Abstracts for the 13th International Congress on Twin Studies

Seoul, South Korea, June 4–7, 2010

TWINS AND SIBLINGS: DIFFERENCES IN IQ AND PERSONALITY RELATIONS

O. Alexeeva[1], M. Egorova[2], I. Kozlova[1], S. Pyankova[2]

[1] *Psychological Institute of Russian Academy of Education, Moscow, Russia*

[2] *Psychology Department, Lomonosov Moscow State University, Moscow, Russia*

It has been suggested that association between IQ and personality traits varies as the function of birth order and can be one of the reasons of the low sibling intrapair similarity as compared with intrapair similarity of fraternal twins. Differences in IQ and personality relations in the samples of MZ twins, DZ twins and siblings (firstborns and later-borns) were investigated to examine the importance of the structure of psychological traits for the intrapair similarity of twins and siblings. The study comprised samples of adolescents from the Moscow Longitudinal Twin Study (148 pairs) and the Moscow Sibling Study (70 pairs from two child families). Methods included WISC-III, Eysenck Junior Personality Questionnaire, Sensation Seeking Scale, Locus of Control and Differential Treatment Questionnaire. Results revealed (1) differences in intrapair correlations of DZ twins and siblings (e.g., .71 vs. .25 for IQ, .15 vs. .00 for Extraversion, .47 vs. .26 for Sensation Seeking), (2) differences in IQ — personality relations (MZ and DZ twins' structures of relations resembled those of younger siblings), and (3) regression analyses revealed a significant relationship between siblings' IQ and differential treatment. Data was analyzed with reference to the theory considering the advantages of the firstborn children.

INTRAUTERINE ENVIRONMENT AND COGNITIVE DEVELOPMENT IN YOUNG TWINS

E. E. Antoniou,[1] T. Fowler,[1,2] E. Thiery,[3] T. Southwood,[4] S. van Gestel,[5] N. Jacobs,[5,6] J. Van Os,[6] S. Gopalakrishnan,[1] C. Derom,[6] M. P. Zeegers[1,7]

[1] *Unit of Genetic Epidemiology, Department of Public Health, Epidemiology and Biostatistics, University of Birmingham, UK*

[2] *Department of Public Health, Heart of Birmingham Teaching PCT, Birmingham, UK*

[3] *Association for Scientific Research in Multiple Births, Ghent, Belgium*

[4] *Department of Paediatrics, University of Birmingham, UK*

[5] *Department of Human Genetics, University Hospital Gasthuisberg, Katholieke Universiteit Leuven, Belgium*

[6] *Department of Psychiatry and Neuropsychology, School for Mental Health and Neuroscience, Maastricht University Medical Centre, The Netherlands*

[7] *Department of Complex Genetics, Cluster of Genetics and Cell Biology, Nutrition and Toxicology Research Institute, Maastricht University Medical Centre, The Netherlands*

Background: Previous work suggests that a mixture of genetic and environmental factors impacts on cognitive development. These must include those operating in the intrauterine environment. Low birth weight is linked to cognitive deficits and lower IQ later in life. However, specific intrauterine factors of potential importance for cognitive development, such as chorionicity and umbilical cord abnormalities have not yet been investigated. *Methods:* 663 twin pairs, aged 7–15 years completed the WISC-R and scores were available for Performance, Verbal and Total IQ measures. The intrauterine factors used in the analysis were birth weights, placental weight and morphology, cord knots, cord length and cord insertion. Random effects regression models were used to compute expected IQ scores for the varying levels of the intrauterine markers adjusting for gender and gestational age. The genetic and environmental influences on IQ were estimated and the association between IQ and the intrauterine factors was examined in a bivariate twin analysis. *Results:* Twins with lower birth weight had lower IQ scores ($p <$ 0.01), as did twins with false knots ($p =$ 0.02). High heritability estimates ranging from 70 to 82% were found for total, performance and verbal IQ. The bivariate analysis suggested that the etiology of IQ is largely distinct from that of birth weight and cord knots, and that non shared environment may influence these relationships. No significant relationship was found between the remaining intrauterine factors and IQ scores. *Conclusion:* Non shared prenatal influences may explain the relationship between the intrauterine environment and IQ.

CAN EPIGENETICS BE USED TO IDENTIFY GENES INVOLVED IN EYE DISEASE?

P. Baird

University of Melbourne, Australia

Over 600 twin pairs were collected as part of the genes in myopia (GEM) study and of these a number of monozygotic (MZ) twins were identified as discordant for eye phenotypes. Birthweight has also been associated with various eye diseases and we wished to assess whether epigenetic changes might play a role in explaining this MZ discordance. As a feasibility study we identified a total of 16 (MZ) monozygotic twin pairs from our cohort who were discordant for birthweight (> 0.5kg) but had no presenting medical conditions and were not discordant for eye disease. The sample consisted of 3 male and 13 female MZ twins with an age range of 18 to 82.5 years (mean 50.2, median 54.2) at examination. DNA from each individual was run in duplicate across Human Methylation 27 (Illumina) arrays, each comprising 2CpG islands over approximately 12,000 genes. All data were assessed for quality control and resulted in the removal of 2 twin pairs. Two twin pairs produced no significant difference in methylation in genes between the pair and 3 twin pairs resulted in the majority of assessed genes as showing significant methylation differences between the pair. These twin pairs were removed from further analysis to leave a total of 9 twin pairs. Significant differences in methylation status were detected for between 7–812 genes depending on the twin pair. No one significant gene difference was detected in methylation in all twin pairs. However, a total of 340 significantly methylated genes appeared in at least 2 twin pairs, with 8 of these genes appearing in at least 4 twin pairs and only one gene in 5 (55%) twin pairs. These genes included several receptors including the insulin receptor and angiotensin receptor as well as a cell adhesion gene that warrant further follow up. These findings indicate that methylation patterns do show significant differences between identical twins and that extensive bioinformatic follow up is required to explain the mechanism of action of these genes before their role can be confirmed in explaining this discordance.

SOCIAL–ECONOMIC STATUS AND DIMENSIONS OF FAMILY ENVIRONMENT AS PERCEIVED BY PARENTS OF RUSSIAN ADOLESCENT TWINS

P. Barsky[1], S. Malykh[1], E. Gindina[1], M. Lobaskova[2]

[1] *Laboratory of Developmental Behavior Genetics, Psychological Institute of Russian Academy of Education, Moscow, Russia*

[2] *Udmurtia State University, Izhevsk, Russia*

The aim of our study was to investigate the perceptions of family environment in parents of adolescent twin children, as well as correlations between the social-economic status (SES) and dimensions of psychological climate in the family. The Russian version of the

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

Family Environment Scale (FES: Moos & Moos, 1981) questionnaire was administered to parents (mothers, in most of the cases) of male and female monozygotic and dizygotic twins, who were living in Russia (the children were aged from 12 to 17 years old); data from 242 families were collected. Socio-economic status was assessed by means of a custom developed short questionnaire (questions were directed at the presence of material conveniences at the family). Eighty three percent of families have reported having moderate to severe economical grievances, but only 22% reported that their overall economical condition is worse than the average family has. The obtained scores of parents of twins on FES questionnaire scales were factor-analyzed using Principal Components method with Varimax rotation. Five dimensions of family environment were derived as the result of factor analysis: (1) Achievement-Control-Expressiveness; (2) Cohesion-Organization; (3) Intellectual-Cultural and Active-Recreational orientations; (4) Moral-Conflict; (5) Independence. The only significant correlation between FES and SES was small, but significant positive correlation of 'Active-Recreational and Intellectual-Cultural orientation' dimension and overall level of SES. No significant effects of children's gender and zygosity were found. Small negative effects of children's age at SES and family's 'Cohesiveness' were found. The results of our study indirectly support the 'equal environments assumption' for the currently assessed dimensions of family environment and SES, but the roughness of assessment should be taken into account when interpreting the data.

SUBJECTIVE WELLBEING AND RELIGION: INVESTIGATING EFFECTS OF GENE BY ENVIRONMENT INTERACTION

M. Bartels[1,2], G. A. H. M. Willemsen[1], N. van der Aa[1,2], T. C. E. M. van Beijsterveldt[1], D. I. Boomsma[1]

[1] *Department of Biological Psychology, VU University, Amsterdam, the Netherlands*

[2] *EMGO+ Institute, VU University Medical Center, Amsterdam, the Netherlands*

Pursuing happiness is a goal for nearly every human being and striving for happiness is one of the major life purposes. In a large sample of adolescent twins and their siblings happiness has been found to be part of the overall construct of subjective wellbeing (SWB). Individual differences in Subjective Wellbeing are partly accounted for by genetic factors. Half of this sample of adolescent twins and siblings (total sample is 7952 individuals, 6255 twins and 1697 siblings) reported that they were raised religiously. Over 90% of individuals without a religious upbringing reported no current religious affiliation, compared to about 20% of the individuals with a religious upbringing. In the current study we investigate the effects of a religious upbringing and current religious affiliation on subjective wellbeing and test for the moderating effects of religion on the heritability of SWB. Previous studies demonstrated how the relative magnitude of genetic influences on a behavioral outcome may be attenuated in environments in which choices are more limited by external factors compared with environments in which individuals have more personal choices, which would be resulting in lower heritability estimates in the religious group versus the non-religious groups. Preliminary twin correlations, though, suggest the opposite by indicating a higher heritability of SWB in the religious group versus the non-religious group. Furthermore, these preliminary analyses indicate that individuals that are religious but not currently active in church activities (28% of the total sample) are happier than non-religious individuals and individuals that are religious and active in church activities.

TWIN METHYLATION DIFFERENCES AT THE SEQUENCE LEVEL

J. T. Bell[1,2], C. L. Hyde[3], J. M. Harris[1], G. J. Brock[3], F. M. K. Williams[1], W. Jun[4], G. Burgess[5], S. John[3], T. Spector[1]

[1] *Department of Twin Research and Genetic Epidemiology, Kings' College London, London, UK*

[2] *Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford, UK*

[3] *Pfizer Global Research & Development, Groton, CT, US*

[4] *Beijing Genomics Institute BGI, Chinese Academy of Sciences CAS, Beijing, China*

[5] *Pfizer Global Research and Development, Sandwich Laboratories, Sandwich, U.K*

Monozygotic (MZ) twins discordant for complex trait phenotypes allow for the dissection of non-genetic risk factors to the phenotype. Recent studies of discordant MZ twins have identified epigenetic factors as a susceptibility component in complex phenotypes, for example, in systemic lupus erythematosus. DNA methylation is a recognized key epigenetic mechanism involved in gene regulation and disease. We examine DNA methylation profiles in 25 MZ twin-pairs that were discordant for pain sensitivity. Pain sensitivity was assessed using heat-shock pain temperature scores and co-twin discordance was based on a set of threshold criteria. DNA methylation profiles from whole blood samples were obtained using high-resolution genome-wide MeDIP-sequencing data. Preliminary analyses examined the distribution of DNA methylation patterns genome-wide. We compared methylation profiles in gene-poor to gene-rich regions, including in the vicinity of promoters, gene-body, and 3' UTR regions, and in relation to functionally significant or conserved sequence motifs. To assess the contribution of DNA methylation to pain sensitivity we first examined power to detect differentially methylated regions (DMRs) that contribute to pain sensitivity differences. We will present preliminary results assessing the role that epigenetic mechanisms play in complex trait phenotypes.

DEPRESSION IN ADOLESCENTS: TWIN STUDY ON RUSSIAN ADOLESCENT SAMPLE

A. P. Belova and S. B. Malykh

Laboratory of Developmental Behavioral Henetics, Psychological Institute of Russian Academy of Education, Moscow, Russia

In order to find out whether there is any genetic contribution for liability to depressiveness in adolescents, a twin study in Moscow, Bishkek and Izhevsk was conducted. 223 twin pairs and their mothers participated in the survey. Among them, there was 72 MZ twin pairs and 124 DZ twin pairs aged between 13 and 17. All adolescents answered the Children Depression Inventory (CDI by M. Kovacs) questionnaire by themselves, in a set of other emotion-related questionnaires. Parents also assessed similar depressiveness symptoms in their children. Twin zygosity was defined by means of questionnaire filled by twins' mothers. As a result we have found out that the genetic contribution was higher among boys and elder teenagers (15–17 years), while for girls and younger teenagers (13–14 years) genetic influence was not as pronounced.

NATIONWIDE COMPARISON OF PERINATAL OUTCOME OF INDUCED VERSUS NATURAL TWINS IN THE NETHERLANDS 2000–2007

A. Bensdorp, C. Hukkelhoven, B. W. Mol, C. B. Lambalk

Department of Obstetrics and Gynaecology, Academic Medical Center AMC, Amsterdam, Perinatal Registration Netherlands (PRN), Utrecht, Division of Reproductive Medicine, VU University, Amsterdam, The Netherlands

Introduction: There are indications that dizgyotic(DZ) multiple pregnancies fare better compared to induced DZ multiples. We aimed to compare pregnancy outcome of natural DZ twins and those after the various ways of fertility treatment. *Material & Methods:* Data were obtained from the Dutch Nationwide Obstetric Registration over the years 2000–2007. We extracted information of primiparous opposite sex twin pair deliveries to warrant dizygosity (>16 wks of gestation) after natural conception or after ovulation induction(OI), after intrauterine insemination (IUI) or after IVF/ICSI. Data were extracted on maternal age at the time of delivery; highest measured

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

diastolic blood pressure measured anywhere during the pregnancy; duration of pregnancy (weeks); mode of presentation and delivery; birthweight, sex, APGAR score, perinatal mortality and maternal postpartum complications. *Results:* The total number of (Boy/girl) deliveries available for the analysis was 9369. There were 3285(52%) births after natural conception, 611(7%) after IUI, 570(6.0%) after OI and 4823(35%) after IVF/ICSI. Maternal ages were slightly higher after IVF and IUI compared to OI and natural conception: 32.5, 32.5, 29,6 and 30.1 years respectively. Hypertension (diastolic pressure > 90mmHG) occurred in 19.9% of the pregnancies after IVF/ICSI, 24.4% after IUI, 23.0% after IO and 24.3% after natural conception. There were 2 maternal mortalities both after natural conception pregnancy. The percentage of mothers with blood loss > 1000ml was 12.8%, 10.8%, 10.4% and 12.6% for IVF/ICSI, IUI, OI and natural conceptions respectively. Perinatal mortality (stillbirth plus mortality within 28 days after birth) was respectively 2.3%, 4.1%, 3.9% and 2.8% after IVF/ICSI, IUI, OI and natural conception. The average birthweight was 2395 588 g per child after IVF/ICSI, 2387 ± 636 g after IUI, 2300 ± 641 g after OI and 2339 ± 629 g after the natural conception. APGAR scores were 9.1, 9.0. 9.0 and 9.1 respectively. *Conclusions:* Our data indicate to an overall slightly higher rate of adverse outcome of perinatal outcome of multiple deliveries but only after IUI or OI and not IVF/ICSI. Compared to natural conception, birthweight and gestational age were not lower after any mode of assisted conception. We confirm our remarkable previous contra-intuitive finding that women undergoing IVF/ICSI have a lower risk for developing hypertensive disorders during pregnancy.

AN INVESTIGATION INTO THE RELATIONSHIP BETWEEN SOFT TISSUE BODY COMPOSITION AND BONE MINERAL DENSITY IN A YOUNG ADULT TWIN SAMPLE

L. H. Bogl[1], A. Latvala[2], J. Kaprio[1,2,3], A. Rissanen[4], K. H. Pietiläinen[1,3,5]

[1] *The Finnish Twin Cohort Study, Department of Public Health, University of Helsinki, Helsinki, Finland*

[2] *Department of Mental Health and Substance Abuse Services, National Institute for Health and Welfare, Helsinki, Finland*

[3] *Institute for Molecular Medicine, Helsinki, Finland*

[4] *Obesity Research Unit, Department of Psychiatry, Helsinki University Central Hospital, Helsinki, Finland*

[5] *Department of Medicine, Helsinki University Central Hospital, Helsinki, Finland*

The purpose of this study was to investigate the relationship of fat mass (FM) and lean mass (LM) with bone mineral density (BMD) independent of genetic effects and to assess the extent to which genetic and environmental influences explain the associations between these phenotypes. Body composition and BMD were measured at the whole-body and 6 regional sites using dual-energy X-ray absorptiometry in 57 MZ and 92 DZ twin pairs, aged 23–31 years, chosen to represent a wide range of intrapair differences in BMI (0.1 to 15.2 kg/m^2). To adjust for height, LM and FM were divided by height squared in genetic model fitting. In multiple linear regression analysis adjusted for height, intrapair differences in both, FM and LM were independently associated with intrapair differences in BMD at most skeletal sites. At the whole-body, LM was a significantly stronger predictor ($p < .01$) of BMD than FM in both zygosity groups. Additive genetic factors explained 86% (95% CI: 79–91%), 78% (95% CI: 66–86%) and 69% (95% CI: 45–76%) of the variation in whole-body BMD, LM and FM, respectively. Additive genetic factors also accounted for 66–84% of the covariance between LM and BMD and for 39–70% of the covariance between FM and BMD depending on the skeletal site. The genetic correlation between LM and whole-body BMD ($r_g = .44$) was greater than that of FM and whole-body BMD ($r_g = .23$). In conclusion, our data indicate that peak BMD is influenced by acquired body weight as well as genetic factors. In addition, LM and BMD may have more genes in common than do FM and BMD in young adulthood.

COMPARISON OF NATURAL AND DZ TWINS IN THE DUTCH TWIN REGISTRY: A DEVELOPMENTAL STUDY

D. I. Boomsma

VU University, Amsterdam, The Netherlands

Since 1987 the Netherlands Twin Register (NTR) recruits newborn twins shortly after birth. The development of these twins is followed in longitudinal survey studies. Approximately every 2 years parents complete mailed questionnaires which track growth, motor, behavioral and emotional development of the children. From age 7 years onwards, surveys are also sent to the teachers of the twins. At age 12 years data on standardized tests for educational attainment are collected. From age 14 years onwards, the twins (and their sibs) complete self-rating questionnaires. Over the period of data collection, we see a substantial increase in the number of twins born after IVF: in 1990 less than 6% of twin pairs who registered with the NTR were born after IVF, in 2005 this was almost 22% and since then seems to decrease slightly. In this presentation we will compare the development of IVF twins to matched control twins. We look at growth, the age at which the twins reach specific milestones, at the prevalence of Internalizing and Externalizing problems and at educational attainment.

A TWIN YEAR IN REVIEW: BEHAVIOR AND PSYCHIATRY

D. I. Boomsma

VU University, Amsterdam, The Netherlands

There are few aspects of human behavior that have not been investigated using the classical twin design. I will review studies from psychology, behavioral sciences and psychiatry. The past few years saw studies of voting behavior (Hatemi et al., 2007), willingness to take economic risks (Zhong, et al., 2009), truancy in high school (van der Aa et al., 2009) outcomes in the classic trust game (Cesarini et al., 2008), humor (Vernon et al., 2008), self-reported G-spot in women (Burri et al. 2009), and sexual performance during first intercourse in men (Santtila et al., 2009). Additionally, the trend to investigate aspects of human behavior in increasingly large samples of twins and their family members is continuing and shows promise for the detection of non-additive genetic effects, genotype-by-sex and by-age interactions. In psychiatry, childhood psychopathology is studied in longitudinal samples, there is an increasing interest in personality disorders such as borderline personality disorder (Aggen et al., 2009 Distel et al., 2009), obsessive–compulsive disorder and in eating disorders for example. Over the past few years, we also see an increase in the number of studies that combine imaging approaches with clever selection of twins concordant or discordant for major psychiatric disorders. To conclude my talk, I will discuss whether there is room for the classical twin design in the current era of molecular genetic studies. The answer is yes: the classical twin design holds promises for the study of gene expression, epigenetics, metabolomic and proteomic projects and gene-environment interaction. The study of special groups, such as monozygotic discordant twin pairs, can be a very powerful approach to search for causal genes underlying monogenetic and complex disorders.

GENETIC ANALYSIS OF LONGITUDINALLY MEASURED IQ, EDUCATIONAL ATTAINMENT AND EDUCATIONAL LEVEL IN DUTCH TWIN-SIB SAMPLES

D. I. Boomsma[1], C. E.M. van Beijsterveldt[1], I. van Soelen[1], S. Franić[1], C.V. Dolan[2], D. Borsboom[2], M. Bartels[1]

[1] *VU University Amsterdam, The Netherlands*

[2] *University of Amsterdam, The Netherlands*

There is a substantial interest in the genes that underlie the large heritability of IQ. However, traditional psychometric tests are time-consuming and often require extensive training in administration and scoring. Here we explore to what extent IQ during childhood and adolescence is predicted from educational attainment as measured by standardized tests at age 12 years (CITO scores) and educational level during high school (3 levels). A previous study in a smaller

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

sample and without information on educational level revealed that there is overlap ranges between CITO and IQ assessed at age 5, 7, 10, and 12, with the correlations increasing as children get older[1]. IQ data are available from different studies that examined children at ages 5 through 18 years who took part in studies of the Netherlands Twin Register at the VU University Amsterdam[2] and consist of longitudinal measures of psychometric IQ in four groups of twins and include a high scoring group (N_1 = 1951, N_2 = 587, N_3 = 1080, N_4 = 852), their siblings (N_1 = 95, N_2 = 260, N_3 = 53) and parents (N_2 = 350) at twin's ages 5, 7, 9, 10, 12, 15, 17, and 18 years. Phenotypic correlations between IQ measures and educational attainment and educational level are substantial and all measures show moderate (IQ in early childhood) to substantial heritability (all other measures). If these associations are mediated by common genetic factors, this suggests that GWA studies of educational level and attainment may enlighten us about the genes for IQ.

1. Bartels, M., Rietveld, M.J.H., Van Baal, G.C.M., Boomsma, D.I. (2002) Heritability of Educational Achievement in 12-year-olds and the overlap with Cognitive Abilities. *Twin Research*, 5(6), 544–554.

2. Boomsma DI, de Geus EJ, Vink JM, Stubbe JH, Distel MA, Hottenga JJ, Posthuma D, van Beijsterveldt TC, Hudziak JJ, Bartels M, Willemsen G. Netherlands Twin Register: from twins to twin families. Twin Res Hum Genet. 9(6):849–57, 2006.

GENETIC AND ENVIRONMENTAL COMPONENTS OF POSTNATAL WEIGHT GAIN IN THE FIRST MONTH OF LIFE

S. Brescianini[1], S. Giampietro[2], R. Cotichini[1], C. Fagnani[1], R. Lucchini[2], M. De Curtis[2]

[1] *Centro Nazionale di Epidemiologia, Sorveglianza e Promozione della Salute, Istituto Superiore di Sanità, Rome, Italy*

[2] *Dipartimento di Pediatria, 'Sapienza' Università di Roma, Rome, Italy*

Postnatal nutrition and subsequent weight gain or loss in the neonatal period is likely regulated by both the environment and the genetic background. Comparing monozygotic (MZ; genetically identical) and dizygotic (DZ; genetically similar) twins allows us to estimate the heritability of postnatal weight gain. This study selected a very homogenous set of MZ twins, DZ twins and a group of singletons paired by gestational age and birthweight that met the following inclusion criteria: gestational age between 30 and 36 weeks, birthweight between 1250 and 2200 grams, and length of stay (LOS) > 12 days. For twins, we excluded opposite sex pairs and pairs that differed by more than 20% in terms of birthweight. The outcome measure of this study is daily weight gain expressed in grams per kilogram per day (g/kg/day) during the period between the nadir day and the day of discharge. The average difference between members of each pair was computed in the three groups of newborns and heritability was estimated using twin data only. The within pair differences of the outcome measure are lower for MZ twins that for DZ twins and singletons suggesting a high genetic component. The total variance of the phenotype under study is explained by two sources of variation, additive genetic (A) and unique environment (E) components (A = 91% (95% CI: 78%–96%) and E = 9% (95% CI: 4%–22%)). This high heritability estimate could suggest using this set of criteria to identify genes that regulate postnatal weight gain or loss.

BUILDING A UNIQUE U.S. TWIN REGISTRY: HOW I LOST MY DRIVERS LICENSE AND FOUNDED A TWIN REGISTRY

D. Buchwald[1], E. Strachan[2], N. Afari[3], C. Hunt[1], J. Goldberg[4]

[1] *Center for Clinical and Epidemiologic Research and Department of Medicine, University of Washington, Seattle, Washington, USA*

[2] *Center for Clinical and Epidemiologic Research and Department of Psychiatry, University of Washington, Seattle, Washington, USA*

[3] *Department of Psychiatry, University of California, San Diego, California, USA*

[4] *Center for Clinical and Epidemiologic Research and Department of Epidemiology, University of Washington and Vietnam Era Twin Registry, Seattle VA Epidemiologic Research and Information Center, Seattle, Washington, USA*

The University of Washington Twin Registry (UWTR) is a community-based registry of twins established in 1999. Twins are identified by the Washington State Department of Licensing when they apply for driver's licenses and identification cards and are then disclosed to the UWTR for recruitment into the registry. The recruitment process is ongoing and as of February 2010, 3,345 adult twin pairs have enrolled in the registry. The UWTR has already worked with numerous investigators, both national and international, on diverse research topics including pain, inflammation, immunity, obesity, eating behaviors, sleep behaviors, and DNA structural variations. In October 2009, the UWTR was awarded a Grant Opportunities award from the NIH to support a massive expansion of the Registry. Recruitment efforts are expected to quadruple and we predict membership in the UWTR will grow beyond 10,000 twin pairs over the next three years. In conjunction with these recruitment efforts, the UWTR has launched a registry-wide initiative that will collect biological samples from 6,000 twin pairs. In addition, the UWTR is embarking upon two exciting Scientific Integration Projects that are part of the Grant Opportunities award. Project 1 examines how the built environment influences activity and eating behaviors in twins. Project 2 focuses on deep phenotyping pain perception using state-of-the-art psycho-physiological measures to examine the link between pain perception and genes thought to correlate with pain conditions. Together these efforts will produce a terrific new resource for twin research in the United States.

GENETIC AND ENVIRONMENTAL INFLUENCES ON FEMALE SEXUAL DYSFUNCTIONS: RESULTS OF A GENOME-WIDE ASSOCIATION STUDY IN AN UNSELECTED UK TWIN POPULATION

A. Burri, L. Cherkas, T. Spector

Twin Research and Genetic Epidemiology, King's College London, UK

Background: Previous studies have shown moderate heritability for female sexual dysfunctions (FSD) and identified correlated genetic and non-shared environmental influences that account for the comorbidity between the subdomains of FSD. So far, however, no study has tried to identify potential genetic variants that are unique or common to the different domains of sexual dysfunction. *Methods:* The twin sample was drawn from the TwinsUK registry and consisted of 1489 female twins (aged 18-85 years). For multidimensional assessment of FSD over the past 4 weeks the widely applied Female Sexual Function Index (FSFI) was used. In addition, a modified version allowing assessment of sexual problems over lifetime was sent to the twins. *Results:* In line with recent studies in genetic epidemiology our model fitting analyses found moderate heritabilities for FSD, ranging from 18% to 34% for both points of time. No evidence for significant shared environmental influences were found, whereas phenotypic variance in all domains was best explained by unique environmental effects. Given the significant additive genetic effects underlying FSD, we performed genome-wide association scans (GWAS) to try and ascertain genes that might have an influence on FSD. Results of the GWAS will be presented. *Discussion and Conclusion:* Results of univariate heritability analysis suggest that additive genetic effects underlie the variation in FSD providing a clear rationale for more genetic research in the field of FSD.

PILOT STUDY COMPARING TWO EQUIPMENTS FOR ASSESSING BODY FAT% AND TOTAL BODY WATER AS PART OF THE RESEARCH-PROGRAM IN GEMINAKAR II

H. Cederholm[1], C. Dalgård[2], K. Kyvik[3]

[1] *Institute of Regional Health Services Research, University of Southern Denmark, Denmark*

[2] *Institute of Environmental Research, University of Southern Denmark, Denmark*

[3] *Institute of Regional Health Services Research, University of Southern Denmark, Denmark*

GEMINAKAR II (GK II) is a longitudinal twin study among 756 twin pairs within the population-based Danish Twin Registry recruited at age 18-67 years in 1997 to 2000 with the purpose to investigate the importance of genes, family and individual environment for the development of insulin resistance, abdominal adiposity and cardiovascular risk factors. This twin-cohort is now invited to participate in a follow-up study. Interviews, physical examinations including various anthropometric measurements and blood sampling are taking place in a mobile examination center. Accurate methods

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

for assessing body composition are important in studies investigating metabolic and cardiovascular risk factors. In epidemiologic studies there may be some restraints regarding equipments. We therefore compared measures of body composition by using bioelectrical impedance analysis by two different equipments that vary in user-friendliness and price. Body fat% and total body water (TBW) were measured using Bodystat 1500MDD Whole Body analysis (Bodystat) and Tanita BC545 Segmental Body Composition Analyser (Tanita). The pilot study includes preliminary data from 36 twins, 18 male and 18 female, aged 30 to 67 years. Body mass index (BMI) was significantly lower in women compared with men (22.4 vs. 25.6, $p = .0047$). Our results demonstrate strong correlation between Bodystat and Tanita derived mean body fat% and TBW ($r = 0.93$, $p < .001$, and $r = 0.96$, $p < .001$, respectively). However, Tanita overestimated body fat% and underestimated TBW compared to Bodystat in general and the difference in body fat% increased with increasing BMI in men. Our pilot study shows that the more user-friendly and inexpensive equipment, the Tanita, measures higher body fat% and lower TBW compared to Bodystat. Furthermore, this difference may be more pronounced in obese men. This should be taken into account when comparing measures of body fat% across studies. However, the difference may be a result of different equations used to calculate body fat% from impedance.

GROWING PAINS SHARES GENETIC DETERMINANTS WITH THE RESTLESS LEGS SYNDROME

D. Champion, C. Flynn, A. Taylor, T. Jaaniste

Department of Anaesthesia and Pain Medicine, Sydney Children`s Hospital, Randwick, NSW, and Medical School, University of New South Wales, Kensington, Australia

Growing pains (GP), a prevalent idiopathic disorder of early childhood, is familial but there are no published twin and family or genetic studies.Our recent community study has added to the evidence that there is individual and familial association with the primary restless legs syndrome (RLS) which is genetically determined. GP and RLS share several clinical characteristics but differ in age distribution and in the urge to move the legs for brief relief of sensory symptoms in the latter. The primary aims of this study were to investigate the genetic influence on GP and to explore the individual and familial relationships between GP and RLS. Through the Australian Twin Registry (ATR), we identified 168 twin pairs in the age range 3–16 with potential GP in at least one individual. Standard questionnaires were mailed to each family addressing zygosity, GP, adult and pediatric RLS, and 101 families (60%) responded. The final data set meeting criteria for analysis included 88 twin families. In 34 monozygous (MZ) twin pairs, 25 were concordant for GP (74%), and the casewise concordance rate was 0.85. In 54 dizygous (DZ) twin pairs, 12 were concordant for GP (22%) and the casewise concordance was 0.36. The concordance ratio MZ/DZ was 3.3. Chi squared (corrected) analysis for 2 independent binary samples MZ and DZ was 20.5, P less than 0.001. Mothers' history of GP was 50% and fathers' was 41%, while sibling (DZ co-twin and all siblings) life prevalence was 33%. Of individual twins with GP, 23.2% also met criteria for RLS. Of the individual twins without GP, 7.8% had RLS. Parents with RLS: 39.1% of mothers and 24.2% of fathers. Pedigree diagrams displayed the remarkably close associations between GP and RLS including 2 sets of female MZ twins one with GP and the other with RLS. We concluded that GP is genetically influenced and shares genetic determinants with RLS.

Acknowledgements: The ATR, Prof John Hopper, and Prof Sam Berkovic for facilitation and for essential guidance.

CHROMOSOMAL POLYMORPHIC VARIATIONS HELP DETERMINE ZYGOSITY IN SAME SEX TWIN PREGNANCIES

S.-D. Chang[1,2], Y.-L. Chang[3]

[1] *Department of Obstetrics and Gynecology Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Tao-Yuan, Taiwan*

[2] *Department of Pediatrics, Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Tao-Yuan, Taiwan*

[3] *Department of Obstetrics and Gynecology, Chang Gung Memorial Hospital, Linkou Medical Center, 5, Fu-Shin Street, Kweishan, Taoyuan, Taiwan*

Chromosomal variable features such as variations in the size of (peri-centromeric) heterochromatin of chromosomes 1, 9, 16, and Y and the nucleolar organization region (NOR) of acrocentric chromosomes and a small pericentric inversion of chromosome 9,inv(9) (p12q13) are known to occur in the general population, as harmless normal variants. When encountered in genetic amniocentesis for twins, these chromosomal variants may play a role in determining their zygosity. In an eight year period from January 2002 to the end of 2009, genetic amniocentesis-fetal karyotyping had been performed on 246 sets of twins with indications varying from advanced maternal age, abnormal fetal aneuploidy screening, abnormal fetal structural findings by ultrasound, to parental anxiety. Amniotic fluid was cultured followed by conventional chromosomal analysis in the cytogenetic laboratory of the Ob-Gyne department. 21 sets of twins (8.5%) were found to possess polymorphism markers in their karyotyping. In five sets, both twins had the same polymorphic variations. In the remaining 16 twin sets where polymorphism occurred in only one twin, seven were of the same sex with their variable features encompassing increased short arm stalk length (13pstk+ and 22pstk+), double satellites (14pss), increase in heterochromatin length (1qh+ and 16qh+), and two cases of inv(9). During early twin gestation, chorionicity determination by ultrasound finding of peak or T sign is vital in counseling the patients for their perinatal outcomes. For those escaping chorionicity diagnosis and moving into the 2nd trimester, amniocentesis findings of polymorphism markers in one co-twin of same sex twin sets is very useful in telling their zygosity, as in our seven cases. For example, due to the presence of the chromosomal variable feature in only one twin, they must be dizygotic twins, hence dichorionic; a very valuable piece of information for future obstetric management.

PLACENTAL GENES EXPRESSION LEVEL IN INTRAUTERINE GROWTH RESTRICTED FETUSES: USING A MONOZYGOTIC TWIN MODEL – IMPLICATION FOR THE PLACENTAL ROLE OF 'FETAL PROGRAMMING' FOR ADULT DISEASE

Yao-Lung Chang[1], Chuan-Chi Kao[1], Tzu-Hao Wang[2]

[1] *Department of Obstetrics and Gynecology, Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Tao-Yuan, Taiwan*

[2] *Department of Obstetrics and Gynecology, Chang Gung Memorial Hospital, Linkou Medical Center, Kweishan*

Purpose: This study was designed to examine a prospective series of MC twins with selective intrauterine growth restriction (sIUGR), in order to investigate the global placental gene expression profile between the IUGR and appropriate for gestational age (AGA) fetuses. *Materials and methods:* The placentas were collected prospectively from women who gave birth to live-born MC twin pregnancies at the Chang Gung Memorial hospital, two to three pieces of placenta about 0.5cm^3 from each placenta territory before cutting the placenta; about midway from vascular equator and individual cord insertion, at the middle layer of placenta midway between maternal and fetal surfaces. Gene expression profiles in placenta were analyzed with the human U133A GeneChip (Affymetrix, Santa Clara, CA, http://www.affymetrix.com), and the manufacturer's protocol was strictly followed. *Results:* We list the 20 most up-regulated (fold-change) and down-regulated genes in the sIUGR twin placenta territory comparing to the AGA placenta territory in MC twin pregnancies with sIUGR. *Conclusion:* In IUGR caused by hypoperfusion due to small placenta, the placenta gene expression levels could be changed in human pregnancy. The different placenta leptin, 11-HSD2 and Glut3 expression levels between sIUGR and

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

AGA placenta territory in the two genetic identical twins in MC twin pregnancy could give us a clue how the role of placenta works in the fetal programming for adult disease.

CLUES TO GENETIC SUSCEPTIBILITY TO BREAST CANCER: A STUDY OF BREAST CANCER CONCORDANT TWIN PAIRS

S. Cho, T. Mack, A. Hamilton
Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA

A positive family history, present in about 30% of breast cancer cases, has been shown to double a woman's risk of breast cancer. The genetic factors responsible are largely unknown, although the relatively high penetrant genes BRCA1/2 may account for 3%. Genes of lower penetrance may also affect breast cancer risk, and a likely group of such genes are those that regulate the production, intracellular transport, and metabolism of estrogen. Previous studies of these susceptibility genes have not been conducted with women with high familial risk. This study included identical twins with differing genetic risks (i.e. concordant for breast cancer pairs vs. discordant pairs) as well as unaffected controls. DNA samples were obtained from 136 concordant pairs, 152 discordant pairs and 137 controls. DNA has been extracted and stored for conducting additional genetic testing using these samples. A total of 368 single nucleotide polymorphisms (SNPs) have been assayed along 16 genes using the Illumina System. The genes included AIB1, COMT, COX2, CYP17, CYP19, CYP1A1, CYP3A4, ESR1, ESR2, GPR54, GSTP1, IGF1, IGFBP3, P160, and PR. The SNPs selected were haplotype tagging SNPs that were selected to cover the variation across the entire length of each of the genes. Of those SNPs, we will present data on associations and interactions between polymorphisms in CYP17 and COMT and risk of breast cancer. Previous studies have linked the variants of these estrogen metabolism genes with breast cancer. This study demonstrates important methods of using twins to identify specific genes related to development of breast cancer.

RECENT ADVANCES OF THE PET AND FMRI AND THEIR APPLICATIONS TO THE NEUROIMAGING STUDIES OF HUMAN BEHAVIORS AND DISEASES

Z.-H. Cho[1]
[1] *Neuroscience Research Institute, Gachon University of Medicine and Science, Incheon, Korea*

Along with the increasing demand for molecular imaging in humans, PET has become an indispensible imaging tool for the diagnosis of metabolic abnormalities as well as brain functional studies based on molecular dynamics. We have also witnessed great progresses in ultra high resolution MR imaging using UHF MRI, such as 7.0T. Based on these two systems, a PET-MRI system has been developed using an ultra high resolution PET, HRRT (High Resolution Research Tomography), and an Ultra-High Field MRI 7.0T, creating a mode of molecular fusion imaging at the highest level of resolution and sensitivities of currently available technology. Recent results obtained from the new PET-MRI fusion imaging system will be demonstrated and future perspectives of this new PET-MRI will be discussed.

A LONGITUDINAL STUDY OF EPIGENETIC VARIATION IN TWINS

C. Chung, Y. Wong, A. Caspi, B. Williams, I. W. Craig, R. Houts, A. Ambler, T. E. Moffitt, J. Mill
Institute of Psychiatry, King's College London, UK

DNA methylation is a key epigenetic mechanism involved in the developmental regulation of gene expression. Alterations in DNA methylation are established contributors to inter-individual phenotypic variation and have been associated with disease susceptibility. The degree to which changes in loci-specific DNA methylation are under the influence of heritable and environmental factors is unknown. In this study, we quantitatively measured DNA methylation across the promoter regions of the dopamine receptor 4 gene (DRD4), the serotonin transporter gene (SLC6A4/SERT) and the monoamine oxidase A gene (MAOA) using DNA sampled at both ages 5 and 10 years in 46 MZ twin-pairs and 45 DZ twin-pairs (total n = 182). We observed high levels of MZ twin discordance in DNA methylation and dynamic changes in individual DNA methylation across all three regions between ages 5 and 10 years. Variation in DRD4 DNA methylation was mostly attributable to environmental factors that were shared among children growing up in the same family whilst inter-individual differences in SERT DNA methylation were primarily attributable to unique environmental factors experienced by each child in the family, and not to shared events or heritable factors. We observed a more complex pattern of results for the MAOA amplicon with noticeable sex differences in twin concordance at both ages and for change over time, as expected for a gene mediated by X-inactivation. Our longitudinal-developmental study suggests that DNA methylation differences are apparent already in early childhood and there are DNA methylation differences between genetically identical individuals (i.e. MZ twins). Moreover, environmental influences are important factors accounting for interindividual DNA methylation differences and individual differences in methylation over time are not stable. While these findings confirm the utility of DNA methylation as a biomarker of environmental influences, they also identify new and important concerns about using cross-sectional approaches to studying and drawing inferences in epigenomics.

TEACHER EFFECTS IN EARLY LITERACY DEVELOPMENT: EVIDENCE FROM A STUDY OF TWINS

W. Coventry
University of New England, Australia

It is often assumed that differences in teacher characteristics are a major source of variability in children's educational achievements. We examine this assumption for early literacy achievement by calculating the correlations between pairs of twin children who either shared or did not share a teacher in kindergarten, Grade 1, and Grade 2. Teacher effects — or, more strictly, classroom effects — would show up as higher correlations for same-class than for different-class twin pairs. Same-class correlations were generally higher than different-class correlations, though not significantly so on most occasions. On the basis of the results, we estimate that the maximum variance accounted for by being assigned to the same or different classrooms is 8%. This is an upper-bound figure for a teacher effect because factors other than teachers may contribute to variation attributable to classroom assignment. We discuss the limitations of the study and draw out some of its educational implications.

DNA METHYLATION ANALYSIS IN MULTIPLE TISSUES FROM TWIN PAIRS AT BIRTH REVEALS BOTH GENETIC AND *IN UTERO* ENVIRONMENTAL/STOCHASTIC COMPONENTS TO HUMAN NEONATAL EPIGENOME ESTABLISHMENT

J. M. Craig[1,3], M. Ollikainen[1,3], K. R. Smith[2], E. J. Joo[1,3], H. K. Ng[1,3], R. Andronikos[1,3], B. Novakovic[1,3], N. K. Abdul Aziz[1,3], J. C. Carlin[2,3], R. Morley[1], R. Saffery[1,3]
[1] *Developmental Epigenetics, Murdoch Childrens Research Institute, Royal Children's Hospital, Melbourne, Australia*
[2] *Clinical Epidemiology and Biostatistics Unit, Murdoch Childrens Research Institute, Royal Children's Hospital, Melbourne, Australia*
[3] *Department of Paediatrics, University of Melbourne, Parkville, Victoria, Australia*

We propose that the human epigenome is in constant flux from conception to death, due to both stochastic and environmental factors. This hypothesis is testable with monozygotic (MZ) twins and may explain the incomplete penetrance and variation in age at onset and severity of diseases observed between MZ siblings. Genomic imprinting is an epigenetic phenomenon that inactivates one allele of a gene by methylation of CpG sites in a parent-of-origin-dependent manner. Imprints are established in the germline, are propagated stably during development, and may be especially sensitive to envi-

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

ronmental factors. Differential methylation of imprinting control regions (ICRs) is involved in the regulation of the transcription of their target genes. There is evidence that MZ twins can have different epigenetic marks but at present it is unclear when such differences first arise and how prevalent they are across different tissues. In order to address this, we examined methylation of four differentially methylated regions (associated with IGF2/H19 locus) in multiple birth tissues derived from 91 twin pairs: 56 monozygotic and 35 dizygotic. Tissues included cord blood-derived mononuclear cells and granulocytes, human umbilical vein endothelial cells, buccal epithelial cells and placental tissue. This represents two embryonic germ layers and extra embryonic tissue. Considerable variation in methylation was observed between tissues in all individuals and between unrelated individuals in specific tissues. Most interestingly, methylation discordance was also present in individual tissues within all twin pairs with dizygotic (DZ) twins showing greater variability than monozygotic (MZ) pairs. These data highlight the contribution of both *in utero* environmental exposures and underlying genetic factors to the establishment of the neonatal epigenome, and confirm the *in utero* period as a sensitive time for the establishment of epigenetic variability in humans. This has implications for the effects of maternal environment on the development of the newborn epigenome and supports an epigenetic mechanism for the previously described phenomenon of 'fetal programming' of disease risk in humans.

EPIGENETIC STUDIES OF A NEWBORN TWIN COHORT: INSIGHTS INTO PRENATAL DEVELOPMENT

J.M. Craig[1], R. Andronikos[1], M. Ollikainen[1], E.J. Joo[1], N. Carson[1], X Li[1], B Weinrich[1], L. Gordon[2], R. Morley[1], J Galati[3], K Smith[3], J. Carlin[3], G. Smyth[4], R. Saffery[1]

[1] *Developmental Epigenetics Group, Murdoch Childrens Research Institute (MCRI), Royal Children's Hospital and Department of Paediatrics, University of Melbourne Parkville, Victoria, Australia*

[2] *Bioinformatics Unit, MCRI & Centre for Epidemiology and Biostatistics, MCRI, Victoria, Australia*

[3] *Clinical Epidemiology and Biostatistics Unit, Murdoch Childrens Research Institute (MCRI), Royal Children's Hospital, Victoria, Australia*

[4] *Bioinformatics Division, Walter and Eliza Hall Institute of Medical Research, Parkville, Victoria, Australia*

Recently, there has been an increasing focus on epigenetic differences as a source of phenotypic discordance within monozygotic twin pairs. Information is also emerging about 'epigenetic drift' as exemplified by studies showing greater epigenetic discordance in older twin pairs. Most epigenetic marks are erased from the genome after fertilization, with re-establishment occurring early in embryonic development and evidence suggests that the prenatal period involves epigenetic remodeling on a scale unparalleled postnatally. We hypothesize that that the prenatal epigenetically-driven developmental program is plastic and can vary from the norm via random and intrauterine environment-driven epigenetic change, and as a result, that epigenetic divergence can be identified in MZ twins at birth. This study forms part of a larger study — the Peri/postnatal Epigenetic Twins Study — a newly-established cohort of 250 mothers and twin pairs. This study aims to investigate epigenetic variation and its association with birthweight discordance, maternal nutrition and fetal genotype. The study also involves a longitudinal component, with data and samples from 18 month old twins currently in progress. Results will be presented from the first phase of the study that aims to identify gene expression and methylation differences within newborn monozygotic twin pairs, in multiple cell types, and to relate these to phenotypic discordance. This presentation will focus on results obtained from genome-wide expression and methylation profiling and from the analysis of imprinted genes, both in multiple cell lineages.

PARENTHOOD IN MULTIPLE BIRTH: A REVIEW OF THE LITERATURE

L. M. da Costa Andrade[1], M. M. Ferreira Pereira da Silva Martins[2], M. J. da Costa Marques Martinho[1]

[1] *Professora Adjunta da Escola Superior de Enfermagem do Porto, Portugal*

[2] *Professora Coordenadora da Escola Superior de Enfermagem do Porto, Portugal*

The experience of parenthood in multiple birth has profound implications on family life. Since this experience occurs with the birth of twins, it is a question that we place. In order to improve our understanding on this phenomenon we propose to develop a literature review of empirical results. To achieve this review we intend to follow the phases recommended by the Cochrane. *Question Formulation:* Which moments do families identify as being particularly significant in twin parenthood experience. *Location, selection and critical evaluation of studies:* To this end and as a source of information we used the following electronic databases: EBSCO, SCielo, SAGE, B On, Cinahl, PsycINFO, PubMed. To be able to identify relevant studies we established different criterias which were included in the study and which were based on the reading of the abstract of 73 articles. From these articles we selected four. In a second phase, we proceeded with the reading of the articles that were quoted and as a final result we obtained a total of 20 articles. *Data collection:* in the data collection and in the research method that was used we considered the participants, the fields or variables in the study, and the results obtained in the studies. *Analysis and presentation of the data and interpretation of the data:* based on parity and on the diversity of the results disclosed in the studies. The major implications that parenting has on personal, marriage and family life are evident. The fact that this experience occurs in twin birth implies that it has greater influence in the results of the implications that derive from it. The conclusions of several of these studies also clearly demonstrates the importance that they have in their understanding by the health professionals, and the experience of parenthood in twin pregnancies as a facilitator and promoter of a more effective intervention with twin families.

DO FRUIT AND VEGETABLES MODIFY THE ASSOCIATION BETWEEN OBESITY AND INFLAMMATORY RISK MARKERS OF CARDIOVASCULAR DISEASE? A STUDY IN A HEALTHY DANISH TWIN POPULATION

C. Dalgård[1], A. -L. Hasselbalch[2], T. I. A. Sørensen[2], K. O. Kyvik[3]

[1] *Institute of Public Health, Dept. of Environmental Medicine, University of Southern Denmark, Denmark*

[2] *Institute of Preventive Medicine, Copenhagen University, Denmark*

[3] *Institute of Regional Health Research, and The Danish Twin Registry, Institute of Public Health, Dept. of Epidemiology, University of Southern Denmark, Denmark*

Obesity is characterised by a chronic, low-grade inflammation and several of the inflammatory risk markers are associated with and predict the development of insulin resistance, type 2 diabetes, and cardiovascular disease. Current evidence suggests that levels of inflammatory markers are determined by environmental, clinical and genetic factors. For instance, an inverse association between the intake of fruit and vegetables and inflammation has been demonstrated. No studies have previously determined whether genetic variation modifies the association between fruit and vegetable intake and the level of inflammation. In 1997–2000, a Danish twin sub-cohort, named GEMINAKAR, was established within the population-based Danish Twin Registry with the purpose to investigate the relative influence of genetic and environmental factors on the metabolic syndrome, obesity and cardiovascular risk factors. The GEMINAKAR population includes 756 complete zygosity determined twin-pairs, ranging from 18 to 67 years of age and initially free of known diabetes or cardiovascular disease. A clinical examination, including measures of bodyweight and height, and a questionnaire survey concerning physical health and health-related behaviour has been carried out. Dietary assessment was performed using a validated food-frequency questionnaire. A total of 1131 twins had complete information on body mass index, energy intake from fruit and vegetable, and C-reactive protein (CRP) and were

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

included in the analyses. Individuals with high CRP levels had lower fruit and vegetable intake. The addition of body mass index to the model did not change this. The independent relationship between CRP levels and fruit and vegetable intake and body mass index was stronger in men. This relationship was not influenced by genetics as assessed in very simple regression models and more in depth analysis of this aspect will be carried out and presented. In conclusion, this simple and preliminary analysis demonstrated that twins with higher energy intake from fruit and vegetable intake had significantly lower CRP levels and the association was independent of body mass index and genetic factors.

GENES, ECONOMICS AND HAPPINESS

J.-E. De Neve[1], J. H. Fowler[2], B. S. Frey[3]
[1] *London School of Economics and Political Science, London, UK*
[2] *Political Science Department, University of California, San Diego, USA*
[3] *Institute for Empirical Research in Economics, University of Zurich, Switzerland*

Research on happiness has produced valuable insights into the sources of subjective wellbeing. A major finding from this literature is that people exhibit a 'baseline' happiness that shows persistent strength over time, and twin studies have shown that genes play a significant role in explaining the variance of baseline happiness between individuals. However, these studies have not identified which genes might be involved. This article presents evidence of a specific gene that predicts subjective wellbeing. Using data from the National Longitudinal Study of Adolescent Health, we show that individuals with a transcriptionally more efficient version of the serotonin transporter gene (5HTTLPR) are significantly more likely to report higher levels of life satisfaction. Having one or two alleles of the more efficient type raises the average likelihood of being very satisfied with one's life by 8.5% and 17.3%, respectively. This result may help to explain the stable component of happiness and suggests that genetic association studies can help us to better understand individual heterogeneity in subjective wellbeing.

PERINATAL OUTCOME OF TWIN PREGNANCIES IN WOMEN OF ADVANCED AGE

I. Delbaere
Ghent University, Belgium

In singleton pregnancies, advanced maternal age (> 35 years) is associated with increased obstetric and perinatal risks. In contrast to singletons, current evidence concerning the association between advanced maternal age and perinatal outcome in multiple pregnancies is not well-documented. The purpose of this study is to assess the outcome of twin pregnancies in women of advanced age (≥ 35 years) compared to women aged 25 to 29 years old. We compared perinatal outcome of twin pregnancies in primiparae aged 35 or older (N = 240) to twin pregnancies in primiparae aged 25 to 29 years (N = 940). Observed outcomes were adjusted for mode of conception, hypertension during pregnancy, level of education and zygosity/chorionicity. In twin pregnancies, maternal age of 35 or over is associated with a lower incidence of preterm birth [Adjusted Odds Ratio (AOR) 0.59, 95% Confidence Interval (CI) 0.44 – 0.79] and low birthweight (AOR 0.75, 95% CI 0.58 – 0.98) compared to younger women. Differences in zygosity and chorionicity between both cohorts do not seem to affect these results. Our results show that twins of older primiparae are not exposed to higher risks of preterm birth and low birthweight in comparison with twins of younger mothers. On the contrary, preterm birth and low birthweight rates are significantly higher in twin pregnancies of women aged 25 to 29 years old than in women aged 35 years or older.

GEOMETRIC MORPHOMETRIC ANALYSES OF FACIAL SHAPE IN TWINS

C. G. Demayo[1,4], A. L. Sinco[2], M. L. Bonachita-Sanguila[3], M. A. J. Torres[1,4]
[1] *Department of Biological Sciences, College of Science and Mathematics, MSU-Iligan Institute of Technology, Iligan City, Philippines*
[2] *Biology Department, College of Arts and Science, Xavier University, Corrales Avenue, Cagayan de Oro City, Philippines*
[3] *Father Saturnino Urios University, Butuan City, Philippines*

Twin pairs represent a unique window into the role of heredity in the determination of any human trait. A primary characteristic by which humans present themselves to the external world is via the anatomy of their facial shape. Thus, facial images are becoming increasingly significant in biometrics research. In this study, the method of geometric morphometrics such as superimposition and Procrustes fitting were used to generate facial and ear shape variables in the form of relative warps of landmarks derived from perceived identical twins. Sixty pairs of twins participated in the study. A digital camera was used to photograph the subjects in neutral mode facing front. The shapes of the face were then summarized using a total of 39 landmark points from the face. Heritability was measured as concordance in the shapes of the face of each member of pair of twin. Specifically, correlation between the relative warp scores of the pairs of twins was used to test for heritability. Results showed that facial shapes of the twins had a moderate to highly positive correlation indicating that the landmark points established on one twin can also be observed in the other twin. Furthermore, the probability values of each correlation coefficient revealed that there is a significant linear relationship of the landmarks between twin 1 and twin 2 indicating a high degree of heritability of facial shapes. The results of the study underscore the utility of geometric morphometrics in the study of inheritance and variability of traits in organisms.

METHYLOMIC PROFILING IN TWINS DISCORDANT FOR MAJOR PSYCHOSIS

E. Dempster, R. Pidsley, L. Schalkwyk, T. Toulopoulou, M. Picchioni, E. Kravariti, R. Murray, J. Mill
Institute of Psychiatry, King's College London

Studies of major psychosis (schizophrenia and bipolar disorder) have focused primarily on the interplay between genetic and environmental risk factors. Genetic studies have uncovered polymorphisms in a number of loci that appear to mediate the risk for disease, but many of these associations are characterized by nonreplication, small effect sizes, and significant heterogeneity. In addition, there are several epidemiological, clinical, and molecular peculiarities associated with both schizophrenia and bipolar disorder that are difficult to explain with traditional gene- and environment-based approaches; such features include incomplete phenotypic concordance between monozygotic twins, a fluctuating disease course with periods of remission and relapse, sexual dimorphism, peaks of susceptibility to disease coinciding with major hormonal rearrangements, and parent-of-origin effects. These observations have led to speculation about the importance of epigenetic factors in mediating susceptibility. Because monozygotic twins share a common DNA sequence, the study of discordant twins represents an ideal design for investigating the contribution of epigenetic factors to disease etiology. We have performed genome-wide methylomic profiling on DNA samples obtained from a unique set of monozygotic twins discordant for major psychosis. A number of genes were found to show significantly different DNA methylation profiles between affected and unaffected individuals. Significant findings have been subsequently assessed in post-mortem brain tissue and ongoing clinical samples from affected individuals.

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

A FUNCTIONAL MRI STUDY IN MONOZYGOTIC TWINS CONCORDANT AND DISCORDANT FOR OBSESSIVE-COMPULSIVE SYMPTOMS

A. den Braber[1], D. van 't Ent[1], D. van Minde[1], D. C. Cath[2], D. I. Boomsma[1], E. J.C. de Geus[1]
[1] *Department of Biological Psychology, VU University, Amsterdam, The Netherlands*
[2] *Department of clinical and health psychology, Utrecht University, Utrecht, The Netherlands*

Obsessive–compulsive disorder (OCD) is characterized by recurrent and intrusive thoughts and subsequent behaviors to reduce distress caused by the obsessions. Neuroimaging studies in OCD patients point to a cortico-striatal-thalamo-cortical network deficit. However, there are large differences between studies. Apart from methodological differences, this may reflect differences in patient recruitment leading to the differential influence of environmental and genetic risks for OCD among studies. To distinguish between the genetic and environmental neurobiology of OCD we assessed fMRI parameters during performance of the Eriksen flanker task in monozygotic (MZ) twins concordant or discordant for ratings on the Padua Inventory Revised Abbreviated Obsessive Compulsive Symptoms (OCS) scale. Twin-pairs who score concordant high on this scale are considered at higher genetic risk for OCD than concordant low scoring twins. Discordant high twins are considered at higher environmental risk for OCD than their low scoring co-twins. Our sample consisted of 23 concordant high, 28 concordant low and 20 discordant twin pairs. The Eriksen flanker task measures selective attention and inhibitory control. It has been suggested that abnormal inhibitory networks are implicated in the pathophysiology of OCD. Relative to concordant low twins, concordant high twins showed increased blood-oxygen-level-dependent (BOLD) signal to response interference in right anterior cingulate cortex and right thalamus. Reduced BOLD responses were noted in the left inferior parietal lobule and right middle temporal gyrus. Compared to their low scoring co-twins, discordant OCS high twins showed increased BOLD to incongruent flankers in the left middle temporal gyrus, left cingulate gyrus, left dorsolateral prefrontal cortex, right inferior parietal lobule, right globus pallidus and left putamen. Decreased BOLD was noted in the left superior frontal gyrus, right fusiform gyrus and left superior parietal lobule. Our study demonstrates OCS related increments as well as decrements in the amount of BOLD signal, during inhibition of distracting information. The observed locations of brain changes are in line with the common hypothesis of a dysregulation of cortico-striatal-thalamo-cortical circuitry during inhibition in OCD. Because partly distinct brain areas are involved in OCS of 'genetic' versus 'nongenetic' origin we conclude that genetic and environmental risk factors for OCD may act on different brain structures.

THE GENESIS OF MULTIPLE GESTATION

C. Derom
Ghent University, Belgium

Twins are not a homogeneous group. According to their origin, zygosity and chorionicity, essential differences exist. Spontaneous dizygotic (DZ) twinning is clearly associated with multiple ovulation, is heritable and suggested to be an index of high fecundity. Maternal factors such as higher age, race and increased parity are also known factors influencing DZ twinning. As a result of the modern methods of treatment of infertility the rate of twin births has almost doubled in industrialized countries. Zygosity and chorionicity distribution are totally different in spontaneous and iatrogenic twins and, contrary to the common belief, not all iatrogenic twins, whether conceived after assisted reproduction technology or artificial induction of ovulation only, are DZ: some 5% are monozygotic (MZ). The causes of MZ twinning remain elusive. MZ twinning events appear to occur very soon after fertilization, presumably spanning a time frame of as much as a week or more after conception. The estimates for the timing of splitting of the embryo are based on the examination of the placental anatomy at birth. Three subtypes of MZ twins can be recognized: the dichorionic-diamnionic (DCDA) pairs (early, before the 4th day after fertilization), the monochorionic-diamnionic (MCDA) pairs (intermediate, between the 4th and the 7th day post fertilization) and the monochorionic-monoamnionic (MCMA) pairs (late, after the 8 day post fertilization). What is true for twins is also true for triplets. In spontaneous triplets around 25% are trizygotic (all three children different), 50% DZ (two alike, one different) and around 20% MZ (all 3 alike). MZ twins can be either MC, DC or trichorionic. In iatrogenic triplets the great majority is TZ. According to these early embryological events important differences exist. Perinatal mortality is much higher in MZMC than in DZ and MZDC twins, especially before birth. MZMC twins suffer a more adverse prenatal environment and have larger intra-pair birthweight differences compared to MZDC twins. The sex proportion at birth in DZ twins is the same as that of singletons and is lowered in MZ twins. To a small extent in DC and MCDA twins and a much greater extent in the monoamnionic variety, according to our data of East Flanders. Other important biological phenomena's that varies between MZMC and MZDC twins are X-inactivation and the degree of epigenetic dissimilarity.

UNDERSTANDING GENE-ENVIRONMENT INTERACTIONS IN ADOLESCENT ALCOHOL USE AND EXTERNALIZING BEHAVIOR

D. M. Dick
Virginia Commonwealth University, USA

An accumulating body of evidence suggests that genetic influences on adolescent alcohol use and externalizing behavior are moderated by several aspects of the environment. In data from the Finnish twin studies, we have previously shown that genetic influences on adolescent alcohol use and externalizing behavior vary as a function of neighborhood factors, such as urban/rural residency, whereby genetic influences are greater in urban settings and common environmental factors are more important in rural settings (Rose et al., 2001 Dick et al., 2001) parental monitoring, such that genetic influences are higher under conditions of lower parental monitoring (Dick et al., 2007) and peer alcohol use, such that genetic influences are greater when an adolescent has more substance-using peers (Dick et al., 2007). Similar findings have also been reported in independent twin samples (e.g., Legrand et al., 2007 Button et al., 2005). Together they suggest that environments that exert more social control constrain the expression of genetic predispositions, whereas other environments allow greater opportunity for the expression of genetic influences. This raises question as to whether there is anything specific and important about each of these different environmental factors (parenting, peers, neighborhoods, etc), or whether they all simply operate through a shared mechanism. We explore this question in data from FinnTwin12, a population-based Finnish twin study consisting of all twins born over a five year period in Finland, using data collected at age 14. We first tested the factor structure across relevant environmental domains assessed in the study. Subsequently, we tested the moderating influence of the overarching environmental factor(s) versus environment-specific residual variance. These analyses aim to help us understand what aspects of the environment are most relevant in moderating the importance of genetic influences on adolescent alcohol use and externalizing behavior.

ARE GENETIC AND ENVIRONMENTAL COMPONENTS OF VARIANCE IN MAMMOGRAPHIC DENSITY MEASURES THAT PREDICT BREAST CANCER RISK INDEPENDENT OF WITHIN-TWIN PAIR DIFFERENCES IN BODY MASS INDEX?

G. S. Dite, J. Stone, J. L. Hopper
Centre for Molecular, Environmental, Genetic and Analytic Epidemiology, The University of Melbourne, Carlton, Australia

Background: To understand the potential roles of mammographic density on breast cancer risk it is important to take into account negative confounding with age and body mass index (BMI). Furthermore, a previous US twin study found evidence that the covariance structure might depend on the extent to which twin pairs differ in BMI, with potential implications for interpretation.

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

Methods: Using a computerized thresholding technique, we measured mammographic dense area for 557 MZ and 394 DZ twin pairs aged 40 to 70 years from Australia and North America. After adjusting for age and BMI, we calculated estimates of variance, covariances, correlations and, under the assumptions of the classic twin model, genetic and environmental components of variance, within and across categories defined by within-air differences in BMI, under a bivariate normal model using the software FISHER. *Results:* The variance, MZ correlation, and difference between MZ and DZ correlations were not constant with BMI difference category (all $p < .001$). The most parsimonious model predicted that the genetic variance component was constant but the environmental component increased almost 3-fold across the BMI difference categories ($p < .001$). *Conclusion:* The genetic and environmental causes of variation in measures of mammographically dense area that predict breast cancer might be quite complex.

GENETIC AND ENVIRONMENTAL INFLUENCES ON CHILDREN'S FOOD INTAKE AND OBESITY IN A CANADIAN TWIN BIRTH COHORT

L. Dubois[1,2], M. Girard[2]

[1] *Department of Epidemiology and Community Medicine, University of Ottawa, Ottawa, Canada*

[2] *Institute of Population Health, University of Ottawa, Ottawa, Canada*

The aim of this research is to study the etiology of human obesity. The genetic and environmental influences on food intake and on body weight were analyzed in a population-based sample of more than 600 pairs of 5-year-old twins. Sex differences in gene-environment etiology were also explored. Analyses used data from the *Quebec Newborn Twin Study (QNTS),* a population-based Canadian birth cohort of 672 twin pairs. This cohort has been followed longitudinally from birth and data on breastfeeding and diet factors instrumental to the development of obesity were collected at the age of 5 months, 1.5, 2.5, 4, and 5 years. Heritability of weight was moderate at birth while common environmental factors accounted for almost half of the variance. Influence of family environment disappeared by 5 months and genetic effects were high (approximately 90%) for both sexes at 5 months and 5 years. Adjustment of weight for height yielded similar results as for weight alone. Slight but significant sex-limitation of genetic effects was observed at 5 months. Overall, genetic factors accounted for 40% of birthweight variance, with intrauterine environment influences explaining almost half. However, genetic factors accounted for most of the variance in weight. These results do not imply a lack of environmental effects on body weight, but rather a lack of: (1) environmental effects that are *independent* from genetic liability, and/or (2) a lack of significant environmental *variation* in the population (e.g., uniform nutritional habits) that leaves genetic differences between children to generate most of the variance in weight. In order to get a better understanding of this issue, we analyzed the part that is: (1) inherited (from the genes) and (2) environmental (shared and unshared) observed by the impact of differences in food intake and in body weight. The results indicate that food intake may act interactively or independently from other environmental factors (e.g. socioeconomic status), on body size. Physical activity was used as a covariate in the analysis. The results of this research improve our knowledge of the factors responsible for the development of overweight and obesity in childhood. The research is important for the development of nutrition recommendations and public health interventions in childhood, adapted to the short- and long-term prevention of obesity at the level of the population.

DEPRESSIVE SYMPTOMS AND ALCOHOL USE ARE GENETICALLY AND ENVIRONMENTALLY CORRELATED ACROSS ADOLESCENCE

A. C. Edwards[1], J. Kaprio[2], R. J. Rose[3], D. M. Dick[1]

[1] *Virginia Institute for Psychiatric & Behavioral Genetics, Virginia Commonwealth University, Richmond VA, USA*

[2] *Department of Public Health, University of Helsinki, Helsinki, Finland*

[3] *Department of Psychological and Brain Sciences, Indiana University, Bloomington IN, USA*

Depressive disorders and alcohol use are frequently positively associated during adolescence. The purposes of this study were to assess the heritability of each phenotype across adolescence; to investigate the extent to which their association is due to a shared liability in the form of genetic and/or environmental factors common to both phenotypes; and to examine changes in the nature of this shared liability across adolescence. We used a sample of Finnish twins (N = 1282) for whom depressive symptoms and alcohol use had been assessed at ages 12, 14, and 17.5. We tested different hypotheses about the genetic and environmental components of variance affecting these phenotypes at each age and across ages. The heritability of depressive symptoms is relatively consistent across adolescence (~40–50%), with a similar proportion of variance accounted for by unique environmental factors, and small shared environmental influences (< 10%). The heritability of alcohol use varies across time (a2 = 0.25–0.44), and is heavily influenced by shared environmental variance at age 14. Modest to moderate genetic (rA = .26–.59) and environmental (rC = .30–.63) correlations between phenotypes exist at all ages, and these correlations decrease over time. The association between depressive symptoms and alcohol use during adolescence is at least partially attributable to genetic and environmental influences shared by both phenotypes. The nature of these common factors is temporally dynamic.

ACADEMIC ACHIEVEMENT OF TWINS AND PECULIARITIES OF SHARED AND NONSHARED ENVIRONMENT

M. Egorova, N. Zyrianova, O. Parshikova, Y. Chertkova

Psychology Department, Lomonosov Moscow State University, Moscow, Russia

The aims of the Russian national twin study of academic achievement are (1) to compare the academic achievement in twins and singletons during primary and secondary schools; (2) to describe the trends of twins' schooling in general and in particular subjects; and (3) to evaluate the impact of genetic and environmental (shared and non-shared) influences into the twins' academic achievement. The sample consisted of 2282 twin pairs and 4065 of their singleton classmates, ages 7–17 years; cohorts born between 1982 and 1997. The analysis shows that twins tend to be behind in primary school, till the 5th grade, and further have only few disadvantages as compared with singletons. There are significant differences between twins and singletons in Russian language and Mathematics in primary school and in learning Russian language in 7–11 grades. The school performance of twins as well as singletons decreases from 2–4 to 7–11 grades. Various features of shared environment (such as age and education of parents number of children in the family number of siblings older/younger, than twins age difference between twins and the nearest sibling) and nonshared environment (such as intrapair twins' relations (if there is a leader in the twin pair)) apply as independent variables in regression analysis.

DIFFERENCES IN SPORT PERFORMANCE AND PERSONALITY TRAITS BETWEEN A PAIR OF MONOZYGOTIC TWINS

O. Enji[1], H. Daisuke[2], O. Aiko[3]

[1] *Department of Education, Shiga University, Shiga, Japan*

[2] *Osaka Electro-Communication University, Osaka, Japan*

[3] *Department of Education and Welfare, Biwakogakuin University, Shiga, Japan*

Genetic constitution and years of physical training are prerequisites for making Olympic athlete. However success may be largely influenced by personality traits (Klissouras et al. 2001). Here we report

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

about differences in personality traits observed between a female pair of monozygotic twins. The twins both engaged in the same sport and had a long-term athletic training together. However, only one twin successfully became a Japanese Olympic player, and the other twin went no further than being a member of Japan's national youth team. The subjects are a pair of female monozygotic twins who both attained a high level of athlete performance of the sport. They are now 33 years old, and both have retired form competition. The twin zygosity was determined by a self-report inventory, and the accuracy of this diagnosis is reported over 90% (Ooki, et al., 1991). The Yatabe-Guilford (YG) personality inventory (Tsujioka, et. al., 1982) was administered for the twins. This inventory comprised 12 subscales. Each subscale consisted of 10 items on a three-point rating scale. The score of each subscale was ranged from 0 to 20 points. With this inventory, personality is also classified into five types in reference to each subscale score. They both had high scores in the category of the extroverted way of thinking, and showed very low scores in such categories as lack of cooperativeness, depression, inferiority feelings and nervousness. This result confirms to the accounts of psychological profiles of athletes reported in previous studies. However, we observed certain marked intrapair differences in the following three categories: lack of objectivity, rhathymia, and ascendance. The Olympic player scored extremely low in lack of objectivity (1 point) and rhathymia (2 points) in contrast to the other twin showing just better than the average: 8 points for the former and 7 for the latter. Further, as for ascendance, the Olympic player scored higher than the other twin: 7 points to 12 points. In personality types, the Olympic player was classified into the calm type that indicates stable emotions and excellent social adaptation, while the other twin was classified into the average type.

SHARED GENETIC EFFECTS BETWEEN PARENT-REPORTED ASTHMA AND WHEEZING IN YOUNG ITALIAN TWINS

C. Fagnani, V. Patriarca, L. Penna, C. D'Ippolito, G. Di Giovambattista, S. Brescianini, M. A. Stazi
Istituto Superiore di Sanità, Rome, Italy

Parent-reported asthma and wheezing among 399 twin pairs aged 8-17 years from the population-based Italian Twin Registry were examined for evidence of genetic overlap by using the twin design and quantitative genetic methods. Zygosity was assessed by standard questions on physical resemblance. According to the answers, there were 145 monozygotic (MZ) and 254 dizygotic (DZ) pairs. Lifetime prevalence rates in twins as individuals, as well as probandwise concordance rates and tetrachoric correlations in MZ and DZ pairs were estimated for asthma and wheezing. Furthermore, a bivariate Cholesky decomposition was fitted to the two traits using the software Mx. The lifetime prevalence rates were 8.6% for asthma and 27.3% for wheezing, and were in keeping with the estimates previously reported in a large survey in Italian children within the International Study of Asthma and Allergies in Childhood (ISAAC project). Probandwise concordance rates in MZ and DZ pairs were .76 and .34 respectively for asthma, and .75 and .59 respectively for wheezing. Cross-twin/within-trait correlations in MZ and DZ pairs were .95 and .53 respectively for asthma, and .88 and .66 respectively for wheezing, suggesting a large genetic influence on asthma and more moderate genetic effects on wheezing for the latter trait, a substantial shared environmental contribution was also evoked. Susceptibilities to asthma and to wheezing were largely correlated (.85) at the individual level. Furthermore, higher cross-twin/cross-trait correlations in MZ (.57 and .58) than in DZ pairs (.33 and .38) were consistent with overlapping genetic effects between asthma and wheezing. A Cholesky decomposition encompassing additive genetic, shared and unshared environmental sources of variance and covariance provided a heritability estimate of .84 (95%CI: .36-.99) for asthma and .44 (95%CI: .08-.80) for wheezing. The model also provided a bivariate heritability estimate of .66 (95%CI: .32-.96), indicating that two-thirds of total covariance in susceptibilities to asthma and to wheezing were explained by genetic factors common to the traits. These results show common genetic effects for asthma and wheezing. For the congress, the above analyses will be replicated on a larger sample including additional twin pairs of different age groups whose recruitment is still ongoing.

HERITABILITY AND GENETIC RELATIONSHIP OF CHILDHOOD SPEECH DISORDERS, STUTTERING, AND CLUTTERING, BASED ON SELF-REPORTED DATA FROM ADULT TWINS

C. Fagnani[1], S. Fibiger[2], A. Skytthe[3], J. V. B. Hjelmborg[4]
[1] *Genetic Epidemiology Unit, Istituto Superiore di Sanità, Rome, Italy*
[2] *Speech and Hearing Department, Centre for Rehabilitation, Region of Southern Denmark, Odense, Denmark*
[3] *The Danish Twin Registry, Institute of Public Health, University of Southern Denmark, Odense, Denmark*
[4] *Department of Biostatistics, Institute of Public Health, University of Southern Denmark, Odense, Denmark*

Genetic influence and mutual genetic relationship for adult self-reported childhood speech disorders, stuttering, and cluttering were studied. Using nationwide questionnaire answers from 34,944 Danish twins, a multivariate biometric analysis based on the liability-threshold model was performed in order to estimate heritability of the traits and genetic correlation between them. The lifetime prevalence rates were in agreement with previous reports, and were higher for males than for females for all three traits. The probandwise concordance rates were always substantially higher for monozygotic compared to dizygotic pairs, suggesting genetic influence. Multivariate biometric analyses showed that additive genetic and unique environmental factors best explained the observed concordance patterns. Heritability estimates for males/females were .71/.87 for childhood speech disorders, .78/.80 for stuttering, and .53/.65 for cluttering. For each trait, the same genes were suggested to affect liability in males and females. Furthermore, high genetic correlations between the traits were obtained; the estimates for childhood speech disorders and stuttering were .71/.79 for males/females, for childhood speech disorders and cluttering .73/.56, and for stuttering and cluttering .53/.57. Substantial unique environmental correlations between the traits were also found in both genders. With the limitations related to self-reporting from adult age, this study demonstrates substantial genetic influence on the traits of childhood speech disorders, stuttering, and cluttering, and mutual genetic relationship between them.

RISK OF DEMENTIA IN TWINS WITH PARKINSONIAN DISORDERS

A. L. Feldman[1], U. K. Eriksson[1], A. L. V. Johansson[1], M. Gatz[2], N. L. Pedersen[1,2], K. M. Wirdefeldt[1]
[1] *Karolinska Institutet, Department of Medical Epidemiology and Biostatistics, Stockholm, Sweden*
[2] *University of Southern California, Department of Psychology, Los Angeles, United States*

Parkinson's disease is the most common type of Parkinsonian disorder, which includes the Parkinsonism symptoms tremor, rigidity and bradykinesia. The etiology of dementia associated to Parkinson's disease and other Parkinsonian disorders is complex. Patients with Parkinsonian disorders, and, in some cases, their relatives, have a greater risk of developing dementia than the general population. This may be due to natural progression of Parkinson's disease into dementia, comorbidity or shared genetic and/or environmental etiology between the diseases. Using hospital and cause of death registry diagnoses as well as data from clinical work-ups for dementia and Parkinsonian disorders in the Swedish Twin Registry, we studied whether there is shared etiology between Parkinsonian disorders and dementia. Cases in twin pairs discordant for Parkinsonian disorders were matched on zygosity, sex and birth year to five twin controls each. Relative risk of dementia in Parkinsonian disorder cases, matched controls and their respective twin partners was estimated using conditional logistic regression. We found that the relative risk of dementia was increased in twin partners of Parkinsonian disorder cases compared to twin partners of controls, indicating that Parkinsonian disorders and dementia share etiology. When stratifying for zygosity, we found that monozygotic twin partners of

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

Parkinsonian disorder cases had a 5-fold increased relative risk of dementia, whereas in dizygotic twin partners of Parkinsonian disorder cases there was no increased relative risk of dementia compared to controls. This indicates that the shared etiology is genetic and not environmental.

WHAT IS THE RESEARCH INVOLVING TWINS AND LOW BACK PAIN TELLING US? A SYSTEMATIC REVIEW

P. Ferreira[1], M. Ferreira[1], C. Maher[2], J. Hopper[3], R. Huxley[2], C. Alcantara[1], L. McGrath-Cadell[1]

[1] *Faculty of Health Sciences, University of Sydney, Sydney, Australia*

[2] *The George Institute for International Health, University of Sydney, Sydney, Australia*

[3] *Australian Twin Registry, University of Melbourne, Melbourne, Australia*

Most existing interventions are not effective in the prevention of low back pain (LBP). The lack of adjustment for genetic confounding is a potential flaw in the design of original studies examining risk factors for LBP. We conducted a systematic review of the literature to identify and describe twin studies that investigated risk factors for LBP. To be included studies had to be prospective observational studies involving twins and exposure factors could be genetics or environmental. The following databases were searched: MEDLINE, CINAHL, LILACS, Web of Science and EMBASE. Five studies, all with participants from the Danish Twin Resister, satisfied the inclusion criteria. Participants included in the studies were either older (aged over 70 years) or younger (aged less than 22 years). Follow-up periods varied between two and eight years. The exposure factors were highly variable between studies including physical activity, measurements of muscle performance such as grip strength, measurements of cognitive function, depression, socioeconomic status, body mass index, smoking, alcohol consumption, and diseases such as asthma. No risk factor was found to be consistently associated with the risk of developing LBP and physical activity appears to be a protective factor (OR = .59 CI .42–.83). Adjustment for genetic confounding was performed in two studies. Being LBP a costly and leading cause of disablement twin studies could lead to major breakthroughs in the area and help in the design of effective preventative interventions.

EXAMINING THE POSSIBLE RELATIONSHIP BETWEEN CHILDREN'S IQ AND PROXIMITY OF PARENTAL BIRTH PLACE

S. Fran, M. G. E. Frantsen, T. C. E. M. van Beijsterveldt, D. I. Boomsma

Department of Biological Psychology, VU University Amsterdam, The Netherlands

Inbreeding depression, or the reduction in the mean phenotypic value resulting from parental genetic relatedness, has been shown to occur for a number of traits, including intelligence. The effects of inbreeding on IQ have been well documented (e.g. J. Bashi, 1977, *Nature*. 266(5601), 440-42), with an average decrease of 4.4 IQ points associated with a ten percent increase in probability of parents carrying identical genes at the relevant loci (D. S. Falconer, T. F. C. Mackay, 1989, *Introduction to Quantitative Genetics*, Longman, London). In the current study we assume that proximity of parental birth place can be used as an index of probability of one's parents being genetically related, and investigate the relationship between proximity of parental birth place and longitudinally measured verbal, performal, and full scale IQ in children at ages 5, 7, 9, 10, 12, 15, 17, and 18. Data are obtained from the Netherlands Twin Register at the VU University Amsterdam and consist of longitudinal measures of cognitive abilities in four samples of twins (N_1 = 1951, N_2 = 587, N_3 = 1080, N_4 = 852), their siblings (N_1 = 95, N_2 = 260, N_3 = 53) and parents (N_2 = 350). Cognitive abilities are assessed using several different measures (Revised Amsterdam Children Intelligence Test (RAKIT), Wechsler Intelligence Scale for Children (WISC), Raven's Standard and Advanced Progressive Matrices (SPM, APM), and Wechsler Adult Intelligence Scale (WAIS)), the choice of test depending on the participants' age. Employing mixed modeling to control for familial clustering, we will examine the relationship between proximity of parental birthplace and children's IQ, as well as the possible dependence of such relationship on the child's age.

EARLY LEXICAL DEVELOPMENT IN JAPANESE-SPEAKING 12-, 18-, AND 24-MONTH-OLD TWINS

K. K. Fujisawa[1], T. Kobayashi[2], J. Ando[1]

[1] *Keio University, Tokyo, Japan*

[2] *NTT Communication Science Lab, Kyoto, Japan*

Elaborate investigations by Rutter et al. (2003) provided clear evidence that English-speaking twins lag behind single-born children in their language development at 20 and 36 months under conditions where obstetric and neurological complications were highly controlled. Although this suggests the existence of language delays in twins after the onset of the vocabulary spurt at around 18–20 months, it remains unclear when their language delays emerge compared with those of singletons. This study addresses the question by investigating whether twins lag behind singletons as regards vocabulary size during the earliest stages of lexical development at 12, 18 and 24 months. We used a vocabulary-checklist method based on maternal reports (Japanese MacArthur-Bates Communicative Development Inventory, Watamaki & Ogura, 2004) to measure the vocabulary size of Japanese-speaking twins and singletons aged 12, 18, and 24 months. The participants were 88 twins (52 boys, 36 girls) and 130 singletons (60 boys, 70 girls) aged 12 months, 206 twins (87 boys, 119 girls) and 274 singletons (126 boys, 148 girls) aged 18 months, and 186 twins (92 boys, 94 girls) and 111 singletons (49 boys, 62 girls) aged 24 months. The mothers with twins reported their vocabulary sizes for timings corrected based on their gestational age. Productive vocabulary scores were investigated in 2 (gender: girls vs. boys) x 2 (birth: twins vs. singletons) ANOVAs for each age group (12-, 18- and 24-month-olds). An analysis of the 12- and the 18-month-olds showed no significant effects of birth (12-month: $F(1,211) = 3.262$, ns 18-month: $F(1,475) = .004$, ns), and no significant interactions (12-month: $F(1,211) = .899$, ns 18-month: $F(1,475) = .227$, ns), indicating that 12- and 18-month-old twins did not lag behind singletons regardless of gender. An analysis of the 24-month-olds yielded a significant interaction, $F(1,289) = 6.369$, $p < .05$, indicating that male twins achieve significantly lower scores than male singletons (twins: $M = 143.8$, singletons: $M = 231.4$ words Bonferroni correction: $p < .0005$) in contrast to the fact that there is no significant difference between females twins and singletons (twins: $M = 254.5$, singletons: $M = 251.7$ words). This study provides no sign of any language delay in twins younger than 18 months, and reveals its emergence at 24 months but only in males. Since Nazzi & Bertoncini (2003) proposed that the period around 18–20 months corresponds to a shift from a purely word-referent associationist mode to a referential lexical acquisition mechanism, the language delay in twins might not be due to association, but to some sort of referential mechanism.

PARENT AND LABORATORY-ASSESSED INHIBITORY CONTROL AND RELATED BEHAVIOR PROBLEMS AT 7–8 YEARS OF AGE

J. R. Gagne[1], M. K. Vendlinski[1], K. Lemery-Chalfant[2], H. Goldsmith[1]

[1] *Department of Psychology, University of Wisconsin-Madison, USA*

[2] *Kathryn Department of Psychology, Arizona State University, USA*

Inhibitory control (IC) is a dimension of child temperament involving the ability to regulate behavior. In middle childhood, low levels of IC are associated with higher levels of non-clinical behavior problems, and the behavioral disorder that is most strongly associated with IC in childhood is ADHD. Multiple twin studies indicate that IC is genetically influenced (J. R. Gagne & K. S. Saudino, in press J. R. Gagne & H. H. Goldsmith, in press). In addition, researchers have examined genetic and environmental covariance between IC and behavior problems in toddlerhood (J. R. Gagne & K. S. Saudino, in preparation) and school age (K. Lemery-Chalfant, L. Doelger, H. H. Goldsmith, 2008, *Infant and Child Development, 17,* 365–385). The present study investigates both parent- and lab-assessed IC and behavior problems at 7–8 years of age. Participants included 231 MZ and 385 DZ twin pairs from the Wisconsin Twin Project (WTP). IC was assessed in the laboratory using the Tower of Patience episode

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

of the Laboratory Temperament Assessment Battery (Lab-TAB H. H. Goldsmith et al., 2001, Unpublished manual) and by mothers using the Children's Behavioral Questionnaire (CBQ M. K. Rothbart, S. A. Ahadi, K. L. Hershey, & P. Fisher, 2001, Child Development, 72, 1394–1408). Externalizing, conduct, and attention/impulsivity behavior problems were rated with the MacArthur Health Behavior Questionnaire (HBQ J. M. Armstrong et al., 2003, Manual for the MacArthur Health and Behavior Questionnaire). Phenotypic correlations between parent and lab-assessed IC and behavior problems ranged from –.10 to –.62. These correlations were all negative, indicating that children with lower IC had higher behavioral maladjustment. MZ correlations exceeded DZ correlations, suggesting the presence of genetic influences. Univariate analyses indicated that genetic influences were significant (heritabilities ranged from .40–.77). Trivariate Cholesky decomposition models yielded variance components that were consistent with previous analyses, and significant genetic correlations between parent and lab IC (.26–.27), and between both IC assessments and behavior problems (–.21– –71). GRANT SUPPORT: R01MH059785.

TWIN STUDY ON DNA REPAIR EFFICIENCY AND HEALTHY HUMAN AGING

C. Garm[1,2], T. Stevnsner[2], V. Bohr[3], K. Christensen[1]

[1] *Institute of public health – Epidemiology, University of Southern Denmark, Denmark*

[2] *Institute of Molecular Biology, Aarhus University, Denmark*

[3] *National Institute on Aging, NIH, Baltimore, USA*

The stability of our genome is constantly challenged by exogenous and endogenous damaging agents. It has been estimated that more than 100.000 DNA lesions occur in each mammalian cell per day. Accumulation of DNA damage is thought to play a critical role in the aging process, and may lead to errors in DNA replication and transcription causing point mutations or chromosomal rearrangements. However, the cells have several DNA repair pathways protecting them from mutations. DNA damage and decline of mitochondrial function has been implicated in cancer, aging, and neurodegenerative diseases. An aim of this study is to test whether healthy aging is associated with a low level of DNA damage, high DNA repair capacity, and functional mitochondria. We hypothesize that the co-twin with the best aging phenotype also tends to have the least DNA damage, the highest DNA repair capacity, and the healthiest mitochondria. A selected group of 20- to 75-year-old twins (40 MZ pairs and 40 DZ pairs) from the Danish Twin Registry are included in this study. Through tests and questionnaires we have achieved information on physical and cognitive function, and hospitalizations etc. The study involves molecular investigation of the DNA repair capacity and mitochondrial function in isolated monocytes from the selected twins by different assays. Using the comet assay and the fluorometric analysis of DNA unwinding (FADU) assay we analyze the DNA repair capacity. DNA damage response is investigated by flow cytometric measurements of gH2AX and XRCC1 foci. Fluorometric measurements of TMRM provide information about mitochondrial function. In this study MZ and DZ correlations for DNA repair capacity, DNA damage repair, and mitochondrial function will be determined to assess the overall influence of genetic factors in DNA repair. According to the preliminary data we have identified a tendency of higher intrapair differences in DNA damage response in the DZ twins compared to MZ twins. The association between intrapair differences identified by this molecular approach and the intrapair differences in health and functioning will be estimated. Additionally, age-related changes in DNA repair and mitochondrial functions will be investigated in these differentially aged twins.

ALCOHOLIC BEVERAGE PREFERENCE IN RELATION TO QUANTITY OF ALCOHOL CONSUMPTION AND GENERAL HEALTH

L. M. Geels[1], J. M. Vink[1], J. H. D. A. Van Beek[1], M. Bartels[1], M. H. M. de Moor[1], G. Willemsen[1], D. I. Boomsma[1]

[1] *Department of Biological Psychology, VU University Amsterdam, The Netherlands*

Moderate alcohol consumption and wine consumption in particular have repeatedly been linked to a decrease of health risks. In this study we look at stability over time of alcoholic beverage preference (beer, wine or liquor) and examine if alcoholic beverage preference is related to sex, age, self-perceived general health, quantity of alcohol consumption and twin versus non-twin status. Questionnaire data on alcohol preference, consumption and general health were available in a population based sample of 8078 twins and 2767 siblings who participated at least once in surveys collected in 1995, 2000 and 2009. The associations between sex and alcohol preference and between twin-sib status and alcohol preference were determined by testing the differences in proportions. Linear mixed models were used to examine effects of alcohol preference (3 levels) on self-perceived health and quantity of alcohol consumption and to look at interaction effects between preference and sex. First results indicate sex differences in alcoholic beverage preference: beer is preferred most among men, whereas among women wine is most popular. Twins and siblings do not appear to differ in which beverage they prefer. Linear mixed models showed interaction effects of sex and beverage preference on both self-perceived health and quantity of alcohol consumption, where men who preferred beer considered themselves healthier than women who preferred beer. Beer-preferring men also had a higher average alcohol consumption than women with the same preference. Over time, wine drinkers are most stable in their preference and liquor drinkers are least stable. Changes in preferred beverage over time are mostly towards wine.

SECULAR TRENDS IN GESTATIONAL AGE AND BIRTHWEIGHT IN TWINS

M. Gielen

Department of Population Genetics, Genomics and Bioinformatics, Maastricht University Medical Centre, Maastricht, The Netherlands

Background: In recent decades, the overall rate of preterm births has increased, as well as the prevalence of multiple gestations. The aims of the present study were to see whether there has been a decrease in gestational age for live-born monozygotic and dizygotic twins and a simultaneous change in birthweight, and to evaluate the contribution of fertility treatment and Caesarean sections in two large European twin cohorts. *Methods:* Cross-sectional study of 6,310 live-born twin pairs, born between 1964 and 2007, from the Belgian East Flanders Prospective Twin Survey and 14,712 twin pairs, born between 1990–2006, from the Netherlands Twin Register. Multiple regression analyses were performed with gestational age as outcome variable, and multilevel analysis with birthweight as outcome variable. All analyses were performed with and without adjustment for zygosity, parity, maternal age, mode of conception and delivery and, for the analyses of birthweight, gestational age. *Results:* Gestational age decreased in a linear fashion from 1964 to 2007 with a decrease of 0.25 days per year in a similar way for monozygotic and dizygotic twins. Changes in birthweight depended on gestational age: up to 32 weeks birthweight decreased and after 32 weeks birthweight increased. The frequency of infertility treatment and Caesarean sections, primiparity and advanced maternal age increased over the years, but none of these factors influenced this secular trend. *Conclusions:* The decrease in gestational age and change in birthweight in twins is a source of concern, especially for very preterm births, for whom birthweight decreased. For twins born after 32 weeks, an increase in birthweight was observed and this is very likely the explanation for the decrease in gestational age.

AN ITALIAN TWIN STUDY ON PSYCHOLOGICAL WELL-BEING IN YOUNG ADULTHOOD

A. Gigantesco[1], C. Fagnani[1], G. Alessandri[2], E. Medda[1], E. Tarolla[1], M. A. Stazi[1]
[1] *Istituto Superiore di Sanità, Rome, Italy*
[2] *Psychology Department, 'Sapienza' University of Rome, Rome, Italy*

The twin method was applied to investigate the genetic and environmental architecture of six dimensions of psychological wellbeing (PWB), that is, autonomy, positive relations, purpose in life, self-acceptance, environmental mastery and personal growth, as assessed by the shortest 18-item version of the Ryff's Scales of Psychological Well-Being. The study sample included 742 twins (284 complete pairs, 174 unmatched twins) aged 23–24 years from the population-based Italian Twin Registry. Zygosity was determined by standard questions regarding physical similarity. Of the 284 complete pairs, 137 were monozygotic (MZ) and 147 were dizygotic (DZ). Out of the 174 unmatched twins, 73 twins were from MZ pairs and 101 from DZ pairs. A confirmatory factor analysis was performed with the software Mplus. Factor scores were derived for the six PWB dimensions under the best-fitting model and were used for biometric analysis. Twin correlations were estimated and interpreted under the assumptions of the twin design. Furthermore, a Cholesky decomposition incorporating additive genetic, nonadditive genetic and unshared environmental latent sources of variance and covariance was fitted to the six PWB dimensions using the software Mx. MZ cross-twin/within-trait correlations were substantial (range: .33–.65), and resulted higher than DZ correlations (range: .09–.26), suggesting genetic effects on each dimension. Except for autonomy and personal growth that correlated modestly (.28) at the individual level, phenotypic correlations were generally moderate to extremely high (range: .42–.94). Cross-twin/cross-trait correlations were larger in MZ (range: 0.30-0.62) versus DZ pairs (range: .06–.25), pointing to a genetic link between the dimensions. The best-fitting Cholesky model included additive genetic and unshared environmental effects. Genetic factors accounted for a moderate to substantial proportion of variance in the six PWB dimensions, with heritabilities between 37 and 64%. Genetic correlations were very high (range: .77–.99), indicating that genetic factors that influence the expression of the different facets of PWB may be shared to a large extent. Unshared environmental correlations were also substantial to high, with the exception of autonomy with the dimensions of purpose in life (.22), self-acceptance (.09) and personal growth (.01). These findings may guide attempts to design intervention strategies aimed at promoting physical and mental health, which are known to be linked with PWB.

EMOTIONAL AND BEHAVIORAL PROBLEMS AMONG RUSSIAN ADOLESCENT TWINS AS REPORTED BY PARENTS

E. D. Gindina[1], S. B. Malykh[1], M. M. Lobaskova[2]
[1] *Laboratory of Developmental Behavior Genetics, Psychological Institute of Russian Academy of Education, Moscow, Russian Federation*
[2] *Department of Psychology, Udmurt State University, Izhevsk, Russian Federation*

The aim of the present study was to assess behavioral and emotional problems in Russian adolescent twins using the ratings of their parents and comparing these to those of their single-born peers. We have also analyzed sex and age differences in the parental scores of adolescents' behavioral and emotional problems. The sample included 490 twin and 540 single-born adolescents aged 10–17 years from different Russian regions. Parents were asked to complete the Child Behavior Checklist (Achenbach T., 1991, Manual for the Child Behavior Checklist/4-18 & 1991 Profile, Burlington: University of Vermont, Department of Psychiatry). No significant differences were found between parental ratings of behavioral and emotional problems of twins and single-born children. Delinquent behavior scores increased with age. Girls scored significantly higher than boys on Withdrawn/Depressed, Anxious/Depressed and Somatic Complains scales; boys scored significantly higher on Attention Deficit/Hyperactivity Problems, Delinquent Behavior and Aggressive Behavior scales. Girls had significantly higher scores on the Internalizing scale and boys had significantly higher scores on the Externalizing scale. Overall, the results were in line with those of the most studies conducted in other countries.

HOW DID THAT HAPPEN? CORRECTING ZYGOSITY ASSIGNMENT IN THE VIETNAM ERA TWIN REGISTRY

J. Goldberg[1], C. W. Forsberg[2], J. Sporleder[2], N. Smith[1]
[1] *Vietnam Era Twin Registry, Seattle Epidemiologic Research and Information Center, Veterans Affairs Puget Sound Health Care System, and Department of Epidemiology, University of Washington, Seattle, Washington, USA*
[2] *Vietnam Era Twin Registry, Seattle Epidemiologic Research and Information Center, Veterans Affairs Puget Sound Health Care System, Seattle, Washington, USA*

The accuracy of the zygosity classification in twin registers is essential for valid inference. The goal of this study was to evaluate zygosity classification in the Vietnam Era Twin (VET) Registry using DNA markers and construct an updated zygosity classification algorithm for all twins in the Registry. The VET Registry includes 7,369 male twin pairs who served in the military during the Vietnam era. In the late 1980's all twins completed a zygosity questionnaire that included 20 question items; military record information, including blood group, was also available for twin pairs. From in-person studies using the VET Registry twins in the period 1990–2009 DNA was available from 612 twin pairs. DNA microsatellite markers from 28 sites were obtained for each individual and concordance across all sites was used to classify zygosity. Logistic regression was used to construct predicted probabilities of DNA-based zygosity using items from the zygosity questionnaire. Twins were classified according to this new zygosity assessment and compared with the original zygosity assignment using measures of overall agreement, sensitivity, and specificity. The concordance of the original and DNA-based classification of zygosity was high ($k = .85$, $p < .0001$) sensitivity for monozygosity was 89.1% (96% CI 86.6-91.1) and specificity was 98.3% (95% CI 96.6–99.2). Errors in the original zygosity assignment were primarily due to monozygotic twins that were misclassified as dizygotic based on discordant military record blood groups. Removing the military record blood group data from the original zygosity classification markedly improved the accuracy of classification ($k = 0.95$, sensitivity = 97.5 (95% CI 96.0–98.4), specificity = 97.5 (95% CI 95.5–98.6)). Using the DNA-based zygosity prediction model an updated zygosity was assigned to all pairs in the Registry. In summary, zygosity assigned using responses to twin similarity questions was highly predictive of DNA-based zygosity. Augmenting zygosity classification using administrative data, from military or other records systems, should only be done with considerable caution.

UPDATING ZYGOSITY IN THE UNIVERSITY OF WASHINGTON TWIN REGISTRY

Jack Goldberg[1], Carolyn Noonan[2], Eric Strachan[3], Niloo Afari[4], Dedra Buchwald[5]
[1] *Center for Clinical and Epidemiologic Research and Department of Epidemiology, University of Washington and Vietnam Era Twin Registry, Seattle VA Epidemiologic Research and Information Center, Seattle, Washington, USA*
[2] *Center for Clinical and Epidemiologic Research, University of Washington, Seattle, Washington, USA*
[3] *Center for Clinical and Epidemiologic Research and Department of Psychiatry, University of Washington, Seattle, Washington, USA*
[4] *Department of Psychiatry, University of California, San Diego, CA, USA*
[5] *Center for Clinical and Epidemiologic Research and Department of Medicine, University of Washington, Seattle, Washington, USA*

The assignment of zygosity is essential for any twin registry. The University of Washington Twin Registry was created in the early 1990's as a unique community-based sample derived from drivers license records. Zygosity questions were included in a baseline survey administered to all twins in the Registry. These questions include: peas in a pod similarity and how often parents, relatives, teachers, and strangers have difficulty telling the twins apart. These self-reported questions were used to assign zygosity. Based on recently obtained biological markers we now evaluate and update our zygosity classification. The Registry has enrolled 3,192 twin pairs. Blood samples were collected from 188 same-sex twin pairs who participated in clinical studies using the Registry. These

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

samples were used to measure a series of highly polymorphic genetic markers. Concordance on these genetic markers was used to determine zygosity. A logistic regression model was developed to predict marker-based zygosity from the self-reported zygosity questions. The new zygosity classification is compared to the original zygosity assignment using measures of agreement, sensitivity and specificity. Using genetic markers we determined that 131 pairs were monozygotic and 57 pairs were dizygotic. Overall chance corrected agreement of the self-report zygosity assignment and the marker-based assignment was 96%. Our previous zygosity classification was 100% sensitive and 76% specific for monozygosity. The original and updated predicted probabilities of zygosity were highly correlated (r =.98). Our results indicate that zygosity assignment based solely on questionnaire data was highly accurate. A new marker-based prediction algorithm improves zygosity assignment and is now available to users of the Registry.

POPULATION CYTOGENETICS OF ABORTIONS AND VANISHING TWIN

H. K. Goswami, A. Rangnekar
Retired Professors of Genetics and Gynaecology & Obstetrics, Bhopal (MP), India

Twins and multiple births are universal and vary from 08 per thousand to 15 or more per thousand births. Triplets and multiple births vary from 1 to 2 per 100,000 births and even rare octuplets are also on records. Our studies during 1965–1992 had revealed that twinning is particularly more common and depends on mothers' genotype, age, consanguinity levels assisted by geographical and climatic factors. Pedigree studies revealed mother dependent predisposition for twinning because it is the mother who has to have all anatomical, immunogenetic and physiological carry-over biological load in order to defy many of the environmental factors. Father best role has to offer deleterious/defective gene free male gamete because in our population cytogenetic studies, fathers contributing a chromosome aberration cause recurrent abortions in more than 30% cases. Cytogenetic studies on 300 couples (G-banded metaphases) have indicated 48% fetal loss due to chromosomal aberrations. Two simple facts had emerged during, family surveys and hospital data (1965-1990s) that inbreeding status influences twinning as well as fetal loss (data on 3.4 million births). Mothers who sporadically bleed during 7–10 weeks of gestation yet continue pregnancy and deliver a normal child and or, also deliver twins/triplets also have sporadic bleeding during pregnancy (SBDP, Goswami, 1983). This was understood as a vanishing twin supporting demonstrable evidences of gynecologists where a missing sac was explicitly observed on ultrasound examination of the uterus/abdomen. Out of 18 couples studied wherein female parent had demonstrated vanishing twin, either of the parent has had shown hyperploid counts and chromosome translocations involving chromosome 1, 16 and marker dots (discovered by Goswami, 1986). Molecular cytogenetic studies can further explain on possible relationship with specific chromosomes triggering vanishing twin.

SOME TRIPLETS OFFER CO TWIN CONTROL STUDY AS EVIDENCE FOR MONOOVULAR DISPERMIC DIZYGOTIC TWINS

H. K. Goswami
Retired Professor of Genetics, Bhopal, India

Literature on twins and twinning has always indicated a possibility of third category of twins, that is, an ovum after release somehow gets divided in to two and both the ova get fertilized to produce twins. So practically, such co-twins will have preferential dominance of traits inherited from the mother, though these can be of different sex and show variables in paternal gene expressions because of two different sperms fertilizing the sister-ova. During our extensive field work and family studies we have had chosen a battery of three categories of traits (minimum 25 traits) for scoring concordance: (1) Biochemical tests include (i) OAB blood groups (ii) percentage of HbF (Foetal haemoglobin) as adjudged by cellogel electrophoresis and laser densitometer for quantitative estimation (Goswami et al., 2002); (2) Anthropometric traits include (i) Skin colour, (ii) Hair colour and curliness, (iii) Eye-colour, (iv) shape and size of the ear lobe/deformity (v) Tongue rolling (vi) tongue gliding (vii) tongue twisting (viii) polydactyly/syndactyly (ix) hairiness on face/limbs including hairy ear rims (if males above 20 yrs) (x) Tasting ability of PTC and or Mannose sugar; (3) Typical/special features in both parents: (i) presence of moles if anywhere, (ii) Forelock of hairs on frontal lobe (iii) Any personalized feature(s) in either parent which can not be casually seen or examined (e.g., a dark skin lesion on the back or thigh of melanosis of Ito). Since most of these 17 to 20 traits are autosomal and polygenic in inheritance their concordance to specific parental trait offer strong genetic support for their biased affinity. In such triplets, two cotwins express exact concordance for the maternal traits while the third one shows discordance for many. Even among three cotwins, one may differ in blood group and heredity persistence of foetal haemoglobin (HPFH). These co-twins cannot be monozygotic in origin because in that event, no biased concordance for many maternal genes and discordance for paternal would occur because MZ twins arise after fertilization. For compilation of tabulated data each trait was given 3 points for concordance and 1 point for discordance. Intrapair correlations indicated that there are certain twin pairs for whom we could opine with 95% confidence that they have expressed more genes from the mother than from the father. Earlier, Goswami (1978) had shown induction of amitotic divisions under the influence of oral contraceptive pills on plant root tip cells. So a question was included in the proforma for mothers' interview 'whether she had taken oral pills quite irregularly or any hormonal treatment'. Hormonal pills have positive correlation with such a possibility (Goswami, 1983). Follow up on only 07 triplets with their parents has extended validity for the battery of above tests. An hypothesis that an ovum soon after release may be amitotically divided into two, probably under the influence of hormonal impact, gets a plausible support.

TWINS WITH ORAL CLEFT IN DENMARK 1936–2004

D. Grosen[1], C. Bille[1], I. Petersen[1], J. Krabbe Pedersen[1], A. Skytthe[1], J. C. Murray[1,2], K. Christensen[1]
[1] *Research Centre for the prevention of Infant Mortality and Congenital Illnesses, Institute of Public Health, University of Southern Denmark, Odense, Denmark*
[2] *University of Iowa, Department of Pediatrics, Iowa City, USA*

Objective: To estimate the prevalence of isolated oral cleft (OC) among twins and compare it to the prevalence among singletons. To estimate the concordance rates and heritability for OC. *Design*: A population-based cohort study. *Setting*: Denmark. *Participants*: All twins (N = 207) and singletons (N = 7966) with isolated OC born from 1936 to 2004 in Denmark. The participants were ascertained by a linkage between The Danish Facial Cleft Database, The Danish Twin Registry and The Danish Civil Registration System. *Main outcome measures*: OC prevalence and prevalence proportion ratio (PPR) for twins versus singletons. OC concordance rates and heritability estimates for the twins. The analysis will be stratified for the sub-phenotypes: Cleft lip with cleft palate and cleft palate only. *Results*: The prevalence of OC for twins was 18.7 per 10,000 (95% confidence interval 16.3 to 21.5) and for singletons 16.6 per 10,000 (95% confidence interval 16.2 to 17.0) no statistically significant difference (PPR = 1.13 95% confidence interval 0.97 to 1.31). For the monozygotic twins we found the same pattern with a PPR = 1.29 (95% confidence interval 0.85 to 1.96) for the period 1968 to 2004. Significantly different (p < .001) concordance rates were found for cleft lip with or without cleft palate (50 % vs. 7.7% for mono- and dizygotic twins respectively). For cleft palate the concordance rates were 33% vs. 7.4% for mono- and dizygotic twins respectively, but not statistically significantly different (p = .1504). For both phenotypes the corresponding heritability estimates were above 90%. *Conclusion*: The similar prevalence for twins and singletons indicate that no special etiology is present for twins with OC. The concordance rates and heritability estimates show a very strong genetic component in OC etiology.

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

GENETIC AND ENVIRONMENTAL COVARIATIONS BETWEEN EMOTIONAL PROBLEMS AND CONDUCT PROBLEMS IN SOUTH KOREAN TWIN CHILDREN

N. Ha[1], M. J. Jin[1], S. Koo[1], O. Jo[1], B. Kim[1], K. Kim[1], J. Yoo[1], Y. W. Shin[1], M.-H. Hyun[1] & Y.-M. Hur[2]

[1] *Chung-Ang University, Republic of Korea*

[2] *Mokpo National University, Republic of Korea*

The present study investigated how genetic and environmental factors contributed to the relationship between emotional problems and conduct problems during childhood. Emotional Problems and Conduct problem scales were given to mothers of 603 pairs of South Korean twins (mean age= 8.5y, SD of age= 2.9y) by telephone interview. Phenotypic correlation between the two scales was 0.21 in the present sample. Univariate model fitting analyses indicated that while genetic, shared environmental, and nonshared environmental factors explained the variance of emotional problems, only shared and nonshared environmental factors were important in explaining individual difference in conduct problems. Bivariate model-fitting analyses showed that the phenotypic relationship between childhood conduct problems and emotional problems were completely explained by common shared environmental factors.

EFFECTS OF LI4 ACUPRESSURE ON LABOR PAIN IN THE FIRST STAGE OF LABOR

A. Hamidzadeh

Gynecology Department, Sahrood Medical Science University, Shahrood, Iran

The purpose of the present study was to determine the effect of LI4 acupressure on labor pain during the first stage of labor. A randomized controlled trial was performed on 100 parturient women who were randomly assigned to two groups. In the case group (n = 50), LI4 acupressure, and in the control group (n = 50) touch of this point, was performed. Data collected from the VAS (visual analogue scale) were used for analysis. Pain score was measured before, immediately after intervention, 20, 60 minutes after intervention and then each hour until delivery. The two groups were not significantly different regarding maternal age, gestational age, parity and gravidity, cervical dilatation and median pain score before intervention. Mean pain score was significantly lower among the case group compared to the control group at immediately after intervention, 20, 60 and 120 minutes after intervention (p = 0/001). LI4 acupressure was effective for decreasing pain in women during labor. LI4 acupressure can be an effective nursing management for women in labor.

GENOME WIDE STUDIES OF MYOPIA IDENTIFY ASSOCIATIONS ON CHROMOSOME 15

C. J. Hammond[1], P. G. Hysi[1], T. L. Young[2], A. Fernández-Medarde[10], D. A. Mackey[3,4], T. Andrew[1], A. M. Solouki[5,6], A. W. Hewitt[4], S. Macgregor[7], J. R. Vingerling[5,6], Y.-J. Li[2], M. K. Ikram[6], L. Y. Fai[8], P. C. Sham[8], L. Manyes[10], A. Porteros[10], M. C. Lopes[1], F. Carbonaro[1], S. J. Fahy[1], N. G. Martin[7], C. M. van Duijn[6], T. D. Spector[1], J. S. Rahi[9], E. Santos[10], C. C. W. Klaver[5,6]

[1] *Department of Twin Research and Genetic Epidemiology, King's College London, St Thomas' Hospital, London, United Kingdom*

[2] *Center for Human Genetics, Duke University, Durham, North Carolina, United States of America*

[3] *Lions Eye Institute, University of Western Australia, Centre for Ophthalmology and Visual Science, Perth, Australia*

[4] *Centre for Eye Research Australia, University of Melbourne, Royal Victorian Eye and Ear Hospital, Melbourne, Australia*

[5] *Department of Ophthalmology, Erasmus Medical Center, Rotterdam, the Netherlands*

[6] *Department of Epidemiology, Erasmus Medical Center, Rotterdam, the Netherlands*

[7] *Genetics and Population Health, Queensland Institute of Medical Research, Brisbane, Australia*

[8] *Department of Psychiatry, University of Hong Kong, Hong Kong, China*

[9] *MRC Centre of Epidemiology for Child Health, Institute of Child Health, University College London, Guilford Street, London, UK*

[10] *University of Salamanca, CIC-IBMCC (CSIC-USAL), 37007 Salamanca, Spain*

Myopia and hyperopia are at opposite ends of the continuum of refraction — the measure of the eye's ability to focus light — which is an important cause of visual impairment and which twin studies confirm is a highly heritable trait. We conducted a genome-wide association study in a cohort of 4,270 British Caucasians from the TwinsUK cohort, and identified polymorphisms in a large region on chromosome 15 in strong association with refractive error (best p = 7.9 × 10-8). These findings were validated in six other Caucasian adult cohorts with an overall 13,414 subjects (best combined p = 1.8 × 10-9). An additional locus on chromosome 15, reported by the Rotterdam Study, was replicated in the TwinsUK cohort. Both these results, associated with retinal signaling genes, show a biologically convincing and replicated association with myopia, and provide novel molecular mechanisms for further study of intervention to prevent the most common cause of visual impairment.

RELATIONAL COMPLEXITY MEASURES OF COGNITIVE PROCESSING: HERITABILITY AND ASSOCIATION WITH IQ

N. K. Hansell[1], B. P. Zietsch[1,2], N. G. Martin[1], D. Birney[3,4], G. Andrews[5], D. H. Shum[6], G. S. Halford[2,6], M. J. Wright[1]

[1] *Queensland Institute of Medical Research, Brisbane, Australia*

[2] *School of Psychology, University of Queensland, St Lucia, Australia*

[3] *School of Psychology, University of Sydney, Sydney, Australia*

[4] *Accelerated Learning Laboratory, University of New South Wales, Sydney, Australia*

[5] *School of Psychology, Griffith University, Gold Coast Campus, Australia*

[6] *School of Psychology, Griffith University, Mt Gravatt Campus, Australia*

We report results from the first genetic study of relational complexity (RC) measures of cognitive processing. RC theory proposes that many higher cognitive processes (e.g. reasoning, language comprehension, and memory operations) can be characterized as involving complex relations and RC is defined as the number of independent sources of variation that are related in a single step of a cognitive task. The RC metric applies to conscious, controlled processing, and in terms of Baddeley's working memory model, relational processing corresponds most closely to the computational functions of the central executive. Data have been collected on three RC tasks (Latin Squares, Nterms Task, and Sentence Task) on approximately 230 twin pairs. Preliminary results show good correlations with full-scale IQ and suggest moderate heritability.

TWINS BORN FOLLOWING ASSISTED REPRODUCTIVE TECHNOLOGY: PERINATAL OUTCOME AND ADMISSION TO HOSPITAL

M. Hansen[1], L. Colvin[1], B. Petterson[1], J. J. Kurinczuk[2], N. de Klerk[1], C. Bower[1]

[1] *Centre for Child Health Research, Telethon Institute for Child Health Research, The University of Western Australia, Australia*

[2] *The National Perinatal Epidemiology Unit, University of Oxford, UK*

Compared with spontaneously conceived (SC) singletons, adverse perinatal outcome, neonatal intensive care unit (NICU) admission and hospital admission in infancy are more common in those born following Assisted Reproductive Technology (ART). Similar comparisons for twins have shown conflicting results. We used record linkage between four population based health registers to investigate perinatal outcome and hospital admission during the first 3 years of life for all twin children born in Western Australia between 1994 and 2000 [700 ART and 4097 SC]. ART twins had a greater risk of adverse perinatal outcome including preterm birth, low birthweight and death compared with SC twins of unlike-sex. In their first year of life, ART twins had a longer birth admission were 60% more likely to be admitted to a NICU and had a higher risk of hospital admission. The increased risk of hospital admission continued in the second and third year but was not statistically significant in the third year. Couples undertaking ART should be aware that in addition to the known increased perinatal risks associated with a twin birth, ART twins are more likely than SC twins to be admitted to a NICU and hospitalized in the first 3 years of life.

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

SOURCES OF EPIGENETIC VARIATION IN THE MHC

J. R. Harris[1], K. Gervin[2], G. Gilfillan[2], H. E. Akselsen[2], M. Hamerø[2], R. Moe[2], H. Gjessing[1], D. E. Undlien[2,3], R. Lyle[2]

[1] *Division of Epidemiology, Norwegian Institute of Public Health, Oslo, Norway*

[2] *Department of Medical Genetics, Oslo University Hospital, Oslo, Norway*

[3] *Institute of Medical Genetics, Faculty Division Ullevål University Hospital, University of Oslo, Oslo, Norway*

Epigenetics refers to changes in gene expression arising from factors not coded in the DNA sequence. DNA methylation is an important epigenetic mechanism for development and phenotypic expression. Disturbances in DNA methylation leading to aberrant gene expression have been implicated in the etiology of many diseases, and variation in DNA methylation may also contribute to the risk of common disease. Whereas genetic variation at the sequence level (SNPs and CNVs) has been studied extensively, little is known regarding the extent and function of epigenetic variation. It may arise due to stochastic processes, genetic influences or environmental factors. Thus, understanding the causes of methylation will help elucidate disease etiology and could provide a 'window' for understanding environmental effects by revealing where modifications of the DNA may have occurred in response to specific experiences or exposures. Findings indicate an age-related divergence in the epigenome of identical twins. This was more pronounced among pairs who had different lifestyles, and gene expression correlated with these epigenetic differences[1]. This study uses a twin model to explore genetic and environmental influences on epigenetic variation in the classical human Major Histocompatibility Complex (MHC). A major strength of our study is that we have isolated and biobanked different lymphocyte subpopulations (CD19+, CD8+, CD4+ and CD4+CD25+) from identical (MZ) and fraternal (DZ) twin pairs. Here, we report results from analysis of CD4+ cells using data from healthy Norwegian twins including 49 MZ and 40 DZ pairs. Bisulphite sequencing was conducted of 1670 individual CpG sites distributed in 176 regions in the MHC. The regions sequenced include CpG islands, the 5'end of genes and non-coding conserved regions. Variation in DNA methylation was considerable, both between and within regions. Heritability of this variation is low: ~6% for individual CpGs and ~11% for amplicons. Estimats of heritability varied for different regions of the genome, with the 5' prime region of genes having higher heritability (16%) than either CpG islands (6%) or conserved non-coding regions (11%). Our data suggest modest genetic influences on DNA methylation variation.

1. Fraga MF, Ballestar E, Paz MF, et al. Epigenetic differences arise during the lifetime of monozygotic twins. Proc Natl Acad Sci USA 2005 102(30): 10604–9.

OBESITY IN ADULTHOOD: INTERPLAY BETWEEN NATURE AND NURTURE

A. L. Hasselbalch

Institute of Preventive Medicine, Copenhagen University Hospitals, Copenhagen Capital Region, Denmark

Both between and within societies, large variation in the prevalence of overweight and obesity exists. This variation is caused by differences in environmental exposures as well as genetic differences between individuals, resulting in differentiated susceptibility to environmental exposures. The evidence for genetic influence on anthropometry has previously been established and has been estimated to be 60–70% based on twin studies. These inter-individual differences can, however, not explain the increase in obesity prevalence during the past 70 years. Environmental factors must therefore play an important role in the obesity epidemic. Habitual diet is one of many environmental factors that potentially contribute to the inter-individual differences in body fat mass, but although extensively studied, only limited evidence for associations between habitual dietary intake and anthropometry exists. Differences in habitual dietary intake are also partly determined by differences in genes influencing, i.e., smell and taste preferences. But, so far, only few studies have investigated genetic influences on dietary intake in adults and the interplay between diet, genes and obesity. The proportion of variation in dietary intake explained by variation in genes differs between the dietary traits under study but for the majority of dietary variables the genetic influence is estimated to be in the range of 20–50%. One reason for the difficulties in detecting associations between diet and anthropometry could be that genetic background influences both the exposure variable — diet, as well as the outcome variable — anthropometry, and thereby works as a confounder on the association. Twin data offer a unique opportunity to study the complex interplay between genes, diet and anthropometry either by using models like the gene-environment interaction model or by focusing on differences within the monozygotic twin pairs in order to control for potential confounding by genetic variation and shared environment on the association between habitual diet and body fat.

GUANGZHOU TWIN REGISTRY AND GUANGZHOU TWIN EYE STUDY

M. He

State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-Sen University, Guangzhou, China

The Guangzhou Twin Registry, initiated in 2005, is a population-based registry of twins born between 1987 and 2000. To date, over 9700 pairs of twins, regardless of their health and medical history, were enrolled in the database using the Official Household Registry of Guangzhou City. The twins were subsequently verified by door-to-door visits based on the registry address. The primary goal of this registry is to develop a resource for genetic epidemiological studies on common diseases in the southern Chinese population. The initial focus is to distinguish the genetic and environmental determinants of eye diseases, in particular myopia and glaucoma. About 700 pairs of twins living close to the Zhongshan Ophthalmic Center were examined for the first phenotyping examination, questionnaire administration and DNA collection in 2006. An annual eye examination and other phenotype data collection were carried out for up to 2009 and scheduled for at least 5 years follow up in order to investigate the changes in phenotypes including the myopia progression, physical development and other general health phenotypes. Recruitment and examination of adult twins aged 50 years and over is underway in the same city. The investigation on eye diseases (Guangzhou Twin Eye Study) has produced more than 10 publications in the top Ophthalmology peer-review journals.

HERITABILITY OF BLOOD PRESSURE AND ITS LONGITUDINAL CHANGES IN CHILD AND ADOLESCENT CHINESE TWINS

M. He

State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-Sen University, Guangzhou, China

Purpose: To estimate the genetic and environmental effects on systolic blood pressure (SBP) and diastolic blood pressure (DBP) and 3-year changes in Chinese twins aged 6 to 19 years. *Methods:* Twins aged 6 to 19 years were recruited from the Guangzhou Twin Registry and the data on blood pressure were collected with a standard digital blood pressure monitor (Omron, HEM713C, Tokyo) between 2006 to 2009. Zygosity for all same-sex twin pairs was ascertained by 16 multiplex STR (powerplex 16 system, Promega) and zygosity in opposite-sex twin pairs was considered as dizygotic without a need for genotyping. Heritability was estimated using a univariate structural variance component genetic model in cross-sectional analysis and a bivariate Cholesky model in longitudinal changes using the Mx program. *Results:* 1024 pairs (652 MZ and 372 DZ) of twins participated in the study and provided cross-sectional data for BP averages and heritability estimates. Of these, 450 pairs (259 MZ and 161 DZ) also participated in the study in 2006, providing data on 3-year longitudinal BP changes. Based on cross-sectional data, the age- and sex- adjusted intraclass correlation coefficients (ICC) between twin pairs were .60 for SBP and .47 for DBP in MZ, while these figures were .31 and .37 in DZ. Additive genetic variance and unique environmental variance estimates in the

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

best-fitting models were .56 (95%CI: .52–.61) and .44 (95%CI: .39–.49) for SBP and .46 (95%CI: .40–.51) and .54 (95%CI: .49–.60) for DBP. The phenotypic correlation between SBP at 2006 and SBP at 2009 was .48 but reduced to .39 after adjusting for age, sex and their interaction. These figures for DBP were .34 and .27. Bivariate Cholesky model-fitting analyses suggested that 57% of the SBP and 59% of DBP correlation was attributable to shared genetic effects. Shared random environmental factors were not detected. *Conclusions:* The estimated heritability for blood pressure is similar to what has been reported in Caucasian and African population. The longitudinal changes of blood pressure are largely determined by shared genetic effects.

LATEST RESULTS FROM THE GUANGZHOU TWIN EYE STUDY

M. He

State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-Sen University, Guangzhou, China

The Guangzhou Twin Registry, initiated in 2005, is a population-based registry of twins born between 1987 and 2000. To date, over 1200 pairs of twins aged 7 to 15 years, as well as their parents, were examined. The zygosity of all same-sex twin pairs was determined by 16 multiplex STR genotyping (Powerplex 16 system, Promega, Madison) while the zygosity in opposite-sex twin pairs was considered as dizygotic. The enrolled twins were examined annually for the traits potentially with progression. A wide range of traits related to eye diseases were collected. In this symposium, we will briefly summarize the major findings on heritability of refractive error (myopia) and its longitudinal changes, the transmission of genetic and environmental effects from parents to children, as well as the recent work on genome-wide association study.

ADOLESCENT TWIN RELATIONSHIPS: EVIDENCE FOR CHANGE IN HERITABILITY OVER TIME

P. Heath[1], M. K. Vendlinski[1], N. L. Schmidt[1], K. Lemery-Chalfant[2], H. Hill Goldsmith[1]

[1] *Waisman Center, Department of Psychology, University of Wisconsin-Madison, Madison, Wisconsin, USA*

[2] *Department of Psychology, Arizona State University, Tempe, Arizona, USA*

This study examines the heritability of facets of adolescent twin relationships and interpersonal experience at two ages. The Twin Inventory of Relationships and Experiences (TIRE) was administered to monozygotic (N = 242) and same-sex dizygotic (N = 222) twins participating in the Wisconsin Twin Project (mean age = 14.2yrs). A subsample of twins (MZ N = 144, SSDZ N = 102) was tested approximately 2 years later (mean age = 16.1yrs). The TIRE assesses child relationship patterns with parents, the co-twin, and peers across 10 factors: 5 parent factors (negative parenting, positive parenting, differential parental criticism, mother preference, and father preference), 3 co-twin factors (closeness, quarrels/fights, and dominance), and 2 peer factors (peer conduct problems and differential peer conduct problems). At age 14, twin report yielded moderate heritability estimates for one parenting factor, negative parenting (h^2 = .58), and two co-twin factors, dominance (h^2 = .66) and closeness (h^2 = .26). Heritability estimates were weak for the remaining 7 factors (h^2 < .15). At age 16, heritability estimates changed in several notable ways. Heritability for negative parenting was lower (h^2 = .36) in the older age group. The father preference factor, with estimated heritability near zero at age 14, showed higher estimated heritability in older adolescents (h^2 = .56). Heritability for twin dominance and closeness was negligible at age 16. Finally, one peer relationship factor, peer conduct problems, was substantially heritable (h^2 = .62). Heritability estimates were weak for the remaining 5 factors (h^2 < .15). In most cases, heritability decreased over time. There was a modest reduction in heritability over time for negative parenting, suggesting that while environment plays a stronger role in negative parenting for older children, features of the child continue to influence the negative parenting factor. This is inconsistent with previous research suggesting that heritability of parent-child relationship factors increased with age [McGue, M. et al., 2005, *Develop Psych, 6,* 971–984]. Consistent with previous literature, two factors exhibited substantial increase in estimated heritability: Father preference and peer conduct problems. Previous literature suggests adolescents likely choose friend groups who share heritable behaviors like conduct problems leading to high heritability estimates for aspects of peer relationships [Pike, A. & Eley, T.C., 2009, Journal of Adolescence, 32, 519–533]. Before presentation we will examine whether the heritability of TIRE dimensions is moderated by age.

A CLOSER LOOK AT THE DEVELOPMENTAL ETIOLOGY OF HIGH IQ

J. Hewitt, A. Brant, R. Corley, S. Wadsworth, J. DeFries

Institute for Behavioral Genetics, University of Colorado, Boulder, USA

Recent twin and family studies have found that, in magnitude of genetic and environmental effects, the etiology of high IQ is similar to that of individual differences in the normal range (Haworth et al., 2009, *Behavior Genetics, 39*, 359–370; Kirkpatrick et al., 2009, Behavior Genetics, 39: 409–416). Our own longitudinal analysis of twins studied from infancy to young adulthood (age 1–16; Colorado LTS) also suggests that the etiology of developmental stability and change is also common to the entire IQ distribution (Brant et al., 2009, *Behavior Genetics, 39,* 393–405). We extend our analyses here to include biological and adoptive siblings from the Colorado Adoption Project. The sample consists of 1058 sibling pairs (266 MZ pairs, 219 DZ twin pairs, 335 biological siblings pairs and 240 adoptive siblings pairs) and allows consideration of the contributions made by twin specific environments, nonadditive genetic influences and assortative mating to variation in the phenotype. The longitudinal nature of the sample allows for examination of stability and change in etiological influences over time and ability level. Results bolster those previously reported for the twin sample, with broad heritability increasing over time and overall shared environmental effects decreasing. When the sample was classified into those with high IQ (above the 85th percentile) and those in the normal range (below the 85th percentile), estimates of variance components were not significantly different from those for the entire distribution. Implications for sample selection in gene-finding efforts and possible explanatory mechanisms for the pattern of results are discussed.

CANCER IN DANISH TWINS: ENVIRONMENTAL AND GENETIC FACTORS

J. V. B. Hjelmborg[1], A. Skytthe[2], T. Martinussen[1], K. Christensen[2], K. O. Kyvik[3], N. V. Holm[2,4]

[1] *Institute of Public Health, Department of Biostatistics, University of Southern Denmark*

[2] *Institute of Public Health, Epidemiology, University of Southern Denmark*

[3] *Institute of Regional Health Services Research, University of Southern Denmark*

[4] *Department of Oncology, Odense University Hospital, Denmark*

In 2000, a collaborative study among the Danish, Swedish, and Finnish Twin Registries demonstrated that environmental factors played a major role in the causation of cancer, although a relatively larger than expected heritability for a few specific sites, such as breast, colorectal, and prostate cancer was demonstrated. However, the Danish contribution in that study was limited to birth cohorts 1870 to 1930. With a recent linkage of the Danish Twin Registry with the nationwide cancer Danish Cancer Registry the number of twins with a cancer diagnosis has increased 4-fold from 3,572 twins to 14,134 twins. The linkage included all birth cohorts in the Danish Twin registry (1870-2004) and covered cancers diagnosed 1943 through 2006. Preliminary results for female breast cancer confirm the role of genetic factors with of concordance rates of .21 for monozygotic twins and .12 for dizygotic twins. For prostate cancer the concordance rates were .21 and .06 for monozygotic and dizygotic twins respectively. Based on statistical modeling we will be present estimates of the relative importance of genetic and environmental factors to the causation of cancer for these and other major sites.

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

MODELING TIME-VARYING GENETIC INFLUENCE

J. Hjelmborg[1], T. Martinussen[1], M. Gerster[1], C. Fagnani[2], J. Kaprio[3]
[1] *Institute of Public Health, Department of Biostatistics, University of Southern Denmark*
[2] *National Centre of Epidemiology, Surveillance and Health Promotion—Italian Institute of Health, Rome, Italy*
[3] *Department of Public Health, University of Helsinki, Helsinki, Finland*

We present a flexible method for studying time-varying genetic influence using longitudinal twin data. In many studies longitudinal responses and covariates are measured in twin pairs for the purpose of quantifying how the variation due to genetic effects may vary over time. Several approaches have been taken exploiting various structures of the data (e.g. multivariate and growth curve models). We adapt dynamic point process models allowing for flexible time-representation and measurements at any time; for example, age at measurement, which forms the basis for modeling time-dependent within pair correlations and further time-varying heritability. Simulations indicate that the method is feasible for detecting various patterns of time-varying genetic influence from samples comparable in size and number of measurements to those used in other studies. The method is applied to Finnish longitudinal BMI data and we investigate how the pattern of genetic influence might vary from young to middle aged adults.

MACULAR CHARACTERISTICS IN OLDER TWINS

R. E. Hogg
Queens University, Belfast, United Kingdom

Age-related macular degeneration (AMD) is a devastating condition that results in a profound loss of central vision. AMD is traditionally categorized into early (drusen and pigmentary irregularities) and late (geographic atrophy, choroidal neovascularization (CNV) and disciform scarring) stages on the basis of retinal morphology. Various features have been associated with the early stages of the disease such as increased fundus auto fluorescence (FAF) and decreased macular pigment. Identifying the mechanisms that underlie such age-related traits poses several challenges. Firstly, such changes tend to lie along a continuum complicating the distinction between normal ageing and early pathology. Secondly, the etiology of AMD is known to be multifactorial involving a complex interplay between genetic predisposition, systemic factors and environmental exposure. We used a classical twin study in an attempt to disentangle such influences. All MZ and DZ twin pairs over the age of 50 enrolled on the Australian Twin Registry (ATR) were invited to take part. Each twin underwent a standard questionnaire including detailed medical and dietary histories, a comprehensive eye examination and intra-ocular photography. Some twin pairs without evidence of advanced AMD also had FAF photographs taken from which the peak macular pigment density(PMPD), spatial distribution of macular pigment(SpMPD) and difference in fundus auto fluorescence(termed MSE or mean standard error) between twin pairs was derived. When comparing PMPD within pairs a significantly higher correlation was found within MZ pairs as compared to within DZ pairs, represented by Pearson correlations (r) of 0.99 (95% CI 0.93–1.00) and 0.22 (95% CI –0.34–0.71) respectively indicating a strong genetic component. SpMPD was similar for MZ and DZ twin pairs (p = 0.551 mean difference, 0.047 ± 0.079). SpMPD showed a slightly higher correlation within DZ twin pairs (r = 0.63 95% CI 0.32–0.83) than MZ twin pairs (r = 0.48 95% CI –0.02–0.83), although this difference was not statistically significant, thus unlikely to be heritable. MSE levels were significantly higher in DZ (OD, 52.09 ± 8.753 OS, 50.9 4 ± 9.833) than MZ (OD, 40.76 ± 7.806 OS, 41.89 ± 8.239) twins, implying that factors associated with FAF levels are more likely to be environmentally driven rather than genetic. Twin studies therefore provide a powerful experimental paradigm by which to investigate the complex relationships involved in age-related disorders.

INFERENCE ON CAUSATION FROM ELIMINATION OF FAMILIAL CONFOUNDING (ICE FALCON)

J. L. Hopper
Centre for Molecular, Environmental, Genetic and Analytic Epidemiology, School of Population Health, The University of Melbourne, Victoria, Australia

Inference on Causation from Elimination of FAmiliaL CONfounding (ICE FALCON) is an approach to the analysis of data for pairs of traits measured for pairs of related individuals that tests the hypothesis that at least part of the association between two traits is due to a causal relationship. It is well known that finding an exposure to be associated with a disease or condition does not of itself prove that the exposure is a cause; the exposure could be associated with the real cause. For example, people who smoke tend also to be drinkers, and vice versa. Therefore, if smoking causes lung cancer there will also be an association between alcohol consumption and lung cancer that is not causal. This is called 'confounding'. We make inference about causation by trying to eliminate it. We do this by considering smoking and alcohol consumption together as predictors of lung cancer; if smoking is causal we should find that there is no association between drinking and lung cancer once smoking has been taken into account. The same principle applies in Ice Falcon, only this time we study the association between a person's outcome (e.g., disease) and both their own exposure and the exposure for their twin. If an exposure is causal, and correlated in pairs of relatives, then a person's risk of the disease will depend on their relative's exposure. For example, if the disease is breast cancer and the exposure is having a high-risk mutation in a breast cancer susceptibility gene like BRCA1 or BRCA2, then a woman who has a sister who carries a mutation is at increased risk (because she has a probability ½ of being a carrier as well). However, if one knows the exposure of the woman herself, in terms of her breast cancer risk it becomes irrelevant what her sister's status is for that exposure. That is, we make inference about causation, this time by trying to eliminate *familial* confounding. We have developed a regression approach that fits a person's outcome (Y_{self}) against one or both of their own exposure (X_{self}) and/or their relatives' exposure ($X_{relative}$). The method will only work if X_{self} and $X_{relative}$ are correlated – so if this method is Applicable a twin design is the most appropriate. It is straightforward to allow for Y_{self} and $Y_{relative}$ to be correlated; for example, if Y is continuously distributed, by using a bivariate normal model (and perhaps a suitable transformation) and fitting the correlation. The method can also be applied if Y is a binary or ordinal variable by using a suitable generalised linear modelling. We will demonstrate application of this approach to outcome and exposure data for twin and sibling pairs, and also to repeated/longitudinal measures for the same individual. It can also be applied when X is a measured genetic variant, either rare as in the example above or common, and has the potential to help resolve issues about the clinical significance of so-called 'unclassified variants'. This method might open up twin research to a new group of researchers.

AUSTRALIAN TWIN REGISTRY — REALISING THE FULL POTENTIAL OF RESEARCH INVOLVING TWINS TO IMPROVE THE HEALTH AND WELLBEING OF ALL AUSTRALIANS

J. L. Hopper, D. Foley, N. de Klerk, J. Boadle
Australian Twin Registry, University of Melbourne, Melbourne, Australia

The Australian Twin Registry (ATR) was established in the late 1970s as a national volunteer registry of Australian twin pairs of all zygosity types and ages who are willing to consider involvement in health and medical research studies. As an openly shared resource, the ATR provides researchers with access to an established infrastructure and a network of scientists and administrative staff who are experienced in twin research. The ATR does not undertake research itself but acts as facilitator. The ATR's core functions are:

- maintenance of an up-to-date database containing contact details and baseline information for twin members willing to participate in research

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

- collaboration with researchers applying to the ATR to ensure that projects are of significant scientific merit and are appropriately described to ensure the ability of potential participants to provide informed consent
- judicious management and administration of approach to eligible twin members to inform them of a new research project, determine their interest in participation, and seek their permission to release their contact details to the researcher
- governance of the ATR in a fair, transparent and equitable manner.

Supported 2010–14 by an Australian National Health and Medical Research Council (NHMRC) Enabling Grant the ATR has facilitated more than 450 studies producing 586 peer-reviewed publications using a variety of designs including classic biometrical twin and twin family studies, co-twin control studies, intervention studies, longitudinal studies, and studies of issues relevant specifically to twins. The ATR currently holds details for 35,970 sets of twins and triplets. Of these 27,674 (76.9% — 27,473 twin sets and 201 triplet sets) are currently willing to be involved in research studies. The membership consists of 7,757 active junior sets (< 18 years) and 19,917 active senior sets (=> 18 years), and include all sex and zygosity twin types, from all states and territories in Australia. Current studies utilizing the ATR are run by a wide range of local and overseas researchers. Australian and international researchers, with an Australian collaborator, are welcome to apply to access the facility. Information on how to apply can be found at *www.twins.org.au* or by emailing *admin@twins.org.au*.

HERITABILITY OF LUNG FUNCTION: A TWIN STUDY AMONG NEVER-SMOKING ELDERLY WOMEN

M. Hukkinen[1], J. Kaprio[1,2], U. Broms[1], A. Viljanen[3], D. Kotz[4], T. Rantanen[3], T. Korhonen[1]

[1] *Department of Public Health, University of Helsinki and National Institute for Health and Welfare, Helsinki, Finland*

[2] *Department of Public Health and Institute of Molecular Medicine, University of Helsinki and National Institute for Health and Welfare, Helsinki, Finland*

[3] *Gerontology Research Center, Department of Health Sciences, University of Jyväskylä, Jyväskylä, Finland*

[4] *CAPHRI School for Public Health and Primary Care, Maastricht University Medical Centre, Maastricht, the Netherlands*

Most studies on heritability of lung function have been conducted in smokers and nonsmokers using cross-sectional study design. However, smoking patterns may confound the contribution of genetic factors. We investigated heritability of forced expiratory volume in one second (FEV1) and forced vital capacity (FVC) longitudinally, excluding the effects of smoking. Initially the sample included 217 female twin pairs aged 63–76 years, ever-smoking prevalence being about 14%. Questionnaire data were collected and medical examination and laboratory measurements, including spirometry, were performed at baseline in 2000 and at follow-up, in 2003. Bivariate structural equation modeling, restricted to never smokers with adequate spirometry performance (n = 339), was used to estimate genetic and environmental influences on two consecutive measurements of FEV1 and FVC, respectively. Also correlations between baseline and follow-up estimates were calculated. Genetic modeling was conducted using age, BMI, physical activity and lung health as covariates. Pairwise correlations suggested that genetics explain a significant proportion of the variance in FEV1 and FVC. The best fitting quantitative genetic models included additive genetic and nonshared environmental effects (AE model). Heritability estimates of 32% and 36% for FEV1 while 41% and 37% for FVC were found at baseline and at follow-up, respectively. The genetic correlation between the FEV1 heritability estimates approached unity, whereas the correlation between FVC estimates was 0.80. In never-smokers one-third of the variation in FEV1 and FVC is explained by additive genetic and two-thirds by nonshared environmental effects. Genetic effects on FEV1 are common to consecutive measurements, whereas FVC is affected by genetic innovations at follow-up. Thus, along ageing no new genes would emerge influencing the observed variance in FEV1 whereas FVC appears to be affected by new genes that become significant in a relatively short time scale and explain as much as 14% of total variance at follow-up.

HOW TO PROVIDE IT SUPPORT FOR A RELIABLE BIOBANK – EXPERIENCES FROM THE DANISH TWIN REGISTRY

L. Hvidberg

Institute of Public Health, University of Southern Denmark, Odense C, Denmark

The biobank system (containing approx. 300,000 single fractions of biological material from 35,000 participants in 38 different cohort studies) is one of the crucial pillars in our Health Research Support System. The other pillars are: project, participant, phenotype and genotype systems. The vision for the Health Research Support System is to assist the ongoing research by managing projects, project participants, biological material, data from questionnaires and surveys, and genotype data. The system must be accessible for various research groups but without compromising the security. The individual groups must be able to see only their own projects and the biological materials and data belonging to these projects. The biobank system has been created as a bank, in which you can deposit biological material (blood, blood spots, hair, saliva, urine etc.) into an account (named a biosurvey). Subsequently the material can be purified, transferred to another biosurvey, or withdrawn from the biosurvey if it is being sent to another research group or laboratory. The data model of the biobank consist of 3 components:

1. Account description (biosurvey)
   - To which project does the account belong?
   - What types of samples (blood, hair etc.) are coming in?
   - Into what types of purifications/extractions are these samples to be divided?

   The basic principle is that the types of samples are not intermingled in the boxes, i.e. one box contains only one type (e.g., serum, plasma, hair or DNA).
2. Freezer administration
   - What closets (freezers, shelving units, filing cabinets) are available? What type of drawers and how many drawers are there room for and where are they situated?
   - What drawers (racks, shelves, drawers) are available? What types of boxes and how many boxes are there room for and in which closet is it situated?
   - What boxes (boxes, binders) are there? What types of tubes and how many tubes are there room for and in which drawer is it situated?
   - What tubes (tubes, envelopes, plastic pockets) are available? In which box is it situated?
3. Withdrawal management
   - To which project is the withdrawal linked?
   - From what samples do we need a withdrawal and how much?
   - Where should the extraction be sent to?

NEUREGULIN 1 ASSOCIATION WITH NICOTINE DEPENDENCE

K. Jackson, J. Chen, K. S Kendler, X. Chen

Virginia Institute for Psychiatric and Behavioral Genetics, and Department of Psychiatry Virginia Commonwealth University, VA, USA

Smoking is highly comorbid with many mental disorders, the most significant ones are schizophrenia, bipolar disorder and major depression. Neuregulin 1 (NRG1) is a leading candidate for schizophrenia, however, its role in smoking and nicotine dependence (ND) is not clear. The aim of this study is to examine if variants in the NRG1 gene are associated with ND. We first tested the association of SNP markers with ND, the Fagerström Test for ND (FTND) and the number of cigarettes smoked per day (numCIG) in the control subjects of the study of molecular genetics of schizophrenia supported by the genetic association information network (MGS-GAIN) and MGS-nonGAIN samples, and selected four representative SNPs to be replicated in selected subjects from the Virginia Adult Twin Study of Psychiatric and Substance Use Disorder (VA-Twins). Of the 4 markers tested, rs2976514 showed significant association in the

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

VAT-twins (ND, p = .0077 FTND, p = .0132). If we consider the phenotypes are correlated and we correct only for 4 markers tested, then this marker reaches experiment-wide significance.

OPPOSITE SEX TWINS AND ITS EFFECT ON REPRODUCTIVE HEALTH AND REPRODUCTIVE BEHAVIOR

S. Jahanfar

Royal College of Medicine, Perak; University Kuala Lumpur; No 3 Greentown St., Ipoh, Perak, Malaysia

Introduction: Hypotheses on uterine position effect suggest that diffusion of steroid hormones from one fetus to another through direct transfusion or through fetal membrane, placenta or amniotic fluid could cause similarities in terms of hormonal balance. Twins are in a unique position to prove or disprove this hypothesis. Our objective was to test the hypothesis that female same sex and female opposite sex twins differ with respect to anthropometric measurements, reproductive events and reproductive health behavior. *Method:* One hundred and ninety three monozygotic and dizygotic twins were recruited from two Iran and Malaysia twin database. This sample was inclusive of 176 female-female twins and 17 female with male twins. Reproductive events and behavior were asked though a telephone interview. *Results:* Same-sex twins had a higher risk of gynecological problem, and irregular menstruation than opposite sex twins. Other reproductive events were not found to be significantly different between the two groups indicating that hormonal transition from male to female may not be a valid explanation for reproductive ill health. *Conclusion:* Our study was unique in comparing specific reproductive events in terms of twin gender. Hormonal interactions claimed to influence female was not seen on reproductive events and behavior studied in our opposite sex twins. Further studies can compare opposite gender twins who shared a placenta during intrauterine life with those who had separate placentas.

FETAL ORIGIN HYPOTHESIS AND REPRODUCTIVE HEALTH OF TWINS

S. Jahanfar

Royal College of Medicine, Perak; University Kuala Lumpur; No 3 Greentown St., Ipoh, Perak, Malaysia

Objective: The fetal origins hypothesis suggests that conditions, such as nutritional, program the fetus for the development of chronic diseases in adulthood. Since low birthweight is the general manifestation of twining, it is logical to hypothesize that twins may suffer from ill health. This study aimed at testing the hypothesis that low birthweight twins and normal birthweight twins differ with respect to reproductive events and anthropometric measurements. *Study Design*: This is a cross sectional and observational study. A group of registered twins were interviewed to obtain their birthweight and reproductive history. They were then divided into two groups of low birthweight (n = 87) and normal birthweight (n = 43). Descriptive and comparative statistical analysis were employed considering p = .05 as the significant level. *Result*: Normal birthweight group had a significantly higher mean of adulthood weight (59.77 ± 10.69) when compared with low birthweight (52.78 ± 7.64) (p = .001). Premenstrual symptoms were found more frequently among normal birthweight group (25% vs. 16.7%; p = .03). No other reproductive health variable was found to be significantly different within the two groups. *Conclusion*: Our data does not support the fetal origin theory as none of the reproductive illnesses was found to be higher among low birthweight twin infants.

ETIOLOGY OF OBSESSIONS AND COMPULSIONS: A BEHAVIORAL-GENETIC ANALYSIS

K. L. Jang[1], S. Taylor[1], G. J. G. Asmundson[2]

[1] *Department of Psychiatry, University of British Columbia, Canada*

[2] *Department of Psychology, University of Regina, Canada*

It is unknown whether major subtypes of obsessive-compulsive (OC) symptoms have genetic and environmental factors in common with one another. Also unknown is whether these symptoms are etiologically related to the general tendency to experience emotional distress (negative emotionality). A further issue to be resolved is whether hoarding is etiologically related to other putative OC symptom subtypes. To investigate these issues, a community sample of 307 pairs of monozygotic and dizygotic adult twins yielded scores on six candidate OC symptom subtypes (obsessing, neutralizing, checking, washing, ordering, and hoarding) and two markers of negative emotionality (trait anxiety and affective lability). Genetic factors accounted for 40 to 56% of variance in the eight phenotypic scores (M = 49% variance across the six OC symptom subtypes). Remaining variance was due to nonshared environment. Scores on each phenotype were also decomposed into genetic and environmental factor scores representing, respectively the importance of genetic or environmental factors in shaping a person's phenotypic score. Factor analyses of genetic scores indicated that OC symptoms (including hoarding) and negative emotionality are shaped by a common genetic factor. Factor analyses of the environmental scores indicated two factors one influencing all OC symptoms (including hoarding) and the other influencing obsessions and negative emotionality. Heritabilities and factor structures were largely replicated in subsamples of probands with comparatively severe OC symptoms. The variance due to genetic factors did not vary with age or sex. Gene-environment interactions were identified. Implications for delineating the etiologic architecture of OC symptoms and for diagnostic classification are discussed.

THE DOPAMINE TRANSPORTER GENE (DAT1) POLYMORPHISM IS ASSOCIATED WITH PREMATURE EJACULATION

P. Jern[1], P. Santtila[1], L. Westberg[2], H. Walum[3], C. T. Pedersen[2], E. Eriksson[2], N. K. Sandnabba[1]

[1] *Center of Excellence in Behavior Genetics, Department of Psychology, Åbo Akademi University, Turku, Finland*

[2] *Department of Pharmacology, Institute of Neuroscience and Physiology, University of Gothenburg, Gothenburg, Sweden*

[3] *Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden*

Previous research has suggested brain dopamine (DA) neurotransmission to be involved in the control of ejaculation. Furthermore, quantitative genetic studies indicate a partly hereditary background to premature ejaculation. The aim of the present study was to investigate whether the dopamine transporter gene (DAT1) polymorphism is associated with premature ejaculation. Retrospective self-reports of four indicators reflecting ejaculatory function — anteportal ejaculation, number of penile thrusts, ejaculation latency time, and feeling of control over ejaculation — and saliva samples for DNA analysis were obtained from 1,290 men aged 18–45 years (M = 26.9, standard deviation = 4.7) with sexual experience. Calculations of allelic effects were computed using the Generalized Estimating Equations module of SPSS 17. Carriers of the 10R10R genotype had scores indicating a lower threshold to ejaculate on each of the indicators compared to the combined 9R9R/9R10R carrier group. The differences were significant both for a composite score measuring ejaculatory function, and for variables measuring anteportal ejaculation, number of thrusts, and feeling of control over ejaculation, but not for ejaculation latency time. The effect of the polymorphism remained significant after controlling for age, homosexual experience, having a regular sexual partner, level of sexual desire, and frequency of sexual activity, hence suggesting that it is not secondary to an association between the studied polymorphism and some other aspect of sexual behavior, but due to a specific influence of DA on ejaculation. The findings of the present study support results of previous studies indicating involvement of dopaminergic neurotransmission in ejaculation.

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

A BIVARIATE ANALYSIS OF SOCIABILITY AND PROSOCIAL BEHAVIORS AMONG SOUTH KOREAN TWIN CHILDREN

M. J. Jin[1], Y.W. Shin[1], N. Ha[1], S. Koo[1], K. Kim[1], B. Kim[1], J. Yoo[1], O. Jo[1], M. Ho Hyun[1] & Y.-M. Hur[2]

[1] *Chung-Ang University, Republic of Korea*

[2] *Mokpo National University, Republic of Korea*

Genetic influences on individual differences in sociability and prosocial behaviors have been well documented. The present study addressed two research issues. First, is childhood sociability phenotypically related to prosocial behaviors? Secondly, do genetic factors play a significant role in the phenotypic relationship between sociability and prosocial behaviors in children? Mothers of 603 pairs of South Korean twins completed the Sociability scale from the EAS temperament survey and the Prosocial Behavior scale from the Strengths and Difficulties Questionnaire. A modest but significant association was found between the two scales (r = .25). Bivariate model-fitting analyses indicated that this relationship was mediated by both genetic and nonshared environmental factors.

CHANGES OF GENETIC AND ENVIRONMENTAL INFLUENCES ON EMOTIONAL PROBLEMS DURING CHILDHOOD AND EARLY ADOLESCENCE IN SOUTH KOREAN TWINS

O. Jo[1], S. Koo[1], B. Kim[1], K. Kim[1], J. Yoo[1], N. Ha[1], M. Jin[1], Y. Shin[1], Y.-M. Hur[2]

[1] *Chung-Ang University, South Korea*

[2] *Mokpo national University, South Korea*

Twin studies that investigated childhood emotional problems among Asians are relatively rare. The main purpose of the present study was to examine genetic and environmental influences on emotional problems in South Korean children. Six hundred and three pairs of twins aged from 3 to 13 years completed five items of the emotional problems scales in the Strengths and Difficulties Questionnaire (SDQ). Twin correlations and model-fitting analyses were carried out. Although twin correlations suggested the importance of shared environmental influences, these effects did not attain statistical significance in model-fitting analyses. Two major conclusions were drawn from analyses: First, genetic and nonshared environmental factors were important in childhood emotional problems in South Korean twin children, second, during childhood genetic factors in emotional problems increase with age (35% –> 57%), whereas environmental factors decrease with age (65% –> 43%).

EVALUATION OF EPIGENETIC DISCORDANCE IN UMBILICAL VEIN ENDOTHELIAL CELLS FROM NEWBORN MZ TWINS

E. Joo[1,3], L. Gordon[2], M. Ollikainen[1], R. Andronikos[1,3], A. Oshlak[4], G. Smyth[4], R. Saffery[1,3], J. Craig[1,3]

[1] *Developmental Epigenetics, Murdoch Childrens Research Institute, Royal Children's Hospital, Parkville, Victoria, Australia*

[2] *Bioinformatics, Murdoch Childrens Research Institute, Royal Children's Hospital, Parkville, Victoria, Australia*

[3] *Department of Paediatrics, University of Melbourne, Parkville, Victoria, Australia*

Monozygotic (MZ) twins are widely considered to share an identical genetic profile as they are derived from a single fertilized zygote. In light of this, it has been assumed that environmental factors are responsible for the phenotypic differences that occur within most MZ pairs. Recently, evidence has emerged that epigenetics may play a role in the mechanism underlying environmental influence on the underlying genome, potentially explaining the phenomenon of 'fetal programming', linked to increased disease risk later in life. DNA methylation (of cytosine within CpG dinucleotides) is the most widely studied epigenetic mechanism is known to be sensitive to environmental influences such as diet and lifestyle. A study by Fraga et al. (2005) showed that MZ twins show increasing levels of DNA methylation discordance with age, with greater differences seen in pairs who have shared less of their environment over their lifetimes. However, little data are available on the level of epigenetic change accumulated *in utero*. We hypothesise that fetal development represents a particularly sensitive time for environmental influence on epigenetic marks, and that differences in epigenetics and gene expression at birth will reflect differences in intrauterine microenvironment. To test this hypothesis, we examined genome-wide methylation and expression profiles, using Illumina Infinium methylation arrays and expression arrays, in purified populations of Human Umbilical Vein Endothelial Cells (HUVECs) collected at birth from 8 MZ pairs. These cells represent an excellent model for studying factors that may program later disease risk associated with suboptimal endothelial function in humans. We observed a range of within-pair expression and methylation discordances and have characterized a set of genes that differ most widely in expression and methylation within pairs that are known to play a role in response to environment. We have also characterized a set of genes associated with birthweight, many of which have previously been linked to cardiovascular disease.

THE ECONOMIC SITUATION OF FAMILIES WITH MULTIPLES: A RISK FOR THE WELLBEING OF THE FAMILY?

M. Kaihovaara-Huhta[1], J. Hyväluoma[2]

[1] *Finnish Multiple Births Association, Jyväskylä, Finland*

[2] *Family Research Centre, University of Jyväskylä, Finland*

Uncertainty of livelihood is often a matter of fact in families with multiples. According to international studies the costs incurred for the family by the birth of multiples are substantial and higher than the costs incurred by the birth of an equal number of children one at a time. In addition, the costs spread over a relatively short period in multiple families, the biggest expenditure occurring while the multiples are infants. (Ellison & Hall 2003; Campbell etc. 2004.) In this paper we will present results from a nation-wide study on multiple families' psychosocial wellbeing and economic survival. The data was collected in context with the project 'Good beginning to parenting multiples' organized by Finnish Multiple Births Association. The collection of data took place in the form of an Internet questionnaire in autumn 2009. The Internet questionnaire was filled in by a representative random sample of 2500 mothers of multiples and their spouses in Finland. The response rate was 47%. Even though the parents of multiples described themselves on an average as fairly well-paid, almost half of the respondents announced that it was hard to cover their expenditure with their income. Compared to other families with children, difficulties in livelihood were more common among single multiple parents and multiple parents with infants or toddlers and among multiple families with 4 or more children altogether. The results revealed that financial concerns of multiple families strain the wellbeing of the entire family. Financial concerns reflected clearly on the mental wellbeing of the parents of multiples. Parents of multiples who were in a difficult economic situation felt clearly worse mentally than other parents in a difficult economic situation. Parents with multiples are highly stressed more often than other parents. The challenges brought about by parenting multiples, combined with economic concerns, may create considerable problems for the wellbeing of the multiple family. The financial situation reflects negatively also to the relationship between parents. Challenging economic situation is more likely to put pressure on and increase disagreements in the relationship. The economic situation affects also children's wellbeing. Parents, who felt it easy to cover expenses with their income, considered their children's overall wellbeing positively more often than those parents who were less well-off. In those families who had difficulty covering their expenses, children were reported to suffer from sleeping problems more often and children followed directions and requests more rarely than in well-off families. The paper gives suggestions for a discussion on what kinds of impact the financial situation of the multiple families can adduce.

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

SOURCES OF CUMULATIVE CONTINUITY IN PERSONALITY: A LONGITUDINAL MULTIPLE-RATER TWIN STUDY

C. Kandler[1], W. Bleidorn[1], R. Riemann[1], F. M. Spinath[2]
[1] *University of Bielefeld, Bielefeld, Germany*
[2] *University of Saarland, Saarbruecken, Germany*

This study analyzed the etiology of rank-order stability and change in personality over a period of 13 years in order to explain cumulative continuity with age. NEO- five factor inventory self- and peer report data from 696 monozygotic and 387 dizygotic twin pairs reared together were analyzed using a combination of multiple-rater twin, state-trait, and autoregressive simplex models. Correcting for measurement error, this model disentangled genetic and environmental effects on long- and short-term convergent valid stability, on occasional influences, and on self- and peer report-specific stability. Genetic factors represented the main sources that contributed to phenotypic long-term stability of personality in young and middle adulthood, whereas change was predominantly attributable to environmental factors. Phenotypic continuity increased as a function of cumulative environmental effects on trait variance and decreasing occasion-specific effects with age. Our findings suggest that genes and environments transact in a complex interplay resulting in the typical patterns of personality development.

LIFE EVENTS AS ENVIRONMENTAL STATES AND GENETIC TRAITS AND THE ROLE OF PERSONALITY

C. Kandler[1], W. Bleidorn[1], R. Riemann[1], F. M. Spinath[2]
[1] *University of Bielefeld, Bielefeld, Germany*
[2] *University of Saarland, Saarbruecken, Germany*

A long tradition of research on life events has shown that occurrence of many life events is not entirely random. Most measures of life events show genetic influences that can be attributed largely to genetic influences on personality. Longitudinal studies have reported on continuity of individual differences in the frequencies of certain life events and have shown that personality affects life events rather than vice versa, but these studies have not examined the role of genetic influence. Our longitudinal twin study focused on the genetic and environmental sources through which personality influenced the experience of life events and vice versa. Unlike personality, which showed both genetic and environmental influences on substantial continuity over time, continuity of controllable positive, controllable negative, and uncontrollable negative life events was moderate and tended to show only genetic influences. Significant associations between personality and life events were specific to certain personality traits and aspects of life events, primarily directional from personality to life events, and basically genetically mediated. In addition, we found some small and basically environmental mediated effects of life events on personality traits. We discuss the full range of results in terms of Scarr & McCartney's developmental theory of genotype-environment correlation.

THE TWIN NURSES PROJECT: A WEB-BASED COHORT STUDY OF WORK-STYLE AND LIFESTYLE OF JAPANESE ADULTS

K. Kato[1,2], F. Inui[1,3], K. Hayakawa[1]
[1] *Osaka University Graduate School of Medicine*
[2] *School of Nursing, Senri Kinran University*
[3] *School of Health Science, Kio University*

As one of the study projects administered by Osaka University Center for Twin Research in Japan, the Twin Nurses Project has been launched in March 2010. The Project aims to investigate influences of not only lifestyle factors but also work-style factors (e.g., working time, shift work, work-related stressors, the type of labor, human relationship at work) on health outcomes, particularly psychosomatic symptoms such as chronic fatigue, chronic pain, irritable bowel, depressive mood, anxiety, and other symptoms that are medically unexplained. The recruitment of participants and all the data collection using questionnaires are conducted exclusively via the Project's website (http://twin-nurse.jp). Apart from general information about the Project, only participants can access the Project's online services such as blog-like newsletters, summaries of previous research outcomes, and SNS-like interactive bulletin board system where the participants can communicate with one another. In addition, each participant has his or her personal page, where the history of his or her responses to previous questionnaires can be browsed. As the first wave of recruitment, we have been publicizing our Project via an organization for psychiatric nurses. We will then extend the recruitment to other specialties of nursing. Because a high rate of early job separation among nurses is a significant issue in Japan, we expect that our Project will contribute to the improvement of nurses' work–life balance and resulting reduction in early job separation rate, as well as the elucidation of underlying etiology of the above-mentioned psychosomatic symptoms.

GENE-ENVIRONMENT INTERACTIONS BETWEEN DEPRESSIVE SYMPTOMS AND SMOKING QUANTITY

K. Keskitalo-Vuokko[1], T. Korhonen[1,2], J. Kaprio[1,2]
[1] *University of Helsinki, Helsinki, Finland*
[2] *Institute for Health and Welfare, Helsinki, Finland*

The association between smoking and depression is well-established. However, relative importance of genetic and environmental factors underlying this association causality remains unclear. The aim of this study was to investigate genetic and environmental interactions between depressive symptoms measured by the Beck Depression Inventory (BDI) and current number of cigarettes smoked per day (CPD) using quantitative genetic modeling of twin data. Both gene–environment correlation (rGE = the genetic control of exposure to different environments) and interaction (GxE = the genetic control of sensitivity to different environments) were examined. The data were drawn from the Older Finnish Twin cohort's third study wave. Questionnaires were sent in 1990 to same-sexed twin pairs born between 1930–1957 and participating in earlier survey(s). Data on total of 12,064 individuals were available for analyses including 3004 pairs with known zygosity (1087 MZ, 1917 DZ). The BDI sum scores ranged from 0 to 49 (mean 5.2). CPD was measured as a categorical variable and replies on all response alternatives (1 = 0, 2 =< 5, 3 = 5–9, 4 = 10–14, 5 = 15–19, 6 = 20–24, 7 = 25–39, 8 => 40) were obtained. Based on the univariate modeling, additive genetic (A) and specific environmental (E) factors were adequate to explain the variation of both traits, while common environmental (C) effects were not significant in any of the further models. Bivariate Cholesky composition revealed that the phenotypic correlation (r = 0.09) between BDI and CPD was explained by shared genetic (rg = 0.18) and environmental (re = 0.08) factors. The linear GxE models were built in two ways (1) using CPD as the trait and BDI as the moderator and (2) vice versa. The moderating effects were significant in both A and E variance components, and the value of both components increased with increasing moderator value. The model incorporating rGE showed that the moderator effects loaded on unique paths and not on the genetic or environmental factors shared between CPD and BDI. In conclusion, these analyses provide evidence that both shared genetic and environmental effects as well as gene–environment interactions underlie the comorbidity of smoking and depression. The analyses examining the linearity of the GxE interaction are underway and the results will be presented in the conference.

EMOTIONALITY AS GENETIC AND ENVIRONMENTAL RISK FACTORS IN CHILDREN'S HYPERACTIVITY PROBLEMS

K. Kim[1], B. Kim[1], J. Yoo[1], Y. Shin[1], M. Jin[1], S. Koo[1], O. Jo[1], N. Ha[1], M.-H. Hyun[1] & Y.-M. Hur[2]
[1] *Chung-Ang University, Republic of Korea*
[2] *Mokpo National University, Republic of Korea*

Children's temperaments have been well documented to be predictors of problem behaviors in childhood and adolescence. The present

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

study explored two research questions. First, is childhood emotionality significantly related to hyperactivity problems? Second, how do genetic and environmental factors mediate the phenotypic relationship between hyperactivity and emotionality in children? Mothers of 603 pairs of South Korean twins completed the Emotionality and the Hyperactivity problems scales. The phenotypic relationship between the two scales was .30. The results of model-fitting analyses indicated that whereas both common genetic and common nonshared environmental factors explained this phenotypic relationship, the contribution of the genetic factors was larger than that of the nonshared environmental factors. Sixty per cent of the phenotypic correlation was attributable to common genetic factors that influence both hyperactivity and emotionality, while 40% was due to common nonshared environmental factors.

THE GENETIC AND ENVIRONMENTAL CONTRIBUTIONS TO THE CO-OCCURRING INTERNALIZING AND EXTERNALIZING BEHAVIORS: A LONGITUDINAL TWIN STUDY

K. J. Kim

Department of Human Development, Virginia Polytechnic Institute and State University, Blacksburg, Virginia, United States of America

Comorbidity has gained momentum in the field of developmental psychopathology since the National Comorbidity Survey (Kessler et al., 1991) revealed that 52% Americans aged 17–54 have at least two or more diagnosable psychiatric disorders, regardless of their awareness of the disorders. Although a large body of studies examined the prevalence rates and configurations of the co-occurrence profile, little is known about the developmental course of co-occurring internalizing and externalizing behaviors from adolescence to adulthood. Much less has been informed on the influence of genotype and environment on variation in the co-occurrence of internalizing and externalizing behaviors. The two-fold purpose of the present investigation was to examine two areas of interest: (1) twin pairs' developmental trajectories of co-occurring internalizing and externalizing behaviors over a 15-year period; and (2) the genetic, shared, and non-shared environmental influences on similarities and dissimilarities in the growth of the co-occurrence of internalizing and externalizing behaviors. The present study was conducted by a secondary data analysis for a four-wave longitudinal panel study called the National Longitudinal Study of Adolescent Health (Bearman, Jones & Udry, 1997). More than 20,000 students in the 7th through 12th grades and their parents were included in the first wave (1994) of the study (N = 20,745). The current investigation focused on 425 monozygotic and 782 dizygotic twin pairs who participated in the study for all four waves of data collection. At the initiation of the project, the mean age of these individuals was 12.78 with a range from 11 to 13 years in age. Growth curve analyses revealed that the initial level of internalizing behavior, on average, did not predict that of externalizing behavior (b = –.01). However, the initial level of externalizing behavior significantly predicted the initial level of internalizing behavior (b = .62, p < .01). Within twin-pair analyses showed that genetic factors explained the association between males' externalizing and internalizing problem behaviors; while non-shared environmental factors were robust predictors of the association between females' externalizing and internalizing problem behaviors. The findings from this investigation provide important evidence regarding specific roles that genetic and environmental factors play in increasing risk for and resilience to young adults' co-occurring internalizing and externalizing behaviors.

HOW TO CREATE A RELIABLE BIOBANK? EXPERIENCES FROM THE DANISH TWIN REGISTRY

S. Knudsen

The Institute of Epidemiology, University of Southern Denmark, Odense, Denmark

The biobank connected to The Danish Twin Registry is hosted by The Institute of Epidemiology, University of Southern Denmark. Currently the biobank contains approx 300,000 single fractions of biological material from both Danish twins as well as cohorts of oldest-old Danish individuals. All together we store biological material from approx 35,000 participants in various cohort studies. The biobanked material typically consists of blood, dried blood spots, check swabs and saliva for use in DNA analyses. Furthermore we store plasma, serum and urine for analyses of various analyses like vitamins, hormones etc. For selected projects we additionally store samples of hair, viable cells and samples for extraction of RNA.

The poster will demonstrate the following items:

- Using the database
- Storage of various sample types
- Structure and maintenance
- Safety, control etc.

THE EFFECTS OF TWIN INFANTS' TEMPERAMENT ON MATERNAL PARENTING STRESS: COMPARISON WITH SINGLETON INFANTS

E.-Y. Koh, Y. Lee

Department of Child & Family Studies, Yonsei University, Seoul, Korea

The present study examined the effects of twin infants' temperament on maternal parenting stress, comparing with singleton infants. The subjects included 30 mothers of twin infants and 32 mothers of singletons who resided in Seoul or suburbs. The subjects were first-time parents of 13–18 month old infant(s). Temperament of infants was measured by the Early Childhood Behavior Questionnaire Very Short Form(ECBQ-VSF; Putnam, Gartstein & Rothbart, 2009). Korean-Parenting Stress Index (K-PSI; Choeong, Lee, Park & Kim, 2008), consisting of infant-related parenting stress and parent-related parenting stress was used to measure mother's parenting stress. T-test, correlation and regression analyses were used for the statistical analysis. The results of this study were as following: First, twin infants' mothers tended to have more parent-related parenting stress than singletons' mothers. Second, in the case of twin infants the negative affect among infants' temperaments explained for infant-related parenting stress only. On the other hand, negative affect and effortful control explained for singleton mothers' entire parenting stress. Third, the level of temperamental similarity between the twins was not correlated with the level of their mothers' parenting stress. In conclusion, the effects of temperament on mothers' parenting stress were found in both twin and singleton infants, but the temperament of infants seemed more influential for the singleton mothers' stress than for the twin group.

CIGARETTE SMOKING AND NICOTINE DEPENDENCE AND DEPRESSION: MECHANISMS OF CO-OCCURRENCE

T. Korhonen

National Institute for Health and Welfare and University of Helsinki, Helsinki, Finland

The aim of this presentation is to review and discuss alternative mechanisms explaining co-occurrence of cigarette smoking and nicotine dependence and depression — based on evidence from longitudinal population studies and genetically informative twin and family studies. A common finding in cross-sectional studies is that cigarette smokers have a greater likelihood of lifetime depression or more current depressive symptoms than nonsmokers and those with depressive disorders tend more often to be smokers than asymptomatic subjects. Although this association is well established, there are competing hypotheses for its explanation. First, pre-existing depressiveness may predict onset of smoking and/or progression to nicotine dependence. Conversely, long-term heavy tobacco exposure may increase the risk of depression. Also, bidirectional predictive associations have been demonstrated. Further, smoking and depression may share common etiologic risks, such as shared genetic or environmental factors. Correlations between genetic components (r_A) of smoking and depression have been investigated in limited number of twin and family studies, with inconsistent results. For example, in Finland we have found different results depending on study design and phenotype used. In the population-based older Finnish Twin

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

Cohort a longitudinal association between persistent smoking and incidence of self-reported depressive symptoms among adult males was observed (OR: 1.8, 95%CI: 1.3–2.5). Based on the bivariate cholesky decomposition, such association was only modestly accounted for by underlying shared genes ($r_A = 0.2$). However, different estimates were seen when analyzing twin pairs selected for and enriched by cigarette smoking and applying phenotypes of lifetime DSM-IV diagnoses of nicotine dependence (ND) and major depressive disorder (MDD) among ever smoking twins. The association between phenotypes was even stronger: those with ND diagnosis had significantly higher likelihood for lifetime MDD (OR:2.4; 95%CI:1.7–3.3), while genetic modeling produced a substantially higher genetic correlation ($r_A = 0.7$). The Finnish example demonstrates that genetic correlations may be sensitive to variation in phenotypic definitions of smoking behavior (persistent smoking, nicotine dependence) and depression (self-reported symptoms, diagnosed MDD) as well as in study design and sample characteristics.

ONE STEP FORWARD, TWO STEPS BACK: EXPLAINING THE SLOW PROGRESS WITH UNDERSTANDING THE ORIGINS OF INDIVIDUAL DIFFERENCES IN MATHEMATICS

Y. Kovas[1,2,3], S. J. Docherty[2], R. Plomin[2]
[1] *Psychology Department, Goldsmiths College, London, UK*
[2] *Social, Genetic and Developmental Psychiatry Centre, King's College, UK*
[3] *New York University in London, London, UK*

Recent twin research has revealed a strong genetic basis to mathematics. Molecular genetic research has begun to identify DNA polymorphisms that contribute to variation in mathematical ability. However, our research suggests that the mechanisms of this contribution are extremely complex, which explains why the progress in this area has been slow. Here we present the results from the UK longitudinal, population-based Twins' Early Development Study demonstrating these complex mechanisms. First, our research suggests that many DNA polymorphisms contribute to mathematical ability, and each of them has only a small and probabilistic contribution to the person's position on the 'mathematical ability continuum'. Second, although many of the same genetic effects continue to be important for mathematics across development, new genetic effects also come on line at each age. Third, many of the DNA polymorphisms that contribute to variation in mathematical ability at a particular age also contribute to variation in other learning abilities at the same age, but less so at other ages. Finally, our research shows that the effects of genes on mathematical ability may not be the same in different environments. For example, genetic risk of poor mathematical performance seems to be mediated by the way children experience and perceive their learning environment — so that the effects of the risk genes are suppressed when the child's classroom experiences are positive. We discuss the importance of the awareness of these complexities for future research and for ultimate progress in understanding the origins of mathematical achievement and underachievement.

PERINATAL ENDOCRINOLOGY OF TWINS

E. A. M. Kuijper,[1] J. C. F. Ket,[2] C. B. Lambalk[1]
[1] *Division of Reproductive Medicine, Department of Obstetrics and Gynaecology, VU University medical center (VUmc), Amsterdam, The Netherlands*
[2] *Medical Library, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands*

Introduction: The intra-uterine (over)exposure to androgens and estrogens is said to influence disease development in later life. To date little is known about the perinatal hormone levels during and shortly after pregnancy in both singleton and twin pregnancies. Therefore, the aim of this study was to review the available data on perinatal hormone exposure of the fetus. *Methods:* Literature searches were conducted in PubMed and Embase.com. The following search terms were used in Pubmed: ((“Pregnancy”[Majr] OR (“Pregnancy Trimester, Second”[Mesh] OR “Pregnancy Trimester, Third”[Mesh])) AND ((((((((“Follicle Stimulating Hormone” [Mesh:noexp] OR “Luteinizing Hormone”[Mesh])) OR “Estrogens”[Mesh:noexp]) OR “Testosterone”[Mesh:noexp]) OR “Androstenedione”[Mesh]) OR “Sex Hormone-Binding Globulin” [Mesh]) OR “Anti-Mullerian Hormone”[Mesh])) OR “Inhibins” [Mesh:noexp]) AND (“Epidemiologic Studies”[Mesh])) NOT (“Reproductive Techniques, Assisted”[Mesh])), and Embase.com: ((‘follitropin’/exp OR ‘luteinizing hormone’/exp OR ‘estrogen’/exp OR ‘testosterone’/exp OR ‘androstenedione’/exp OR ‘sex hormone binding globulin’/exp OR ‘muellerian inhibiting factor’/exp OR ‘inhibin’/exp) AND ‘umbilical cord blood’/exp]). *Results:* These searches resulted in 158 papers. Two reviewers will select the eligible studies, when discordance existed, a uniform decision will be made by re-evaluating the study. Results from these studies will be discussed.

PROJECT ‘GOOD BEGINNING TO PARENTING MULTIPLES’ (2009–2011)

U. Kumpula
Finnish Multiple Births Association, Finland

The poster will present the aims and some results of the Project ‘Good beginning to parenting multiples’. The project is organized by Finnish Multiple Births Association. The aims of the project are (1) to get information of the economic survival and psychosocial well-being of families with multiples by a nation-wide study, (2) to make a free guide book for all mothers and fathers expecting multiples and (3) to have family training for families expecting multiples offered by professional public health care staff. This poster will present the results of the study (1). The study was made by University of Jyväskylä in Finland. The poster will present all the main results of economic survival of families with 0–18 year old multiples (oral presentation in COMBO-session will focus on that), but also the psychosocial wellbeing of families with multiples. Also the poster will present what the parents regard as the most rewarding and most pressuring in being a parent of multiples and how parenting multiples reflects to the relationship between parents. The poster will present the content of the guide book (2) and describe more in detail how the book opens the ‘landscape of the mind’ when having multiples, not forgetting the basic information and practical advice when having multiples. The poster will also present a tested family training model. (3). The aim of the training is to provide information and peer support for the families preparing for the multiple births and living with the multiples. The poster will tell how the project is carried out to have the public health care take responsibility for the training. The project is funded by non-profit organizations: Finland’s Slot Machine Association (RAY) and Alli Paasikivi Foundation.

ASSOCIATION OF MIDLIFE OBESITY AND RELATED METABOLIC DISORDERS WITH OLD AGE COGNITION

V. S. Laitala
University of Helsinki, Helsinki, Finland

Objective: Epidemiological studies suggest a relationship between midlife metabolism and old age cognition. We examined the effect of midlife BMI and related metabolic conditions on old age cognition and whether there was evidence from direct causal pathways behind these associations in a large sample of Finnish twins. *Methods:* Midlife variables of 2606 twin individuals were based on postal questionnaires and registry records. Old age cognitive status was measured by using a validated telephone interview. *Results:* Midlife BMI, cardiovascular disease, hypertension and diabetes were each associated with old age cognition when adjusted for sex, education and age at the interview. Similarly, overweight increased the risk for mild impairment of cognitive function and dementia. Cardiovascular disease diminished the mean cognitive score also among discordant twin pairs (b-estimate = 1.10, p value =.012). Weight gain more than 1.7 kg/m2 and loss more than 2 kg/m2 within an average of 5.6 years were associated with lower cognitive performance independently of BMI. An additive genetic correlation explained the association between BMI and old age cognition (rA = –0.12, 95% CI –0.21 –0.03), but adjustment for education led to loss

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

of significance (rA = –0.06, 95% CI –0.16 0.03). *Conclusions:* Midlife metabolic diseases, especially diabetes, are independently associated with impaired cognition in old age. Even a more subtle weight change than suggested previously was associated with old age cognition in our study. There was evidence from direct causal pathway between cardiovascular disease and old age cognition, while the correlation between midlife BMI and old age cognition was explained mostly by genetic factors.

OVARIAN AGEING AND TWINNING

C. B. Lambalk, J. Vink, E. Van der Stroom, D. I. Boomsma

Division of Reproductive Medicine, VU University Medical Center, Department of Biological Psychology, VU, Amsterdam, The Netherlands

Dizygotic twinning is the result of fertilization of multiple follicles that develop during one ovulatory cycle. Consequently multiple embryos occur and when they implant multiple pregnancy and delivery results. Significant factors contributing to natural DZ multiples are heredity, increased maternal age and higher parity. To a lesser extent smoking and increased body mass index contribute. Older women are at higher risk for DZ twinning because they have a strongly increased risk of multiple follicle growth. This is < 5 % in women < 25 years of age and increase to about 25 % when women are over 35 years and the result of diminished ovarian feedback from the due to ageing smaller sized monthly available cohort of follicles. Consequently Follicle Stimulating Hormone (FSH) goes up allowing all follicles present to develop and if more then one present all grow and ovulate. With familial twinning elevations of FSH are also a characteristic feature. One mechanism by which hereditary twinning may occur is via a hereditary mechanism of advanced ovarian ageing. There are indications that twinning is associated with earlier menopause (Gosden et al., *Hum Reprod,* 22, 2142–2152, 2007) So possibly advanced biological ageing may be responsible for the multiple follicle growth in familial twinning along mechanisms identical to that in normally aging women. In a study published a decade ago we showed that FSH was often elevated in mothers of a familial DZ twin but no clear signs of limited ovarian feedback could be observed. Oestradiol levels and Inhibin A and B levels were normal and FSH was elevated compared to controls (Lambalk et al., *J Clin Endocrinol Metab*, 83, 481–486, 1998). Recently another hormone from small non developing follicles has been indicated as a good and more subtle estimate for ovarian aging namely Anti Mullerian Hormone (AMH). Lower and undetectable levels are associated with biologically ovaries of advanced age. We now determined AMH in the residual serum of the 16 mothers of DZ twins and their 14 controls from the previous study. This could reveal if the twin mothers of our study at younger age may already have shown some subtle features of limited ovarian reserve indicating protracted organ ageing. The average AMH levels were not different: 2.13 +/– 0.50 microgram/L the twin mothers and 1.85 +/– 0.60 in the controls. The average calendar age was 35 years in both groups. Among the 16 familial twin mothers as many as 7 had elevated FSH values over 10 U/L in the early follicular phase compared to 1/14 in the control (p <0.04). Their AMH was very low compared to the 9 twin mothers with normal FSH values: 0.57 +/– 0.15 and 3.37 +/– 0.88 microgram/L (p = .016) whereas Inhibin B and Inhibin A were slightly but not significantly lower. None of the twin mothers, all now over the age of 45 years, reported early menopause (< 45 yrs). Our data indicate that among mothers with familial DZ twins elevated FSH occurs often and does seem to be associated with signs of limited ovarian reserve. These findings support the hypothesis that with familial DZ twinning potentially inheritance of processes that advance ovarian ageing can be responsible.

RE-EXAMINING THE DIMENSIONALITY OF PARENTAL SOCIALIZATION: A MULTIVARIATE GENETIC ANALYSIS

S. J. Latendresse[1], R. J. Rose[2], R. J. Viken[2], L. Pulkkinen[3], J. Kaprio[4], D. M. Dick[1]

[1] *Virginia Institute for Psychiatric and Behavioral Genetics, Virginia Commonwealth University, Richmond, Virginia, United States of America*

[2] *Department of Psychological and Brain Sciences, Indiana University, Bloomington, Indiana, United States of America*

[3] *Department of Psychology, University of Jyväskylä, Jyväskylä, Finland*

[4] *Department of Public Health, University of Helsinki & National Public Health Institute, Helsinki, Finland*

Parenting has long been regarded as one of the most influential early socialization environments, with evidence of prospective associations with a number of psychosocial outcomes throughout adolescence, and even into adulthood. Historically, parental socialization has been conceptualized along two purportedly orthogonal dimensions of parental affect and parental control. In practice, arbitrary thresholds have been used to distinguish between 'high' and 'low' levels of each of these dimensions (e.g., median splits), effectively yielding four distinct parenting styles. In turn, an extant literature now describes the many quantitatively meaningful differences existing between these qualitatively derived styles of parenting. While recent studies have challenged both the orthogonality of parental affect and control, and the unidimensionality of each of these constructs, none has yet examined the associations between various parenting practices/environments within a genetically informative framework. Evidence from the twin literature suggests that parenting is a product of both genes and environments, as univariate analyses have shown that heritability significantly contributes to variability within a number of individual parenting behaviors. In this study, we used data from *FinnTwin 12*, a population-based, epidemiological sample consisting of five consecutive birth cohorts of Finnish twins (1983-87), to test the etiological structure underlying associations between numerous adolescent-reported parenting behaviors at two distinct developmental periods. Findings demonstrate a pattern of inter-correlated parenting dimensions (subdimensions), with multiple shared genetic and environmental sources of variability at age 12, but no trace of heritability in perceptions of parenting by age 14. Moreover, findings are generally consistent across sexes. As such, parental socialization appears to be a more complex, multidimensional construct than was originally believed, and which, in early adolescence, is partially attributable to genetic transmission.

GENETIC AND ENVIRONMENTAL INFLUENCES ON MEASURES OF PROCESSING SPEED: THE OLDER AUSTRALIAN TWINS STUDY

T. Lee[1,2], M. Mosing[3,4], M. J. Wright[3,4], J. N. Trollor[1,5], J. D. Henry[6], A. Lammel[1], D. Ames[7], N. G. Martin[3,4], P. S. Sachdev[1,2]

[1] *Brain and Ageing Research Program, School of Psychiatry, Faculty of Medicine, University of New South Wales, Australia*

[2] *Neuropsychiatric Institute, Prince of Wales Hospital, Sydney, Australia*

[3] *Genetic Epidemiology Laboratory, Queensland Institute of Medical Research, Australia*

[4] *School of Psychology, University of Queensland, Australia*

[5] *Intellectual Disability Mental Health, School of Psychiatry, Faculty of Medicine, University of New South Wales, Australia*

[6] *School of Psychology, University of New South Wales, Australia*

[7] *National Ageing Research Institute, University of Melbourne, Australia*

This study represents the first Australian study of genetic influence on cognitive functions of the elderly, with a genetically informative sample of twins aged 65 and above. It has attempted to confirm the findings of studies conducted in other countries, and to extend their findings by employing several measures of processing speed in the same population. Processing speed is one of the basic elements of cognitive functions and it has been regarded as a 'common mechanism', which mediates general cognitive decline. Studies of normal ageing have shown that up to 79% of age-related variance in many cognitive functions can be explained by age-related variance in measures of processing speed. The present study examined the genetic and environmental influence in five measures of processing speed: Trail Making Test A, Digit Symbol, Stroop, Simple Reaction Time (SRT) and Complex Reaction Time (CRT). Additive genetic factors

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

explained 59% of the variance in Stroop, 51% in Digit Symbol, and 41% and 36% in SRT and CRT respectively. No genetic contribution was found for Trail Making Test A. Digit Symbol and Stroop, and Digit Symbol and CRT shared the same genetic factors, whereas similar environmental influences (70%) were shared by SRT and CRT. The substantial environmental influence found in the various measures of processing speed would prompt the need to identify potentially modifiable environmental factors.

THE CHINESE NATIONAL TWIN REGISTRY: WHAT HAVE WE DONE AND WHERE TO GO?

L. Li, W. Gao, J. Lv, W. Cao, S. Zhan, H. Yang, Y. Hu

Department of Epidemiology and Biostatistics, School of Public Health, Peking University, Beijing, China

The Chinese National Twin Registry (CNTR) is the first and largest population-based twin registry in China. It was established in 2001. The primary goal of this program is the establishment of a national population-based twin registry from several regions representing north, south, urban, and rural areas in China. A secondary goal is to study genetic contributions to complex diseases, and to test associations of candidate genes with related phenotypes. The recruitment of twins in the registry was achieved mainly through the three-tiered prevention and health system (village, township and county level) in China; 8,342 twin pairs have been enrolled in the registry. Based on the baseline registry, a twin cohort including 579 pairs was established. Continued research includes study on zygosity determination, the secular trend of twin birth ratios and its associated factors, the intermediate phenotypes of cardiovascular and cerebrovascular diseases in adult twins, psychological studies in adult twins, and study on multidimensional assessment of health status in adult twins. Taking advantage of China's large numbers of twin pairs, the CNTR has gradually developed appropriate methodology for the Chinese twins' registry. A twin cohort was established. The blood samples were collected and stored for etiological study. The CNTR has become an important national and international resource for a broad range of research. The current state and future plans for the CNTR will be discussed in this symposium.

TWIN REGISTRY IN SOUTHWESTERN CHINA (TRISC): EXPLORING THE EFFECTS OF GENETIC AND ENVIRONMENTAL FACTORS ON MENTAL HEALTH WELLBEING IN CHILDREN AND ADOLESCENTS

T. Li[1,2], Y. Huang[1], X. Zhang[1,3], X. Ma[1], D. Collier[2], P. C. Sham[3]

[1] *Mental Health Center, West China Hospital, Sichuan University, Chengdu, Sichuan, PR China*

[2] *Institute of Psychiatry, King's College London, UK*

[3] *Department of Psychiatry, Hong Kong University, Hong Kong, PR China*

Object: The purposes of the Twin Registry in Southwestern China (TRiSC) are to explore effects of genetic and environmental factors on behavioral development and psychopathology in children and adolescents. In the present study, we focused on variables of interest such as IQ, cognitive processing speed and personality in order to examine the influence of age and sex on IQ, cognitive processing speed and personality, and to investigate the role of genetic and environmental factors in the relationship between IQ and personality. 366 pairs of twins aged between 6 and 16 years old and their parents were recruited from Chengdu and Chongqing, based on the demographic information of twins from primary and middle school, and the Chinese Birth deficit registry. The twins were assessed by using the Wechsler Intelligence Scale for Children (WISC-R), coding, symbol search and Eysenck Personality Questionnaire, and their parents completed the general health questionnaire. There is moderate heritability on the total IQ and verbal IQ, while shared environmental factors played important roles on the variance of performance IQ. The heritability of IQ, verbal IQ and performance IQ were higher in older children and adolescent than that in younger children. There is moderate to high heritability on the processing speed, but coding and symbol search may reflect different dimensions of processing speed. The coding test is more stable, with fewer changes in different sex and age groups. There is moderate to high heritability on personality, but there are some variances in different dimensions. There are significant effects of common environmental effects between IQ and different dimensions of personality. The heritability of the observed phenotypic correlation between IQ and personality were higher in older children and adolescents.

BEIJING TWIN PROJECT ON MENTAL HEALTH PROBLEMS AMONG CHINESE ADOLESCENTS

X. Li

Institute of Psychology, Chinese Academy of Sciences

The Beijing Twin Project on Mental Health Problems among Chinese Adolescents was launched in 2005 in the Institute of Psychology, Chinese Academy of Sciences (CAS). The main purposes of this project are: (1) to establish a behavioral genetics lab in the Institute of Psychology, CAS, (2) to collect an adolescent twin sample in Beijing, and (3) to investigate several developmental issues of adolescent behavioral and emotional problems using this twin sample. The first and second purposes have been achieved. More than 2,000 pairs of twins in Beijing primary and high schools were identified and enrolled in the study. Among them, 1,352 pairs and their parents agreed to participate in this study. The age range of the main body of the sample was from 10 years to 18 years. There are 800 pairs of monozygotic (MZ) twins (386 pairs are male, 414 pairs are female), 311 pairs of dizygotic (DZ) twins (141 pairs are male, 170 pairs are female), and 241 pairs of opposite-sex twins. The MZ:DZ ratio in our sample is 2.57, which is similar to previous reports among east Asian population. We are interested in three mental health outcomes of adolescents: anxiety, depression and externalizing behavior problems, for the reason that they all have high prevalence rates among Chinese adolescents, and they have adverse consequences on the children's development. A variety of factors were measured as hypothesized predictors or consequences of the three mental maladjustments. These factors include social variables such as parenting style, sibling relationship, life events, and peer delinquency physical variables such as height, weight, pubertal onset, and pubertal stage cognitive variables such as emotion regulation and effort control. In order to study the emotional and behavioral changes during adolescence longitudinally and prospectively, we planned to follow up these children from their adolescence to adulthood. In order to study the genetic bases of vulnerability to these mental health problems, association study was put forward. Buccal cells were collected and genome DNA was extracted. Genotyping was conducted for several polymorphisim loci in a couple of candidate genes, such as 5-HTT and DRD4. The behavioral data and the gene data were analyzed jointly to investigate how individuals with different genotypes responded to the risk environmental factors, especially, how their anxiety, depression and externalizing behavior levels changed when they encountered risk environmental factors.

PREVALENCE AND HERITABILITY OF EARLY-ONSET MIGRAINE

L. Ligthart, N. van der Aa, M. Bartels, D. I. Boomsma

Department of Biological Psychology, VU University, Amsterdam, the Netherlands

Migraine is a severe and common headache disorder. The heritability of migraine headache is commonly estimated at 30–50%. The disorder is around 2 to 3 times more prevalent in women than in men, particularly between puberty and menopause. The prevalence of migraine peaks around the age of 35–40 years. The first onset of migraine usually occurs during adolescence, with a peak incidence at the age of 10–11 years in boys, and 14–17 in girls. Here, we investigate the heritability of early-onset migraine and test the hypothesis that individuals with a strong genetic predisposition to migraine develop their first attack relatively early in life. We analyzed migraine data from several cohorts of adolescent twins and their singleton siblings from the Netherlands Twin Registry (NTR). Questionnaire data were collected in 8,355 adolescent twins from three age cohorts (13–14, 15–16, and 17–19 years), and 1,004 of

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

their non-twin siblings. Migraine was assessed with a questionnaire that included items on the migraine symptoms defined by the International Headache Society. These items were analyzed with Latent Class Analysis (LCA) to empirically classify individuals as affected or unaffected for migraine headache. Results of genetic models will be presented, including prevalence and heritability estimates in the adolescents. These findings in adolescents will be compared to previous findings for heritability of LCA based migraine diagnosis in adult NTR samples.

PREVENTION STRATEGIES FOR PREMATURE DELIVERY IN MULTIPLE PREGNANCY? FACTS AND FICTION

A. C. Lim

Department of Obstetrics & Gynaecology, Academic Medical Centre Amsterdam, the Netherlands

Despite the enormous advance in neonatal care during recent years, preterm birth remains the major cause of handicaps in children without congenital anomalies or genetic disorders. Almost 50% of women with a multiple pregnancy deliver before 37 weeks of gestation, while 9% deliver before 32 weeks. Effective strategies for the prevention of preterm birth in multiple pregnancies have yet to be established, despite the large amount of research that has already been conducted in this subject area. Although in one trial progesterone appeared to be effective in both singleton and twin pregnancies with second trimester cervical shortening, the proportion of twin pregnancies in that trial was only small (24 twin vs. 226 singleton pregnancies) and the effect of progesterone in women with a twin pregnancy was not statistically significant. Three large trials in unselected multiple pregnancies did not show a reduction of preterm birth after the use of progesterone. Two treatment strategies that have been explored in the past even seem to have a detrimental effect on unselected multiple pregnancies. A Cochrane review showed that women with an uncomplicated twin pregnancy who were hospitalized for bed rest had a significantly higher risk of delivering before 34 weeks (OR 1.8; 95% CI 1.01–3.3). In an individual patient data meta-analysis, cerclage in multiple gestations was also found to increase pregnancy loss or death before discharge from the hospital (OR 5.9; 95% CI 1.1–30). An intervention that deserves further research is the vaginal pessary. Retrospective studies on this treatment have shown promising results and several randomized controlled trials are currently being conducted. Past efforts to find a preventive treatment for preterm birth have mostly focussed on the group of women with a multiple pregnancy as a whole. Although it is true that this entire group is at increased risk of preterm birth as compared to singleton pregnancies, it is very likely that the individual risk varies and that a subgroup of women with a multiple pregnancy is at an even higher risk of delivering preterm. Interventions are possibly only effective in this high-risk group. Cervical length measurement during the second trimester may be a useful instrument for identifying women who are at increased risk of preterm birth.

OUTCOME OF EXPECTANT MANAGEMENT IN CASES OF DISCORDANT STRUCTURAL FETAL ANOMALIES IN MULTIPLE PREGNANCIES

I. H. Linskens[1], R. M. van Elburg[2], D. Oepkes[3], J. M. G. van Vugt[1], M. C. Haak[1]

[1] *Department of Obstetrics and Gynecology, VU University Medical Center, Amsterdam, the Netherlands*

[2] *Department of Neonatology, VU University Medical Center, Amsterdam, the Netherlands*

[3] *Department of Obstetrics, LUMC, Leiden University Medical Center, the Netherlands*

Objective: Routine obstetric ultrasound increasingly leads to detection of structural fetal anomalies. In multiple pregnancies with one abnormal twin, counseling on management strategies is complicated. Our aim was to analyze this process and the outcome of multiple pregnancies with one abnormal fetus. *Patients:* Ultrasound and outcome data of multiple pregnancies between January 2007 and July 2009 from a tertiary fetal medicine center were analyzed retrospectively. Structural anomalies were classified as central nervous system, cardiovascular, thoracic, abdominal, urinary tract, facial, skeletal and placenta/cord/membranes. *Results:* In total 231 pregnancies (6 MCMA, 62 MCDA, 155 DC twins and 8 triplets), 470 fetuses, were studied. Mean maternal age at ultrasound was 33.8 ± 4.5 years. Anomalies were seen in 37 fetuses (7.9%), predominantly central nervous system anomalies $n = 5$, skeletal anomalies $n = 7$, urinary tract anomalies $n = 6$ and single umbilical artery $n = 4$. In four cases multiple congenital anomalies were seen; 3 of which karyotyping confirmed Trisomy 13. Selective fetal reduction with KCL was performed in 3 cases of severe but non-lethal anomalies (2 × neural tube defect/1 × abdominal anomaly) in DC twins. In two MC cases (concordant Trisomy 13/conjoint twin) the whole pregnancy was terminated. The remaining cases were managed conservatively after counseling, in three cases spontaneous fetal loss was observed. In 5 cases with very severe or lethal anomalies parents opted for comfort care for the affected fetus with good outcome for the unaffected co-twin. In all these cases neonatal death of the affected twin occurred, as expected. Median gestational age at delivery was not significantly different for twins without structural anomalies and twins with one abnormal fetus (Kruskal Wallis; $p = .46$). *Conclusion:* In our data we found a tendency towards conservative management on request of the patient of those twins discordant for very severe/lethal anomalies to avoid the risk of selective reduction for the unaffected co-twin. Fetal reduction was only opted for in a small number of cases with severe but non-lethal anomalies in DC twins. Termination of the complete pregnancy was only performed in MC twins with concordant anomalies.

PRENATAL SCREENING IN TWINS ANNO 2010

I. H. Linskens, J. M. G. Van Vugt

VU University Medical Center, Department of Obstetrics and Gynecology, Amsterdam, the Netherlands

Obstetricians and other health care professionals are confronted with an increasing rate of multiple pregnancies. This increasing twinning rate is associated with increasing maternal age at conception and widespread use of assisted reproductive technologies. Twin pregnancies are at increased risk for adverse pregnancy outcome compared to singletons. Prenatal screening aims to identify women at a certain risk for carrying a fetus with a certain abnormality. Prenatal testing for Down syndrome (DS, trisomy 21) has become part of the routine obstetric care. The past decade prenatal screening for DS has developed from primarily second trimester serum screening towards first trimester screening. Earlier diagnosis with first trimester assessment is preferable to second trimester. In this presentation we will focus on recent development in both second trimester and first trimester DS screening in multiples. An update on both conventional and new ultrasound and biochemical screenings markers will be included. Moreover prenatal screening is also shifting from fetal chromosomal abnormalities solely towards screening for maternal health and adverse outcome of the pregnancy. Recent advances in maternal health screening in multiples will be included in the presentation.

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

DIGITAL QUANTIFICATION OF HUMAN EYE COLOR HIGHLIGHTS GENETIC ASSOCIATION OF THREE NEW LOCI

F. Liu[1], A. Wollstein[1,2], P. G. Hysi[3], G. A. Ankra-Badu[3], T. D. Spector[3], D. Park[4], G. Zhu[4], M. Larsson[4], D. L. Duffy[4], G. W. Montgomery[4], D. A. Mackey[5], S. Walsh[1], O. Lao[1], A. Hofman[6], F. Rivadeneira[7], J. R. Vingerling[6,8], A. G. Uitterlinden[6,7], N. G. Martin[4], C. J. Hammond[3], M. Kayser[1]

[1] *Department of Forensic Molecular Biology, Erasmus University Medical Center Rotterdam, The Netherlands*

[2] *Cologne Center for Genomics (CCG), University of Cologne, Cologne, Germany*

[3] *Department of Twin Research & Genetic Epidemiology, King's College London, London, United Kingdom*

[4] *Queensland Institute of Medical Research, Brisbane, Australia*

[5] *Centre for Ophthalmology and Visual Science, Lions Eye Institute, University of Western Australia, Perth, Australia*

[6] *Department of Epidemiology, Erasmus University Medical Center Rotterdam, The Netherlands*

[7] *Department of Internal Medicine, Erasmus University Medical Center Rotterdam, The Netherlands*

[8] *Department of Ophthalmology, Erasmus University Medical Center Rotterdam, The Netherlands*

Previous studies have successfully identified genetic variants in several genes associated with human iris (eye) color; however, they all used simplified categorical trait information. Here, we quantified continuous eye color variation into hue and saturation values using high-resolution digital full-eye photographs and conducted a genome-wide association study on 5,951 Dutch Europeans from the Rotterdam Study. Three new regions, 1q42.3, 17q25.3, and 21q22.13, were highlighted meeting the criterion for genome-wide statistically significant association. The latter two loci were replicated in 2,261 individuals from the UK and in 1,282 from Australia. The /LYST /gene at 1q42.3 and the /DSCR9/ gene at 21q22.13 serve as promising functional candidates. A model for predicting quantitative eye colors explained over 50% of trait variance in the Rotterdam Study. Over all our data exemplify that fine phenotyping is a useful strategy for finding genes involved in human complex traits. In an ongoing collaborative study of human hair color, we performed a genome-wide association study in 15,758 participants from Rotterdam Study, Twins UK study, and the Brisbane Twin Nevus Study Australia. Some results are presented and discussed.

COMMON GENETIC VARIANTS NEAR THE BRITTLE CORNEA SYNDROME LOCUS ZNF469 INFLUENCE THE BLINDING DISEASE RISK FACTOR CENTRAL CORNEAL THICKNESS

Y. Lu

Queensland Institute of Medical Research, Australia

Central corneal thickness (CCT), one of the most highly heritable human traits (h^2 typically >0.9), is important for the diagnosis of glaucoma and a potential risk factor for glaucoma susceptibility. We conducted genome-wide association studies in five cohorts from Australia and the United Kingdom (total N = 5058). Three cohorts were based on individually genotyped twin collections, with the remaining two cohorts genotyped on pooled samples from singletons with extreme trait values. The pooled sample findings were validated by individual genotyping the pooled samples as well as additional samples also within extreme quantiles. We describe methods for efficient combined analysis of the results from these different study designs. We have identified and replicated quantitative trait loci on chromosomes 13 and 16 for association with CCT. The locus on chromosome 13 (nearest gene FOXO1) had an overall meta-analysis p-value for all the individually genotyped samples of 4.6×10-10. The locus on chromosome 16 was associated with CCT with p = 8.95×10-11. The nearest gene to the associated chromosome 16 SNPs was ZNF469, a locus recently implicated in Brittle Cornea Syndrome (BCS), a very rare disorder characterized by abnormal thin corneas. Our findings suggest that in addition to rare variants in ZNF469 underlying CCT variation in BCS patients, more common variants near this gene may contribute to CCT variation in the general population.

STUDYING THE EXTENT AND FUNCTION OF EPIGENETIC VARIATION IN TWINS

R. Lyle[1], K. Gervin[1], G. Gilfillan[1], H. E. Akselsen[1], M. Hamerø[1], R. Moe[1], H. Gjessing, J. Harris[2], and D. E. Undlien[1,3]

[1] *Department of Medical Genetics, Oslo University Hospital, Oslo, Norway*

[2] *Division of Epidemiology, Norwegian Institute of Public Health, Oslo, Norway*

[3] *Institute of Medical Genetics, Faculty Division Ullevål University Hospital, University of Oslo, Oslo, Norway*

The phenotypic differences between individuals are an outcome of genetic and epigenetic variation. Whereas variation at the sequence level (SNPs and CNVs) has been studied extensively, much is still unknown regarding the extent and function of epigenetic variation. Disturbance in DNA methylation leading to aberrant gene expression has been shown to be involved in many diseases, and variation in DNA methylation may contribute to the risk of common disease. The aim of this study is to explore variation and patterns of epigenetic variation using twins. Since each cell type has its own epigenome, we have isolated different lymphocyte subpopulations ($CD19^+$, $CD8^+$, $CD4^+$ and $CD4^+CD25^+$) from more than 350 twin pairs. We have used both region-specific and genome-wide analyses. First, we studied DNA methylation in the classical human major histocompatibility complex (MHC). The MHC is a gene dense and highly polymorphic region on human chromosome 6p21.3, containing genes with a broad range of functions within the innate and adaptive immune systems. We performed extensive bisulphite sequencing of 1670 individual CpG sites distributed in 176 regions in the classical human Major Histocompatibility Complex (MHC) in 49 monozygotic (MZ) and 40 dizygotic (DZ) healthy Norwegian twin pairs. Regions of interest include CpG islands, the 5'end of genes and non-coding conserved regions. We observed significant variation in DNA methylation both between and within regions. Interestingly, the heritability of this variation is low, ~6% for individual CpGs and ~11% for amplicons, suggesting DNA methylation variation is not under strong genetic control. Second, we are using genome-wide methods to examine disease discordance in monozygotic twins. We have performed genome-wide methylation analyses using both Infinium arrays and bisulphite sequencing using the Illumina platform. In parallel, covalent histone modifications were examined by chromatin immuno-precipitation (ChIP).

EDUCATION AND MORTALITY: CAUSALITY OR SELECTION? A TWIN APPROACH

M. Madsen[1,2], A. M. Andersen[1], K. Christensen[1,2], P. K. Andersen[3], M. Osler[1,4,5]

[1] *The Danish Ageing Research Centre*

[2] *The Danish Twin Registry, University of Southern Denmark*

[3] *Department of Biostatistics, University of Copenhagen*

[4] *Department of Social Medicine, University of Copenhagen*

[5] *Research Centre for Prevention and Health, Glostrup University Hospital*

Objectives: A strong relationship between mortality and education has been widely demonstrated. However, the causality of the association has been questioned, suggesting that underlying factors influencing both education and mortality risk account for the association. The discordant twin design allows us to isolate the effect of education by means of adjustment for genetic and environmental confounding per design. If twin pairs discordant for educational status differ in mortality risk, it will suggest an independent effect of education, whereas a lack of association will point to other explanations, that is, childhood environment and genetic confounding. *Methods:* The study is register-based and includes data from the Danish Twin Registry and Statistics Denmark. Using Cox regression, we estimated hazard ratios (HR) for mortality according to highest attained education among 5,260 monozygotic (MZ) and 11,088 dizygotic same sex (DZSS) twin pairs born 1921–1950. Follow-up lasted from 1980–2008 and analyses were conducted separately for zygosity (MZ and DZSS), gender and birth cohorts. Standard and intra-pair analyses were compared. *Results:* Expected social differences in mortality were demonstrated in the standard analyses, comparing > 7 years to ≤ 7 years of education. In the intra-pair analyses, the associations between education and mortality were

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

generally attenuated and most estimates were close to 1 (HR = 1.02 (CI 95% (0.77–1.36) to HR=1.12 (CI 95% 0.77–1.62)), except for men born 1921–35 who displayed estimates of the same magnitude as in the standard analysis. For the largest educational contrasts (≤ 7 years vs. 15+ years), education still seemed to have an independent effect on mortality risk. We found no significant effect modification of education by zygosity. *Conclusions:* Since associations were attenuated in the intra-pair analyses and no differences in effect were observed among MZ and DZSS twin pairs, the results are most compatible with an effect of early environment in explaining the educational inequality in mortality. However, for males born 1921-35, there might be a more direct effect of education on mortality. Large educational differences were still reflected in mortality risk within twin pairs.

THE INDIVIDUAL DIFFERENCES IN TEMPERAMENT IN RUSSIAN ADOLESCENT TWINS AND SINGLETONS

S. Malykh[1], E. Gindina[1] and M. Lobaskova[2]

[1] *Laboratory of Developmental Behavior Genetics, Psychological Institute of Russian Academy of Education, Moscow, Russia*

[2] *Udmurtia State University, Izhevsk, Russia*

We have conducted the comparative analysis of means on the M. K. Rothbart's temperament questionnaire in twins and singletons, both groups aged 10 to 17 years old. Non-twin children from the younger group (10–14 years old) had higher scores on Activation Control, Inhibitory Control, Attention, Frustration, Aggression and Depression scales, that is, on Effortful Control and Negative Affectivity. Younger group of adolescent twins (10–14 years old) are less frustrated, aggressive and depressive, and at the same time, the have lower self-regulation scores in comparison to singletons. Non-twin children from the older group (15–17 years old) reported having higher scores on Fear, Sadness, and Affective and Associative Perceptual Sensitivity scales. Twins of this age have higher Sociability scores. The slightly higher emotional background is more characteristic of twins then singletons. The gender differences were also found for the scales of M. K. Rothbart's temperament questionnaires. Female twins from the 10- to 14-year-old group have higher scores on Affiliation, Depression, Fear and High Intensity Pleasure scales male twins from this younger age group had higher scores on Activity. Female twins from the 15- to 17-year-old group have higher scores on Fear, Sadness, Affective and Associative Perceptual Sensitivity male twins from this older age group have higher Activation Control and Higher Intensity Pleasure. It's worth mentioning that gender differences in twins are less pronounced that in general sample of singletons, but the main patterns remain: boys are more active and girls are more emotional.

FAMILY CHANGES IN TWIN PREGNANCIES

L. A. M. Manue

ESEP, Portugal

The studies developed in recent decades brought about a more effective intervention with families, but the complexity and diversity associated, continually places us new questions. In this context, the understanding of how the family reorganizes and adapts to twin parenthood is still little explored. The objective of this study is to search for specific experiences, of how the families adapt to twins, and how family cohesion after the birth of twins evolves. To this end, we developed a quantitative, longitudinal, descriptive, correlation of repeated measures study between 2001 and 2009. The sample consisted of 35 families with twins born in 2001 in a hospital located in the North of Portugal, and of which 29 cases finished the monitoring process. The instruments of data collection were questionnaires carried out in five moments where the three latter were self-filled and sent and received by conventional mail. The study focused on the control of the following variables: socio-demographic characteristics, perception of family functioning, family cohesion, family adaptability, the nature of the pregnancy, concerns about the future, resources recognized by the family, depression and allocation of family roles. To operationalize it, we used the following instruments: FACES III (Family Adaptability and Cohesion Evaluation Scale) – Olson H. Portner, J. and Lavee, Y.(1985) family rating scale APGAR family is a scale developed by Smilkstein (1978) EPDS (Edinburgh Postnatal Depression Scale) rating scale of depression of Cox, Holden, & Sagovsky (1987). The results show that: families have changes in their functioning from the birth of the child until the age of six women have mainly their spouses' support. The family changes occur at cohesion and adaptability level suggesting broken up and chaotic families. The social support recognized by the family focus on the extended family, the nursery school and the health center. The major difficulties perceived by families are economic, social participation and availability of time.

BASIC ASPECTS OF MATERNAL SPEECH TO TWIN AND NON-TWIN INFANTS IN THE COURSE OF EARLY INFANCY

M. Markodimitraki[1], T. Kokkinaki[2]

[1] *Department of Preschool Education, University of Crete, Rethymnon, Crete, Greece*

[2] *Department of Psychology, University of Crete, Rethymnon, Crete, Greece*

This longitudinal and naturalistic study aimed to investigate the emotional and the verbal expressions, the focus and the syntactical form of maternal speech to twin and non-twin infants in the course of early infancy. Nine first infant-mother twin and nine infant-mother non-twin dyads were observed (through video recording) during spontaneous interactions at home, from the second to the sixth month after birth in a Greek sample from Crete. The groups were matched on maternal age, infant gender and family socioeconomic and education level. It was hypothesized that differences would be evident in certain aspects of maternal speech to twins compared to non-twins, summarized as follows: (a) negative emotional expressions and emotional mismatching than positive facial expressions of emotional and emotional matching would be more frequent in the course of maternal speech to twin infants compared to non-twin infants, (b) maternal speech during twin infant–mother dyadic interaction would be more directive (contain fewer questions), less infant-focused and less responsive to infant cues than that of maternal speech to non-twin infants. Preliminary results from the microanalysis of three infant–mother twin and three infant–mother non-twin infants will be presented and discussed in the frame of the theory of innate intersubjectivity.

THE INTERACTION OF TWIN AUTISTIC BROTHERS WITH TEACHERS AND PEERS IN A SPECIAL NURSERY UNIT: A CASE STUDY

M. Markodimitraki, M. Kypriotaki, M. Ambartzaki, M. Linardakis

Department of Preschool Education, University of Crete, Rethymnon, Crete, Greece

The aim of the present study is to explore interactions between dizygotic autistic twins of preschool age with their teachers and peers in a Special Nursery Unit. We observed interaction episodes in a naturalistic setting for 4 days (1 day per week for a whole month). Data analysis was carried by nonparametric tests due to the small size of the sample. Results showed significant differences between the twins: proximity to the teachers during interaction is higher with the first born than with the second born twin. The firstborn displays negative feelings before interaction episodes that usually turn into positive during the episodes. The secondborn twin displays a rather stable emotional condition before, during and after interactions. Further, he involves in interaction episodes more frequently than the firstborn (65% in comparison to 35% of the firstborn). There were no significant results regarding interactions with peers. It is more likely that the twins are going to make the first step in order to come into contact with peers although it is the teachers who always initiate interactions with the two brothers. Besides, both teachers initiate interaction more frequently with the secondborn, which results in a higher involvement with interaction games (75%). When the firstborn is involved in an interaction episode, this takes the form of solitary play in a dyad, or interactive play.

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

INTERVENTION IN FAMILIES WITH TWINS

M. M. Martins
ESEP, Portugal

This describes an intervention developed between 2001 and 2009 by a multidisciplinary group of Centro Hospitalar Alto Ave (1 social assistant, 8 nurses and 2 doctors) and Escola Superior de Enfermagem do Porto (2 professors), recognizing that there is a high incidence of twins in the population they serve and that the current intervention addressed to these families is no different from that addressed to the vast majority of families using the services. They proposed to develop a longitudinal study that favors a better understanding of their experiences guiding the monitoring/follow-up process of families with twins, by the health professionals. We believe that to intervene with these families, as a facilitator of the recovery of the changes occurred, it is important to get to know about them and see how they live, and the transitions that occur in preparation for, and during, parenthood; the socio-cultural context in which they live, allowing us to create intervention and follow-up programs focused on the duality, 'multiple pregnancy: multiple pleasure or multiple jobs'. In this respect and trying to provide a more effective and appropriate intervention to the socio-cultural context we highlight the following interventions:

- The distribution of a handbook of twins that focuses on aspects of instrumental cases such as: home organization, particular emphasis being given to the father, raising awareness to the need to share tasks with the mother, strengthening of the individuality of twins, awareness of a greater willingness of the family in general and of the mother in particular, to live under greater stress, feel more tired and eventually live in economic hardship, alert the family of the mothers increased need to rest in the early days, but also, alert that it is important that the couple spend some time together;
- Establish health surveillance aimed at families with twins and an effective involvement of the father;
- Create a gender database from the social service of the hospital centre where the study took place; and
- Organize regular twin meetings.

The support given to families requires two types of decision making: on one hand, an effort to develop a partnership with each family, providing them with assistance in accordance with their values and priorities, and on the other hand, a new attitude from the professionals who care for and treat these individuals.

CONTRIBUTIONS OF TWIN STUDIES TOWARDS ELUCIDATING DISEASE ETIOLOGY

N. G. Martin
Queensland Institute of Medical Research, Australia

Well-conducted twin studies are able to completely change the way we view problems and to re-orient entire research programs. For instance, autism had been attributed to a variety of causes, such as emotional coolness in the mother, until a landmark twin study found much higher concordance in MZ than DZ twins. For decades, the focus of research on attention deficit hyperactivity disorder (ADHD) in children was on the possible role of dietary imbalance, food additives and the like. Several recent twin studies, however, have found heritabilities for ADHD around 0.8, suggesting a very major role for genetic factors. It is harder to obtain good evidence for rare diseases, but by systematically asking all Canadian patients with multiple sclerosis whether they were a twin, researchers collected a large enough sample to show an MZ concordance of 26% versus a DZ concordance of 2%. Recent successes in finding QTLs for multiple sclerosis can in part be attributed to the impetus from these striking findings in twins. More recent successes of the twin method in elucidating disease etiology will be discussed.

DNA METHYLATION PROFILES IN MONOZYGOTIC TWINS

N. G. Martin
Queensland Institute of Medical Research, Brisbane, Australia

Twin studies have provided the basis for genetic and epidemiological studies in human complex traits. As epigenetic factors can contribute to phenotypic outcomes, we conducted a DNA methylation analysis in white blood cells (WBC), buccal epithelial cells and gut biopsies of 114 monozygotic (MZ) twins as well as WBC and buccal epithelial cells of 80 dizygotic (DZ) twins using 12K CpG island microarrays. An intraclass correlation (ICC)-based comparison of matched MZ and DZ twins showed significantly higher epigenetic difference in buccal cells of DZ co-twins ($P = 1.2 \times 10^{-294}$). Although such higher epigenetic discordance in DZ twins can result from DNA sequence differences, our in silico SNP analyses and animal studies favor the hypothesis that it is due to epigenomic differences in the zygotes, suggesting that molecular mechanisms of heritability may not be limited to DNA sequence differences.

A GENOMEWIDE ASSOCIATION STUDY OF NICOTINE AND ALCOHOL DEPENDENCE IN AUSTRALIAN AND DUTCH POPULATIONS

N. G. Martin
Queensland Institute of Medical Research, Brisbane, Australia

Persistent tobacco use and excessive alcohol consumption are major public health concerns worldwide. Both alcohol and nicotine dependence (AD, ND) are genetically influenced complex disorders that exhibit a high degree of comorbidity. To identify gene variants contributing to one or both of these addictions, we first conducted a pooling-based genomewide association study (GWAS) in an Australian population, using Illumina Infinium 1M arrays. Allele frequency differences were compared between pooled DNA from case and control groups for: (1) AD, 1224 cases and 1162 controls; (2) ND, 1273 cases and 1113 controls; and (3) comorbid AD and ND, 599 cases and 488 controls. Second, we carried out a GWAS in independent samples from the Netherlands for AD and for ND. Third, we performed a meta-analysis of the 10,000 most significant AD- and ND-related SNPs from the Australian and Dutch samples. In the Australian GWAS, one SNP achieved genomewide significance ($p < 5 \times 10^{-8}$) for ND (rs964170 in *ARHGAP10* on chromosome 4, $p = 4.43 \times 10^{-8}$) and three others for comorbid AD/ND (rs7530302 near *MARK1* on chromosome 1 ($p = 1.90 \times 10^{-9}$), rs1784300 near *DDX6* on chromosome 11 ($p = 2.60 \times 10^{-9}$) and rs12882384 in *KIAA1409* on chromosome 14 ($p = 4.86 \times 10^{-8}$)). None of the SNPs achieved genomewide significance in the Australian/Dutch meta-analysis, but a gene network diagram based on the top-results revealed overrepresentation of genes coding for ion-channels and cell adhesion molecules. Further studies will be required before the detailed causes of comorbidity between AD and ND are understood.

THE UNIVERSITY OF MINNESOTA INITIATIVE ON THE GENETICS OF HIGH COGNITIVE ABILITY

M. McGue, R. M. Kirkpatrick, M. Miller, W. G. Iacono
Minnesota Center for Twin and Family Research, Department of Psychology, University of Minnesota, Minneapolis, Minnesota, USA

As part of the consortium on the Genetics of High Cognitive Ability (GHCA) the University of Minnesota will be analyzing IQ data from 1196 pairs of monozygotic twins, 686 pairs of dizygotic twins, 209 pairs of biological siblings, and 406 pairs of adoptive siblings, a total of 4994 individuals. All twins and siblings were in early to late adolescence when assessed and completed an abbreviated version of either the Weschler Adult Intelligence Scale-Revised (if age 16 or older) or the Weschler Intelligence Scale for Children-Revised (if younger than 16). We also have IQ data on over 3500 parents of the twins. Although the Minnesota sample is unselected for IQ, it is still informative for the genetics of high cognitive ability both because the large sample size allows us to identify individuals with exceptional levels of cognitive ability and because earlier analyses by

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

multiple groups suggests that the genetics of high cognitive ability is likely to be largely continuous with the genetics of normal range cognitive ability. By the summer of 2010 we will have genome wide association study (GWAS) data on all the Minnesota samples. Specifically, participants will have been genotyped on approximately 660K SNP markers using Illumina's 660W Quad array. In this presentation we will begin by describing the Minnesota samples, including their biometric properties. We will then discuss the challenges associated with our GWAS analysis of the complex family structure of the Minnesota samples, using a candidate-gene study to illustrate our approach.

IS HIGH COGNITIVE ABILITY ASSOCIATED WITH A LOWER GENOMIC BURDEN OF COPY NUMBER VARIANTS?

A. McRae, M. Wright, N. Hansell, P. Visscher, G. Montgomery, N. Martin
Queensland Institute of Medical Research, Brisbane, Australia

The heritability of IQ is 50–80% yet GWAS studies have so far failed to identify any SNPs replicably associated with it, suggesting that there must be very large numbers of common variants of small effect, large numbers of rare variants of large effect, or a combination. Copy number variants (CNVs) such as chromosomal deletions may have large (mainly negative) effects on IQ and are most likely to be rare. We have typed the Illumina 610k SNP array on ~1700 teenage twins and sibs from ~750 families, who have been tested at age 16 on a comprehensive range of cognitive tasks, including IQ tests. CNVs have been scored from the SNP array data using the QuantiSNP program. Preliminary results comparing scored CNV distributions in high and low IQ quantiles will be presented.

HERITABILITY OF CAROTID INTIMA-MEDIA THICKNESS AND ARTERIAL STIFFNESS: PRELIMINARY RESULTS FROM AN ITALIAN TWIN STUDY

E. Medda[1], C. Fagnani[1], R. Cotichini[1], L. Nisticò[1], M. Salemi[1], D. L. Tarnoki[2], A. D. Tarnoki[2], F. Fanelli[3], C. Baracchini[4], Z. Garami[5], M. A. Stazi[1]
[1] *Genetic Epidemiology Unit, Istituto Superiore di Sanità, Rome, Italy*
[2] *Department of Radiology and Oncotherapy, Semmelweis University, Budapest, Hungary*
[3] *Department of Radiological Sciences, Sapienza University, Rome, Italy*
[4] *Department of Neurosciences, University of Padua, Padua, Italy*
[5] *The Methodist Hospital DeBakey Heart and Vascular Center, Houston, USA*

Carotid intima-media thickness (IMT) and arterial stiffness are early markers of atherosclerosis. The aim of this study is to estimate heritability and to assess the environmental component on the onset of atherosclerosis. The sample is part of an international collaboration (Hungary, USA, Italy) and preliminary results refer to Italian twins. 67 monozygotic (MZ) and 60 dizygotic (DZ) twin pairs (mean age 57.1 ± 11years) were visited and answered to a behavioral questionnaire (lifestyle, happiness, etc). TensioMed Arteriograph was used to measure the arterial stiffness parameters (Augmentation index on brachial artery, AIxbra and Pulse Wave Velocity on aorta, PWVao); carotid IMT (CCA proximal and distal on both sides, internal carotid artery, ICA) was measured by ultrasound. Average values of the IMT on each side were used in the analysis. Intraclass correlation coefficients and univariate quantitative genetic models were used to determine the relative contribution of genes and environment to the variation of IMT and arterial stiffness. All results are age adjusted. The intraclass correlation coefficients for CCA proximal and distal were higher in MZ than in DZ twins (MZ = 0.29, DZ = 0.12 and MZ = 0.53, DZ = 0.18, respectively) and the estimated broad heritability was 0.29 (95%CI: 0.07–0.46) and 0.46 (95%CI: 0.28–0.60). No difference between MZ and DZ intraclass correlations was detected for ICA IMT. Intraclass correlations of AIxbra parameter differ slightly across MZ and DZ twins (0.45 *vs* 0.40) and most of the variation in AIxbra values is explained by shared (C = 0.32) and unshared (E = 0.53) environmental component. Considering PWVao, MZ twin pairs show higher correlation coefficients compared to DZ pairs, resulting in a heritability estimate of 0.48 (95%CI: 0.28–0.64) and an individual-specific environmental contribution of 0.52 (95%CI: 0.36–0.72). Our data show a moderate genetic effect on IMT and arterial stiffness and also highlight the importance of unshared environment in the variability of the investigated parameters. The sample for the final analysis will include additional 50 twin pairs whose recruitment is currently ongoing, and psychological factors as possible protective factors against atherosclerosis will also be considered.

GWAS FOR FINGER RIDGE-COUNT

S. E. Medland
Genetic Epidemiology, Queensland Institute of Medical Research, Brisbane, Australia

The finger ridge count (a measure of pattern size) is one of the most heritable complex traits studied in humans and has been considered a model human polygenic trait in quantitative genetic analysis. Here, we report the results of the first genome-wide GWAS scan for finger ridge count in two samples from QIMR. Our analyses revealed multiple regions of interest. Individual SNP and gene level results will be reviewed.

SKEWED X-INACTIVATION AND SURVIVAL: A 13-YEAR FOLLOW-UP STUDY OF ELDERLY TWINS AND SINGLETONS

J. Mengel-From, I. Petersen, M. Thinggaard, L. Christiansen, K. Christensen
The Danish Twin Registry, Epidemiology Unit, Institute of Public Health, University of Southern Denmark, Odense, Denmark

Epigenetics is a topic which has gained increasing interest during the last decade. The biological phenomenon of X-chromosome inactivation is a branch of epigenetics uniquely observed in females across a variety of species. Women have two X-chromosomes of which one is arbitrarily inactivated whereas the other X-chromosome actively expresses the gene encoded products, thus defining two cell lines distributed in a mosaic pattern. Usually X-inactivation is detected in blood using an assay abbreviated HUMARA. Using this methodology it has previously been shown, that elderly women have a higher degree of skewness (DS) of X-inactivation than younger female twins. A DS higher than 50% illustrates that one cell line is more abundant than the other. Here we analyzed the DS at intake and the chance of survival in a 13-year follow-up study, including 361 elderly twins (74-92 years of age) from the Longitudinal Study of Aging Danish Twins (LSADT), 118 singleton women (92-93 years of age) and 21 centenarians. Skewed X-inactivation was not systematically associated with chance of survival, and twin intrapair analyses also showed no significant association (proportion = 0.58 95% CI 0.49-0.66) for the twin with the highest DS to survive longer than the co-twins. This study revealed no consistent association between X-inactivation and survival in elderly twins and singletons.

THE ASSOCIATION BETWEEN BREASTFEEDING AND CHILD'S LATER ADULT DEPRESSION: THE ROLE OF ESTROGEN RECEPTOR GENE POLYMORPHISM

P. Merjonen[1], M. Jokela[1], J. Salo[1], T. Lehtimäki[2], L. Keltikangas-Järvinen[1]
[1] *Department of Psychology, Institute of Behavioral Sciences, University of Helsinki, Finland*
[2] *Laboratory of Atherosclerosis Genetics, Department of Clinical Chemistry, Centre for Laboratory Medicine, Tampere University Hospital and Medical School, University of Tampere, Finland*

Recent research has demonstrated that adult vulnerability to depression may have its origins in genetic factors and early childhood, emphasizing the value of life-course studies of depression. Our objective was to test the interactive effect between estrogen receptor 1 (ESR1) rs2234693 and breastfeeding when predicting the child's later depression in adulthood. A sample of 1209 boys and girls from the Cardiovascular Risk in Young Finns study was followed from 3, 6, 9, 12, 15, and 18 years of age in 1980 until 2007 (30-45 years of age). Adulthood depressive symptoms were self-reported by the participants using the Beck's Depression Inventory in 2007. Breastfeeding was reported by the mothers in 1983, and several confounding factors from childhood were controlled for. Breastfeeding tended to predict lower adult depression although not consistently, while the ESR1 genotype was not associated with depression. A significant interaction between breastfeeding and ESR1 was found to

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

predict participants' depression (p =.004), so that C/C genotype carriers that had not been breastfed had a higher risk of depression than T allele carriers (40.5% vs. 13.0%) while there were no genotypic differences among those who had been breastfed. In sex-specific analysis, this interaction was evident only among women. Child's genes and maternal behavior may interact in the development of child's adult depression, so that breastfeeding may buffer the inherited depression risk possibly associated with the C/C genotype of the ESR1 gene, especially among women.

PARENTAL EDUCATION LEVEL MODERATES THE IMPORTANCE OF GENETIC AND ENVIRONMENTAL INFLUENCES ON ADOLESCENT SMOKING

J. L. Meyers[1], U. Broms[2], A. C. Edwards[1], J. Kaprio[3], D. M. Dick[1]

[1] *Virginia Institute for Psychiatric & Behavioral Genetics, Virginia Commonwealth University, Richmond VA, USA*

[2] *Department of Public Health, University of Helsinki and National Institute for Health and Welfare, Helsinki, Finland*

[3] *Department of Public Health, University of Helsinki, Finland, National Institute for Health and Welfare, Helsinki, Finland; Institute for Molecular Medicine, Helsinki, Finland*

Although there is a substantial literature on the role of parental education level in adolescent substance use, most effects have been studied outside the context of genetically informative designs. Using a genetically informative twin-family design, we studied the role of parental education on adolescent smoking at ages 14 (1539 twin pairs) and 17 (1420 twin pairs) using data from the population-based Finnish Twin study, FinnTwin12. We find significant main effects of parental level of education on adolescent smoking at age 14 and 17; among twins, at age 14, where both parents had achieved an academic matriculation diploma (received after successful completion of upper secondary school in Finland), 33% have smoked compared to 43% observed in those twins where neither parent had achieved this diploma. Similarly at age 17, among twins where both parents had achieved an academic matriculation diploma, 60% have smoked compared to 73% observed in those twins where neither parent had achieved this diploma. In addition, we find a significant moderation effect associated with parental education: among twins where both parents had achieved an academic matriculation diploma, genetic influence assumed greater importance on adolescent smoking patterns. These trends were evident at ages 14 (h^2 = 0.58) and 17 (h^2 = 0.72). However, this effect appeared to be due largely to initiation of smoking. Among smokers, the opposite effect was observed, whereby genetic influences assumed less importance on the frequency of smoking among twins with more highly educated parents. These analyses suggest that the etiology of adolescent smoking may vary as a function of parental education level, but that the moderating effects associated with parental education are complex.

COMMEMORATING COMBO'S 30TH ANNIVERSARY WITH THE 1ST INTERNATIONAL MULTIPLE BIRTHS AWARENESS WEEK

G. Moore

Co-Vice Chair COMBO 2007–2010, Chair/Director of Communications, Multiple Births Canada 2008-2010

In 2007, at the ICTS in Ghent, Belgium, Multiple Births Canada presented its achievement in initiating and delivering effective National Multiple Births Awareness Days in Canada. Using strategies shared during that presentation, some COMBO delegates returned to their home countries and began holding successful national events of their own. During the 2007 Congress COMBO representatives voted to investigate the possibility of coordinating what would be the 1st International Multiple Births Awareness Week in 2010 to commemorate the 30th Anniversary of COMBO. Discussions since then indicate there is a keen interest in hosting the event later this year and using the opportunity to draw attention to the Declaration of Rights and Statement of Needs of Twins and Higher Order Multiples first adopted by COMBO in 1995/Updated June 2007. Distributing the English version of the 1st International Multiple Births Awareness Week media kit, Gail Moore will instruct delegates on the steps involved in bringing this milestone event to their countries. Delegates will be invited to provide input on timing for the event as well as suggestions for future International Multiple Births Awareness Weeks. Discussions will also include the possibility of hosting the event every three years in the fall after every ICTS.

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

R. Morley, S. Raj, J. Hopper

The University of Melbourne, Australia

Introduction: 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 (ATR), aims to recruit twins prenatally and collect prospective data and samples. *Method:* Recruitment and data and sample collection will depend on women with twin pregnancies across Australia choosing to join and contribute. Logistic challenges have included:

- dealing with ethical and legal issues
- getting information about MATCH to all women with a pregnancy
- obtaining fully informed consent
- getting data sent to MATCH
- optimising chorionicity determination
- optimising collection and processing of samples, and transfer to the bio-repository

Results: We have designed an attractive folder as a resource for women expecting twins, in collaboration with obstetricians, neonatologists, nutritionists and parents of twins. It is available in 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, as well as educational material for midwives and ultrasonologists. *Conclusion:* A pilot of MATCH Victoria, Australia collected pregnancy-related data and biological samples from 77 women in 13 different hospitals. The data and samples collected include socio-demographic data, obstetric history and maternal health data, maternal bloods at 28 weeks gestation, and cord bloods or Guthrie cards. Access to MATCH is available to Australian researchers, and international researchers with an Australian collaborator. Researchers are welcome to apply to utilise the MATCH data. Information on how to apply can be found at *www.twins.org.au* or by emailing *admin@twins.org.au*.

GENOME-WIDE ASSOCIATION STUDY ON SELF-RATED HEALTH

M. Mosing[1,2], K. J. H. Verweij[1,2], S. E. Medland[1], S. D. Gordon[1], M. J. Wright[1,2], D. R. Nyholt[1], G. W. Montgomery[1], N. G. Martin[1,2]

[1] *Genetic Epidemiology, Queensland Institute of Medical Research, Brisbane, Queensland, Australia*

[2] *School of Psychology, University of Queensland, Brisbane, Queensland, Australia*

Self-rated health questions have been proven to be a highly reliable and valid measure of overall health as measured by means of other indicators in all population groups. It also has been shown to be a very good predictor of mortality and the need for services, and is positively correlated with clinical assessments. Furthermore, higher self-rated health has been associated with absence of chronic diseases, severe diseases, disabilities, functional limitations, and with higher physical activity, and better psychosocial wellbeing. Heritability of self-rated health has been investigated by several twin studies, estimating genetic factors to account for 25–64% of the variance in the liability of self-rated somatic health. Furthermore, a large longitudinal twin study showed that the heritability of self-rated health was greatest at age 16 with 0.63 (95% confidence intervals (CI): 0.56–0.67) and declined steadily to age 25 with heritability being 0.33 (CI: 0.25–0.41) with moderate correlations between the

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

different health ratings at different ages (r = 0.33–0.61). These correlations were mainly due to genetic factors. As self-rated health has been shown to be moderately heritable, it would be interesting to explore what specific genes are influencing this trait. This knowledge would help to understand the biological pathways related to an individual's subjective rating of health. The aim of the present study was to identify SNPs underlying the heritability of self-rated health by conducting a genome-wide association analysis in a large sample of 7000 Australian individuals aged 18–92. Results and implications of the study will be presented and discussed.

HERITABILITY OF NEURAL SYNCHRONY AND CAUSAL NETWORKS ASSOCIATED WITH RESPONSE INHIBITION IN A GO/NO-GO TASK

Viktor Mueller[1,2], Andrey P. Anokhin[3], Ulman Lindenberger[1,2]

[1] *Center for Lifespan Psychology, Max Planck Institute for Human Development, Berlin, Germany*

[2] *School of Psychology, Saarland University, Saarbrücken, Germany*

[3] *Washington University School of Medicine, St.Louis MO, USA*

Response inhibition is one of the key aspects of adaptive regulation of goal-directed behaviour, and its impairment is a core dysfunction in neuropsychiatric disorders such as ADHD and addiction. Event-related brain potentials elicited in Go/NoGo tasks indicate that the brain activation during the task is located more anterior in the NoGo condition as compared with the Go condition. Genetic model-fitting analysis in monozygotic and dizygotic twins showed that about 60% of the variance in the amplitudes of the frontal No-Go N2 and P3 amplitudes can be attributed to genetic factors, suggesting that these ERP components may index genetically transmitted individual differences in brain activity related to conflict detection and response inhibition. However, averaged ERP waveforms provide only limited information about the underlying neuronal dynamics. This study examined heritability of event related brain dynamics associated with the execution and inhibition of motor responses using the different synchronisation (e.g., Evoked and Whole Power, Phase Locking Index, Phase Coherence) and MVAR (MultiVariate AutoRegressive) measures in 218 young female twins (69 MZ and 40 DZ pairs). The subjects completed a cued version of the Continuous Performance Test consisting of serially presented letters; the subjects were instructed to respond quickly if an O was followed by an X ('Go' condition), to withhold their response if O was followed by a non-X letter ('No-Go' condition), and to ignore all other letters. Compared to Go trials, NoGo trials produced greater synchronization in the later time window, at the slightly higher frequency and in the more anterior regions. This was accompanied by an increase of induced (non-phase locked) alpha activity after 300 ms practically over the whole cortex with a centro-parietal maximum. Genetic model-fitting analysis showed that both phase synchronization and MVAR measures show significant heritability and can serve as indicators of genetically transmitted individual differences in neural substrates of response inhibition.

META-ANALYSIS ON HERITABILITY OF BMI IN PRE-ADOLESCENCE, YOUNG ADULTHOOD AND LATE ADULTHOOD

C. Nan[1], B. Guo[1], C. Warner[1,2], T. Fowler[1,3], T. Barrett[4], K. Khan[5], D. Boomsma[6], T. Nelson[7], K. Whitfield[8], G. Beunen[9], M. Thomis[9], J. Ordoñana[10], J. Deeks[1], M. Zeegers[1,11]

[1] *Department of Public Health, Epidemiology and Biostatistics, University of Birmingham, United Kingdom*

[2] *Mental Health Commissioning, NHS Cambridgeshire, Cambridge, United Kingdom*

[3] *Department of Public Health, Heart of Birmingham Teaching PCT, United Kingdom*

[4] *School of Clinical and Experimental Medicine, University of Birmingham, United Kingdom*

[5] *Research and Development Department, Birmingham Women's Hospital, United Kingdom*

[6] *Department of Biological Psychology, VU University, Amsterdam, the Netherlands*

[7] *Health and Exercise Science and Colorado School of Public Health Colorado State University, Fort Collins, Colorado, United States of America*

[8] *Department of Psychology and Neuroscience, Duke University, Durham, North Carolina, United States of America*

[9] *Department of Biomedical Kinesiology, Katholieke Universiteit Leuven, Belgium*

[10] *Department of Psychobiology, University of Murcia, Spain*

[11] *Department of Complex Genetics, Maastricht University Medical Centre, the Netherlands*

Increased body mass index (BMI) is a worldwide health issue that could be related to genes, environment or an interaction between both. We performed a meta-analysis and a raw data analysis to investigate genetic and environmental influences on BMI in pre-adolescence (9–11 years), young adulthood (18–22 years) and late adulthood (49–65 years). Nine published papers and an additional four raw datasets from the East Flanders Prospective Twin Study (EFPTS), Netherlands Twin Registry (NTR), Carolina African American Twin Study of Aging (CAATSA) and Murcia Twin Register (MTR) were included. This comprised a total of 7,980 monozygotic (MZ) and 9,719 dizygotic (DZ) healthy twin pairs. We used intra-pair twin correlations for structural equation modeling (SEM), which showed that the heritability of BMI increases significantly with each increasing age category. Overall, heritability of BMI remains high over all age categories ranging from 59% to 79%, while unique environmental influences increased from 13% to 41% with increasing age. The remainder of the variance could be explained by common environmental influences, which decreased with age. The pooled raw data analysis showed similar results. The significant age effect could be explained by the expression of different genes, variation in magnitude of gene expression, gene-environment interactions or cohort effects. The increasing importance of the unique environment could be due to diverging lifestyles as twins become older, and should be taken into account when studying genetic and environmental influences on BMI.

GENETIC CONTRIBUTION TO THE RELATIONSHIP BETWEEN SOCIAL ROLE FUNCTION AND DEPRESSIVE SYMPTOMS IN ELDERLY TWINS

R. Nishihara,[1] F. Inui,[1,2] K. Kato,[1,3] R. Tomizawa,[1] Y.-P. Cai,[1,4] K. Hayakawa[1]

[1] *Department of Health Promotion Science, Osaka University School of Medicine, Osaka 565-0871, Japan*

[2] *Department of Nursing, Hakuho Women's College, Nara 636-0011, Japan*

[3] *Department of Nursing, International University of Health and Welfare at Odawara, Kanagawa, Japan*

[4] *Beijing University of Chinese Medicine Dongzhimen Hospital, Beijing, China*

Social role function is the capacity to maintain interpersonal relationships and is essential for being independent in the community. Limitations in social role function often coexist with depressive symptoms, suggesting a possible common mechanistic basis. We investigated whether the observed association between these traits is mainly due to genetic or environmental influences. Our sample included 92 monozygotic and 31 dizygotic male twin pairs aged over 65 years. Our results show that genetic influence was the major contributor to the relation between social role function and depressive symptoms, and individual unique environmental influence was important for overall variation in each trait. We concluded that focusing on an individual's unique environment is an essential approach for maintaining social role function and psychological wellbeing.

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

HERITABILITY OF TYPE 1 DIABETES MELLITUS IN A COHORT OF ITALIAN TWINS

L. Nisticò[1], A. Galderisi[2], R. Cotichini[1], C. Fagnani[1], V. Toccaceli[1], M. A. Stazi[1], D. Iafusco[2] and the Italian Study Group on Diabetes of the Italian Society of Paediatric Endocrinology and Diabetology-ISPED

[1] *Genetic Epidemiology Unit, CNESPS, Istituto Superiore di Sanità, Rome, Italy*

[2] *Department of Paediatrics, Second University of Naples, Naples, Italy*

We identified a population-based cohort of Italian twin pairs with at least one diagnosed with type 1 diabetes mellitus (T1DM) to estimate concordance in monozygotic (MZ) and dizygotic (DZ) twins, co-twin recurrence risk and disease discordance time, genetic and environmental components of susceptibility variance to T1DM. Twins were identified linking the Italian Twin Registry with 13,354 T1DM patients records, provided by diabetologists of 35 centers from all over Italy (Sardinia excluded). Out of the 148 pairs/triplets identified, 77 pairs and 1 unlike sex triplet have been enrolled so far. DNA has been collected from saliva of 61 pairs. Zygosity in same sex pairs was assigned by genotyping nine microsatellites or by standardized questionnaire on physical resemblance when DNA was not available: 29 are MZ (17 males) and 48 are DZ (12 and 18 same sex males and females, respectively, and 18 unlike sex). Mean age at diagnosis was 8 yrs (1.1–2.5) in first affected twins and 1.7 yrs (1.4–19.9) in concordant co-twins. Proband-wise concordances were significantly different (p = .007) between MZ (43.2% [95% CI 23.3–63.2]) and DZ pairs (11.3% [0–23]). Five years after the diagnosis in the index twins' cumulative incidences were 35% in MZ co-twins and 6% in DZ co-twins. In concordant pairs, MZ co-twins developed T1DM within 34 days — 5.2 years (median 1.1 yrs) and DZ co-twins within 0 days — 7 yrs (median 4.7 yrs) from diagnoses of the index twins. In discordant pairs, median follow-up times are 4.45 yrs (range: .4–19.0) for MZ and 6.8 yrs (.2–31.8) for DZ unaffected co-twins. Under an ACE model, heritability (A) was estimated at .633 (.159–.893), while contributions of familial (C) and individual-specific (E) environmental effects were .154 (0–.546) and .213 (.107–.366), respectively. This study confirms the substantial contribution of genetics in T1DM susceptibility, with a significant role of individual specific factors. These results are in line with those observed in Finnish and Danish populations. Final results on a larger sample will be shown at the congress.

DISSECTING THE ROLE OF GENES AND ENVIRONMENT IN THE ESTABLISHMENT OF THE NEONATAL EPIGENOME: DNA METHYLATION ANALYSIS OF PLACENTAL TISSUE FROM TWIN PREGNANCIES

B. Novakovic[1,2], H.K. Ng[1,2], M. Ollikainen[1], J. Craig[1,2], R. Saffery[1,2]

[1] *Developmental Epigenetics, Murdoch Childrens Research Institute, Royal Children's Hospital, Victoria, Australia*

[2] *Department of Paediatrics, University of Melbourne, Parkville, Victoria, Australia*

Normal cellular functioning and identity during development are dependent on the correct establishment and maintenance of epigenetic profile (including DNA methylation at CG dinucleotides). Disruption of this process is recognized as a potential cause of adverse outcomes during pregnancy and longer-term health risk. The establishment of epigenetic marks is sensitive to environmental cues including the availability of micronutrient methyl-donor precursors (such as folate, and B group vitamins) and alcohol, drugs, toxins and viruses, which influence DNA methyltransferase activity. The placenta establishes a link that facilitates the exchange of nutrients, gas and waste between maternal and fetal circulations, and proper placentation requires a coordinated series of genome-wide, locus-specific epigenetic modifications that precisely regulate gene expression at key points in development. Numerous lines of evidence implicate poor (insufficient) placentation in the aetiology of adverse pregnancy outcomes (such as intra uterine growth restriction and pre eclampsia) and potentially longer term health risk in later life. Evidence from animal and human studies also suggests that maternal factors (such as diet) are very important in determining the epigenetic profile of the developing pregnancy (fetus and placenta). For example, specific phenotypic consequences of epimutations *in utero* can be reversed in animal models by dietary interventions during pregnancy. The placenta represents the site of maximal exposure of the developing pregnancy to potentially adverse environmental agents, anticipated to cause changes to the neonatal epigenome. This in turn is likely to be dependent on the underlying genetic background of the developing fetus. In order to begin to understand the factors regulating this process *in utero*, we are profiling DNA methylation, at both the genome-wide and locus-specific level, in placental tissue of newborn DZ and MZ twins. Results to date indicate a wide variation in methylation levels both within and between twin pairs, with considerable evidence for a contribution of underlying genetic factors in the establishment of the neonatal epigenome. Recent data also implicates periconceptual maternal alcohol consumption as a modifier of placental DNA methylation profile.

THE LINKS BETWEEN SIBLING RELATIONSHIPS IN JAPANESE PRESCHOOL TWINS WITH THEIR ADJUSTMENT

M. Nozaki[1], K. K. Fujisawa[2], J. Ando[2], T. Hasegawa[1]

[1] *Department of Cognitive and Behavioral Science, Graduate School of Arts and Sciences, The University of Tokyo, Japan*

[2] *Department of Humanities & Social Science, Faculty of Letters, Keio University, Japan*

In early/middle childhood siblings whose ages were different, sibling relationship quality was associated with the older siblings' adjustment, controlling for the children's relationships with parents (Pike et al., 2005). In addition, Pike et al. (2005) suggested that positivity within the sibling relationship was more strongly linked with child adjustment than was sibling conflict. Twin siblings are nearly equal in developmental stage and have common social experience. We hypothesized that sibling relationship in twins were different from that in siblings whose ages were different. In this study we investigated links between sibling relationships in Japanese preschool twins with their adjustment. Twin children in this study were part of the Tokyo Twin Cohort Project (ToTCoP, Ando et al., 2006). Participants were 67 mothers of twin children. Mean age of children was 5.18 years old (SD = .09). The children consisted of 36 MZ twins (15 boy–boy pairs and 21 girl–girl pairs) and 31 DZ twins (12 boy–boy pairs and 19 girl–girl pairs). Their mothers answered the Strengths and Difficulties Questionnaire (SDQ, Goodman, 1997) and Maternal Interview of Sibling Relationships (MISR, Stocker et al., 1989). SDQ is composed of five factors prosocial behavior, hyperactivity, emotional problem, conduct problem and peer problem. MISR is composed of two factors sibling positivity and sibling negativity. As a result, sibling positivity was positively correlated with sibling negativity (r = .25, p < .05). In addition, sibling positivity was positively correlated with SDQ prosocial behavior (r = .43, p < .01). Sibling negativity was positively correlated with SDQ conduct problem (r = .29, p < .05) and negatively correlated with SDQ peer problem (r = –.26, p < 05). This study showed that sibling relationships in Japanese preschool twins had link with their adjustment. The link was different from the case of siblings whose ages were different, in that both positivity and negativity within the sibling relationship were linked with child adjustment.

COMMON GENETIC VARIANTS ASSOCIATED WITH BREAST CANCER AND MAMMOGRAPHIC DENSITY MEASURES THAT PREDICT DISEASE

F. Odefrey[1], J. Stone[2], L. C. Gurrin[2], G. B. Byrnes[2,3], C. Apicella[2], G. S. Dite[2], J. N. Cawson[4], G. G. Giles[5], S. A. Treloar[6], D. R. English[2], J. L. Hopper[2], M. C. Southey[1]

[1] *Department of Pathology, University of Melbourne, Melbourne, Australia*

[2] *Centre for Molecular, Environmental, Genetic, and Analytic MEGA Epidemiology, University of Melbourne, Melbourne, Australia*

[3] *International Agency for Research on Cancer IARC, Lyon, France*

[4] *St. Vincent's Hospital, University of Melbourne, Fitzroy, Victoria, Australia*

[5] *The Cancer Council Victoria, Melbourne, Australia*

[6] *Centre for Military and Veterans' Health, The University of Queensland, Brisbane, Australia*

Background: Mammographic density (MD) adjusted for age and BMI is a heritable risk factor for breast cancer. We aimed to determine if recently identified common variants associated with small gradients in breast cancer risk are associated with MD. *Methods:* We

genotyped 497 monozygotic (MZ) and 330 dizygotic (DZ) twin pairs and 634 of their sisters from 903 families for 12 independent variants. Mammographic dense area, percent dense area and non-dense area were measured by three observers using a computer thresholding technique. Associations with MD measures adjusted for age, BMI and other determinants were estimated: (a) cross-sectionally using a multivariate normal model for pedigree analysis (Px), and both (b) between-sibships and (c) within-sibships using orthogonal transformations of outcomes and exposures. A combined test of association (Pc) was derived using the independent estimates from (b) and (c). We tested if the distributions of P-values across variants differed from the uniform distribution (Pu). All P-values were two-sided. *Results:* For dense area and percent dense area, the distributions of Pc-values were not uniform (both Pu<0.007). Consistent with their breast cancer associations, rs3817198 (LSP1) and rs13281615 (8q) were associated with dense area and percent dense area (all Px and Pc<0.05), and rs889312 (MAP3K1), rs2107425 (H19) and rs17468277 (CASP8) were marginally associated with dense area (some Px or Pc <0.05). *Conclusion:* At least two common breast cancer susceptibility variants are associated with the MD measures that predict breast cancer. These findings could help elucidate how those variants, and the MD measures, are associated with breast cancer susceptibility.

LIFESTYLE FACTORS AFFECTING THE DECLINE OF HIGHER-LEVEL FUNCTIONAL CAPACITY IN ELDERLY TWINS

T. Ohno, S. Ogata, K. Hayakawa, R. Nishihara

Department of Health Promotion Science, Faculty of medicine, Osaka University, Osaka, Japan

The purpose of this study is to clarify the life style factors affecting the higher-level functional capacity of Japanese elderly twins by co-twin control analysis in MZ twins. The mailed questionnaires survey was conducted for 533 pairs of Japanese twins aged 65 years old and over. Responses from 494 subjects were analyzed. The Tokyo Metropolitan Institute of Gerontology (TMIG) Index of Competence was included in the questionnaires to measure basic characters, anamnesis and Higher-level Functional Capacity. Health Practice Index (HPI) was included in the questionnaires to measure health habits as life style factors. In MZ twins, TMIF-IC indicated the significant intrapair correlation on all measures. In DZ twins, TMIF-IC did not indicate any significant relation on measures of the active capacity and the intellectual activity. However, there was significant intrapair correlation on measures of the social activity and Instrumental Activities of Daily Living (IADL) in DZ twins. In male MZ twins, TMIF-IC indicated the moderate positive correlation between the intrapair difference on the active capacity and intrapair differences on the sleeping hours and also on the extent of feeling stressful. Those who had more exercise habits than the other within the pair tended to get higher scores of the active capacity. Those who had less exercise habits than the other within the pair tended to get lower scores of the active capacity.

IMPACT OF THE INCREASING NUMBER OF MULTIPLE BIRTHS ON THE LOW BIRTHWEIGHT AND PRETERM DELIVERY DURING THE LAST THIRTY YEARS IN JAPAN: VITAL STATISTICS, 1975–2008

S. Ooki

Department of Health Science, Ishikawa Prefectural Nursing University, Ishikawa, Japan

Background: Despite the rapid increase in multiple births because of the widespread use of fertility treatments, there is no clear epidemiologic evidence that estimates the long-term impact of multiple births on the low birthweight and preterm delivery rates in Japan. *Methods:* Japanese vital statistics of multiple live births presented by the Ministry of Health, Labor and Welfare were gathered and reanalyzed. Secular trends of relative risk and population attributable risk percent of multiple births for low birthweight (<2500g), very low birthweight (<1500g), and extremely low birthweight (<1000g) using 1975–2008 vital statistics and premature delivery (before 37, 32 and 28 weeks) using 1979–2008 vital statistics were calculated with singletons as the reference group. *Results:* Multiple births rates increased twice during the past two decades, and about 2% of all neonates are now multiples. The population attributable risk percent tended to increase as a whole during the same period concerning all categories, and recently reached around 20%. *Conclusions:* The public health impact caused by the rapid increase in multiple births remains large in Japan, and should not be ignored.

HERITABILITY OF MEDICAL PRESCRIPTION COMPLIANCE IN ADULT FEMALE TWINS

J. R. Ordoñana,[1] S. A. Burt,[2] J. F. Sánchez-Romera,[1] M. J. Tornero,[1] F. Pérez-Riquelme,[3] I. Rebollo-Mesa[4]

[1] *Murcia Twin Registry, Area of Psychobiology, University of Murcia, Spain*

[2] *Department of Psychology, Michigan State University, USA*

[3] *Murcia Health Council, Department of Public Health, Murcia, Spain*

[4] *MRC Centre for Transplantation, King's College of London, UK*

Introduction: Poor adherence to medical prescription and subsequent treatment failure is a key issue for health care. Adherence to treatment regimens among patients in developed nations averaged for most common chronic diseases has found to be only about 50% (WHO, 2003). Prevalence of medication discontinuation or nonadherence is highly variable across samples and health conditions. Dose, kind of medication, or treatment length are related to compliance to medical prescriptions, but also factors like memory difficulties, anxiety, depression, neuroticism, and low conscientiousness. Our objective was to explore genetic and environmental effects on individual differences in adherence to medical prescription in adult female twins. *Methods:* The data comprised adult female twins from the Murcia Twin Register (Spain) (212 MZ and 259 DZ pairs). Mean age = 51.4 (*SD* 7.67, Range = 41–67). Treatment adherence was assessed through a single question about usual treatment compliance with four levels. Responses were dichotomized between Always and Inconsistent. Zygosity was ascertained by questionnaire. Genetic analyses were conducted to quantify genetic and environmental influences on variation in this behavior. *Results:* Most of the sample reported following medical prescriptions about treatment consistently (74.6%). Tetrachoric correlations for treatment compliance were higher for MZ twins [MZ: .328 (IC 95%: .061, .560) DZ: 0.102 (IC 95%: –.136, .332)]. Genetic analyses suggest that an AE model offered the best fit to the data. The proportions of variance explained were A: .30, E: .70. No effect for common environmental factors was apparent. *Conclusion:* Preliminary results suggest that genetic differences may affect the probability of following the recommendations from medical personnel regarding drug prescription and treatment.

GLOBAL HUMAN PROTEOME PROJECT AND DISEASE BIOMARKER DISCOVERY FOR PERSONALIZED MEDICINE

Y.-K. Paik

HUPO President Yonsei Proteome Research Center, Yonsei University, Seoul, Korea

With the advent of proteomics, we are now facing with the new field of drug related research area such as pharmacoproteomics and proteomics diagnostics in relation to personalized medicine. In the first part of my talk, I will address some issues related to the current state of proteomics-based biomarker discovery with respect to the personalized health intervention. There will be some discussions on the future perspective on the HUPO's role in advancing proteomics technology applications and the future impact of proteomics on medicine, science, and society. Major emphasis will also be placed on a need for launching a Gene-Centric Human Proteome Project (GC-HPP) through which all representative proteins encoded by the genes can be identified and quantified in a specific cell and tissue. In the second part of my presentation, I will focus on the clinical proteomics and its application to the future medicine with respect to liver cancer biomarkers. Although the field of clinical proteomics progresses very well, many challenges still remain with respect to standard operating procedures for both clinical specimen handling

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

and reduction of sample complexity and the ability to detect proteins and peptides present in low amounts. The traditional concept of a disease biomarker is shifting toward a new paradigm, namely that an ensemble of proteins or peptides would be more efficient than a single protein/peptide in the diagnosis of disease. Thus, I will address these questions and stress the coordinated use of genomics and proteomics in tandem, which can offer mechanistic triangulation of liver cancer biomarker data, and discovery and validation of newly discovered liver cancer biomarker on the critical path to personalized health interventions.

A GENOME-WIDE LINKAGE SCAN FOR DIZYGOTIC TWINNING

J. N. Painter[1], G. Willemsen[2], D. Nyholt[1], C. Hoekstra[2], D. L Duffy[1], A. K Henders[1], L. Wallace[1], S. Healey[1], L. A. Cannon-Albright[3], M. Skolnick[3], N. G. Martin[1], D. I. Boomsma[2], G. W. Montgomery[1]

[1] *Molecular Epidemiology, Genetic Epidemiology and Neurogenetics Laboratories, Queensland Institute of Medical Research, Brisbane, Australia*

[2] *Department of Biological Psychology, VU University Amsterdam, Amsterdam, The Netherlands*

[3] *Division of Genetic Epidemiology, Department of Internal Medicine, University of Utah, Salt Lake City, USA*

The tendency to conceive dizygotic (DZ) twins is a complex trait influenced by genetic and environmental factors. To search for new candidate loci for twinning we conducted a genome-wide linkage in families with multiple cases of DZ twins. Non-parametric linkage analyses including 523 families containing a total of 1115 mothers of DZ twins (MODZT) from Australia and New Zealand (ANZ) and The Netherlands (NL) produced four linkage peaks above the threshold for suggestive linkage, including a highly suggestive peak at the extreme telomeric end of chromosome 6 with an exponential (exp)LOD score of 2.813 (p = 0.0002). Since the DZ twinning rate increases steeply with maternal age independent of genetic effects, we also investigated linkage including only families where at least one MODZT gave birth to her first set of twins before the age of 30. These analyses produced a maximum expLOD score of 2.718 (p = 0.0002), largely due to linkage signal from the ANZ cohort, however, ordered subset analyses indicated this result is most likely a chance finding in the combined dataset. Linkage analyses were also performed for two large DZ twinning families from the USA, one of which produced a peak on chromosome 2 in the region of two potential candidate genes. Sequencing of FSHR and FIGLA, along with INHBB in MODZTs from two large NL families with family-specific linkage peaks directly over this gene, revealed a potentially functional variant in the 5' untranslated region of FSHR that segregated with the DZ twinning phenotype in the UT family. Our data provide further evidence for complex inheritance of familial DZ twinning.

INDEPENDENT AND COMMON PATHWAY MODELS FITTED TO CHINESE TWIN DATA ON MULTIPLE SUB-PHENOTYPES PREDISPOSING TO METABOLIC SYNDROME

Zhengchang Pang[1,2], Shuxia Li[3], Dongfeng Zhang[2], Haiping Duan[1], Torben A. Kruse[4], Kaare Christensen[3], Kirsten O Kyvik[3,5], Qihua Tan[3]

[1] *Qingdao Center for Disease Control and Prevention, Qingdao, China*

[2] *Dept of Public Health, Qingdao University Medical School, Qingdao, China*

[3] *Epidemiology, Institute of Public Health, University of Southern Denmark*

[4] *Dept of Clinical Genetics, Odense University Hospital, Denmark*

[5] *Institute for Regional Health Service Research, University of Southern Denmark, Denmark*

The common genetic and environmental components in the development of sub-phenotypes associated with metabolic syndrome have been investigated using data on twins. Statistical analyses fitting bivariate (Hasselbalch et al. 2008) and multivariate (Benjamin et al., 2007) models to Danish twin data have shown that, on top of the common genetic components for clusters of physiologically similar endophenotypes, independent genetic and environmental mechanisms are important in characterizing the different phenotypes and in contributing to the development of metabolic syndrome. We study this issue by fitting independent and common pathway models to the Chinese twin data of 695 pairs (405 monozygotic and 290 dizygotic pairs) on selected multiple sub-phenotypes including BMI, HDL, LDL, fasting glucose, total cholesterol (TC), triglycerides (TG), that are associated to metabolic syndrome. Results from model fitting showed that the independent pathway model outperforms the common pathway model according to AICs and confirm the existence of common factor genetic component (chi-squared = 259.3, df = 6, $p = 0$) and common factor shared environmental component (chi-squared = 232.7, df = 6, $p = 0$) in these phenotypes while at the same time support the independent genetic and environmental mechanisms for individual phenotypes. The consistent conclusions from Chinese and Danish data emphasize the complex nature in the etiology and pathogenesis of metabolic syndrome.

THE PERINATAL OUTCOMES OF TWIN-TO-TWIN TRANSFUSION SYNDROME BASED ON CLINICAL STAGE: FOR 10 YEARS' EXPERIENCES (2000–2009)

H. Park, S. Kim, S. Lee, S. Hwang, J. Seo, S. Jun

Department of Obstetrics and Gynecology, Gil Hospital, Graduate School of medicine, Gachon University of Medicine and Science, Incheon, Korea

Objectives: Twin-to-twin transfusion syndrome (TTTS) is a very serious complication in monochorionic twins. We reviewed the effectiveness and usefulness of clinical stage by Quintero in diagnosis and treatment of TTTS through our hospital's reports on the previous 10 years. *Method:* In our previous study (between March 2000 and June 2004) we reported the clinical outcomes in 12 cases of TTTS among 236 twin pregnancies. Between July 2004 and 2009, there was another 15 cases of TTTS among 240 twin pregnancies. We report the perinatal outcomes for 27 cases of TTTS, which were classified by Quintero's clinical staging between 2000 and 2009. We examined all cases of placentas after delivery and confirmed the exact chorionicity. Clinical state was decided at the time of initial diagnosis and any changes of clinical progress were observed during 24 hours after birth by ultrasonography. *Results:* (1) There were 147 cases in dichorionic twins, and 89 cases in monochorionic twins and 15 cases of monochorionic twins were diagnosed as TTTS (16.9%). (2) We divided these 15 cases of TTTS into five stages (I–V). There were 6 cases of stage I, 0 cases of stage II, 1 case of stage III, 2 cases of stage IV, and 6 cases of stage V. (3) After including previously reported data, the perinatal outcomes were related with the clinical stage at diagnosis and time intervals between diagnosis and birth, and these associations were statistically significant ($p < .05$). But no difference was found in gestational weeks at diagnosis, at delivery times, birthweight or birthweight discordance. (4) 12 amnioreductions were performed for the treatment of TTTS and the neonatal survival rate was 66.7% (16 out of 24 twin births) which were consisted of stage I-III as 81%, and stage IV–V as 37%). *Conclusions:* Early diagnosis and aggressive amnioreduction for prolonged gestation in TTTS may improve the fetal survival rate.

NO EVIDENCE OF HIGHER 10-YEAR PERIOD PREVALENCE OF DIABETES AMONG 77,335 TWINS COMPARED WITH 212,894 SINGLETONS FROM THE DANISH BIRTH COHORTS 1910–89

I. Petersen[1], M. M. F. Nielsen[2], K. Christensen[1]

[1] *The Danish Twin Registry, University of Southern Denmark, Odense, Denmark*

[2] *Department of Endocrinology, Odense University Hospital, Odense, Denmark*

Aim: To compare the prevalence of diabetes of twins with that of singletons. *Introduction:* Few small studies have demonstrated higher prevalence of diabetes and type 2-diabetes precursors among Danish twins compared with singletons as well as among monozygotic twins compared with dizygotic twins. *Material and methods:* The study is based on a linkage between the Danish Twin Registry (DTR) and databases held by Statistics Denmark. The sample consists of all twins from the DTR born 1910-89 and a 5% random sample of each birth year drawn from the total Danish population. The study included non-emigrated Danish-born survivors at January 1, 1997. We identified diabetes patients by means of the redeemed prescriptions registered in the Danish Medical Register (ATC-codes A10A* and A10B*), Health Insurance Register (glucose measurements and

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

podiatry treatments), and the National Patients Register (ICD10 codes E10, E11, E12, E13, E14, O24, and H360). Gestational diabetes was excluded. It is not possible to distinguish between Type 1- and Type 2-diabetes based on Danish Health Registers but we identified a subgroup of the diabetes patients who, at some point during the 10-year follow up time, had either been diagnosed as non-insulin dependent diabetics (ICD10-code E11) or redeemed a prescription on anti-diabetics (ACT-code A10B*) as type 2 diabetics. This subgroup comprised 66% of all identified diabetes patients in our sample. We calculated 10-year period prevalence stratified for sex, 10-year birth cohorts, and twin/singleton status as well as zygosity (monozygotic versus same-sex/opposite-sex). The analyses were conducted on basis of the total case sample as well as on the sub-sample consisting of type 2-diabetics. *Results:* In spite of the large sample size in the present study we were not able to confirm the findings in previous small studies of Danish twins and singletons demonstrating a higher occurrence of diabetes in twins compared with singletons. Likewise we did not find any evidence of a higher occurrence of diabetes among monozygotic twins compared with dizygotic twins. The results remained unchanged when restricting to the subsample consisting of type 2-diabetics.

VANISHING TWINS IN IN-VITRO FERTILIZATION (IVF)

A. Pinborg
Fertility Clinic, Rigshospitalet, Copenhagen University, Denmark

Since the first IVF baby was born in 1978 more than one million children have been born after assisted reproductive technology (ART). During the 1990ties most European countries succeeded in reducing the triplet births, however due to the double embryo transfer policy twins still account for beyond 20% of the ART children born. It is well known that the outcome of twins is poorer than for singletons, however another consequence of double embryo transfer is that one in ten in vitro fertilization (IVF) singletons are born after a vanishing twin pregnancy. Two-thirds of these loose their co-twin during the first and second trimester, but even if spontaneous reduction sets on early in pregnancy this influences the survivor, as the surviving fetus carry higher neonatal risks including low birth weight, preterm birth, intrauterine growth retardation, neonatal deaths and admission to neonatal intensive care unit. Presumably also long-term outcomes such as cerebral palsy are increased with higher prevalence the later in pregnancy the co-twin disappears. Recently it has also been shown that there is a highly significant increase in the risk of congenital anomaly in survivors from a multiple conception following early loss of a conceptus. Hence by implementing single embryo transfer to the good prognosis IVF patients we will benefit not only from reduced twin birth rates also the outcome of IVF singletons will improve. In some European countries multiple birth rates have already been reduced from 25% to less than 15% by introducing elective single embryo transfer to the good-prognosis patients and there is now general consensus that the optimal IVF outcome is a singleton healthy baby. Countries should aim for national guidelines regarding embryo and patient selection criteria for elective single embryo transfer.

BEHAVIORAL GENETICS IN THE ERA OF MOLECULAR GENETICS: LEARNING ABILITIES AND DISABILITIES AS EXAMPLES

Robert Plomin
King's College London, London, UK

Twin analyses of complex phenotypes such as learning abilities and disabilities are alive and well even in this era of molecular genetics. I will present recent examples that go beyond merely estimating heritability, using learning abilities and disabilities as examples. Three findings from twin research stand out for their far-reaching implications. First, common disorders are the quantitative extreme of the same genetic factors responsible for genetic influence throughout the normal distribution (the Common Disorders are Quantitative Traits Hypothesis). Second, the same set of genes is largely responsible for genetic influence across diverse domains (the Generalist Genes Hypothesis). Third, experiences are just as influenced genetically as are behaviors and genetic factors mediate associations between widely used measures of the environment and behavioral outcomes (the Nature of Nurture Hypothesis).

THE GENETICS OF HIGH COGNITIVE ABILITIES: AN OVERVIEW

R. Plomin, C. M. A. Haworth
Social, Genetic and Developmental Psychiatry Centre, Institute of Psychiatry, King's College London, London, UK

The purpose of this symposium is to bring together researchers interested in the genetics of high cognitive abilities. The presenters, all members of a consortium called the Genetics of High Cognitive Abilities (GHCA), contributed to the first-ever collection of papers on the genetics of high cognitive abilities which was published as a special issue of the journal *Behavior Genetics* in 2009. The GHCA Consortium also collaborated on the first adequately powered study of high general cognitive ability (*g,* aka *intelligence*) in a mega-analysis of data from 11,000 twin pairs across six studies from four countries. High *g,* defined as the top 15%, yielded a heritability estimate of 0.50 which was similar to the estimate for the entire distribution. High cognitive abilities are likely to represent the quantitative extremes of the same genetic factors responsible for normal variation in cognitive abilities as well as for low cognitive abilities. However, a key question is whether high cognitive abilities merely represent the absence of 'risk' alleles for low cognitive abilities or whether there are genes that are 'risk' alleles for high cognitive abilities? There are hundreds of genes for which one allele is known to decrease cognitive abilities. The effect is nonsymmetrical (nonadditive) in that the other allele has no average effect on the phenotype in the population. Are there other genes with a nonsymmetrical effect in the other direction — with alleles that enhance cognitive abilities? To what extent is the heritability of high cognitive abilities due to such 'increasing' alleles rather than merely the absence of 'decreasing' (risk) alleles? Results from our genome-wide association studies of *g,* mathematics and reading generally confirm that most associations involve 'symmetrical' effects but when 'nonsymmetrical' effects emerge they are in the direction of decreasing alleles rather than increasing alleles. However, the research available so far is limited to moderately high cognitive abilities (top 15%). The genetics of high cognitive abilities might well differ for truly exceptional ability. The GHCA Consortium is currently obtaining DNA from a sample of 2000 individuals with IQs above 160 (4 standard deviations above the mean) in preparation for a genome-wide association analysis of exceptionally high *g.*

PRETERM BIRTH, SOCIAL DISADVANTAGE, AND COGNITIVE COMPETENCE

F. Rasmussen[1], C. Ekeus[2], K. Lindström[3], F. Lindblad[4,5], A. Hjern[6,7]
[1] *Child and Adolescent Public Health Epidemiology Group, Department of Public Health Sciences, Karolinska Institutet, Stockholm, Sweden*
[2] *Department of Women and Children Health, Karolinska Institutet, Stockholm, Sweden*
[3] *Department of Clinical Sciences and Education, Sachs Childrens Hospital, Stockholm, Sweden*
[4] *Department of Neuroscience, Child and Adolescent Psychiatry, Uppsala University, Uppsala, Sweden*
[5] *Stress Research Institute, Stockholm University, Stockholm, Sweden*
[6] *Centre for Health Equity Studies, Karolinska Institutet, Stockholm, Sweden*
[7] *Centre for Epidemiology, National Board of Health and Welfare, Stockholm, Sweden*

The aim was to study the impact of a range of gestational ages (GAs) on cognitive competence in late adolescence and how this effect is modified by contextual social adversity in childhood. This was a register study based on a national cohort of 119 664 men born in Sweden from 1973 to 1976. Data on GA and other perinatal factors were obtained from the Medical Birth Register, and information on cognitive test scores was extracted from military conscription at the ages of 18 to 19 years. Test scores were analyzed as *z* scores on a 9-point stanine scale, whereby each unit is equivalent to 0.5 SD. Socioeconomic indicators of the childhood household were obtained

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

from the Population and Housing Census of 1990. The data were analyzed by multivariate linear regression. The mean cognitive test scores decreased in a stepwise manner with GA. In unadjusted analysis, the test scores were 0.63 stanine unit lower in men who were born after 24 to 32 gestational weeks than in those who were born at term. The difference in global scores between the lowest and highest category of socioeconomic status was 1.57. Adjusting the analysis for the childhood socioeconomic indicators decreased the effect of GA on cognitive test scores by 26% to 33%. There was also a multiplicative interaction effect of social adversity and moderately preterm birth on cognitive test scores. This study confirms previous claims of an incremental association of cognitive competence with GA. Socioeconomic indicators in childhood modified this effect at all levels of preterm birth.

INTELLIGENCE, SMOKING HABITS AND NICOTINE DEPENDENCE AMONG SWEDISH MALE TWIN PAIRS

F. Rasmussen[1], K. Modig Wennerstad[1], K. Silventoinen[2], P. Tynelius[1], L. Bergman[3], J. Kaprio[4]

[1] *Department of Public Health Sciences, Karolinska Institute, Stockholm, Sweden*

[2] *Population Research Unit, Department of Sociology, University of Helsinki, Finland*

[3] *Department of Psychology, University of Stockholm, Sweden*

[4] *Department of Public Health, University of Helsinki, Finland, National Institute for Health and Welfare, Helsinki, Finland; Institute for Molecular Medicine, Helsinki, Finland*

Associations between intelligence (IQ) and smoking status reported in previous studies might be biased by residual confounding and it is unknown to what extent correlations between these phenotypes can be explained by pleiotropy. We examined associations between IQ at age 18 and smoking status and nicotine dependence in adulthood in a large population of Swedish male twins born 1951–84. IQ was assessed at military conscription, and data on smoking and nicotine dependence was collected by computer-assisted telephone interviews or by a web-questionnaire when the twins were 22–47 years of age. Nicotine dependence from smoking and from snuff use was measured with the Fagerström Nicotine Dependence scale, FTND. Logistic regression models estimated with generalised estimating equations were used to explore associations between IQ and smoking status among the twins as individuals as well as between and within twin pairs. Univariate and bivariate biometrical models of IQ and nicotine dependence were estimated using the Mx package. A strong inverse association between IQ and smoking status was observed in un-paired analyses over the entire range of the IQ distribution. Within- and between-pair analyses showed that SES and/or psychosocial factors explained most of the inverse IQ-smoking relationship. These analyses also indicated that nonshared and genetic factors contributed only slightly (and non-significantly) to the IQ-smoking association. Analysis of twin pairs discordant for IQ and smoking status displayed no evidence that non-shared factors contribute substantially to the association. In addition, the results showed an inverse association between IQ and nicotine dependence. Analyses of the genetic and environmental contributions to the association between IQ and nicotine dependence are ongoing and results will be presented at the meeting.

TRAJECTORIES OF ATTENTION PROBLEMS IN CHILDHOOD

S. C. C. Robbers[1,2], F.V.A. van Oort[1], T. J. C. Polderman[1,2], M. Bartels[2], G. H. Lubke[4], F. C.Verhulst[1], D. I. Boomsma[2], A. C. Huizink[1,3]

[1] *Department of Child and Adolescent Psychiatry, Erasmus University Medical Center — Sophia, Rotterdam, the Netherlands*

[2] *Department of Biological Psychology, VU University Amsterdam, the Netherlands*

[3] *Department of Education, Faculty of Behavioral and Social Sciences, University of Amsterdam, Amsterdam, The Netherlands*

[4] *University of Notre Dame, Department of Psychology, Notre Dame, IN*

The first aim of this study was to identify developmental trajectories of attention problems in male twins followed from age 6 to 12 years. Second, we investigated whether singletons follow similar trajectories. Maternal longitudinal ratings on the Attention Problems (AP) subscale of the Child Behavior Checklist were obtained for a sample of 6,161 male twins from the Netherlands Twin Register and for a comparable general population sample of 662 male singletons. Trajectories were analyzed by growth mixture modeling (GMM) in twins, and subsequently in singletons. Teacher longitudinal ratings on the AP subscale of the Teachers' Report Form were available for 3,506 male twins and 580 male singletons, and were used for cross-sectional mean comparisons at each age. We identified three linear trajectories, i.e. stable low (84%), increasing (9%), and decreasing (7%). Singletons followed three similar trajectories, with similar class proportions. Intercepts of the trajectories did not differ between twins and singletons, but the decreasing trajectory decreased at a slightly higher rate for twins than for singletons. Teacher ratings yielded no pattern in differences in mean levels of attention problems between twins and singletons. In conclusion, the development of attention problems in boys from age 6 to 12 years can be characterized by stable low, increasing, and decreasing developmental trajectories. Twins and singletons are largely comparable with respect to the development of attention problems in childhood. Our findings confirm the generalizability of twin studies to singleton populations with regard to attention problems in middle and late childhood.

A TWIN STUDY EXPLORING THE ASSOCIATION BETWEEN PRENATAL AND NEONATAL COMPLICATIONS AND AUTISTIC SPECTRUM DISORDERS

A. Ronald

University of London, UK

Obstetric factors and pre-, peri-, and neonatal problems have been found to be associated with autistic spectrum disorders (ASD). It is not clear from existing data to what extent these early complications are environmentally caused, and thus could be considered an environmental risk factor for ASD, or if they may be a result of existing genetic abnormalities in a fetus who later develops ASD. The first part of the study took a dimensional approach. Neonatal events and later autistic-like traits in the general population were assessed, using a prospective design. Parents of 13,690 18-month-old twins enrolled in the Twins Early Development Study (TEDS), a representative community sample born in England and Wales, reported on the twins' birth complications. At ages 7–8, parents and teachers completed questionnaires on social and nonsocial autistic-like features and parents completed the Childhood Asperger Syndrome Test. Correlations between prenatal and neonatal events and autistic-like features were weak, both in the whole sample (r = .00–.07) and at the 5% quantitative extreme (phenotypic group correlations = .01–.11), after controlling for socioeconomic status and cognitive ability. Differences in monozygotic (MZ) twins' neonatal problems correlated weakly with their difference scores on autistic-like features (r = .01–.06). In the second part of the study, twin pairs with suspected ASD in TEDS were assessed in early adolescence using the ADOS and ADI-R diagnostic instruments and parents completed the Obstetric Enquiry Scale during this assessment. MZ differences between ASD symptoms and neonatal complications were examined in this diagnosed group using differences correlations and within-pair mean group comparisons. These findings are discussed in light of their implications for the role of prenatal and neonatal complications as risk factors for ASD.

THE PERINATAL EPIGENETIC TWIN STUDY (PETS)

R. Saffery[1,3], R. Morley[1], M. Ollikainen[1], R. Andronikos[1,3], E.J. Joo[1,3], J. Carlin[2,3], S. Healy[1], T.Vaiano[1], N. Brooks[1], G. McIlroy[1], A. Czajko[1], J.M. Craig[1,3]

[1] *Developmental Epigenetics, Murdoch Childrens Research Institute, Royal Children's Hospital, Victoria, Australia*

[2] *Clinical Epidemiology and Biostatistics Unit, Murdoch Childrens Research Institute, Royal Children's Hospital, Victoria, Australia*

[3] *Department of Paediatrics, University of Melbourne, Parkville, Victoria, Australia*

Introduction: Considerable evidence in animal models, and circumstantial evidence in humans, implicates the *in utero* period as a major determinant of neonatal epigenome and the establishment of disease risk for a host of phenotypic variation emerging throughout the life course. *Aims:* Collection of extensive maternal environmental and dietary information during pregnancy, with associated collection of maternal blood and multiple birth specimens in twin pregnancies

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

provides a unique opportunity to examine the contribution of genetic, epigenetic and environmental factors to the establishment of the neonatal epigenome in humans. *Methods:* The Peri/Postnatal Epigenetic Twin Study (PETS) involved recruitment of over 250 mothers with twin pregnancies, with collection of extensive dietary, lifestyle, and reproductive data, maternal blood, and birth specimens, including cord blood, cord vein endothelial cells, and inner cheek (buccal) cells. This resource provides a unique opportunity to investigate both genetic and environmental contributions to epigenome establishment. *Results:* Approximately 300 women pregnant with twins were approached for recruitment into this study. Of these 287 consented to participate, and of these, full questionnaire data and maternal blood were collected from 251 births. Birth biospecimens, including cord blood (both twins, 188; one twin only, 21), human umbilical vein endothelial cells (HUVECS; 218 pairs), buccal cells (233 pairs) and placenta (148 pairs), were collected and stored at either -70^{0}C (blood serum, plasma, buccal cells, placenta biopsies), or processed for cell isolation and storage in liquid nitrogen (Cord Blood Mononuclear Cells, HUVECs). *Conclusions:* Comprehensive data/biospecimen collection from this unique cohort provides the foundation for investigating the complex interplay between genetic and environmental factors in the establishment of the neonatal epigenome. Longitudinal analysis will enable the 'predictive' power of neonatal epigenetics to be fully explored in relation to adverse health outcomes in later life.

SEROTONIN RECEPTOR 2A GENE MODERATES THE EFFECT OF CHILDHOOD NURTURING ENVIRONMENT ON SOCIAL ATTACHMENT IN ADULTHOOD

J. Salo[1], M. Jokela[1], P. Merjonen[1], T. Lehtimäki[2], L. Keltikangas-Järvinen[1]
[1] *Institute of Behavioural Sciences, University of Helsinki, Helsinki, Finland*
[2] *Laboratory of Atherosclerosis Genetics, Department of Clinical Chemistry, Centre for Laboratory Medicine, Tampere University Hospital, Tampere, Finland*

The ability to form and maintain social attachments is a central factor underlying mental health. Traditionally, the development of attachment is assumed to be influenced by environmental factors, mainly the early relationships with caregivers. However, there may be genetically based differences in how individuals respond to parental care. There is preliminary evidence that serotonergic genes may moderate the association between early parental care and attachment in infancy. Our aim in the current study was to extend the scope to adulthood and to examine whether a variant of the serotonin receptor 2A gene moderates the effect of childhood maternal nurturance on social attachment in adulthood. We analyzed prospective, longitudinal data from a subsample of 913 healthy women and men derived from a population-based Finnish sample called the Cardiovascular Risk in Young Finns study. Childhood maternal nurturance was self-reported by the participants' mothers in 1980 by a self-report measure reflecting the emotional significance of the child to the mother. Social attachment was measured twice, in 2001 and 2007, using two self-report measures filled by the participants: the Relationship Questionnaire (Bartholomew & Horowich, 1991), which assesses adult attachment styles, and the reward dependence temperament scale of the Cloninger's Temperament and Character Inventory. The subsample was genotyped for the HTR2A T102C (Rs6313) polymorphism. We found high childhood maternal nurturance to be associated with high reward dependence (B = 0.76, SE = 0.27, p = .004) and low avoidant attachment (B = -0.27, SE = 0.10, p = .005) in adulthood, but, when genotypic data was taken into account, the effect of maternal nurturance was present strongly among carriers of the T/T genotype group (e.g. reward dependence: B = 3.15, SE = 0.85, p < .001), and only weakly in the T/C or C/C genotype groups (e.g. reward dependence: B = 0.54, SE = 0.28, p = .06). Thus, high maternal nurturance seemed to benefit mostly the T/T genotype carriers of the HTR2A gene T102C variant in terms of social attachment. On the basis of our results it seems that genetic factors may moderate the association between childhood nurturing environment and child's later social attachment in adulthood.

THE DOPAMINE TRANSPORTER GENE (DAT1) POLYMORPHISM MODERATES THE EFFECTS OF ALCOHOL USE ON AGGRESSIVE BEHAVIOUR IN MEN

P. Santtila, A. Johansson, B. von der Pahlen, N. K. Sandnabba
Center of Excellence in Behavior Genetics, Department of Psychology, Åbo Akademi University, Turku, Finland

We were interested in identifying whether the dopamine transporter gene (DAT1) polymorphism influences aggressive behavior in men and, more specifically, whether it moderates the effects of alcohol on aggressive behavior. The present study involved 1,598 Finnish men (M = 26.3, SD = 4.8 years; range 18–45) of which 867 were twin individuals and 423 their brothers. Alcohol use was assessed using the Hazardous Alcohol Use subscale from the Alcohol Use Disorders Identification Test (AUDIT; Saunder et al., 1993). Aggressive behavior was assessed using the physical and verbal aggression items from the Buss and Perry Aggression Questionnaire (AQ; Buss & Berry, 1992). We found main effects of both the DAT1 polymorphism (p < .046) and alcohol use (p < .015) on aggressive behavior. Men with at least one 10R allele evidenced lower levels of aggressive behavior compared to individuals homozygous for the 9R allele. Men with higher scores on the alcohol use measure reported higher levels of aggressive behavior. The interaction between DAT1 and alcohol use was also significant (p < .032). Men with at least one 10R allele reported more aggressive behavior if they had high alcohol use scores (r = .27, p < .001) whereas this was not true of the men homozygous for the 9R allele (r = .02, p < .887). The implications of the results will be discussed.

COPY NUMBER VARIATIONS IN SHORTSIGHTEDNESS (MYOPIA)

M. Schache
Centre for Eye Research Australia, University of Melbourne, Royal Victorian Eye and Ear Hospital, Melbourne, Australia

Myopia is a complex disease influenced by genetic and environmental factors. Many genome-wide linkage and candidate gene association studies have been undertaken for myopia but these have had little impact on our understanding of its causative genetic variants. We hypothesize that copy number variations (CNVs) may play a role in myopia and to date the role of CNVs in myopia is relatively unexplored. To test this hypothesis we undertook a pilot study using a subset of twins from the Genes in Myopia (GEM) study. For the pilot study, 87 unrelated individuals including 51 myopic cases and 36 controls were genotyped using the Illumina Human610-Quad BeadChips. Output data was analyzed using the PennCNV software package for CNV calling. Frequencies of CNVs were compared between cases and controls using the Fisher Exact test. The quality of data from the pilot study was high with the average oligonucleotide call rate for each sample being 99.84% ± 0.07. A total of 3,250 CNVs were identified. Of these, 14 CNVs showed a statistically significant difference (p > .05) between myopic cases and controls including 8 deletions and 6 duplications. These CNVs were located in 11 chromosomal regions including 1p13, 2p21, 2q33, 3q26, 4p16, 4q32, 4q32, 6p21, 6p21, 14q11, 15q11. One of these CNVs appears to be novel whilst the remaining 13 have been previously reported in the Database of Genomic Variants. In conclusion, this pilot study suggests that CNVs do play a role in the development of myopia.

AKAIKE INFORMATION CRITERION IS NOT APPROPRIATE FOR IDENTIFYING THE 'TRUE' MODEL: BAYESIAN INFORMATION CRITERION IS PREFERABLE

D. F. Schmidt, J. L. Hopper
The University of Melbourne, Centre for Molecular, Environmental, Genetic and Analytic Epidemiology, School of Population Health, Melbourne, Victoria, Australia

A commonly used tool in model-based analysis of twin data is the Akaike Information Criterion (AIC). We argue that selection of a hypothesis based solely on choosing the model with the lowest AIC

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

score is inappropriate when one is attempting to identify the 'true' model from amongst a finite set of parametric models. The AIC is designed to provide an estimate of the expected performance of a fitted model in terms of prediction of future data arising from the true distribution, and as such offers no guarantees that it will select the true model, even as the sample size grows. As an alternative we suggest that the Bayesian paradigm as an attractive alternative; the primary advantage being that the Bayesian approach allows one to examine and weigh the models by their posterior probabilities. In particular, the Bayesian Information Criterion (BIC), which is designed as a large sample approximation to the marginal probability, offers a simple, tractable alternative to AIC which is guaranteed to select the true model as the sample size grows. Additionally, the BIC provides a straightforward way to compute weights for each of the parametric models, allowing the evidence for and against particular hypotheses to be weighed in a more informative manner than simply choosing the model with the lowest information score. We will illustrate the implications of this for classic twin modeling by reference to the published literature.

SUICIDAL BEHAVIORS IN TWINS WHOSE CO-TWINS DEATHS WERE SUICIDES AND NON-SUICIDES

N. L. Segal
California State University, Fullerton

Identifying individuals at risk for suicide-related behaviors is a significant problem for mental health professionals. Genetically informative samples can address hereditary and experiential influences on suicide-related behaviors. Epidemiological twin studies of suicide have implicated both genetic and non-genetic factors. The Fullerton Twin Loss Study, which has been ongoing at CSU Fullerton since 1991, has studied the loss experience in over 650 twin survivors. Twins complete an extensive Twin Loss Survey by mail; embedded within the survey are questions pertaining to the cause of the co-twins' death, as well as suicidal attempts and ideation on the part of participants. In the present study, the frequency of suicide-related behaviors was compared in twins from two survivor groups: (1) those whose co-twins' deaths were suicides (monozygotic [MZ]: n = 47; dizygotic [DZ]: n = 31), and (2) those whose co-twins' deaths were nonsuicides (MZ: n = 347; DZ: n = 170). The frequency of suicide attempts among suicide survivors was significantly higher in MZ (8/47, 17%) than DZ twins (0/31, 0%) (Fisher's Exact Test, $p < .01$). The frequency of suicidal ideation did not differ between the two types of twins (MZ: 56.4%; DZ: 65.6%). In contrast, the frequency of suicide attempts among nonsuicide twin survivors did not differ between MZ (2.0%) and DZ twins (3.5%), as expected. In addition, the frequency of suicidal ideation did not differ between these MZ (28.5%) and DZ twin survivors (24.4%). It was concluded that twin concordance for suicidal attempts most likely reflects a genetic predisposition than a behavioral reaction to the loss.

MONOZYGOTIC TWINS SWITCHED AT BIRTH: ISSUES AND FINDINGS FROM THE RECENT CANARY ISLANDS CASE

N. L. Segal, I. Blandón–Gitlin
Department of Psychology, California State University, Fullerton, California, United States of America

There is a rare class of reared apart twins whose separation is due to the inadvertent switching of one twin infant with an unrelated non-twin infant in the hospital nursery. This unfortunate event creates presumed DZ twins (in reality, a same-age unrelated sibling pair) raised by the twin's parents, and a single child (in reality, a singleton twin) raised by non-biological parents. There have been five documented cases of switched at birth twins. These cases have been reported in Switzerland, Puerto Rico (2 cases), Poland and Canada. The sixth most recently reported switch occurred thirty-six years ago, in Spain's Canary Islands. Following the twin's chance reunion in 2001, the case was reported publicly in May 2008 and drew considerable interest. The focus of attention was a lawsuit brought by the twins and their families against the Nuestra Senora del Pino Hospital, in Las Palmas, for emotional damages. However, switched at birth twins raise many issues of considerable scientific and social significance: (1) Two genetically informative pairs are created when twins are switched at birth. How similar are the behavioral and physical characteristics of the separated co-twins, compared with the unrelated siblings? (2) Most reunited twins are happy to find one another. What are the psychological consequences of discovering an unknown twinship that was interrupted due to hospital error? (3) Lawsuits involving switched at birth non-twins have been based on disruption of the biological parent-child bond. What additional part does disruption of the twin relationship play in lawsuits involving switched at birth twins? (4) Maternal uncertainty, rarely considered seriously, appears to be increasing. How can this phenomenon be explained, and what hospital procedures can insure that mothers and infants are matched correctly? In September 2009, the senior author visited the Canary Islands to interview and test the twins and unrelated sister (e.g., BMI, self-esteem, personality), family members and the attorneys working on the case, and to interview an expert on newborn infant identification. The aim of this visit was to obtain information on the questions listed above. A review of switched at birth twin cases and discussion of issues and questions raised by the Canary Islands case and others will be presented.

THREE-DIMENSIONAL CRANIOFACIAL DISCORDANT MONOZYGOTIC TWINS WITH CLEFT LIP AND PALATE: A MODEL FOR IDENTIFYING DEFORMATIONS OF CLEFT

R. Shibazaki-Yorozuya[1], Y. Asama[1], F. Ohkubo[2], K. Kadomatsu[2], Y. Kako[3], Y. Hosaka[2], K. Maki[1]
[1] *Department of Orthodontics, Showa University Cleft Palate Treatment Centre, Japan*
[2] *Department of Plastic and Reconstructive Surgery, Showa University Cleft Palate Treatment Center, Japan*
[3] *Department of Pediatrics, Showa University Cleft Palate Treatment Center, Japan*

Craniofacial deformations of cleft monozygotic twins (MZ) have reported by means of lateral cephalometric radiographs since 1954. However, it is hard to investigate whether which areas are effected by clefts or not in craniofacial region in two-dimensional data. The objective of this report is to investigate those regions in three-dimension for treatment of their craniofacial deformities by comparing in monozygotic twins with/without cleft lip and palate. Three couples of monozygotic twins with/without cleft lip and alveolus (2couples; UCLP; 4, 16 year-old, 1 couple; UCLA; 4 year-old) discordant for nonsyndromic clefting were studied. Three-dimensional Cone–Beam CT data had taken, and three-dimensional superimposition and three-dimensional linear/angle were measured within twins. Immature/mature twins with/without cleft showed Skeletal Cl In all couples except mature cleft co-twin. Comparison within twins, twins with cleft showed wider midface than that of co-twins without cleft. However, morphology of mandibles are the same as co-twins who are with no cleft. Those findings suggested that cleft might effect on not only maxilla (maxillofacial width) but also temporal bone and midface including orbital position, however, cleft might not accelerate mandibular growth.

ENVIRONMENTAL INFLUENCES ON THE COVARIATION BETWEEN PROSOCIALITY AND CONDUCT PROBLEMS IN SOUTH KOREAN TWIN CHILDREN

Y. Shin[1], M. Jin[1], S. Koo[1], O. Jo[1], B. Kim[1], K. Kim[1], J. Yoo[1], N. Ha[1], M. Hyun, Y.-M. Hur[2]
[1] *Chung-Ang University, Republic of Korea*
[2] *Mokpo National University, Republic of Korea*

The present study explored the issue of genetic and environmental influences on the relationship between prosociality and conduct problems during childhood. Mothers of 603 pairs of South Korean twins completed the Prosocial Behavior and the Conduct problems scales. The phenotypic correlation between the two scales was –.35. Cross-twin correlation was slightly higher among dizygotic than among monozygotic twins suggesting that the relationship between the two phenotypes may be influenced by common environmental influences. The model-fitting results were consistent with the results

from correlational analyses. Although children's prosociality was heritable trait, common environmental influences significantly mediated the relationship between procosiality and conduct problems. These results suggest that prosociality can be environmental protective factors for children's conduct problems.

GENETIC REGULATION OF GROWTH IN ASIAN AND CAUCASIAN POPULATIONS SYMPOSIUM: THE ROLE OF PSYCHOSOCIAL CONSEQUENCES IN THE GENETICS OF ANTHROPOMETRIC MEASURES

K. Silventoinen
Department of Social Research, University of Helsinki, Finland

Childhood is a crucial phase of the human life cycle for the further development of many psychosocial factors, and thus good understanding on factors affecting childhood development is crucial when creating optimal living environment for children. Studies from both Asian and Caucasian populations have shown that childhood growth in height and weight is strongly genetically regulated. Less research is available on other anthropometric measures, but strong genetic component is found also for head circumference. Strong genetic tracing in height and relative weight is present during the growth period, but also new genetic variation emerges during growth. There is evidence on moderate common environmental effect in relative weight in childhood, but this effect seems to disappear already in adolescence when children get more freedom to make own choices in eating and physical exercise. Genetic regulation of relative weight in the Japanese population seems to be very similar than it is in Caucasian populations. This is interesting since Japan does not differ from western countries only for its ethnic composition, but also the prevalence of obesity is much lower in Japan than in many western countries suggesting that Japan can be regarded as relatively less obesogenetic environment. The results in several countries both in Asia and Europe thus show that at least in affluent societies the physical development of the child is strongly genetically regulated. Further studies are needed to reveal whether these genetic factors also explain the associations between physical development in childhood and psychosocial factors in adulthood or whether they are explained by environmental factors.

HERITABILITY OF POST PRANDIAL B-CELL FUNCTION IN A DUTCH TWIN FAMILY STUDY

A. M. C. Simonis-Bik[1], D. I. Boomsma[2], J. M. Dekker[3], M. Diamant[1], E. J. C. de Geus[2], L. M. 't Hart[4], R. J. Heine[1], M. H. H. Kramer[5], J. A. Maassen[1], A. Mari[6], G. Willemsen[2], E. M. W. Eekhoff[1]
[1] *Diabetes Center, VU University Medical Center, Amsterdam, The Netherlands*
[2] *Biological Psychology, VU University, Amsterdam, The Netherlands*
[3] *EMGO Institute for Health and Care Research, VU University Medical Center, Amsterdam, The Netherlands*
[4] *Molecular Cell Biology and Medical Statistics, Leiden University Medical Center, Leiden, The Netherlands*
[5] *Internal Medicine VU University Medical Center, Amsterdam, The Netherlands*
[6] *CNR Institute of Biomedical Engineering, Padova, Italy*

Type 2 diabetes mellitus is a multi factorial disease with an increasing prevalence around the world. Deterioration of the b-cell function plays a crucial part in the development of diabetes. Genetic influences are responsible for a part of the individual differences in b-cell function, which have been estimated in different research settings, but never with the most physiological challenge test; for example, the mixed meal tolerance test. We recruited 77 same-sex twin families from the Netherlands Twin Register, including 51 MZ twin pairs, 21 DZ twin pairs, 5 twins without their co-twin and 34 same-sex siblings of the twins. All 183 healthy participants (77 male) were of European origin and aged 20-49 years. Before and after the consumption of a standardized meal blood samples were taken for blood glucose, insulin and C-peptide levels. We calculated 17 often used (classical as well as model derived) parameters of b-cell function and postprandial glycemia, the waist circumference and insulin sensitivity. All genetic analyses were carried out in Mx, a structural equation modeling program. In the univariate analyses the MZ and DZ/sibling correlations were assessed with age and sex as covariates. A genetic triangular model was used to decompose the total variance into components A,C and E or A,D and E. Likelihood-ratio tests were employed to identify the most parsimonious model. Under this model we estimated the heritability of each variable individually. Three sets of variables were selected for multivariate analyses to reveal to which extent genetic factors influencing post prandial b-cell function overlap with those influencing waist circumference and insulin sensitivity. We will present the MZ and DZ/ sibling correlations and heritability estimates under the most parsimonious model. We will also show the decomposition of the heritability of waist, insulin sensitivity and the 4 most important post prandial b-cell function measurements.

NOVEL USES OF TWINS IN THE ERA OF MOLECULAR GENETICS: EXAMPLES FROM EPIGENETICS AND GENE EXPRESSION

T. Spector
King's College London, London, UK

Recent rapid advances in DNA and RNA genotyping technologies have allowed us to use twins in ways we couldn't have imagined ten years ago. The use of Copy number variants (CNVs) and methylation changes has shown us that MZ twins can no longer considered completely identical. These changes may occur at different points in life. We also now have a whole range of novel phenotypes that can be tested in twins, such as 26,000 gene expression arrays — which have different levels of heritability and the new field of metabolomics — which can provide 26,000 different metabolite ratios, picking up subtle errors of inborn metabolism. Genome-wide Methylation arrays of 500,000 markers will soon be available — picking up important sites of epigenetic change. As we move into the phase of whole genome sequencing — uncovering rare individual mutations, the twin model — both classical and the discordant MZ twin approach will have a major role in unraveling the complex interaction between genes and environment.

GENETIC EFFECTS ON AGE-RELATED CATARACT: EVIDENCE FROM AN ITALIAN TWIN STUDY

M. A. Stazi[1], R. Cotichini[1], C. Fagnani[1], L. Ferrigno[1], M. Ferri[1], A. Gregorio[2], C. Rinaldi[2], S. L. Williams[2], and G. Maraini[2]
[1] *Istituto Superiore di Sanità, Rome, Italy*
[2] *Section of Ophthalmology, University of Parma, Parma, Italy*

The twin design was used to estimate the genetic contribution in nuclear and cortical cataracts. Out of the 620 twins aged 50-85 identified by the General Register Office of the city of Parma, 379 participated. Twins were invited to the Eye Clinic of the University of Parma, where they were administered a questionnaire regarding environmental risk factors for cataract, underwent ocular examination with lens photographs, and donated a blood sample for DNA extraction. Lens status was 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. Zygosity was assessed by standard questions on physical resemblance. A total of 646 images for the 379 twins (758 eyes) were available for grading analysis. Biometric models were fitted to data from monozygotic (MZ) and dizygotic (DZ) twins with the software Mx to estimate genetic and environmental effects on nuclear and cortical cataract. For each type of cataract, the models were adjusted for age, gender, sunlight exposure and the other type of cataract. Cortical grading score was dichotomized using standard cut-offs and the occurrence of cortical cataract in at least one eye was considered for nuclear cataract, both the occurrence in at least one eye and the log-transformed opacity score in the worse eye were examined. For dichotomous nuclear cataract, six concordant and no discordant pairs were observed among MZ twins, while there were seven concordant and 10 discordant pairs among DZ twins. This corresponded to tetrachoric twin correlations of 1.00 (95%CI: 0.84–1.00) in MZ and 0.60 (95%CI: 0.03–0.92) in DZ pairs. The

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

tetrachoric correlations for cortical cataract were 0.76 (95%CI: 0.24–0.97) and 0.17 (95%CI: –0.43–0.68) in MZ and DZ pairs respectively. Heritabilities were 0.80 (95%CI: 0.15–1.00) for nuclear cataract and 0.76 (95%CI: 0.24–0.97) for cortical cataract. For nuclear grading score, twin correlations were 0.74 (95%CI: 0.54–0.84) and 0.23 (95%CI: 0.03–0.42) in MZ and DZ pairs, resulting in a heritability of 0.74 (95%CI: 0.54–0.84). Our data showed large genetic effects on nuclear and cortical cataract, independently of each other and of age, gender and sunlight exposure.

VASCULAR RISK FACTORS AND COGNITIVE CHANGE IN OLDER WOMEN: A TWIN STUDY

C. J. Steves
King's College London, UK

Cognitive decline with age is one of the most feared aspects of growing old. Ageing is associated with changes in cognitive function in the normal population over the age of 50, especially fluid abilities such as working memory, speed of processing and reaction time. Maintenance of these abilities as we age contributes to preservation of autonomy, independence and quality of life. Recent research has indicated that some of these changes may be vascular in origin, some of which may be modifiable. This study utilizes a well characterized cohort of 381 Caucasian female twins aged over 60 who have 10 year longitudinal data on cognitive performance, measured using the Cambridge Neuropsychological Test Automated Battery, vascular endo-phenotypes and vascular risk factors. Data are presented on these associations, as well as heritability estimates and discordant twin analyses, and associations with candidate genes involved in vascular damage. Our data reveals potentially interesting insights into the genes and pathways linking vascular and cognitive ageing.

PRELIMINARY RESULTS FROM A TWIN STUDY OF PERSONALITY, PSYCHOLOGICAL DISTRESS, AND HSV-1 REACTIVATION

E. Strachan[1], M. Saracino[2], J. Goldberg[3], D. Buchwald[4], A. Wald[5]
[1] *Department of Psychiatry and Behavioral Sciences, University of Washington, Seattle, Washington, USA*
[2] *Department of Allergy and Infectious Diseases, University of Washington, Seattle, Washington, USA*
[3] *Department of Epidemiology, University of Washington, Seattle, Washington, USA*
[4] *Department of Medicine, University of Washington, Seattle, Washington, USA*
[5] *Departments of Medicine, Epidemiology, and Laboratory Medicine, University of Washington, Seattle, USA; and Vaccine and Infectious Disease Institute, Fred Hutchinson Cancer Research Center, Seattle, USA*

Herpes simplex virus (HSV) is a very common infection in humans with clinical disease outcomes that range from asymptomatic to severe. The reasons for clinical phenotype variability are not understood but psychological distress may be a relevant co-factor. There are, however, gaps in the research linking distress and HSV. First, many studies do not link immune modulation to actual morbidity. Second, clinical symptoms are relatively rare compared to the presence of infectious virus in the mouth or genital area. Third, most studies are not sufficiently sensitive to establish the distress-disease chronology. As such, studies demonstrate a temporal association between distress and lesions but not a causal direction. Finally, stable personality traits that may impact stress attributions have not typically been measured in HSV research. HSV-1 infection in twin pairs provides a unique opportunity to measure the impact of both personality factors and psychological distress on the phenotype of infections. We have developed accurate methods to objectively quantitate the frequency and magnitude of HSV-1 reactivation on mucosal surfaces, using real-time quantitative PCR. We are enrolling 25 HSV-1 concordant MZ and 25 HSV-1 concordant DZ twin pairs from the University of Washington Twin Registry into a prospective study in which the participants collect swabs of the oral mucosa daily for 60 days to determine the frequency and magnitude of oral HSV shedding, and clinical severity of disease, as measured by days with oral lesions and symptoms. These data will be combined with measures of psychological distress focused on different time intervals and account for stable personality traits including neuroticism, extraversion, and conscientiousness. We will present data on 13 pairs who have completed the protocol. We hypothesize that psychological distress will predict viral shedding and lesions and that personality factors will partially mediate the effect of distress on shedding and lesions.

CROSS-POPULATION DISPARITY IN GENETIC AND ENVIRONMENTAL EFFECTS ON ENDOPHENOTYPES ASSOCIATED WITH METABOLIC SYNDROME

Q. Tan[1,4], S. Li[1], Z. Pang[2,3], D. Zhang[3], T.A Kruse[4], K. Christensen[1], K. O. Kyvik[1,5]
[1] *Epidemiology, Institute of Public Health, University of Southern Denmark*
[2] *Qingdao Center for Disease Control and Prevention, Qingdao, China*
[3] *Dept of Public Health, Qingdao University Medical School, Qingdao, China*
[4] *Dept. of Clinical Genetics, Odense University Hospital/Clinical Institute, University of Southern Denmark*
[5] *Institute for Regional Health Service Research, University of Southern Denmark*

Genetic epidemiological studies using data on family and twins have shown that both genetic and environmental factors contribute to the development of metabolic syndrome together with their interplay. Among the factors studied, ethnicity is an interesting topic because it can help to reveal important (adaptive) gene-environment interaction effects that underlie the etiology of metabolic syndrome. Meanwhile ethnic disparities in the pathophysiology and pathogenesis of the sub-phenotypes associated with metabolic syndrome can have an important impact on prevention and management. Recently, the cross-population comparison on genetic and environmental effects in the development of these phenotypes has only been conducted[1,2], although with limited scopes. For example, Hur et al.[1] performed a cross-population comparative study on genetic influences on body height, weight, and BMI between Caucasian and East Asian adolescent twins and reported no ethnic difference in the genetic control over these phenotypes. By comparing Danish and Chinese twin data, we obtain consistent conclusion on the 3 phenotypes. However, our preliminary results comparing lipid phenotypes (apolipoprotein A, total cholesterol, triglycerides, LDL, HDL, etc) in the Chinese twins with published results on Danish twins of similar age range[3] have shown that the Danes have a higher genetic control over lipid phenotypes than the Chinese while variations in these phenotypes are more determined by individual's unique environment in the Chinese (take total cholesterol for example, the additive genetic components are 0.49 with 95% CI: 0.18–0.58 in Chinese and 0.74 with 95% CI: 0.55–0.80 in Danes while the unique environmental components are 0.52 with 95% CI: 0.42–0.63 in Chinese and only 0.24 with 95% CI: 0.20–0.29 in Danes) indicating perhaps an important environmental adaption in two populations from different environments. Such findings can have an important impact on public health policy especially for the Chinese whose life style is under steady westernization.

1. Hur YM, Kaprio J, Iacono WG, Boomsma DI, McGue M, et al. Genetic influences on the difference in variability of height, weight and body mass index between Caucasian and East Asian adolescent twins. *Int J Obes (Lond)*, 32(10):1455–1467, 2008.
2. Ordoñana JR, Rebollo-Mesa I, González-Javier F, et al. Heritability of body mass index: a comparison between the Netherlands and Spain. *Twin Res Hum Genet*, 10(5):749–756, 2007.
3. Fenger M, Benyamin B, Schousboe K, Sørensen TI, Kyvik KO.Variance decomposition of apolipoproteins and lipids in Danish twins. *Atherosclerosis,* 191(1):40–47, 2007.

EXTREME SIMILARITY OF SECONDARY SKIN STRUCTURES IN THE FACES OF A REPRESENTATIVE PAIR OF CONCORDANT MZ TWINS

D. Teplica[1], L. Keith[2], D. Keith[3]
[1] *Section of Plastic Surgery, The University of Chicago, USA*
[2] *Department of Obstetrics and Gynecology, Northwestern University Medical School, Chicago, USA*
[3] *The Center for Study of Multiple Birth, Chicago, USA*

More than 220 pairs of MZ twins underwent photographic documentation of facial anatomy using highly standardized rotational imaging

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

techniques. Dermatologic evaluation of secondary skin features showed either concordance or mirroring in each twin pair. Older twins exhibited more identifiable features whether they had spent their adult lives in the same or different environments. Younger pairs demonstrated fewer evaluatable skin features and were less useful for study. Extreme similarity, concordant or mirrored, was found to a degree not previously documented in the literature. Allowing for slight variations in the degree of expression and differential rates of embryologic tissue migration within a given dermatome increased the observed similarity. We present the detailed analysis of one representative non-mirrored pair. Features distinct from the background skin were tabulated for each side of the face. Eighteen findings were identified on both the right side of Twin A and on the right of Twin B. Each matched for diagnosis and relative position ($p < .0001$). On the left side, Twin A exhibited 17 distinct findings, in contrast to 16 in twin B. However, 16 of the 17 had the same diagnosis and relative positions in both twins ($p < .0001$). A single wrinkle crease was the only feature out of 35 that was present on both sides of the same twin. The chance of having 34 out of 35 skin findings occur with the same diagnosis, relative position, and laterality in two separate individuals (using published estimates of 50% for the inheritance of individual skin structures) is 1 in 2 billion. We conclude that the accepted estimate for heritability of skin structures is wrong, since similar concordance was also observed on opposite sides of twin pairs who exhibited mirroring of facial shape. It is extremely unlikely that environmental factors play any significant role in the development of common skin features in this or any other twin pair studied to date, as environment cannot unilaterally affect anatomic development on one side of one twin and only the same side (or only the mirror opposite side) of the other twin in a consistent way for each separate skin structure.

CHANGES IN PERCEIVED AGE AND MORTALITY IN DANISH TWINS

M. Thinggaard, J. Mortensen, K. Christensen

Danish Twin Registry and Danish Aging Research Center, Institute of Public Health, University of Southern Denmark, Odense C, Denmark

Objectives: Facial expression is widely used by clinicians as a general indication of a patient's health, and it has been shown to be associated with mortality and important ageing phenotypes. The purpose of this study was to determine whether change in perceived age predicts survival even after controlling for genetic confounding. *Methods:* In 2001, 1826 twins (175 MZ pairs, 212 DZ pairs and 1052 single twins) had their face photographed. Ten nurses gave an estimation of the age of the person, and the mean of the age estimates for each twin was used as the twin's perceived age (PA). PA was shown to be associated with mortality, but also that this association seemed to decline over the follow-up period. In 2005, 898 twins (58 MZ pairs, 68 DZ pairs and 646 single twins) of the 1826 twins had their face photographed again. Survival of the twins was determined up to January 2010, by which time 243 (27%) of the 898 had died. *Results:* The change in PA, adjusted for age and gender, predicted survival during 5 years' follow-up (hazard ratio = 1.07, p = .001). Similar results were obtained if both level and change of PA were included in the model (hazard ratio = 1.07, p = .002). The measure of PA in 2005 also predicted survival (hazard ratio=1.06, p = .001). In the intra-pair analysis we found that there was a likelihood that the twin with the biggest change in PA died first and that this likelihood increased with increasing discordance in the change within the twin pair—that is, the bigger the difference in change in PA, the more likely that the twin with the biggest change died first. Stratifying this analysis with zygosity showed no major differences between MZ and DZ. *Conclusion:* Change in PA from 2001 to 2005 when evaluated independently predicts survival and has similar effect as the PA measure in 2005. Hence, an instantaneous measure might be just as good as measuring over time. Further analysis where the change is evaluated within each twin (adjacent pictures taken four years apart) might shed more light on this. The intra-pair analysis indicates that controlling for genetic factors do not have an impact on this association.

LIFESTYLE AND ENVIRONMENTAL FACTORS AFFECTING INTRA-PAIR DIFFERENCES OF DEPRESSIVE SYMPTOMS IN AGED IDENTICAL TWINS

R. Tomizawa, S. Saiki, T. Ohno, R. Nishihara, K. Hayakawa

Department of Health Promotion Science, Graduate School of Medicine, Osaka University, Japan

Objective: This study aims to clarify the lifestyle and environmental factors affecting the intra-pair differences of depressive symptoms in aged identical twins in their later adulthood. *Methods:* The self-reported questionnaire survey was conducted for 120 twin pairs aged over 60 years old. The questionnaires included GDS 15 (Geriatric Depression Scale 15 Item Version), Breslow's seven item (Body Mass Index, alcohol intake, smoking, sleeping, breakfast intake, physical exercise, and minimal snacking), ADL, economic situations and stress, subjective health feeling and the life events. Data was analyzed by Kruskal-Wallis Test and One-way layout Analysis of Variance. *Results:* There was no significant difference of intra-class correlation coefficients of GDS scores between monozygotic and dizygotic twins. When the data was analyzed individually as a person, not as a pair, it was shown that the GDS score tended to be inversely proportional to IADL score in male twins. Subjective health feeling, economic situation and physical exercise also tended to show an inverse proportion to GDS scores in male twins ($p < .01$). In female twins, subjective health feeling tended to show an inverse proportion to GDS score ($p < .05$). *Conclusion:* It was assumed that depressive symptoms in later adulthood were strongly related to lifestyle and environmental factors.

TWIN STUDY ON SALIVARY PROTEIN INTERACTIONS IN THE PERCEPTION OF ASTRINGENCY

O. Törnwall[1], C. Dinnella[2], K. Keskitalo-Vuokko[1], J. Kaprio[1,3,4], M. Perola[3,4], E. Monteleone[2], H. Tuorila[1]

[1] *University of Helsinki, Finland*

[2] *Università di Firenze, Italy*

[3] *National Institute for Health and Welfare, Finland*

[4] *Institute for Molecular Medicine, University of Helsinki, Finland*

Astringency is a shrinking and puckering perception at the epithelium caused by an exposure to phenolic compounds found in a wide range of foods and beverages. Astringent substances react with salivary proteins to form insoluble and soluble aggregates, leading to perceived astringency. Physiological individual variation of saliva characteristics is a well-recognised factor modulating the sensitivity to astringency induced by phenolic stimuli. The aim of this study was to evaluate the genetic effects on the astringency perception by investigating the saliva compositions in monozygotic (MZ) and dizygotic (DZ) twins. A total of 180 twins (21–25 year of age, 86 males, 94 females) participated in the study. The sample included 71 full pairs (22 MZ, 48 DZ, 1 XZ) and 38 individual twins. Sensory evaluation (liking and intensity) of perceived astringency was recorded as responses to an apple juice with added tannic acid (0.15%) relative to untainted apple juice. The subjects donated two saliva samples, collected after 12 hours of fasting and after the stimulation with apple juice that contained tannic acid. The difference in the stimulated and rested concentrations of total salivary proteins (SPtot), phenols (Phs), amylase (Am), proline rich proteins (PRPs), histatin (H), cystein (C) and mucin (M) were measured. For the analysis of Am, PRPs, H, C and M only the full twin pairs (9 MZ, 43 DZ) were used. The MZ and DZ within-pair correlations (r) did not greatly differ for SPtot, Phs, H and C. In the individual protein components of the saliva, the correlations within pairs were higher in MZ twins: for Am, rMZ = .77 & rDZ = .31, for PRPs rMZ = .58 & rDZ = .31, and for M rMZ = .44 & rDZ = .13. The sensory data did not indicate large differences in correlations between MZ and DZ pairs, possibly due to the limitations of the chosen phenotypes. The present data implies that genetic factors may influence some of the salivary components, but ideally a larger sample would be needed to resolve this.

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

Research in this area is still in its infancy, and further studies are needed to understand the implications of the perceived astringency and salivary protein composition.

HERITABILITY OF EATING BEHAVIOR IN SELECTED PHILIPPINE ETHNIC GROUPS

M.A. J. Torres

Obesity is an increasing problem in the Philippines and is a major risk factor for chronic diseases such as diabetes, hypertension and cardiovascular diseases. However, very little is known about the heritability of behavioral traits, particularly that of eating behavior, that are tightly associated with obesity. This study was conducted to determine variability and heritability of eating behavior among ethnic groups in Iligan City, Philippines. The sample is comprised of people from diverse cultural backgrounds including Filipino Chinese, Ilonggo, Cebuano, Iliganon, Maranao, Tausog and Lumads. The Eating Behavior Questionnaire (EBQ) was used as an instrument to assess eight dimensions in eating style: food responsiveness, enjoyment of food, emotional overeating, desire to drink, satiety responsiveness, slowness in eating, emotional under-eating and fussiness. Heritability coefficients (h^2) were calculated and associations between the eating behavior of the parents and the offspring were also computed using Pearson's *r*. Results showed differences in the heritability values among the eight dimensions of eating style across ethnic groups. Also, variations in the eating behavior were observed based on the results of the MANOVA of the EBQ score matrix. The results of this study are discussed in the light of how heritability of eating behavior would differ among populations that differ in the distribution of environmental risk factors for obesity.

DETERMINANTS OF INFANT GROWTH IN FOUR AGE WINDOWS: A TWIN STUDY

R. N. H. Touwslager[1,2], M. Gielen[3,4,5], C. Derom[6], A. L. M. Mulder[1,2], W. J. M. Gerver[1,2], L. J. Zimmermann[1,2], A. J. Houben[7,8], C. D. A. Stehouwer[4,7,8], R. Vlietinck[6], R. J. F. Loos[9], M. P. Zeegers[3,4,5]

[1] *Department of Pediatrics, Maastricht University Medical Centre, The Netherlands*

[2] *Maastricht School for Oncology and Developmental Biology (GROW), The Netherlands*

[3] *Department of Complex Genetics, Cluster of Genetics and Cell Biology, Maastricht University Medical Centre, The Netherlands*

[4] *Nutrition and Toxicology Research Institute Maastricht (NUTRIM), The Netherlands*

[5] *Unit of Genetic Epidemiology, Department of Public Health and Epidemiology, University of Birmingham, United Kingdom*

[6] *Department for Human Genetics, Faculty of Medicine, Catholic University of Leuven, Belgium*

[7] *Department of Internal Medicine, Maastricht University Medical Centre, The Netherlands*

[8] *Maastricht School for Cardiovascular Diseases (CARIM), The Netherlands*

[9] *Medical Research Council Epidemiology Unit, Institute of Metabolic Science, Cambridge, United Kingdom*

Context: Low birthweight is related to disease risk later in life. A proposed underlying mechanism is accelerated growth. *Objective:* The study aimed to identify determinants of infant growth in four age windows. We hypothesized that the influence of environmental factors would decrease in time. *Design, setting, participants:* The sample consisted of 424 twin pairs from the East Flanders Prospective Twin Survey. Multilevel regression analysis with birthweight, gestational age, sex, chorionicity, parental heights, parity, smoking, gestational hypertension, gestational diabetes, breast feeding and educational level as determinants was used. Intra-pair growth correlations were calculated. *Main outcome measure:* Growth: g/kg/day (0–1 month) and change in weight *z* score (0–6, 6–12 and 12–24 months). *Results:* 250 grams increase in birthweight decreased growth by 0.84 g/kg/day ($p < .0001$) and by –0.27 ($p < .0001$), –0.08 ($p = .0001$) and –0.01 ($p = .70$) *z* scores from 0–6, 6–12 and 12–24 months. One week increase in gestational age increased growth by 0.35 g/kg/day (p=.0008) and by 0.23 ($p < .0001$), 0.10 ($p < .0001$) and 0.03 ($p = .40$) *z* scores from 0–6, 6–12 and 12–24 months. From 12–24 months, 10 cm increase in paternal height increased growth by 0.29 z-scores ($p = .004$). The difference in intra-pair growth correlation between monozygotic and dizygotic twins increased from no difference from 0–1 month ($p = .39$) to a monozygotic:dizygotic ratio that approximated 2:1 from 12-24 months ($p = .001$). *Conclusion:* From 0–1 month, environmental factors influence growth, whereas genetic factors become more important over time. This is a first step in identifying age windows for future counseling and interventions on the effects of accelerated growth.

PERCEPTION OF BEING BULLIED AND PARENTAL CARE AND NEGLECT DURING CHILDHOOD AND THE DEVELOPMENT OF ADULT OBESITY: A CO-TWIN CONTROL STUDY

M. Vámosi[1], B. L. Heitmann[2], M. Thinggaard[4], K. O. Kyvik[3,4]

[1] *Health Promotion, Institute of Public Health, University of Southern Denmark, Denmark.*

[2] *Research Unit for Dietary Studies, Institute of Preventive Medicine Center for Health and Society, Copenhagen University Hospitals, Denmark*

[3] *Institute of Health Services Research, University of Southern Denmark, Denmark*

[4] *The Danish Twin Registry, Epidemiology, University of Southern Denmark, Denmark*

Background: The etiology of adult obesity is still poorly understood. It has been shown that overweight children suffer from adverse psychological events, but less is known about the potential effects of adverse psychological factors among normal weight children for later development of obesity. The objective of this study was to examine if the exposure of perception of being bullied and parental care and neglect during childhood could be associated with the development of adult obesity. *Methods:* Adult twin pairs aged between 20 and 50 years discordant for BMI were identified from the Danish Twin Registry. Criteria for being discordant were that one of the twins had a normal BMI and the co-twin a BMI > 30 kg/m^2. A total of 146 complete pairs fulfilled the criteria for election and were invited to an interview and a physical examination in 2006. A part of the questionnaire was the bullying questionnaire developed by Olweus. Another part of the questionnaire was the parental care and neglect questionnaire developed by Bufilco et al. Data were analyzed by means of a growth-curve model and an intra-pair comparison. *Results:* In total 236 twin individuals participated, giving a participation rate of 81.7%. The results showed that three of the questions related to childhood bullying: 'How often were you bullied in school' ($p = .02$), 'I was made a fool of' ($p = .03$) and 'Schoolmates spread lies about me' ($p = .002$), were associated with adult obesity. Furthermore the results showed that adult obesity at the age of 20 seemed associated with perceived maternal antipathy ($p = .04$) and perceived maternal neglect ($p = .01$) but no association with perceived paternal antipathy or neglect was found. This study demonstrates that perception of being bullied and that of lack of maternal care and neglect during childhood seems to have a potentially negative influence on adult weight.

GENETIC FACTORS IN ALCOHOLIC BEVERAGE PREFERENCE IN DUTCH TWINS

J. H. D. A. Van Beek, J. M. Vink, M. H. M. de Moor, M. Bartels, L. M. Geels, G. Willemsen, D. I. Boomsma

Department of Biological Psychology, VU University Amsterdam, The Netherlands

Alcoholic beverage preference is associated with the development of alcohol use disorders (AUD). A preference for drinking wine is found to be associated with a lower risk of AUD independent of the amount of alcohol consumed for both genders. A preference for beer is associated with a higher risk for AUD in women drinking weekly, but not in men. Preferring spirits is not associated with the risk for AUD nor neither gender (e.g. Flensborg-Madsen et al., Journal of Studies on Alcohol and Drugs, 2008, pp. 371–377). Therefore, it is important to explore the mechanism underlying beverage preference. We present results of a large twin study in which we investigated whether genetic differences could explain variability in beverage preference. Data on beverage preference (beer, wine or spirits) were available in a sample of 8,078 twins (1,455 complete MZ-twin pairs 1,556 complete DZ-twin pairs) registered with the Netherlands Twin Register. Beverage preference was measured in surveys in 2009, 2000 and 1995. If data on beverage preference was available on multiple surveys, the latest survey was taken in which both twins indicated their preference. Beverage preference was treated as an ordinal variable according to the alcohol percentage of the beverage

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

type. A threshold model with two thresholds was fitted to the data with age as covariate. First, polychoric twin correlations were estimated in a saturated model. Next, genetic models were fitted to the data, including additive genetic effects, shared environmental factors and unique environmental influences. First results show that genetic factors can partly explain differences in beverage preference. These genetic factors appear to be different for men and women.

GENETIC INFLUENCES ON INDIVIDUAL DIFFERENCES IN EXERCISE AND SEDENTARY BEHAVIOR DURING ADOLESCENCE

N. van der Aa, E. J. C. de Geus, D. I. Boomsma, M. Bartels
Department of Biological Psychology, VU University, Amsterdam

Regular exercise is thought to be a key contributor to health (Berlin & Colditz, 1990), whereas a sedentary lifestyle is proposed to be one of the main causes of the rise in obesity that starts at increasingly younger ages (Martinez-Gonzalez et al., 1999). Studying exercise behavior and sedentariness during adolescence is of particular interest because the declining prevalence observed for exercise participation is most prominent during adolescence. Sedentary behavior is often addressed as the opposite of exercise behavior, but exercise behavior and sedentariness might have different underlying etiologies. The objective of this study is to investigate the degree to which genetic and environmental influences affect variation in adolescent exercise and sedentary behavior. In addition, we examined if exercise and sedentary behavior are associated and if the same genetic and environmental factors influence exercise and sedentary behavior. Data on regular leisure time exercise and sedentary activities were analyzed in 8,355 adolescent twins and in 1,004 of their non-twin siblings from three age cohorts (13–14, 15–16, and 17–19 years), coming from 3,405 families. Exercise behavior was assessed with survey items about type of regular leisure time exercise, frequency, and duration of the activities. Sedentary behavior was assessed with survey items about frequency of watching TV, gaming, and activities on the internet. The prevalence of moderate exercise behavior declined from age 13 to 19 years, whereas the prevalence of vigorous exercise behavior remained constant across age cohorts. A small decline in the prevalence of sedentary behavior was also observed across age cohorts. Variation in exercise and sedentary behavior was largely accounted for by genetic factors, whereas shared environmental factors only accounted for a substantial part of variation in exercise behavior in girls aged 13–14 years. A correlation close to zero was found between exercise and sedentary behavior. We hypothesize that genetic effects on exercise ability may explain the high heritability of exercise behavior during adolescence. Moreover, our results clearly suggest that exercise and sedentary behavior are not associated.

GENETIC ETIOLOGY OF CANNABIS USE INITIATION AND PROBLEMATIC USE: A META-ANALYSIS OF TWIN STUDIES AND A GENOME-WIDE ASSOCIATION STUDY

K. J. H. Verweij[1,2,3], B. P. Zietsch[1,2], M. T. Lynskey[4], S. E. Medland[1], M. C. Neale[5], A. Agrawal[4], N. G. Martin[1], D. I. Boomsma[3], J. M. Vink[3]
[1] *Genetic Epidemiology, Queensland Institute of Medical Research, Brisbane, Queensland, Australia*
[2] *School of Psychology, University of Queensland, Brisbane, Queensland, Australia*
[3] *Department of Biological Psychology, VU University, Amsterdam, the Netherlands*
[4] *Department of Psychiatry, Washington University School of Medicine, St Louis, MO, USA*
[5] *Virginia Institute for Psychiatric and Behavioral Genetics, Virginia Commonwealth University, Richmond, VA, USA*

Because cannabis use can be associated with social, physical and psychological problems, it is important to know what causes some individuals to initiate cannabis use and a subset of those to become problematic users. A systematic literature search identified 28 twin studies on cannabis use initiation and 24 studies on problematic cannabis use. The proportion of total variance accounted for by genes (A), shared environment (C), and unshared environment (E) in (1) initiation of cannabis use and (2) problematic cannabis use was calculated by averaging corresponding A, C, and E estimates across studies from independent cohorts and weighting by sample size. For cannabis use initiation, A, C, and E estimates were 48%, 25% and 27% in males and 40%, 39% and 21% in females. For problematic cannabis use A, C, and E estimates were 51%, 20% and 29% in males and 59%, 15% and 26% in females. Confidence intervals of these estimates were considerably narrower than those in the source studies. These results indicate that vulnerability to both cannabis use initiation and problematic use was significantly influenced by genetic as well as environmental (C and E) influences. The next step is to find the specific genetic variants that are involved in the vulnerability to cannabis use. Identification of these genes should broaden our understanding of underlying biological pathways related to cannabis addictive behavior and could aid prevention and intervention of (problematic) cannabis use. We performed two genome-wide association analyses on lifetime cannabis use and problematic cannabis use with approximately 1500 Australian twins. Results of the genome-wide association analyses will be presented and discussed.

THE HERITABILITY OF GENERAL FACTORS OF PERSONALITY EXTRACTED IN FOUR DIFFERENT DATASETS

L. Veselka, J. Aitken Schermer, P. A. Vernon
University of Western Ontario, Canada

We have extracted a general factor of personality in four different datasets, all of which have used adult MZ and DZ twins as participants. In study 1, 254 pairs of MZ twins and 98 pairs of DZ twins completed the NEO-PI-R and the Mental Toughness Questionnaire (MT48). Factor analysis of the 5 NEO factors plus 4 factors from the MT48 yielded a strong first unrotated (general) factor accounting for 46% of the variance. In study 2, the same samples of twins completed the NEO-PI-R and the Trait Emotional Intelligence Questionnaire (TEIQue). Factor analysis of the five NEO factors plus 15 trait EI facets from the TEIQue yielded a GFP accounting for 37% of the variance. In study 3, 666 pairs of MZ twins and 526 pairs of DZ twins completed the short forms of the HEXACO Personality Inventory and the TEIQue. Factor analysis of the 6 HEXACO dimensions and 4 TEI factors yielded a GFP accounting for 33% of the variance. In study 4, 250 pairs of MZ twins and 200 pairs of DZ twins completed the Supernumerary Personality Inventory and 3 questionnaires measuring the Dark Triad traits: narcissism, Machiavellianism, and sub-clinical psychopathy. Factor analysis of the 10 traits assessed by the SPI and the 3 measures of the Dark Triad yielded a GFP accounting for 26% of the variance. MZ correlations were larger than DZ correlations for the GFPs extracted in each study. Univariate behavioral genetic model fitting showed that additive genetic and non-shared environmental factors fully accounted for individual differences in these factors, with heritabilities ranging from 46% to 53%. These results are compatible with those of several previous studies and lend support to the existence of a heritable general factor of personality.

A BEHAVIORAL GENETIC STUDY OF HUMOR STYLES AND MENTAL TOUGHNESS

L. Veselka[1], J. A. Schermer[2], R. A. Martin[1], P. A. Vernon[1]
[1] *Department of Psychology, University of Western Ontario, London, Ontario, Canada*
[2] *Management and Organizational Studies, University of Western Ontario, London, Ontario, Canada*

The present study investigated the relations between mental toughness and the four major humor styles — two positive (affiliative, self-enhancing), and two negative (hostile, self-defeating). Participants were 152 monozygotic (MZ) adult twin pairs and 67 dizygotic (DZ) adult twin pairs from North America. They completed the MT48 assessing individual differences in global mental toughness and in its eight factors (commitment, control, emotional control, control over life, confidence, confidence in abilities, interpersonal confidence, challenge). Individual differences in humor styles were assessed via the Humor Styles Questionnaire (HSQ). Positive correlations were noted between all of the mental toughness factors and the positive humor styles, with all but one association reaching significance.

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

Conversely, negative associations were found between all mental toughness factors and the negative humor styles, with the mental toughness factors of control, emotional control, confidence, confidence in abilities, and interpersonal confidence exhibiting significant correlations. Subsequent behavioral genetic analyses of these phenotypic correlations revealed that they were primarily attributable to common genetic and nonshared environmental factors. The implications of these findings regarding the potential effects of humor styles on wellbeing, and the possible selective use of humor by mentally tough individuals is discussed.

THE STUDY OF EARLY DEVELOPMENT OF BEHAVIOR CONTROL IN TWINS

G.Vilenskaya
Institute of Psychology, Russian Academy of Sciences, Russia

This paper describes a part of longitudinal study of early mental development and development of behavioral control. This study was worked out in the laboratory of developmental psychology IPRAS. The researches considered genetic environmental contributions in behavior regulation are relatively small in number (Malykh et.al., 1998, Yamagata et.al., 2005). Despite the small size of the sample longitudinal research allowed us to detect a dynamics of genetic-environmental determination of behavioral control and its components. The behavioral control is a psychological level of behavior regulation, a way of psychological resources composition for goal achievement. It consist of three components: emotional control, cognitive control and control of actions. Twins (24 pairs of MZ and 21 pairs of DZ) were traced longitudinally. Children visited at the ages 4, 8, 12, 18, 24, 30, 36 months. They were tested by BSID-II for estimating of cognitive control and control of action. The emotional control was measured by 'Baby's Day Questionnaire' (Balleyguier, 1981). This test evaluated the child's temperament, considered as the style of emotional regulation and the type of family education. The heredity of the emotional component of behavior control increased with age and displayed in the most part of temperamental features. One of the features which had a great and early presented genetic contribution is the mood and intensity of emotional reactions which were estimated by the scale of Unpleasant Sensations (from 'Baby's Day'). We proposed that this feature modulated the manifestation of other emotional control features. In older children, genes defined activation level and behavior orientation. The shared environment made an essential contribution in development of behavior control in twins. The family characteristics related to the organization of child behavior by parents (rigidity, strictness) had most strong relations to emotional control, especially for MZ twins. For DZ parental love and indulgence are more important than in MZ. The age-related dynamics of genetic-environmental contributions in emotional control was demonstrated a decrease in heredity between 18 and 24 months. With other data about age dynamics of behavioral control it supported a proposition about crucial character of this period for behavioral control development. In this period a child is very open to environmental influences. It suggested that internal and external developmental conditions are inextricably associated and of greater importance of inherited individuality of children.

GENETIC AND ENVIRONMENTAL INFLUENCES ON SEXUAL SOCIALIZATION

M.Westerlund, P. Santtila
Department of Psychology, Center of Excellence in Behavior Genetics, Åbo Akademi University, Turku, Finland

Sexual socialization refers to the process where the individual through social interaction gains and internalizes culturally specific knowledge, values and attitudes about sexuality. The aim of the present study is to investigate gene-environment correlations (rGE) on adolescents' sexual socialization experiences by conducting polymorphism analyses. rGE refers to unique individual experiences (such as exposure to certain environments) that are correlated with the individual's genotype. Using DNA samples it is possible to explore whether interindividual genetic differences in a candidate gene (i.e. genetic polymorphisms) are related to variance in a phenotype. Also, if individuals with different genetic variants differ in their exposure to environmental factors (i.e. gene-environment correlation) can be investigated. A previous study (Westerlund, Santtila, Johansson, Jern, & Sandnabba, submitted) showed that genetic effects influenced sexual socialization in men (52%) and women (46%) in a Finnish sample of twins and their siblings. Evidence for rGE and indications of qualitative sex differences were also found. Genetic and environmental influences were examined using twin modeling. The present study will explore these findings further by examining the associations between polymorphisms and adolescents' sexual socialization experiences using partly the same sample as the previous study (Westerlund et al., submitted). The sample is a Finnish population-based sample of twins and their siblings called Genetics of Sex and Aggression (GSA). The polymorphisms will be analyzed from 4400 DNA samples that were returned within the data collection. Repeat polymorphisms in the genes coding for the androgen receptor, estrogen receptor, vasopressin receptor 1A, and dopamine transporter will be performed using PCR amplification followed by fragment analysis. Single nucleotide polymorphisms (SNPs) in the genes coding for the oxytocin receptor, vasopressin receptor 1a, estrogen receptor alpha, estrogen receptor beta, progesterone receptor, among others. Totally 30 SNPs will be analyzed in these genes using Sequenom technology. All DNA analyses will be completed within the Q1/2010 and analyses concerning the associations between various polymorphisms and adolescents' sexual socialization experiences can be undertaken immediately. A previous study (Walum et al., 2008) offers encouraging results regarding the present study by having found an association between one of the human AVPR1A repeat polymorphisms (RS3) and some men's lacking capability to engage in long-term relationships. Results of the present study will be ready well in time in order to be presented at the ICTS congress.

THE ROLE OF PSYCHOSOCIAL FACTORS IN THE GENETICS OF ANTHROPOMETRIC MEASURES

G.Willemsen, E. J.C. de Geus, D. I. Boomsma
Department of Biological Psychology, VU University Amsterdam, Amsterdam, the Netherlands

Socioeconomic status (SES) has consistently been associated with body composition. In current days in Western populations, average height is higher and average body mass index (BMI) is lower in individuals in higher socioeconomic circumstances. Previous studies have shown genetic factors to be important determinants of height and BMI. Using data from the Netherlands Twin Register, we found that in the Dutch population height is almost completely under genetic control (heritability 89-90%, Silventoinen et al., 2003), while genes were also the main determinant of individual variation in BMI (heritability between 64-81% depending on age and sex, Schousboe et al., 2003). As SES-indicators such as educational attainment are also highly heritable, the association between body composition and SES may be due to common genes. However, in populations from Finland and the USA, the association between height and SES was found to be nongenetic, though genetic factors may play a role in the association between SES and body weight. In the present study, we examine the association between SES and body composition indices and explore whether educational attainment may moderate the heritability of body composition in the Dutch population. As part of a large biobank project, height, weight, waist circumference and hip circumference were obtained during a home visit in 9,528 participants (twins and their family members) of the Netherlands Twin Register. For 6,546 participants survey information on their own educational attainment (after age of 25 years) and for 6,239 participants information on parental educational attainment is currently available. Results show that body composition indicators are significantly associated with educational attainment in the expected direction, with increased height and decreased BMI, waist and hip circumference in higher educational attainment, even after correction

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

for age and sex. Similar results were seen for parental educational attainment. Data are available for 3670 twins (1353 complete twin pairs), and twin correlations indicate high heritability for educational attainment and body composition indicators. First analyses suggest that, at best, the moderating effects of educational attainment on body composition are small.

COMPARING MATERNAL CHARACTERISTICS IN MZ AND DZ TWIN MOTHERS: WHAT DOES IT TELL US ABOUT DZ TWINNING?

G. Willemsen, T. van Beijsterveldt, D. I. Boomsma

Department of Biological Psychology, VU University Amsterdam, Amsterdam, the Netherlands

Family history, increased parity or gravidity and increased maternal age are known to increase the risk of spontaneous DZ twinning. However, these factors only explain part of the variation in dizygotic twinning. To gain more insight into the mechanisms that underlie DZ twinning we compared mother of spontaneous DZ twins with mothers of monozygotic (MZ) twins. MZ twinning presents a random process that may happen to any woman having children. As such, mothers of MZ twins present an ideal comparison group, possibly even better than mothers of singletons. For the twin mother comparison, we first used survey data collected in 19,357 twin mothers of the Netherlands Twin Register. Twin mother comparisons confirmed the association between DZ twinning and maternal age and gravidity. In addition, mothers of spontaneous DZ twins were taller, had a higher BMI and had smoked more often prior to the twin pregnancy than mothers of MZ twins. We further confirmed the familial risk for DZ twinning and showed that mothers of spontaneous DZ twins had a shorter time to conceive than mothers of MZ twins. A second dataset available for twin mother comparisons consists of interview data that were collected for a study on the genetics of DZ twinning. Women were selected into the study if they were part of a sister pair that both had had twins. Using within-pair and between-pair comparisons, we examined the association between DZ twinning and maternal age at twin birth, parity, body composition, smoking behavior and natural menstrual cycle regularity. We compared data separately for sister-pairs in which both sisters had spontaneous DZ twins (N = 133) and sister-pairs in which one sister had spontaneous DZ twins and the other sister had monozygotic or non-spontaneous DZ twins (N = 117). No significant differences in means and variances, prevalence or correlations were found within or between sister-pairs. High correlations between sister pairs suggest that twinning is explained by familiarity and these high influences of familial similarities possibly overshadow the relation between DZ twinning and maternal characteristics found in the population based studies.

GENETIC AND ENVIRONMENTAL INFLUENCES ON BLOOD PRESSURE AND BODY MASS INDEX IN HAN CHINESE: A TWIN STUDY

T. Wu[1,2], H. Snieder[2,3], L. Li[1], W. Cao[1], S. Zhan[1], J. Lv[1], W. Gao[1], X. Wang[3], X. Ding[3], Y. Hu[1]

[1] *Department of Epidemiology and Biostatistics, Peking University Health Science Center, Beijing, China*

[2] *Unit of Genetic Epidemiology and Bioinformatics, Department of Epidemiology, University Medical Center Groningen, University of Groningen, the Netherlands*

[3] *Georgia Prevention Institute, Department of Pediatrics, Medical College of Georgia, Augusta GA, USA*

The familial aggregation of blood pressure (BP) may partly be due to the familial aggregation of obesity caused by genetic and/or environmental factors influencing both. Gene-obesity interactions are expected to result in different heritability estimates of BP at different obesity levels. However, the latter hypothesis has never been tested. The present study included 1243 monozygotic and 833 dizygotic twins (mean ± SD age: 37.81 ± 9.82; range: 19.1–81.4) from the Chinese National Twin Registry. Body mass index (BMI) was used as the index of general obesity. Outcome measures were systolic BP (SBP) and diastolic BP (DBP). Quantitative genetic modeling was performed using Mx software. SBP and DBP heritabilities were 46% (30%–62%) and 30% (14%–48%), respectively. Positive correlations of BMI with SBP (r = .26) and DBP (r = .27) were largely due to genetic factors (around 85%). Six and 7% of the total variance for SBP and DBP, respectively, could be attributed to genetic factors that also influence BMI. The gene–obesity interaction analysis showed that both common and unique environmental influences on SBP increased with increasing level of BMI, resulting in a lower heritability at higher BMI levels, while for DBP, the heritability remained unchanged at higher BMI levels. Our results suggest that correlations between BP and BMI are mainly explained by common genes influencing both. Additionally, higher BMI may reduce the penetrance of genetic vulnerability to elevated SBP through a larger impact of environmental effects. These conclusions may prove valuable for gene finding studies.

GENETIC AND ENVIRONMENTAL INFLUENCES ON BLOOD PRESSURE AND BODY MASS INDEX IN THE NAS-NRC WORLD WAR II VETERAN TWIN REGISTRY

T. Wu[1], W. F. Page[2], H. Snieder[1]

[1] *Unit of Genetic Epidemiology and Bioinformatics, Department of Epidemiology, University Medical Center Groningen, University of Groningen, the Netherlands*

[2] *Emeritus director of NAS-NRC WWII Veteran Twin Registry*

The familial aggregation of blood pressure (BP) may partly be due to the familial aggregation of obesity caused by genetic and/or environmental factors influencing both. Gene-obesity interactions are expected to result in different heritability estimates of BP at different obesity levels. The latter hypothesis has never been tested. The present study included 11914 monozygotic and 15152 dizygotic white male twins (mean ± SD age: 20.2 ± 2.28; range: 15.5–33.5) from the National Academy of Sciences-National Research Council (NAS-NRC) World War II Veteran Twin Registry. Systolic BP (SBP) and diastolic BP (DBP) as well as height and weight were measured at the induction physical examination. Body mass index (BMI) was used as the index of general obesity and calculated as weight(kg)/height(m)^2. Quantitative genetic modeling was performed using Mx software. SBP, DBP and BMI heritabilities were 39% (37%–41%), 30% (28%–32%) and 81% (80%–82%), respectively. Positive correlations of BMI with SBP (r = .14) and DBP (r = .09) were largely due to genetic factors (78% and 84%, respectively). Only 1% of the total variance for SBP and DBP could be attributed to genetic factors that also influence BMI. The gene–BMI interaction analysis showed that BMI did not have any modifying effect on genetic and environmental influences of SBP. However, the additive genetic effect on DBP slightly decreased with BMI, resulting in attenuated heritability for DBP at higher BMI levels. Our results suggest that correlations between BP and BMI are mainly explained by common genes influencing both. Moreover, higher BMI levels may reduce the penetrance of genetic vulnerability to elevated DBP, although this modifying effect is minor. These conclusions may prove valuable for gene finding studies.

HERITABILITY OF NEUROLOGICAL SOFT SIGNS: A PRELIMINARY STUDY IN CHINESE HEALTHY TWINS

T. Xu[1,2,3], R. C. K. Chan[1,2]

[1] *Neuropsychology and Applied Cognitive Neuroscience Laboratory, Institute of Psychology, Chinese Academy of Sciences, Beijing, China*

[2] *Key Laboratory of Mental Health, Institute of Psychology, Chinese Academy of Sciences, Beijing, China*

[3] *Graduate School, Institute of Psychology, Chinese Academy of Sciences, Beijing, China*

Neurological soft signs (NSS), which occur more frequently in schizophrenia patients, are potential endophenotypes for schizophrenia. Numerous studies have reported increase rates of NSS in nonpsychotic relatives of schizophrenic patients. However, the heritability estimates from twins study are relatively few. The current study attempted to examine the heritability of NSS in 23 healthy monozygotic and dizygotic healthy Chinese twin pairs using the Cambridge Neurological Inventory. We applied the structural equation modeling to estimate the contributions of additive genetic,

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

shared environmental and unique environmental effect. Genetic factors accounted moderately for the total variation in NSS (h^2 = 0.53). The heritabilities of motor coordination and disinhibition subscales are 0.58 and 0.56, respectively. In particular, several items showed significant correlations included Fist-Edge-Palm of left hand (r = 0.75), Fist-Edge-Palm of right hand (r = .49), mirror movement of left hand finger thumb opposition (r = .51), and mirror movement of left hand diadockinesia (r = 0.67). The current findings suggest NSS are heritable in healthy Chinese twins. Future studies recruiting larger healthy and clinical samples are required for a more powerful investigation of genetic analysis in NSS.

PARENTAL DISCIPLINES EXERT SHARED-ENVIRONMENTAL INFLUENCES ON ADOLESCENTS' MORAL BEHAVIORS: A JAPANESE TWIN STUDY

S. Yamagata, C. Shikishima, J. Ando
Keio Twin Research Center, Keio University, Tokyo, Japan

Although several studies examined univariate genetic and environmental etiology of moral behaviors or phenotypic association between moral behaviors and parental disciplines, study that examined bivariate genetic and environmental association between moral behaviors and parental disciplines is scarce. The present study examined the association by a mail survey to 569 twin pairs and their parents. Twin adolescents were asked about three types of moral behaviors (returning things one borrowed, not talking about someone behind their back, not telling lies) across two situations (about friends or family members). Parents were asked about frequency with which they have been strict with their twin children when they observed the six types of immoral behaviors of their twin children above. The results of univariate analysis showed that adolescents' moral behaviors were largely under nonshared environmental influences, with small genetic and shared environmental influences. Both maternal and paternal disciplines were largely under shared environmental influences, with small genetic and nonshared environmental influences. Results of a trivariate analysis showed that near-zero phenotypic correlations between moral behaviors and parental disciplines (r = –.01 for both maternal and parental disciplines) were due to mixture of negative genetic and positive shared-environmental correlation that cancel out each other. The genetic and shared-environmental correlations were statistically significant for only fathers' disciplines. These results suggest that along with immoral 'child effects' that elicit harsh disciplines from their fathers, there are also harsh 'fathers' effects' that reduce adolescents' immoral behaviors.

TWIN STUDY ON LOW/NON-RESPONSE TO HBV VACCINATION IN INFANTS

W. Yan[1], H. Sun[2], K. Yan[1], Q. Wang[1], L. Dou[2], X. Sun[3], Y. Li[4]
[1] *School of Public Health, Xinjiang Medical University, Uruqmi, Xinjiang , China*
[2] *People's hospital of Xinjiang Uygur Automous Region, Urumqi, Xinjiang China*
[3] *The First Affiliated Hospital of Xinjiang Medical University, Urumqi, Xinjiang China*
[4] *Women and Children Health Care Center of Urumqi, Urumqi, Xinjiang China*

The prevalence of HBV infection in Chinese population is reported over 7.18% (1–59 years old) (2006 national survey). HBV vaccination to new born infants has been included in China national free vaccination programs since 2002(vaccinate at 0th, 1st, and 6th month after birth); however, 10–15% of newborns who complete full course of vaccination show low/non-response, which is defined by WHO as producing anti-HBV antibody level lower than 10 mIU/ml. Previous studies documented that both genetic and environmental factors played roles in the impaired response to HBV vaccination, however how large is the genetic influence remains unclear. The current study aims at investigating the heritability of low/non-response to HBV vaccination by using the traditional twin study design. Han and Uygur ethnic twins born from March 1, 2009-December 30, 2011 and received full course of HBV vaccination will be recruited in our study (180 pairs for each ethnicity). The infants' anti-HBV antibody level will be examined at 12th month and 18th month of age respectively. The following information will also be collected by medical record and interviewing parents: (1) parents' information, include demographic and anthropometrics, personal disease history, history of HBV infection, life styles, as well as information related to pregnancy, such as age at pregnancy, weight gain and etc. (2) the baby's information, include general information about birth, growth and development measurements, breeding history, and disease history. Statistical analyses include the heritability of low/non-response to HBV vaccination (qualitative trait), heritability of anti-HBV antibody level at 1 year of age and reduction of antibody during 6–12 months after vaccination (quantitative trait), if there is gene-environmental interaction or ethnic difference in these heritability of the traits of interest. The current sample size ensures sufficient power (over 0.80) to identify the heritability of the quantitative trait when it is over 0.2. This study is the first twin study on cause of impaired response to HBV vaccination that will provide valuable information to improve HBV vaccination protection rate in Chinese population.

GROWTH CHARTS OF LENGTH AND HEIGHT FROM BIRTH TO SIX YEARS OF AGE IN JAPANESE TRIPLETS

Y. Yokoyama[1], M. Sugimoto[2], H. Kurokawa, K. Silventoinen[3], J. Pitkäniemi[3], J. Kaprio[3,4]
[1] *Department of Community Health Nursing, Osaka City University, Osaka, Japan*
[2] *Nishinomiya City Public Health Center, Nishinomiya, Japan*
[3] *Department of Public Health, University of Helsinki, Helsinki, Finland*
[4] *Department of Mental Health and Alcohol Research, National Public Health Institute, Helsinki, Finland*

Aim: There are only few previous studies on the postnatal growth, especially length/height growth, of triplets in the world, while a number of studies on the postnatal growth of twins have been conducted. We analyzed the characteristics associated with the growth in length and height of Japanese triplets from birth to six years of age and present the growth charts for them. *Methods:* The study included 354 mothers and their 1,061 triplet children, who were born between 1978 and 2006. Data were collected through a mailed questionnaire sent to the mothers asking for information recorded in medical records. Data on triplets' length and height growth, gestational age, sex, parity, and maternal age at delivery were obtained from records in the Maternal and Child Health Handbooks, which is provided by the authorities after a report of pregnancy. *Results:* Birth length showed the strongest contribution to height of triplets from one to six years of age. In addition, birthweight was also a significant contributing factor to height from one to three years of age. Compared to the 50th percentile of the growth standard for the general population of Japan, the length and height deficit of the triplets was approximately 15% at birth (male, –7.0 cm female, –7.0 cm), decreased within the first year of age, and fluctuated between 2 % and 5 % until six years of age (male, –3.7 cm female, –3.3 cm). *Conclusion:* Triplets have lower birth length and subsequent height than singletons. In spite of the catch-up growth during the first year of life, they are behind singletons even in mid-childhood. This study provides height growth curves for use in triplets.

THE DIAGNOSTIC STABILITY AND HERITABILITY OF ALCOHOL DEPENDENCE

E. Ystrom
Norwegian Institute of Public Health, Norway

Background: The assessment of a lifetime history of DSM-IV alcohol dependence (AD) has in epidemiological samples been found to be moderately reliable. Furthermore, AD has been found to be substantially heritable (i.e., 50% ?0%) in a range of different populations. However, in these studies, errors of measurement could not be discriminated from the true unique environmental effects. *Aim:* To, first, predict reliable reporting of AD second, investigate the heritability of AD as a function of diagnostic confidence and third, to estimate the heritability and environmentality of AD without measurement error. *Methods:* Measures of AD was obtained twice by personal interview in twin pairs participating in a large population-based study. *Results:* Reliability of AD was moderate (k = .55,

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press

tetrachoric r = .77). In men, reliable reporting of AD was predicted by number of AD symptoms, treatment seeking, duration of episode, and DSM-IV criterion 5 (i.e., a great deal of time is spent in activities to obtain the substance, use the substance, or recover from its effects). In women, reliability of AD was predicted by treatment seeking and negatively predicted by time 1 abstinence (significantly different from males). Constructing an index of caseness for men from the aforementioned predictors, the heritability of AD increased as a function of diagnostic confidence. Including error of measurement into a multivariate twin model comprising both occasions of measurement, the estimated heritability of the liability to AD in men increased substantially (from 54% to 71%). About 37% of what was conceived as environmental effects in fact turned out to be measurement error, when two assessments of AD in men were used. *Conclusion:* Diagnostic stability in AD can be predicted by characteristics relevant for the disorder, and differentially so in men and women. Lifetime AD appears to be a moderately reliable disorder of high heritability.

GENOME-WIDE LINKAGE SCAN FOR QTL AFFECTING BMI IN CHINESE TWINS USING HIGH DENSITY SNP MARKERS

D. Zhang[1], S. Li[2], Z. Pang[1,3], T.A. Kruse[4], K. Christensen[2], K. O. Kyvik[2,5], Q. Tan[2]

[1] *Dept of Public Health, Qingdao University Medical School, Qingdao, China*

[2] *Epidemiology, Institute of Public Health, University of Southern Denmark*

[3] *Qingdao Center for Disease Control and Prevention, Qingdao, China*

[4] *Department of Clinical Genetics, Odense University Hospital, Denmark*

[5] *Institute for Regional Health Service Research, University of Southern Denmark*

The body mass index (BMI) is a very important phenotype associated with obesity and metabolic syndrome. As such, the phenotype has been of great interest for genetic epidemiology studies using methodologies from phenotype-based heritability estimation to molecular marker-based genetic linkage scan to map QTLs linked to BMI with results from the former indicating a strong genetic dissection and from the latter pointing to multiple genomic loci in linkage with BMI. In a recent study by Kettunen et al.[1], two common BMI loci have been confirmed on Chromosomes 3 and 7 using multicenter data from 6 populations of European origin possibly indicating evolutionarily preserved genetic mechanisms from the two loci across these populations. We performed a genome-wide linkage scan on BMI in 63 pairs of Chinese dizygotic twins using the Affymetrix SNP 6.0 array containing very high density genetic markers of about 1 million SNPs. Data analysis using the variance component model in Merlin localized the highest linkage (lod score = 4, genome-wide p value < .05) on Chromosome 7 at the same location (7q36) as from the multicenter study. The results from a population of large ethnic and cultural difference to the Europeans reconfirm the existence of an evolutionarily preserved genetic control over BMI but might have been developed very early in history. Our analysis also identified multiple unique loci on Chromosomes 1, 8, 12, 14, and 21 with lod scores of 2.8, 2.7, 2.4, 2.1 and 1.8 possibly suggesting population specific genetic effects developed over history as a result of environmental adaption.

1. Kettunen J, Perola M, Martin NG, et al. Multicenter dizygotic twin cohort study confirms two linkage susceptibility loci for body mass index at 3q29 and 7q36 and identifies three further potential novel loci. Int J Obes (Lond). 2009;33(11):1235–1242.

GENERALIZED LINEAR MIXED MODEL IN THE ESTIMATION OF HERITABILITY IN TWIN STUDIES

J. Zhang

State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-sen University, Guangzhou, China

The generalized linear mixed model (GLMM) has been widely used in epidemiology. It allows statistical processes in the widely available SAS/ R/S-plus package. Therefore, we propose generalized linear mixed models with two random effects to analyze the latent genetic and environmental effects in twin studies. We illustrate this method using data on anterior chamber depth and axial length, and continuous ocular biometric traits collected in the Guangzhou Twin Eye Study. We compare results between generalized linear mixed model and the structural equation model based on the data on the twin pairs. Furthermore, we demonstrate the advantages of using this model in the data collected in extended twin families when the parental data were added and with increased number of random effects. SAS procedures and syntax are included in the appendix.

GENETIC CORRELATES OF ORGASM RATE IN FEMALE TWINS, AND IMPLICATIONS FOR UNDERSTANDING 'FEMALE ORGASMIC DISORDER'

B. P. Zietsch[1,2], G. F. Miller[3,2], J. M. Bailey[4], N. G. Martin[2]

[1] *School of Psychology, University of Queensland, Brisbane, Australia*

[2] *Genetic Epidemiology Laboratory, Queensland Institute of Medical Research, Brisbane, Australia*

[3] *Psychology Department, University of New Mexico, Albuquerque NM, USA*

[4] *Department of Psychology, Northwestern University, Evanston, IL, USA*

Women vary greatly in their how frequently they orgasm during sexual activity. In particular, a large proportion of women rarely or never experience orgasm. Failure to consistently reach orgasm characterizes 'female orgasmic disorder' (DSM IV), but it is unclear whether or not this truly reflects a biological dysfunction. The evolutionary origins and adaptive functions of female orgasm are crucial in clarifying this issue, but they remain contentious. Different theories lead to different expectations for the adaptively 'optimal' rate of orgasm, and at least one theory regards orgasm rate as entirely irrelevant to females' fitness. Most of all, a lack of empirical research has limited progress on the problem. To address this, we use data from a community sample of 2,914 female twins who completed a survey on wide ranging topics including orgasm rates during intercourse, other sex, and masturbation. We examined phenotypic and genetic correlations between female orgasm rates and: personality traits (Extraversion, Neuroticism, Psychoticism, and Impulsivity); occupational, educational, and marital status; sexual history, behavior, and attitudes; and gender identity (masculinity–femininity). Most mental disorders are associated with high Neuroticism and/or Psychoticism, and/ or impaired social, educational, or occupational functioning. However, individual differences in orgasm rates were essentially unrelated to these traits, both phenotypically and genetically. Similarly, most adaptive accounts of the female orgasm predict associations with traits related to fitness, relationships, or sexual history and strategies. Again though, individual differences in orgasm rates were essentially unrelated to these traits. Indeed, orgasm rate during intercourse, other sex, and masturbation, while themselves heritable, were genetically uncorrelated with every other trait we looked at. These results challenge the idea that low orgasm rates are dysfunctional in females, and also pose major problems for adaptive accounts of the female orgasm.

https://doi.org/10.1375/twin.13.3.246 Published online by Cambridge University Press