

twin research and human genetics

The official journal of the **International Society for Twin Studies** and the **Human Genetics Society of Australasia**

Covering all areas of
human genetics
with an emphasis on
twin studies, genetic
epidemiology, psychiatric
and behavioral genetics,
and research on
multiple births in the
fields of epidemiology,
genetics, endocrinology,
fetal pathology, obstetrics
and pediatrics.

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Nicholas G. Martin

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Twin Research and Human Genetics is the official journal of the International Society for Twin Studies and, as such, is the successor journal to *Acta Geneticae Medicae et Gemellologiae*, which was founded in 1952 by Luigi Gedda. He edited it until its cessation in 1998, with Paolo Parisi as Acting Editor and then Executive Editor from 1968 to 1992. *Acta* became the official journal of ISTS when the society was established in 1974. The subtitle *Twin Research* was adopted in 1979. It was published by The Mendel Institute in Rome, except for the years 1979 to 1983, when it was published jointly with Alan R. Liss in New York.

Twin Research itself was founded in 1998 by Robert Derom, who edited it in 1998 and 1999. It has been edited by Nick Martin since 2000. It was published by Stockton Press (which became part of Nature Publishing Group) from 1998 to 2000, and since 2001 has been published by Australian Academic Press.

The title *Twin Research and Human Genetics* was adopted from the beginning of Volume 8 in 2005 and is a translation of *Acta Geneticae Medicae et Gemellologiae*, Luigi Gedda's original title.

In 2008, *Twin Research and Human Genetics* was also adopted as the official journal of the Human Genetics Society of Australasia.

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TWINS AND SIBLINGS: DIFFERENCES IN IQ AND PERSONALITY RELATIONS

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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 (first-borns 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

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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 esti-

mates 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

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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 ($> 0.5\text{kg}$) 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

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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

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

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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

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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

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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

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Introduction: There are indications that dizygotic (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