ABSTRACT

Behavior Genetics Association 42nd Annual Meeting Abstracts

Symposia

Advanced genetic epidemiology with OpenMx

This symposium will focus on developments in statistical modeling with OpenMx. Hermine Maes will discuss the extended twin kinship design. Sarah Medland will discuss implementation of GWAS analyses. Steve Boker will present on dynamical systems analysis. Michael Neale will present regime switching models for study of substance use behaviors.

Beyond the back cross: Recent research on the genetics of nonhuman animal behavior

Like the twin method, studies of nonhuman animal behavior have long been recognized as an important tool in understanding the genetics of a wide range of human behavioral phenotypes. Moreover, studies of nonhuman animals are key to understanding the evolutionary processes underlying variation in simple and complex behavioral phenotypes. Much of the genetics of nonhuman animal behavior has been conducted in mice, fruit flies, and similar organisms. However, there is growing interest in studying avian and nonhuman primate species given their complex behavioral repertoires, and, in the case of nonhuman primates, their phylogenetic proximity to humans. The symposium will provide an overview of this research. The studies presented involve a wide range of species, behavioral phenotypes, and cutting-edge quantitative and molecular genetic methods. The first speaker symposium will be Kees van Oers who will describe his work on the genomics of personality variation in wild and captive great tits. Next, Hideaki Abe will discuss his findings on the association between copy number variation and tonic immobility in the chicken. The third speaker will be Mark Adams who will describe his work on the evolution of personality, focusing on the genetic and environmental variance underlying personality and subjective well-being in orangutans. The next speaker will be Kazunori Yamada who will describe the genetic differences between two groups of Japanese macaques that differ in levels of aggressive behavior. Finally, Nicky Staes, will present her preliminary results on the association between personality and variants of oxytocin and vasopressin genes in bonobos.

Challenging the latent trait perspective: A phenotypic network view and its consequences for gene-finding studies

The field of behavioral genetics currently struggles with the "missing heritability" problem, i.e., identified genetic variants explain only a small fraction of the heritability estimates obtained in twin and family-studies, while a large proportion of the heritability remains unaccounted for. Various reasons for this missing heritability have been coined, including statistical reasons (e.g., lack of statistical power due to the combination of small genetic effect sizes and insufficient sample size), genetic reasons (e.g., genetic heterogeneity, inapposite focus on variation in DNA structure), and substantial overestimation of the family-based heritability estimates due to violation of the genetic additivity assumption ("phantom heritability"). Misspecification of the phenotypic model (i.e., the phenotype generating mechanism) can also result in the failure to identify genes responsible for observed phenotypic variation, but this possible cause for the missing heritability has not entertained much attention in the literature. We wish to organize a symposium specifically dedicated to this issue. Specifically, we aim to discuss the current unilateral reliance in genetic studies on the latent trait model for psychiatric and psychological traits, and contrast this model to a relatively recent alternative phenotypic model, namely the network perspective. The symposium consists of four presentations, followed by a general discussion. In the first contribution, the two phenotypic models will be compared in conceptual detail, and consequences of the network model for genetic studies are discussed. In the second contribution, simulation is used to show how under the network model, associated genetic variants become untraceable using standard methodology. The third contribution explains analytically why this is so. Finally, in the fourth contribution, depression data are analysed to illustrate how genotype-phenotype data can be used to distinguish between the two alternative phenotypic models. We wish to wrap up the symposium with a general discussion, which will be hosted by Prof Conor V. Dolan.

Exploring gene–environment correlation: Unraveling the relationships between genotype, phenotype and environment

An increasing body of evidence demonstrates genetic involvement in environmental exposure, or gene–environment correlation (rGE) (Kendler & Baker 2007). Understanding rGE is likely to prove crucial in refining our understanding of the aetiology of complex disorders. We can approach rGE in at least two ways: First, we can explore the
is now well established at between 50 and 70%, much less is known about the developmental processes and contextual factors that give rise to heritable variation in cognition and achievement. In this symposium, researchers present new work on the developmental and contextual dynamics of the genetics of cognition across the lifespan. Daniel Briley presents results of a comprehensive meta-analysis of longitudinal twin-family studies of cognition in both childhood and adulthood. He finds that while genes contribute substantially to intellectual stability, and nonshared environments contribute largely to intellectual instability, increasing stability of cognition over development is attributable to increasing stability of both genetic and environmental factors. Angela Brant presents results from both cross-sectional and longitudinal datasets indicating a categorical shift in heritability of intelligence that occurs later in development for more intelligent individuals. Sara Hart examines both gene–environment correlation and interaction with regards to peer relations and reading performance. Her results indicate that better readers pair with less antisocial friends, who in turn moderate nonshared environmental influences on reading outcomes. In the last three talks Kristen Jacobson, Terrie Vasilopoulos, and Timothy Bates each present results of recent projects that extend to adulthood previously published findings of gene-by-SES effects on cognition in childhood. Kristen Jacobson’s longitudinal results indicate that while parental education interacts with genetic, shared environmental, and nonshared environmental variation in Vocabulary IQ in adolescence, it only interacts with shared environmental variation in Vocabulary IQ in young adulthood. Terry Vasilopoulos finds that present socioeconomic status moderates nonshared environmental variation, but not genetic variation, in general cognitive ability in middle adulthood. Finally, Tim Bates presents positive evidence for gene-by-childhood SES effects on cognition in an age heterogenous sample of adult twins. Robert Plomin serves as discussant.

Gene–environment interplay in the timing of reproductive maturation

Individual differences in the timing of reproductive milestones are robustly associated with adverse outcomes in psychological well-being and achievement. Yet the timing of reproductive maturation is not random, but predicated in genes and sociobehavioral experiences canaleal many years earlier. The purpose of this symposium is to unite emerging genetically-informed research on reproductive timing, with an especial emphasis on rethinking causal assumptions regarding the environmental origins and pathogenic effects of early reproductive development. The first paper focuses on early life antecedents of reproductive maturation, examining whether ecological stressors such as low socioeconomic status and biological father absence moderate genetic influences on age of first sexual intercourse may be expressed. The second paper examines how earlier pubertal maturation may increase vulnerability to deviant peer influences and corresponding substance use during adolescence. Lastly, the third paper considers the long-term sequelae of earlier age of first childbirth, applying a co-twin control design to ascertain whether associations between adolescent childbearing and low academic and economic achievement may in fact be attributed to third variable environmental confounds. The panel discussant has particular expertise in theories of reproductive maturation, and how these may be confirmed or questioned through the use of behavioral genetic designs. All three papers share an interest in critically evaluating—and perhaps refuting—conventional and causal assumptions of earlier reproductive timing. Collectively, the results from these papers hold considerable promise for redefining the existing psychosocial hypotheses of sexual development, and underscore the need to consider genetic influences when examining the adverse correlates of reproductive milestones across the lifespan.

Genetic and environmental influences on cognition across time and context

Although the population-average heritability of cognition in adulthood is now well established at between 50 and 70%, much less is known about the developmental processes and contextual factors that give rise to heritable variation in cognition and achievement. In this symposium, researchers present new work on the developmental and contextual dynamics of the genetics of cognition across the lifespan. Daniel Briley presents results of a comprehensive meta-analysis of longitudinal twin-family studies of cognition in both childhood and adulthood. He finds that while genes contribute substantially to intellectual stability, and nonshared environments contribute largely to intellectual instability, increasing stability of cognition over development is attributable to increasing stability of both genetic and environmental factors. Angela Brant presents results from both cross-sectional and longitudinal datasets indicating a categorical shift in heritability of intelligence that occurs later in development for more intelligent individuals. Sara Hart examines both gene–environment correlation and interaction with regards to peer relations and reading performance. Her results indicate that better readers pair with less antisocial friends, who in turn moderate nonshared environmental influences on reading outcomes. In the last three talks Kristen Jacobson, Terrie Vasilopoulos, and Timothy Bates each present results of recent projects that extend to adulthood previously published findings of gene-by-SES effects on cognition in childhood. Kristen Jacobson’s longitudinal results indicate that while parental education interacts with genetic, shared environmental, and nonshared environmental variation in Vocabulary IQ in adolescence, it only interacts with shared environmental variation in Vocabulary IQ in young adulthood. Terry Vasilopoulos finds that present socioeconomic status moderates nonshared environmental variation, but not genetic variation, in general cognitive ability in middle adulthood. Finally, Tim Bates presents positive evidence for gene-by-childhood SES effects on cognition in an age heterogenous sample of adult twins. Robert Plomin serves as discussant.

Genetics and intervention

There is great variability in the way individuals respond to interventions, and genes, and their interaction with the environment, are a key potential explanation. Interactions between genes and interventions can be studied experimentally, and the underlying mechanisms by which interventions create changes in behaviour can be further understood. Much of the research in this area has focused on understanding genetic influences on drug response, but a new era of genetically sensitive interventions now includes behavioural and environmental interventions. In intervention research, heterogeneity is the norm, but when it comes to selecting treatments we require greater accuracy than the average treatment response to be able to assign effective and personalised interventions. Understanding heterogeneity is important for three reasons. First, using this information we should be able to design and deliver better, more personalised interventions. Second, heterogeneity can hide treatment efficacy, meaning some beneficial interventions are discarded even though they were effective for some individuals. Finally, heterogeneity is a window on the mechanisms of the intervention. By investigating why the intervention works for some and not others, we can generate new hypotheses about how the intervention works. This symposium represents the breadth of research within genetics and intervention, including data from both experimental and observational studies, drug and behavioural interventions as well as molecular genetic and twin analyses.

Genetic research of autism and ADHD: Commonalities, achievements and challenges

Autism Spectrum Disorders (ASD) and Attention Deficit/Hyperactivity Disorder (ADHD) are common neurodevelopmental conditions
that are typically diagnosed in childhood. ADHD and ASD often co-occur and there is compelling evidence for a partly shared etiology. Moreover, research in the past decades indicates that the conditions have some important commonalities.

Findings from twin and family studies suggest that both conditions are highly heritable in childhood, with heritability estimates of around 80% for clinical autism and autistic traits and around 75% for ADHD and ADHD traits. The few studies conducted in older cohorts suggest that the heritability may be substantially lower at later stages in life, but whether measurement artefacts can explain these findings remains as yet unclear. Despite the high heritability of autism and ADHD and a large effort from molecular genetic studies to find the genes involved in both conditions, the etiology of the majority of cases remains unexplained. Moreover, both ASD and ADHD are associated with impairments in cognitive functioning, both in general intelligence and specific cognitive abilities such as executive functioning and social cognition. Therefore it is thought that cognitive endophenotypes may aid the search for susceptibility genes, and may improve our understanding of the pathways between genes, cognition and a clinical diagnosis. Because of these commonalities we feel that cross-pollination between autism and ADHD research can be of great benefit to both disciplines. In this symposium 2 four speakers from four different research labs will discuss their findings from twin studies of ADHD and/or autism. The discussant, Dr Angelica Ronald, who has expertise in the comorbidity of ASD and ADHD, will highlight the achievements and challenges common to both research fields. The discussion will also focus on future research directions, with the aim to facilitate cross-discipline research collaborations.

\[ G \times E \text{ in the presence of } rGE: \text{ Methodological pitfalls and practical solutions} \]

Genes rarely influence health and mental health in isolation. Rather, genetic vulnerabilities are necessary but not sufficient in the etiology of disorders because environmental factors influence the expression of genetic vulnerabilities. Accurately identifying such gene-by-environment interactions \((G \times E)\) is of critical importance for genetic research on mental health, including etiological theory, prevention, and design of molecular studies. Indeed, candidate moderating environments are often traits that are themselves subject to genetic influences (e.g., socioeconomic status). Gene–environment correlation \((rGE)\), arising when genetic influences on a candidate environment are shared with those on a phenotype of interest, is equally as important as \(G \times E\). Allowing for \(rGE\) is essential in investigations of and tests for \(G \times E\), as is accounting for \(G \times E\) when quantifying \(rGE\). Purcell (2002) proposed a widely adopted method for extending biometric twin models to accommodate both \(rGE\) and \(G \times E\). In this methodologic symposium, Rathouz et al. will advance Purcell’s approach to the next level with new models and computational tools for testing \(G \times E\). Van der Sluis et al. will then explore settings within the Purcell framework giving rise to false detection of \(G \times E\). Finally, Molenaar et al. will return to the more classic setting of detecting \(G \times E\) when the environment is unmeasured.

Positive psychology and well-being

Twin and family studies revealed that 40–50% of the variance in happiness is explained by genetic factors (Bartels & Boomsma, Behav Genet 39(6):605–615, 2009). However, all previous studies on the causes of individual differences were based on studies with adolescents and adults. For many phenotypes, like intelligence and psychopathology a change in genetic architecture is observed over age. The current study aims to reveal the causes of individual differences in happiness in children aged 2 and 3. Maternal reports on happiness have been collected in the survey studies of the Netherlands Twin Register. Mothers of twins were invited to report on their children’s level of happiness on a 5-point scale (How would you rate the level of happiness of your child in general?). Information is available for 792 twin pairs at age 2 and 1,575 twin pairs at age 3. The first analyses indicate that about 70% of the children are reported to be always or almost always happy. Less than 1% of the children are unhappy all the time. MZ correlations are estimated at 0.85, while the DZ correlations are estimated at 0.65. This indicates that variance in happiness in young children has a genetic component and that shared environmental influences might also play a role. However, rater effects may be present in the shared environmental contribution and need to be explored through collection of paternal ratings.

The 2012 National Longitudinal Survey of Youth Kinship Links:
Conducting behavior genetic research using the NLSY79 and NLSY-children data

This symposium describes the status of the National Longitudinal Survey of Youth datasets (the NLSY79 original data and the NLSY-Children data) as increasingly valuable databases for conducting research in behavior genetics and other developmental disciplines. Such research has been conducted by our team and other BG researchers for over 20 years. With the recent release of new direct indicators of sibling relatedness, the datasets are expanded substantially in sample size, in flexibility, and has improved reliability and validity features. The thousands of phenotypes in the NLSY data include measures of cognitive development, childhood problem behaviors and adolescent delinquency, workplace and economic indicators, family, fertility, and reproductive behavior, social interaction variables, school and educational information, and many other domains. For many of these variables, there exist longitudinal streams collected across up to 40 years. Two additional features make the NLSY even more valuable to BG researchers. First, the NLSY administrators are in the process of collecting biomarkers to do DNA assays in future rounds of the survey. Second, the NLSY79 and the NLSY-children are linked in that the NLSY79 females are the mothers of the NLSYC, supporting unique and powerful cross-generational research designs. The papers in this symposium describe the overall scheme of the NLSY to support high-quality BG research, present validity analyses, describe the online archive that has been developed to facilitate NLSY BG research, describe some methodological innovations that have emerged from use of the NLSY kinship links, and present an empirical biometrical analysis to illustrate the use of the new kinship links within the context of a sophisticated biometrical design.

What have modern genetic studies told us about depression?

Depression is a heritable illness and its more severe and recurrent forms have a heritability comparable to that of schizophrenia and bipolar. It has also been subject to the largest GWAS of a psychiatric disorder. However, GWAS has as yet failed to find multiple genes for depression. Future studies of depression need to take account of the issues surrounding diagnosis and life course of depression, the implication of the GWAS results for considerations of the genetic architecture of depression and how family and phenotype studies may inform us. Gerome Breen will review the results of the PGC GWAS
Stability and change in anxious depression as a function of genes and environment.

A longitudinal twin and GWA study from age 3 to 65 years

Abdel Abdellaoui; VU University, Amsterdam, the Netherlands
Meike Bartels; VU University Dorret Boomsma; VU University, Amsterdam
Gareth Davies; Avera Institute for Human Behavioral Genes
Conor Dolan; University of Amsterdam Lot Geels; VU University, Amsterdam
Maria Groen-Blokhuis; VU University
Jouke Jan Hottenga; VU University, Amsterdam Kenneth Kendler;
VCU-VIPBG Christel Middeldorp; VU University Michel Nivard;
VU University Paul Schet; University of Texas, MD Anderson
Cancer Center Patrick Sullivan; USDA Jenny van Beek; VU University,
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Gonneke Willemsen; VU University, Amsterdam

Symptoms of Anxiety and Depression are moderately stable from childhood into adulthood. For example, among subjects suffering from any anxiety disorder or depression at 26 years, 50% had received the diagnosis for the first time before 15 years of age. Thus, half of the adults with anxiety or depression had already suffered from these disorders at childhood. If the same genes contribute to the symptoms throughout the lifespan, this would imply that variation in age has little bearing on the role of genes. Alternatively, if different genes are important at different ages, variation in age among the participants in gene finding studies may lower the power to detect genetic variances. Research addressing these lifespan questions is scarce.

Longitudinal survey data on anxious depression were collected in 7,863 monozygotic and 15,815 dizygotic twin pairs registered at the Netherlands Twin Registry (NTR). The majority of twins participated in more than one survey. A genetic simplex model was chosen to analyze the longitudinal data. This model allows the assessment of the stability and change in the effects of genetic (A) and environmental (C, common) & E (unique) factors over time by modeling the extent to which effects are transmitted from one time point to the next (stability), and the extent to which “new” effects (innovations) come into play.

The genetic variance initially observed in childhood appears to account for a small proportion of the total variance in adults. At every age in childhood, new genetic variance influences anxious depression. We find a very stable genetic pattern in adulthood: no novel genetic variance is detected and the same genetic variance plays a role from age 30 till age 65. We follow up this analysis by applying a multivariate genome-wide association study on these data to tease out actual genetic variants related to anxious-depression symptoms.

The association between copy number variants in chicken chromosome 1 and tonic immobility

Hideaki Abe; Kyoto University Kenji Nago; Aichi Agricultural Research Center Akihiro Nakamura; Aichi Agricultural Research Center Miho Inoue-Murayama; Kyoto University

Tonic Immobility (TI) is a state of paralysis found in animals, such as rodents and birds, and is mostly exhibited when individuals feel threatened by a predator. TI shares common features with catalepsy and other abnormal behaviors. To identify genetic variants associated with individual differences in chicken (Gallus gallus) TI, we examined the copy number variants (CNVs) in chromosome (chr) 1. To these ends we first measured TI duration and induction score of newly-hatched Nagoya (i.e., Japanese native chickens) and White Leghorn chicks, and detected significantly longer TI duration and higher induction score in Nagoya breed than those of White Leghorn. We then used array comparative genomic hybridization (array CGH) to compare approximately 60 Mb region of chr 1 between Nagoya chicks with long and short TI duration. Array CGH analysis enabled us to identify dozens of candidate loci and genes harboring CNVs. We confirmed the heterogeneity of amplifications in some of these candidate loci by following quantitative PCR. Further statistical analyses are underway to examine the association of candidate CNVs with TI scores. Additionally, we report on the progress of comparative studies on avian neurotransmitter related genes and their possible effects on phenotypic variation.

Using next generation sequencing to investigate methylation patterns associated with alcohol use behaviors

Shaunna Clark; Virginia Commonwealth University Karolina Aberg; Virginia Commonwealth University Srilaxmi Nerella; Virginia Commonwealth University Joseph McClay; Virginia Commonwealth University Linying Xie; Virginia Commonwealth University Alexandra Hudson; Virginia Commonwealth University Wenan Chen; Virginia Commonwealth University Guimin Gao; Virginia Commonwealth University Swedish Schizophrenia Consortium; Virginia Commonwealth University Jozsef Bukzar; Virginia Commonwealth University Christina Hultman; Karolinska Institutet Patrik Magnusson; Karolinska Institutet Patrick Sullivan; University of North Carolina Edwin van den Oord; Virginia Commonwealth University

Twin studies suggest that genetic factors play a role in various aspects of drinking behavior. Identifying specific genetic variants, however, has proven difficult and the predictive power of the reported variants is typically modest. DNA methylation studies represent a complement to genetic studies focusing on sequence variation.

Methylation studies of alcohol have historically been restricted to candidate genes or very small sample sizes. This study makes a huge leap forward by using next generation sequencing to screen the 30.6 million human methylation sites for association with drinking behaviors.

We performed methylome-wide association studies (MWAS) in a sample of ~700 individuals using two phenotypes related to alcohol habits: if participants ever used alcohol and in what frequency they drink. To investigate all CpGIs in the human genome, we enriched for the methylated genomic fraction using a methyl-CpG binding domain (MBD) protein capture system followed by next generation
sequencing. Each sample had, on average, 31.9 million reads, to yield a total of 19.7 trillion reads for all individuals.

After quality control and data reduction, 4.2 million high quality blocks were left for the association testing. The MWAS showed a number of highly significant findings with a top $p$ value of 3.30E-09. Among the top results were blocks located in, for example, ELOVL2 and PDE4B for ever using alcohol and ATF1 for frequency of alcohol use. PDE4B has previously been linked to alcohol response while ELOVL2 and ATF1 have been associated with comorbid psychiatric disorders. Future directions include replication of the top findings in an independent sample of 560 individuals using targeted pyrosequencing and a network analysis to examine if any of the top results cluster into the same network. Once the results are replicated, we will have ascertained the first collection of CpG sites identified using MWAS for alcohol use.

**The majority of genetic variation in orang-utan personality and subjective-well being is nonadditive**

Mark Adams; University of Sheffield

Quantitative genetic modeling using extended family designs indicates that nonadditive genetic effects, such as dominance and epistasis, play a large role in personality variation. Recent selection on human personality has been put forward as one possible explanation of this genetic structure. To test whether this genetic feature is unique to humans, I estimated additive and nonadditive genetic variance in personality and subjective well-being of zoo-housed orang-utans using an animal model. More than half of the genetic variance in these traits could be attributed to nonadditive genetic effects, modeled as dominance. Subjective well-being had genetic overlap with personality, though less so than has been found in humans or chimpanzees. Since a large portion of nonadditive genetic variance in personality is not unique to humans, the nonadditivity of human personality is not sufficient evidence for recent selection of personality in humans. Nonadditive genetic variance may be a general feature of the genetic structure of personality in primates and other animals. Furthermore, although nonadditive genetic variance is stated as evidence for recent selection in the evolutionary psychology literature, evolutionary theory shows that it instead tends to be the outcomes of long-term selection pressures.

**The genetics of cannabis withdrawal**

Arpana Agrawal; Washington University in St. Louis
Alan Budney; University of Arkansas for Medical Sciences
Nick G. Martin; Queensland Institute of Medical research
Michael Lynskey; Washington University School of Medicine

DSM-5 is considering the inclusion of cannabis withdrawal as part of its repertoire of symptoms of cannabis use disorders. Cannabis withdrawal has been found in epidemiological and clinical studies to be both reliable and valid—its symptoms include irritability, anger and aggression, depressed mood, nervousness/anxiety, psychomotor agitation (restlessness), insomnia, decreased appetite/weight loss and physical symptoms (e.g. stomach pain). Utilizing a Australian sample of adult (27–40 years) male and female (63 %) identical and fraternal twins, we examine the genetic underpinnings of cannabis withdrawal in the context of existing diagnostic criteria. Of the full sample, 2.276 (69 %) of the twins reported a lifetime history of cannabis use. Of the withdrawal criteria, and consistent with clinical studies, irritability (11 %) was the most commonly reported, followed by restlessness and sleep difficulties (10.8 %). Physical symptoms were uncommon (e.g. stomach pains reported by 1.4 %). Twelve percent of the sample met criteria for proposed DSM-5 withdrawal, the heritability of which was 72 %. The heritability of individual criteria varied from 0.58 for decreased appetite in male twins to 0.24 for physical symptoms in both sexes. Sex differences were apparent with no evidence for heritable influences on irritability/anger and sleep difficulties in females or for depressed mood in males. Underlying the 7 criteria was a single factor, with factor loadings ranging from 0.71 to 0.92. The cannabis withdrawal factor was heritable in men ($h^2 = 0.40$, 95 % CI 0.26–0.55) and in women ($h^2 = 0.46$, 95 % CI 0.33–0.56). Shared environmental influences were important in females ($c^2 = 0.27$, 95 % CI 0.13–0.38) but not males. As with dichotomous measures, genetic influences on the withdrawal factor overlapped completely with genetic influences on a factor representing DSM criteria for abuse and dependence. Our analyses reveal a genetic basis for cannabis withdrawal and individual withdrawal symptoms, adding further support for the addition of this clinical important criterion to DSM-5.

**Whole genome linkage analysis in a large multigenerational family from Brazil and case control exploration of linkage regions**

Shaza Alsabban; KCL

Substantial evidence from family and twin studies confirms the importance of genes in influencing susceptibility to bipolar disorder (BPD). GWAS uncovered a few genetic variants that only explain a fraction of the total heritability of BPD, and linkage studies have not been able to identify consistent and replicable findings. Large multigenerational families are powerful samples for mapping complex disease as they segregate fewer disease causing genes than a collection of independent nuclear families. This study performed a whole-genome linkage scan of a large multigenerational family from Brazil (BBF) segregating a severe form of BPD and unipolar depression with the aim of localising and identifying genetic variants that contribute to the development of BPD. The BBF is one of the largest reported in the literature; 308 family members were interviewed using the Structured Clinical Interview for DSM-IV Axis I Disorders and Kiddie-SADS-Present and Lifetime Version and 321 family members were genotyped using the Affymetrix 10 K array. Parametric and non-parametric linkage analyses were performed using four hierarchical phenotype models that included variation of BPD and unipolar depression diagnoses. Four significant linkage regions were identified on chromosomes 2p23.1–p22.3, 3p25.3–p24.1, 11p15.4, and 12q24.22–q24.32, and four suggestive linkage regions were identified on chromosomes 1p22.2–p21.3, 1q21.1–q21.3, 12p12.3, and 22q11.21–q12.1 which either conferred specific risk to BPD, unipolar depression, or provided evidence for a general mood disorder liability. To determine the role of the identified linkage regions in sporadic bipolar and depression cases, a case control association analysis using bipolar and depression case control cohorts was performed. None of the linkage regions identified in the BBF were found to be associated with BPD or depression. This study aims to determine the functional variants within the identified linkage regions that may be contributing to the development of BPD in the BBF through sequencing analysis, which is already underway.
Corticotrophin-releasing hormone genes and stress-related phenotypes

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Simone White; VIPBG/VCU Roxann Roberson-Nay; VCU-VIPBG
Nicole Nugent; Alpert Brown Medical School Suzanne Thomas;
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MUSC Kenneth Ruggiero; MUSC Joel Gelerter; Yale Glenn Saxe; NYUMC Karestan Koenen; Columbia University

Genes regulating the HPA axis, such as corticotrophin-releasing hormone (CRH) and CRH type 1 receptor gene (CRHR1) are implicated in stress-related phenotypes. Here we examine variation in CRH genes in stress-related studies: (1) a laboratory investigation of cortisol response to stress (Trier Social Stress Test; TSST); (2) a longitudinal study of posttraumatic stress disorder (PTSD) in pediatric injury patients; and (3) an epidemiologic study of PTSD in hurricane-exposed adults. In the context of a larger study examining the role of stress on substance craving, two SNPs within CRH were examined in relation to core-n cortisol post-TSST in a sample of 205 subjects (114 alcoholics, 63 marijuana dependent subjects, and 28 controls). Adjusting for covariates (i.e., education, racial/ethnic status, gender) and controlling for baseline cortisol, rs6991010 was associated with cortisol level after the TSST. In the injury study 103 children were assessed in the hospital in the acute aftermath of their injury and followed prospectively. Nine SNPs in CRHR1 were examined in relation to initial PTSD symptom level and symptom trajectory over time. After correction for multiple testing, rs12944712 was significantly associated with initial PTSD symptoms, and PTSD symptoms over time. The third study examined 12 SNPs (80% of common variation) in CRHR1 in relation with post-hurricane PTSD symptoms in an epidemiologic sample of 626 adults exposed to Florida hurricanes in 2004. Results show that rs12938031 was significantly associated with post-hurricane PTSD symptoms. Notably, the two significant CRHR1 SNPs across samples are in high LD with each other. This study is the first to examine CRH gene variation in a laboratory model of a stressor, a longitudinal study of children, and an epidemiologic study of adults. Results underscore the importance of CRH variation with regard to the basic stress response, and CRHR1 variation and risk of PTSD. Implications will be discussed.

Genetic stability and change of personality traits in adulthood: A 7-year longitudinal study

Juko Ando; Keio University

Genetic influences on stability and change of personality traits in adulthood have not been well-investigated compared to in childhood and old age. The current study examined genetic and environmental stability and change of the big five traits (Neuroticism, Extraversion, Openness to experiences, Agreeableness, Conscientiousness) during adolescence and young adulthood over about seven-year interval. Longitudinal twin data of the Japanese version of NEO-PI-R at time1 (1998–2001) and NEO-FFI (the short version of the NEO-PI-R at time2 (2005) were available from the Keio Twin Project. Mean ages (SD) at time1 and at time2 were 19.9 (3.8), and 26.0 (4.2) respectively (mean age difference was 6.2 (1.5). Phenotypic stability were substantially high (r = 0.53–0.62). Bivariate Cholesky analyses indicated that those phenotypic stabilitys were mainly mediated by both genetic (0.33–0.40) and nonshared environmental (0.19–0.24) factors. Significant novel genetic contribution emerged at time 2 for all of the five traits and, especially for Openness to experience, it was significant dominance effect (about 16%).

Heritability of individual differences in the neural correlates of prediction error

Andrey Anokhin; Washington University School of Medicine

Evaluation of action outcome and the detection of discrepancy between the real result of action and the representation of the desired result (prediction error) is a fundamental mechanism of adaptive self-regulation of goal-directed behavior. This neural mechanism is reflected by feedback-related negativity (FRN), an event-related brain potential (ERP) component evoked by “error” feedback. Recent studies showed that individual differences in feedback-related neural activity are correlated with personality traits and psychopathology, however, little is known about the genetic and environmental origin of these individual differences. Here we investigated heritability of ERP components associated with feedback processing in adolescent twins (n = 436, including 92 monozygotic and 126 dizygotic pairs) using a gambling task in which binary choices could result in monetary gains or losses. Consistent with previous studies, both losses and gains elicited a large P3 wave, but losses compared to gains elicited a distinct negative deflection of potential at 320 ms. The amplitude of P3 potential elicited by both gains and losses was highlyheritable, with 51 and 48% of observed variance explained by genetic factors, respectively. FRN amplitude showed modest but significant heritability (27%). Furthermore, this brain phenotype showed significant association with a functional polymorphism of the catechol-O-methyltransferase gene (COMT, rs4680), with val allele being associated with attenuated neural response to negative feedback. These results indicate that individual differences in brain activity related to feedback processing in adolescents are significantly influenced by genetic factors and suggest that feedback-related ERPs can serve as intermediate phenotypes (endophenotypes) in genetic studies of individual differences and psychopathology characterized by abnormal processing and utilization of feedback information.

Young children’s drawings of the human figure are associated with intelligence a decade later, for mostly genetic reasons

Rosalind Arden; King’s College London Maciej Trzaskowski;
Institute of Psychiatry Victoria Garfield; Goldsmiths, University of London Robert Plomin; King’s College London

Do young children’s drawings of the human figure predict later intelligence? And if they do, to what extent is the co-occurrence genetic in origin?

We conducted the largest study of children’s figure drawing in early childhood (N = 14,565 at age four), and the first genetically-sensitive design. We investigated the relationship between objective measures of the children’s drawing (from the McCarthy Scales of Children’s Abilities) and intelligence at ages 7, 12 and 14 (indexed by a composite of two verbal and non verbal tests at each age). We also explored the sources of differences in drawing ability. Although it seems intuitive that the largest influence on twins’ drawings would be their co-twin, parents and family background, we found, strikingly, that genetic differences exert a greater influence on children’s figure-drawing than between-family differences. Drawing scores at age 4 correlated phenotypically with intelligence (at age 4 r = 0.33, N = 14,050, at age 14 r = 0.19, N = 4,622). Human figure drawing at age 4 was as heritable as intelligence at age 4 (both 29%). The genetic correlation between drawing at age 4 and intelligence at age 14 was 0.45; the genetic influence on drawing at age 4 was significant and detectable on intelligence a decade later even when
intelligence at age 4 had been partialled out. These findings tell us that
drawing a human figure is a stable indicator of intelligence in early
childhood and that one of the most ‘cultural’ of all human behaviors has
an important genetic component, distinct from intelligence—at least in
early childhood where we have measured it.

Biometric analysis of complex NLSY pedigrees:
Introducing a conditional autoregressive biometric (CARB) mixed model

David Bard; University of Oklahoma William Beasley; Howard Live
Oak Kelly Meredith; University of Oklahoma Joseph Rodgers;
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Over the last decade, behavior genetics has experienced an explosion
of new advanced methods for biometric analysis. Most of these meth-
ods rely on some form of a mixed effects model and involve either
maximum likelihood (ML) estimation (Guo & Wang 2002; McArdle
& Prescott 2005; Rabe-Hesketh, Skrondal, & Gjessing 2008; van den
Oord 2001) or Bayesian Markov Chain Monte Carlo (MCMC)
methods (Lindon Eaves & Erkanli 2003; Eaves et al. 2005; van
den Berg, phanie, Beem, & Boomsma 2006). In this paper, we present
a new version of the MCMC biometric model that falls into the class
of methods recently proposed for analysis of complex pedigrees in
the animal and forestry sciences (Finley, Banerjee, Waldmann, &
Ericsson 2009; Hallander, Waldmann, Wang, & Sillanpaa 2010;
Steinsland & Jensen 2010; Waldmann 2009).

We review the connections between the new method and Gaussian
Markov Random Field models for spatial analyses and present
results from a simulation study comparing this new approach to its
most popular ML competitors. Special focus is also given to the new
method’s reduction of computational complexity and its improved
flexibility for handling complex models and family structure. Finally,
sample BUGS code and data preprocessing algorithms (available
through the NlsyLinks R package) are provided for common bio-
metric analyses (e.g., ACE & ADE models), and an application of the
new method is presented for height and weight phenotypes of com-
plex pedigrees of the NLSY Children dataset.

Happiness in very young children:
What are the causes of individual differences?

Meike Bartels; VU University Toos van Beijsterveldt; VU University,
Amsterdam Dorret Boomsma; VU University, Amsterdam

Twin and family studies revealed that 40–50 % of the variance in
Happiness is explained by genetic factors (M. Bartels and D.I. Boom-
sma 2009, Behav Genet 39(6):605–615). However, all previous studies on
the causes of individual differences were based on studies with
adolescents and adults. For many phenotypes, like intelligence and
psychopathology a change in genetic architecture is observed over age.

The current study aims to reveal the causes of individual differ-
ences in Happiness in children aged 2 and 3.

Maternal reports on Happiness have been collected in the survey
studies of the Netherlands Twin Register. Mothers of twins were
invited to report on their children’s level of Happiness on a 5 point scale
(How would you rate the level of Happiness of your child in general?)

Information is available for 792 twin pairs at age 2 and 1,575 twin
pairs at age 3. The first analyses indicate that about 70 % of the
children are reported to be always or almost always happy. Less than
1 % of the children are unhappy all the time. MZ correlations are
estimated at 0.85, while the DZ correlations are estimated at 0.65. This
indicates that variance in happiness in young children has a
genetic component and that shared environmental influences might
also play a role. However, rater effects may be present in the shared
environmental contribution and need to be explored through collection
of paternal ratings.

Childhood socioeconomic status magnifies genetic
individual differences in adult cognition

Timothy Bates; University of Edinburgh Gary Lewis; Edinburgh
University Alexander Weiss; University of Edinburgh

While the heritability of intelligence has been shown to co-vary with
socioeconomic status (SES) in young samples where shared envi-
ronment is still a substantial influence, these effects have not been
examined in mid- to late-life, when shared environmental effects are
reduced. Using 1,694 twins assessed on IQ aged 24–84, we tested
for interactions between SES and genetic, family-environmental, and
unique-environmental effects. Support for interactions of gene \times
SES were found (increasing SES was associated with greater genetic
variance in intelligence). Mean intelligence scores were also signifi-
cantly and positively linked to childhood SES. No significant evi-
dence for environment \times SES interactions was found. Socioeco-
omic status appears to amplify genetic variation in intelligence, with
effects enduring into late life. By contrast interactions between SES
and shared environment appear to wash out by late adolescence. The
results support a model in which increased resources cause enduring
amplification of genetically based differences in ability among higher
SES offspring, raising mean ability levels as a consequence.

Different understandings of the same marriage:
A genetically informed study of spouses’ marital
functioning

Christopher Beam; University of Virginia Eric Turkheimer;
University of Virginia Robert Emery; University of Virginia Paul
Lichtenstein; Karolinska Institutet David Reiss; Yale Erica Spotts;
George Washington University Jody Ganiban; George Washington
University Jenae Neiderhiser; The Pennsylvania State University

Prior research suggests that marital relationships matter more to wives
than husbands (Cross & Madson 1997, Psychol Bull 122:5–37). Many
propose that this difference underlies the reason for their different
causes and consequences of marital quality (Kiecolt-Glaser & Newton
2001, Psychol Bull 127:472–503; Fincham, Beach, Harold, &
Osborne 1997, Psychol Sci 8:351). One study found different genetic and
environmental origins for spouses’ marital quality scores to help
explain this gender difference (Spotts, Prescott, & Kendler 2006, J
Fam Psychol 20:605–613). We explore the possibility that genes and
environments operate similarly in husbands and wives but lead to
different interpretations of the same marital processes. Using confir-
matory factor analytic methods designed to assess idiosyncratic
differences in the measurement of individuals’ behavior (Nesselroade,
Gerstorf, Hardy, & Ram 2007, Measurement 5:217–235), we test the
hypothesis that husbands and wives differ on marital functioning at
the observable, measurement level but not in their underlying genetic
and environmental structures.

Using a representative sample of 909 Swedish twin pairs (male =
350, female = 559) and their spouses from The Offspring Study in
Sweden (TOSS, Neiderhiser & Lichtenstein 2008), we will analyze
spousal responses to items on the Dyadic Adjustment Scale (Spanier 1976) the Marital Instability Scale (Booth, Johnson, & Edwards 1983), and the Marital Adjustment Scale (Locke & Wallace 1987). We will evaluate whether the factor loading patterns, the latent marital traits and their underlying etiological influences, or both are invariant between husbands and wives. Because factor loadings link observed behaviors to unobservables, evidence of different factor loading patterns will provide support for our hypothesis that the same etiological processes lead spouses to different understandings of the same marriage. Future research will be proposed to study why marriages have different causes and consequences for husbands and wives.

**NlsyLinks: An R package facilitating BG research with the NLSY**

William Beasley; Howard Live Oak Joseph Rodgers; University of Oklahoma David Bard; University of Oklahoma Kelly Meredith; University of Oklahoma

The NLSY has provided behavioral genetic researchers with a nationally representative family-based kinship sample since the first sibling links were released in the early 1990s. Today we discuss the newest version of the links that incorporate new survey items into our improved linking algorithm, which identifies the level of genetic relatedness among twins, siblings and cousins. The substantive presentations in this symposium demonstrate how the new links provide (a) increased flexibility, (b) higher power and (c) access to spatially-inspired techniques. This presentation focuses on the mechanical aspects of the links. First, the algorithm is discussed, and then the companion R package is introduced.

The NlsyLinks package takes over many of the manual and error-prone tasks required in BG research, such as data manipulation and specification of biometrical models. Entire univariate ACE analyses can be completed with fewer than ten lines of code. The package’s documentation and vignettes initially showcase basic analyses, which should lower the barriers of entry facing those new to the NLSY or BG research. The example analyses progressively grow in complexity to latent models, which should help experienced researchers be more efficient with their existing analyses. As a result, a wide range of behavior genetic researchers are relieved of many mechanical details and can dedicate more time to their substantive efforts.

**Early profiles of temperament: Characterization and influences of genes and environment**

Charles Beekman; The Pennsylvania State University Jenae Neiderhiser; The Pennsylvania State University Kristin Buss; The Pennsylvania State University Jody Ganiban; George Washington University Laura Scaramella; University of New Orleans Leslie Leve; Oregon Social Learning Center Daniel Shaw; University of Pittsburgh David Reiss; Yale

Evidence is mounting that child temperament is an important mechanism underlying development in the domains of psychopathology, school adjustment, and resiliency. While there is evidence that genes substantially influence specific dimensions of temperament (Saudino 2005), less is known about whether genes influence how multiple dimensions of temperament co-occur within individuals.

Participants were children, adoptive parents, and birth mothers from 361 linked family units drawn from the first cohort of the Early Growth and Development Study. Adoptive parents rated their child’s temperament at child ages 9, 18, and 27 months. The temperament of adoptive parents and birth mothers was also assessed.

Using the full constellation of measured temperament dimensions as indicators, Latent Profile Analysis (LPA; Muthen & Muthen 2000) was used to estimate profiles of child temperament. Four profiles best fit the data at 9 months (Fig. 1a); High Reactive, Low Reactive, Positive Reactive, and Negative Reactive. Three profiles best fit the data at 18 (Fig. 1b) and 27 months (Fig. 1c); Positive Reactive, Negative Reactive, and Fearful.

Children with birth mothers who had higher levels of reward dependence (e.g., more sociable, warm, tender-hearted) were 1.4 times less likely to be members of the Fearful Profile as opposed to the Positive Reactive profile at 18 months, X2 (2, N = 315) = 6.1, p < 0.05; indicating genetic influences on membership. Children who had adoptive mothers with higher levels of temperamental harm avoidance were 1.4 times more likely to be in the Negative Reactive Profile at 18 months as opposed to the Positive Reactive Profile, X2 (6, N = 320) = 26.4, p < 0.01; indicating environmental influences on membership.

Results replicate and expand prior temperament findings and provide direct evidence for specific genetic and environmental influences on profiles of child temperament.

**Consanguinity and democracy: Is there a link?**

Edward Bell; Brescia University College, at UWO
Michael Woodley; University of Arizona

We examine the issue of whether the principle of inclusive fitness (kin selection) is relevant to national levels of democracy. Specifically, we address the hypothesis that consanguinity (marriage and subsequent mating between second cousins or closer relatives) is an important though often overlooked predictor of democracy. Measures of consanguinity and democracy correlate substantially in a sample of 70 nations (r = −0.632, p < 0.001), and consanguinity remains a significant predictor in multiple regression and path analyses involving several key control variables. The data suggest that where consanguineous kinship networks are numerically predominant and share a common statehood, democracy is unlikely to develop. Although the results are preliminary, possible explanations for these findings include the idea that restricted gene flow arising from consanguineous marriage facilitates a rigid collectivism that is inimical to individualism and the recognition of individual rights, which are central elements of the democratic ethos. Furthermore, high levels of within-group genetic similarity may discourage cooperation between different large-scale kin groupings sharing the same nation, inhibiting democracy.

**The genetic architecture of economic and political preferences**

Daniel Benjamin; Cornell University David Cesarini; New York University Matthijs van der Loos; Erasmus University Rotterdam Chris Dawes; New York University Philipp Koellinger; Erasmus University Rotterdam Patrik Magnusson; Karolinska Institutet Chris Chabris; Union College Dalton Conley; New York University David Laibson; Harvard University Magnus Johannesson; Stockholm School of Economics Peter Visscher; University of Queensland Diamantina Institute

Preferences are fundamental building blocks in all models of economic and political behavior. We study a new sample of comprehensively
genotyped subjects with data on economic and political preferences and educational attainment. We use dense single nucleotide polymorphism (SNP) data to estimate the proportion of variation in these traits explained by common SNPs and to conduct genome-wide association study (GWAS) and prediction analyses. The pattern of results is consistent with findings for other complex traits. First, the estimated fraction of phenotypic variation that could, in principle, be explained by dense SNP arrays is around one-half of the narrow heritability estimated using twin and family samples. The molecular- genetic-based heritability estimates, therefore, partially corroborate evidence of significant heritability from behavior genetic studies. Second, our analyses suggest that these traits have a polygenic architecture, with the heritable variation explained by many genes with small effects. Our results suggest that most published genetic association studies with economic and political traits are dramatically underpowered, which implies a high false discovery rate. These results convey a cautionary message for whether, how, and how soon molecular genetic data can contribute to, and potentially transform, research in social science. We propose some constructive responses to the inferential challenges posed by the small explanatory power of individual SNPs.

Inclusion of SNP data in the CCC model for drug use and abuse

Jocilyn Bergin; Virginia Commonwealth University
Michael Neale; Virginia Commonwealth University

In drug studies, if an individual does not initiate drug use it is typically not possible to assess their level of drug abuse or dependence. One approach to this problem is to collect data from relatives and use the causal-common-contingent (CCC) structural equation model of drug use and abuse. The aim of this study was to compare logistic regression and structural equation modeling tests for association between single nucleotide polymorphisms (SNPs) and liability to initiation and dependence.

Drug use/abuse and SNP data were simulated using the mvnorm function in R for 5,000 and 10,000 sibling pairs. The following values were used: minor allele frequency = 0.3; drug use/abuse correlation = 0.5; sibling correlation-use = 0.3; sibling correlation-abuse = 0.4; cross sibling use/abuse correlation = 0.2; and allelic effect-use = 0.00, 0.05 or 0.1. The allelic effect on abuse was set as the allelic effect of abuse (0.00, 0.05, or 0.1) + the value of the allelic effect on use* use/abuse correlation. Phenotypic and sibling correlations were varied. CCC models were run for each set of allelic effect combinations, phenotypic, and sibling correlations. The full model was run and SNP effects of use or abuse were removed. Logistic regressions models predicting SNP were also used. Abuse was coded in each of the following three ways: true simulated value; abuse = 0 when use = 0; and abuse = missing when use = 0.

Results show that the CCC model accurately estimates the true G × E effects of SNPs on drug use and abuse. Higher correlations yielded more accurate estimates. The CCC models were more precise than regression models. Regression models that most closely resembled the models where actual values were used were those where abuse = 0 when use = 0. However, this coding introduced bias into the results.

The CCC model accurately estimates SNP association with drug use and abuse phenotypes in large samples. The method compares favorably with some regression-based alternatives.

Common and specific genetic effects on ADHD and initial sensitivity to cigarettes in female adolescent twins

Cinnamon Bidwell; Brown University Rohan Palmer; Division of Behavioral Genetics, Rhode Island Hospital & Brown University
Andrew Heath; Washington University School of Medicine
Pamela Madden; Washington University Kathleen Bucholz;
Washington University School of Medicine John McGuey;
Providence VAMC/Brown University Valerie Knopik; Division of Behavior Genetics, RI Hospital/Brown University

Background: Attention-Deficit Hyperactivity Disorder (ADHD) is highly heritable and a robust predictor of adolescent smoking initiation, even after controlling for comorbid Conduct Disorder (CD) (e.g. B.F. Fuemmeler et al. 2007, J Pediatr Psychol 32:1203–1213). There is also evidence that ADHD symptoms may qualify genetic influences on initial sensitivity (IS) to cigarettes (Bidwell et al. 2011, Nicotine & Tob Res 14:229–233). This study aimed to examine common and specific genetic effects among ADHD symptom dimensions and IS to cigarettes while accounting for CD in female adolescent twins.

Methods: We examined age-adjusted rank normalized scores for DSM-IV Inattentive (IN) and Hyperactive-Impulsive (HI) subtypes of ADHD, CD, and IS to cigarettes in 3,753 respondents from the Missouri Adolescent Female Twin Study. DSM-IV ADHD was assessed via parent interview when the twins were adolescents. DSM-IV CD and IS (i.e. 7 items reflecting subjective responses to first experiences with cigarettes) were assessed by twin self-report. A multivariate Cholesky was used to partition the variance and covariance among the traits.

Results: Based on the results of the full Cholesky, each phenotype was at least moderately heritable (46, 76, 87, 29 % for CD, IN, HI, and IS, respectively), with modest shared environmental effects. The genetic relationship between ADHD and IS was driven by common and trait-specific genetic factors (a common genetic factor accounted for 54 % of the genetic covariance between IN and IS and 30 % of the covariance between HI and IS). There was also evidence for ADHD-subscale-specific genetic factors and tobacco sensitivity specific genetic effects. Common genetic effects on CD and ADHD accounted for only 11 % of the genetic effect on IS.

Conclusion: The covariation between ADHD subtypes and initial sensitivity to tobacco is primarily explained through a genetic factor common with CD. In addition, ADHD-specific and tobacco specific genetic effects are significant contributors.

Evidence of polygenic enrichment in Irish high-density Schizophrenia families

Tim Bigdeli; Virginia Commonwealth University

Although the combined evidence of family, twin, and adoption studies supports a substantial aggregate genetic component for Schizophrenia, there is no evidence of either Mendelian inheritance in affected families nor genes of large effect in the general population. Recent GWAS of Schizophrenia provide strong support for a substantial common polygenic contribution of a large number of small effects. However, the respective contributions of rarer or structural variation have not yet been realized. Of interest herein is the supposition that the occurrence of multiple cases in a family supports segregation of a transmissible genetic risk factor, as opposed to a de novo mutation giving rise to a sporadic case. Multiply-affected families could, therefore, be enriched for larger, common effects. We sought to assess the predictive value of...
polygenic findings reported by the Psychiatric GWAS Consortium (PGC), as applied to a sample of Irish high-density Schizophrenia families (ISHDSF). Using genome-wide SNP data available for affected and unaffected relatives, as well as a larger panel of imputed SNP genotypes, we constructed per-individual polygenic risk scores based on the PGC analysis. Per-family averages of this score, calculated from the normalized scores for all family-members irrespective of individual affection status, were shown to be significantly elevated (mean Z-score = 0.69). Because families were clustered geographically, we addressed whether the observed enrichment for polygenic effects could exhibit regional differences. Preliminary findings indicate a non-random distribution of family means across the historical counties of Ireland and Northern Ireland. In summary, we have demonstrated empirically that the unaffected members of multiply-affected Schizophrenia families may be significantly enriched for widely-replicated, common polygenic effects.

Dynamical systems analysis in twin research

Steve Boker; University of Virginia Michael Neale; Virginia Commonwealth University Kelly Klump; Michigan State University

An approach is proposed for decomposing twin-pair differences in estimated parameters of a differential equation model into additive genetic, common environment and unique components. The approach is evaluated using first- and second-order latent differential equation models fit to simulated data. An example is discussed in application to daily-burst measures of ovarian hormones from a sample of young twin women.

Is higher IQ associated with a longer sensitive period in cognitive development? Evidence from biometrical and clinical studies

Angela Brant; University of Colorado Boulder John Hewitt; University of Colorado Boulder Yuko Munakata; University of Colorado at Boulder Robert Plomin; Kings College London

A higher IQ score is associated with a prolonged trajectory of structural brain development, which has been hypothesized to reflect an extended period of environmental sensitivity. Collective consideration of developmental changes in IQ-related brain measures and of behavioral genetic studies of IQ provides some circumstantial evidence for this proposition. I will present results from two studies in our lab that have tested this hypothesis more directly. First, results from a behavioral genetic study of IQ using a large-cross-sectional twin sample and a longitudinal replication set of twins, adoptive siblings and biological siblings demonstrate that the much-replicated finding of a gradual increase in genetic influence on IQ (and decrease in shared environmental influence) reflects a more categorical shift that happens later in development for individuals of higher IQ. This pattern is consistent with the sensitive period hypothesis but is less readily accounted for by active gene–environment correlations. Second, we aimed to bolster these variance components results by demonstrating extended influence in higher scoring individuals of a single accurately measurable environmental variable with a large influence on IQ. Phenylalanine level in Phenylketonuria sufferers has both of these characteristics, and there is some evidence that its influence on IQ is limited to childhood. I will present preliminary results from analysis of data from the 137 early-diagnosed US sufferers and their families collected as part of the PKUCS longitudinal study. Implications of these analyses for understanding the factors behind the emergence of high IQ during development will be discussed.

Self-assessed intelligence, personality and measured IQ: Phenotypic and genetic associations

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Phenotypic and genetic associations between self-assessed intelligence, personality and measured IQ were explored using 732 Croatian twins (15–22 years old). Data was collected on cognitive ability, self-assessed intelligence (SAI), and Five-Factor Model personality traits via mail. Significant phenotypic associations were found: measured IQ correlated positively with self-assessed intelligence and Openness, and negatively with Neuroticism and Extraversion. Also self-assessed intelligence correlated positively with Openness. Subsequent bivariate genetic analyses revealed that these phenotypic associations were mainly due to overlapping genetic influences. Multivariate analyses indicated that around 20 % of IQ variance could be explained by SAI and personality traits (Neuroticism, Extraversion, Openness). In combination with other recent findings from behavior genetics, this result supports the idea of pleiotropy and generalist genes.

What have modern genetic studies told us about depression?

Gerome Breen; King’s College London Shaza Alsabban; KCL. Michel Nivard; VU University Christel Middeldorp; VU University

Depression is a heritable illness and its more severe and recurrent forms have a heritability comparable to that of schizophrenia and bipolar. It has also been subject to the largest GWAS of a psychiatric disorder. However, GWAS has as yet failed to find multiple genes for depression. Future studies of depression need to take account of the issues surrounding diagnosis and life course of depression, the implication of the GWAS results for considerations of the genetic architecture of depression and how family and phenotype studies may inform us. GEROME BREEN will review the results of the PGC GWAS for depression of ~10k cases and ~10k controls and review the findings from the field of GWAS and linkage in depression. SHAZA AL-SABBAN will present genetic studies of a uniquely large family with over 80 cases of mood disorders and present genomewide significant linkage for two loci for depression. MAXIME NIVARD will present a study on the stability and change in anxious depression as a function of genes and environment, including a longitudinal twin and GWA study from age 3 to 65 years in the Netherlands Twin Registry. CHRISTEL MIDDELDORP combined a twin and GWA study to examine how symptoms of anxiety and depression during childhood and adolescence are influenced by similar genetic factors as major depression in adulthood via calculation of polygenic risk scores in a sample of 3,266 subjects from the Young Netherlands Twin Register.
Continuity of genetic and environmental influences on cognition across the life span: A meta-analysis of longitudinal twin-family studies

Daniel Briley; University of Texas at Austin
Elliot Tucker-Drob; University of Texas at Austin

The rank-order stability of many traits, including cognitive abilities, increases over the lifespan. Continuity of genetic influences has been posited as a key component of stability of psychological traits over time, but it is also possible that different genes contribute to cognition during different periods of development. How continuous or innovative are the genetic and environmental influences on cognitive development? A number of longitudinal twin-family studies of cognition have been published over the past two decades that have documented the stability of genetic and environmental influences on cognition over circumscribed periods across the lifespan. In an effort to quantitatively synthesize these effects and piece together results from various periods of development, we searched for published studies of cognition that reported raw genetically-informative longitudinal correlations and/or parameter estimates from longitudinal behavior genetic models. We identified 138 combinations of time points and measures from 15 independent samples. In total, longitudinal data came from 4,374 monozygotic twin pairs raised together, 7,491 dizygotic twin pairs raised together, 34 monozygotic twin pairs raised apart, 78 dizygotic twin pairs raised apart, 228 adoptive sibling pairs, and 250 non-adoptive sibling pairs. We fit longitudinal correlated factors models to data from each pair of time points. Estimates were aggregated by weighting by the inverse of both the sampling variances and the number of data points per sample, and correcting for non-independence. Cross-time genetic correlations and shared environmental correlations were substantially larger than cross-time nonshared environmental correlations. Cross-time correlations for each component tended to be low during early childhood, increase sharply over child development, and remain relatively high from adolescence through late adulthood. These results indicate that while genes contribute substantially to trait stability, increasing trait stability over development is attributable to increasing stability of both genetic and environmental factors.

Phenotypic and genetic structure of anxiety sensitivity in adolescence and early adulthood

Hannah Brown; Institute of Psychiatry
Maciej Trzaskowski; Institute of Psychiatry
Helena Zavos; Institute of Psychiatry
Fruhling Rijssijk; Institute of Psychiatry
Alice Gregory; Goldsmiths
Thalia Eley; Institute of Psychiatry

Anxiety sensitivity, an enhanced sensitivity towards symptoms of anxiety with a belief they are harmful, has been implicated as a risk factor in a range of emotional disorders, especially anxiety. However, whether it is a unitary or multifaceted construct is unclear. Factor analyses support both unitary and multifaceted constructs, with varying numbers of anxiety sensitivity dimensions identified across studies. Furthermore, there is disagreement about the relationship between these dimensions, some data suggesting hierarchical factor solutions, others correlated. Subjects completed anxiety sensitivity questionnaires at three time points spanning adolescence and young adulthood. Phenotypic, confirmatory factor analysis (CFA) identified the number of anxiety sensitivity dimensions and genetic (twin) analyses examined the structure and etiological relationships between these dimensions. CFA revealed comparable statistical support for three- and four-factor models across time points but only the three-factor model, depicting Physical, Social and Mental anxiety-related concerns delineated distinct facets. Genetic analyses on the three-factor model supported a common pathway model across time points with a latent “anxiety sensitivity” factor and three lower-order dimensions each influenced by dimension-specific and general etiological influences. Taken together, phenotypic and genetic analyses supported a hierarchical structure of anxiety sensitivity with three lower-order dimensions representing Physical, Social and Mental concerns.

Do non-shared environmental influences persist over time? An examination of minutes

S. Alexandra Burt; Michigan State University
Kelly Klump; Michigan State University

Behavioral genetic research has argued that differential twin perceptions of an objectively shared or family-wide event (e.g., parental conflict) can yield effectively nonshared or child-specific child outcomes, whereby only one twin engages in more pathological behavior as a consequence of this shared experience. However, prior research has yet to resolve the extent to which their findings were due to differential perceptions of a shared event or exposure to nonshared events. The current study will address this issue by examining whether differential perceptions of an objectively shared experience (i.e., parental marital conflict) can have effectively nonshared outcomes (i.e. differential externalizing). Participants will include 500 population-based twin pairs from the Twin Study of Behavioral and Emotional Development in Children, one study in the Michigan State University Twin Registry (MSUTR). The Children’s Perceptions of Interalternal Conflict inventory (Nigg et al. 2009) will be used to assess twin-specific perceptions of interparental conflict. The Child Behavior Checklist (Achenbach & Rescorla 2001) will be used to measure externalizing behavior for each twin. Analyses will be conducted using both a monozygotic twin differences design and co-twin control design, a statistically powerful counterfactual approach for identifying nonshared environmental mediation (Burt, Donnellan, Humbad, Hicks, McGue, & Iacono 2010; McGue, Osler, & Christensen, in press). We expect that discordance in twins’ perceptions of their parents’ conflict will predict discordance in their externalizing behaviors, such that the twin appraising the conflict more negatively will engage in more externalizing behaviors than his or her co-twin.

Can objectively shared events have effectively nonshared effects? Associations between differential perceptions of marital conflict and child externalizing behavior

S. Alexandra Burt; Michigan State University
Kelly Klump; Michigan State University
Early adverse environments and genetic influence on age at first sexual intercourse: Evidence for gene–environment interaction

Marie Carlson; University of Texas at Austin Kathryn Harden; University of Oregon

Youth who experience adverse early environments initiate sexual activity earlier, on average, than youth from more advantaged circumstances. Evolutionary theories have posited that ecological stress at home and early father absence are causally linked to earlier reproductive and sexual onset. Alternatively, behavioral geneticists have emphasized the role of common genetic factors mediating this association (i.e., passive gene–environment correlation). Using a large, epidemiological sample of twins and full sibling pairs (MZ = 263, DZ = 236, FS = 654) from the National Longitudinal Study of Adolescent Health, the present study attempts to reconcile these broader perspectives by testing for gene–environment interactions between several markers of environmental risk (father absence, low socioeconomic status, racial/ethnic minority status, and gender) and the genetic influences on age at first sex. Consistent with our predictions, we found that markers of disadvantage, specifically low SES and biological father absence before age 10, were associated with suppressed genetic influences on age at first sex. Although \( G \times E \) interactions for race/ethnicity and gender did not reach statistical significance in univariate interaction models, the interaction effects were in the hypothesized direction, with lower genetic influences evident among racial/ethnic minorities and males. Results from a multivariate model with these four moderators entered simultaneously showed significant \( G \times E \) interactions for SES, race/ethnicity, and gender; father absence was no longer a significant moderator. These results are most consistent with Bronfenbrenner and Ceci’s biocological model (1994), whereby proximal processes serve to increase the magnitude of genetic variance in environments/circumstances that are marked by advantage.

Cumulative genetic and environmental predictors of youth alcohol use, abuse, and dependence

Jennifer Carrano; Boston College

Alcohol use among adolescents and young adults is a significant public health issue, as rates in youth are higher than among any other age group and because early use is associated with a higher risk of later abuse/dependence and a higher incidence of related risk-taking behavior. Thus, the goal of this study is to examine genetic and environmental
predicators of youth alcohol use, abuse, and dependence in an effort to better understand the etiology of these behaviors. This study expands upon extant research by being the first to utilize a genetic risk score approach to assess the aggregate effect of several dopaminergic polymorphisms on alcohol use, by incorporating cumulative measures of environmental risk and promotive factors, and by examining gene–environment interactions and gender differences in substance use predictors, thus allowing for a more comprehensive assessment of environmental and genetic influences than has been done in the past.

Data were drawn from a longitudinal sample of approximately 15,000 youth who participated in surveys and DNA sampling in the National Longitudinal Study of Adolescent Health. Weighted multi-level poisson regression models assessed trajectories of alcohol use from adolescence (ages 12–18) into adulthood (ages 24–32) and how those trajectories were influenced by environmental and genetic contexts. Weighted zero-inflated negative binomial regression analyses examined main and interactive effects of environmental risk and promotive factors and genetic risk scores on clinically significant alcohol abuse and dependence in early adulthood. Analyses also examined gender differences in alcohol use predictors. Results provide a better understanding of the etiology of alcohol use and provide evidence of the utility of GRS methods for studying genetic influences on alcohol use. Further, findings add to what is still a rather sparse and contradictory literature on genetic effects on alcohol use and help clarify discrepant findings regarding gender differences in alcohol use etiology.

Early maternal age at childbearing and risk for ADHD in offspring

Zheng Chang; Karolinska Institutet Paul Lichtenstein; Karolinska Institutet Brian D’Onofrio; Indiana University Niklas Långström; Karolinska Institutet Henrik Larsson; Karolinska Institutet

Background: Women who give birth at younger ages (e.g., teenage mothers) are more likely to have children who exhibit behaviors problems, in particular antisocial behaviors. However, the link between early maternal age and offspring ADHD has not been established. In addition, it is not clear whether early maternal age at childbearing is causally associated with poor offspring outcomes or confounded by familial factors.

Methods: We used a population-based cohort of children born in Sweden between 1992 and 1998 (N = 720,764), using linkage of national registries. Children and their mother were identified from the Multi-generation Registry. Offspring ADHD (n = 13,963) were identified from the National Patient Registry (NPR) and the Prescribed Drug Registry (PDR). First, survival models were used to analyze the association between early maternal age and offspring ADHD among unrelated individuals. Second, we compared the risk of ADHD among differentially exposed siblings within nuclear families to control for familial background factors.

Results: Results showed that early maternal age at childbearing (maternal age <20) was significantly associated with the risk of ADHD in offspring (Hazard ratio = 2.22, 95% CI 2.06–2.38). Comparison of differentially exposed siblings indicated no within family association. Adjusted model showed that maternal age at first birth (MAFB) accounted for the observed association.

Conclusions: Early maternal age increased the risk of offspring ADHD. However, the absence of within-family association suggests that familial factors shared by siblings account for the association. Interventions for reducing ADHD should target risk factors that shared in a teenage-mother family.

An investigation of genetic and environmental influences on the association between fertility and lifespan in male and female twins

Elizabeth Chereji; University of Southern California Margaret Gatz; University of Southern California Nancy Pedersen; Karolinska Institutet Carol Prescott; University of Southern California

Research on the existence and direction of the relationship between fertility and lifespan has yielded mixed results. One evolution-based theory, the disposable soma theory (DST), proposes a trade-off between fertility and lifespan with natural selection favoring allocation of resources toward reproduction at the expense of longevity. Under the DST, females are expected to experience the majority of the adverse consequences of fertility relative to males, as females experience higher direct costs of reproduction. The present study used a large, population-based dataset from the Swedish Twin Registry to test whether additional children are related to decreased lifespan (as proposed by the DST) and whether demographic covariates explain any relationship found. Data from pairs of twins were analyzed to elucidate whether the association between fertility and lifespan is accounted for by individual-level factors or by genetic and environmental factors shared by family members. Fertility and longevity information from female and male twins (N = 15,622) born 1901–1925 were analyzed using survival analysis. Contrary to the DST, women with children had a significantly longer lifespan relative to those who were childless [males without kids (ref) = 1.00, males with kids = 1.06, females without kids = 1.20, females with kids = 1.27]. Although women in general lived longer than men, the survival advantage associated with parenthood was similar for the sexes and the effect did not depend on number of offspring. Adjustments for demographic factors and co-twin fertility did not alter the prediction for an individual’s survival, indicating that the association is attributable to individual-level factors associated with fertility rather than family-level environmental or genetic factors shared by co-twins. These results, derived from a large, population-based sample, are inconsistent with the disposable soma theory as applied to modern humans.

Cross-cultural study of academic achievement of twins

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This study is a part of comparative research of academic achievement of school-age twins and singletons in Russia and Azerbaijan. The aim of this part of the study was to analyze the impact of shared and non-shared influences into the twins’ academic achievement. The sample consisted of more than 2,000 pairs of MZ and DZ twins aged 7–19 and more than 4,000 singletons. We analyzed the scholastic measures of Reading, Literature, Foreign Language, Mathematics, History, Science, several other school subjects and general measures. The results show that

1) the family structure is a significant factor, having an influence on scholastic achievement of twins;
2) there are some cultural peculiarities, mediating these influences.
Does parental emotional support moderate genetic influences on early externalizing behaviors?

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Previous research has revealed that parental emotional support moderates the association between psychosocial adversities and the development of externalizing behaviors (e.g., Kim-Cohen, Moffitt, Caspi, & Taylor 2004; McLeod & Smith 2002). Yet, relatively little is known about the mechanisms of this protective effect of positive parenting against the development of externalizing behaviors. This longitudinal study examines gene × environment interaction in the development of externalizing behaviors among approximately 600 twin pairs at ages 4 and 5 years from a nationally representative sample of children born in the United States in 2001. Parental emotional support was rated by trained coders using video recordings of parent–child interactions in the context of a semi-structured task. It was hypothesized that parental emotional support would suppress genetic influences on externalizing behaviors. Structural equation modeling was employed to estimate the moderation effect of parental emotional support on genetic and environmental contributions to age 5 externalizing, unique of and carried over from age 4 externalizing. We additionally fit models to a replication sample of approximately 1,500 pairs of siblings at ages 4–5 years and ages 6–7 years, in which maternal emotional support was assessed using the Home Observation for Measurement of the Environment.

The aetiological covariation between inattention, reading difficulties and reaction time variability in a general population sample of twins

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Attention deficit hyperactivity disorder (ADHD) and reading difficulties (RD) are both highly heritable and show substantial comorbidity. Bivariate twin analyses indicate that the comorbidity is largely driven by shared genetic influences, with RD showing stronger phenotypic and genetic association with inattention than with hyperactivity-impulsivity symptoms. Similarly, recent findings also suggest that reaction time variability (RTV) shows greater aetiological overlap with inattention than with hyperactivity-impulsivity symptoms in a general population of twins (Kuntsi et al., under review). However, little is known about the association between RD and RTV, and to what extent does RTV play a role in the between-inattention and RD. This study investigates the extent to which aetiological influences between inattention and RD are independent of the aetiological factors underlying RTV.

We used multivariate structural equation modelling on IQ, parent and teacher ratings on ADHD symptoms, parent ratings on RD and a measure of RTV obtained from a 4-choice reaction time task and a go/no-go inhibition task from a general population sample of 1,312 twins aged 7–10 years.

Inattention symptoms showed moderately strong phenotypic and genetic correlations with both RD (rPh = 0.51; rA = 0.62) and with RTV (rPh = 0.27; rA = 0.33). The phenotypic and genetic correlations between RTV and RD were 0.20 and 0.30, respectively. 74% of the phenotypic covariation between inattention and RD was due to additive genetic (A) factors; 55% of which was independent of the overlapping genetic influences in common with RTV. 81% of the covariation due to unique environmental (E) factors was not shared with the other phenotypes. Our results suggest that the co-occurrence between inattention symptoms and RD is driven by largely genetic factors, around half of which also contribute to the aetiology of RTV.

A genetically informed study of disordered eating pathology in adolescent twins

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Although lifetime prevalence rates for eating disorders remain low in adolescent female populations (Hoek & van Hoeken 2003, Int J Eat Disord 34:383–396), disordered eating attitudes and behaviors can have deleterious outcomes for the well-being of young women (Swanson et al. 2011, Arch Gen Psychol 68:714–723). Prior research demonstrates that weight concerns correlate with body dissatisfaction in young girls (Davison, Markey & L.L. Birch 2000, Appetite 35:143), and dieting awareness is present in girls as young as eight years of age (Hill & Pallin 1998, Int J Eat Disord 24:405–413). Additionally, early adolescence to young adulthood appears to be the period of highest risk for the development of eating disorders (Hoek & van Hoeken 2003, Int J Eat Disord 34:383–396). Among the disordered eating behaviors, dietary restraint is dangerous because it may lead to more a serious eating disorder. Presently, we investigate potential causal hypotheses for how cognitive and behavioral aspects of disordered eating predict dietary restraint.

Using a sample of 191 female twin pairs (M age = 18.11, SD = 1.87) from the Michigan State University Twin Registry, we conducted three quasi-experimental twin studies to evaluate the selection and causal processes underlying the observed correlation between dietary restraint scores and body dissatisfaction, binge eating behavior, and weight preoccupation scores. Although body dissatisfaction and binge eating contain underlying genetic components, we observed a significant shared environmental correlation but not a significant genetic correlation between restraint behavior and body dissatisfaction and binge eating. Conversely, we observed a significant genetic correlation but not a significant shared environmental correlation between weight preoccupation and dietary restraint. In all three analyses, we found that the nonshared environmental sources of body dissatisfaction, binge eating, and weight preoccupation predict individual differences in dietary restraint.
Gene-environment interplay in adult depression symptomatology: Initial findings from iGEMS

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The consortium on Interplay of Genes and Environment across Multiple Studies (iGEMS) aims to understand the joint impact of the social environment and genetic factors on the course of adult development and aging. Towards this goal, we are creating a large and informative research resource by harmonizing data collected in longitudinal twin studies from Denmark, Sweden and the USA. In total, iGEMS includes data on over 16,000 twin individuals including over 2,600 MZ and 4,400 DZ twin pairs aged between 24 and >95 years at their initial assessment and followed for as many as 26 years in up to 9 follow-up assessments. One initial focus was depressive symptomatology, assessed in iGEMS studies either with the CESD or the CAMDEX. These two scales have been harmonized using IRT methods in a new sample that completed both measures. Similar procedures have been applied to the different social-environmental measurements, used in the different twin studies (e.g., perceived SES). We present results from analysis of baseline data from all of the twin studies using the harmonized measure of depression to address the following questions: (a) How does depressive symptomatology change across the adult lifespan? (b) Do genetic influences on depression become more or less important with age? (c) Is the heritability of depression moderated by gender or age? (d) Is there evidence for possible G × E? Mean scores show the characteristic U-shaped pattern by age, greater depression among women than men and a cross-over in the oldest years. Phenotypic variance increases with age, largely due to significant increases in nonshared environmental variance. Initial tests of G × E in MZ twins, testing for heterogeneity of within-pair differences in depression scores, were significant for the full sample, within country, and within sex. These findings represent a demonstration of successful data harmonization, point to important etiological underpinnings of age differences in depressive symptoms including gene–environment interplay, and inform our future efforts to investigate the role of social factors in the etiology of depression symptoms among other health and well-being outcomes.

The etiology of reading: A nuclear twin family design study in twin children and their parents

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Reading in the early years of primary school is highly heritable according to estimates derived from twins or twins and siblings. The limit of using just twins and siblings is that, to ensure the models are identified, the lesser of either genetic dominance or the common environment are fixed to zero. To date, no research has used parents in addition to twins to partition the genetic architecture of childhood reading. This research fits Nuclear Twin Family Design (NTFD) models to reading measured by the TOWRE in both the parents and their twin children. The children were assessed at preschool, kindergarten, and grades 1 and 2. As expected, the NTFD results showed dominance and the common environment were larger than when assessed with just twins, while additive genetic effects were smaller. However, the NTFD is not without its limitations, not least, the correlation between parents and twins may be underestimated to the extent the TOWRE measure of reading does not capture the same ability in parents and children. Models were re-fitted to accommodate this bias. The range of NTFD estimates are considered relative to those of studies using just twins.

Maternal outcomes associated with teenage childbirth: A quasi-experimental study of educational attainment and economic disadvantage

Claire Coyne; Indiana University Niklas Långström; Karolinska Institutet Paul Lichtenstein; Karolinska Institutet Brian D’Onofrio; Indiana University

Teenage childbirth is associated with higher rates of lifetime poverty, lower educational attainment and the receipt of social welfare benefits. The current study used genetically informative data from multiple Swedish national registries to test whether the association between teenage childbearing and teen mother’s poor educational and socioeconomic outcomes as adults is consistent with a causal association or due to confounding selection factors. The sample included longitudinal data for 1,117,806 mothers born between 1955 and 1970. Multi-level, logistic and Cox regression models were used to test the association both between and within families. Sibling-comparisons (half sisters, full sisters, DZ and MZ twin sisters) were used to control for unmeasured genetic and environmental factors.

In population-wide analyses teenage mothers were at increased risk for low educational achievement (OR = 3.58). The association was attenuated in the comparison of half (OR = 2.28) and full (OR = 3.59) sisters but remained robust. The comparisons of DZ (OR = 4.17) and MZ (OR = 2.22) twin sisters showed that teenage childbearing remained a strong predictor of low educational achievement. Similarly, population-wide, mothers who began childbearing as teenagers were more likely to be in the lowest quintile of family income at age 35 (OR = 1.25). The pattern persisted when comparing sisters (OR = 1.17), including MZ twin sisters (OR = 1.56).

Cox regression models tested the association between teenage childbearing and ever receiving social welfare benefits. The population-wide association (HR = 3.11) was somewhat attenuated in the comparisons of half (HR = 1.53) and full (HR = 1.61) sisters. DZ (HR = 1.37, 95 % CI = 1.14–1.65) and MZ (HR = 1.73, 95 % CI = 1.36–2.21) twin sister comparisons showed that teenage childbearing still predicted the receipt of social welfare benefits. Overall, the results are consistent with a causal association between teenage childbearing and educational attainment and economic disadvantage later in life.

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A network perspective on modeling the relationship between genes and psychopathology

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The potential success of behavioral genetic studies in unraveling the genetic underpinnings of psychological disorders crucially depends on correctly modeling the genotype-phenotype relationship. In the current dominant approach, a psychological disorder is modeled as a latent variable that is the common cause of a variety of symptoms. Subsequently, one examines whether genes predict the (dichotomized) sum score on symptoms of a disorder: if so, then those genes are said to be associated with that disorder. Despite moderate to high heritability of psychiatric disorders, however, this strategy has so far hardly yielded groundbreaking results: typically, identified genetic polymorphisms account for less than 2% of the genetic variance.

The network perspective (Borsboom 2008; Cramer, Waldorp, van der Maas & Borsboom 2010), in contrast, views psychological disorders not as latent variables but as networks of directly, causally related symptoms: e.g., insomnia → fatigue → concentration problems. From this network perspective, the assumption that genes impact all symptoms of one disorder (i.e., using the sum score) is less compelling since it is likely that the relations between symptoms are partially driven by different sets of genetic polymorphisms: e.g., the more physiological homeostatic processes that are involved in the relation between sleep and fatigue vis-à-vis the more cognitive processes that are probably involved in the relation between depressed mood and suicidal thoughts. If this is true, then gene hunting based on a phenotypic sum score might be ill-advised because it will only capture genetic variance shared among symptoms and relations between them (Cramer, Kendler, & Borsboom 2011).

Heritability of the trajectory of body mass index across the adult life span

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Being overweight or obese in midlife is linked to poor health. However, the association between weight and health in late life is less well understood, with indications that weight maintenance may be an indication of health and survival. Body Mass Index (BMI) is highly heritable in midlife, but less is known about the heritability of the trajectory of BMI across the life span. BMI values from early adulthood (25 years of age) to old–old age (96 years of age) were available for 425 twin pairs taking part in the Swedish Adoption/Twin Study of Aging (SATSA). Among both men and women BMI values increased until the age of 65, then the increase leveled off with a significant decline starting at the age of 80 years. Variability in BMI was larger in women compared to men across age. A full 3-part piecewise biometrical growth model indicated that the heritability of BMI change from 25 to 65 years of age was moderate in women and men (0.33 and 0.38, respectively) and higher than between ages 65–80 (0.04 and 0.12) or 80+ years (0.20 and 0.02). Rearing environment also contributed to change in BMI (range, 0.13–0.34). For both men and women the unstandardized variance components for the genetic and non-shared environmental effects increased over age. The study results highlight that both genetic and non-shared environmental effects must be considered in a longitudinal context to understand BMI development across the adult life span.

A Genome-wide association study of non-pathological cognitive ageing

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Cognitive decline is a feared aspect of growing old. It is a major contributor to lower quality of life and loss of independence in old age. We investigated the genetic contribution to individual differences in non-pathological cognitive ageing in five cohorts of older adults. We undertook a genome-wide association analysis using 549,692 single nucleotide polymorphisms (SNPs) in 3,511 unrelated adults in the Cognitive Ageing Genetics in England and Scotland (CAGES) project. These individuals have longitudinal cognitive data from which phenotypes measuring each individual’s cognitive changes were constructed. One single nucleotide polymorphism (SNP)—rs2075650, located in TOMM40—had a genome-wide significant association with cognitive ageing ($p = 2.5 \times 10^{-8}$). This result was replicated in a meta-analysis of three independent Swedish cohorts ($p = 2.41 \times 10^{-6}$). An APOE haplotype, previously associated with cognitive ageing, was found to have a significant effect on cognitive ageing in the full CAGES sample ($p = 2.18 \times 10^{-8}$, females, $p = 1.66 \times 10^{-11}$, males, $p = 0.01$). Fine SNP-mapping of the TOMM40/APOE region identified both APOE (rs429358; $p = 3.66 \times 10^{-11}$) and TOMM40 (rs11556505; $p = 2.45 \times 10^{-8}$) as loci with SNPs that were associated with cognitive ageing. Conditional analyses of these loci suggest that they are not independent effects. Results from gene-based and functional annotation analyses will also be presented. In conclusion, the APOE/TOMM40 region was found to be significantly associated with non-pathological cognitive ageing. The identity and mechanism of the causal variant(s) remains unclear.

Putting nature and nurture on the map: visual analysis of geocoded twin data

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Twin studies allow us to estimate the relative contributions of nature and nurture to human phenotypes by comparing the resemblance of identical and fraternal twins. Variation in complex traits is a balance of genetic and environmental influences; these influences are typically estimated at a population level. However, what if the balance of
nature and nurture varies depending on where we grow up? We used statistical and visual analysis of geocoded data from over 6,700 families to show that genetic and environmental contributions to 45 childhood cognitive and behavioural phenotypes vary geographically in the United Kingdom. This has implications for detecting environmental exposures that may interact with the genetic influences on complex traits, and for the statistical power of samples recruited for genetic association studies. More broadly, our experience demonstrates the potential for collaborative exploratory visualization to act as a lingua franca for large-scale interdisciplinary research.

Negative affectivity, political contention and turnout: A genopolitics field experiment

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Recent genopolitics and political psychology research suggests individuals’ biological differences matter for political participation. Some studies demonstrate that individual differences interact with the environment to affect political behavior but have failed to account for the possibility that individuals self-select into their environments. To test the interaction between innate predispositions and an exogenous environmental influence, we conducted a field experiment during the 2010 California midterm elections. We randomly assigned subjects to receive a postcard mobilization treatment designed to induce an emotional response to the degree of political competition in the election. We tested the hypothesis that subjects who are genetically predisposed toward negative affectivity will be less likely to vote after treatment exposure. To our knowledge, this is the first study in political science to measure genetic moderation of a field experimental treatment, and it suggests experimental approaches can benefit from the inclusion of genetically and other biologically informative covariates.

Additive genetic variation in risk to schizophrenia across African American and European American populations

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Schizophrenia is a highly heritable disorder (~0.7–0.8) with a prevalence rate of ~1%, but with prominent variation between populations (McGrath 2006). However, to date, few studies have specifically examined whether SNPs associated with schizophrenia are shared across populations or, rather, are population specific. We used a recently developed method (Lee et al. 2011) to determine the extent to which additive genetic variance in liability to schizophrenia tagged by common SNPs is shared across African American (AA) and European American (EA) populations (AA n = 2,006; EA n = 4,796) in the Molecular Genetics of Schizophrenia (MGS) samples. Using 771,112 genome-wide SNPs that passed rigorous quality control procedures, we estimate the genetic variance in liability to schizophrenia associated with these SNPs that is shared across the two populations (n = 6,802) to be 0.20 (SE 0.06) and the variance that is unique within each population to be 0.21 (SE 0.07). Constraining all of the genetic variance to be shared between populations results in a model with a significantly worse fit. However, AAs are known to be highly admixed. By limiting the analysis to EAs and only low-admixed AAs (n = 5,893), we find no evidence for shared genetic variance between the two populations (point estimate of 0, SE 0.08) and unique genetic variance within ethnicities to be 0.39 (SE 0.09). These findings suggest that common causal variants are likely to be important factors in the etiology of schizophrenia in both African and European descent populations, but also suggest that GWAS results from EA populations cannot typically be extrapolated to populations of African descent. Further work is needed to disambiguate whether the lack of shared genetic variance tagged by SNPs is a result of unique causal variants or different LD structures in the two populations.

Effects of genetic variation in the dopaminergic system on leisure time exercise behavior

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Despite its well-known benefits, regular leisure-time exercise behavior drops from childhood to adolescence and reaches unacceptable low proportions in adulthood, with the majority of people in the United States and Europe not engaging in regular exercise at the recommended level for the past two decades. Twin studies provide evidence that genetic influences contribute strongly to individual differences in exercise behavior. Previous findings in human subjects and animal research suggest that part of the genetic variation that leads to differences in exercise behavior may be found in the dopaminergic midbrain reward systems. In this study we tested the effects of multiple (functional) SNPs and VNTRs on leisure time exercise behavior in genes coding for elements in the dopaminergic signaling pathway. SNPs in the DBH (rs1611115, rs2519152), COMT (rs4680), DRD1 (rs265981), DRD2 (rs1800497), DRD4 (rs1800955, rs3758653) and DAT (rs2652511, rs40184) genes as well as VNTRs in DRD4, DAT1, DRD5 and MAOA genes were typed in 2,013 subjects from twin families in the age ranges from 7 to 12 (parental report) and 14 to 50 (self report). Using linear mixed modeling, the genetic predictors were tested for association in the young and adolescent/adult samples with age and sex as additional covariates and taking familial relationships into account. No significant association between any of the dopaminergic and variants leisure time exercise behavior was found (p’s > 0.098). This was true for a continuous measure of weekly MET hours spent on exercise as well as for a dichotomy between vigorous exercisers (>16 MET hours weekly) versus non-exercisers. We conclude that obvious candidate genes in the dopaminergic pathway are not strongly associated with regular leisure time exercise behavior. Genome wide association for exercise behavior in large samples might be the only appropriate way forward.
**Do extraversion and sensation seeking causally influence exercise? A longitudinal genetically informed analysis**

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Extraversion and sensation seeking are positively correlated with exercise behavior, in adolescence and in adulthood. In epidemiological studies on exercise it is often assumed that these correlations reflect causal effects of personality on exercise, but this has not been thoroughly tested. Since personality does not stabilize before mid-adulthood, an alternative hypothesis is that personality and exercise mutually influence each other over time. Another alternative hypothesis is that genetic pleiotropic mechanisms, such as the hypothalamic drive to be active, explain the observed correlations.

These hypotheses were tested by analyzing data from twins and their siblings aged 13–32 who participate in the longitudinal survey study of the Netherlands Twin Register. Exercise behavior (MET hours/week) was assessed in 1991, 1993, 1995, 2002, 2004 and 2009. Sensation seeking (Sensation Seeking Scale) and extraversion (Amsterdame Biografische Vragenlijst) were assessed in 1991, 1993, 1997, 2000 and 2002. Data were restructured such that age blocks of 2 years represent the time points. As a first step, cross-sectional bivariate and co-twin control analyses were applied to a subsample of 2,768 complete twin pairs.

The phenotypic correlation with exercise is 0.12 for extraversion and 0.17 for sensation seeking. Extraversion and sensation seeking are correlated 0.31. For extraversion and exercise, the intrapair difference correlation was 0.10 in both MZ and DZ pairs, and genetic and environmental correlations \( r = 0.08 \) vs. \( r = 0.04 \) were both significant \( (p < 0.001) \). For sensation seeking and exercise, the intrapair difference correlation was nonsignificant in MZ pairs \( r = 0.04 \). The unique environmental correlation was also nonsignificant \( (r = 0.01) \), in contrast to the genetic correlation \( r = 0.16; p < 0.001 \).

These preliminary results suggest that the association of extraversion with exercise is causal, but that the association between sensation seeking and exercise is due to pleiotropic effects. Longitudinal analyses will be conducted to confirm these findings.

**Do boys with a male teacher perform and behave better at school? A discordant monozygotic twin design**

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Educational achievement of girls is increasing compared to that of boys at the same time that the number of female teachers in primary school education is rising. Since same-gender teachers are said to enhance educational achievement, some blame the lack of male teachers for a poorer performance of boys. Our objective is to determine whether teachers’ gender has an effect on educational achievement and behaviour problems in a unique sample of twins discordant for teachers’ gender. The Netherlands Twin Register has collected over 6,000 surveys from teachers of 12-year old twins. Some of those twins attended separate classes with a female and a male teacher. Therefore, this study can adopt a unique design with the comparison of 73 monozygotic twin pairs, who are genetically identical and perfectly matched on family background, but discordant for teachers’ gender. Teachers rated the proficiency of their students on arithmetic, language, reading, and physical education, and assessed their classroom behaviour. In addition, data on a national educational achievement test was available. Analyses of the data from the discordant twin pairs showed that the interaction between teachers’ and students’ gender was significant (or approached significance) for the teacher ratings of all school subjects. Both male and female teachers seem to give higher ratings to same-gender students. Boys taught by a male teacher had higher scores on all scales of the educational achievement test. However, the difference was only significant for the subscale study skills. There were no differences in behaviour problems, including attention problems, between 12-year old boys and girls with a male or a female teacher.

**GWAS of behavioral disinhibition in a selected adolescent sample**

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Behavioral disinhibition (BD) is a construct encompassing risky and impulsive behaviors. It is strongly heritable, perhaps even more so than its component phenotypes (e.g. Young et al. (2000) Am J Med Genet (Neuropsychiatric Genetics) 96:684–695). Although GWAS have been conducted on phenotypes that fall under the umbrella of BD (such as alcohol dependence [Treurlein et al. (2009) Arch Gen Psychiatry 66:773–784] and conduct disorder [Dick et al. (2011) Mol Psychiatry 16:800–808]), few studies have searched genome-wide for genetic influences on the overall BD construct. The Center for Antisocial Drug Dependence (CADD) provides a unique sample of adolescents over-selected for high BD characteristics, such as substance problems. The current sample was comprised of over 1,700 unrelated adolescents drawn from the ongoing studies within the CADD. Individuals were selected for genotyping based on demonstrating average to high levels of BD at their first assessment, between ages 13 and 19. BD was evaluated as a composite score of age- and sex-corrected substance abuse/dependence, conduct disorder, and novelty seeking measures. All individuals were genotyped on the Affymetrix 6.0 array and genotype calls were refined using BeagleCall. We will present results from this GWAS of BD in the context of discussing how examining genetic effects on the higher-order BD phenotype may inform our understanding of specific BD-related behaviors, and vice versa.

**Gene–trait interactions: What they mean and why they matter**

Colin DeYoung; University of Minnesota

Why is it so difficult to identify specific genetic variants that account for more than a tiny percentage of known genetic variance in phenotypes? Commonly invoked explanations for this “missing
heritability” include massive polygenicity, epistasis, and gene–environment interactions. Gene–trait interaction is another concept useful for understanding the lack of obvious genetic main effects. Both genes and environments are distal contributors to human behavior, but the brain is the proximal driver of behavior. Functional variation in a gene creates variation in the brain system in which it is expressed. However, to understand the consequences of that variation, one must understand not only its effect on the particular brain system in which it is expressed, but also how that affected system interacts with other brain systems that vary across individuals. In other words, to understand the effect of variation in a single gene, we must understand how it interacts with its context in different individuals. Modeling the brain accurately enough to accomplish this task is extremely difficult. However, one method to begin studying how single genes interact with variation in the rest of the organism is to investigate gene–trait interactions. A psychological trait reflects a characteristic pattern of psychological function (and, therefore, of brain function), which has its origin in the cumulative effects of both the genome and the environment. A trait, therefore, describes variation in the general organismic context in which any single gene operates. To illustrate gene–trait interaction, I describe a research program revealing dramatic genetic moderations of behavior and brain function associated with externalizing behavior (the general tendency toward aggression, impulsivity, antisocial behavior, and drug abuse). In multiple samples, variations in the dopaminergic genes COMT and DRD4 interact with level of externalizing to predict cognitive abilities as well as neural activity measured with fMRI.

Integrating quantitative and molecular genetics to characterize gene–environment interaction

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It is widely accepted that gene–environment interactions (G × E) are theoretically important in most psychiatric and substance use disorders. However, characterizing G × E has been a topic of hot debate. Candidate G × Es have been controversial and difficult to replicate. In parallel to the rapid growth in candidate G × E studies, there has been an explosion of interest in characterizing G × E using twin data, though these literatures have developed largely in isolation. However, unlike the controversy and failures to replicate that have riddled the candidate G × E study literature, latent G × E demonstrated in twin data have been far more robust. Here we propose an integration of twin and molecular methodology to better characterize G × Es. Rather than studying single candidate genes and associated interaction effects, we use genome-wide information to characterize an individual’s genetic risk. We studied three candidate environments previously hypothesized to moderate the relative importance of genetic effects on adolescent alcohol use: parental monitoring, peer deviance, and stressful life events. First we tested for moderation of overall genetic effects with each of these environmental variables using twin data; then we tested for moderation of aggregate measured genetic risk at the level of polygene scores creating using GWAS data. In all five cases where we found significant moderation of genetic effects in the twin model, we also found moderation at the level of the aggregate measured genotypic scores. In the one case where there was no moderation of genetic variance found in the twin model, there was also no moderation at the level of the polygene score. We believe these results provide a compelling demonstration of the utility of this approach and suggest that integrating twin and molecular studies is an important means by which to advance our understanding of G × E.

Psychiatric problems associated with preterm birth: A population-based, quasi-experimental study

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Preterm birth is associated with increased risk for subsequent psychiatric problems. Most researchers have drawn strong causal inferences regarding the consequences of preterm birth. Yet, preterm birth is associated with numerous environmental risks that are themselves predictive of subsequent difficulties, and family- and twin-based studies also have shown that genetic factors, primarily passed down from the mother, influence gestational length. Environmental confounding and shared genetic liability, therefore, could account for part or all of the increased risk associated with preterm birth. The aim of the current study was to explore the associations between shortened gestation and numerous indices of psychiatric problems in a large prospective Swedish cohort study while comparing differentially exposed siblings to account for all genetic and environmental factors that make siblings similar. The study included 2.3 million offspring born between 1973 and 1997. The pattern of findings for psychiatric problems were somewhat domain-specific. When compared to offspring born at term (37–43 weeks of gestation), offspring born at earlier gestational ages were at greater risk for severe psychopathology (HRGA: 23–28 weeks = 3.17, p < 0.0001), autism (HRGA: 23–28 weeks = 3.24, p < 0.0001), and ADHD (HRGA: 23–28 weeks = 2.35, p < 0.0001) in unadjusted models. In the subsequent analytical models that included measured covariates and compared differentially exposed siblings we found that the association were independent of measured selection factors and background familial factors shared by siblings. In contrast, early gestational age was associated with suicide attempts in the population (HRGA: 23–28 weeks = 1.73, p < 0.005), but the association was largely attenuated when comparing differentially exposed siblings. The findings suggest that environmental factors specifically associated with preterm birth, consistent with a causal inference, accounts for increased risk for many psychiatric problems. But, increased risk for suicidal behavior was due to factors shared by siblings, suggesting familial background factors confound the association.

Testing models of genes and environment in development of adolescent depression

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Cross-temporal patterns of variances and covariances between depression scores of monozygotic (MZ) and dizygotic (DZ) twin pairs (N = 1,412) on the Mood and Feelings Questionnaire in the longitudinal Virginia Twin Study of Adolescent Behavioral Development (“VTSSAD”) are analyzed to identify the principal genetic and environmental processes underlying adolescent change in depression. Phenotypic variance and cross-temporal correlations between adjacent measures increase with age. Correlations between repeated measures decay with increasing interval between measurements.

Two theoretical models are tested individually and jointly for both genetic and environmental components. The first (“random regression”) assumes observed changes in the covariance structure result from the unfolding of inherent random individual differences in the
overall levels and rates of linear and quadratic change in liability to depression over time. The second ("autoregression") assumes changes are due to individual time-specific random effects that persist and accumulate with more of less fidelity over time. Expected patterns of age-related changes in variance and cross-temporal correlation are described for different versions of the two models. Both models make predictions that are superficially similar.

Maximum-likelihood (ML) parameter estimates are obtained for a range of models of varying complexity in the attempt to identify parsimonious models for the salient genetic and environmental influences.

Genetic effects are consistent with the gradual unfolding of inherent genetic differences in the overall liability to depression and correlated differences in the rates of change with age. There is little evidence of age-specific genetic effects or the persistence of genetic innovations over time. The environment also creates significant individual differences in overall levels of depression and rates of change with age. However, in contrast to genetic effects, effects of time-specific environmental experiences persist with some degree of fidelity across subsequent occasions of measurement. Implications of these differing genetic and environmental mechanisms for understanding the etiology of depression are considered.

**Heritability of SWAN-measured ADHD in adolescents and adults**

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The heritability of ADHD for adolescents when measured using the Strengths and Weaknesses of ADHD symptoms and Normal Behaviour (SWAN) scale is lower than when scales of severity (for example, the Australian Twin Behaviour Rating Scale; ATBRS) are used. This is essentially due to a higher DZ correlation for SWAN rated behaviours.

This study will examine data from 1,187 (621 female and 566 male) adolescent twins and their siblings aged from 10 to 18 to determine whether this result can be replicated. The heritability of the inattentive and hyperactive-impulsive subtypes of ADHD will also be estimated in a sample of 2,179 (1,094 female and 1,085 male) adult twins and their siblings aged from 19 to 46 as only one other study has examined the heritability of ADHD in adults and this was as a total score.

This study has three aims; first to estimate the heritability of ADHD using the SWAN scale for both adolescents and adults. The second is to infer developmental changes in genetic and environmental variance components contributing to symptom expression across age groups. A third aim is to explore how these effects may vary across sex.

A non-scalar sex limitation model will be used to test sex specific genetic and environmental effects in both age cohorts. Additionally, standard ACE, ADE and sub-models will be fitted to find the most parsimonious and essentially the most appropriate description of the genetic and environmental effects influencing the variation of ADHD symptoms within our sample. Results to be presented.

**Measured and latent genetic influences shared across internalizing disorders**

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Twin studies have demonstrated that a variety of internalizing problems, including major depression, anxiety, and phobias, are influenced by a common genetic factor. However, which genes underlie this common factor remains unclear. Here, we explored the extent to which a single latent genetic factor influenced four internalizing disorders in a population-based sample of young adult Finnish twins. A single common genetic factor accounted for nearly all of the genetic variance of each disorder in both men and women. Genetic covariance across phenotypes ranged from 0.04 to 0.36 in men, and 0.17 to 0.43 in women. We then conducted a genome-wide association analysis on the resulting genetic liability factor scores, in an effort to determine which genes underlie a general liability to internalizing problems. No marker met the conservative genome-wide significance threshold. The most strongly implicated genes in gene-based association tests include genes previously associated with internalizing phenotypes (NPY, NVL, PAWR); genes associated with alcohol-related phenotypes (MBNL2, NPY); multiple nicotine acetylcholine receptors and other genes associated with smoking-related phenotypes; and multiple transcription factors. Thus, our results represent replication of previous genetic associations with internalizing problems; support widely reported genetic correlations between internalizing and substance use phenotypes; and suggest previously unidentified risk genes. Further study is warranted in larger samples and in samples with repeated measures of internalizing problems.

**Sensation seeking and child responsiveness:**

**Examining evocative genotype–environment correlations with parental warmth and hostility**

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Sensation seeking is a heritable temperamental trait that is part of a sensory profile defined by an increased need for stimulation and decreased response to and registration of the surrounding environment. High sensation-seeking children have evidenced genetic susceptibility to lower quality parenting and increased behavioral problems later in life (A. Raine et al. 1998, Arch Gen Psychiatry 55:745–751; B.E. Sheese et al. 2007, Dev Psychopathol 19:1039–1046). However, it is unknown whether the genetic underpinnings of these child characteristics elicit differential parenting behavior in mothers and fathers in predicting child social behavior.

The present study examined the evocative influence of birth mother’s sensation seeking using the BIS/BAS self-report scales (C.S. Carver & T.I. White 1994, J Person Soc Psychol 67:319–333). Sensation seeking was included in separate models of adoptive parent reported hostility-to-child, via adoptive mother’s perception of unre sponsiveness in the toddler, in predicting child social disruption. Families from the Early Growth and Development adoption study were assessed at 27 and 54 months of age. Using path analysis, child
unresponsiveness at 27 months was examined as a mediator between sensation seeking and adoptive parent measures at 27 months and found to be significantly predicted by birth mother sensation seeking (0.15*). Toddler unresponsiveness predicted adoptive mother and father hostility (0.28***, 0.29*), indicating an evocative genotype–environment correlation. Adoptive mother and father hostility each predicted within-rater report of later child social disruption at 54 months (0.17*, 0.26*), as did cross-rater report of father hostility to mother’s report of child social disruption (0.14*), with passive genotype–environment correlation controlled for given the absence of genetic relation between adoptive parents and child. Results highlight the evocative nature a genetic liability for sensation seeking manifested as child unresponsiveness may play in eliciting differential parenting techniques and the influence on subsequent child social behavior.

**Therapygenetics: Predicting response to CBT in child anxiety from specific genetic markers**

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**Background:** Child anxiety disorder is a chronic debilitating condition. Cognitive Behavioural Therapy (CBT) is successful in approximately 60% of cases, with poor response associated with greater severity, comorbidity and parental psychopathology, implicating genetic influence. The twin literature has shown that genetic influences interact with both negative and positive environmental influences, thus genes may predispose individuals to respond well or poorly to a psychological treatment. The Serotonin Transporter Promoter Polymorphism (5HTTLPR) has been associated with responsivity to the environment. Specifically, the short (S) allele has been associated with increased depression in the presence of stress, and with better outcomes in the absence of stress, and may thus be a marker of environmental responsivity.

**Methods:** We examined the role of the SS genotype in predicting anxiety diagnosis and response to CBT in child anxiety disorders, using a gene–environment interaction approach. Children aged 6–13 years with a primary diagnosis of anxiety disorder undergoing CBT provided DNA (N = 559, 357 from white European ancestry).

**Results:** There was an association between the 5HTTLPR and treatment response at follow-up. Individuals with the SS genotype were 20% more likely than the SL/LL group, to be free of their primary or all anxiety diagnoses by follow-up. This finding was independent of significant influences of pre-treatment symptom severity, and comorbid mood disorder on treatment response. Children with the SS genotype also showed a significantly greater reduction in symptom severity by follow-up than those with the other genotypes.

**Discussion:** Treatment offers the ideal opportunity to test for gene–environment interaction with a positive environment, and as the timing can be predicted this design allows for pre-treatment assessment. If replicated, these findings suggest that in time it could be possible to predict which children are least likely to benefit from CBT alone and would benefit from an enhanced treatment package.

**Is facial emotion recognition a true endophenotype for childhood aggression?**

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Aggressive behavior in childhood and adolescence poses a significant problem to parents and mental health professionals alike, and it characterizes many common DSM-IV DSM-IV psychological disorders in children. A better understanding of the developmental origins of these behaviors is needed for large-scale treatment/prevention. It has been previously demonstrated that aggression and antisocial behavior have a substantial genetic component, with heritability estimates averaging ≥50%, yet molecular genetic studies have been unable identify any genetic loci showing consistent associations with these phenotypes. This failure may be due, at least in part, to the complexity of behavioral traits, which are likely to develop from collections of simpler neurocognitive/ neuropsychological traits or “endophenotypes” that are more directly influenced by gene expression. Facial emotion recognition (FER), an individual’s ability to reliably discriminate among simple facial expressions (e.g. happy, sad, angry, and fearful), has been previously examined as a putative endophenotype for complex behavioral and emotional outcomes, including aggression. Nonetheless, previous studies have primarily examined associations between FER and outcomes of interest using correlational methods, and it is thus unclear whether FER represents a “true” endophenotype in that it shares common underlying genetic influences with these outcomes. The current study utilized quantitative genetic methods to better understand the nature of these associations. In a sample of ~160 childhood and adolescent twins, ACE models were first used to decompose the variance in (1) participants’ behavioral responses to an FER task designed to tap one’s ability to recognize facial emotions and (2) a composite measure of the twins’ aggression calculated from maternal ratings. Next, Cholesky decompositions were used to model their covariance and allow us to infer to what extent to which common genetic and/or environmental influences may underlie these phenotypes.

**The association of childhood antisocial behavior and social cognitive deficits with the vasopressin receptor 1a gene (AVPR1a)**

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Animal studies in voles and mice have implicated several neuropeptide genes in pair bonding, mating strategies, social recognition, and affiliative behavior, in particular a 428-bp repeat sequence in the promoter region of the Arginine Vasopressin Receptor 1a Gene (AVPR1a). Studies in humans also have begun to examine associations between AVPR1a and various traits and disorders. In our clinic-referred sample of 641 children and their parents, we tested for associations between two promoter VNTRs (RS3 and RS1) in AVPR1a and various forms of antisocial behavior and social cognition. We found association of the RS3 VNTR with Callous-Unemotional traits (Multi-Allelic: 2 = 24.9, 11 df, p = 0.006) with overtransmission of the 326 allele (Z = 2.87, 106 transmissions, p = 0.0041) and undertransmission of the 334 and 336 alleles (Z = -3.01, p = 0.0020 and Z = -3.11, p = 0.0018, respectively), but not with the other psychopathic trait dimensions (Narcissism or Impulsivity) nor with reactive or proactive aggression or symptoms of ODD or CD. The 326 allele of RS3 was also associated with hostile perceptual biases (p = 0.00086) and general deficits in intention-cue detection (p = 0.00048; multivariate test of both
dimensions; \( p = 0.00030 \). These findings are interesting, given the specificity of RS3’s association with Callous-Unemotionality but not with other aspects of antisocial behavior, its association with both social cognitive deficits and biases, and that the same 326 allele that was related to these phenotypes in our sample was associated with poorer marital quality and spousal closeness in a Swedish twin sample. These results suggest a role for AVPR1a and perhaps other neuro-peptide genes in children’s antisocial behavior and its social cognitive underpinnings.

**Genetic variance in lung function drives variation in aging of spatial ability and processing speed**

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Longitudinal studies document an association of pulmonary function with cognitive function in middle-aged and older adults. Previous analyses have identified a genetic contribution to the correlation of pulmonary function with cognitive function [Emery et al. (1998). J. Gero, 53, P311–P317]. The goal of the current analysis was to apply the biometric dual change score model to consider the possibility of temporal dynamics underlying the genetic covariance between aging trajectories for pulmonary function and cognitive abilities. Longitudinal twin data from the Swedish Adoption/Twin Study of Aging were available from 806 twins ranging in age from 50 to 88 years at the first measurement wave. Participants completed up to six assessments covering a 19-year period. Measures at each assessment included standardized indicators of cognitive functioning tapping four cognitive domains: verbal ability, spatial ability, memory, and processing speed. In addition, spirometry was used to measure pulmonary function at each assessment with Forced Expiratory Volume in the first second (FEV1), a widely used indicator of pulmonary function. Model-fitting indicated that genetic variance for FEV1 was a leading indicator of variation in age changes for spatial and speed factors. There was no evidence that declines in cognitive function led to subsequent decline in pulmonary function. Thus, these data indicate a genetic component to the directional relationship from decreased pulmonary function to decreased cognitive function, underscoring the importance of maintaining pulmonary function for maintenance of cognitive performance.

**Developmental trajectories in syndromes with intellectual disabilities: Fragile X, Williams-Beuren, and Wolf-Hirschhorn**

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Individuals with intellectual disabilities (ID) are thought to constitute 2–3% of the general population. However, there have been relatively few published studies of trajectories of cognitive-behavioral development in children with ID, and none for those with subtelomeric deletions. The purpose of our study was to compare the developmental trajectories of children with different genetic disorders. To that end, we recruited 106 children diagnosed with one of three genetic disorder syndromes: Fragile X, Williams-Beuren, and Wolf-Hirschhorn, and assessed their cognitive abilities and adaptive behavior skills at two different time points. Of those recruited, we were able to retest 61 children 2 years after their initial test. We then computed the differences in their IQ and adaptive behavior scores, and compared the difference scores as a function of genetic disorder, with age at initial testing and initial IQ or adaptive behavior score as covariates. Results show that genetic disorder and initial IQ score affect IQ difference scores; but, only genetic disorder affected adaptive behavior score difference scores. Our results suggest that different gene-brain-behavior patterns exist for each of these genetic disorders.

**Shared genetic bases between Mendelian disorders and a polygenic trait? Testing for an association between genes underlying autosomal recessive cognitive disorders and full-scale IQ**

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A recent investigation into the genetic etiology of human height indicated a partial overlap between genetic variants affecting skeletal growth defects and those affecting height in adult humans (H. Lango Allen et al. 2010, Nature, 467(7317):832–838). Extending the idea of an overlapping genetic basis between a Mendelian disorder and a classic polygenic trait, we performed an association study in which we examined the effect of 43 genetic variants implicated in autosomal recessive cognitive disorders on cognitive abilities in an unselected Dutch population.

All available single-nucleotide polymorphism markers (SNPs) located in the 43 genetic variants of interest (1,227 SNPs in total) were tested for an association with cognitive abilities in a sample of 1,316 Dutch individuals (1,299 children, 107 adults) from 662 families. SNP-based association tests were carried out using a multilevel regression model with random intercepts to control for the covariance structure within families. In addition, gene-based testing was performed using the GATES and the VEGAS method. The results compellingly suggest an association between the phenotype and the genetic variants of interest, with genes ELP2, TMEM135, PRMT10, and RG57 showing the strongest association. This association was empirically evaluated by subjecting random samples of 1,227 SNPs from intragenic regions of the genome to the same analyses as the 1,227 SNPs of interest. The marked difference between the results obtained for the random samples and those obtained for the SNPs of interest corroborates the present findings.

**Wellness and well-being across five years in the lives of middle-aged men**

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Little is known about the underlying dynamics of the association between health and well-being. The goals of this longitudinal study were to determine: (1) the extent to which wellness (defined as self-rated health) and well-being were influenced by similar or different genetic and environmental factors; (2) whether the underlying
structure of different types of well-being and wellness was similar over time, and (3) what accounted for associations between wellness and well-being measures in a 5-year follow-up. Participants were 724 male twins from the Vietnam Era Twin Study of Aging (VETSA) who were, on average, age 55 at time 1 (T1) and 60 at time 2 (T2). Well-being measures at both times included: psychological well-being, life satisfaction, self-esteem, and depressive symptoms. Wellness was based on SF-36 self-rated physical health. All measures were significantly correlated both and were significantly heritable. These measures also showed high levels of stability over the 5 years, with phenotypic correlations ranging from 0.53 to 0.67.

Within each time, a 2-factor common pathway model fit the data well. At both times, psychological well-being and self-esteem loaded most strongly on Factor 1, which was highlyheritable ($h^2 = 0.71/0.67$ at T1/T2 respectively). Life satisfaction loaded most strongly on Factor 2. This factor was only weakly heritable ($h^2 = 0.12/0.08$ at T1/T2) and was dominated by unique environmental influences. Self-rated health and depressive symptoms loaded on both factors; but only self-rated health included significant measure-specific genetic influences. Unlike the well-being measures, most (79 %) of the genetic and environmental influences on self-rated health were measure-specific at both times. Ways in which genetic or environmental influences accounted for associations between well-being and self-rated health over time varied depending on the well-being measure.

Etiology of stability and change in executive functions from late adolescence to adulthood

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Executive functions are higher-level cognitive abilities that enable us to control our own thoughts and actions. Often associated with the brain’s frontal lobes, they continue to develop into early adulthood. Our previous research suggests that when measured with latent variables that reduce task impurity and measurement error, executive functions in late adolescence are highly heritable and diverse, in that separable executive functions (response inhibition, working memory updating, and set shifting) have different genetic influences. We report results of an ongoing follow-up study on the etiology of stability and change in these three components of executive function from age 17 to age 23. This study included re-tests of nine indicators of three executive function components as well as assessments of clinically relevant variables that might be associated with EF changes (such as depression). Preliminary results (559 individuals) indicate that individual differences in executive functions are quite stable across a 6-year time span (phenotypic latent variable correlations range from 0.86 to 1.0). However, there is evidence for change, particularly in the factor that is common to multiple executive functions (Common EF) and the factor specific to set shifting (Shifting-specific). Multivariate twin models suggest that stability is due almost entirely to high genetic correlations across time; there is no new genetic variance at age 23. Change is due to small nonshared environmental influences at age 23 (8–15 %). Despite the high stability, phenotypic analyses revealed that the change in the Common EF factor significantly correlated with changes in depression symptoms from age 17 to age 23. The results suggest that individual differences in executive functions are quite heritable and stable by late adolescence, yet are still sensitive to recent events or problems.

Gender differences in preschool temperament: A multi-method twin study approach

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The temperament dimensions of fear, activity level (AL) and inhibitory control (IC) emerge in early childhood and are considered precursors to several important developmental outcomes. Despite extensive research on these three aspects of early temperament, few investigations have examined the influence of child gender in a methodologically comprehensive, genetically informative sample. Participants included 714 twins (357 pairs) assessed at 36 months of age ($M = 157.67$ weeks, $SD = 3.49$). The sample was 50 % female and approximately one-third of the children were MZ twins (33.5 % MZ, 38.2 % same-sex DZ, 28.3 % opposite-sex DZ). We used mother and father ratings as well as the Laboratory Temperament Assessment Battery (Lab-TAB) to assess preschool temperament. Boys had higher levels of AL and lower levels of fear and IC than girls. Both boys and girls with elevated levels of fear showed lower AL and higher IC than those with low fear ratings, and those with high levels of IC had lower levels of AL. Correlations within the three dimensions across assessment modalities were positive and significant, although mother and father agreement within dimensions was always higher than parent by Lab-TAB agreement. In general, the patterns of twin correlations by gender were both reflective of the results for the full sample and fairly consistent across gender within an assessment category. Genetic analyses revealed significant genetic influences on parent-rated temperament, but only for fear as assessed in the lab. Phenotypic associations were largely due to nonshared environmental covariance for parent ratings, and to shared environmental covariance in the laboratory. These findings suggest that both the child’s gender and the status of the rater should be considered when interpreting phenotypic and genetic analyses of preschool temperament.

Genetic, prenatal, and environmental contributions to children’s weight trajectories from infancy to preschool

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Childhood obesity rates have risen dramatically over the past 30 years. Current research indicates that children’s home environment, along with genetic and prenatal factors contribute to childhood obesity. Few studies, however, have examined the unique effects of these factors on weight trajectories. The current study utilized an adoption design to differentiate between genetic, prenatal, and postnatal environmental contributions to children’s weight across early childhood.

Participants were from the Early Growth and Development Study (EGDS), a nationwide, longitudinal study that includes 361 adoptees, along with their birth parents (BPs) and adoptive parents (APs). Children’s weight percentile rankings based on the US Centers for Disease Control 2000 growth charts were computed at ages 9-, 18-, 27-, and 54-months. APs’ BMI and restrictive feeding practices, measured at 54 months, were included as indices of postnatal environmental risk factors for obesity. Data regarding two suspected prenatal risk factors for childhood obesity (pregnancy weight gain, smoking during
pregnancy) were collected from Birth Mothers at approximately 4 months postpartum. Last, birth mothers’ prepregnancy BMI was used as an indicator of the adopted children’s genetic risk for obesity.

Structural equation modeling was used to assess stability and sources of change in children’s weight trajectories. Preliminary analyses indicate that children’s weight percentile rankings were highly stable after 9-months. Smoking during pregnancy and birth mothers’ prepregnancy BMI were associated with children’s birthweights. Furthermore, birth mothers’ BMI and weight gain during pregnancy were positively related to the children’s weights at 27- and 54-months. In contrast to previous studies, AP’s BMI and restrictive feeding practices were not associated with children’s weight. This pattern of results highlights the contributions of genes and prenatal influences to children’s weight trajectories.

Maternal smoking during pregnancy and offspring conduct problems: The evidence for the association using genetically-sensitive designs

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A number of studies report an association between maternal smoking during pregnancy (MSDP) and offspring conduct disorder, ADHD, and criminal behavior. Past studies have utilized genetically sensitive (e.g., twin and adoption) designs and biologically-related epidemiological designs to examine smoking in pregnancy effects on offspring development. Each has strengths and weaknesses; however, all have limitations in disaggregating prenatal, genetic, and postnatal influences on development. We aimed to explore the relationship between MSDP and child conduct problems, controlling for mother–child genetic-relatedness in examining prenatal and postnatal influences using a complement of research designs.

Three longitudinal studies were employed: The Christchurch Health and Development Study (CHDS) (a longitudinal cohort study, N = 1,265), Early Growth and Development Study (EGDS) (a longitudinal adoption study, N = 361) and Cardiff IVF study (genetically related and unrelated families, N = 888). Associations between MSDP measured as number of average cigarettes/day (0, 1–9 or 10+) and parent-reported child conduct problems (age 4–10 years) were analysed in genetically-related (e.g., CHDS and IVF sperm donation) and genetically-unrelated (e.g., EGDS and IVF egg and embryo donations) mother–child pairs. A number of confounds were used to control for child-rearing environment (e.g., child gender, maternal age at birth, family SES, and maternal hostile parenting). A significant dose–response relationship between MSDP and child conduct problems was observed in each of the samples (β = 2.93 (IVF genetically-related pairs), 2.76 (CHDS), and 1.70 (EGDS), all p < 0.05), with the exception of the IVF genetically-unrelated pairs (β = 0.24, p > 0.05).

Associations remained statistically significant after adjusting for child-rearing environment and other covariates. The findings across studies suggest that there is a complex relationship between MSDP and child conduct problems, which is unlikely to be explained by the child-rearing environment only or by passive gene–environment correlation. Prenatal exposure to smoking however appears as a significant factor underlying offspring conduct problems, even when common genetic factors are controlled.

Genetic influences on victimization during preschool play with unfamiliar peers

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Peer victimization appears heritable, but it is unclear whether the traits that confer genetic risk require time and familiarity with a bully to manifest or whether novel and short interactions demonstrate similar genetic risk. It also is unclear whether victimization is heritable for preschool-aged children. We examined 20-min, peer-play interactions between 5-year-olds, pairing one twin at a time with an unfamiliar, same-sex peer. Victimization was defined as receiving aggression (physical or verbal) from the play partner. We also examined the behavioral, temperamental, and emotional constructs that might be associated with victimization in this unfamiliar interaction. Results demonstrated that victimization was 62 % heritable. Surprisingly, no parent-rated behaviors were significantly associated with victimization, indicating that children may behave atypically in novel play interactions with a stranger.Victimized children tended to be more aggressive during the interaction, give fewer commands, enjoy the interaction less, and be enjoyed by their play partner more. This difference in enjoyment combined with the low use of commands suggests that victimized children may not be assertively communicating their own needs and opinions during play. Cross-twin analyses indicated some differences between monozygotic and dizygotic twin pairs. Specifically, MZ twins whose co-twins demonstrated higher aggression and less commanding behaviors were more likely to be victimized. Dizygotic twins did not demonstrate a similar pattern, again supporting the importance of genetic influences in victimization. This study demonstrates genetic influences on victimization in children as young as 5-years-old, even in short interactions with unfamiliar peers. Children’s behaviors during peer interactions, rather than parent-reported behaviors, may better predict victimization in this age group. These results have implications for the point of intervention for children being victimized and they stress the importance that social skills and assertive communication skills training may have in decreasing victimization in young children.

The genetic factor structure of cannabis use and symptoms of abuse and dependence

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To determine the number of genetic factors underlying the DSM-IV criteria for cannabis dependence, we conducted structural equation twin modeling for seven dependence criteria and an ordinal stem based on three screening questions in 2,467 personally interviewed male and female twins from the Virginia Adult Twin Study of Psychiatric and Substance Use Disorders, who reported lifetime cannabis use. The best-fit twin model required single genetic and unique environmental factors along with criterion-specific unique environmental factors. The single genetic factor was defined by high loadings on the stem item related to quantity as well as time spent using or recovering from cannabis use, along with preoccupation and activities given up. Genetic factor scores derived from these two factors differentially predicted patterns of comorbidity, educational status and other historical/clinical features of cannabis dependence.
Examining associations between acetylcholine receptor genotype and personality

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Acetylcholine is a neurotransmitter strongly involved in cognitive function. It binds to cholinergic receptors that influence brain development and plasticity throughout childhood and adolescence, and research has implicated genes that influence acetylcholine function in differential response to “expected uncertainty” in the environment (e.g. Yu & Dayan 2005). In humans, individual differences in neural systems that process this kind of uncertainty appear to manifest in traits related to negative emotionality, perceptual attention, working memory, and Big Five Openness/Intelligence (Grazioplene et al., Under Review; Markett et al. 2011; Winterer et al. 2007). The Multidimensional Personality Questionnaire (MPQ) includes Stress Reaction, which measures how frequently and intensely an individual experiences negative emotions; the Absorption scale of the MPQ describes the extent to which individuals think imaginatively and become immersed in perceptual stimuli, and Absorption is a good marker of Openness/Intelligence (Tellegen & Waller 2008; Markon et al. 2005). Based on previous research pointing to a role for acetylcholine genetics in behavioral phenotypes, we hypothesize that variation in cholinergic receptor genes will be related to Stress Reaction and Absorption as measured by the MPQ. We will also explore associations between intelligence and cholinergic receptor SNPs. Results are forthcoming; analyses will be carried out using MPQ scores and GWAS data from the Minnesota Twin Registry. Genotyping for all twins was completed using the Illumina-660W-quad beadchip, and has identified 43 single nucleotide polymorphisms across 5 genes that code for cholinergic receptor subtypes. Single nucleotide polymorphisms for association analyses will be identified using the implementation of ‘‘Tagger’’ in the Haploview software package. Analyses of personality-genetic associations will be carried out in R and OpenMx for all SNPs, using models that account for both zygosity and sex of twins.

The influence of early anesthesia exposure on ADHD

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Recent retrospective studies have shown an association between anesthesia exposure early in life and later learning and behavioral problems, in particular Attention Deficit Hyperactivity Disorder (ADHD). A previous study by the Netherlands Twin Register (NTR) confirmed the association between anesthesia exposure and Educational Achievement (EA) and Learning Problems (LP), but showed that undergoing anesthesia at an early age may be considered an indicator of a genetic vulnerability rather than a causal factor for LP and EA.

The aim of the current study was to attempt to replicate the association between anesthesia and ADHD and establish whether the association can be explained by a shared (genetic) vulnerability. Within the NTR, data on anesthesia exposure under age 3 were available from maternal reports at age 2 and 3. ASEBA and Conners’ ADHD-associated phenotypes as rated by mothers, fathers and teachers were available for twins at age 7, 10 and 12 (n = 12,103). A significant higher score on all ADHD-related scales was observed for children exposed to anesthesia under age 3. However, in twin pairs discordant for early anesthesia exposure, the unexposed twin had similar scores as the exposed twin. Therefore, the association between early anesthesia exposure does not appear to be causal, but rather due to a shared vulnerability that puts children at risk for both early anesthesia and ADHD. A follow-up study in which detailed information about the type of surgery and duration of anesthesia is collected will address the question whether this conclusion also holds for severe exposures.

A closer look on the heritability of life-satisfaction: Twin effects and the role of personality

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One of the major goals in the area of “Positive Psychology” is to get a better understanding of subjective well being and especially life satisfaction that is someone’s cognitive evaluation of its quality of life. Currently, there is still an ongoing discussion about the degree of trait and state characteristics of life satisfaction and the role of personality within this process. On the one hand, life satisfaction shows stability over time, a substantial genetic component and a strong relation to personality, suggesting the existence of a “happy personality”. On the other hand, studies postulate that life events, situational circumstances and specific domain satisfaction can affect one’s global life satisfaction. The purpose of the present study was to analyze the etiology of life satisfaction using a genetically sensitive multi-group design (GSMGD). Moreover, we investigated the relationship of life satisfaction and personality with respect to common genetic and environmental effects. Our sample combined data from identical and fraternal twins, siblings, mother–child and grandparent–child pairs with a total of 1,308 couples. This GSMGD allowed the simultaneous testing of additive and non-additive genetic effects, shared and non-shared environmental effects and twin-specific environmental effects. The analyses showed that the relationship of life satisfaction and personality could be explained by common genetic and environmental effects considering twin- and non-twin-specific environmental effects. Our results support an integrative model of life satisfaction influenced by both variable situational factors and stable dispositional factors such as personality.

Socioeconomic status (SES) and children’s intelligence (IQ): In a UK-representative sample SES moderates the environmental, not genetic, effect on IQ

Ken Hanscombe; Institute of Psychiatry Maciej Trzaskowski; Institute of Psychiatry Claire Haworth; Institute of Psychiatry Oliver Davis; King’s College London Philip Dale; University of New Mexico Robert Plomin; King’s College London

Background: The environment can moderate the effect of genes—a phenomenon called gene–environment (G × E) interaction. Several studies have found that socioeconomic status (SES) modifies the heritability of children’s intelligence. Among low-SES families, genetic factors have been reported to explain less of the variance in intelligence; the reverse is found for high-SES families. The evidence however is inconsistent. Other studies have reported an effect in the opposite direction (higher heritability in lower SES), or no moderation of the genetic effect on intelligence.

Methods: Using 8,716 twin pairs from the Twins Early Development Study (TEDS), we attempted to replicate the reported moderating
effects of SES on children’s intelligence at ages 2, 3, 4, 7, 9, 10, 12 and 14: i.e., lower heritability in lower-SES families. We used a twin model that allowed for a main effect of SES on intelligence, as well as a moderating effect of SES on the genetic and environmental components of intelligence.

**Results:** We found greater variance in intelligence in low-SES families, but minimal evidence of G × E interaction across the eight ages. A power calculation indicated that a sample size of about 5,000 twin pairs is required to detect moderation of the genetic component of intelligence as small as 0.25, with about 80% power—a difference of 11 to 53% in heritability, in low- (−2 standard deviations, SD) and high-SES (+2 SD) families. With samples at each age of about this size, the present study found no moderation of the genetic effect on intelligence. However, we found the greater variance in low-SES families is due to moderation of the environmental effect—an environment–environment interaction.

**Conclusions:** In a UK-representative sample, the genetic effect on intelligence is similar in low- and high-SES families. Children’s shared experiences appear to explain the greater variation in intelligence in lower SES.

### “Bad friends” moderate the nonshared environmental influences on reading performance: Florida Twin Project on Reading

Sara Hart; Florida State University Christopher Schatschneider; Florida State University Jeannette Taylor; Florida State University

**Purpose:** The development of reading is a dynamic process involving a complex interplay among genetic and environmental influences. Peer effects are often considered to be important in the development of reading, although little is known about how friends, particularly “bad friends”, affect the etiology of reading development.

**Methods:** Participants included twins drawn from the Florida Twin Project on Reading (n = 470). Each twin completed a questionnaire concerning the extent to which his or her friends participated in anti-social or illegal behaviors (M = 3.72, SD = 0.27, range = 2.0–4.0; lower scores represent more bad behaviors). Reading comprehension was measured using FCAT results from statewide testing (M = 334.201, SD = 56.22, range = 100–500).

**Results:** FCAT and “bad friends” were significantly correlated (r = 0.10, p < 0.05). A genetic × environmental interaction model was fit to the data, with the best fitting model suggesting a significant moderation for bad friends on the unique nonshared environmental influences of FCAT scores. This moderation effect was positive, in that nonshared environmental variance in FCAT was greater when the twins’ had fewer bad friends (i.e., having better quality friends). Additionally, there was a high genetic correlation between bad friends and FCAT scores (rg = 1.00), suggesting genetic niche picking in that genetic factors influencing FCAT scores are associated with selecting friends.

**Conclusions:** It has been suggested that peers have an influence on academic outcomes, and in the behavioral genetic context friends are commonly cited as sources of possible nonshared environmental influences. These data suggest that poor quality friends confine the nonshared environmental variance in reading achievement, whereas in the presence of higher quality friends, the overall twin specific environmental variance increases. This result, coupled with the indication of genetic niche picking, suggests that better readers tend to pick higher quality friends, and in turn these friends have a great influence on the child specific environmental variability in reading outcomes.

### The genetic and environmental pathways between IQ, education and social attitudes

Pete Hatemi; Penn State University Brad Verhulst; Virginia Institute of Psychiatric and Behavioral Genetics Nick G. Martin; Queensland Institute of Medical research

Long has the public, media and scholarly discourse focused on the relationship between intelligence, education and attitudes. Educational socialization is among the most celebrated determinant of social and political orientations (Verba 2001). Recently however, several studies have also proposed a connection between lower IQ and social conservatism (Hodson and Busseri 2012), whose roots are purportedly evolutionary or genetic in nature (Kanazawa 2010). Here, we test these propositions by conducting a series of analyses to explicate the connection between IQ, education and attitudes. We separate attitudes into several social, defense and economic factors, and find that IQ is related to attitude domains in different ways. That is, a simple conservative or liberal connection to IQ is misleading. Rather high IQ is linked to both economic conservatism and social liberalism. We then conduct multivariate genetic analyses to explore the import of genetic and environment pathways from IQ and education to attitude constructs. Results are discussed.

### Genetic and environmental links between mental health and illness

Claire Haworth; King’s College London Robert Plomin; King’s College London

Moderate inverse correlations are typically found between positive mental health and mental illness. We aimed to investigate the role of genes and environments in explaining this relationship. 2,500 pairs of 16-year old twins from the UK Twins Early Development Study (TEDS) contributed data on subjective happiness and life satisfaction, as well as symptoms of depression and anxiety. These measures were combined into composites representing positive mental health (well-being) and internalising symptoms. Twin analyses indicate that wellbeing is moderately heritable (44%), with moderate non-shared environmental influence (47%) and minimal shared environmental influence (9%). Similar estimates were found for internalising symptoms, with moderate heritability and non-shared environmental influences (39 and 53%, respectively). The majority of the phenotypic correlation of −0.52 between wellbeing and internalising symptoms was explained by common genetic factors (44%), but non-shared environmental influences also explained a significant proportion (41%) of this phenotypic correlation. This study provides evidence of genetic and environmental overlap between mental health and illness, and supports the theory of mental health and illness being partly (but not entirely) correlated dimensions. The significant overlap between these dimensions suggests that the study of positive psychological wellbeing, for which it is easier to recruit samples, is an important method for identifying both the genetic and environmental risk factors for mental illness. Nevertheless, these dimensions are also partly distinct, which is particularly surprising when we focus on internalising symptom scores in an unselected population rather than clinical diagnoses. 70% of the genetic and 83% of the non-shared environmental influences on wellbeing are independent of those on internalising symptoms, indicating that there are significant genetic and environmental factors to identify for wellbeing that go beyond the absence of mental illness.
‘Verbal’ and ‘clinical’ language impairment at 4 years: Etiology and outcomes at age 12

Marianna Hayiou-Thomas; University of York Philip Dale; University of New Mexico Robert Plomin; King’s College London

The etiology of developmental language impairment (LI) at 4 and 12 years, as well as the relationship between the two, was examined using longitudinal data from the Twins Early Development Study.

At 4, two definitions of LI were used: (a) ‘Verbal LI’, defined on the basis of low (<−1.25 SD) scores on a parent-reported measure of expressive vocabulary (N = 332 (MZ) and 190 (DZs) probands), or (b) ‘Clinical LI’, defined as having seen a medical professional or speech-language therapist, following parental concern about their child’s language development (N = 273 (MZ) and 250 (DZs) probands). The 12-year language measure was a latent factor composite of 4 web-administered receptive language tests (<−1.25 SD).

It was found that: (a) ‘Verbal LI’ is more predictive of poor language performance at age 12 than ‘Clinical LI’ (Odds Ratios of 2.8 and 1.1 respectively); (b) while ‘Verbal LI’ reflects poor oral language abilities, ‘Clinical LI’ reflects speech difficulties (based on measures of speech and language function, as well as parent-reported concerns); (c) ‘Clinical LI’ is substantially and significantly more heritable than ‘Verbal LI’ (a2 = 0.73 and 0.18 respectively).

Overall, parental concern is more likely to be aroused by speech than by language problems, and this seems to be the marker of a more heritable disorder. However, the more heritable disorder is not the more persistent one; rather, early language—as opposed to speech—impairment, with its substantial environmental underpinnings, is more likely to persist into early adolescence.

The association between cognitive abilities and the postsynaptic proteome of central excitatory synapses

William Hill; University of Edinburgh Gail Davies; University of Edinburgh Mike Croning; University of Edinburgh Antony Payton; University of Manchester leone Craig; University of Aberdeen Michael Horan; University of Manchester William Ollier; University of Manchester John Starr; University of Edinburgh Neil Pendleton; University of Manchester Seth Grant; University of Edinburgh Timothy Bates; University of Edinburgh Ian Deary; University of Edinburgh

General cognitive ability accounts for a substantial proportion of the variation in any large battery of cognitive tests, and it is predictive of important life events, including health. General ability is substantially heritable, but whereas no single gene has been reliably associated with general intelligence, 40–50% of narrow sense heritability has been traced to alleles in linkage disequilibrium with commonly occurring single nucleotide polymorphisms (SNPs). The lack of replicable variants associated with cognitive ability is due to insufficient sample size to detect small effects, however by testing for associations between cognitive abilities and networks of genes, there is an increase in power thus reducing the sample size required. In this study, associations between cognitive abilities and genes previously linked to long-term potentiation/depression are examined. The human postsynaptic proteome comprises a large set of proteins organized into multiprotein complexes that regulate a range of innate and learned behavioral responses. In humans, mutations in these genes result in over 130 brain diseases including many cognitive disorders. We examined proteins of all the postsynaptic proteome and specific subsets that form complexes associated with Membrane Associated Guanylate Kinase (MAGUK) scaffold proteins (called MASC) and the NMDA receptor. Data from 8,191 individuals drawn from five cohorts with phenotypes for general fluid-type cognitive ability, crystallized-type cognitive ability, memory, and speed of processing and who were genotyped using an Illumina610-Quadv1 chip will be presented. A gene-based association approach using VEGAS will be reported, testing whether genes responsible for these proteins show an enriched association with cognitive ability compared to other brain-expressed genes and an estimate of the proportion of variance in these cognitive abilities that is due to proteins involved in neuronal plasticity.

Genetic and environmental influences on the association between temperament in toddlerhood and personality in adolescence

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We examined the association between two core components of temperament (negative emotionality and behavioral inhibition) in toddlerhood and their associations with personality traits (extraversion, harm avoidance, neuroticism, novelty seeking, and reward dependence) in adolescence in a sample of 401 twin pairs from the Colorado Longitudinal Twin Study. Both parental report and observational measures were used to assess negative emotionality and behavioral inhibition in twins at 14, 20, 24, and 36 months. Parental report measures included the Differential Emotion Scale (DES), the Toddler Temperament Scale and Emotionality, Adaptability, Sociability (EAS) Temperament Survey. Observational measures included independent ratings of the participants’ negative emotionality and behavioral inhibition during a variety of tasks. Personality in adolescence was assessed via the short form of the Eysenck Personality Questionnaire (EPQ) at age 12 and 17 and the Temperament and Character Inventory (TCI) at age 12 and the Tridimensional Personality Questionnaire (TPQ) at age 17. We hypothesized that behavioral inhibition during toddlerhood will be inversely associated with novelty seeking in adolescence, whereas negative emotionality during toddlerhood will be positively associated with neuroticism in adolescence. Significant associations between parent-reported behavioral inhibition and negative emotionality in toddlerhood and harm avoidance at age 12 and 17 were observed. Shared environmental influences contributed to the covariation between negative emotionality and behavioral inhibition in toddlerhood and harm avoidance at age 12, whereas genetic influences contributed to the covariation between negative emotionality and behavioral inhibition in toddlerhood and harm avoidance at age 17.

Genetic predictors of antidepressant side effects

Karen Hodgson; Institute of Psychiatry Oliver Davis; King’s College London Katherine Aitchison; Institute of Psychiatry Rudolf Uher; Institute of Psychiatry Anne Farmer; Institute of Psychiatry Peter McGuinness; Institute of Psychiatry

The unwanted effects associated with antidepressant medications are key determinants of treatment adherence in depression and genetic
Genetic overlap between autistic traits and theory of mind impairments

Rosa Hoekstra; The Open University Francesca Happé; Institute of Psychiatry, King’s College Angelica Ronald; Birkbeck/Institute of Psychiatry

Background: People with autism tend to show impairments in Theory of Mind, reflected in poor performance on tests such as the Reading the Mind in the Eyes Task (RMET). Broader autism phenotype family studies suggest that individual differences in RMET performance may be under familial influence. The aims of the present study were to (i) explore the association between RMET performance and quantitative autistic traits in a community-based twin sample; (ii) to establish the heritability of RMET performance; and (iii) to explore the aetiology of the association between RMET scores and autistic traits.

Methods: A sample of 7,093 12-year-old twin pairs completed an online version of the RMET. Parents rated the autistic-like behaviours of their children using the Childhood Autism Spectrum Test. A measure of the twins’ vocabulary ability was also available. The genetic aetiology of RMET and autistic traits was explored using structural equation modelling.

Results: Autistic traits were negatively related to RMET performance; this association was mainly due to social and communication difficulties; the association between RMET performance and restricted, repetitive behaviours and activities (the non-social traits characteristic for autism) was not significant. The association between social and communicative difficulties and RMET performance remained significant even when vocabulary ability was taken into account. Individual differences in RMET performance were moderately heritable (35 %), whilst social communicative autistic traits were under strong genetic influence (76 %). The association between RMET performance and autistic traits was entirely due to genetic influences.

Conclusions: This study suggests that Theory of Mind ability is partly influenced by genes and that this cognitive process, long hypothesised to relate to social communicative autism symptoms, is indeed linked to these traits at a genetic level. Using the RMET as a quantitative endophenotype for autism may help elucidate the pathways between genes and a clinical autism diagnosis.

Longitudinal analysis of marriage and desistence from antisocial behavior in a sample of young adult twin and sibling pairs

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Research suggests that married individuals tend to be less prone engaging risky behaviors, but the processes underlying this relation remain in question. Recent behavioral genetics cross-sectional research using twin and sibling pairs suggests that this relation is not solely due to between-family selection effects. Other behavior genetic research has explored desistence from antisocial behavior (ASB) as a function of marriage as well. Findings from independent samples suggest that marriage indeed predicts desistence from antisocial behavior above any beyond familial selection effects. While the behavioral genetics literature is in accordance regarding the role of concurrent marital status on ASB and desistence from ASB, none has examined the relation between marriage and the trajectory of ASB. Using Waves I-IV of the National Longitudinal Study of Adolescent Health, we modeled ASB as a linear growth curve and examined the causal nature of deviations in the trajectory of ASB attributable to marital status. Age was controlled for in all analyses. Results suggest that marital status is associated with concurrent deviations in the ASB trajectory (such that married individuals report fewer antisocial behaviors) but not future deviations, and this relation remains while controlling for between-family confounds. These effects were less pronounced for females. Consistent with findings from other studies, it appears that marriage fosters reduction in antisocial behavior (particularly for males), and that this relation cannot be entirely explained by genetic or shared environmental selection factors.

Understanding links among remembered parental bonding, friendship satisfaction, and depressive symptoms

Briana Horwitz; The Pennsylvania State University Chandra Reynolds; University of California Riverside Susan Charles; University of California, Irvine Jena Neiderhiser; The Pennsylvania State University

The degree of parental warmth received during childhood and satisfaction with interpersonal relationships during adulthood is associated with adults’ depressive symptoms. Environmental explanations are often used to explain these links such that the quality of early parent–child bonds form the basis of a cognitive working model that gives rise to adult’s interpersonal relationship satisfaction and their depressive symptomatology, in turn. An alternative explanation is that individuals’ own inheritable characteristics play a role in shaping the quality of parenting they receive during childhood, interpersonal relationship satisfaction in adulthood, and depressive symptoms. The current study examined whether genetic and environmental factors associated with adults’ remembered parental warmth during childhood and current friendship satisfaction explain individual differences in depressive symptoms.

Participants consisted of monzygotic (N = 216) and same- and opposite-sex dizygotic (DZ) twin pairs (N = 585) from the MacArthur Foundation Survey of Midlife Development in the United States (MIDUS). The sample ranged in age from 25 to 74 years old (M = 45 + 12.05), and 55 % of the sample was female. Adults’ who reported receiving less warmth from parents during childhood and who were less satisfied with their current friendships had greater depressive symptomatology. Parameter estimates could be constrained to be equal.
across males and females in the multivariate case. Findings from the most parsimonious Cholesky model revealed that the association between remembered parental bonding, friendship satisfaction, and depressive symptoms was accounted for by a common genetic factor. This factor explained 19% of the genetic variance in depressive symptoms. An additional genetic factor common to friendship satisfaction and depressive symptoms explained the majority of the genetic variance (81%) in depressive symptoms. Results suggest that remembered parental warmth received during childhood and especially adults’ current friendship satisfaction are integral for understanding heritable influences on depressive symptoms.

**Familial risk and cognitive impairment in major depression: A monozygotic twin-pair study**

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Neuropsychological deficits associated with episodes of major depression (MD) remain even after symptom remission and also occur in non-depressed family members. These findings imply such deficits are associated with familial risk for MD rather than a consequence of experiencing MD. We studied performance on measures of attention, working memory, general cognitive functioning, verbal learning, and visuospatial construction among 158 MZ twins from the Virginia Adult Twin Study of Psychiatric and Substance Use Disorders (Kendler & Prescott 2006). We hypothesized attention and working memory would be related to familial risk for MD and consequently would be impaired in twin pairs concordant or discordant for lifetime history of MD compared to never-depressed pairs. In contrast, we expected no differences among groups on general cognitive ability, verbal learning, or visuospatial processing. Data were analyzed by regressing the neuropsychological outcomes on personal MD history, indices of MD episode severity, and co-twin MD history using structural models that constrained the regression weights to be equivalent across members of the twin pair. Covariates included age, gender, current mood symptoms, and parental MD history. The results were partially supportive of our hypotheses. Pairs for whom one or both twins had experienced MD had lower scores on attention, working memory, and visuospatial processing compared to twin pairs with no history of MD. There was no effect of MD history associated with general cognitive functioning or verbal learning. These findings support the theory that deficits in attention are tied to familiarly transmitted liability and may be markers of risk for the development of major depression.

**Some results on the genetic architecture of human intelligence**

Stephen Hsu; University of Oregon

Quantitative traits such as height and intelligence are controlled by many loci, each of small effect. While this makes discovery of individual loci difficult, there is a complementary property: the average genetic distance between pairs of individuals will increase significantly and detectably as phenotype difference increases. This phenomenon can be explored using novel “global” statistical techniques. Analysis of data from the ALSPAC birth cohort reveals that genetic distance increases by approximately 35 SNPs per standard deviation of difference in g; a “genius” (someone of exceptional cognitive ability) dimers from an ordinary person by roughly 100 (perhaps 200 at most) polymorphisms which affect intelligence. This leads to a crude estimate of ten thousand causal loci affecting intelligence. We also find that genetic entropy increases with below average phenotype: there are more genotypes corresponding to below average g than to above average g. Equivalently, there are more common variants (MAF < 0.5) with slightly negative effect on g than with positive effect. The typical MAF for g-associated SNPs is roughly 0.1. Similar results are found for height.

**Change in heritability of substance use behavior through development: Exploring the longitudinal role of shared environment**

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Robin Corley; University of Colorado
Boulder Sally Wadsworth; University of Colorado Michael Stallings; University of Colorado

While it is clear both genetic and environmental factors influence substance use, few studies have described how the heritability of substance use liability changes throughout development. As social and peer environment radically change during the transition from early adolescence into adulthood, we might expect the magnitude of environmental influence to peak at particular time points. While many cross-sectional studies have shown moderate to substantial influences of shared environment on substance use in adolescence (Walden et al. 2004; Buchanan et al. 2009), longitudinal analyses of adoptive pairs may be particularly useful in describing and explaining key periods of environmental influence. One strength of the adoptive design is that sibling resemblance is a direct estimate of shared environment, whereas the resemblance of biological sibling pairs can be due to both shared environment and genetic influences. In the current study, we draw upon the Colorado Adoption Project, a longitudinal study following adoptive children, matched controls, and their families in order to examine the change in genetic and environmental influences on cigarette, alcohol, and marijuana use from adolescence into adulthood. We tested sibling similarity among 34–76 adoptive sibling pairs (varies by assessment age) and 49–97 biological sibling pairs on substance use behaviors. Measures included both substance use initiation and substance use frequency. Preliminary results show evidence for genetic influences on tobacco and marijuana initiation to be substantial during early adolescence (14–16) and adulthood (after 21), and a period of increased shared environmental effects around age 16 through 18. For alcohol use, genetic effects tended to emerge earlier with shared environmental effects increasing in early adulthood, where most subjects were users of alcohol. We plan to investigate time-specific environmental variables (e.g. family cohesion, parental monitoring, peer influences) to determine which factors contribute to sibling resemblance for substance use from adolescence into adulthood.

**Comparing the effects of three measures of marital conflict on the etiology of conduct problems**

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Kelly Klump; Michigan State University S. Alexandra Burt; Michigan State University

Marital conflict has been found to be consistently associated with negative child outcomes, including child conduct problems. Moreover, there is some evidence to suggest that the relationship between marital conflict and child conduct problems is primarily
environmental in origin. The current study sought to extend these findings to a gene–environment interaction (G × E) framework, evaluating genetic and environmental influences on conduct problems at various levels of three separate measures of marital conflict. A sample of 418 twin pairs from the Michigan State University Twin Registry, ranging in age from 6 to 10 years of age, will be examined. Conduct problems in the twins will be measured using an average of reports from both mothers and fathers on the Child Behavior Checklist and reports from the Semi-Structured Clinical Interview for Children and Adolescents, a child self-report instrument based on an interview conducted by masters-level clinicians. Marital conflict will be examined using three different measures: an average of both parents’ self-reports of marital conflict on the Dyadic Adjustment Scale, dyadic conflict assessed via observational methods using the Brief Romantic Relationship Coding Scheme, and the Conflict Frequency scale from the Children’s Perception of Interparental Conflict Measure. The use of multiple informant reports for both the assessment of marital conflict and child conduct problems is a key strength of the current study, as existing research often relies on parent report alone. Results will reveal whether genetic, shared environmental, and nonshared environmental influences of conduct problems vary across levels of marital conflict and across different measures of marital conflict. Implications of our results will also be discussed.

Examining the reciprocal relationship between maternal negativity and child negative emotionality during adolescence

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Previous research indicates consistent links between children’s difficult temperament characteristics and parenting behaviors. However, it is likely that this effect is dynamic and mutual. The current study utilized a cross-lagged, biometric design to assess and understand the reciprocal relationship between negative emotionality and maternal negativity across adolescence. These issues were examined within the Nonshared Environment in Adolescent Development project, a nationwide study that included sibling pairs who varied in regard to genetic relatedness, and resided together in nondivorced or stepfamilies. This study focused on a subset of NEAD families (N = 395) who were assessed two times, 3 years apart. This sample included five types of sibling pairs: MZ twins (NMZ = 63), DZ twins (NDZ = 75), Full Siblings (NFS = 153), Half Siblings (NHS = 60), and Unrelated Siblings (NUS = 44). The average ages of the children were 13.5 (sibling 1) and 12.1 years (sibling 2) at Time 1. Mothers’ and fathers’ ratings were combined to form a composite measure of Child Negative Emotionality. A composite measure of Mother Negativity was also created and included self- and child-reports, and observational ratings.

Child Negative Emotionality and Maternal Negativity were moderately stable, and correlated within each age and over time. At Time 1 and 2 the associations were primarily explained by genetic factors. The cross-lagged paths from Maternal Negativity to Child Negative Emotionality and vice versa were significant (β’s = 0.08). The results support a bidirectional model: Maternal Negativity and Child Negative Emotionality at Time 1 predicted modest changes in each other over time. 67% of the cross-lagged effect of Child Negative Emotionality (Time 1) on Maternal Negativity at Time 2 and 62% of the cross-lagged effect of Maternal Negativity (Time 1) and Child Negative Emotionality at Time 2 were accounted for by child-based genetic factors. Results are consistent with the child effects model.

Developmental changes in moderating effects of parental education on individual differences in vocabulary IQ from adolescence to young adulthood

Kristen Jacobson; The University of Chicago Terrie Vasilopoulos; University of Chicago

Prior research in several samples of children and adolescents has found moderating effects of parental socioeconomic status (SES) on genetic and environmental influences on measures of youth cognition. As parental SES increases, genetic variance of cognition increases, and shared environmental variance decreases, resulting in higher heritabilities among youth raised in more economically privileged families. However, studies examining moderating effects of parental SES on heritabilities of cognition in adult samples often fail to find significant moderating effects on genetic variance in cognition, although decreasing environmental variance results in similar patterns of increased heritability with higher levels of parental SES. This pattern of results suggests that genetic variance of cognition may be less amenable to moderating effects of childhood SES after a certain developmental period, although this hypothesis has not been tested directly in longitudinal studies. Using data from 2,747 twins and siblings (including N = 1,246 complete pairs) from the National Longitudinal Study on Adolescent Health who have valid data on vocabulary IQ at both Wave 1 (average age = 15.9, range = 11–20) and Wave 3 (average age = 21.8, range = 18–26), we tested moderating effects of parental education levels using a bivariate model of covariance between Wave 1 and Wave 3 vocabulary IQ. Significant moderating effects of parental education were found for genetic, shared environmental, and nonshared environmental variance at Wave 1, while only the moderating effects on shared and nonshared environmental variance at Wave 3 were significant. Heritabilities of vocabulary IQ increased from 0.22 (−2 SD) to 0.70 (+2 SD) at Wave 1, while increases in heritability of vocabulary IQ were less marked at Wave 3 (0.42–0.65). These results confirm that while parental education has a lasting effect on environmental variation in verbal IQ from adolescence to early adulthood, genetic variance of verbal IQ is not affected by childhood socioeconomic status in early adulthood.

Does regular exercise help to maintain low BMI? How?

Wendy Johnson; University of Edinburgh Kirsten Kyvik; University of Southern Denmark Thorkild Sorensen; Institute of Preventive Medicine

Epidemiological studies consistently report moderate benefits from regular exercise in maintaining healthy body weight and reducing excess weight. Body weight, however, is substantially heritable, as is the tendency to exercise. This raises the possibility that exercise does not exert strictly causal effects on body weight, but instead that common genetic and/or environmental factors influence levels of both physical activity and body weight. Moreover, some evidence indicates that genetic variance in body weight may be lower in those who are physically more active (Silventoinen et al. 2009). We explored this question further in the GEMINAKAR sample, a subset of the Danish Twin Registry consisting of 625 adult twin pairs that have provided extensive data on exercise and fitness habits and body mass index (BMI). Genetic variance and nonshared environmental variance both decreased by a
factor of 2 across a 4-standard deviation range of physical activity, while shared environmental variance was very low and constant. Genetic correlations were more strongly positive when physical activity was high. In contrast, shared environmental correlations were more strongly negative when physical activity was high. We interpreted these results to indicate that people show different genetic and environmental responses to lack of physical activity. The environmental influences for activity appeared to act to reduce BM, but genetic influences tended to act to increase it. There was no association between BMI and level of physical activity in this sample, and overall levels of obesity were relatively low compared to those in many populations.

Genetic and environmental influences on rumination and depression

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Rumination is a pattern of cognition that involves repetitively and passively focusing on symptoms of distress and on the possible causes and consequences of these symptoms. Evidence suggests that rumination increases risk for depression by enhancing the effects of depressed mood on thinking, impairing effective problem solving, interfering with instrumental behavior, and eroding social support. Although some studies have sought to identify specific biological mechanisms behind rumination through examining the association between rumination and candidate genes, no studies to date have examined the magnitude of genetic and environmental influences on this construct, nor the potential for common genetic and environmental influences underlying rumination and depression. The current study sought to address these deficits in the literature by examining the etiology of rumination and depression and estimating the magnitude of shared and specific etiological influences.

Two hundred sixty-four twin pairs from Colorado’s Longitudinal Twin Study were assessed in early adulthood (age 21–26) with three measures of rumination and measures of depressive symptoms and diagnosis. Results from biometrical modeling indicated modest to moderate heritability of rumination (h2 = 17–30 %) and depression (h2 = 28–50 %) and a genetic correlation between these constructs of nearly 1, suggesting that most of the genetic factors influencing rumination and depression are common to both phenotypes. Results also indicated a substantial influence of the nonshared environment on rumination (e2 = 37–76 %) and depression (e2 = 42–63 %), as well as a modest influence of shared environmental factors on each phenotype (c2 = 0–14 %). This study represents the first to examine the genetic structure of rumination and will provide valuable contributions to etiological models of depression.

Does the lowering of heritability coefficients of attention problems and inattention in adolescence reflect genetic or environmental changes?

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Heritability estimates of ADHD, ADHD symptoms (e.g., inattention, IA), and related traits (e.g., Attention Problems, AP) are high in childhood but thereafter. We investigated whether this is due to genetic or environmental changes or to methodological effects.

Subjects comprised mono- and dizygotic twin pairs (n > 10,000) from the Netherlands Twin Register.

AP was assessed at ages 7, 10, 12, 14, and 16, using the AP scale from the Achenbach System of Empirically Based Assessment. At age 7, 10, AP was rated by mothers, fathers, and teachers; at age 12 by mothers, fathers, teachers, and the twins themselves; at ages 14, and 16 by the twins themselves. IA was assessed at ages 7, 10, and 12, using parent, teacher, and self-ratings on the Conner’s IA Scale.

Behavior genetic modeling showed that the amount of genetic variance in IA and AP was constant over measurement occasions, whereas the amount of environmental variance in AP increased with the switch from a same rater (e.g., mother, father) to different raters (twins themselves). As a result heritability coefficients of IA and AP rated by others were higher than those of self-rated AP, except when IA and AP were rated by different teachers rather than the same teacher and heritability coefficients of IA and AP at age 7 and 10 were higher than those of AP at age 14 and 16.

Because at age 12 the heritability coefficient of AP as rated by twins themselves was lower than heritability coefficients of AP as rated by parents and the same teacher, and were comparable to heritability coefficients of AP rated by different teachers, we conclude that the relatively low estimated heritability of ADHD, ADHD symptoms, and related traits after childhood is— at least partially—due to the use of ratings by different raters rather than the same rater.

Genetic and environmental links between personality traits and political attitudes

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This study examined genetic and environmental sources of variance in two core political attitudes: acceptance of inequality and resistance to change. Based on an extended twin family design including twins’ parents and spouses, genetic and environmental transmissions as well as different sources of spouse correlations were taken into account. Furthermore, I examined the proportion of genetic and environmental variance in political attitudes that could be accounted for by genetic and environmental variance in Big Five personality traits using self- and other reports. Analyses revealed that variance in political attitudes showed multiple environmental (e.g., generation-specific social homogamy, spouse- and twin-specific effects) and genetic sources (e.g., additive effects and epistatic interaction, genotypic assortative mating). A substantial proportion of genetic variance could be accounted for by genetic variance in personality traits. Acceptance of inequality showed negative links to openness and agreeableness. Resistance to change was positively related to extraversion and conscientiousness and negatively related to openness. These links were primarily mediated by genetic effects. The results provide support for multiple sources of variance in political attitudes and for the position that Big Five personality traits and political attitudes are systematically related due to common genetic factors.

Education, height and reproduction: The role of genetic and environmental factors

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Background: Sexual selection is the key force shaping evolution together with natural selection. It is speculated whether sexual
selection is present also humans. The strongest candidates for traits affected by sexual selection in humans are height and education reflecting material and social resources in childhood. We analyzed how height and education are associated with reproductive success and how genetic and environmental factors affect these associations using a twin study design.

Data and methods: Education, height and zygosity were assessed using postal questionnaires in 1972 and 1981 in 1,076 monozygotic and 2,445 same-sex dizygotic complete twin pairs born 1950–1957 in Finland (response rates 89 and 84 %). Information on live births as of June 2009 was extracted from the national population register. The associations between reproductive success measured as completed number of children and age at first birth with height and education were analyzed using Cholesky decomposition. The analyses were carried out by the Mx statistical software.

Results: Men with average stature and highest education had the best reproductive success. In females height was not associated with number of children but short women had somewhat earlier age at first birth. Women with low education had more children when compared to better educated women. The association between education and having any children was explained by genetic factors in men (rA = 0.28) and women (rA = 0.44) and genetic factors also explained the association between height and age at first birth in women (rA = 0.18).

Conclusions: Average rather than tall stature is associated with better reproductive success in males. The association between height, education and reproduction are explained by genetic factors. This suggests that other factors, such as personality or hormonal factors showing high heritability, lie behind of these phenotypic associations rather than causal effects of height and education on reproductive success such as speculated previously.

Genome-wide complex traits analysis and extensions: Important tools for behavioral genetics

Matthew Keller; University of Colorado at Boulder

Genome-wide complex traits analysis (GCTA) uses genome-wide single nucleotide polymorphisms (SNPs) to estimate pairwise relationships between all individuals in a sample, and uses a random-effects model to estimate the additive genetic variation attributable to all SNPs. Here, I describe two extensions to this approach. The first uses genome-wide SNP data to estimate the degree to which SNPs that predict schizophrenia in individuals of European descent also predict schizophrenia in individuals of African descent (de Candia et al. 2012). The second uses shared haplotypes of different sizes to estimate the pairwise relationships, which allows insight into the allelic spectrum of causal variants (Keller et al. 2012). Both approaches provide information that could never be discerned using traditional, family approaches to estimating heritability. I argue that the GCTA method and extensions of it provide exciting new methodological avenues to researchers interested in understanding the genetic basis of behavioral phenotypes.

Genetic and familial–environmental influences on risk for drug abuse: A national Swedish adoption study

Kenneth Kendler; VCU-VIPBG Kristina Sundquist; Lund University Hermine Maes; Virginia Commonwealth University Jan Sundquist; Lund University

Context: Prior research suggests that drug abuse (DA) is strongly influenced by both genetic and familial-environmental factors. No large-scale adoption study has previously attempted to verify and integrate these findings.

Objective: To determine how genetic and environmental factors contribute to risk for DA.

Design: Follow-up in 9 public data bases (1961–2009) of adoptees and their biological and adoptive relatives.

Setting: Sweden.

Participants: 18,115 adoptees born 1950–1993; 78,079 biological parents and siblings; 51,208 adoptive parents and siblings.

Intervention(s): None.

Main Outcome Measure(s): DA recorded in medical, legal or pharmacy registry records.

Results: Risk for DA was significantly elevated in adopted away offspring of biological parents with DA (OR = 2.09, 95 % CI 1.66–2.62), in biological full and half-siblings of adoptees with DA (OR = 1.84, 1.28–2.64 and OR = 1.41, 1.19–1.67, respectively) and in adoptive siblings of adoptees with DA (OR = 1.95, 1.43–2.65). A genetic risk index (including biological parental or sibling history of DA, criminal activity and psychiatric or alcohol problems) and an environmental risk index (including adoptive parental history of divorce, death, criminal activity, alcohol problems; and an adoptive sibling history of DA, psychiatric or alcohol problems) both strongly predicted risk for DA. Including both indices along with sex and age at adoption in a predictive model revealed a significant positive interaction between the genetic and environmental risk indices.

Conclusions: DA is an etiologically complex syndrome strongly influenced by a diverse set of genetic risk factors reflecting a specific liability to DA and a vulnerability to other externalizing disorders and by a range of environmental factors reflecting marital instability, and psychopathology and criminal behavior in the adoptive home. Adverse environmental effects on DA are more pathogenic in individuals with high levels of genetic risk. These results should be interpreted in the context of limitations of the diagnosis of DA from registries.

Copy-number variants and general cognitive ability

Robert Kirkpatrick; University of Minnesota Matthew McGue; University of Minnesota William Iacono; University of Minnesota Michael Miller; University of Minnesota Saonli Basu; University of Minnesota Nathan Pankratz; University of Minnesota

The genetic markers typically used in GWAS are common SNPs. The contribution of rare or non-SNP markers to the heritable variance of quantitative traits has received far less research attention. We present and discuss the results of analyses which predict general cognitive ability from copy-number variants (CNVs), using a sample of N = 6,202 Caucasian participants from 2,197 families. This sample combines participants from two longitudinal studies, a twin-family study and an adoption-family study. We operationalize cognitive ability as Full-Scale IQ on the WAIS-R or WISC-R, as appropriate for participant age. We identify and call CNVs from genome-wide SNP probe-intensity data from the Illumina 660 W Quad array. Guided by an initial, small-sample study by Yeo et al. (2011, PLoS ONE 6(1): e16339), we aggregate CNV calls into four mutational burden scores. Contrary to hypothesis, data analysis indicates that both count and length (in kilobases) of copy-number deletions are positively associated with IQ at nominal significance level. However, neither association survives correction for multiple testing, and we conclude that these data provide no clear evidence of association between mutational burden and IQ. We discuss possible future analyses that narrow the utilized CNV set, for example, to CNVs in/near genes or to de novo mutations.
Exploring the intergenerational transmission of parenting behavior: A meta-analysis of the etiology of parenting

Ashlea Klahr; Michigan State University S. Alexandra Burt; Michigan State University

Extant research has strongly indicated that parenting behaviors are transmitted across generations (Conger, Belsky, & Capaldi 2009), such that adults often parent in much the same way that they were parented as children. Some have suggested that this intergenerational transmission may be directly mediated via observational learning processes or indirectly mediated via child development outcomes which impact subsequent parenting. An alternative possibility is that parenting behavior is genetically transmitted from one generation to the next. Indeed, a sizeable body of literature has identified genetic influences on parenting. However, heritability estimates vary widely across study and parenting phenotype. In addition, researchers have employed two primary study designs for examining the etiology of parenting; child-based and parent-based designs. The conclusions which can be drawn from these two study types are distinct and yet this distinction is not consistently explicated within the existing literature. The goal of the current meta-analysis was to quantitatively synthesize the existing research examining the etiology of parenting at the level of the child and the parent and to identify potential moderators of this etiology. We examined the etiology of parental warmth, control, and negativity at both the level of the child and the parent using existing twin and adoption studies of parenting ($n = 30$). Our results revealed significant effects of both child-driven genetic influences (i.e., non-passive gene-environment correlation) and parental genetic makeup on parental behavior. However, our findings also highlighted the importance of shared and non-shared environmental contributions to parenting. In addition, etiological contributions to parenting were found to differ across mothers and fathers and across child age. Theoretical implications of these findings for the intergenerational transmission of parenting will be discussed.

Epigenetics of maternal cigarette smoking during pregnancy and child neurobehavioral outcomes

Valerie Knopik; Division of Behavior Genetics, RI Hospital/Brown University Matthew Maccani; Rhode Island Hospital; Brown University John McGearly; Providence VAMC/Brown University

The period of in utero development is one of the most critical windows during which adverse in utero exposures may both influence the growth and development of the fetus but also its future postnatal health and behavior. Maternal cigarette smoking during pregnancy remains a relatively common but nonetheless hazardous in utero exposure, and previous studies have associated it with reduced birth weight, poor developmental outcomes, and increased risk for diseases and behavioral disorders later in life. Current research suggests that many of the mechanisms whereby maternal smoke exposure may dysregulate key pathways crucial for proper fetal growth and development may include epigenetic modes of regulation. Maternal cigarette smoking during pregnancy has been associated with aberrant DNA methylation and dysregulated expression of microRNA, but a deeper understanding of the epigenetics of maternal cigarette smoking during pregnancy as well as how these epigenetic changes may affect later offspring health and behavior remains to be elucidated. This presentation seeks to explore many of the previously described epigenetic alterations associated with maternal cigarette smoking during pregnancy, assesses how such alterations may have consequences for both fetal growth and development as well as postnatal health, behavior and well-being, and recommends future directions for this new and exciting field of research.

The influence of personality disorders on longitudinal stability of anxiety

Gun Peggy Knudsen; Norwegian Institute of Public Health Kristian Tambs; Norwegian Institute of Public Health Jack Hettema; Virginia Institute for Psychiatric and Behavioral Genetics Ragnhild Ørstavik; Norwegian Institute of Public Health Espen Roysamb; University of Oslo Nikolai Craikowski Kenneth Kendler; VCU-VIPBG Ted Reichborn-Kjennerud; Norwegian Institute of Public Health

Background: Anxiety disorders tend to develop in adolescence and usually persist through adult life with episodes of remission and relapse. Twin studies have shown that both genetic and environmental etiological factors have significant impact at several distinct time points. Generally, long term stability is mainly influenced by genetic factors, while change usually is related to environmental factors. Comorbidity between anxiety disorders and personality disorders (PD) is common and presence of PDs predicts increased severity, functional disability, and poorer treatment outcomes. Little is known about how PDs influence the stability of anxiety disorder.

Aim: The present study aims to examine the longitudinal association between PDs and anxiety disorders.

Method: Anxiety disorders and PDs were measured at two time points, mean inter wave interval 10 years, in a young Norwegian twin population. In 1999–2004, 2,800 twins underwent psychiatric interviews assessing all axis I and axis II disorders. In 2010–2011, 2,284 twins participated in a follow-up study of the major axis I disorders and six PDs. Mean age of the twin population was 28.2 and 38.4 years at the two time points. Initially, the incidence of new anxiety disorders as a function of individual PD criteria count at baseline will be examined. Secondly, multivariate models will be fitted in Open Mx with PD criteria count and anxiety disorder at each time point. This will provide estimates of how genetic risk factors indexed by PDs impact on the stability of anxiety disorder over a 10 year period in early adulthood.

Preliminary descriptives: The lifetime prevalence of any anxiety disorders (GAD, panic disorder, social phobia, specific phobia and agoraphobia) was 21.2% at the second time point (tetrachoric correlation 0.66 for any anxiety at the two time points). At this time, there were 307 twins with a new anxiety disorder.

Mapping the genetic association between general cognitive ability and cortical surface area

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The genetics of cortical regionalization may not map one-to-one onto traditional cortical regions that have been based on structure or
function, rather than genetics. Advances in understanding the genetics of brain-cognition associations may thus come from efforts to map the cortex without constraints based on pre-defined boundaries. The most prominent model of the cortical regions associated with general cognitive ability (GCA)—the parietal-frontal integration theory (P-FIT)—is based on a mix of neuroimaging studies of cortical volume, a smaller number examining cortical thickness, and other functional imaging studies. Few studies have examined genetic associations between cortical phenotypes and GCA, and virtually no attention has been paid to the different genetic influences of different cortical phenotypes as they relate to GCA. For example, cortical thickness and surface area—which we have shown to be genetically independent—may have different associations with GCA. Here we present the first examination of the association of cortical surface area to GCA. Participants were 514 middle-aged male twins (ages 51–59) in the Vietnam Era Twin Study of Aging (VETSA). In part, because area size has functional relevance, we expected cortical surface area to be more strongly related to GCA than cortical thickness. We compared continuous (vertex-wise) genetic correlation maps of a well-validated GCA measure with both surface area and thickness. As expected, GCA was more widely associated with surface area than thickness. Significant genetic correlations with surface area were mostly in frontal and temporal-parietal regions, particularly anterior frontal and anterior temporal. There was a dissociation with thickness, which was mostly associated with pre- and post-central regions. Interestingly, the map of surface area—but not thickness—associations was generally consistent with the P-FIT model. This finding suggests that previous studies, such as those examining volume, may have been primarily tapping the surface area component of volume.

### Pubertal timing and peer influence on delinquency: A social network approach

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**Background:** Individuals who experience puberty relatively early are at risk for a range of poor developmental outcomes, including delinquency and substance abuse (Mendle, Turkheimer, & Emery 2010). In addition to direct effects of puberty on risky behavior, early pubertal timing may confer risk by increasing vulnerability to peer influence. This possibility is consistent with evidence that the social reorientation of adolescence is driven in part by the cascade of hormonal events that occur with pubertal onset (Forbes & Dahl 2010; Nelson et al. 2005).

**Methods:** We used structural equation modeling to determine whether pubertal timing moderated genetic and environmental influences on individual delinquency and on exposure to delinquent peers. Data were drawn from a nationally representative sample of 390 same-sex adolescent twins (“targets”) and their close friends, identified by peer nominations. Delinquency, including substance use and criminal activity, was assessed using self-report. Exposure to delinquent peers was defined as the mean level of delinquent behavior that was reported by individuals in the target’s peer group. Pubertal timing was defined as the deviation of an individual’s self-reported development from the mean level of development reported by same-age peers.

**Results:** Pubertal timing moderated environmental influences on individual risk-taking: shared environmental influences were most important for early maturing adolescents. Pubertal timing also moderated environmental influences on affiliation with delinquent peers—in this case, the nonshared environment was most important for early maturing adolescents. A gene–environment correlation was found, with the same genes influencing substance use and exposure to delinquent peers; this relationship was not moderated by pubertal timing.

**Conclusions:** These results suggest that early pubertal timing increases vulnerability to environmental influences on delinquent behavior and exposure to delinquent peers. Furthermore, our findings are consistent with previous research identifying gene environment correlation in peer effects on adolescent risk-taking behavior (Harden et al. 2008).

### Is smoking during pregnancy dangerous for the offspring? Estimating gene–environment correlation in a children of siblings design using a National Swedish Cohort

Ralf Kuja-Halkola; Karolinska Institutet Brian D’Onofrio; Indiana University Niklas Långström; Karolinska Institutet Henrik Larsson; Karolinska Institutet Paul Lichtenstein; Karolinska Institutet

Maternal smoking during pregnancy (SDP) has been associated with adverse outcomes in offspring, such as poor academic achievement (AA), higher rate of violent criminal convictions (VC), and born small for gestational age (SGA). Studies have suggested that associations between SDP and outcomes later in offspring’s life (e.g. AA and VC) are due to familial confounding, and thus not causal, while associations with pregnancy related outcomes (e.g. SGA) seem to be at least partly causal.

We performed within-siblings analyses to assess possible familial confounding between the exposure (SDP) and the three outcomes AA, VC and SGA. Next, we performed bivariate analyses between SDP and each of the three outcomes using structural equation models. Because the exposure is caused by mothers and the outcome is measured in offspring we need information on relatedness in three generations, therefore a children-of-sibling design was used. We partitioned the variance into genetic, shared and unique environmental components and estimate the genetic and environmental correlations; hence we assess whether possible familial confounding is due to genetics (i.e., passive gene–environment correlation) and/or shared environments. We treated SDP and SGA as binary variables, VC as a time-to-event variable, and AA as a continuous variable.

We used a linkage of several national Swedish registries to obtain information on the exposure, outcomes and covariates. In Swedish antenatal care SDP has been registered since 1983, and the linkage includes data until 2009. SGA exist for all births in Sweden (N = 2,027,617). AA is measured as grades from secondary school (children aged about fifteen) since 1999 (N = 906,785). Official records on criminal convictions are used for VC (N = 1,001,675).

### The separation of ADHD inattention and hyperactivity-impulsivity symptoms: Pathways from genetic effects to cognitive impairments and symptoms

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Both shared and unique genetic risk factors underlie the two symptom domains of attention deficit hyperactivity disorder (ADHD):
inattention and hyperactivity-impulsivity. The developmental course and relationship to co-occurring disorders differs across the two symptom domains, highlighting the importance of their partially distinct etiologies. Familial cognitive impairment factors have been identified in ADHD, but whether they show specificity in relation to the two ADHD symptom domains remains poorly understood. A better understanding of the underlying risk pathways is required for the development of targeted interventions.

We aimed to determine, using a multivariate genetic model fitting approach, whether different cognitive impairments are genetically linked to the ADHD symptom domains of inattention versus hyperactivity-impulsivity. A population twin sample of 1,314 children, ages 7–10, was individually assessed on a 4-choice reaction time task and a go/no-go inhibition task.

Reaction time variability (RTV) showed substantial genetic overlap with inattention, as observed in a genetic correlation of 0.68, compared to a genetic correlation of 0.34 with hyperactivity-impulsivity. Commission errors (CE) showed low genetic correlations with both hyperactivity-impulsivity and inattention (genetic correlations of 0.18 and 0.10, respectively). The genetic correlation between RTV and CE was also low and non-significant at −0.13, consistent with the etiological separation between the two indices of cognitive impairments.

Two key cognitive impairments phenotypically associated with ADHD symptoms, captured by reaction time variability (RTV) and commission errors (CE), showed different genetic relationships to the two ADHD symptom domains. Overall, the findings extend a previous model of two familial cognitive impairment factors in combined subtype ADHD by separating pathways underlying inattention and hyperactivity-impulsivity symptoms.

**Short and long-term effects of nonparental child care on internalizing and externalizing problems: A behavior genetic study in Dutch twins**

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**Objective:** To explore the effect of formal child care on (1) mean problem behavior scores and (2) the relative importance of additive genetic factors in childhood problem behavior.

**Method:** Mothers of respectively 11,849, 8,901 and 5,627 Dutch twins aged 3, 5 and 7 years reported on internalizing/anxiety and externalizing/aggressive behavior of their children. Cross-sectional genetic analyses were performed with the effects of child care, birth cohort, socio-economic status and sex modeled on the means and on the additive genetic, common environmental and unique environmental variance components.

**Results:** Mean problem behavior was higher for children that went to formal child care; the effect was most pronounced for externalizing/aggressive behavior of boys from low SES families. However, in general effect sizes were small. Child care moderated the relative importance of genetic factors for anxiety at age 5 with higher estimates for the formal–child-care than for the home-care group. In addition, the relative importance of genetic factors was lower for children born after 2000 than those born before.

**Conclusions:** Formal child care poses no environmental trigger for genetic factors to become relatively more important, except for anxiety at age 5. This suggests that anxiety, for which normally the family environment plays an important role, its expression is more genetically driven when children receive formal child care. Effects of child care on mean problem behavior were small. It is argued that other aspects that differ between families of formal-child-care and home-care children could possibly—partly—account for the differences.

**Family income in early childhood as a causal risk factor for offspring attention-deficit/hyperactivity disorder**

Henrik Larsson; Karolinska Institutet Amir Sariaslan; Karolinska Institutet Niklas Längström; Karolinska Institutet Brian D’Onofrio; Indiana University Paul Lichtenstein; Karolinska Institutet

**Objectives:** Studies have found negative associations between socioeconomic indices and Attention-Deficit/Hyperactivity Disorder (ADHD), but the causal nature of this association is unclear. We aimed to determine the extent to which the association between family income in early childhood and ADHD depends on confounded familial background factors by using relevant covariates and a quasi-experimental design.

**Methods:** This study used a birth cohort of all offspring born in Sweden between 1997 and 2003 (N = 629,059). Diagnosis of ADHD was assessed via the Swedish National Patient Register and the Swedish Prescribed Drug Register. Annual family income during the offspring’s first five years in life was collected prospectively via a Swedish Integrated Database for Labour Market Research (LISA). The analyses prospectively predicted ADHD diagnosis while controlling for statistical covariates and comparing differentially exposed siblings to minimize confounding.

**Results:** Low family income during the offspring’s first five years was associated with an increased rate of ADHD. This estimate was attenuated when measured family-wide and offspring-specific confounders were included in the model, but was still associated with an increased rate of ADHD. The within-family estimates (i.e., adjusted for unmeasured selection factors) were also significant even after adding offspring-specific confounders and offspring-specific mediators (Incident rate ratio with 95 % confidence intervals: 1.10 [1.02; 1.20]).

**Conclusions:** The results show that reduced family income in early childhood was associated with increased risk for ADHD. The association remained even after controlling for genetic and environmental selection factors, which highlight family income in early childhood as a potential causal risk factor to ADHD.

**The mechanistic role of callous-unemotionality in the association between CHRM2 and trajectories of externalizing behaviors**

Shawn Latendresse; Virginia Institute for Psychiatric and Behavioral Genetics

Recent findings have shown that CHRM2, a gene previously linked with liability for a range of externalizing disorders and affiliated personality dimensions, is also associated with discrete patterns of externalizing problems spanning adolescence (Latendresse et al. 2011). In addition, a growing body of evidence suggests that there is a significant degree of phenotypic covariation between externalizing psychopathology and callous-unemotionality (Blair et al. 2006; Frick & Viding 2009), one of the hallmarks of psychopathic personality. Personality theorists have historically posited that attributes such as this are dispositional in nature, generally reflecting some underlying genetic architecture. In this way, personality has been considered a
proxy for one’s genes, such that any association between personality and behavior is indirectly the result of these biological underpinnings. Michel (1968), however, suggested that personality is less “trait” and more “state”, in that it is largely contingent on the surrounding context. Mechanistically, these two theoretical perspectives can be tested via mediation and moderation models, respectively. Thus, in the present study, we use data from a subset of 452 participants from the Child Development Project, an on-going epidemiological study of individuals followed annually from kindergarten through age 25, to test whether pre-adolescent measures of callous-unemotionality mediate and/or moderate the influence of CHRM2 on trajectories of self-reported externalizing behavior across adolescence. Results of our analyses both rule out mediation and implicate moderation as the mechanism by which this specific gene exerts an influence over the developmental course of externalizing problems. Implications of these findings are discussed, as are potential limitations and areas for future inquiry.

Are childhood verbal and motor development associated with cognitive performance in young adulthood: A co-twin control analysis among twins discordant for their development as reported by parents

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Cognitive abilities are stable across the lifespan, but it is uncertain whether variation in early verbal and motor development predicts cognitive outcomes in adulthood. We used parental report and neuropsychological test data from two longitudinal population-based birth cohort studies of Finnish twins to explore these associations. In FinnTwin16 and FinnTwin12, a family questionnaire was filled in by the parents when the twins were 16 and 11–12 years, respectively. Parents reported retrospectively on differences between co-twins in verbal and motor developmental outcomes in childhood. Cognitive functioning was assessed with neuropsychological tests of verbal and spatial ability, processing speed, attention, working memory, executive functioning and learning in sub-samples of 602 and 812 twins from FinnTwin16 and FinnTwin12 in young adulthood (age ranges: 23–30 and 21–24 years). In conditional logistic regression analyses of same-sex twin pairs discordant for their development, indicators of verbal development (age of speaking words, age of learning to read, verbal expression in childhood, grades in primary school) were positively related to each other, as were indicators of motor development (age of walking, manual dexterity and general motor development before school age, agility in school age). Monozygotic twins were less often discordant for their development than same-sex dizygotic twins. Age of speaking words was not systematically associated with cognitive performance but twins who learned to read earlier, were more advanced in verbal expression in childhood or had higher grades in primary school outperformed in each case their co-twins in most cognitive domains in young adulthood. These associations were mostly limited to DZ pairs, indicating genetic continuity between childhood verbal development and cognition in young adulthood. In some cases similar but smaller differences were also observed in MZ pairs, suggesting developmental continuity independent of genetic influences. Childhood motor development was not systematically associated with cognitive performance in young adulthood.

Quantitative trait loci that influence antisocial drug dependence in adolescence: A replication analysis

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Familial factors, including shared genetic risk, may account for the observed comorbidity between externalizing problems and substance use disorders in adolescents. A combined phenotype capturing dependen- ce vulnerability (DV) was constructed in a set of adolescent probands and their families. Stallings et al. (2005) reported evidence of QTLs for DV on 3q24–3q25 and 17q12 in 249 proband-sibling pairs. That sample has been extended with an additional 645 proband-sibling pairs. The original sample was genotyped using 374 microsatellite markers which only provided limited information content. Greater information content and coverage was achieved in the replication sample using a common pool of 37,000 SNPs assembled from the multiple Affymetrix platforms on which the replication sample was genotyped. The created SNP pool provides full genome coverage for the entire sample. Regression based QTL mapping procedures were used in a replication analysis of the previous findings, and in secondary analyses to look for novel QTLs.

Genetic and environmental influences on children’s inhibitory control: An adoption study

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Deficits in inhibitory control have been associated with short- and long-term problems across the lifespan, including elevated rates of ADHD, depression, drug abuse, and antisocial behavior. Both genetic and family-level influences have been associated with inhibitory control. For example, heritability estimates in young children’s inhibitory control processes from twin studies have ranged from 40 to 80 %, and effective parenting skills have been linked to improved child inhibitory control skills. However, work in this area has been limited by a dearth of genetically-informed research designs that include a focus on measured environmental mechanisms. The current study used data from a prospective adoption design (The Early Growth and Development Study) to examine processes related to the intergenerational transmission of risk for deficits in inhibitory control. The sample included 361 linked sets of children adopted at birth, their adoptive parents, and their birth parents. Children’s inhibitory control was measured as the percentage of correct trials during a computer-based go no-go task at age 6. Adoptive mother’s harsh discipline was measured using a standardized parenting questionnaire, and birth parent inhibitory control was measured using the same go no-go task as the child completed. Results indicated independent associations of birth parent inhibitory control and adoptive mothers’ discipline on child inhibitory control, suggesting two pathways of risk: the first via genetic transmission, and the second via exposure to harsh parenting. Additional analyses indicated that
children’s poor performance on the go-no-go task was associated with mother and father ratings of the child’s ADHD and inattention symptoms using standardized assessments, suggesting the validity of the go-no-go task as an indicator of symptoms of psychopathology. The utility of the adoption design to inform researchers and clinicians as to the underlying etiology of behavior and help identify environmental targets for intervention will be discussed.

The heritable origins of ingroup favoritism: Testing a norm-conformity theory

Gary Lewis; University of California, Santa Barbara Timothy Bates; University of Edinburgh

In-group favoritism is ubiquitous and has a known heritable basis in humans. The mechanisms underlying favoritism, however, remain obscure. Recent theories suggest that favoritism emerges from systems concerned with the maintenance of social norms. Here, in three studies, we demonstrate that heritable elements of norm-conformity substantially overlap with the heritable bases underlying in-group favoritism. In Study 1, traditionalism and in-group favoritism were assessed in a nationally-representative sample of adult US twins. Traditionalism accounted for approximately a quarter of the genetic variance in favoritism. Study 2 confirmed this association in an independent sample of adult US twins and with a different measure of norm-conformity: Right-wing authoritarianism (RWA). In this study, heritable influences on RWA fully accounted for the heritable effects on in-group favoritism. Study 3 examined the role of personality on RWA and favoritism. Big Five traits, especially low openness and high conscientiousness, accounted for around one-third of the common genetic variance underlying RWA and in-group favoritism. Taken together, these studies suggest that in-group favoritism reflects a specialized system evolved to detect and reinforce normative social practices, the sensitivity of which is in turn partially influenced by basic dimensions of personality.

Migraine with and without major depression are genetically different disorders

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Twin and family studies suggest that major depressive disorder (MDD) and migraine are genetically correlated. Here, we use polygenic risk prediction to investigate whether MDD-related migraine has a different genetic basis than migraine unrelated to MDD.

Genome-wide association analyses (GWA) were performed in the Radiant-UK sample (MDD-discovery) and the Australian Twin Migraine (ATM) sample (migraine-discovery). The results of these analyses were used to calculate a polygenic risk score for MDD and migraine for individuals in the NTR/NESDA sample (NTR/NESDA-target). The NTR/NESDA-participants came from two cohort studies in the Netherlands, which collected data on both DSM-IV diagnosed MDD and migraine. The number of SNPs that overlapped between discovery and target samples was 249,917 for ATM, and 416,030 for Radiant-UK. For each individual in the target sample, we calculated the number of score alleles they possessed, weighted by the log odds ratio from the discovery sample. Logistic regression analyses were performed in the target sample to assess whether the aggregate (polygenic) scores reflected migraine and/or MDD risk. We tested for a higher mean score in migraine cases (all, with MDD, without MDD) and MDD cases (all, with migraine, without migraine), when compared to controls unaffected for both conditions.

The polygenic scores for MDD significantly predicted MDD in the NTR/NESDA-target sample, regardless of the presence of comorbid migraine. However, these scores did not predict migraine without MDD. Polygenic scores for migraine significantly predicted migraine, regardless of MDD status, but migraine was not significantly predictive of MDD without migraine.

These results suggest that the ‘pure’ forms of migraine and MDD are genetically different. Most likely, the observed genetic correlation between migraine and MDD in population based samples is explained by individuals who have comorbid migraine and MDD. This is consistent with MDD-related and non-MDD related migraine being genetically different disorders.

Parental schizophrenia and increased offspring suicide risk: Exploring the causal hypothesis using cousin comparisons

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Background: Little is known about suicide risk among offspring of parents hospitalized for schizophrenia and the mechanisms behind this association.

Methods: We applied a nested case–control design based on linkage of Swedish population-based registers. Among 12- to 30-year-old offspring, we identified 68,318 offspring with suicidal behavior (attempted and completed suicide) and their parents. Five healthy control-parent pairs were matched to each suicidal case-parent pair and conditional logistic regression used to obtain odds ratios. Further, to disentangle familial confounding from causal environmental mechanisms, we compared the population based suicide risk with the risk found within full-cousins and half-cousins differentially exposed to parental schizophrenia.

Results: Offspring of parents with schizophrenia had significantly increased suicide risk after accounting for socioeconomic status, parental suicide and offspring mental illness (odds ratio [OR] = 1.65, 1.50–1.81). Suicide risks in offspring of schizophrenic mothers and fathers were similar in magnitude; so were risks across different developmental periods. Importantly, offspring suicide risk remained essentially unchanged across genetically different relationships; offspring of siblings discordant for schizophrenia had equivalent risk increases within full-cousins (OR = 1.95, 1.68–2.30) and half-cousins (OR = 1.73, 1.19–2.50).

Conclusions: Parental schizophrenia was associated with increased risk for offspring suicide, independent of the gender of the schizophrenic parent, and persisting into adulthood. The suicide risk in offspring remained unchanged when comparing genetically different relationships, which suggests that environmental mechanisms; that is, the experience of having a schizophrenic parent, increases offspring suicide...
risk. These findings should inspire increased attention to suicidal ideation and prevention efforts in offspring of parents with schizophrenia.

Direct and indirect relations between reactive and proactive aggression, facial emotion recognition, and MAOA-uVNTR/5-HTTLPR

Devon LoParo; Emory University Courtney Ficks; Emory University Irwin Waldman; Emory University

Research has demonstrated that individuals high in antisocial traits tend to have difficulty recognizing fearful and sad facial expressions, though researchers have not attempted to link these deficits to specific forms of aggression, such as reactive and proactive aggression. Further, no studies to date have examined associations of facial emotion recognition with specific genes. Two genetic markers frequently studied in association with aggression are a repeat sequence in the promoter region of the monoamine oxidase A gene (MAOA-uVNTR) and a polymorphic region of the serotonin transporter gene (5-HTTLPR). These genes are active in brain regions involved in aggression and facial emotion recognition, such as the amygdala, indicating that facial emotion recognition deficits or biases may serve as an endophenotype for aggression. In a sample of 180 twins genotyped for the MAOA-uVNTR and 5-HTTLPR, we found that the MAOA-uVNTR risk allele was associated with fewer correct fear recognitions, more fear commission errors, and more sad commission errors on a facial emotion recognition task, while the 5-HTTLPR risk allele was associated with fewer correct sad recognitions and more sad commissions. We also found that fewer correct fear recognitions, more fear commissions, and the MAOA-uVNTR risk allele were associated with reactive aggression, while more fear commissions was also associated with proactive aggression. In addition, we found that correct fear recognitions and commissions mediated the relation between the MAOA-uVNTR and reactive aggression. These results suggest that impaired fear recognition is related to both reactive and proactive aggression. Further, the influence of MAOA-uVNTR on reactive aggression seems to act in part through impaired fear recognition, indicating that facial emotion recognition may be a useful endophenotype for reactive aggression. Future studies should extend these findings by evaluating other criteria for the validity of these endophenotypes and examining other aspects of social cognition as endophenotypes for aggression.

Network phenotypes and missing heritability

Gitta Lubke; University of Notre Dame, VU University, Amsterdam Michel Nivard; VU Denny Borsboom; University of Amsterdam

Nivard and colleagues demonstrate with simulated data that misspecification of the phenotype in twin and GWA models can lead to missing heritability. Specifically, they consider the case where the phenotype is measured by multiple items that mutually affect each other, and where SNPs modify the strength of these interrelations. They show that using a crude simplification of the phenotype as is done in typical gene finding studies results in severe underestimation of genetic variance. Motivated by these simulation results, we chose a small, three-symptom network as an example to show analytically the consequences of incorrectly specifying the phenotype. Different scenarios for SNP effects are investigated, and analytical results are presented for the cases that (1) ACE-type twin models, or (2) typical GWA models are fitted to univariate simplifications of network phenotypes.

ADRB2, white matter integrity and cognitive ageing in the Lothian Birth Cohort 1936

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Background: Non-synonymous mutations arg16gly (rs1042713) and gln27glu (rs1042714) in the adrenergic β-2 receptor gene (ADRB2) play a role in human neurodevelopment, and have been associated with adult cognitive function and brain white matter integrity in previous studies (L. Penke et al. 2010, Behav. Genet. 40 [2], 146–156).

Objectives: The current study aimed to firstly replicate previous reported findings in a larger sample of healthy older adults, and secondly extend the number of cognitive domains and white matter tracts assessed.

Methods: The current sample was the Lothian Birth Cohort 1936. This sample had been cognitively assessed at age 11 years with further cognitive assessment and diffusion-tensor MRI performed in older age around 73 years (n = 762).

Results: Previous findings in a sub-sample (n = 162) of this cohort were not replicated, but novel significant associations were found. Most notably, integrity of the left arcuate fasciculus mediated a significant association between rs1042714 and the Digit Symbol Coding test of processing speed. No associations survived correction for false discovery rate.

Discussion: The arcuate fasciculus has been suggested to underlie parieto-frontal cortical integration, a proposed foundation of higher cognitive ability (R.E. Jung and R.J. Haier 2007, Behav Brain Sci 30, 135–187). The mediation reported here may reflect the general role that this tract plays in subserving cognitive functioning in addition to the high sensitivity of the Digit Symbol Coding task in detecting subtle cognitive dysfunction. Significant associations did not survive correction for multiple testing and require further replication in independent samples.

Professional science master’s: A new graduate degree for behavioral genetics

Carol Lynch; Council of Graduate Schools Toni Smolen; University of Colorado Boulder

In recent years we’ve seen a marked decrease in applicants to graduate programs in behavioral genetics. Concern about the lack of jobs for PhDs, who are typically 35–40 years old before they obtain their first permanent position, leads students who might have been
interested in a PhD to look elsewhere. Our undergraduate courses are filled with students, many of whom might consider a career in behavior genetics if we could increase their employment opportunities outside of academia. We need to create degree options that are less time consuming than a doctoral program, with reasonable prospects for employment following graduation. The Professional Science Master’s (PSM) is an innovative graduate degree designed to allow students to pursue advanced training in science or mathematics while simultaneously developing workplace skills valued by employers. PSM programs consist of graduate training in an emerging or interdisciplinary area, along with professional components that may include internships and “cross-training” in professional skills, such as business, ethics, communication, and regulatory affairs. Programs are developed with advice from employers and are designed to dovetail into professional career opportunities. PSM programs now number about 250 at about 115 institutions. The four largest fields, together comprising 80% of fall 2011 enrollments, are biology/biotechnology, mathematics and statistics, environmental sciences, and computational sciences. These programs attract students who are not interested in a doctorate, but want a degree that leads to a science-based career in innovative organizations and that prepares them for advancement. PSM graduates experience almost 100% employment and many programs—especially in biomedical fields—report more demand for graduates than they can supply. Given the student interest in relevant fields, and the employment opportunities in business and the public sector, adding these degrees to our academic offerings would provide an opportunity for behavioral geneticists to contribute to innovation and economic growth.

Heritability of the neural mechanisms of cognitive control

Christine Macare; University of Bonn Ulrich Ettinger; University of Bonn

Imaging genetics relates inter-individual variation in brain activity to molecular genetic variation. A fundamental assumption of this approach however is the heritability of brain activity frequently assessed by the blood oxygen level dependent (BOLD) response. Ninety-six healthy same-sex twins composed of 60 mono- (MZ: 28 males, 32 females) and 36 dizygotic (DZ: 22 males, 14 females) twins underwent functional magnetic resonance imaging (fMRI) during the antisaccade task, a measure of cognitive control and an established schizophrenia endophenotype. BOLD signal contrasting activation during antisaccades and prosaccades showed strong activations in the fronto-parietal-subcortical network including bilateral frontal eye fields (FEF), bilateral supplementary eye fields (SEF), bilateral intraparietal sulcus (IPS), bilateral dorsolateral prefrontal cortex (DLPFC), bilateral ventromedial prefrontal cortex (VMPFC) and right supramarginal gyrus (SMG). Twin correlations indicated familial influences in the insula, anterior cingulate cortex, IPS, SMG, DLPFC and temporo-parietal junction (TPJ). However, the correlations were of small to moderate magnitude (rMZ: 0.11–0.37; rDZ: 0.03–0.27). Behavior genetic modeling of the activation in TPJ provided tentative evidence for additive genetic influences (51%; 95% confidence interval: 0–75). Despite replication of the neural underpinnings of antisaccade task performance, behavior genetic modeling did not show evidence for significant genetic influences on these activations. Limitations of the current study as well as implications for future imaging genetics research will be discussed.

Methylation of 11-beta hydroxysteroid dehydrogenase 2 in the human placenta is associated with newborn neurobehavioral outcomes

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Background: In utero development is a sensitive period during which disruption or modification of the prenatal environment can impact the neurodevelopment of the fetus. Recent work has investigated influences of the prenatal environment on alterations to the functional epigenome of the placenta [1]. In the placenta, the HSD11B2 gene encoding the 11-beta hydroxysteroid dehydrogenase enzyme is responsible for the inactivation of maternal cortisol, is regulated by DNA methylation, and has been shown to be susceptible to stressors from the maternal environment [2,3].

Methodology/Principal Findings: DNA methylation of the HSD11B2 promoter region in the placenta of 185 healthy newborn infants was measured by pyrosequencing. Expression of the HSD11B2 gene in the same placenta was measured by Real-Time PCR. Associations between DNA methylation extent of the HSD11B2 promoter region and infant and maternal characteristics, including newborn neurobehavioral outcomes as assessed by the NICU Network Neurobehavioral Scales (NNNS), were investigated. HSD11B2 promoter methylation extent is significantly negatively correlated with HSD11B2 gene expression (p = −0.24, p < 0.02). Controlling for confounders, increased HSD11B2 methylation extent is associated with reduced scores of quality of movement (p = 0.04).

Conclusions/Significance: This study is one of the first to link epigenetic alterations of placental genes and early life neurobehavioral outcomes in a human population. Our findings enhance our understanding of epigenetic control of the HSD11B2 gene, which is central to HPA axis development, and correlate these epigenetic alterations to altered infant neurobehavioral development, suggesting a potential mechanism for the developmental origins of infant neurological health. Future investigations include examining epigenetic alterations as a mode by which the prenatal environment may influence trauma-associated neurobehavioral disorders in children.

OpenMx modeling of extended twin (ET) kinship designs

Hermine Maes; Virginia Commonwealth University Michael Neale; Virginia Commonwealth University Lindon Eaves; VIPBG, Virginia Commonwealth University

The extended twin kinship design allows the simultaneous testing of additive and non-additive genetic, shared and individual-specific environmental factors, as well as sex differences in the expression of genes and environment in the presence of assortative mating and...
combined genetic and cultural transmission. It also handles their
correlation to the (co)variation of multiple phenotypes. We further
extend the model by allowing for genotype × age or genotype ×
environment interaction using the piecewise style, and apply it to
smoking data from the Virginia 30,000.

Parental negativity and adolescent externalizing
problems: Using the extended children of twins
model to clarify genotype–environment correlation

Kristine Marceau; Pennsylvania State University Briana Horwitz; The
Pennsylvania State University Jurgita Narusyte; Karolinska Institutet
Jody Ganiban; George Washington University Erica Spotts; George
Washington University Paul Lichtenstein; Karolinska Institutet David
Reiss; Yale Jenae Neiderhiser; The Pennsylvania State University

The present study tested the mechanisms underlying the association
between negative parenting and adolescent externalizing problems.
The data used were a large Swedish sample of twin mothers and
fathers and their adolescent offspring (Twin and Offspring Study in
Sweden, adolescents aged 11–22, = 15.5, SD = 2 years) in combi-
nation with a large US-based sample of adolescent twins and sib-
lings and their parents (Nonshared Environment in Adolescent
Development, adolescents aged 11–22, = 15.7, SD = 2.5 years).
Data analyses were performed using the novel Extended Children of
Twins (ECOT) model (Narusyte, J., Neiderhiser, J. M., D’Onofrio, B.,
Reiss, D., Spotts, E. L., Ganiban, J., & Lichtenstein, P. (2008).
Testing different types of genotype–environment correlation: An
extended children-of-twins model. Dev Psychol 44(6):1591–1603).
The ECOT model estimates the genetic influences of parents’ and
adolescents’ on the association between negative parenting and ado-
lescent externalizing problems and can discern whether passive and/
or evocative genotype–environment correlation operates in the asso-
ciation between parenting and child behavior, or whether parenting
exerts a direct environmental influence on child behavior. Results
suggest that evocative genotype–environment correlation explains the
association between maternal and paternal negativity and adolescent
externalizing problems. Parental negativity did not exert a direct
environmental effect on adolescents’ externalizing problems, nor was
there evidence of passive genotype–environment correlation. Results
suggest that parental negativity in adolescence is a reaction to children’s
genetically influenced characteristics, rather than an environmental
influence exacerbating adolescents’ behavior problems.

Common variants of large effect: Do they exist,
do they matter?

Nicholas Martin; Queensland Institute of Medical Research

In general, gene variants with large effects (such as those for diseases
showing Mendelian inheritance) tend to be uncommon or rare whereas polymorphic variants (with minor allele frequency over 1 %)
have small effects. Genome-wide association studies have relied on
common tagging polymorphisms and have mainly identified small
effects; around 1.2 relative risk for case–control studies and 1 % of
variance for quantitative phenotypes. Combining data in meta-anal-
yses allows detection of smaller effects, and in the near future typing
of SNPs with frequency down to 0.1 % may detect larger ones.
The focus of this presentation is on exceptions to the rule; what can be
learned by identifying SNPs with larger allelic effects, and are larger
effect sizes found for endophenotypes than for disease?

Data come from the QIMR twin and family studies, in which around 8,000 adults and 3,000 adolescents have genome-wide SNP
typing and a wide range of measured phenotypes, including around 30
biochemical risk factors or biomarkers measured in serum or eryth-
rocytes. From this resource, we have extracted data on the rela-
tionships between allele frequency and effect size for each phenotype,
assessed the frequency distribution of effect sizes, and identified SNP-
phenotype combinations where the proportion of phenotypic variance
explained is over 5 % in our populations.

Substantial effects associated with typed or imputed SNPs have
been found for bilirubin, cholinesterase, transferrin and uric acid.
Other phenotypes including most lipids, liver function tests, iron
markers and renal function tests showed significant hits, consistent
with results from other groups, but accounting for only small propor-
tions of the phenotypic or genetic variance. The phenotypes showing large SNP effects do have associations with disease or
involvement in essential metabolic steps, but the gene variants persist at high frequencies in European (and in most cases, other) popula-
tions.

An assessment of gene-by-environment interaction
effects on neuropsychological phenotypes related
to developmental dyslexia: The role of the DYX1C1,
DCDC2, KIAA0319 and ROBO1 genes
and of specified putatively hazardous factors

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Eugenio Medea Michel Maziaede; Centre de Recherche de l’Institut
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Institute Eugenio Medea

Developmental Dyslexia (DD) is a heritable condition characterized
by an impairment of reading abilities in spite of normal intelligence
and adequate educational opportunities typically diagnosed in the
first school years. The etiology of DD involves multiple interacting
risk factors, which can be either genetic or environmental, under-
lying a continuously distributed liability. While the genetic and
environmental contributions to DD have been studied extensively,
the effects of identified genetic risk susceptibility and of specified
environmental hazard factors have usually been investigated sepa-
ately.

In the light of the relevance of a more comprehensive approach to
enhance genomic investigation of DD, we assessed gene-by-envi-
ronment (G × E) interactions on DD-related quantitative phenotypes.
The presence of G × E effects and their direction were investigated
for four DD-candidate genes and for a set of putative environmental
hazardous factors in 168 nuclear families in which at least one
member had DD, by implementing a general test for G × E inter-
action in sib pair-based association analysis of quantitative traits (van
der Sluis et al. 2008).

Taken together, our data show some significant interactions
between specified environmental moderators and the selected DD-
candidate genes’ markers for the considered DD-related neurophe-
notypes. These results are consistent with the diathesis-stress rather
than the bioecological model of G × E interactions, whereby a less
supportive familial environment may lead to greater genetic liability from detrimental DD-susceptibility genes’ alleles, which would remain undetected in more supportive environments.

Although these data are preliminary and need replication in larger independent samples, we have provided initial evidence that the joint analysis of identified genetic risk susceptibility and measured putatively hazardous factors can be evaluated in the study of the aetiology of DD, and may assist in identifying/preventing the occurrence of DD.

Estimating heritability of personality from family research: Biometrical analyses and the collective influence of SNPs

Lindsay Matteson; University of Minnesota Michael Miller; University of Minnesota Matthew McGue; University of Minnesota William Iacono; University of Minnesota

Research has shown that personality traits predict many important life outcomes just as strongly as other variables do, such as cognitive ability and socioeconomic status. Data from twin and family studies have suggested a moderate heritability of personality traits, but genome-wide association studies (GWAS) on personality have identified few causal variants. Some have suggested that psychological phenotypes are so polygenic that effect sizes of individual single nucleotide polymorphisms (SNPs) are too small to be observed with our current sample sizes. One thing we might do to identify the "missing heritability" is to consider the influence of all SNPs together; the collective influence of all SNPs represents a lower-bound estimate of additive genetic effects. In the current study, we wished to estimate the proportion of variance in personality that can be explained by all SNPs and compare it to the biometrical estimates of heritability from the same sample. Our phenotypes consisted of the three higher-order factors from the Multidimensional Personality Questionnaire (MPQ): positive emotionality (PEM), negative emotionality (NEM), and constraint (CN). For the biometrical analyses, we used Mx statistical software to model the variance–covariance structure of twin and adoption data from the Minnesota Twin and Family Study (MTFS) and Sibling Interaction and Behavior Study (SIBS) at the University of Minnesota. For the genetic analysis, we first estimated pairwise genetic relationships between individuals from the MTFS and SIBS. We excluded one individual from any pair that had an estimated coefficient of relatedness greater than 0.025, and then we used restricted maximum likelihood to estimate the variance in personality explained by all SNPs. Results of these analyses are forthcoming.

Method: We sought to explain the heritability of maternal negativity, paternal negativity and negative life-events via their associations with oppositionality, delinquency, physical aggression, depression and anxiety in a UK sample of 1,102 twin pairs aged 15 years (range 13–17). Three Cholesky decomposition models were used, one for each environmental measure.

Results: All environmental measures were moderately heritable. Cholesky models showed that the heritability of each was entirely accounted for by its association with the behavioural phenotypes. Genetic factors involved in maternal negativity were correlated with oppositionality (r = 0.55), delinquency (r = 0.39), depression (r = 0.60) and anxiety (r = 0.46). Genetic factors involved in paternal negativity were correlated with delinquency (r = 0.37) and depression (r = 0.48). Genetic factors involved in negative life events were correlated with oppositionality (r = 0.57), delinquency (r = 0.87), physical aggression (r = 0.50), depression (r = 0.57) and anxiety (r = 0.36).

Conclusions: Results demonstrate that the heritability of putative environmental measures can be entirely accounted for by their association with behavioural phenotypes, with different combinations of phenotypes explaining the heritability of different environmental measures. As such we highlight specific behaviours that may operate as the link between genes and our 3 environmental measures. Such links may take the form of passive, active or evocative rGE.

Using openMx for GWAS

Sarah Medland; QIMR Karin Verweij; QIMR Joseph Powell; University of Queensland

Genome wide association studies (GWAS) typically examine evidence for association at the univariate level in samples of unrelated individuals. There are a limited number of programs designed to analyse family based data and these methods typically assume the covariance structure can be fully accounted for by an AE model. Within the context of behavioural genetics there are a wide range of univariate and multivariate models that we may want to adopt either as a background to association or alternatively as a vehicle for conducting multivariate association analyses. One mechanism for implementing these methods is to fit the models using openMx. We will discuss the feasibility and practical considerations of this approach and introduce a purpose built R package designed to assist researchers in running large scale GWAS analyses with user specified covariance structures.

Multivariate models of BMI, intelligence, and fertility using the NLSY-children kinship links

Tom McAdams; King’s College London Alice Gregory; Goldsmiths Robert Plomin; King’s College London Thalia Eley; Institute of Psychiatry

An increasing body of evidence shows that many environmental measures are heritable, demonstrating genetic involvement in environmental exposure (Kendler & Baker 2007). Multivariate genetic analyses demonstrate that the heritability of environmental measures can be partially explained via their association with heritable behavioural phenotypes (Button et al. 2007; Pike et al. 1996; Saudino & Plomin 1997). In the present study we sought to expand on this work by including multiple behavioural phenotypes in an attempt to explain ALL of the heritability of three environmental measures.

Genes of experience: Explaining the heritability of putative environmental variables

Tom McAdams; King’s College London Alice Gregory; Goldsmiths Robert Plomin; King’s College London Thalia Eley; Institute of Psychiatry

Multivariate models of BMI, intelligence, and fertility using the NLSY-children kinship links

Kelly Meredith; University of Oklahoma Joseph Rodgers; University of Oklahoma William Beasley; Howard Live Oak David Bard; University of Oklahoma

Previous studies have identified heritability in BMI, intelligence, and measures of sexual readiness and behavior. Further, studies have indicated that intelligence is related to both sexual activity (Kanazawa & Raymiers 2009) and biological variables such as height (Harden & Mendel 2011). Bivariate biometrical models have even indicated that the correlation between height and intelligence is explained by common genetic sources of variance (Silventoinen et al. 2006). A Life History perspective motivates potential links among these three
theoretical domains. To our knowledge, however, no study has used biometrical analysis to partition variance and evaluate the relationship between all three outcomes.

Our newly developed kinship linking algorithm identified 10,512 shared-household kin pairs, including half siblings, full siblings, and twins, in the National Longitudinal Survey of Youth Children (NLSYC). In this study, we use these NLSYC kinship links to evaluate both univariate and multivariate biometrical models involving measures of BMI, intelligence, and sexual outcomes. Our univariate models are consistent with findings from previous studies. Our multivariate models, which we fit using OpenMx, include Competing Pathway Models and Cholesky Models to evaluate overlapping sources of variance and time-related patterns of shared variance. We present the best-fitting models within each category, and provide Life History interpretations.

On early genetic and environmental antecedents of hostility

Päivi Merjonen; University of Helsinki

Objective: Hostility is a multidimensional construct having wide effects on society through social and health problems related to it. Thus, identifying and managing early-life factors that contribute to hostility may have public health significance. This review consists of my previous studies of breastfeeding, early mother–child relationship, and genetic constitution as predictors of hostility.

Methods: Studies are based on the Young Finns study which was launched in 1980 with 3,596 3- to 18-year-old boys and girls who have been followed up for 27 years. Information on breastfeeding and child-rearing attitudes was reported by parents in 1980 or 1983 and hostility has been followed by the participants 12, 17, 21 and 27 years after the baseline when the offspring were 15–45 years old. Hostility was measured with the Cynicism Scale (MMP), Distrustful attitudes (SCL-90R) and Anger (BDHI) scales. Also their genome was covered by genotyping around 550,000 SNPs for which by genotype imputation 2.5 million could be used in genome-wide association analysis (GWA).

Results: Breastfeeding as well as warm mother–child relationship predicted lower levels of hostility in adulthood (ps < 0.05). Associations were independent of several child-, mother-, or family-related factors. HTR2A rs6313 was found to moderate the association between maternal child-rearing attitudes and hostile attitudes. Also in GWAS some potential areas in chromosomes 7, 14, 17, and 22 were suggestively associated with some hostility scales. Also their genome was covered by genotyping around 550,000 SNPs for which by genotype imputation 2.5 million could be used in genome-wide association analysis (GWA).

GWAS of genetically informed measures of alcohol consumption and problems in the Finntwin12

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To date, several GWAS on alcohol dependence have been published without producing robust, replicable genetic association signals. One such problematic aspect of conducting genetic analyses on alcohol dependence is the imprecise and heterogeneous nature of the phenotype. Results from our previously published twin analyses indicate that different aspects of alcohol consumption and problems are genetically heterogeneous. In the present study, we examine the genetic architecture of five measures of alcohol consumption and problems within the Finntwin12, a large population-based twin study. We used the resulting genetic factor structure to create genetic factor scores for each individual. We then conducted a genome wide association study in the same twin sample utilizing the information gained from the twin analyses; in addition to analyzing our primary phenotype of interest, DSM4 Alcohol Dependence symptoms, we also analyzed two genetic factor scores that emerged from the multivariate twin analyses. GWAS data was available on 1,069 individuals (406 MZs; 614 DZs) who were genotyped on the Illumina 670K Custom Array. GWAS analyses indicated that no individual single nucleotide polymorphism (SNP) met criteria for the genome wide significance threshold, however many SNPs were approaching this threshold, including SNPs located within genes DOK7, UKP1B, FXYD6 and TSHZ2. Additionally, we ran gene-based analyses that produced a number of top gene results including AMPD2, FGF5, and HSPA2. In parallel to twin analyses, some of the top genes were shared across the alcohol phenotypes, while others were exclusively associated with
Are symptoms of anxiety and depression during childhood and adolescence influenced by similar genetic factors as major depression in adulthood?

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Symptoms of anxiety and depression (SxAnxDep), are influenced by many genetic variants, each with a small effect. Consequently, genome wide association (GWA) studies should be performed on the largest samples possible. One way to increase sample sizes is to pool data from subjects of different ages. This only makes sense if similar genetic factors influence a trait across age.

Results from three twin studies suggested that genetic effects for SxAnxDep are transmitted from childhood onwards, but that new genetic effects also come into play during adolescence and young adulthood.

Here, we use a different approach to investigate the overlap between genetic factors influencing major depressive disorder (MDD) in adults, on the one hand, and SxAnxDep in childhood and adolescence, on the other. GWA data as well as data on SxAnxDep are available in a sample of 2,557 dizygotic twins and siblings from 1,652 families from the Netherlands Twin Register. SxAnxDep were assessed at age 3, 5, 7, 10, 12, 14, 16 or 18 years with age-appropriate versions of the Achenbach System of Empirical Based Assessment. All subjects had participated at least once. The computation of polygenic scores is based on the GWA results of the MDD meta-analysis from the Psychiatric Gwas Consortium (PGC), including nine samples with a total of 18,759 adults. Linear regression analyses were performed from subjects of different ages. This only makes sense if similar genetic factors influence a trait across age.

Comparison of methods that use inferred genetic similarity from GWAS data, even for ostensibly unrelated subjects, to draw conclusions about effects of quantitative trait loci

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The classical twin method suggests substantial heritability for most behavioral phenotypes (30% or greater), yet GWAS projects using millions of SNPs on thousands of subjects have identified loci accounting for a total of less than 1% of variance for most traits. Because of this, much interest in the past couple of years has focused on the problem of how else we might use GWAS data to discover clues about unknown trait loci such as their chromosomal locations, their total effect on trait variance or their minor allele frequencies. Traditional linkage methods can use close relatives of known shared ancestry to identify chromosomal regions containing trait loci even in the absence of population-level association of any markers with the trait. Such linkage methods have extremely low statistical power without very large samples of related pairs. Related approaches use average identity-by-descent proportion over a genomic region (e.g., a chromosome) for relative pairs to attempt a broader-based assessment of genetic effect. The most recently-developed methods attempt to detect genetic similarity between all possible pairs of a large number of ostensibly unrelated individuals. These include the Yang et al. (& Visscher) (2010, Nat Genet) Genome-wide Complex Trait Analysis (GCTA) and the Browning and Browning (2011, AJHG) fastIBD method. The currently very popular Yang/Visscher GCTA approach uses restricted maximum likelihood (REML) to compute a variance proportion. Questions remain about the power and sensitivity of these methods in the presence of various kinds of effects and how results should be interpreted. Using data produced by computer simulation under several different models, varying parameters such as allele frequencies, effect sizes, numbers of trait loci, association and linkage of trait loci with markers, we compare analytical methods and present findings.
Sibship-based association analysis with imputed sibling genotypes

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Many registries include phenotype data from multiple family members. However, in GWA studies often not all family members are included for genotyping. When phenotypic data of multiple family members are available, while genotypic data are limited to a subset of family members, limiting the association analysis to the ‘complete data’ participants wastes information. An alternative is to exploit the genetic relations among relatives to impute genotypes of relatives lacking genotypic data (Visscher & Duffy 2006). This study investigates the power advantages of using imputed genotypes in sibling based association analysis.

In simulated data, we consider the design in which 1 sibling is genotyped and the design in which 1 sibling and 1 parent are genotyped. In both designs, we impute up to 3 siblings, and we limit the association analyses to the sibling data.

First we compare two statistical approaches: the mixture model, which involves the full distribution of the imputed genotypes, and the dosage model, in which the mean of the conditional distribution features as the imputed genotype.

Second, we investigate the effect on power of misspecification of the background covariance structure. Family-based association analysis requires statistical modeling of the background covariance structure. As such modeling is of interest regardless of whether genotypes are imputed or not, we evaluate the effect of background misspecification both in the “all sibs genotyped” setting and in the dosage model.

We illustrate the imputation procedure in a sibship-based association analysis with imputed sibling genotypes aimed at replicating 112 of the 180 height SNPs reported by Lango Allen et al. (2010). Height data were available for 17,195 sibs in 8,310 families. In 2,164 families 2,410 siblings (and 1,437 parents) were genotyped and 3,502 additional siblings had height but no genotype data.

Association between androgen receptor gene (AR)
CAG repeat length and externalizing behavior

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Testosterone has been related to physical aggression and behavioral problems in animal and human studies of impulse control, self-regulation, and mating competition. Testosterone exerts its effects on gene expression in part by binding to the androgen receptor. It is thus important to examine the androgen receptor gene (AR) and its relations with externalizing problems. Shorter CAG repeats in a polymorphism in AR is associated with increased efficiency of androgen binding to the receptor and greater AR gene expression. Past research has found that the CAG repeat polymorphism is associated with aggressive personality traits and criminal behavior in adult males, such as impulsivity, psychopathicism, and rape. Nonetheless, there are mixed findings regarding the direction of the association between CAG repeat length and externalizing problems. Studies have also focused primarily on adult males, with not many studies on children or females. In our sample of 200 clinic-referred and control children ($M = 10.13$ years old, $SD = 3.4$), we collected their DNA and obtained maternal ratings of their children’s DSM externalizing and internalizing symptoms. We used generalized linear modeling with general estimating equations to test for the relations between CAG repeat length and different problem dimensions. Controlling for age, sex, and ethnicity, we found positive associations between children’s mean CAG repeat length and reactive aggression, hyperactivity, and hyperactive-impulsivity. There were no associations between mean CAG repeat length and proactive aggression, inattention, Oppositional Defiance Disorder, or Conduct Disorder. Future research should explore the effect of the CAG repeat length on specific subtypes of aggression and other related traits, which may explain the inconsistent positive and negative associations found in the literature. It is also important to study multiple polymorphisms within AR to better capture genetic variation in the androgen gene, its function, and its overall effect on aggression and other externalizing and internalizing behavior problems.

Genotype by environment interactions when the environment is unmeasured:
Comparing two approaches

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Using the traditional ACE model, a lot of effort has been devoted to the identification of genotype by environment interactions ($G \times E$) in various domains of research. In many cases, the environmental variables are measured variables, allowing the use of the moderation model proposed to test for $G \times E$ (Purcell 2002). However, in some cases, relevant environmental variables are lacking or difficult to identify. In these cases there are two possible approaches to test for $G \times E$: (1) the heteroscedasticity approach (Jinks & Fulker 1970; van der Sluis et al. 2006; Molenaar et al., in press) in which it is tested whether environmental influences are variable across the additive genetic factor, A; and (2) the extended DeFries-Fulker regression method (LaBuda 1986; Cherney et al. 1992; Detterman 1992; Brand et al. 2012) in which it is tested whether the phenotypic variable interacts with the common environment factor, C, and/or the A factor. In this talk, both approaches are compared to see to what degree they are different. Results are illustrated on a real dataset.

Correlates of processing speed difficulty in patients with mitochondrial disease

Heather Moore; Newcastle University Mike Allerhand; University of Edinburgh Michael Tre nell; Newcastle University Ian Deary; University of Edinburgh Doug Turnbull; Newcastle University Grainne Gorman; Newcastle University

Introduction: Mitochondrial diseases are a group of inherited disorders that predominantly affect organs with high energy requirements including muscle, heart and brain. Neurological impairment remains one of the hallmarks of mitochondrial disease and cognitive impairment is one of the least understood aspects of its phenotypic expression. Recently, slowed processing speed has been reported in a small number of patients with mitochondrial disease.

Aims: To systematically investigate processing speed, this is an important, low level cognitive ability, in a large cohort of patients with mitochondrial disease.
**Methods:** Cognitive data were recorded using the Wechsler Test of Adult Reading, the Symbol Search (Wechsler Adult Intelligence Scale-III) and the Speed of Comprehension test (Speed and Capacity of Language Processing) in patients attending the NHS Specialised Services Clinic in Newcastle. Three hundred and fourteen patients were assessed.

**Results:** Nonverbal processing speed declined 0.023 SD per year ($p < 0.01$), whereas verbal processing speed did not ($p = 0.12$). Adjusting for baseline age and premorbid cognitive functioning, mitochondrial disease severity, as measured by the Newcastle Mitochondrial Disease Adult Scale, had a significant effect on verbal ($p < 0.01$) and nonverbal processing speed ($p < 0.01$). Non-verbal processing speed decreased by 0.03 SD per 1% increase in disease severity; verbal processing speed by 0.025 SD. The effect was similar at all ages.

**Conclusion:** Disease burden has a significant detrimental effect upon both verbal and non-verbal processing speed in patients with mitochondrial disease and may be an important contributor to cognitive and functional difficulties. We propose, in future, to explore this effect over time.

**Genetic influences on flow proneness and its relationship to behavioral inhibition and locus of control**

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Flow is a subjective experience of high but effortless attention, loss of self-awareness, control, and enjoyment that can occur during active performance of challenging tasks and has been shown to be associated with personality, specifically with low neuroticism and high conscientiousness. The first study aimed to investigate genetic and non-genetic influences on flow-proneness (FP) in 444 adult twin-pairs. Our second study further explored the genetic architecture of the relationship between flow-proneness and personality, in particular behavioral inhibition (BI) and locus of control (LoC)—both highly related to neuroticism and conscientiousness. All three traits (i.e., FP, BI, and LoC) are influenced by dopaminergic neural systems. Data were collected using an on-line administration of the Swedish Flow Proneness Questionnaire (assessing FP in three major domains of life: work, maintenance, and leisure), the Adult Measure of Behavioral Inhibition, and the Locus of Control Scale. We found moderate (0.29–0.35) heritabilities for the flow scales. Genetic influences were almost entirely shared for the three flow scales and genetic correlations between the scales were very high (0.81–0.97), suggesting that the same genes influence FP independently of domain. Non-shared environmental influences were largely specific to each flow scale. The relationship between FP and the two personality traits (BI and LoC) was entirely explained by shared genetic influences. However, this shared genetic factor only explained a small part of the genetic influences on BI and LoC. Accordingly, genetic correlations were only moderate ranging between 0.33 and 0.42 with the environmental correlations being close to zero. We conclude that an individual’s general proneness to experience flow is influenced by the same genetic factors regardless of domain, while specific environmental factors appear to be of importance for within-individual differences between domains. The relationship between FP with LoC and BI, respectively, is entirely due to shared genes.

**Regime switching models for substance use data:**

Michael Neale; Virginia Commonwealth University Shaunna Clark; Virginia Commonwealth University

Latent growth curve mixture modeling (LGCM) is a popular approach for the analysis of repeated measures data. The population is assumed to consist of at least two subgroups, and individuals within these groups conform to a particular estimated growth curve model throughout the measurement period. For certain behaviors, this fidelity to a single growth curve model may not describe the data accurately. One example is substance abuse data, where use patterns may include periods of abstinence and periods of heavy use. An enhancement to LGCM is to allow for regime switching [C.V. Dolan et al., Structural Equation Modeling 2005 12:94–119]. In this model, class membership is not static throughout the occasions of measurement; probabilities of switching between classes are estimated as well. The use of the R package OpenMx to construct and this model is described. The extension of the model to data collected from relatives is also discussed. Application to data on substance use reveal a limited number of classes but substantial probabilities of switching between them.

**Pregnancy illegal drug use and toddler emotional reactivity: Genetic and parenting influences and their interaction**

Jena Neiderhiser; The Pennsylvania State University Charles Beekman; The Pennsylvania State University Gordon Harold; University of Leicester Leslie Leve; Oregon Social Learning Center Daniel Shaw; University of Pittsburgh Jody Ganiban; George Washington University David Reiss; Yale

We examine the effects of pregnancy use of illegal drugs, genetic influences, and parenting on toddler emotional reactivity (ER) using a prospective adoption design. Genetic influences on toddler ER are included via birth mother (BM) lifetime drug abuse and parenting via adoptive mother (AM) self-reports of overreactive parenting. The sample is part of the Early Growth and Development Study; 561 sets of BMs and adoptive parents linked through the adopted child and 208 birth fathers. The Life History Calendar method is used to assess BM pregnancy substance use and lifetime drug use is assessed using symptom counts on the CIDI-SF and diagnosis of drug abuse or dependence on the CIDI. Parenting is assessed using parent self-reports of overactive parenting behavior. Consistent with literature that children have lower ER when exposed to drugs prenatally, toddler ER at 18 months was assessed via parent reports from the CBC.

Findings indicate a direct negative effect of pregnancy use of illegal drugs, genetic influences, and parenting on toddler emotional reactivity (ER) using a prospective adoption design. Genetic influences on toddler ER are included via birth mother (BM) lifetime drug abuse and parenting via adoptive mother (AM) self-reports of overreactive parenting. The sample is part of the Early Growth and Development Study; 561 sets of BMs and adoptive parents linked through the adopted child and 208 birth fathers. The Life History Calendar method is used to assess BM pregnancy substance use and lifetime drug use is assessed using symptom counts on the CIDI-SF and diagnosis of drug abuse or dependence on the CIDI. Parenting is assessed using parent self-reports of overactive parenting behavior. Consistent with literature that children have lower ER when exposed to drugs prenatally, toddler ER at 18 months was assessed via parent reports from the CBC.

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Genetic architecture of the pro-inflammatory state in an extended twin-family design

Melanie Neijts; VU University, Amsterdam Jenny van Dongen; VU University, Amsterdam Eco de Geus; VU University, Amsterdam Gonneke Willemensen; VU University, Amsterdam Dorret Boomsma; VU University, Amsterdam

Introduction: The pro-inflammatory cytokines TNF-α and IL-6, and the acute phase proteins CRP and fibrinogen are characteristic of the pro-inflammatory state that serves as a risk factor for many diseases including major depression and heart disease. In addition, it is suggested to be the reason for the co-morbidity between the two. We extended the classical twin design with non-twin siblings and parents in the largest set of twins with data on TNF-α, IL-6, CRP and fibrinogen to date. The large sample size and the extended twin-family design allows us to estimate the extent of additive (A) and dominant (D) genetic effects, as well as shared (C) and unique (E) environmental factors with high precision.

Methods: Between January 2004 and July 2008, 9,530 participants registered in the Netherlands Twin Registry were visited at home for collection of blood and urine samples. CRP, fibrinogen, TNF-α, and IL-6 values were determined in fasting blood samples. Genetic analyses were performed using structural equation modeling in the software package Mx. First, a non-restrictive, fully parametrized model was fitted to the data to freely estimate the sample descriptive and covariance structures among relatives. Next increasingly restricting models were fitted to the data in order to arrive at the most parsimonious model that explained the data best.

Results: A moderate but consistent degree of heritability was found for all immune parameters, ranging from 27 to 41%. For TNF-α and for CRP in females, dominance was implicated. E was implicated in all parameters. A small part of the variation in fibrinogen and CRP was due to C as well.

Conclusions: Genetic factors play a significant role in explaining individual variation in the pro-inflammatory state. These heritability estimates provide a clear numerical target for ongoing genome-wide screens attempting to find the actual genetic variants underlying the pro-inflammatory risk profile.

Exome sequencing of an isolated Chilean population affected by Specific Language Impairment (SLI)

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Speech and language impairments that are a primary deficit and have no obvious cause (e.g. a comorbid neurological disorder like autism) are diagnosed as Specific Language Impairment (SLI). SLI affects 5–8% of preschool children and represents a lifelong disability associated with an increased risk of behavioural disorders, social problems and literacy deficits. SLI is highly heritable and twin studies indicate a strong genetic basis. Nonetheless, the underlying genetic mechanisms are expected to be multifactorial and, to date, only three risk variants have been identified. One way to increase the power to detect contributory genetic factors is to study isolated populations derived from relatively recent shared ancestors (founder populations). In 2008, Villanueva described a founder population with a particularly high incidence of SLI (10 times that expected). They inhabit the Robinson Crusoe Island, which lies 677 km to the west of Chile and was colonised in the late 19th century by 8 European and Amerindian families. 77% of the current island population have a colonising surname and 14% of marriages involve consanguineous unions. More than 80% of language impaired individuals can be traced to a pair of founder brothers. This population thus has a short (5-generations) and well-documented history and represents a unique resource which could make valuable contributions to the elucidation of genetic mechanisms underpinning SLI.

We applied exome sequencing technologies to five language-impaired individuals from this population and identified nine non-synonymous coding changes or splice site mutations that were present in at least three of the five affected individuals sequenced. Sequencing of the entire cohort identified a single non-synonymous coding change that was significantly more frequent in cases than controls (genotype frequencies of 46 and 11% respectively, \( p = 4.48 \times 10^{-7} \)). We suggest that this rare coding variant may contribute to the elevated frequency of SLI in this population.

Genetic and environmental influences on gender specific income differences

Camilla Nexoe; VIPBG Virginia Commonwealth University Brad Verhulst; Virginia Institute of Psychiatric and Behavioral Genetics Lindon Eaves; VIPBG, Virginia Commonwealth University

Previous research has demonstrated that the additive genetic components of a wide range of phenotypes vary across the lifespan (Eaves et al. 2008; Hatemi et al. 2009). Interestingly, for several social traits shared environmental factors dominate the pattern of transmission during childhood and early adolescence, and then markedly drop after the child leaves the family home when additive genetic factors take on greater importance (Hatemi et al. 2009). This study focuses on income differences between opposite sex dizygotic twin pairs (DZO) in order to explore sex specific effects on the means that are masked when focusing on variance decomposition methods. Using cross sectional data from adult twins aged 17–93 (Virginia 30,000), we find male DZO twins (\( M = 4.85, SD = 2.01 \)) have significantly higher incomes than females (\( M = 3.03, SD = 1.83 \)) (\( t(2,373) = 22.84, p = 0.0000 \)). Importantly, there are no significant differences between levels of education for DZO twin pairs, suggesting sex differences in income are not based on previous sex differences in education. Centrally, preliminary analyses suggest that the average inter-pair differences in level of income among DZO twins increase with age. While there is close to no difference in level of income among brother and sister in the late teenage years (\( M = 1.62, SD = 0.88 \) \( M = 1.57, SD = 1.04 \)) (\( t(117) = 0.3056, p = 0.3802 \)), the sex specific differences in level of income is found to be significant in all other age cohorts from 23 years of age and up. Most evident is the mean differences in level of income between brother and sister in the age cohorts 41–46 (\( M = 5.66, SD = 1.71 \)) (\( M = 3.26, SD = 1.89 \)) (\( t(213) = 9.77, p = 0.0000 \)) and 53–58 (\( M = 6.08, SD = 1.56 \)) (\( M = 3.44, SD = 2.07 \)) (\( t(225) = 10.91, p = 0.0000 \)). Implications for gender inequalities in income and education are discussed.
Phenotypic complexity as genetic dark matter: A network explanation of missing heritability

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For many psychiatric disorders, combined effects of candidate SNPs together explain only a fraction of the genetic variance as estimated in twin studies. This phenomenon is known as missing heritability. Available explanations of missing heritability are either based on genetic measurement or focus on methodological issues. We propose an additional mechanism that may produce missing heritability in psychiatry, which emerges from novel models for mental disorders. In this proposed model, psychiatric symptoms directly affect each other (rather than being correlated as a result of the influence of a common latent variable). To show how missing heritability arises from a symptom network, we simulate a network model for major depression, in which symptoms are connected through causal pathways (e.g., insomnia → fatigue → concentration loss). Genetic effects are introduced as modifying the strength of these pathways, so that an individual’s genetic constitution influences the structure of that individual’s network. We simulate data for monozygotic and dizygotic twins to estimate genetic effects, and then attempt to trace these effects to the genes responsible. We show that, even under an extremely simple additive genetic model, 40% of the genetic variance goes missing, in the sense that it becomes untraceable using standard methodology. We propose that explicitly modeling psychiatric disorders as complex phenotypes may increase the chances of identifying their genetic determinants.

Disentangling the relationship between BMI and health-related quality of life

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The relationship between Body Mass Index (BMI) and Health-Related Quality of Life (HRQoL) has been reported in different settings, ages and samples. Both of them are relevant variables from a public health perspective and are strongly associated to morbidity and mortality. There is persistent evidence of high heritability for variation in BMI. Fewer studies have analyzed the relative influence of genetic factors on HRQoL and the available reports show moderate heritability. The current study sought to disentangle the relationship between BMI and HRQoL in a population-based sample of adult female twins. The data comprised 215 MZ and 220 DZ pairs from the Murcia Twin Register, in Spain. Mean age = 55.2 (SD 7.4; Range = 43–69). Height and weight were objectively measured during a personal interview to calculate BMI. HRQoL is based in the descriptive system of the EQ-5D questionnaire. EQ-5D index was obtained using the appropriate value set for Spanish population. As expected, mean BMI was high = 27.65 (SD 5.1) in this sample. Consistent with previous studies, BMI and HRQoL showed a negative significant correlation (r = −0.267). Of the variance associated with BMI and HRQoL, 69 and 33% was attributed to additive genetics respectively, and the rest was attributed to unshared environment. According to bivariate analysis virtually all the phenotypic correlation (99%) between BMI and HRQoL was due to the effect of shared genes. Our results highlight the importance of genetic factors on the relationship between BMI and HRQoL.

The role of conduct disorder in explaining the common genetic influences on initial sensitivity to alcohol and tobacco

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Background: Initial sensitivity to psychoactive drugs, such as alcohol and tobacco, may reflect the impact of psychoactive and pharmacological properties, and are predictive of later use and dependence. Emerging studies suggest common genetic mechanisms across these behaviors (Haberstick et al. 2011, Addiction, 106:215–224; 106:391–399), however, it is unclear how this early indicator of future substance use is etiologically related to one of the most robust predictors of substance dependence, conduct disorder (CD; Riala et al. 2011, Eur Child Adolesc Psychiatry, 20:393–399). This study investigated the extent to which genes and environment contribute to the covariance between CD and the liability for sensitivity to alcohol and tobacco. Methods: 3,753 individuals from the Missouri Adolescent Female Twin Study, who participated at the baseline wave of assessment, were assessed for CD, and sensitivity measures to first experiences with alcohol and tobacco (i.e., During your first cigarette/drink did you experience—cough, heart racing, headache, sleep, etc.). Symptom counts were age-adjusted and rank normalized to better approximate a normal distribution. Phenotypic associations were determined after adjusting for family structure. A trivariate Cholesky was used to partition the variance and covariance between the traits. Results: The heritability estimates for CD and sensitivity to alcohol and tobacco were 60, 28, and 37%, respectively. Genetic and environmental effects on the sensitivity to alcohol and tobacco partially overlapped (rA = 0.40[0.19,0.61], rE = 0.16[0.06,0.26]). The ACE trivariate Cholesky suggested that sensitivity to alcohol and tobacco shared common additive genetic and non-shared environmental factors with CD. Based on the best-fitting model, 60–70% of covariance between drugs was attributable to a common genetic factor. Conclusion: We conclude that conduct disorder partly explains the covariation of alcohol and tobacco sensitivity. Specifically, a portion of the shared genetic effects between is explained by the genetic contribution common with CD.

Genetic patterning of white matter/gray matter signal intensity contrast: A new phenotype for imaging genetics studies

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Variation in signal intensity contrast between white matter and gray matter (Wm/Gm contrast) along the cortical mantel has traditionally
been viewed as a nuisance variable in structural neuroimaging because it complicates the estimation of the gray-white boundary and cortical thickness. More recently, however, this phenotype has been shown to be an informative marker of tissue integrity and possibly of subtle neuropathology. Hypothesized to reflect, at least in part, the degree of myelination of the white matter fibers under the cortical mantle, Wm/Gm contrast decreases substantially during later life and in non-uniform patterns across the cortex. Differences in Wm/Gm contrast have also been observed between samples of normal aging adults and those with Alzheimer’s disease. Such findings suggest that Wm/Gm contrast is highly relevant to understanding brain aging. We recently demonstrated that at the level of predefined regions of interest (ROIs), Wm/Gm contrast is significantly heritable, and that it is genetically distinct from corresponding measures of cortical (gray matter) thickness. In the present study, we expand upon this work and map the heritability of Wm/Gm contrast across the entire cortical surface, independent of predefined ROI boundaries. Data were obtained from 514 male twins ages 51–59 (130 monozygotic pairs, 97 dizygotic pairs, and 60 unpaired individuals) in the Vietnam Era Twin Study of Aging (VETSA). In addition to the examination of heritability, we created continuous (vertex-wise) maps of genetic correlations between several seed points of Wm/Gm contrast and all other points in order to determine if the same or different genes influence this phenotype across the brain. Results further support that Wm/Gm contrast is a meaningful and genetically distinct neuroimaging phenotype. We conclude that, in addition to cortical thickness and cortical surface area, Wm/Gm contrast is essential for understanding the genetic and environmental determinants of brain structure and brain aging.

The 2p12 dyslexia risk locus is associated with general cognitive ability and white matter density

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Candidate genes for dyslexia and specific language impairment (SLI) have been shown to impact upon reading/language-specific traits in the general population. Their effects seemed to affect vary specific cognitive traits. It has been shown that many of the dyslexia risk genes (KIAA0319, DCDC2, DYX1C1 and ROBO1) are involved in cortical development and specifically in neuronal migration. An important, and still unanswered, research question is therefore how genes involved in such a general process as cortical development contribute to the risk for specific disorders. To further explore the impact of disorder-associated genes on cognitive functions, we investigated whether they play a role in broader cognitive phenotypes. We tested a panel of dyslexia (KIAA0319, DCDC2, DYX1C1 and the MRPL19/C2ORF3 locus) and SLI (CMIP and ATCP2C2) genetic risk factors for association with two measures of verbal and non-verbal general cognitive abilities, in the Avon Longitudinal Study of Parents and Children (ALSPAC) cohort (N > 5,000). The MRPL19/C2ORF3 locus showed statistically significant association ($p = 0.00009$) which was further supported by independent replications in four other cohorts. In addition, a fifth independent sample showed association between the MRPL19/C2ORF3 locus and white matter structure in the posterior part of corpus callosum and cingulum, connecting large parts of the cortex in the parietal, occipital and temporal lobes. General cognitive ability, assessed with standardised intelligence tests, is a highly heritable trait, yet very few genetic factors have been identified for influencing this trait. In addition, most of the reported candidate gene studies have lacked adequate sample size in discovery samples and were not supported by independent replications. We conclude that the MRPL19/C2ORF3 locus, originally identified as a dyslexia candidate, is likely to harbour genetic variants associated with general cognitive abilities possibly by influencing white matter structure in localised neuronal regions.

Dissociable genetic influences on continuous performance task indices

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Attention-deficit/hyperactivity disorder (ADHD) is a complex, heritable childhood disorder with unclear etiology. Numerous dopaminergic candidate genes, including the catechol-O-methyltransferase gene (COMT) and the dopamine transporter gene (DAT1), have been examined for association with ADHD, but yielded inconclusive findings. Instead of relying on manifest diagnoses or symptoms, using endophenotypes may yield stronger, more replicable results in molecular genetic studies of ADHD. Deficits in neurocognitive functions have been proposed as putative endophenotypes for ADHD, as individuals with ADHD have been shown to be impaired in various neuropsychological laboratory measures, including the Continuous Performance Task (CPT), a widely-used measure of sustained attention and impulsivity. Distinct indices of CPT performance (i.e., omission and commission errors, sensitivity, and response bias) have been shown to be related to COMT and DAT1, but there have been no studies examining genetic influences on the trajectories of these indices over time (i.e., across blocks). In this study we investigated the association between CPT indices and COMT and DAT1, considering both overall performance as well as performance across blocks. We recruited a large clinically-referred sample who were genotyped for the COMT val108/158met polymorphism and the DAT1 40 bp VNTR polymorphism, and administered a variant of the CPT (i.e., the AX-CPT). Analyses of overall performance indices revealed a marginally significant association between COMT and commission errors and sensitivity, a marginally significant association between DAT1 and response bias, and a significant association between DAT1 and commission errors. Analyses of performance indices across blocks revealed a trend for the interaction between COMT and block for response bias. These results provide support for a role of COMT and DAT1 in distinct overall CPT performance indices, and also suggest that COMT may potentially contribute to response style trajectories across time.

Multivariate, multi-method model of P300 amplitude and externalizing psychopathology: Evidence for a highly heritable combination

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P3 amplitude reduction (P3-AR), a highly heritable event-related potential, is one of the best-documented endophenotypes of disinhibitory/externalizing psychopathology (EXT). Yet, few molecular genetics studies have utilized the information provided by P3-AR to identify putative disease genes. One reason may be that the correlation between diagnostic outcome data measured using interview/self-report and P3-AR data measured using physiologic recording is attenuated by method variance (e.g., variance specific to how each
On the association of common polygenic variation with body mass index across adolescent development: A longitudinal twin study

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There have been few genetically informative longitudinal studies examining the stability of body composition over time. However, there is some evidence to suggest additive genetic effects associated with BMI are relatively stable across adolescence as indicated by genetic cross-time correlations upwards of 0.80. In contrast, the environmental cross-time correlations have been shown to decrease over time and common environment has been shown to be important in early but not late adolescence or adulthood. Furthermore, genome-wide association studies (GWAS) of BMI using large-scale adult samples have yielded 32 robustly associated variants. Of which 23 were associated with BMI in a cross-sectional analysis of children and adolescents. Further research needs to address when in development these variants become important for predicting BMI. Given the dramatic increase of obesity prevalence in both children and adults in developed countries and the numerous negative consequences associated with elevated body weight, future research is warranted to understand the genetic and environmental contributions to BMI trajectories across adolescence. Therefore, the purpose of this research is to utilize a developmental twin study design to (1) test for changes in the relative contributions of genes and environment, (2) test for shared genetic and environmental liability across time, (3) identify factors driving change versus maintaining stability and (4) evaluate association of validated BMI-SNPs across adolescence to develop-mental continuity/change of BMI. BMI was calculated from weight and height collected on up to four waves and ages ranged from 8 to 18 in 2,794 twin participants from the Virginia Twin Study of Adolescent Behavioral Development (ABD). Preliminary results suggest that SNPs in FTO and TNN13K are associated with BMI from age 11 through development and a SNP in MC4R is associated from age 17. Understanding obesity development will aid in identifying obeseogenic vulnerability time-points and facilitate targeted prevention and treatment efforts.

The role of evaluation in the genetic structure of externalizing and internalizing spectra

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Investigations into the genetic structure of common Axis I and II diagnoses and symptoms tend to generate two positively correlated spectra, namely, internalizing and externalizing. In a recent investigation, however, these spectra became negatively correlated after controlling a general factor of psychopathology. We re-interpret this general factor as evaluation, which is the tendency to endorse items based on their perceived valence irrespective of actual content. Thus, the evaluative dimension may cluster items of opposite meaning as long as they have similar valence (e.g., sluggish and manic). Because this dimension appears unlikely to tap a consistent behavioral style, we advocate isolating it from descriptive variance. First, we demonstrate that evaluation is a problem in multivariate genetic structure. Second, we re-analyze published data on Axis I and II diagnoses to show that internalizing and externalizing disorders become inversely related controlling evaluation. Third, we fit a four-factor genetic model (RMSEA = 0.06) to 686 (346 MZ) twins who self-reported on the Dimensional Assessment of Personality Pathology instrument. Subsequently, we rotated the four genetic factors to simple structure using Oblimin, which rendered a positive correlation (r = 0.37) between an internalizing factor (positive loadings included submissiveness and anxiousness) and an externalizing factor (positive loadings included callousness and conduct problems). We then proceeded to isolate evaluative variance onto a separate factor using a partially specified orthogonal target rotation. Whereas all problems loaded in the same direction on the evaluative factor, on one of the non-evaluative factors, internalizing traits (submissiveness, anxiousness) and externalizing traits (callousness, conduct problems) loaded in the opposite direction. We conclude that internalizing and externalizing disorders are similar in that they are both negative, but that they are opposite in the ways they are negative.

ADHD symptoms and atypical hypothalamic–pituitary–adrenal axis functioning: Evidence for familial overlap and moderating effects of oppositional behaviours

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Attention-deficit/hyperactivity disorder (ADHD) has been linked to dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis, indexed by salivary cortisol. Whether this association is explained by co-occurring oppositional symptoms, remains controversial. We aimed to investigate the phenotypic and etiological association of ADHD symptoms with cortisol reactivity, and the moderating effects of co-occurring symptoms. Salivary cortisol was obtained across three time points during a cognitive testing session from a twin sample of 68 male pairs, ages 12–15, who were selected based on consistently high or low parental ADHD ratings. We applied a genetic latent growth-curve model (GMC) to the data, to examine the etiological association of a latent ADHD factor with the intercept (baseline) and slope (rate of change) factors. Correction for selection was accomplished by including the population twin sample ADHD scores (3
index variables) in the model. The correlation between the ADHD latent factor and the slope factor of the GCM was significant (−0.37 (−0.94, −0.05)). This association was due to familial effects (X2 (df = 2) = 6.29, p = 0.04), but we had insufficient power to establish whether this was mainly due to genetic or shared environmental effects. When examining the moderator effects on the slope mean using only the GCM part of the above model, we found ADHD affection status moderated the slope mean (−0.16 (−0.28, −0.04)), with cortisol levels dropping faster for affected individuals. A similar pattern was observed for oppositional behaviours on the slope mean (−0.17 (−0.30, −0.03)), indicating cortisol levels dropped faster as oppositional symptoms increased. Moreover, when modelling the moderator effects of oppositional behaviours, the effect of ADHD affection status was no longer significant. We identified the rate of change in cortisol reactivity as an index of HPA axis activity that shows a familial association with ADHD. However, this association is primarily driven by oppositional symptoms.

The genetics of experience: From passive to active approaches

Robert Plomin; King’s College London Bonamy Oliver; King’s College London

In 1991, a target article in Behavioral Brain Sciences, called ‘The Nature of Nurture,’ pulled together research that pointed to what at first seemed an odd finding: Measures widely used as indices of environmental experience show significant genetic influence (Plomin & Bergeman 1991). Far from being a mere methodological point—that measures ostensibly assessing the environment are contaminated by genetic influence—this finding has profound implications. It leads to a perspective that transcends the traditional passive view of environments as imposed on the individual, to suggest an active model of the environment in which individuals, in ways correlated with their genetic propensities, shape their experiences. This active approach to the genetics of experience is the focus of this presentation. First, we reflect on the nature-of-nurture research over the past 20 years. Next, we discuss the major new development in this area, namely research on the behavioral causes and consequences of genetic influence on environmental measures using multivariate genetic techniques. This new research provides insights into the genetics of experience which could lead to measures of ‘shaped’ experiences rather than ‘imposed’ environments. Third, we consider an exciting development for this field that was not anticipated in the 1991 article: the potential offered by new advances in DNA research to identify genes that contribute to the genetics of experience. The long-term goal is to build an active model of the genetics of experience from the bottom up, by understanding how genotypes use their environments to become phenotypes, at all levels from genes to brain to behavior.

Current DNA arrays account for at least half of the genetic influence on cognitive abilities

Robert Plomin; King’s College London Oliver Davis; King’s College London

For nearly a century, twin and adoption studies have yielded substantial estimates of heritability for cognitive abilities. In common with many medical disorders, recent large-scale genome-wide association studies have struggled to identify the genetic variants that account for this, a puzzle known as “missing heritability”. However, a new approach brings together the strengths of quantitative and molecular genetics, forgoing the identification of individual polymorphisms to estimate the total heritability captured by genotyping arrays. In the same sample of 3,000 12-year-old twin pairs, we directly compared heritability estimates for cognitive abilities with the heritability captured by 1.7 million DNA polymorphisms. We found that polymorphisms tagged by the array account for 60 % of the estimated heritability on average, reaffirming that cognitive abilities are both heritable and highly polygenic, similar to height and weight. Larger sample sizes alone will be sufficient to identify many of the genetic variants that influence human cognition.

Phenotypic and genetic association between attention problems and autistic traits in adults is mainly mediated by attentional switching ability

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ADHD related symptoms and autistic traits often co-occur. The pattern and etiology of co-occurrence are largely unknown, particularly in adults. This study investigated the associations between both traits in detail, and subsequently examined the etiology of these associations, using two independent adult population samples.

Data were collected in a population sample (n = 559, S1) and a population based family sample of twins and siblings (n = 560, S2). In S1 Inattention and Hyperactive symptoms were measured with the CAARS. In S2 the Attention Problem (AP) scale of the YSR, tapping mainly inattention, was used. The abridged version of the Autism-spectrum Quotient (AQ-Short) was administered in both samples to assess five dimensions of Autistic Traits (social, routine, attentional switching, imagination, patterns).

Hyperactive symptoms (S1) did not correlate substantially with the AQ-Short scales. For Inattention (S1) and AP (S2) the correlations with the AQ-Short scales were also low except for a prominent correlation (0.47 and 0.36 resp.) with the attentional switching scale. Analyses in S2 revealed that this association was completely explained by a shared genetic factor.

We report strikingly similar findings in two independent samples, suggesting that the co-occurrence of ADHD related symptoms and autistic traits in adults, is mainly determined by problems related to cognition (inattention problems and switching attention capacity) and not by social or behavioral problems. As the etiology of this association is purely genetic, biological pathways involving cognitive control could be a promising focus of future studies aimed at unraveling genetic causes of these disorders.

Does the maternal immunity hypothesis explain individual differences in cognition?

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The prenatal hormonal environment has lasting influences on brain organization and influences a wide range of phenotypes. For example, prenatal hormonal effects have been used to explain the observation that homosexual orientation is more common in men
with several older brothers, Blanchard (2001) has proposed the maternal immunity hypothesis—that younger brothers have reduced in utero androgen sensitivity due to maternal Y-specific antibodies that develop and accumulate across successive male pregnancies. This hypothesis predicts that the effect should be seen in younger brothers of males but not in younger brothers of females or in younger sisters. Prior studies of the immunity hypothesis have used between-family tests. We used a within-family design to test whether the maternal immunity effect applies to cognitive variables for which androgenization effects have been proposed, based on higher population mean scores among males than females. Data came from >30,000 adolescent sib pairs and triads participating in Project Talent (Flanagan 1962), a representative sample of >400,000 U.S. high school students. We found significant negative effects of older brothers on cognitive performance in males, which persisted after adjusting for family income and total number of siblings. An effect of older brothers was also observed in females, but to a lesser extent. The effect occurred for cognitive abilities for which males had better average performance, including mechanical reasoning and mental rotation, but also for abilities without sex differences. These results are consistent with the maternal immunity hypothesis but also with other biological or social mechanisms associated with being a younger sibling.

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Depressive symptoms and lifetime cigarette use during adolescence

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Depression frequently co-occurs with nicotine dependence. However, the etiology underlying these common conditions is unclear because of their complexity, including common environmental risk factors and biological systems. Further, it is unclear how common risk factors function across important developmental periods such as adolescence. A prospective cohort sample of 1,441 adolescent twin pairs ages 8–18 years from the longitudinal Virginia Twin Study of Adolescent and Behavioral Development (VTSABD) was assessed for lifetime cigarette use and depressive symptoms across three waves. Number of recent depressive symptoms was a significant risk factor for smoking during a subsequent wave in both males and females during early adolescence ($b_{males} = 0.30, p = 0.0001$; $b_{females} = 0.22, p = 0.003$). However, the number of recent depressive symptoms was a significant risk factor for lifetime smoking only among females in later adolescence ($b_{females} = 0.26, p = 0.002$). While sex differences were found in univariate estimates of genetic and environmental effects in lifetime smoking, they were mostly not significant. However, the characterization of shared and specific genetic/environmental contributions between recent depressive symptoms and later smoking across waves indicated different genetic and environmental effects for males and females. These results suggest important implications of the use of smoking phenotypes informed by developmental genetic and environmental trajectories for use in genome-wide association studies as well as for smoking prevention and education.

Locating drunk driving on the externalizing spectrum: A multidimensional scaling approach

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Drunk driving is a major contributor to alcohol-related injury and mortality among social and problematic drinkers. Despite the prevalence of drunk driving, questions remain regarding its etiology and its relation to disordered alcohol use, and relatively little behavioral genetic research has tested the extent to which this association reflects common familial influences or environmental experiences. This investigation used longitudinal data from a sample of 517 same-sex twin pairs from the National Longitudinal Study of Adolescent Health to examine genetic and environmental associations between drunk driving and an array of externalizing behaviors during adolescence and early adulthood. Replicating previous findings, we found evidence for additive genetic and non-shared environmental influences on drunk driving. We conducted multidimensional scaling analyses of the genetic and non-shared environmental covariations among drunk driving and eight other adolescent and early adult externalizing behaviors. In the resulting genetic “map,” drunk driving was located near the center of the radex, reflecting the strength and consistency of its genetic mediacy mediated by externalizing phenotypes. In contrast, non-shared environmental associations were more diffuse. Moreover, whereas the phenotypic association between drunk driving and alcohol dependence symptoms was largely explained by common genetic factors, the majority of the genetic variance in drunk driving was unique of dependence symptoms. Taken together, these results suggested that drunk driving is not simply a symptom of alcohol dependence but rather can be considered a marker of genetic vulnerability to a broad externalizing spectrum.

Negative parenting and externalizing behavior across preschool: A cross-lagged analysis

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Previous research with adolescent and school age children suggests that links between parenting and externalizing behaviors are, in part, explained by child-based evocative effects. The current study used a cross-lagged design to assess evocative processes during the preschool years, when externalizing behavior first emerges. Analyses examined: (1) stability in mother negativity and children’s externalizing behavior; (2) the mutual influence of each construct over time; and (3) the contributions of child-based genetic and environmental factors to stability and change in parenting and externalizing behavior. Participants were drawn from the Boston University Twin Project (BUTP). The BUTP includes 312 same-sex twin pairs (NMZ = 144, NDZ = 168), assessed at ages 2 and 3 years. Mothers’ reported on their own negative disciplinary strategies (Parenting Scale), and their children’s externalizing behavior (Child Behavior Checklist). Analyses identified significant genetic, shared, and nonshared environmental contributions to parenting and externalizing behavior at each age. Phenotypic correlations between constructs ranged from 0.47 to 0.53 within each age. At 2 and 3 years, genetic and nonshared environmental correlations were significant (rg 0.36–0.58, re = 0.33–0.53). Shared environmental factors were only correlated at age 2 ($r_c = 0.41$). Parenting and externalizing behavior were moderately stable over time (β’s 0.54–0.56). Genetic factors
explained stability in externalizing behavior, while genetic and shared environmental factors accounted for stability in parenting. Significant cross-lagged effects were present ($\beta$’s 0.17–0.18), and were explained by children’s genetic makeup and shared environment.

These findings are consistent with evocative child effects: children’s genetically influenced characteristics contributed to the parenting they received within each age and over time, and primarily explained the cross-lagged association between parenting at age 2 and externalizing behavior at age 3. Findings also highlighted children’s shared environment as an important contributor to change and stability in parenting, and early links between parenting and externalizing behavior.

Models and procedures for gene-by-environment interactions in behavior genetic designs:
Computational procedures and simulation results

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In an earlier paper (“New Models and Procedures for Gene-by-environment Interactions in Behavior Genetic Designs”) to which this poster is intended as a companion, we presented new statistical models for examining gene-by-environment interaction ($G \times E$) in behavior genetic designs. As some of those models cannot be estimated with standard statistical software, we have developed new computational algorithms for fitting them. Here, we first present a likelihood formulation and decomposition for these models that facilitates computation considerably. We then present our computational approach using an adaptive numerical integration routine. The method is implemented in the R statistical software environment and utilizes some parallel computing tools available in most installations of R. We also present details of the design and results of simulation studies conducted with these new tools.

New models and procedures for gene-by-environment interactions in behavior genetic designs

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An influential paper by Purcell (2002) proposed a method for testing interactions between latent genetic influences and measured environments ($G \times E$) in the presence of gene-by-measured environment correlation. We (Rathouz et al. 2008) examined statistical aspects of Purcell’s approach and found in preliminary studies that it incorrectly identifies $G \times E$ when it does not exist under some conditions. To address this issue, we proposed a new class of statistical models and suggested how they can be compared to test for $G \times E$. Picking up on that work, in this paper, we first embed Purcell’s model in a broader class of biometric models for $G \times E$, focusing on interpretability of the various members of this class. We then discuss how to fit and test these models, as some are not estimable in standard structural equation modeling software. We present simulation studies examining the statistical operating characteristics of these procedures in twin samples. Finally, we illustrate our approach with an analysis of the moderation of genetic influences on anxiety by birthweight in a community twin sample of children. This paper will be followed up by a companion poster entitled “Models and Procedures for Gene-by-environment Interactions in Behavior Genetic Designs: Computational Procedures and Simulation Results”.

Etiology of change in cognitive abilities from adolescence to early adulthood in the Colorado Adoption Project

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The salience of earlier life on the maintenance and change of cognitive abilities in old age has become increasingly appreciated. However, few behavioral genetic studies have focused on early adulthood period, as it has been presumed that cognitive performance is largely stable. Phenotypic and biometric analysis of latent change from three assessment points spanning 20 years were evaluated in the Colorado Adoption Project (CAP) sample. The current study evaluated cognitive factors developed from the CAP adult battery. At each assessment, the cognitive subtests forming the factors were standardized against the means and standard deviations of the biological parents of the adoptive probands, and identical factor weights applied, which resulted in a common scale to study change across time. The factors included a general cognitive ability factor, as well as verbal, spatial, speed and memory factors. Phenotypic analyses of general cognitive ability trajectories in 796 CAP siblings from 447 families evidenced significant performance declines across ages 16–36 years and increasing variability in performance. Initial biometric analyses conducted in Mx indicated that the increasing phenotypic variance in general cognitive ability was due to increasing genetic variance, whereas shared and nonshared environmental variance contributing to trajectories were small and comparatively stable. Heritability of the intercept (reflecting age 16 performance) and linear change slopes were 0.77 and 0.63, shared environmental effects at 0.09 and 0.33 and non-shared environmental effects at 0.14 and 0.05, respectively. Biometrical models fitted to specific cognitive abilities supported similar patterns of increasing genetic variance for spatial and speed factors, while verbal and memory factors indicated an increasing role for environmental influences. Overall the findings suggest that early adulthood is an important period in which to address emergent etiological factors underlying growth and decline in cognitive performance because it may set pathways for mid- and late-life cognitive health.

Testing a developmental propensity model of conduct problems

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The adverse impact of conduct problems on both the individuals engaging in conduct problems and society makes the examination of its etiology extremely important. We tested the “developmental propensity model” (B. B. Lahey and I. D. Waldman (2003) in B. B. Lahey, T. E. Moffitt, and A. Caspi, eds., Causes of conduct disorder and juvenile delinquency, Guilford Press, New York), which advances specific and testable hypotheses regarding the etiology of conduct problems, proposing three dimensions of temperament (i.e., negative emotionality, daring, and low prosociality) and low
cognitive abilities as distinct components of “antisocial propensity”. The participants were 476 pairs of monozygotic (MZ) and dizygotic (DZ) same-sex twin pairs from the Colorado Longitudinal Twin Study (LTS). Negative emotionality, behavioral inhibition (the inverse of daring), concern and disregard for others (constructs closely related to prosociality), and cognitive ability assessed via parent report and observations between age 14 and 36 months were examined as predictors of conduct problems assessed in middle childhood and adolescence via three sources (parent report from age 4 to 12, teacher report from age 7 to 12, and self report at age 17). Observed disregard for others and cognitive ability were significantly associated with later conduct problems assessed via parent, teacher, and self report, and the covariance between antisocial propensity and later conduct problems was due to shared environmental influences.

Marital hostility and child sleep problems: Direct and indirect effects via hostile parenting

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Sleep problems during early childhood are relatively common and are an early precursor of subsequent adjustment problems. Thus, it is important to understand processes associated with the early exacerbation or amelioration of sleep problems. However, studies examining relations among family processes and child sleep in early childhood are relatively rare and none have jointly considered genetic and environmental influences. The current study examined marital hostility and hostile parenting as predictors of child sleep problems at 4.5 years in an adoption sample ($N = 361$ linked triads). We examined pathways from observed marital hostility at 9 months to child sleep at 4.5 years via hostile parenting at 27 months, controlling for birth parents’ internalizing disorders (i.e., genetic effects). Fathers’ hostile parenting was associated with child sleep problems, and a significant indirect effect was found from fathers’ observed marital hostility to child sleep problems via mothers’ hostile parenting. Mothers’ observed marital hostility was directly associated with child sleep problems; there was no evidence of indirect effects via hostile parenting.

Meta-analysis of educational attainment GWAS:

The Social Science Genetics Association Consortium

Niels Rietveld; Erasmus University Rotterdam Sarah Medland; QIMR Jaime Derringer; University of Colorado Boulder Daniel Benjamin; Cornell University David Cesarini; New York University Philipp Koellinger; Erasmus University Rotterdam The Social Science Genetics Association Consortium; SSGAC

Educational attainment is associated with a variety of health outcomes, from cancer (e.g. Mouw et al. (2008) PLoS ONE 3(11):e3639) to depression (e.g. Ross & Mirowsky (2006) Soc Sci Med 63:1400–1413), and is moderately heritable (e.g. Taubman (1976) Am Econ Rev 66:858–870; Miller, Mulvey, Martin (2001) Econ Educ Rev 20:211–224). We sought to carry out a large-scale meta-analysis of GWAS on educational attainment, implementing a consistent phenotype definition and analytic approach across all contributing cohorts. GWAS results were contributed by 42 cohorts in the discovery stage and 12 additional, independent cohorts in the replication stage, representing educational and genotypic data from 134,125 adult individuals of European ancestry. Educational attainment was coded in terms of years-of-education (according to the International Standard Classification of Education) as well as dichotomously in terms of completion of a college degree. All cohorts imputed genotyped data up to the ~2.5 million SNPs available in HapMap 2. Meta-analyses of the combined discovery and replication stage identified significant SNPs (at $p < 5e-8$) on chromosomes 2, 3 and 6 for years-of-education, and on chromosomes 1 and 2 for the college-degree phenotype.

A longitudinal examination of genetic and environmental influences on homotypic and heterotypic continuity of anxiety disorders and depression

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Longitudinal studies provide valuable information regarding the developmental unfolding and fluctuating nature of psychiatric dysfunction over time. Current data suggests that some disorders exhibit homotypic continuity, onseting in childhood and continuing into adulthood with the same symptom profile and clinical manifestation while other disorders predict development of a different disorder (heterotypic continuity). Of the anxiety disorders, the three more prevalent disorders in childhood include separation anxiety disorder, generalized anxiety disorder, and social phobia. Childhood separation anxiety disorder (SAD) is hypothesized to share etiologic roots with panic disorder (PD), a condition that typically emerges in adulthood while pediatric generalized anxiety disorder (GAD) is hypothesized to share pathophysiologic features with major depressive disorder (MDD). Pediatric social phobia (SoPh), by contrast, exhibits strong developmental continuity with SoPh manifest in adulthood. There is a lack of genetically informed studies examining genetic and environmental contributions to homotypic versus heterotypic continuity. Thus, data from children participating in the Virginia Twin Study of Adolescent Behavioral Development (VTSABD) and those twins who later completed the Young Adult Follow-Up (YAFU) ($n = 1,437$ twin pairs) will be used to examine several hypotheses regarding the developmental relation between pediatric anxiety and depression (SAD, GAD, SoPh, and MDD) and development of adult anxiety and depression (PD, GAD, SoPh, and MDD). We will use multivariate twin modeling to accomplish this goal. Our previous results suggest that childhood SAD and adult onset panic attacks/PD share a robust common genetic diathesis that is not observed for childhood GAD, strongly supporting the hypothesis of a specific genetic etiologic link between the two phenotypes. Here, we extend this analysis examining the genetic and environmental relations between a range of childhood and adult onset disorders using longitudinal twin data.
Validity studies of the 2012 NLSY kinship links using height and weight

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Twenty years ago, three research teams (including ours) developed independent computer algorithms to identify the levels of genetic relatedness among siblings in two linked cohorts of the National Longitudinal Survey of Youth (the NLSY79 and NLSYC data). These kinship algorithms were necessary because genetic relatedness was not directly assessed. Since then, over 50 studies using these kinship links have been published in psychology and behavior genetic, including 6–8 theses/dissertations. Most have been biometrical analyses of child and young adult outcomes using the rich longitudinal structure in the NLSY.

In 2006, questions were added to directly assess relatedness, which further improved the already valuable NLSY kinship information. In particular, hundreds of kinship links were added or adjusted based on the new information. Using a combination of the direct and earlier inferred assessments, we have created virtually complete kinship links for the 10,000 + NLSY79 respondents and the 11,000 + NLSYC respondents. In this paper, I’ll summarize their quality by presenting biometrical analyses of adult height and weight as validity indicators.

We compare results to previous studies of height and weight to verify the performance of the revised NLSY kinship links. Next, we interpret results from the NLSY whose mothers were part of a household probability sample of the US) and identify biometrical gender and race differences in height and weight.

In 1991, Chase-Lansdale et al. published a Developmental Psychology paper (now cited over 160 times) that promoted use of the NLSYC by developmental researchers. Similarly, the current paper—and others in this symposium—are designed to stimulate and support the use of the sibling and broader kinship information in the NLSY datasets by behavior genetic and developmental researchers.

New evidence on the aetiology of specific psychotic experiences from an adolescent general population twin sample

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Background: Psychotic-like symptoms are likely first to emerge in adolescence. If they persist, become more severe, and are associated with distress and impaired function, they comprise an Ultra High Risk syndrome, which carries a very high risk of later developing a psychotic disorder. In light of the paucity of knowledge concerning the aetiology of psychotic experiences in adolescence, the present study aimed to assess the genetic and environmental architecture of a broad range of specific psychotic experiences in adolescence.

Methods: A sample of >5,200 16-year-olds (M = 16.4, SD = 0.7), from a UK-based general population study, was assessed on a battery of six specific psychotic-like experience quantitative scales: paranoia, hallucinations, hedonia, cognitive disorganization, grandiosity (all self report) and negative symptoms (parent report). Extensive psychometric analyses, and univariate and multivariate twin model-fitting analyses, were conducted.

Results: All scales showed high internal consistency and considerable quantitative variation. Exploratory factor analyses revealed a clear six-factor solution, together explaining 45 % of the variance, with each symptom dimension loading on a separate factor. Heritabilities of specific psychotic experiences ranged from 30 to 55 % with the lowest heritability for hallucinations (30 %) and the highest for parent-rated negative symptoms (55 %). All self-rated scales showed considerable nonshared environmental influences (E) (51–58 %), with a lower estimate for parent-rated negative symptoms (E = 17 %). Shared environment was nonsignificant for all scales except hallucinations (C = 13 %) and parent-rated negative symptoms (C = 28 %). Correlations between psychotic experience scales ranged from −0.07 to −0.43. Multivariate models demonstrated that genetic correlations between scales ranged from high (>0.6) to nonsignificant, with high genetic overlap apparent between paranoia and cognitive disorganization, and between paranoia and hallucinations. Overlap in environmental influences also varied across scales.

Conclusions: These results are relevant to models of how to conceptualise psychosis, and provide a science base from which to inform the design of early interventions.

Recruitment and retention biases in a multi-wave population-based twin study

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Longitudinal Finnish twin studies yield information on biases in both initial recruitment and in retention across successive waves of study. We share lessons learned from longitudinal studies that enrolled twins at ages 11–12 (FinnTwin12) and 16 (FinnTwin16).

Recruitment: Fathers of nearly 7 % of 16-year-old twins were lost to study due to death or separation from twins or twins’ mothers. Among all parents consenting to their family’s enrollment, fathers show lower individual response rates than do mothers. Structure of the twin children (SS vs. OS) had no effect on parental permission rates, but family structure did: For 11-year-old twins, parental permission was given by >88 % of all 2-parent families and 85 % of single-parent families absent fathers, but by only 70 % of single-parent families absent mothers. Baseline enrollment was high (>90 % of twins, >87 % mothers and >84 % of available fathers, with pair-wise twin response rates of 88 % at age 16 (and 87 % at age 11–12), but it was moderated by gender (reduced rates among both twin brothers and twins’ fathers), with greater individual and pair-wise enrollment for sister–sister (≈92 %) and sister-brother (≈89 %) than brother–brother (≈85 %) pairs. Retention: Gender influences retention as much as recruitment: these rates fell to 87, 78 and 70 % just 30-months later. Retention of twin brothers from adolescence into early adulthood is lower within both MZ and SSDZ pairs. Loss of twin brothers across assessments is non-random and baseline personality characteristics predict subsequent retention. Quartile membership at age 16 in the 50-item Scale 4 (Pd) of the MMPI illustrates: At age 17 follow-up, 7 % of the highest quartile Pd-scoring twin brothers dropped out against 4 % of those in the lowest quartile; by age 25, these drop out rates increased to 17.9 % against 10.3 %. Effects are clearly greater among males but are as systematic among females.
Differential item functioning in the CAMDEX depression scale across middle age and late-life

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A long-standing and critical issue in the study of aging is the divergence of psychometric and clinical measures of depression. Self-report and interview-based measures show a consistent increase in rates of trait depression with increasing age, but the rate of clinical diagnosis of major depression remains stable or decreases throughout the lifespan (Blazer 2003; Jorm 2000; Newman 1989). While many explanations of this problem exist, one relatively unexplored area is the possibility of a lack of measurement invariance as a function of age.

The present analysis presents tests of differential item functioning on the depression section of the CAMDEX interview schedule, which consists of affective and somatic subscales (McGue & Christensen 1997). Participants for the analysis come from a combined sample of the Middle-aged Danish Twin Study (MADT; Gaist et al. 2000; Johnson et al. 2002) and the Longitudinal Study of Aging Danish Twins (LSADT; Christensen et al. 1999), representing the same population at conjoining ages (MADT: 45–68; LSADT: 70–104). This sample was further split into two subsamples, such that each twin pair placed one member in sample 1 (n = 4,492) and the other in sample 2 (n = 4,553); this split provided a “biologically-matched” comparison sample used for internal replication. Initial analyses support the presence of the two previously defined subscales.

Results for the affective subscale show significant differences in item functioning in the majority of the affective items as a function of age (Items “Happy Life”, “Lonely”, “Nervous” “Worthless” and “Future”: Chi-square = [30.193, 255.971], df = 6, p < 0.0001). Analyses for the somatic subscale show that differential item functioning is limited to a single item relating to coping (Chi-square = 180.754, df = 6, p < 0.0001). These results indicate that changes in depression symptoms over the lifespan are not entirely due to changes in the level of depression, and that the measurement structure of trait depression varies over the lifespan.

Life events and GABRA2 interact to predict adolescent externalizing symptoms: Initial evidence and a replication

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Stressful life events are positively associated with externalizing pathology; furthermore, there is evidence from twin studies that life events moderate genetic influences on externalizing pathology. The present study brings these two lines of evidence together to examine whether life events and variation in GABRA2, a gene implicated in externalizing pathology, interact to predict adolescent externalizing symptoms.

Analyses were carried out in two samples for which relevant data were available: an American community-based sample (Child Development Project [CDP]; analyses limited to Caucasian participants; n = 354; 50 % female), and a Finnish population-based sample (FinnTwin12: all Caucasian participants; n = 789; 52 % female). In CDP, 18 life events and Achenbach adolescent externalizing symptoms were assessed via maternal reports annually between ages 12–17. In FinnTwin12, fifteen life events were assessed via adolescent-report and externalizing symptoms were assessed via the teacher rating form of the Multidimensional Peer Nomination Inventory at age 14. Ten and six GABRA2 SNPs were genotyped in the samples, respectively. Sex was entered as a covariate in all analyses.

Life events and GABRA2 interacted to predict adolescent externalizing symptoms. The results from moderated linear mixed models in CDP indicated that the positive longitudinal covariation between life events and externalizing symptoms was stronger for those with 0 or 1 copies of the minor allele compared to those with 2 copies of the minor allele. Parallel trends were observed in FinnTwin12, though they did not reach significance (ps ranged from 0.08 to 0.26, mean p = 0.16).

In summary, this study provides convergent evidence that GABRA2 may differentially sensitize individuals to stressful life events. Parallel trends in CDP and FinnTwin12 are especially notable in view of sociodemographic and measurement differences between the two samples.

Family involvement and adolescent alcohol use: Potential sources of shared environmental influence

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In order to further knowledge on specific characteristics of the shared environment that contribute to adolescent alcohol use, this study utilized Cholesky decomposition to investigate the effect of family involvement. Using a genetically informed sibling-pair design (adopted vs. nonadopted adolescents, N = 613 pairs), the covariance between family involvement (mom, dad, sibling) and adolescent alcohol use was decomposed into genetic and environmental contributions. Parent involvement was measured in terms of parental knowledge of child activities and parent–child closeness; sibling involvement was measured in terms of spending time together. Shared environmental effects on alcohol use were moderate (c² = 0.23, a² = 0.25, e² = 0.53), were minimal for mom and dad involvement (c² = 0.05–0.06, a² = 0.22–0.35, e² = 0.59–0.73), and substantial for sibling involvement (c² = 0.46, a² = 0.33, e² = 0.21). Fit statistics showed the full ACE model fit better than more restricted models (CE = χ² = 20.72, AE χ² = 137.78, E χ² = 269.90; all on 10 df). Results indicated that only 4 % of genetic and 5 % of nonshared environmental influence was explained by family involvement. In contrast, 100 % of the shared environmental influence was explained by family involvement, largely by sibling involvement (92 %). However, there were few significant paths, which is most likely due to the generally low overall correlations between family involvement and adolescent alcohol use (while significant, r’s ranged from 0.08 to 0.24). Future research questions include examining the contributions of alcohol availability as well as sibling facilitation of alcohol use on adolescent alcohol use. This program of research will lead to better understanding of shared environmental effects on adolescent alcohol use, which ultimately further supports specific environmental intervention and prevention work.
School performance but not neighborhood deprivation and social capital predicts serious adolescent criminality and substance use disorders

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Context: There is an extensive literature on neighborhood effects on criminality but only one population-based study on substance abuse. While studies in the US generally find sizeable neighborhood effects on criminality, studies in Europe have resulted in very modest effects. The causality of neighborhood effects is questioned.

Objectives: To assess the association between neighborhood deprivation and social capital on serious adolescent criminality and substance use disorders in Sweden.

Design: Longitudinal generalized linear mixed effects modeling of the Swedish population born between 1975 and 1989 who had at least one biological full sibling.

Setting: Population-based.

Participants: We studied 171,972 individuals living in the three largest cities in Sweden (Stockholm, Gothenburg and Malmo) who had full information on the individual and contextual level variables.

Results: Neighborhood deprivation and voting participation (i.e. social capital) are not associated with serious adolescent criminality or substance use disorders. The contextual effect of school performance is significantly associated with serious adolescent criminality (RR = 1.19 [1.17; 1.21]) and substance use disorders (RR = 1.14 [1.07; 1.22]). The effect sizes are slightly attenuated after extensive adjustments of observed and unobserved individual and familial confounders.

Conclusions: Factors on the neighborhood context are not causally associated with serious adolescent criminality and substance use disorders Sweden. The performance of schools, however, is an interesting risk factor that is not confounded by familial factors.

Genetic and environmental contributions to separation anxiety: A meta-analytic approach to twin data

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Separation anxiety disorder (SAD) and symptoms (SA) have been studied both epidemiologically and genetically; however, large between-studies discrepancies emerge relative to the role of genetic, shared-, and non-shared environmental influences on these conditions.

Based upon available literature, 18 cohorts and 31,859 subjects belonging to twin samples in Europe, the US and Australia were included in 3 meta-analytic estimations of: the standardized variance components of etiological influences on SAD/SA, and on the effect of sex and rater.

Meta-analytic estimations carried out on all cohorts showed that within-family (genetic 43 % and shared environmental 17 %) factors explain most of individual differences for SAD/SA. Meta-heritability estimates were higher among females (0.52) than males (0.26), while non-shared environmental effects were stronger for the latter (0.74) than for the former (0.41). When SAD/SA was rated by parents, the shared environmental influences were higher than those obtained with self-assessment instruments (0.23 vs. 0.05), but this may reflect an age difference between subsamples.

Adolescents’ MZ differences on autistic traits, internalising traits and their co-occurrence: The role of early NSE trait differences

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Autism spectrum disorders frequently co-occur with anxiety disorders. Previously, we investigated the degree of overlap between autistic and internalising traits in early adolescence and reported significant nonshared environmental influences and overlap between them. The present MZ differences study investigated nonshared environments (NSE) relevant to internalising and autistic trait levels and their co-occurrence. Second, longitudinal changes in these associations were studied. A community sample of 2,450 MZ twins from the Twins Early Development Study was assessed using parent-report of internalising traits at 12 years (Strengths and Difficulties Questionnaire Emotional problems subscale), and autistic traits at 14 years (Autism spectrum Quotient). Univariate MZ difference scores, and MZ difference scores on their co-occurrence (a standardised sum score of both traits) were created. These were correlated with the twins’ differences on earlier manifestations of these traits. Results showed that associations of childhood with adolescent difficulties on the same phenotype were increasing with age (autistic traits: r = 0.10–0.17; internalising: r = 0.05–0.41, p < 0.01).

Personality similarity in unrelated look-alike individuals: Resolving a twin study challenge

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A large number of twin studies have reported genetic influence on personality, yet twin research findings continue to be questioned by some members of the scientific community. A recurring misconception is that MZ co-twins resemble one another in personality due to their similar treatment by others. It is further argued that MZ twins’ similar treatment is triggered by their identical physical resemblance. The present study brings new evidence to this question by examining the similarities in personality and self-esteem of individuals in 23 unrelated look-alike pairs (U-LAs), evenly divided between males and females. The mean age of the participants was 46.21 years (SD = 13.96), and the mean age difference was 6.65 years (SD = 5.63). The U-LAs were identified in Canada with the assistance of photographer Francois Brunelle. Intraclass correlations for the personality scales of the French Questionnaire de Personnalite au Travail and the Rosenberg Self-Esteem Scale demonstrated negligible behavioral resemblance between U-LAs. These results are in striking contrast to those from MZ and DZ twins, both reared apart and together; for example, reported intraclass correlations for neuroticism range between 0.25 and 0.61 for MZ twins, and 0.11 and 0.29 for DZ twins, providing an informative backdrop for discussion. The U-LA findings are especially interesting with reference to DZ twins who do not look nearly as alike physically as U-LAs. It is, therefore, concluded that MZ co-twins’ personality similarity mostly reflects their shared genes, and reactive gene–environment correlation best explains MZ co-twins’ similar treatment by others. Future research directions include analyses of the U-LAs’ responses to first meeting and the nature of their ongoing relationships with one another.
Genetics of decision making: A Japanese twin study using the Allais problem

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Why are some individuals better at rational decision making than others? And why is human decision making often inconsistent and violating the rational assumptions of economics? We investigated the genetic and environmental effects on individual differences in decision making using a classical task of the Allais problem. Approximately 600 pairs of Japanese twins aged 21–47 participated in the study. We identified individual genetic differences in decision making, but also found that larger components were explained by nonshared environment. Subsequent multivariate genetic analysis clarified that decision making using the utility theory was associated with general intelligence, and the association was largely mediated by the genetic factors. In contrast, decision making violating the utility theory was not associated with intelligence, but was in part associated with Cloninger’s temperament traits of novelty seeking and harm avoidance. The association was largely mediated by the genetic factors. It was implied that people can adjust their decision-making behavior according to their genetic disposition.

Genetic and environmental influences on the association between temperament and self-restraint in toddlerhood

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Self-restraint, or the inhibition of a prepotent response, is a moderately heritable and an important developmental process during toddlerhood, and has been shown to predict executive function abilities and behavioral problems later in life. The aim of the present study was to gain a better understanding of the etiology of self-restraint in toddlerhood by examining the association between temperament and self-restraint in a genetically informative sample. Behavioral inhibition (e.g., shyness and fearfulness) is hypothesized to predict higher self-restraint based on earlier research demonstrating increased response latency and effortful control in fearful children, whereas negative emotionality (proneness to fussiness and anger) is hypothesized to predict poorer self-restraint, perhaps due to increased reactivity in unpleasant situations. Attentional control (e.g., focus and persistence) is hypothesized to predict improved self-restraint because earlier research suggests that mechanisms of attention are involved in the development of self-restraint and effortful control. Biometrical genetic analyses were conducted to determine the magnitude of covariance between temperament and self restraint due to genetic, shared environmental, and nonshared environmental influences.

Participants were twins recruited from the Colorado Longitudinal Twin Study (LTS) at the University of Colorado. The present sample included 115 monozygotic (MZ) female twin pairs, 79 dizygotic (DZ) female twin pairs, 106 MZ male twin pairs, and 94 DZ male twin pairs. Data on negative emotionality, behavioral inhibition, and attentional control were assessed via parent report and observations. Self-restraint was assessed in a prohibition task, in which toddlers were asked not to touch an attractive toy. Data were collected at 14, 20, 24, and 36 months.

Results indicated that toddlers with high behavioral inhibition and/or attentional control had better self-restraint, whereas high negative emotionality predicted lower self-restraint. Results of Cholesky decomposition suggested that common genetic influences contributed more to the covariance between temperament and self-restraint than environmental influences.

Marital satisfaction and personality: Using gene–environment interplay to understand mechanisms

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Personality is significantly associated with marital satisfaction. For instance, higher levels of neuroticism in either partner are related to lower marital quality of both partners. Behavior genetic modeling may be particularly important for understanding the mechanisms underlying the associations between marital quality and personality. To date, there have been only a handful of studies that have examined the relationship between personality and marital quality within a genetically informative design (c.f., Spotts et al. 2004a). Research has shown that marital quality is moderately heritable (South & Krueger 2008; Spotts et al. 2004b; Spotts, Prescott, & Kendler 2006), a finding that fits with work showing moderate to substantial heritability of environmental variables (Kendler & Baker 2007). Research has also shown overlap between genetic influences on marital satisfaction and personality (Spotts et al. 2005a), well-being (Spotts et al. 2005b), and internalizing psychopathology (South & Krueger 2008; Spotts et al. 2004a). In the current study, we extend this important work by examining the gene–environment interplay between relationship satisfaction and personality traits in a sample of twins followed longitudinally from adolescence through age 30. All participants completed the MPQ (Tellegen et al., in press) and abbreviated versions of the Dyadic Adjustment Scale (DAS; Spanier 1976). Analyses examine the genetic and environmental overlap between relationship satisfaction and personality. Further, biometric moderation models are used to examine whether relationship satisfaction moderates the genetic and environmental components of variance on personality. Examining these types of gene × environment interactions has the potential to elucidate how environmental risk factors, like marital satisfaction, impact the etiology of personality.

Oxytocin and vasopressin receptor gene polymorphisms and personality in bonobos (Pan paniscus): Preliminary results

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Many studies have reported an important role of genes coding for neurotransmitter receptors in the brain on both human behaviour and personality traits. Studying this association in bonobos and comparing these results with those found in humans might give us better insight in the evolution of human behaviour. In this preliminary study we focus on a SNP “rs53576” in the third intron of the oxytocin receptor gene (OTR) and the VNTR in the promoter region of the vasopressin receptor gene (avpr1a) named “RS3”. In humans, these
polymorphisms are known to have an influence on behavioural traits like aggression, altruism, fear, stress, empathy and trust and personality traits like novelty seeking and persistence. We collected DNA from 55 bonobos (30 females and 25 males) in European and American Zoos and analysed polymorphisms through PCR, fragment analyses and sequencing. We determined personality from the same individuals, by using a 54 adjective questionnaire, filled out by zoo keepers. Using Principal Component Analyses, we found a four factor personality structure in bonobos, similar to the structure found in other apes, with the factors labelled as “Extraversion”, “Conscientiousness”, “Agreeableness” and “Dominance”. Our preliminary genetic analyses indicate that, contrary to humans there is no variation in rs53576 in bonobos. We did find an interesting SNP 99 bp downstream of rs53576, which is absent in humans. In contrast to chimpanzees but similar to humans we found no 360 bp deletion in the promoter region of avpr1a for bonobos, but we did find variation in length of the VNTR in the promoter region ranging from 289 to 315 bp. In humans normal variation lies between 308 and 460 bp and longer repeats are associated with increased mRNA levels in the brain. We will discuss the link between polymorphisms and differences in personality.

Serotonin system gene polymorphisms are associated with impulsivity in a context dependent manner

Scott Stoltenberg; University of Nebraska Christa Christ; University of Nebraska Krista Highland; University of Nebraska

Impulsivity is a risk factor for adverse outcomes and characterizes several psychiatric disorders and risk for suicide. There is strong evidence that genetic variation influences individual differences in impulsivity, but the details are not yet understood. In a cross-sectional study we examined whether polymorphisms in six serotonin system candidate genes and the experience of early life trauma (age 0–12) were associated with individual differences in impulsivity in a non-clinical sample of Caucasian university students (N = 424). We specifically tested potential gender specific, gene–gene (epistatic), and gene × environment (early life trauma) effects. In our main analyses with Barratt Impulsiveness Scale (BIS-11) Total score, there were significant (i.e. p < 0.01 and False Discovery Rate < 0.10) interactions between (1) gender and TPH2 (rs1386483) genotype; (2) gender and HTR2A (rs6313) genotype; and epistatic interactions among (3) 5-HTTLPR and MAOA uVNTR; (4) 5-HTTLPR and rs6313 and (5) HTR1B (rs6296) and rs6313 genotypes. Our results strongly support the explicit investigation of context dependent genetic effects on impulsivity and may help to resolve some of the conflicting reports in the literature.

Investigation of genetic association between cerebellar volume and attention problems in children

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The importance of genetic factors has been established for a wide range of structural brain measures, for example total and regional brain size, volumetric changes and cortical thinning. The cerebellum, one of the last maturing brain areas, is well known for its role in motor skills, and has recently been implicated to be important in cognitive functioning. Cerebellar development also seems to be of importance for healthy development, as it has been implicated in developmental disorders like ADHD. Both cerebellar volume and attention problems are highly heritable in childhood. Whether there is an association between these two measures, and possibly IQ, and how this relation might be influenced by genetic factors will be investigated.

Data from a longitudinal study about development of brain and cognition during puberty, Brainscale, will be used to investigate the relation between cerebellar volume, cognition and attention problems. In total, twins and siblings from 112 families have participated in Brainscale, in which MRI, behavioral, IQ, neurocognitive, physical and hormonal data were collected at two time points (twins age 9 and 12).

At the first measurement 214 twins and 87 older siblings have completed an MRI scan, 140 twins and 59 siblings were scanned again three years later. Measures of total cerebellar volume, IQ and overactive/attention problem behavior rated by both parents (Child Behavior CheckList at ages 3 through 12) were analyzed. Total, gray and white cerebellar volume at age 9 correlate around −0.24 with overactive behavior at age 3. At later ages, no associations were seen with attention problems, although there was a relation between cerebellar volume and IQ (0.30). An extended twin model was used to estimate twin correlations and to model genetic and environmental correlations between phenotypes. Highheritabilities and significant genetic correlations were found between all measures.

Impact of early parental warmth and concurrent punitive discipline on the heritability of young children’s problem behaviors

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The role of parenting in the etiology of behavioral problems during early childhood has long been an important question for psychologists. Both lack of parental warmth and harsh verbal and physical punishment have been associated with childhood problem behaviors (McKee et al. 2007, J Fam Violence 22:187–196). We extend current findings by using the twin design to extrapolate the underlying genetic and environmental factors associated with problem behaviors. We hypothesized, based on previous literature, that parental warmth and harsh punishment would act as moderators of the heritability of problem behaviors. Participants were 315 twin pairs (26.3 % MZs, 34.3 % ssDZs, 39.4 % osDZs) participating in the ethnically diverse (65.3 % Caucasian, 23.8 % Latino, 10.8 % other) longitudinal Arizona Twin Project, mean age 2.61 years (0.21 SD) at time two. Parental warmth was assessed using the Child Rearing Practices Report at time one (12 month assessment), punitive discipline using the Parental Responses to Child Misbehavior scale at time two, and total problem behaviors with the Infant Toddler Social and Emotional Assessment at time two. Using Purcell’s (2002, Twin Res 5:554–571) moderated ACE model, parental warmth significantly moderated the A and E paths (−0.2. −0.402.702, df 385, A 0.68 C 0.02 E 0.30) such that heritability increased as warmth increased. Problem behaviors were not moderated by concurrent harsh discipline. Thus, problem behaviors are more heritable under optimal, warm parenting conditions, whereas the environment has a larger impact when caregivers are more rejecting of their young children. From an evolutionary perspective, parental warmth strengthens familial relationships and enhances children’s learning of moral values (McDonald 1992, Child
Dev 63:753–773). Thus, parental rejection leads to weaker familial bonds that place young children at risk.

**Chaotic home environment is a shared environmental mediator of the relationship between rule breaking disposition and reading achievement**

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Prior research suggests that temperament factors reflecting sociability and attentiveness are positively associated with achievement in children, whereas, chaotic home environment is negatively related to achievement. Further, certain temperament dispositions have been shown to relate to the development of conduct problems, which are often associated with achievement deficits, particularly in verbal domains. The present study begins to combine these literatures by examining a disposition factor called Respect for Rules that is related to the development of conduct disorder and reading comprehension in 201 MZ and 211 same-sex DZ twin pairs age 6–13 participating in the Florida Twin Project on Reading. A bivariate Cholesky model was used to examine the common genetic and environmental influences on the relationship (r = 0.28) between parent-rated Respect for Rules and reading comprehension measured with the Florida Comprehensive Achievement Test (FCAT). The model also allowed for an examination of the mediational role of family income and parent-rated chaos in the home (reverse scored) on the disposition–achievement relationship. Results showed a significant common shared environmental effect on the covariation of Respect for Rules and reading comprehension that was completely accounted for by family income and (reversed) home chaos. These data suggest that a chaotic home environment may relate to the development of problems in both psychological and academic domains that are themselves related to the development of childhood behavior disorders. Future work should examine the development of conduct disorder and other externalizing disorder in relation to Respect for Rules and achievement outcomes in a longitudinal design to provide information on the direction of the associations shown here.

**Nonshared environmental influences on the association between traits of autism and attention-deficit/hyperactivity disorder: A monozygotic twin differences study**

Mark Taylor; Institute of Education Tony Charman; Institute of Education Angelica Ronald; Birkbeck/Institute of Psychiatry

Traits of autism and attention-deficit/hyperactivity disorder (ADHD) show considerable covariation with one another. Nonshared environmental influences are thought to play a modest, yet significant, role in this association. This study explored the specific nonshared environmental influences on this association using a monozygotic (MZ) twin differences design. Parents of 2,043 MZ twin-pairs participating in the Twins Early Development Study (TEDS) completed questionnaires regarding traits of autism (Childhood Autism Spectrum Test [CAST]) and ADHD (Conners Parent Rating Scale ADHD subscale) when twins were aged 12-years. A composite ‘co-occurrence’ score was created by summing z-standardised CAST and Conners scores. Early nonshared environmental influences, including birthweight, birth length, and medical risk factors, have been linked with traits of autism (e.g. Ronald et al. 2010) and ADHD (e.g. Lehn et al. 2007) individually, and were hence included in this study, as were later factors, such as peer problems. The MZ differences design assumes that MZ twins share all their DNA code, meaning any cross-twin differences are caused by nonshared environmental influences. To control for genetic influences, a difference score was created for each measure (including environmental measures, which are still prone to genetic influences) by subtracting one twin’s score from their co-twin’s score. Significant Pearson correlations were found between difference scores in co-occurrence and birthweight (r = −0.13, p < 0.001), birth length (r = −0.08, p < 0.05), general medical factors (r = 0.06, p < 0.001), and peer problems at age 12 (r = 0.30, p < 0.001). Regression-based mediation models suggested that the association between medical risk factors and co-occurrence scores is mediated by verbal ability at age 2. The correlations between MZ difference scores in environmental measures and co-occurrence scores were stronger than the correlations with CAST and Conners scores individually. Hence, these nonshared environmental factors may be associated with greater co-occurrence between traits of autism and ADHD.

**The genetics and behaviours of high- and low-risk sport enthusiasts**

Cynthia Thomson; University of British Columbia Amelia Rajala; University of British Columbia Rebecca Power; University of British Columbia Scott Carlson; University Minnesota Duluth Gregory Michel; University of Bordeaux II Jim Rupert; University of British Columbia

Sensation seeking (SS) involves a desire to seek out new and thrilling experiences and has been linked to both socially unacceptable behaviours such as drug-abuse, and to less stigmatized ‘risky behaviours’ such as high-risk sports (e.g. sky-diving). The sensation of excitement (the ‘high’) associated with these behaviours is related to the release of dopamine. Common variations in dopamine-pathway genes have been associated with approach-related traits, including novelty seeking and extroversion, in some (but not all) studies; however, few studies have measured SS, and none have investigated genetic variations in high-risk sports participants. High-risk sports practitioners often exhibit higher levels of SS than general populations and/or lower risk sport groups, making them an interesting group to study extreme versions of the SS trait. Instead of a cross-sectional design that is often applied to non-pathological personality studies, we used a case–control design with sport as the grouping variable. We recruited high-risk athletes (e.g. free-ride skiers, paragliders, B.A.S.E. jumpers, n = 123) as the ‘cases’ and low-risk athletes (e.g. cross country skiers, golfers, swimmers, n = 125) as the ‘controls’ from Chamonix, France and Western Canada. Using a case–control design we compared genotype frequencies of a functional SNP, the dopamine-4-receptor gene (DRD4) 120-bp duplication. Our preliminary results (n = 53 low-risk and n = 54 high-risk) show no differences in genotype frequencies of the DRD4 120-bp duplication between groups (p = 1.0). We did observe significant differences in personality measures (impulsivity and sensation seeking, p < 0.01), and genotyping of other variants in dopamine and related pathways is currently underway. While our data supports previous studies that have found differences in SS scores between high- and low-risk sport groups, we did not find any evidence that the 120-bp duplication in the promoter of the DRD4 was associated with a predilection for risky sports.
School motivation: A twin study

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Motivation and engagement at school are important predictors of academic achievement. In this study we aimed to investigate the role teachers play in fostering motivation, and specifically whether sharing the same teacher would increase the similarity between twins. Questionnaire data on motivation was collected from more than 4,000 pairs of twins from the UK Twins Early Development Study (TEDS) at ages 9, 12 and 16. Data on self-perceived ability (‘how good do you think you are?’) and liking (‘how much do you like?’) for English, Math and Science were available at ages 9 and 12. At age 16, we assessed motivation using items drawn from the PISA questionnaires, including homework behaviour, attitudes towards English, Math and Science, and overall attitudes towards school. To assess the role of the teacher, we calculated estimates of the genetic and environmental origins of individual differences in motivation separately for those twin pairs who shared the same teacher/classroom and those twins who were in different classrooms. At 9 and 12 years, we found significant heritability (35 % on average) and the absence of shared environmental influences on motivation for all academic subjects. Moreover, there were no differences between estimates for twins in the same versus different classrooms, indicating that the same teaching style does not make children more similar on self-perceived ability or enjoyment of subjects. Results for school attitudes at 16 showed a similar pattern, with moderate heritability and minimal shared environmental influence. Non-shared environmental influences were important at all ages, explaining 65 % of the variance on average at 9 and 12 years. The striking absence of shared environmental influences on motivation, particularly for those twins in the same classroom, questions the assumption that teachers are the key ingredient for inspiring students and motivating them to achieve.

The heritability of “number sense”

Maria Grazia Tosto; Goldsmiths, University of London Yulia Kovas; Goldsmiths College Robert Plomin; King’s College London

Number Sense defines basic skills used when dealing with numerical information without relying on mathematical formal education. These competences allow us to recognise and discriminate quantities and numerosities. Number Sense is present in non-human animals, as well as human infants and adults, suggesting that this trait is evolutionarily conserved. It is possible that variation in the precision of Number Sense is driven by genetic influences to a large extent. It is also possible that these genetic influences overlap with the genetic factors influencing mathematical ability; and that this overlap explains the observed relationship between number sense and mathematical performance. We present the first genetically sensitive investigation into the aetiology of Number Sense adopting the large representative sample of the Twins Early Development Study (TEDS). At 16 years of age 3,800 pairs of MZ and DZ twins were assessed on a measure of Number Sense (approximation of dot numerosities), as well as three measures of mathematical skills and achievement. Sex-limitation model fitting was conducted on the Number Sense measure to examine the aetiology of the variation in this trait for males and females. Contrary to the prediction, individual differences in Number Sense were largely explained by non-shared environment (0.69), with genetic influences of only 0.31, and no shared environment. Further, no gender differences in the aetiology of individual differences in Number Sense ability were found.

The absence of any observed gender differences in Number Sense, or quantitative and qualitative gender differences in the aetiology of its variation, suggests that this ability does not contribute to the observed average gender differences in mathematical ability. The finding of the very strong non-shared environmental influence on variation in Number Sense calls for further study aimed to establish the exact nature of these environments and of the relationship between mathematics and Number Sense abilities.

Examining the interplay of birth mothers’ and adoptive parents’ antisocial behavior in predicting growth in externalizing problems during early childhood

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Early-emerging externalizing problems are predictive of delinquency later in childhood and adolescence, making it crucial to understand the etiology of these problems. Studies of young twins suggest that early externalizing behaviors are moderately heritable, with genetic factors accounting for roughly 50 % of the variance and shared environmental factors accounting for much of the remaining variance. An adoption design is a useful approach to help disentangle genetic and environmental factors that may lead to early externalizing problems. This study utilizes a prospective adoption design, The Early Growth and Development Study, to examine birth mother and adoptive parent antisocial behavior as predictors of growth in early childhood externalizing problems. 361 linked triads (birth mother, adoptive parents, child) were recruited from adoption agencies throughout the United States. Child externalizing problems were assessed at 18, 27, and 54 months using adoptive parent ratings on the Child Behavior Checklist. Birth mother antisocial behavior was assessed with the Elliott Social Behavior Questionnaire. Adoptive parent (mean of adoptive mothers’ and fathers’ scores) antisocial behavior was assessed with the Antisocial Action Scale and the Personality Diagnostic Questionnaire. Covariates included prenatal risks, adoption openness, and the postnatal rearing environment. A latent growth model examined the initial level and growth in externalizing problems from age 18 to 54 months. Adoptive parents’ antisocial behavior predicted higher initial levels of child externalizing problems. There was a significant interaction between birth mother antisocial behavior and adoptive parents’ antisocial behavior when predicting growth in externalizing. Compared to birth mothers with lower levels of antisocial behavior, children of birth mothers with higher levels of antisocial behavior showed steep growth in externalizing problems when raised by adoptive parents with higher levels of antisocial behavior. These findings highlight the interplay of genetic and environmental factors in early-emerging externalizing problems.

Copy number variants (CNV) deletion burden and cognitive abilities

Maciej Trzaskowski; Institute of Psychiatry Robert Plomin; King’s College London

Copy number variants (CNVs) are DNA segments from just a few to millions of bases in size that are deleted or duplicated, which can
lead to the duplication or deletion of whole genes or parts of them. Rare CNVs have been associated with cognitive disorders such as schizophrenia and autism and one small study has reported that deletions are associated with lower IQ. We examined the association between carefully selected CNVs that are likely to be inherited and cognitive abilities in a representative sample of ~3,500 12-year-olds from the Twins Early Development Study (just one twin per pair).

More than 200k non-polymorphic probes were used to identify copy number of 6,000 CNVs on a customized Affymetrix DNA array designed for the Welcome Trust Case Control Consortium 2 (WTCCC2). We analyzed individuals' total deletions expecting that having more deletions would be associated with lower cognitive performance.

Despite the high-quality assessment of the selected CNVs, only 1,316 of the 6,000 met quality control criteria, indicating the difficulties in assessing CNVs. For these CNVs, individuals varied widely in their total number of deletions; our distributions were highly similar to large control samples from the WTCCC2. Similar to our analyses with common SNPs, association analyses using common CNVs did not yield any specific associations. Continuous analysis of the total number of deletions as well as comparisons of cognitive scores for high versus low extreme CNV groups yielded no significant results. Additional analyses of length of deletion, frequency, and functionality also showed no effect. In conclusion, CNV deletions to not appear to importantly influence cognitive abilities.

**Shared and unique genetic and environmental influences on changes in multiple cognitive abilities over 16 years of late adulthood**

Elliot Tucker-Drob; University of Texas at Austin Chandra Reynolds; University of California Riverside Deborah Finkel; Indiana University Southeast Nancy Pedersen; Karolinska Institutet

Aging-related declines occur in many different domains of cognitive function during later adulthood. However, whether a domain-general dimension underlies individual differences in different aspects of cognitive change, and whether domain-general genetic influences on cognitive changes exist, is less clear. We addressed these issues using data from 778 individuals (ages 60–96 years) from the Swedish Adoption/Twin Study of Aging, who had been measured on 11 cognitive variables representative of verbal, spatial, memory, and processing speed abilities up to 5 times over up to 16 years. Multivariante linear growth curve models were applied to the data, with either a 1-factor, a 2-factor, or a 4-factor model superimposed on the changes. The four factor model of changes fit the data best. The factors were highly intercorrelated and could, in turn, be specified to load on a higher order global change factor. On average, 56% of individual differences in changes were global in nature, 18% were domain-specific, and 26% were task-specific. Quantitative genetic decomposition indicated that 29% of individual differences in changes in the global dimension were attributable to genetic influences, but significant domain-specific genetic influences on changes in spatial ability and memory persisted, even after accounting for domain-general contributions. Substantial variation in verbal knowledge change was domain-specific and attributable to nongenetic factors. These findings are consistent with a balanced global and domain-specific account of the genetics of cognitive aging.

**Genome-wide complex trait analysis and the missing heritability problem**

Eric Turkheimer; University of Virginia

The missing heritability problem refers to the gap between heritability estimates for complex human traits based on quantitative genetics and the small magnitude and unreliability of contemporary molecular genetics, especially genome-wide association studies. I review the origins of the missing heritability problem and consider research that has attempted to resolve it by quantifying the joint explanatory power of multiple genetic loci, rather than considering their effects one at a time. In the most advanced form of this research program, Visscher, Yang and colleagues have recently developed a method (Genome-wide Complex Trait Analysis, or GCTA) for computing pairwise genetic similarity among “unrelated” pairs using genome-wide SNP data. They have demonstrated that a substantially higher proportion of genetic variance can be recovered using this method, compared to more traditional methods of gene counting and weighting. I will attempt to place GCTA on a continuum running from quantitative pedigree and family analysis through more contemporary gene-finding technologies. I conclude that GCTA makes an important contribution by demonstrating once and for all that the broad conclusions of human quantitative genetics do not depend crucially on the various statistical and genetic assumptions of twin studies. GCTA does not, however, show the way out of the missing heritability problem. Finally, I anticipate some possibilities for the most recent applications of GCTA, in which it is used to estimate classical genetic parameters without relying on familial relatedness.

**The heritability of the startle blink reflex: A twin study**

Uma Vaidyanathan; University of Minnesota Steve Malone; University of Minnesota Scott Vrieze; University of Minnesota Michael Miller; University of Minnesota Scott Burwell; University of Minnesota Matthew McGue; University of Minnesota William Iacono; University of Minnesota

The startle blink reflex is a widely used physiological index of defensive reactivity in humans. It has also been frequently utilized to study abnormalities in emotional processing in various forms of psychopathology (Lang & McTeague 2009; Grillon & Baas 2003; Vaidyanathan et al. 2009) and is considered to be a potential biomarker of fear and anxiety (RDoC 2011). Only two studies, however, have investigated its heritability using twins (Carlson et al. 1997; Anokhin et al. 2007), revealing somewhat contradictory results. The current study attempted to expand upon these results using both conventional biometric models of heritability and molecular genetic techniques including genome-wide association study (GWAS) and genome-wide complex trait analysis (GCTA) of approximately 520,000 single-nucleotide polymorphisms (SNPs), in a large population-representative sample of approximately 1,300 same-sex male and female monozygotic and dizygotic twins and their parents. For all participants, startle blink data were collected using a typical affective-picture startle paradigm in which blink responses to aversive noise probes were elicited in the context of pleasant, neutral, and unpleasant pictures. Results from the various analyses listed above will be presented and discussed both with a view to reconciling discrepancies between the various methodologies and a broader understanding of the notion of heritability and biomarkers.
Additive genetic variance in AST, ALT and GGT levels and its covariance with problematic alcohol use explained by SNPs

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Plasma levels of the liver enzymes AST, ALT en GGT are markers for oxidative stress and liver injury and predict all-cause mortality. Heritability estimates for AST, ALT and GGT range from 22 to 60 %. Liver enzyme levels are increased by alcohol use, and twin studies suggest that genes which influence (problematic) alcohol use have pleiotropic effects on liver enzymes. Currently, less than 2 % of the genetic variance in liver enzymes has been traced back to actual SNP effects, when only genome-wide significant SNPs are considered. It is still unknown how much of the variation in liver enzyme levels, and how much of its covariation with problematic alcohol use, can be explained when the effects of all measured SNPs are considered jointly. To investigate this question we analyze data on AST, ALT, GGT levels, alcohol consumption and the CAGE (a measure for problematic alcohol use) and SNP data collected from two samples: unrelated individuals enrolled in the Netherlands Twin Register (NTR; $N = 2,402$) and a selection of individuals participating in the Netherlands Study on Depression and Anxiety (NESDA; $N = 1,669$).

The variance and covariance explained by SNPs will be estimated with GCTA (Yang et al. 2010, Nat Genet 42:565–569) and by the method proposed by So et al. (2011, Genet Epidemiol 35:447–456). In addition, the method of So et al. will be applied to meta analysis results from an independent study ($N > 55,000$).

A closer look of the association between attention problems and atopic diseases in a genetic design

Toos van Beijsterveldt; VU University, Amsterdam Meike Bartels; VU University, Amsterdam

In a review on the relation between atopic diseases (asthma and eczema) and Attention-Deficit/Hyperactivity Disorder (ADHD), Schmitt et al. (2010) reported an increased risk of ADHD in children with eczema. As most of the included studies were cross-sectional, it was not possible to determine whether this relationship is causal.

To clarify the association between ADHD and atopic diseases the present study examined the relationship between Attention Problems (AP) and atopic diseases in a group of MZ twin pairs discordant for atopic diseases. A discordant MZ twin design controls for the possible influence of genetic and shared environmental factors, and could lead to a more plausible interpretation of the causality of relationships.

For about 14,000 5-years old twin pairs we had data on both atopic diseases and AP. For a part of these twin pairs (8,200) we have also AP measured at age 7. All measures were obtained by mailed surveys.

At the group level, parents reported more AP in children with asthma than in children without asthma at both ages ($T$-scores at age 5: 50.8 vs. 49.9, $p < 0.001$; $T$-scores at age 7: 51.5 vs. 49.7, $p < 0.01$). The results for eczema were less consistent over time, only at age 7 a significant difference in AP between children with and without eczema ($T$-scores at age 7: 50.7 vs. 49.6, $p < 0.001$) was seen. The first results of the comparisons of AP in MZ discordant twins for atopic diseases revealed no significant differences between twin members. These results suggest that it is unlikely that there is a causal relationship between Atopic diseases and Attention Problems.

Reference

Schmitt I, Buske-Kirschbaum A, Roesner V (2010) Is atopic disease a risk factor for attention-deficit/hyperactivity disorder? A systematic review. Allergy 65:1506–1524

False positives and power in the Purcellian G × E model

Sophie van der Sluis; VU University, Amsterdam

In the commonly used gene–environment interaction model proposed by Purcell in 2002, the variance of trait $T$ is decomposed as a function of environmental moderator $M$. Using simulation, we show that the false positive rate of this model can be much higher than the expected 5 % if $M$ and $T$ are correlated, and if $M$ is correlated between twins as well. We show that a simple extension of the original model can solve this problem, but only if the covariance between $T$ and $M$ is itself not subject to moderation. If the covariance between $M$ and $T$ is itself also subject to moderation, then significant moderation effects on the variance composition of $T$ obtained in a univariate setting should be interpreted with care since such moderation effects can have their origin in either moderation of the covariance between $M$ and $T$, or in moderation of the variance components unique to $T$. A bivariate moderation model is required to disentangle these two possible sources of moderation. If, however, moderation on the covariance between $M$ and $T$ can be ruled out, then testing moderation in a univariate setting is recommended because the power to detect moderation effects is higher in the univariate moderation model compared to the bivariate moderation model.

Charting SNP effects in depression: Abandoning the latent trait perspective

Sophie van der Sluis; VU University, Amsterdam

Following the latent trait perspective, depression is a trait that cannot be observed directly (i.e., latent), and that causes individual differences in depressive symptoms. These symptoms, like “lonely”, “sad” and “crying spells”, are believed to co-vary because they all originate in the same latent depression trait. From this perspective, the latent trait mediates relations between depressive symptoms and putative external correlates like genetic variants: the variant affects the latent trait and via the latent trait the depressive symptoms. Consequently, relations of a specific genetic variant with multiple depressive symptoms should all have the same sign when the symptoms are identical coded, and symptom-specific SNP-effects should be negligible. As genome-wide association studies of depression, which implicitly adhere to the latent trait perspective, have to date identified only a few genetic variants of small effect, testing the correctness of the assumed phenotypic model, and the viability of alternative models, deserves attention. Network perspectives on psychiatric disorders, for example, obviate the need to invoke latent traits and assume that covariance between symptoms...
The genomics of personality in a small passerine bird, the great tit Parus major
Kees van Oers; Netherlands Institute of Ecology

Animals within populations consistently differ in the way they deal with environmental challenges. This phenomenon is often referred to as animal personality. Personality differences have been shown to be wide-spread and to influence fitness in natural populations. Quantitative genetic variation underlying personality differences has been demonstrated in studies both on wild as well as captive populations. Until recently it was impossible to connect this variation to genome-wide molecular genetic variation. Such a connection is essential to identify genes responsible for phenotypic variation and to study the way these genes interact with the environment in which they are expressed, in order to describe or predict micro-evolutionary processes. Here we show the first results of the genomic characterisation of the great tit and its associations with personality in an F2 cross population from lines selected for exploratory behaviour.

The role of executive functioning in the progression from substance use to dependence
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Individual differences in executive functioning (EF) have been hypothesized to play an important role in substance use disorders. Evidence suggests that the three most commonly studied executive functions (‘inhibition’, ‘updating’, and ‘shifting’) are separate but correlated constructs (Miyake et al. 2000). A highly heritable common factor (Common EF) has been shown to account for the covariance among these three executive functions, independent of IQ and perceptual speed (Friedman et al. 2008). In our previous analysis, genetic influences on Common EF were related to genetic influences on substance use and substance dependence vulnerability (Vandeven et al. 2011). Although our measure of substance use (number of substances used repeatedly) was less heritable than our measure of substance dependence vulnerability (average dependence symptoms, or total number of DSM-IV criteria endorsed divided by the number of substances used repeatedly), the genetic correlation between substance use and Common EF was greater in magnitude than the genetic correlation between substance dependence vulnerability and Common EF. For the present study we followed up on this finding by examining (a) distinct substance use transitions and (b) not only multi-substance use, but also alcohol, tobacco, and cannabis use separately. We conducted a biometrical analysis using adolescent twins (16–18 years) who had completed a battery of nine laboratory assessments of executive functioning and a structured clinical interview on substance use. Two substance-related transitions were identified: (1) no use, early onset, or late onset, and (2) among users, dependence versus no dependence (assessed by meeting DSM-IV criteria for dependence on at least one substance). Preliminary findings show greater genetic covariance between Common EF and substance use onset than dependence. However, these findings may be dependent on substance type and the definition of early versus late onset.

Present socioeconomic status moderates non-shared environmental influences on general cognitive ability in late middle age
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Ample evidence supports the moderation of genetic and environmental influences on cognition by socioeconomic status (SES), especially in youth. However, only three studies (Kremen et al. 2005, van der Sluis et al. 2008; Grant et al. 2010) have examined moderating effects of parental SES on adult cognition. None of these studies found evidence for genetic moderation, while two found differential evidence for moderation of shared environmental influences. Furthermore, only van der Sluis et al. examined the influence of contemporaneous SES on variation in adult cognition, reporting increasing non-shared environmental influences on IQ associated with living in more affluent areas. These findings suggest that the mechanism underlying the influence on SES on cognition differs between childhood and adulthood. In the present study, we examined the moderating effect of contemporaneous SES on general cognitive ability in a sample of middle-aged male twins, mean age = 55.4, from the Vietnam-Era Twin Study of Aging (N = 1,237). General cognitive ability was assessed using the Armed Forces Qualification Test, a 100-item test that is highly correlated with Wechsler IQ. SES was indexed by the twin’s lifetime educational attainment (in years). General cognitive ability and education were significantly correlated (r = 0.23, p < 0.001). In a bivariate moderation model, education had significant moderating effects on non-shared environmental influences underlying general cognitive ability. With increasing education, non-shared environmental influences decreased, resulting in an overall increase in the heritability of general cognitive ability. For the highest level of education, the heritability of general cognitive ability was h2 = 0.62, while at the lowest level of education h2 = 0.47. This pattern remained even after adjusting for parental education. Our findings provide no support for the genetic moderation by SES for cognition in adult samples. However, our results do provide evidence that the mechanism by which SES influences cognition in adults is through moderation of non-shared environmental influences.
A genetically informative parallel process growth model of externalizing personality traits and smoking behavior in adolescent twins

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Using a longitudinal sample of adolescent twins we explore the developmental relationship between externalizing personality traits and smoking behaviors. Extant evidence suggests a strong phenotypic relationship between substance use behaviors in general and externalizing traits such as conduct disorder and anti-social personality disorder (Kruger & South 2009), and smoking in particular (Spillane et al. 2010). Individuals with conduct disorder are more likely to try substances earlier and exhibit features of substance dependence, with conduct disorder often preceding the onset of substance use. Further, evidence from the behavioral genetics literature suggests that the relationship between externalizing personality traits and smoking has a shared genetic liability (Hicks et al. 2004; Kendler et al. 2003; Young et al. 2000). We explore the genetic and environmental etiology of smoking initiation using genetically informative longitudinal data. Specifically, we fit parallel or dual process growth models to model developmental trajectories of externalizing traits and smoking behavior during adolescence. Our genetically informative data allows us to decompose the variances and the covariance of the latent intercept and slope factors into additive genetic (a), common environmental (c) and unique environmental variance components. Moreover, based on the fact that this is a developmental sample of respondents, this modeling technique will allow us to explore the correlations between the static and dynamic components of externalizing personality traits and smoking. The implications for the initiation into chronic substance use behaviors will be discussed.

Genome-wide scoring to predict substance use pathology

Scott Vrieze; University of Minnesota Matthew McGue; University of Minnesota Michael Miller; University of Minnesota Brian Hicks; University of Michigan William Iacono; University of Minnesota

Many traits appear to have relatively strong polygenic influences, such that the influence of any single nucleotide polymorphism is low. Work on anthropometric traits and some psychiatric diseases indicate that considering the aggregate effect of all SNPs can provide insight into the broad genetic architecture of a trait. In this study of ~8,000 individuals from ~2,000 nuclear families from the Minnesota Center for Twin and Family Research we consider the aggregate effect of ~500,000 common SNPs on substance use measures of alcohol dependence, alcohol use, drug use, nicotine use, and a measure of behavioral dis-inhibition. To aggregate the SNPs we sum them by their univariate regression weight, employing 10-fold cross-validation to control for bias in estimating predictive validity. Much of the sample is composed of twin families, which allows us to compare the aggregate SNP results to estimates of polygenic effect based on twins as well as genome-wide complex trait analysis (GCTA) developed by Visscher and colleagues. The results suggest significant heritabilities for these traits, and indicate that a polygenic effect based on summed SNP scores can be detected, although at low levels in this moderate-sized sample.

Croatian twin study of body mass index and physical activity

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Earlier studies have established that a substantial percentage of variance in obesity-related phenotypes and in exercise behaviors is influenced by genetic and environmental effects. Heritability estimates from different countries range between 65 and 85 % for body mass index (BMI), while this percentage is somewhat lower for exercise behavior (35–55 %). The aim of this study was to explore the relationship between BMI and physical activity in a sample of Croatian twins. Data on BMI and physical activity (frequency and intensity) were collected from 339 twin pairs (105 MZ and 234 DZ) aged between 15 and 22 years.
Heritability estimates from our study are in line with those obtained in previous studies indicating that genetic factors contribute around 80% to individual differences in BMI, around 60% for the frequency of physical activity (FPA) and around 50% for the intensity of physical activity (IPA). Bivariate analyses indicate that there is a positive genetic ($r_A = 0.21$) and a negative non-shared environmental correlation ($r_E = -0.34$) between FPA and BMI, meaning that the same genetic factors contributing to higher FPA also contribute to higher BMI. On the other hand, same non-shared environmental factors contributing to higher FPA also contribute to lower BMI. Genetic and non-shared environmental correlations between BMI and IPA were not statistically significant.

**Longitudinal exploration of the relationship between antisocial behavior and marriage**

Sarah Ward; University of Minnesota Matthew McGue; University of Minnesota William Iacono; University of Minnesota

Research on antisocial behavior has consistently found a relationship between marriage and desistance from antisocial behavior, though it’s unclear whether or not this relationship is accounted for by selection or causal effects. Previous genetically informative studies have generally found evidence for selection effects, with some additional evidence supporting an additional effect of marriage, above and beyond familial risk or previous levels of antisocial behavior (Burt et al. 2010; Barnes & Beaver 2012). However, there is considerable variation in when people choose to get married, and the timing of marriage may moderate this relationship. This is a longitudinal study of 2,700 male and female twins in the Minnesota Center for Twin and Family Research from adolescence to late adulthood, with antisocial behavior data at four separate time points, from age 17 to age 29. This study allows for full exploration of the longitudinal effect of marriage on an individual’s level of antisocial behavior in young adulthood, and in particular, the effect of age of marriage. The use of twin data allows for the exploration of shared genetic and environmental contributions to both traits across an important developmental period, and the use of discordant twins allows for the examination of selection versus causation effects. The sample also allows for exploration of gender effects on the relationship between marriage and desistance from antisocial behavior.

**Genetic and environmental influences on relationship between anxiety sensitivity and anxiety subtypes in children**

Monika Waszczuk; Institute of Psychiatry Helena Zavos; Institute of Psychiatry Thalia Eley; Institute of Psychiatry

Anxiety sensitivity (AS), a tendency to fear anxiety-related symptoms believing they are harmful, has been implicated as a specific risk factor for panic disorder (PD). However, some previous research has found that AS predicts another closely related disorder—separation anxiety (SA). Yet other studies suggest AS is a broad risk factor for all anxiety subtypes.

Here we examined the genetic and environmental underpinnings of the relationship between AS and PD, SA and a more broad anxiety subtype—general anxiety (GA). Self-ratings of AS and DSM-based anxiety (including PD, SA and GA items) were obtained from 300 eight-year-old twin pairs, selected for child anxiety at age 7. The measures were repeated 2 years later.

Longitudinal correlations revealed that AS was significantly correlated with all anxiety subtypes. Partial longitudinal correlations suggested that AS predicts PD and SA, but not GA. At both times, genetic influences on each measure were moderate, common-environmental influences were negligible and non-shared environmental influences were high.

Within-time association between AS and three anxiety subtypes was largely explained by genetic influences (62–99%). Non-shared environmental influences were moderate (16–40%). Longitudinally, the relationship between AS and PD showed substantial genetic overlap (100%), and overlap was also high for GA (96%) but moderate for SA (43%). Non-shared environmental influences did not contribute to the longitudinal associations.

This study shows that shared genetic factors explain correlations of AS with anxiety subtypes in childhood, both within-time and longitudinally. The results support “Generalist Genes Hypothesis”, which states that the covariation amongst traits tends to be due to shared genetic influences. They also suggest the same underlying covariance pattern between AS and PD, SA and GA; implying that while phenotypically AS is a specific predictor of PD and SA, there are no different genetic and environmental patterns of influence that underlie this relationship when compared to GA.

**Exploring the heritability of education attainment using a parent-offspring model**

Gonneke Willemsen; VU University, Amsterdam Dorret Boomsma; VU University, Amsterdam Marleen de Moor; VU University, Amsterdam

We do not randomly choose our partners; one of the traits that is most significant in partner choice is educational attainment. This makes it difficult to get a proper estimate of the heritability of educational attainment is therefore difficult to establish when only data for twins and siblings are available. However, when both parents and offspring are available it is possible to account for the influence of assortative mating, while at the same time providing more opportunity of detecting dominance influences. In the current study we apply a parent-offspring model to educational attainment data collected in Dutch twins, siblings and parents, using data from the Netherlands Twin Register (NTR). The NTR has included questions on educational attainment in all surveys that were sent out to adults registered with the register. Participants were asked to report on their own education as well on the education of their parents. As parents also reported on their own education, we could establish that children’s reports on parental education were highly reliable. As a result, we have educational attainment in more than 23,000 individuals from more than 9,000 families. As there are clear generational changes in educational attainment due to changes in society and education policy, we will examine both sex and age effects on the assortative mating for and heritability of educational attainment.

**Peers and cigarette smoking: Catalyst to initiation or precursor of regular use?**

Amanda Wills; University of Colorado Greg Carey; University of Colorado

Homogeneity in smoking behavior within a peer group is well established, but its causes are poorly understood. Further compounding this complexity are findings of the differential impact of genes and environment on the different stages of smoking behavior. Here, we use a genetically informative sample to examine the relationship between shared peers and smoking at two stages of the smoking process: smoking initiation and regular use. Our participants were twin pairs from Waves 1 (W1) and 2 (W2) of the National Longitudinal Study of Adolescent Health, a representative study of American adolescents in grades 7–12. For smoking initiation, we
found that the number of shared friends did not correlate with similarity of the twin pair’s smoking behavior at either W1 or W2. For regular smoking at W1, however, greater reported shared friends increased smoking similarity between same-sex fraternal and identical twins, but not opposite-sex fraternal twins. Though at W2, with a reduced sample size, this result was only found for fraternal male twin pairs. Our findings suggest that, the degree to which twins belong to a similar peer group may influence progression to regular smoking, rather than initiation of smoking behavior.

Early-age childbearing, marriage, and mental health in women: A genetically-informed study

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Research indicates an association between higher levels of depressive symptomatology and poor social adjustment and childbearing among women, particularly among women who are early childbearers. A family pattern for early childbearing may also exist: daughters of teenage mothers were 66% more likely to become teenage mothers, after accounting for school performance, maternal education, marital status, number of children, dating history and race factors. Similarly, individual and family background factors partially accounted for the adverse outcomes faced by young mothers who had given birth by age 26. In the present study, we examine the effects of early childbearing (before/after age 25) on mental health in different marital status using female twins from the National Longitudinal Study of Adolescent Health, a representative sample of US population. Preliminary analyses suggest a phenotypic effect of early childbearing on depressive symptoms ($B = -0.24, p < 0.001$), which indicates that later childbearing is associated with less depressive symptoms. Correlations suggest both depressive symptoms ($r_{MZ} = 0.51, r_{DZ} = 0.04$) and early childbearing ($r_{MZ} = 0.82, r_{DZ} = 0.28$) are influenced by genetic factors. Using biometric modeling will we examine the quasi-causality of the observed relation between early childbearing and mental health. We will also examine marriage and cohabitation (child born within/outside of marriage and cohabitation) as a moderator of this association.

Intra-species differences in tolerance and genetic polymorphisms in Japanese macaques (Macaca fuscata)

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Japanese macaques live in highly hierarchical societies and high-ranking monkeys attack subordinates so as to monopolize provisions. Regional differences in the frequency of aggressive behavior are well-documented. We investigate whether these regional differences were associated with frequencies of two aggression-related candidate genes in wild Japanese macaques. To assess the degree of tolerance in the Katsuyama group (Okayama prefecture, Japan) and Awajishima group (Hyogo prefecture, Japan), we conducted feeding experiments. In these experiments we counted the number of monkeys within an 8 m diameter circle in which 7.2 kg of wheat was evenly scattered and the number of agonistic vocalizations emitted by these monkeys. Using DNA obtained from fecal samples, we genotyped 55 females in the Katsuyama group and 75 females in the Awajishima group for polymorphisms of two candidate genes for aggressive behavior: the monoamine oxidase A promoter (MAOALPR) gene and the glutamine repeat in androgen receptor (AR) gene. The Awajishima group was more tolerant: the maximum number of monkeys in the circle was 167 in the Awajishima group and 20 in the Katsuyama group; the frequency of aggression was lower in the Awajishima than in the Katsuyama group. There were significant differences in allele frequency distribution between the groups. Although further studies are necessary, these result suggest that regional differences in tolerance between the two wild groups of Japanese macaques are related to polymorphisms in MAOALPR and AR.

Genetic and cultural transmission of political attitude: A study of Japanese adolescent twins and their parents

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This study examined how political attitude is transmitted from parents to offspring in Japanese families. In March 2009, 533 twin pairs (270 MZ and 263 DZ pairs), their 553 mothers and 459 fathers rated feeling thermometers on Liberal Democratic Party of Japan (LDPJ), the Democratic Party of Japan, and the respective party leaders at the time (Taro Aso and Ichiro Ozawa). Twins also rated their perception of parents’ evaluation to the two party and the leaders, separately for mothers and fathers. For each of twins, mothers, fathers, twins’ perception of mothers and fathers, factor analyses on the four items yield a single principal component, construed as positive evaluation to LDPJ. Phenotypic correlations of the evaluation for spouses, mother-offspring, father-offspring, MZ and DZ twin pairs were $r = 0.46, 0.39, 0.25, 0.56$, and $0.37$, respectively. Under both phenotypic assortment and social homogamy model on the twins’ and parents’ own evaluation, omission of dominant genetic influences yielded better fit. In the absence of dominant genetic influences, social homogamy model ($AIC = 14,838.8$) fit better than phenotypic assortment model ($AIC = 14,841.8$). The parameter estimates were $a^2 = 0.09, c_{T2} = 0.17, c_{R2} = 0.25, e^2 = 0.50$, where $c_{T2}$ represents cultural transmission and $c_{R2}$ represents residual shared environmental influences. Trivariate Cholesky decomposition on twins’ and perceived parental evaluations revealed that all the three evaluations were partly explained by both genetic and shared environmental influences ($a^2 = 0.28, 0.22, 0.22$, and $c^2 = 0.24, 0.40, 0.32$, for twins, perceived mothers and fathers, respectively), and 16% of phenotypic variance of twins’ own evaluation was explained by shared environmental influences common to perceived parental evaluations. These results suggested the importance of cultural transmission of political attitudes in Japanese families.

Increased chromosomal damage in adults with a history of childhood sexual abuse: Moving toward a model of biological mechanism

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Childhood sexual abuse (CSA) is a traumatic life event associated with an increased lifetime risk for psychopathology/morbidity. The long-term biological consequences of CSA-elicited stress on...
chormosomal stability in adults are unknown. The primary aim of this
study was to determine if the rate of acquired chromosomal changes,
measured using the cytokinesis-block micronucleus assay on stimu-
lated peripheral blood lymphocytes, differs in adult female
monozygotic twins discordant for CSA. Monozygotic twin pairs (17
pairs, 34 individuals) discordant for CSA were identified from a larger
population-based sample of female adult twins for whom the expe-
rience of CSA was assessed by self-report. Micronuclei (MN) contain
chromatin from structurally normal or abnormal chromosomes that
are excluded from daughter cells during nuclear division and serve as
a biomarker to assess acquired chromosomal instability. Female
monozygotic twins exposed to CSA exhibited a 1.63-fold average
increase in their frequency of MN compared to their nonexposed
cotwin (Paired t test, t16 = 2.65, p = 0.017). No additional effects of
familial factors were detected after controlling for the effect of CSA
exposure. A significant interaction between CSA history and age was
observed, suggesting that the biological effects of CSA on MN for-
mation may be cumulative. These data support a direct link between
CSA exposure and MN formation measured in adults that is not
attributable to genetic or environmental factors shared by siblings.
Further research is needed to understand whether and how these
DNA-based changes might mediate the association between CSA and
adult psychopathology/morbidity.

Is age of alcohol use initiation a risk indicator
or risk mediator for alcohol use disorders in young
adulthood?

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Introduction: An early age of initiation of alcohol use is associated
with later alcohol use disorders (AUD), and has been proposed to be a
cause of later AUD. Results from twin studies, however, indicate that
the association is non-causal and due to correlated genetic risk
factors.

Aims: To test the causal versus non-causal hypotheses of the rela-
tionship between by age of alcohol use initiation and AUD. A model
where age of initiation of alcohol use is an indicator of genetic or
environmental risk for AUD was compared to a model where the
genetic and environmental associations are mediated through age of
initiation of alcohol use.

Methods: We will utilize a population-based sample of 1,336 Nor-
wegian twins who had initiated alcohol use and responded on a
clinical interview measuring DSM-IV AUD.

Results: Compared to the risk indicator model, the mediation model
had a poorer fit to the data. While 34 % of the observed variation in
age of alcohol use initiation was explained by genetic factors, 96 % of
the covariation between age of initiation of alcohol use and AUD was
explained by common genetic risk factors. The remaining 4 % of the
covariation was explained by individual-specific environmental fac-
tors. Environmental risk factors shared by siblings explained (25 %)
of the variation in age of alcohol use initiation, but did not explain the
covariation with AUD.

Conclusion: The overlap between genetic risk factors for age of
alcohol use initiation and AUD appears to be substantial, whereas
environmental risk factors are more or less distinct. A causal
hypothesis on the relationship between age of alcohol use initiation
and AUD was thus not supported by genetically informative data
from this Norwegian young adult population. This has clear impli-
cations for the potential effect of early interventions against AUD
by reducing age of initiation of alcohol use.

Maintenance of genetic variation in human
personality: Testing evolutionary models by estimating
heritability due to common causal variants
and investigating the effect of distant inbreeding

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Personality traits are basic dimensions of behavioural variation, and
twin, family, and adoption studies show that around 30 % of the
between-individual variation is due to genetic variation. There is
rapidly-growing interest in understanding the evolutionary basis of
this genetic variation. Several evolutionary mechanisms could explain
how genetic variation is maintained in traits, and each of these makes
predictions in terms of the relative contribution of rare and common
genetic variants to personality variation, the magnitude of nonadditive
genetic influences, and whether personality is affected by inbreeding.
Using genome-wide SNP data from >8,000 individuals, we estimated
that little variation in the Cloninger personality dimensions (7.2 % on
average) is due to the combined effect of common, additive genetic
variants across the genome, suggesting that most heritable variation in
personality is due to rare variant effects and/or a combination of
dominance and epistasis. Furthermore, higher levels of inbreeding
were associated with less socially-desirable personality trait levels in
three of the four personality dimensions. These findings are consistent
with genetic variation in personality traits having been maintained by
mutation-selection balance.