largest genome-wide association study (GWAS) of EA to date (EA3, discovery sample) and estimate polygenic scores (PGS) in two independent target samples of young adults with neuroimaging data from Australia (N = 1165) and the USA (N = 723), to examine how the genetic factors underlying educational attainment and cognitive ability relate to brain structure. Higher EA-PGS significantly predicted larger global brain morphometry measures, such as intracranial volume and total surface area (R^2 = 0.006 and 0.016 respectively, $p < 0.001$) in both independent samples. Remarkably, EA-PGS also predicted cortical surface area of three frontal and three temporal regions in both target samples (over and above total surface area). The identified regions have been robustly implicated in language, memory, visual recognition and cognitive processing. Additionally, individuals with higher EA-PGS achieved higher scores in cognitive tests and we demonstrate that these identified brain regions partly mediate the association between EA-PGS and cognitive test performance, accounting for approximately 20% of the variance explained in IQ scores. Altogether, these findings advance our understanding of the neurobiology that underpins educational attainment and cognitive ability and provide focus points for future research.

Update on Australian genetics of depression study

Nick Martin, QIMR Berghofer Medical Research Institute

More than 20.000 depression cases have been enrolled at DNA and GWAS have been obtained on > 16,000 of these. Early results will be presented with a focus on response to anti-depressant medication.

Five ways to analyze 50,000 pairs of related persons in the National Longitudinal Survey of Youth

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With the rise of molecular genetics methodologies like genome-wide complex trait analysis (GCTA), it becomes critical to viscerally understand how these newer methods relate to the older twin and family methods. Such an understanding informs what novel findings may result from the new methods. This presentation uses the National Longitudinal Survey of Youth (NLSY) to exemplify the techniques. The NLSY is an excellent test-bed for a wide array of biometric analysis methods due to its (a) large, representative sample from the United States, (b) copious number of diverse outcomes, (c) longitudinal data collection, and (d) burgeoning cross-generational structure. We analyze both standard and unconventional outcomes from the NLSY in five related ways. First, we analyze outcomes in the standard form of a structural equation model (SEM). Second, the identical analyses are conducted as a multilevel SEM. Third, multiple large blocks of pedigrees are used to include extended relationships such as cousins. Fourth, the entire data are analyzed as a single genetically-related family using the conventional GCTA software. Fifth, multivariate outcomes are studied for the entire data using the OpenMx software. Each of these ways of structuring the analysis for the NLSY allows certain questions to be answered while forcing the researcher to omit or make assumptions about others.

GWAS on the Internet: systematic review of online news and blog articles about GWAS publications from 2005 to 2018

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In this study, we present a systematic review of news and blog articles on GWAS since its inception, combining statistical analysis with text mining techniques. GWAS publications were identified via the NHGRI-EBI GWAS Catalogue and classified into phenotype categories using the ICD-10. Blog and news articles about these studies were identified using the Altmetric database.

As of 19/09/18, there were 3557 GWAS studies on 1945 different traits. We found 5349 different English language websites that mentioned these publications. Only 41.4% of those websites offered original content (not copied from another website). The most researched areas were non-disease traits (e.g., body mass index, educational attainment, metabolic traits, etc.; N = 1197), neoplasms (N = 462), and mental and behavioral disorders (N = 371). However, only 20.1%, 21.4%, and 15.9% of scientific papers in these areas were mentioned in two or more websites, respectively. Year of publication, number of hits, impact factor, and sample size, were positively and significantly associated with number of online mentions. Non-disease traits generated 2.5 times more mentions than predicted by those variables, while behavioral disorders generated 2 times less, suggesting different patterns in public interest. The Top 5 topics in the news were genetics of Alzheimer's disease, depression, breast cancer, intelligence, and asthma. Finally, readability analysis revealed that more than 95% of all online articles required at least university-level reading skills to understand them. Implications for science communication and genetic literacy campaigns will be discussed.

A cross-country, cross-reporter twin study of oppositional defiant disorder

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Oppositional defiant disorder (ODD) is characterized by a persistent pattern of anger, defiance, or vindictiveness that impairs social functioning. Often beginning during preschool years, temporally it precedes most comorbid disorders. Genetics contributes to the etiology of ODD but research that associates parenting practices with ODD has not been conducted in a genetically sensitive design. We examined the heritability of ODD symptoms in two twin cohorts, one Australian and one Dutch. In Australia, mothers (N = 1281) reported ODD for twins at age ~ 14.3 using the SWAN, and twins self-reported (N = 2210) lifetime incidence of ODD at age ~ 27. An overlapping sample on both measures was available on 246 individuals (110 complete pairs). In the Netherlands, mothers (N = 16,584) and fathers (N = 11,676) reported ODD at age ~ 12.2 using the CBCL12, and twins self-reported (N = 4841) ODD at age ~ 16.9 using the YRS. An overlapping sample on parental and self-report was available for 904 monozygotic and 1138 dizygotic complete

pairs. ODD was moderately heritability across all measures and both countries. Heritability was higher in Australia, 59–76% from mothers and self-report, compared to the Netherlands, 37–51% from mothers, fathers, and self-report. The family environment was only influential in the Netherlands. Mothers and fathers report variance decomposition could be equated and implies a high degree of similarity in parental perception of ODD behaviors. In Australia, ODD score from mothers was associated with self-reported ODD. In the Netherlands, parental report of ODD had a small correlation with self-report 4 years later and this correlation was mainly due to genetic factors.

Criteria for DSM-5 personality disorders and risk of alcohol and substance abuse in Norwegian twins

Tom Rosenström, University of Helsinki; Fartein Ask Torvik, Norwegian Institute of Public Health; Eivind Ystrom, Norwegian Institute of Public Health; Steven Aggen, Virginia Commonwealth University; Nathan Gillespie, Virginia Commonwealth University; Robert Krueger, University of Minnesota; Nikolai Olavi Czajkowski, University of Oslo; Kenneth Kendler, Virginia Commonwealth University; Ted Reichborn-Kjennerud, Norwegian Institute of Public Health

Personality disorders (PDs) are associated with alcohol (AUD) and substance use disorders in the general population. However, the DSM-5 definitions of PDs have been criticized and the PDs are highly comorbid with each other. A series of three studies on etiologic specificity and mechanisms behind the PD-AUD associations is discussed. We investigated 2801 Norwegian twins using structured interviews on PDs, AUD, and other substance use. When all 80 DSM-5 PD criteria were adjusted for each other in an Elastic Net regression model, only three specific PD criteria predicted AUD. These specific criteria were for Antisocial (ASPD) and Borderline (BPD) PDs. ASPD and the three specific criteria, self-damaging impulsivity (BPD criterion #4), childhood conduct disorder (ASPD #8), and violations of social norms on lawful behavior (ASPD #1) each mediated over 50% of effects of childhood stressful life events on AUD according to a genetically informative mediation model, whereas BPD appeared as a confounded variable in such mediation model. Finally, a bifactor model indicated that the PD-related AUD risk factors all reflected some latent dimension of risk for all ASPD and BPD criteria rather than more specific factors. These findings are discussed in the light of emerging hierarchical taxonomy of psychopathology and in the context of clinical environments. For example, personality-based indirect indices of substance-abuse risk could be valuable when making decisions regarding prescriptions of potentially addictive drugs.

Well-being, loneliness, and self rated health; what's the chicken and what's the egg?

Meike Bartels, Vrije Universiteit Amsterdam; Margot van de Weijer, Vrije Universiteit Amsterdam; Bart Baselmans, Vrije Universiteit Amsterdam

Existing literature has established that loneliness, characterized by a sense of emptiness, worthlessness, and a lack of control, is negatively associated with well-being. Moreover, self-rated health, a subjective evaluation of one's current health status, has also been pointed out as an important predictor of well-being, due to its high proportion of shared variance with well-being.

The correlation between two variables can reflect reverse causation or unobserved factors that influence both. Mendelian Randomization (MR) can be used to get a better hold on causality by estimating the causal effect of a risk or protective factor on an outcome, provided that genetic variants are known that influence the risk factor.

In order to answer questions like: "Do lonely people become unhappy or is unhappiness the driver for a lonely life", or "are people happy because they are healthy or the other way around", we will apply an MR approach. We will use the summary statistics of large Genome-Wide Association Studies for well-being (Baselmans et al. 2018), loneliness (Abdellaoui et al. 2018), and self-rated health (Harris et al. 2017) and conduct two sample bidirectional MR analyses to establish whether well-being affects loneliness and/or self-rated health, or vice versa.

Using polygenic scores for unbiased SNP-heritability estimation

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In recent years, many methods have been proposed to estimate SNP-based heritability. Methods such as GREML are sensitive to several assumptions about the genetic architecture of traits (e.g., regarding the relationship between MAF, LD, and effect size). In addition, methods using summary statistics, such as LD-score regression, typically suffer from attenuation bias when used to infer SNP-based heritability, as a result of differences in LD between the reference and GWAS samples. Finally, heuristic methods based on polygenic scores (PGSs) also suffer from attenuation bias, as the inferred PGS based on a finite-sample GWAS is a noisy approximation of the true PGS.

However, a major strength of PGS-based approaches is that they are agnostic about the exact genetic architecture of a trait. In addition, the attenuation bias in a PGS-based approach can be ameliorated by constructing different PGSs for the same trait using different GWAS results, and then applying GIV regression, thereby obtaining an unbiased estimate of SNP-based heritability, regardless of the exact genetic architecture of the trait at hand.

In addition to trait architecture, there is a plethora of further statistical nuisances that may bias classical SNP-heritability estimation, such as assortative mating and gene–environment correlations, including population stratification and genetic nurture.

We now combine a within-family design with GIV regression, and investigate the potential of this new approach for unbiased SNP-heritability estimation in the presence of various genetic architectures, as well as genetic nurture and population-level confounds, such as population stratification and assortative mating.

Low back pain, neck pain, and sleep quality. Genetic and environmental relationships

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Background: There is a close relationship between sleep quality and both neck and low back pain, that includes common genetic influences among them. However, this relationship has not been widely studied. Therefore, the aim of this study was to investigate the genetic