Finland who had been followed at 2-10 years, 12-20 years and at 22-30 years of age. Data on depressiveness, psychosomatic symptoms, inter-twin and parent-twin relationships were elicited. Monozygotic (MZ) twins, especially MZ females, reported most often co-twin dependence. When the symptom reporting was evaluated in relation to co-twin dependence no relation was found in depressiveness between dependent and independent twins. Twin's subjective experience about the co-twin dependence appeared to be important for the twin's mental well-being as dependence–independence imbalance within twin pair was associated with elevated levels of depressive symptom reporting, especially in twins who perceived themselves as dependent and the co-twin as independent. Dominance–submissiveness in twin relationships were assessed separately in 3 domains of life: physical and psychological dominance-submissiveness and the role of a spokesperson. Submissiveness in the psychological domain was associated with increased symptom reporting in males of male-female pairs. Among females of same-sex pairs, submissiveness in the psychological domain was associated with depressive symptoms. Egalitarianism, having a good relationship to both parents, seemed to be most beneficial for twins as these twins had the least symptoms. Submissiveness, especially in the psychological domain, to a female twin partner seemed to be stressful, whereas it was easier, especially for females, to be submissive to a male twin partner. This was in contrast to co-twin dependency which was experienced positively towards twin sister.

OBESITY — BIO PSYCHOLOGICAL AND SOCIAL DETERMINANTS: A STUDY AMONG DISCORDANT TWINS

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The traditional view of obesity is to consider it a lifestyle problem caused by either overeating or a low level of physical activity. Recent investigations have demonstrated that other determinants should probably be included among the causes of obesity, for example, parental care in childhood, being bullied during childhood, perceived stress and coping competencies. In order to understand the etiology of obesity it is thus necessary to view it as a product of a dynamic combination of physical, psychological and social factors. In the Danish Twin Registry, 144 pairs of twins (monozygotic as well as dizygotic) are discordant for obesity, that is, one twin has a normal body mass index (BMI; between 20 and 25) and the other has a BMI over 30. These twin pairs have been interviewed about their experiences in childhood, with special focus on parental care, eating patterns, being bullied in childhood, perceived stress and coping behavior. The interviews are supplemented with blood samples and anthropometric measures. The interviews began in April 2006 and the total number of persons to be contacted was 288 of which 236 interviews were completed, which means that 82% of the twins have chosen to participate. Preliminary data indicates that the obese twin suffers from either physical or psychological problems or diseases. They are unhappy with their body size but have given up and food is used as consolation. Moving from home, pregnancies, childbirth or other life events have been the cause of the weight increase in the obese twins. The closest childhood relation was the co-twin and therefore many of the obese twins felt neglected by their parents. Successful prevention of obesity requires broad knowledge and documentation based on both physical, psychological and social studies, to which we hope this project can contribute.

EXPLORATION OF ENVIRONMENTAL RISK FACTORS FOR ASTHMA IN 5-YEAR-OLD DUTCH TWINS

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Research identified several environmental risk factors for asthma and allergic diseases that are shared by family members, such as parental smoking, number of siblings and air pollution. In contrast to these results, a consistent finding from twin studies is that the environment shared by family members does not contribute to the variation in susceptibility to asthma and allergy. The minor role of environmental factors seems remarkable and can probably explained by gene–environment interactions. In the present study we will explore various environmental factors as potential risk factor for asthma and test for gene–environmental interactions. Asthma data was obtained by parental report for about 11,000 5-year-old twin pairs. The following factors were explored as potential environmental risk factors: maternal smoking during pregnancy, partus, number of elderly sibs, amount of child care, breast feeding and birth cohort. A first exploration of the data revealed that prematurity, birth cohort and nonparental child care were significant predictors for asthma. For very preterm babies we observed an almost doubling of the prevalence of asthma (14.3.2%) compared to prevalence of term babies (7.2%). The prevalence of asthma was 5% for the birth cohorts 1986–1989, and increased to 10% for children born in 1996–1999. The results for child care were in an unexpected direction: 7% of children without child care suffered from asthma compared to 10% of the children with child care outside home. For these factors we will test whether the heritability will be different across varying levels.

NEUROPSYCHOLOGICAL FUNCTIONING AND ADOLESCENT AND EARLY ADULT SUBSTANCE USE: BETWEEN- AND WITHIN-FAMILY ANALYSES

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Twin pairs in the FinnTwinn16 study have been assessed for frequency of drinking, drinking to intoxication, and tobacco use at ages 16, 17, 18, and 24-26 (hereafter 25), and for drinking problems at age 18 and 25. A subset of 300 pairs chosen in part based on discordance and concordance for adolescent drinking problems was tested at age 25 on a battery of neuropsychological tests: Trails, Digit Span, Digit symbol, Letter-Number Sequencing, and the CVLT. We report associations between young-adult neuropsychological performance and both adolescent and contemporaneous

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substance use and drinking problems. As 2 siblings are assessed in each family, the same associations can be evaluated between families and within families (i.e., how do within-family differences in adolescent drinking correlate with within-family differences in neuropsychological functioning). Associations between neuropsychological performance and substance use were generally modest or low, although there were significant associations with alcohol problems in particular. Some associations showed a similar pattern between and within families, while for others the within-family associations were substantially different.

SINGLETON, TWIN AND TRIPLET DIFFERENCES AND GENETIC EFFECTS ON HANDEDNESS

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There has been great interest in genetic models of handedness, but twin studies have yielded inconsistent results. There is also a question of whether twins display higher rates of left-handedness than singletons. We studied singleton, twin and triplet differences and genetic and environmental effects on handedness, with information on forced right-handedness, in a sample of 30,335 Finnish subjects aged 18-69. Left-handedness as a child was more common in twins (8.1%) and triplets (7.1%) than in singletons (5.8%). Ambidextrousness was more common in triplets (6.4%) than in twins (3.4%) and singletons (3.5%). Males had a higher rate of left-handedness (8.7%) than females (6.8%) and that sex difference was evident also in singletons, twins and triplets separately. Within left-handers, there were no differences in forced right-handedness between singletons, twins and triplets. Concordance for left-handedness in twins was rare and did not occur more often than by chance. Genetic modeling indicated that additive genetic (A) effects (0.07, 95% CI: 0–0.15) and unique environmental (E) effects (0.93, 95% CI: 0.85–1.00) contributed to childhood handedness (right vs. left). Also an E model fitted the data well. The best model for current handedness was AE: A = 0.27 (95% CI: 0.16–0.37) and E = 0.73 (95% CI: 0.63–0.84), but also the CE model fitted the data well: C = 0.19 (95% CI: 0.11–0.26) and E = 0.81 (95% CI: 0.74–0.89). Despite a sex difference in prevalence, male and female variance components did not differ. We conclude that unique environmental effects explain most of the variance in handedness.

IDENTITY DEVELOPMENT IN ADOLESCENT TWINS AND NONTWINS

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Siblings present a long-lasting and not freely chosen type of social relationship. In our longitudinal study (T1-T3), we assessed dyadic identities, individual evaluations of the siblings' relationships and individual identity development to examine differences between 5 groups of siblings, including monozygotic (MZ) and dizygotic twins (DZ; N = 214, average age 11.2, T1). The Brunswick Dyadic Identity Scale for Siblings (BDISS) was tested for its factorial structure and reliability (Cronbach's Alpha = .88). A German version of the modified Dutch Utrecht-Groningen Identity Development Scales II was used to examine exploration and commitment in the life domains siblings, best friend, intimate friend, and school. It became obvious that MZ twins represent a special group of siblings concerning their dyadic identities. They show continuous higher values in most aspects - only their emotional attachment is not significantly higher than that of other siblings during puberty. DZ twins seem to be closer to the nontwin sibling relationships. In addition, the sex of the siblings of a dyad had a significant influence on dyadic identity. Concerning their individual identity development, hierarchical and nonhierarchical analyses revealed hardly any differences between the different groups of siblings. Only MZ twins derive more self-esteem from their sibling relationships and are therefore not constricted in their individual development.

LONGITUDINAL STUDIES ON CARDIOVASCULAR RISK FACTORS IN ADOLESCENT AND ADULT TWINS

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The clinical expression of cardiovascular disease (CVD) results from long-term exposure to internal or external factors increasing risk, culminating in an acute event. Risk must be regarded as a time-integrated variable, and single measurements of risk factors are inadequate for both clinical and research purposes. Despite theoretical agreement on this point, most twin, linkage or association studies rely on one-off measurements of risk factors. Our twin and family studies include repeated measures of CVD risk factors on adults from 1980 to the present, and also longitudinal studies across adolescence. Adults with repeated measures were tested at mean ages of 23 and 36 years, while adolescent data were available at 12, 14, 16 and 18 years. This presentation will concentrate on biochemical risk factors: plasma low-density lipoprotein- and high-density lipoprotein-cholesterol, triglycerides, uric acid, and markers of fatty liver (ALT and GGT). Data analysis so far has addressed developmental changes, and the relative importance of common and age-specific genetic and environmental factors across adolescence and early adulthood. Examination of correlations shows that those for individuals across time are generally lower than those for members of monozygotic pairs at any particular age. Model-fitting to the data confirms that some genetic effects on cardiovascular risk factors persist across time while others vary not only across adolescence but between the early twenties and mid-thirties. Nonshared environmental effects tend to be occasion-specific and probably represent biological variation and measurement error. These findings have implications for identification of relevant polymorphisms by linkage or association methods.

GENETICS OF BODY MASS INDEX: SHOULD WE TAKE THE INFLUENCE OF CHILD BEARING INTO ACCOUNT?

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As being overweight is rapidly becoming a major health problem, much attention is given to the underlying causes of individual differences in weight and weight gain, including genetic influences. Body mass index (BMI, a frequently used indicator of being overweight) has consistently been shown to be highly heritable in both men and women. However, little attention has been given to the influence of child bearing on the heritability estimates. The aim of the present study is to examine whether having children modifies the genetic influences on BMI. As part of a longitudinal study of the Netherlands Twin Register, data on BMI and childbearing have been obtained in 2864 monozygotic (1284 complete pairs) and 2768 dizygotic female twins (680 complete same-sex pairs) and 1609 female siblings aged 18 or over. Data on female spouses of male twins were available in 695 cases. A first analyses of the data from women shows that the age of having a first child is more comparable in MZ than in DZ twins. In women for whom data are available after age 40, the agreement for the number of children is also higher in MZ than in DZ twins. We see an increase in a women's weight after pregnancy, and the higher concordance in MZ twins for reproductive history may increase heritability estimates for BMI in women. We will analyze the heritability of BMI, as a function of the number of pregnancies.

THE CORRELATION OF BIRTHWEIGHT AND LENGTH OF MULTIPLE BIRTH CHILDREN TO HEIGHT AND WEIGHT OF PARENTS AND GESTATIONAL AGE

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In 2005-2006, the National Organization of Mothers of Twins Clubs, Inc. (NOMOTC) conducted a survey that queried their membership for information regarding the birthweight, birth length, and gestational age of their multiple birth children. Respondents were also asked the prepregnancy height and weight of the mother, total weight gained in the pregnancy and asked to record any problems during the gestational period. The father's height and weight were also asked. Demographic questions such as number of multiple birth children, zygosity and gender rounded out the survey. The questionnaire was distributed to NOMOTC's members via NOMOTC's Notebook, a bi-monthly publication mailed to over 25,000 members, mailed to each of the over 400 clubs that are affiliated with NOMOTC, and available online by downloading a PDF from the NOMOTC website. Completed surveys numbered 733. Information extracted from this study shows the correlation of the mother's height to gestational age of the multiples at time of birth, weight gained by mother correlating to the birthweight of the multiples, complications in pregnancy affecting birthweight and gestational age at birth, etc.

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INVESTIGATING EPIGENETIC BIOMARKERS UNDERLYING PHENOTYPIC DISCORDANCE IN MONOZYGOTIC TWINS

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As the majority of monozygotic (MZ) twins have identical DNA, any phenotypic discordance between them is generally considered to be the result of environmental influences. One of the primary mechanisms mediating the effects of environment is epigenetics — covalent modifications to DNA or packaging histones that result in heritable changes to gene expression in the absence of any primary DNA sequence change. The most widely studied epigenetic modification involves the methylation of cytosine residues to give 5MeC. We are currently collecting various tissue samples from both MZ and dizygotic twin pairs for epigenetic analysis. Genomic DNA from these tissues is initially being analyzed for global genomic DNA methylation levels(5MeC) using inexpensive, high throughput, high-pressure liquid chromatography (HPLC). This is anticipated to reveal the extent of any differences in global genomic DNA methylation levels between twins and within pairs that may be a contributing factor to any observed phenotypic discordance.

ARE GENETIC AND ENVIRONMENTAL CONTRIBUTIONS TO NICOTINE, ALCOHOL AND CANNABIS DEPENDENCE IN MALE TWINS MOSTLY SHARED OR DRUG SPECIFIC?

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Previous twin models have reported overlapping genetic vulnerability between nicotine dependence (ND) and alcohol dependence (AD) and between AD and cannabis dependence (CD). Because ND is often comorbid with AD and CD, we fit a trivariate model to test for genetic and environmental contributions common and specific to all 3 phenotypes. Data were obtained via administration of the Diagnostic Interview Schedule in 1992 to 7869 monozygotic (n = 4264: 1874 pairs, and 516 singletons) and dizygotic (n = 3605: 1498 pairs and 609 singletons) twins from the Vietnam Era Twin Registry. Trivariate genetic model fitting was performed to estimate the magnitude of genetic and environmental contributions to the lifetime co-occurrence of DSM-III-R diagnoses of ND, AD and CD. The best fitting model allowed for additive genetic contributions and unique environmental influences that were common to all 3 phenotypes. Risks for ND, AD and CD were also due to genetic and unique environmental influences specific to each drug. A shared environmental factor only contributed to CD. These results suggest the lifetime co-occurrence of ND, AD and CD is due to common and specific genetic and unique influences, and vulnerability for CD is due to family environmental factors that do not contribute to ND and AD. The majority of genetic variance is shared across drugs and the majority of environmental influences are drug specific.

ASSOCIATION BETWEEN BIRTHWEIGHT AND TEMPERAMENTS IN EARLY CHILDHOOD

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The present study examined the association between body weight at birth, body weight at 24 months, and temperament at 24 months, which were measured by Early Childhood Behavior Questionnaire (ECBQ; Putnam et al., 2006). Data were obtained from mothers of 87 monozygotic and 157 dizygotic twin pairs who participated in Tokyo Twin Cohort Project (ToTCoP; Ando et al., 2006). After controlling for age and gender, birthweight had positive phenotypic correlation with Positive Anticipation, Fear, and Sadness. A series of multivariate genetic analyses revealed that after controlling for gestational age, the association was not significant for Sadness, but birthweight had significant positive nonshared correlation with Positive Anticipation and Fear; for Positive anticipation, birthweight explained 2% of phenotypic variance and 6% of nonshared environmental variance, and for Fear, birthweight explained 1% of phenotypic variance and 2% of nonshared environmental variance. Body weight at 24 months was not associated with either temperaments. These results suggest that differences in prenatal environment partly explain nonshared environmental influences to later temperament.

PHYSICAL GROWTH CHARTS FROM BIRTH TO 6 YEARS OF AGE IN JAPANESE TRIPLETS

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The purpose of this study is to show the characteristics of the physical growth of triplets in childhood and provide growth charts of Japanese triplets. The subjects were 271 mothers and their 813 triplet children. Their mothers in the present study consented to the aim of this study. Data were collected through a mailed questionnaire. For these births, data on bodyweight, height/length, gestational age, sex, parity, maternal pregravid weight and maternal height were obtained from records in the Maternal and Child Health Handbooks which was established by the Maternal and Child Health Law in Japan. Factors that affected bodyweight and height/length were analyzed by stepwise regression analysis. The selected percentiles of body weight and height/length by gestational age and sex were calculated. Smoothing of growth curves was performed by cubic polynominal functions. The size deficit of the triplets compared to the standards for the general population of Japan was calculated. Gestational age, party, birth order and maternal pregravid body mass index affected body weight and height/length in varying degrees. Growth charts of the triplets present growth at selected percentiles from birth to 6 years of age according to sex. The size deficit of the triplets was largest at birth: more than 40% for weight and approximately 15% for length compared to the 50th percentile of the standard for the general population in Japan. Growth charts specifically for triplets are needed, at least for the first 1 to 6 years of age.

ANXIETY IN MOTHERS OF TWINS OR TRIPLETS AS COMPARED WITH MOTHERS OF SINGLETON CHILDREN

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The purpose of this survey was to study anxiety in mothers of twins or triplets as compared with mothers of singleton children. The subjects were 190 mothers of twins or triplets aged less than 6 and 1469 mothers of similarly aged singleton children. The Japanese version of State-Trait Anxiety Inventory (STAI) was used to evaluate their anxiety state. Mothers of twins or triplets showed significantly higher STAI state anxiety scores than those of singleton children. Meanwhile, there was no significant difference in STAI trait anxiety scores between the mothers of twins or triplets and those of singleton children. Mothers of twins or triplets showed greater anxiety during pregnancy than those of singleton children. There were higher rates of mothers who could not have an image for child-rearing during pregnancy or alleviate stress in mothers of twins or triplets than in those of singleton children. STAI state anxiety scores was associated with no image for child-rearing during pregnancy, no way to alleviate stress, maternal health conditions and poorer sleeping conditions. This study indicated a tendency for mothers of twins or triplets to show greater anxiety as compared with those having singleton children. Maternal anxiety was associated with no image for child-rearing during pregnancy, no way to alleviate stress, maternal health conditions and poorer sleeping conditions.

INTERACTION OF GENETIC DETERMINANT OF FORCED EXPIRATORY VOLUME WITH SMOKING AND ASTHMA: A CLASSIC TWIN STUDY

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Genetic influences on lung function measured by the forced expiratory volume in one second (FEV1) have been studied with conflicting results. The aim of this study was to estimate heritability of FEV1 in Caucasian population and to examine the interaction between genetic factors, smoking and asthma on FEV1. Unselected monozygotic (MZ) and

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dizygotic (DZ) twin pairs from the TwinsUK registry were used. FEV1 was measured with a spirometer. Three manoeuvres were performed and the maximum recorded values for FEV1 were obtained. Height and weight were measured at the interview and smoking status and Doctor diagnosed asthma history were obtained by a validated questionnaire. Structural equation modeling implemented in Mx was used in the analysis. A total of 703 MZ and 1753 DZ twin pairs with a mean age of 47 (range 18 - 84) took part. FEV1 was significantly and independently associated with age, sex, height, weight, smoking status, and asthma history (all $p < .01$). The intraclass correlation in FEV1 was .82 and .69 among MZ and DZ twins, respectively, suggesting a genetic component. The correlation in height, weight, smoking status, and asthma history were also significantly higher among MZ than DZ, suggesting genetic influences on these traits. The fact that there was no significant cross-trait cross-twin correlation between these traits and FEV1 — except for height — suggested that the association between FEV1 and these traits is less likely due to sharing common genes. The significant cross-trait cross-twin correlation between FEV1 and height was altered after adjustment for age and sex. By structural equation modeling, the heritability estimate for FEV1 was found to be 68% (95% CI: 64%–72%) after adjustment for age, sex, height, weight, smoking, and asthma history. Further, a significant interaction between genetic factors and smoking on FEV1 existed. The heritability estimate for FEV1 was significantly reduced to 33% (95% CI: 13%–55%) in current smokers. But there was no difference in the heritability estimate between nonsmokers and exsmokers. Similarly, the heritability estimate was significantly reduced to 15% (95% CI: 2 37%) in subjects with asthma. FEV1 heritability is strong in healthy subjects not exposed to smoking. However, in individuals affected by respiratory disease, for example asthma, or in current smokers the magnitude of the genetic contribution to FEV1 is significantly lower.

LACK OF ASSOCIATION BETWEEN LEUKOCYTE TELOMERE LENGTH AND GENETIC VARIANTS IN TWO AGING RELATED CANDIDATE GENES

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Leukocyte telomere length, a putative marker of ageing, is a highly variable but heritable complex trait. In order to determine the possible underlying genetic variants for leukocyte telomere length variation, we conducted an association study of leukocyte telomere length and 2 candidate genes for ageing related traits, *TGFB1* and *KLOTHO*, in a female Caucasian dizygotic twin population. Terminal restriction fragment (TRF) length, an index of telomere length, was measured using Southern Blotting. Six and 4 single nucleotide polymorphisms (SNP) were genotyped in *TGFB1* and *KLOTHO* gene respectively and tested for association. When there is strong LD between SNPs ($r2 > .5$), haplotypic association was investigated using haplotype trend regression approach. All SNPs were in Hardy-Weinberg equilibrium ($p > .05$). No significant association was detected for individual SNPs, under either codominant or completely dominant models ($p > .101$), or two-locus haplotypes ($p = .7497$) with TRF variation. We failed to find any significant association between leukocyte telomere length and 10 SNPs in 2 ageing-related candidate genes, *TGFB1* and *KLOTHO*. This result suggests that while we couldn't exclude minor effects, none of 10 SNPs in these 2 candidate genes showed significant association with the variation of leukocyte telomere length in our cohort. But as it is unclear whether telomere length dynamics is the cause or the effect of the ageing process, it is still possible the genes are associated with ageing via alternate mechanisms.

GENOME-WIDE LINKAGE SCAN FOR 25-OH VITAMIN D SERUM LEVEL IN A FEMALE CAUCASIAN POPULATION

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Vitamin D is a crucial vitamin to maintain normal blood levels of calcium and phosphorus and plays a role in aging, cancer and musculoskeletal health. As 25-hydroxy vitamin D is the most accurate measure of vitamin D in the body, we conducted a genome-wide linkage scan for 25-hydroxy vitamin D serum level in a female Caucasian dizygotic twin population. Subjects consisted of 2054 healthy twin individuals who were derived from TwinUK registry. Serum level of 25-hydroxy vitamin D was measured using radioimmunoassay. Heritability was estimated using Mx. Haseman-Elston algorithm was performed for genome-wide linkage scan. Analyses were stratified into 2 subgroups (winter and summer months) according to the seasons when the measurements were taken. Heritability estimations for 25-hydroxy vitamin D serum level were 45% overall (64% and 43% for in winter and summer months respectively). Linkage signals for 25-hydroxy vitamin D level were observed in 2 quantitative trait loci (QTLs) on chromosome 17 at 105 cM (unadjusted LOD 4.60) and chromosome 15 at 125-130 cM (LOD 2.92) during summer months, and 3 QTLs on chromosome 2 at 125 cM (LOD 2.48), chromosome 9 at 65 cM (LOD 2.61) and 35 cM (LOD 2.45), during winter months. To the best of our knowledge, this is the first genome-wide linkage scan for 25-hydroxyvitamin D levels in healthy individuals. Our results suggested different QTLs might be involved in 2 major 25-hydroxy vitamin D metabolism processes in the body. Further finer mapping in these regions will be useful to replicate potential candidate genes and further identify novel genes underlying the variation of 25-hydroxy vitamin D level.

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