

INTERNSHIPS BIOLOGICAL PSYCHOLOGY VRIJE UNIVERSITEIT AMSTERDAM

The Department of Biological Psychology offers a wide variety of internships, including behavioural genetic and epidemiological topics but also topics related to methodology and mathematics. Internships are open to Bachelor and Master students within the Department of Biological Psychology but also, when sufficient background knowledge is present, for students from other departments and universities.

To apply for an internship, please read through the internship list, choose a topic and follow the relevant procedure, as outlined below.

Bachelor students learning track Genes, Brain and Behaviour

You will be requested by the B-thesis coordinator to indicate the top-3 of topics you are interested in. The B-thesis coordinator will allocate the topics based on the preferences indicated by all B-thesis students. Note that you need to have followed the related minor and methodology 3 course prior to enrolling in the B-thesis course.

Research Master students Genes in Behaviour and Health

Apply for the topic of your interest by providing the supervisor (first listed in case of multiple supervisors) with a brief motivation for your choice and your cv. More information is provided within the RM programme.

All other Bachelor and Master programmes.

Send an email with a motivation letter, CV, and a list of your grades to the Internship coordinator, Dennis van 't Ent (d.vant.ent@vu.nl). If you are interested in multiple topics, please provide a top-3.

LIST OF INTERSHIP POSSIBILITIES

Please find below the internships offered at the Department of Biological Psychology.

Effects of regular exercise on daily-life stress reactivity.

The health benefits of regular exercise behaviour have been extensively documented in epidemiological research but the exact biological mechanisms by which this beneficial effect is generated remain to be elucidated. About 30 years ago a popular hypothesis invoked buffering effects of exercise of physiological stress reactivity as a major explanation. After about a decade of research this hypothesis was abandoned because meta-analysis of randomized training intervention studies showed little impact of regular exercise on laboratory stress reactivity to a variety of mental stress tasks. Despite this, the stress buffering hypothesis is very much alive to date as it seems to resonate strongly with folk wisdom. What is going on? Should we simply dismiss folk wisdom as wishful thinking or did we use the wrong paradigms to study effects of regular exercise on stress reactivity? The aim of the current B-thesis project is to re-investigate the relationship between regular exercise behaviour and stress reactivity, not using artificial laboratory stressors, but looking at stress reactivity to naturalistic settings in daily life with use of the VU-AMS. In addition, two new summary measures of autonomic stress reactivity will be used (Berntson, Norman, Hawkley, & Cacioppo, 2008) that may better capture individual differences in stress reactivity.

Level: B-thesis

Students make use of ambulatory datasets collected in the past to perform data analyses on the effects of regular exercise on ambulatory stress reactivity.

Requirements: This project requires basic statistical skills, knowledge of SPSS and background knowledge on the biology of the ANS.

Supervisors: prof dr. Eco de Geus, Denise van der Mee, MSc.

Berntson, G. G., Norman, G. J., Hawkey, L. C., & Cacioppo, J. T. (2008). Cardiac autonomic balance versus cardiac regulatory capacity. *Psychophysiology*, 45(4), 643-652. doi:10.1111/j.1469-8986.2008.00652.x

Investigating the relationship between affective states and autonomic nervous system activity

In a recently started project in collaboration with Philips, the relationship between (positive & negative) affect and various autonomic nervous system (ANS) activity measures is investigated. The relationship between affect and ANS activity has already been a topic of interest for many years. However, to date the vast majority of these studies have investigated this relationship in a laboratory setting with use of artificial stressors, limiting their ecological validity. This is partially due to a lack of possibilities to measure ANS activity in an ambulatory setting in the past. However, progress is being made in the development of such devices, like the VU-AMS here at the VU. The aim of the current study is dual. Firstly, this study aims to investigate the relationship between affect and ANS activity during daily life with use of the VU-AMS. Secondly, this study aims to validate two wrist watches (one measuring heart rate and one measuring skin conductance) under development at Philips. These watches could provide novel ways to measure ANS activity during prolonged recordings in daily life.

To study these aims participants will perform a variety of task (known to influence ANS activity) at our laboratory while wearing the VU-AMS and the two Philips watches. They will continue to wear these devices during a 24 hour ambulatory measurement to measure ANS activity in daily life. At the laboratory section participants are asked to report their affect after various tasks, by filling in a short questionnaire. During the ambulatory section participants are asked to report their affect (but also main activity, location and social environment) by filling in a short diary on an iPod hourly.

Level: B-thesis & M-thesis

Students gain hands on experience in collecting and handling diverse data types. The student will assist the PhD in participant recruitment, data collection and data cleaning and perform analyses on the laboratory data but additionally perform more involved data analyses combining data from various domains and across laboratory and ambulatory data sets.

Requirements: This project requires basic statistical skills, knowledge of SPSS and background knowledge on the biology of the ANS. Experience with VU-AMS or diary data, R/Matlab and fluency in Dutch is preferred.

Supervisors: dr. Martin Gevonden, prof dr. Eco de Geus, & Denise van der Mee, MSc.

What is the role of the autonomic nervous system in cognitive functioning?

There is a growing body of empirical evidence demonstrating that (intra- and inter-) individual differences in cognitive functioning relate to differences in the activity of the autonomic nervous system (ANS). Indices of heart rate variability, for instance, have been found to associate with verbal memory in middle-aged men and with executive functioning in the elderly. In addition, autonomic nervous system activity is associated with the performance on tasks requiring attention and inhibitory control in both healthy and clinical samples of children. The master thesis student will engage in an in-depth investigation of the association between cognitive task performance (speed+accuracy) and cardiac ANS activity at rest and during the actual execution of the cognitive tasks. For this investigation we have already collected a large dataset on cognitive as well as cardiac ANS functioning in a sample of ~1000 twins and twin family members (Swagerman et al. 2015, *Brain Cognition*, 97:32-9). Measures of cognitive functioning span a broad range of cognitive domains (17 different tasks). Because data were collected in a genetic informative sample they provide the unique opportunity to study genetic and non-genetic contribution to the association. Various student-specific questions on modifiers of the association between ANS and cognition can be formulated, because participants had been interviewed extensively on e.g., education of parents and self, subjective health or well-being, smoking and drinking behaviour, exercise behaviour, and medicine use.

The student will be tasked with (1) careful signal analysis of the ECG and impedance cardiography recordings at rest and during the cognitive tasks to extract measures of cardiac ANS activity, (2) performing analyses to confirm or refute an association between this cardiac ANS activity and the performance in various cognitive domains, and (3) to report on the results of the analyses in a master thesis.

Level: M-thesis

Requirements: Good statistical skills, knowledge of SPSS, and ideally R/Matlab ; background knowledge on the biology of the ANS.

Supervisor: Prof dr. Eco de Geus

Personality and sports preference: are runners introverts, soccer players extraverts, and martial arts adepts sensation seekers?

The link between personality and sports preference has long been established, amongst others by the famous Hans Eysenck (Eysenck, Nias, & Cox, 1982). Recent reviews have reconfirmed this link (Rhodes & Smith, 2006) and the topic seems to be regaining popularity. A major concern with most previous studies, however, is that they have treated leisure time exercise behaviour as a uniform construct by summing all exercise and sports activities that the person engages in into a summary score that either reflects the time spent on exercising, or an estimation of the total energy expended in exercise. The latter is done by multiplying frequency, duration, and an estimate of the intensity of the exercise activities usually expressed as a multiple of the basal metabolic rate, i.e. in MET hours/ weekly.

Although the use of such a summary score is very valuable, it cannot detect more detailed patterns in the tracking of different types of exercise behaviour. Ideally tracking coefficients would be analysed for each sport or exercise activity individually (fitness, soccer, jogging, tennis, karate, etc.) but doing so would significantly reduce the number of available subjects per cell even in very large databases. Therefore, as a compromise, exercise activities could be divided into domains based on three dimensions (1) a team-based or individual nature, (2) a competitive or non-competitive nature, and (3) an externally paced or an internally paced nature. The third of these dimensions is based on the nature of the skills required in the exercise activities (van der Mee et al., 2017). Exercise behaviour in these different domains is likely to be differently associated with different personality traits.

Level: B-thesis & M-thesis

B-thesis students make use of existing datasets to test a differential association of neuroticism, extraversion, and sensation seeking to regular voluntary exercise behaviour in these various domains. At M-thesis level the genetic contribution to these associations is additionally researched using either bivariate twin modelling or polygenic risk scores for the personality traits.

Requirements: This project requires basic statistical skills, knowledge of SPSS and background knowledge on personality theory. At M-thesis level, good statistical skills, knowledge of SEM, OpenMX are required.

Supervisors: prof dr. Eco de Geus, Matthijs van der Zee, MSc.

Eysenck, H. J., Nias, D. K. B., & Cox, D. N. (1982). Sport and personality. In S. Rachman & T. Wilson (Eds.), *Advances in behaviour research and therapy* (pp. 1-56). Oxford: Pergamon Press. (Reprinted from: Not in File).

Rhodes, R. E., & Smith, N. E. I. (2006). Personality correlates of physical activity: a review and meta-analysis. *British Journal of Sports Medicine*, 40(12), 958-965.

van der Mee, D. J., Fedko, I. O., Hottenga, J. J., Ehli, E. A., van der Zee, M. D., Ligthart, L., . . . de Geus, E. J. C. (2017). Dopaminergic Genetic Variants and Voluntary Externally Paced Exercise Behaviour. *Medicine & Science in Sports & Exercise*. doi:10.1249/MSS.0000000000001479

Heritability of objectively assessed physical activity during the week and the weekend.

Voluntary exercise behaviour has been found to be heritable from adolescence onwards. Genetic differences between individuals account for up to 70% of the variance in exercise behaviour. These large-scale population based studies though, are based on self-report and survey-based measures of voluntary exercise behaviour. A disadvantage with this survey method is that a lot of physical activity is not captured because it occurs outside exercise activities (dancing, biking, physical labor at work). Within this project the student will use data on physical activity collected with a hip-worn accelerometer. Resemblance between MZ and DZ twins will be used to estimate the heritability of objectively measured vigorous intensity physical activity, moderate intensity activity, and light intensity physical activity, separately for week days and the weekend.

Level: B-thesis

Requirements: Some experience with basic statistics and SPSS (or comparable programs) is required.

Supervisors: Prof dr. Eco de Geus & Matthijs van der Zee (PhD candidate)

Exercise behaviour and epigenetics in monozygotic twins

Epigenetic mechanisms such as DNA methylation regulate the expression of genes in cells, and may respond to environmental influences. Previous studies have reported that exercise may induce epigenetic changes in cells. For example, directly after exercise, skeletal muscle cells show changes in DNA methylation and gene expression that trigger structural and metabolic adaptations of muscle tissue. Vice versa, epigenetic mechanisms may also influence exercise behaviour. This project aims to investigate if monozygotic twins who differ in voluntary exercise behaviour display differences in DNA methylation in white blood cells. This study may provide novel insights into the effects of exercise behaviour on immune-system related functions. The student will perform statistical analysis of existing DNA methylation data from monozygotic twins and link this to information on exercise behaviour to examine the question which locations in the genome show differences in DNA methylation between monozygotic twins who are discordant for exercise behaviour. The student will perform basic statistical analyses (paired t-tests, correlations) of candidate genes in R or SPSS.

Level: B-thesis.

Requirements: An interest in the topic, experience with basic statistics and some experience with a statistical program such as SPSS or R.

Supervisor: Dr. Jenny van Dongen, Prof. Eco de Geus, Matthijs van der Zee Msc

Epigenetic discrimination of monozygotic twins

In forensic settings, monozygotic (MZ) twins are indistinguishable via traditional DNA profiling because their DNA sequences are identical. Recent studies have therefore explored if epigenetic (DNA methylation) profiles could be used for discrimination of MZ twins. It is known that MZ twins exhibit differences in DNA methylation, but a lot still remains unclear, for instance: are loci that show DNA methylation differences between MZ co-twins unique to each pair or do any loci exist that display variable methylation levels in all MZ pairs? Which DNA methylation differences between MZ twins are stable across time, and which DNA methylation differences are detectable in different tissues? For forensic applications, the epigenetic profile of trace DNA (DNA collected at a forensic scene) should be linked to epigenetic profiles of reference DNA (DNA collected from potential suspects). The tissue source of these materials are usually different (i.e. buccal/cheek cells are an ideal source of reference DNA because they are easy to collect but these cells are not typically left at a crime scene). In this internship project, the student will first perform a literature review on this topic. Next, he or she will analyse existing DNA methylation datasets from the Netherlands Twin Register, including genome-wide DNA methylation in buccal and blood and DNA methylation in longitudinal blood samples to investigate DNA methylation differences between MZ twins and their potential use for discrimination of MZ twins.

Level: M-thesis

Requirements: Experience with programming in R, an interest in the topic.

Supervisor: Dr. Jenny van Dongen, Prof. Dorret Boomsma

The Happiness-Formula

Recently it has been claimed that there is some kind of happiness-formula (see for example Mo Gawdat's book Solve for happiness). In the presentation of this formula differences between people are largely ignored. Is there such thing as a happiness-formula? And which factor play a significant role. In a collaborative project of Hope XXL (hope-xxl.com), Professor Meike Bartels, and Bart Baselmans, information in happiness, flourishing, and satisfaction with life is collected in a sample of about 2000 individuals living in the east of the Netherlands. Besides these well-being measures, we gather information on life-style, living environment, and work. In this project, we would like to sort out if some factors are more important than others factors for overall well-being. We, furthermore, would like to compare these data to population-based data of the Netherlands Twin Register. HOPE XXL wants to ensure that all people can achieve a life they can grade as 'good'. Therefore, they developed a new vision on the future with young people from all over the world. This vision, called the Liemers List, was presented to the United Nations in February 2015. With the current project, we will start to make this vision evidence-based.

Level: B-Thesis

Requirements: basic statistical skills

Supervisor: Prof. dr. Meike Bartels & Bart Baselmans.

Family conflict & self-control in adolescence

Family conflict brings tremendous costs to individuals and society. Although it is reliably associated with multiple problems, the pathways underlying these associations are poorly understood hampering effective interventions. We propose that self-control plays a key role in family conflict because of its foundational function in regulating behaviour, emotions, and cognition. As a result, we hypothesize that coping with family conflict and associated stressors depletes individuals' self-control strength. In order to test this hypothesis, this study aims to investigate the association between family conflict and associated stressors and self-control, expecting them to correlate cross-sectionally and longitudinally. The Netherlands Twin Register includes measures to validly operationalize self-control (ASEBA-SCS) family conflict (e.g. "we fight a lot at home", "Family members get so angry, they throw things") and family stressors (e.g. "someone close passed away", "one of my parents lost their jobs recently"). These measures have been assessed at age 14, and 16 and therefore the present study will focus on adolescence.

Level: B or M-thesis

Supervisors: Prof dr. Meike Bartels, Yayouk Willems, Msc

Reference: Finkenauer, C., Buyukcan-Tetik, A., Baumeister, R., Schoemaker, K., Bartels, M., & Vohs, K. D. (2015). Out of control: Identifying the role of self-control strength in family violence. *Current Directions in Psychological Science*, 24, 261-266

Are optimistic individuals happier or does a half empty glass not influence overall wellbeing?

It sounds obvious that optimistic people are happier. Or could we better say that happy people are more optimistic? This is however more based on folk wisdom and on any evidence-based fact. Individual differences in optimism and wellbeing, such as happiness, are accounted for by genetic differences and differences in environmental influences. About 40% of the variance is accounted for by genes. The open research questions are if there is a significant association between optimism and wellbeing and if so if this is accounted for by overlapping genes. In addition the large-scale longitudinal data of the NTR provide the opportunity to gain insight into the direction of causation. Do optimistic people become happier or are happy people more optimistic?

Level: B-thesis

Requirements: Some experience with basic statistics and SPSS (or comparable programs) is required.

Supervisor: Prof dr. Meike Bartels

Choosing your environment; Differences in environment between happy and unhappy individuals

There has been a fair amount of research, including my own work, into the underlying sources of familial aggregation of wellbeing. A recent meta-analysis reveals that about 35% of the variance in wellbeing is accounted for by genes. Additionally, several studies have attempted to unravel the environmental and social correlates of wellbeing. Main focus has been on income and life events, such as relationship status and employment status. A literature review, however, calls for caution in the interpretation of such determinant studies, due to lack of evidence on the direction of causation. It should also be noted that most of these 'environmental' or 'non-genetic' correlates are actually influenced by genes, necessitating an integrated approach of genetic and environmental research. Focus so far has been on additive models in which independent effects of genes and environment add up to explain individual differences in wellbeing. If, however, genes and environment do not act in an additive manner, as is to be expected for multi-factorial complex traits such as wellbeing, ignoring the presence of gene-environment interplay will lead to biased estimates of the relative importance of both genetic and environmental factors and will provide an incomplete and simplistic picture of the etiology of wellbeing. The proposed thesis focuses on the gene-environment correlation in wellbeing. Gene-environment correlation (r_{GE}) describes the genetic control of exposure to the environment, resulting in a non-random distribution of environments over distinct genotypes. Within this project the results of a genome-wide association study for Wellbeing will be used to compose poly-genic risk scores. This risk scores will then be associated to environmental factor as assessed in the large-scale database of the Netherlands Twin Register. With this project we will gain insight into the "happy environment".

Level: M-thesis

Requirements: this project requires innovative analysis of existing data, knowledge of SPSS (or similar software) is required,

Supervisor: Prof dr. Meike Bartels & Bart Baselmans, MSc

Is the influence of heritable and environmental factors on ADHD symptoms different in highly intelligent individuals (IQ>120) compared to (below) average intelligent individuals?

Attention-deficit/Hyperactivity Disorder (ADHD) is a highly heritable disorder with a prevalence of around 5-7% in children and adolescents. However, the validity of ADHD in individuals with high intelligence is highly disputed, since some argue that high intelligence may 'mimic' the symptoms of ADHD in the absence of the specific pathophysiological pathways for ADHD. Surprisingly, no studies have been conducted examining whether the etiological factors underlying ADHD symptoms in highly intelligent individuals are indeed different from those underlying ADHD in (below) average intelligent individuals. The main aim of this project is to examine this issue using data of the Netherlands Twin Registry. More specifically, it will be examined whether (1) the contribution of genetic and environmental factors to ADHD symptoms is comparable for highly intelligent versus (below) average intelligent individuals and whether (2) the shared genetic factors underlying ADHD and intelligence is moderated by intelligence level.

Level: M-thesis

Requirements: An interest in the topic and some experience with basic statistics, twin analyses and SPSS (or a comparable program) is required.

Supervisors: Dr. Eveline de Zeeuw & Dr. Nanda Rommelse (Radboudumc)

Characteristics of highly intelligent underperformers

Intelligence and school performance are robustly correlated. However, in individual cases large discrepancies can occur between measured IQ and actual school performance. It is not well understood what factors differentiate these highly intelligent underperformers from highly intelligent performers. It may be hypothesized that symptoms of neurodevelopmental disorders (ADHD and/or ASD) and/or weak executive functions may be more prevalent in the former group contributing to an overall lower level of functioning. The main aim of this project is to examine if there are differences between highly intelligent performers and underperformers with respect to these two domains. Data comes from the Netherlands Twin Registry. Highly intelligent individuals are selected based on an IQ score of ≥ 120 . (Under)performing is operationalized as the discrepancy between the CITO school performance data in comparison to the IQ score.

Level: M-thesis

Requirements: An interest in the topic and some experience with basic statistics, twin analyses and SPSS (or a comparable program) is required.

Supervisors: Dr. Eveline de Zeeuw & Dr. Nanda Rommelse (Radboudumc)

Parental psychopathology and its effect on self-control in childhood

Parental psychopathology has been shown to be associated with internalizing and externalizing problems in children. However, most research cannot draw conclusions about the causal pathways underlying these associations. It is possible that the association is merely due to the fact that parents do not only provide the environment in which their children grow up, but also each contribute 50 per cent of their genes. As a consequence the association might reflect genetic transmission instead of an environmental effect. This study will try to unravel which aspects of the family environment have a 'true' causal effect on self-control by using a polygenic score design in which the fact that parents pass, at random, only 50% of their genes to their offspring while 50% of their genes are not transmitted, is utilized. Two scores summarizing the genetic predisposition for different types of psychopathology based on the transmitted and on the non-transmitted alleles can be employed to test for the effect of parental psychopathology on self-control that is not confounded by the offspring's genetic make-up. If the non-transmitted alleles for parental psychopathology are associated with lower self-control in the offspring this provides support for the causal effect of parental psychopathology on self-control.

Level: B- or M-thesis

Requirements: An interest in the topic and some experience with basic statistics and SPSS (or a comparable program) is required.

Supervisors: Dr. Eveline de Zeeuw

The link between self-control and psychopathology

Children vary a lot in their ability to adopt to rules and control their emotions, behaviour and impulses. This so called self-control is a moderate to highly heritable trait with estimates for the heritability ranging from 50 to 80% and shows genetic overlap with psychopathology in adulthood. Much less is known on this link between behavioural control and different types of psychopathology in children. This study will use the classical twin design and the large dataset available in the Netherlands Twin Register to investigate the contribution of genetic and environmental factors to the association between behavioural control and different types of psychopathology (e.g. attention problems, autistic traits, anxiety, depressive symptoms). The aims will be 1) to determine the extent to which self-control overlaps with psychopathology and 2) to determine whether this overlap is due to genetic pleiotropy, i.e. when the same genes, through the same underlying biological mechanisms, affect both phenotypes or to a causal relationship between the two phenotypes.

Level: B-thesis

Requirements: An interest in the topic and some experience with basic statistics, twin analyses and SPSS (or a comparable program) is required.

Supervisors: Dr. Eveline de Zeeuw

Aura without migraine: why do some “migraineurs” not have headaches?

In many patients, migraine headaches are preceded by so-called aura symptoms, which most often manifest as temporary visual disturbances preceding, or coinciding with the start of a migraine attack. Some patients, however, have aura symptoms without headaches. Other patients have migraines but no aura symptoms. Or their headaches disappear as they get older, while the aura remains.

In the NTR, we have collected data on aura symptoms in individuals with and without migraine headaches. This allows us to investigate the relationship between aura symptoms and the migraine attack. Do patients with aura, but without headache, share the typical characteristics observed in migraineurs? For example, are they at increased risk of anxiety, depression, and other pain symptoms? Or are they in fact at a lower risk of these things, which would suggest they are somehow protected against developing headaches?

Level: B-thesis

Requirements: Due to the nature of the dataset, this project is only suited for Dutch-speaking students. Some experience with basic statistics and SPSS/R (or comparable programs) is required.

Supervisor: Dr. Lannie Ligthart

Addiction – a consequence of loneliness? Testing the ‘Rat Park hypothesis’ using a natural experiment in humans

The intriguing findings of the ‘Rat Park experiment’ continue to stir debate even today. This animal experiment showed that drug self-administration in rats (in preference to water) depends heavily on whether they are placed in a cage alone, or in an environment that allows for social interaction. The controversy aside, there are numerous studies persistently showing that loneliness associates with substance use also in humans. Substance use and loneliness are increasingly recognized as serious public health concerns. Evidence suggests that early initiation of substance use (before age 18) ‘opens the gate’ for experimentation with other drugs and progression to escalated use, abuse and dependence. Regular substance use is predictive of health problems, poor educational and professional achievement. Loneliness increases the odds of premature death by ~26%, being as hazardous to our health as smoking or obesity.

However, serious gap in knowledge exists regarding the interpretation of this association, as we are severely limited by the correlational design of the human study: based on the observed associations we cannot distinguish between conditions that lead to substance use and those that are the consequence of substance use. Does loneliness causally increase the likelihood of initiation/regular substance use, or does substance use causally affect loneliness? Or, is there a common underlying factor that increases the vulnerability to both substance use and loneliness? The dramatic advancements in genotyping technologies and statistical methodology provide us with the unprecedented opportunity to test these hypotheses by taking advantage of a natural experiment in humans (enabled by random inheritance of genetic variants).

This project aims to test the nature of the association between substance use and loneliness (is the association causal in nature?), and to test whether substance use is a cause or a consequence of loneliness. The student will test these hypotheses using a recently developed analysis method that allows for causal inferences on the basis of genetic data. The student will analyse data from the

Netherlands Twin Register and publicly available summarized data on genetic associations with substance use and loneliness.

Level: M-thesis

Requirements: A motivated student with interest in the etiology of substance use, experience/motivation to learn R programming, interest in causality.

Supervisor: Dr. Camelia Minica; email: camelia.minica@vu.nl

Lack of gender differences in polygenic risk scores.

Many traits have quite strong sex differences in prevalence, or effect on the trait mean, for example height, major depression, migraine and more. In contrast, the polygenic risk scores for these traits hardly differ between men and women. Usually within the original GWAS meta-analysis male and female individuals either have been analysed separately, or there has been a correction for gender as a co-variate. If this is the case, the effect of gender would be absent in the beta's of the summary stats, and hence we would not find any difference in the risk scores. Hence, we want to download the summary stats for several consortia (Giant, PGC, MAGIC), for which the male and female analysis was done separately (without the NTR). With these stats we can subsequently examine the difference in males and females (if present here) and calculate new gender separate polygenic risks. Then we could test using the Netherlands Twin Register data, whether there is no difference in scores, whether the scores predict the individual genders better (ore reverse), or if it all really does not matter. In this period, you will learn dealing with large genetic datasets and summary statistics, polygenic risk score calculation and other various methods and relevant statistics.

Level: M-thesis.

Requirements: This project some knowledge of linux command line work, statistical skills and knowledge of SPSS (or similar software), basic understanding of genetic principles.

Supervisor: Jouke- Jan Hottenga

Effect of genetic principal components in twin modelling

Within genetic research to find genes it is common practice to add principal components based on SNP data as covariates, in order to correct for possible population stratification. Population stratification can be present at all levels within the studied population, either based on different ethnicity, but also based on other factors like religion or geographic location. Recently a whole new wave of heritability analyses has arisen, which tries to estimate all the genetic variance explained by the measured common SNPs, the GCTA approach. Results from this heritability modelling has shown very different outcomes. An interesting part of these analyses is, that here often PCs are taken into account as well. This in contrast to the classic twin heritability models where this is not the case. Within the Netherland Twin register we have data on multiple phenotypes, we have GWAS SNP data and we have twin families. With the help of an empirical example and simulations of various conditions we want to see the effects on twin heritability, when we are correcting for PCs like GWAS and GCTA. This can be a Bachelor or Master thesis subject. The student will learn how to perform various heritability analyses and to make simulations of the various studied models.

Level: B or M-thesis

Requirements: Statistical skills and knowledge of SPSS (or similar software), basic understanding of genetic principles.

Supervisor: Prof. dr. Conor Dolan & Dr. Jouke- Jan Hottenga

Effects of genome wide SNP imputation on the ancestry estimates of individuals

In genome wide association studies, genotypes are imputed to allow for subsequent meta-analysis of the data and to cover the whole genome with all viable known variants. In addition, principal components (PCs) are often calculated from the SNP data of individuals to estimate their ancestry. These PCs are then used in the association analysis to correct for population stratification. The imputation of genotypes is usually based on a reference panel with mixed ancestry as studies have shown that the results are optimal in this case. An interesting question is however, if the ancestry estimates are also affected by the imputation itself. A further question is how serious an imputation is affected when the ancestry is absent in the reference panel, and another question related to this is why there are small differences between ancestry estimates in monozygotic twins. In order to answer these questions sequence and chip platform data from the Netherlands Twin Register will be (re-)imputed and the effects on the PCs will be calculated. Furthermore we could for example impute the

Neanderthal genome and see the ancestry estimates of this person. The methods learned in this research are cleaning and analyzing genetic SNP & sequence data, determining ancestry by PCs and improve scripting and computer skills.

Level: B or M-thesis

Requirements: his project some knowledge of linux command line work, statistical skills and knowledge of SPSS (or similar software), basic understanding of genetic principles.

Supervisor: Dr. Jouke- Jan Hottenga.

Genetic factor scores in the genomic age

GCTA is a linear mixed model used to estimate the variance attributable to a large number of measured genetic variants. Traditionally such linear mixed modelling was used for prediction in animal breeding, where the aim was to determine the breeding value of the animal or plant. In GCTA, as applied to human data, this aspect is not considered, as the focus is on the estimation of (chip-based or genomic) additive genetic variance. The aims of this project is 1) to consider the estimation of breeding values following GCTA analysis in a manner analogous to that used in animal breeding studies, and 2) determine the relationship of these with additive genetic factor scores as calculated in the classical twin design, 3) to determine the use of breeding values in studying genotype environment interaction and covariance.

Level: B or M-thesis

Requirements: Interest in structural equation modelling and linear mixed modelling

Supervisor(s): Prof. dr. Conor Dolan & Dr. Jouke-Jan Hottenga

Do taller women have more children? Unravelling the connection between female fertility and body composition using genetic information

Previous studies have showed that spontaneous dizygotic twinning is associated with body composition (height, body mass index) and smoking. Mothers of DZ twins differ from other women in the population namely, they are taller, have increased body mass index and are more likely to smoke before pregnancy. However, these results are based on observational studies, and further investigation is needed to disentangle whether these associations are causal in nature. Do taller women have more children? Is there a common genetic cause affecting both body composition and fertility? This study will take advantage of the recent progress made in identifying genes that are related to fertility, spontaneous dizygotic twinning, smoking, and anthropometric traits. The aim of this project is to test these hypotheses using genetic and epidemiologic data on fertility and reproductive behaviour collected at the Netherlands Twin Register, as well as summary statistics from large genome-wide association studies of fertility and anthropometric traits from the Twinning Consortium, the Human Reproductive Behaviour Consortium, and from the GIANT consortium.

Level: B or M thesis

Requirements: experience/motivation to learn R programming, knowledge of SPSS, interest in twin modelling.

Supervisors: Dr. Hamdi Mbarek & Dr. Camelia Minica

Multivariate heritability of metabolic traits highlighting the genetic contribution to metabolite-metabolite interaction networks.

The human metabolome consists of over 50,000 small molecules that are involved in our metabolism. Metabolites are molecules that are inputs or products of (enzymatically catalyzed) chemical reactions. As such they are involved in biological pathways of that underly biological (dys)function.

Although the metabolome is highly dynamic and dependent on environment, the concentrations of metabolites are under genetic control, i.e. metabolic traits are modestly heritable.

The analytics behind metabolomics is based upon modern research techniques such as mass-spectrometry, nuclear magnetic resonance spectrometry, chromatography, chemo-metrics, and statistical methods such as discriminant multivariate analysis and cluster analysis.

The Netherlands Twin Register (NTR) hosts metabolomics data on hundreds of molecules measured in over 5,500 participants. This project entails performing multivariate analyses to assess the heritabilities of metabolites measured in NTR participants by including information on genetic relatedness between participants. As a secondary output of the applied method, the genetic contribution to the traits is obtained. By comparing the metabolite-metabolite interaction networks of the measured concentrations to the 'genetically controlled' concentrations we aim at obtaining

more insight in the genetic contribution to the interaction networks.

Level: B- or M-thesis

Requirements: Motivation to learn (or enhance) your programming skills in python and/or R. Experience in data analysis is an advantage.

Supervisor: Dr. René Pool

Associations between subjective happiness and cortex structure

Differences in wellbeing between individuals spark reason to study the (neuro)biological foundations in order to gain understanding of the mechanisms that underlie a happy and satisfactory life.

Interestingly, some recent studies pointed to an association of subjective happiness with volumes of parietal lobe structures, especially of the precuneus. In the present study we will further investigate possible relations of subjective happiness with regions of the cortex.

Level: B-thesis

Requirements: Experience with basic statistics and SPSS

Supervisor: Dr. Dennis van 't Ent

Assortative mating in the MR-DOC model.

The twin model has been extended to include polygenic instruments to study causality by means of Mendelian randomization (MR DOC model). The twin model is based on the assumption of random mating. How does assortative mating affect the results of the MR-DOC model? This question is address in a simulation study in which twin data are generated subject to various types of assortative mating. The basic question is: is the MR-DOC model robust to assortative mating.

Level: M or B-thesis

Requirements: Interest in statistical modelling of twin data, experience with the R programming environment

Supervisors: Prof. dr. Conor Dolan & Dr. C. C. Minica.

Batch effect in the classical twin design.

Biological phenotyping often involves the processing of biological samples in batches. Batch processing may give rise to batch effects. In downstream statistical analyses, it is important to accommodate batch effect, as they are a source of data clustering. In the classical twin design, such clustering may manifest as false shared environmental effects. Batch-based phenotyping in the classical twin design poses a design issue concerning the allocation of twins to batches. Specifically is it better to allocate twin pairs to batches or individual twins to batches?

Level: M or B-thesis

Requirements: Interest in statistical modelling of twin data, experience with the R programming environment

Supervisors: Prof. dr. Conor Dolan

Testing GxE interaction in the moderated classical twin design using polygenic scores.

The moderated twin model is a bivariate twin model, in which one phenotype is the moderator or the genetic and environmental effects on the second phenotype. The aim of this project is to determine the power to detect moderation using a polygenic score as the moderator rather than a phenotypic moderator. How well can GxR interaction be detected using a relatively weak polygenic score.

Level: M or B-thesis

Requirements: Interest in statistical modelling of twin data, experience with the R programming environment

Supervisors: Prof. dr. Conor Dolan, Dr. Michel Nivard

Within person Phenotype to E transmission difficult... within person A to E transmission doable?

Phenotype to E transmission in the repeated measures twin design amounts to the transmission of Phenotypic effects at time t on the environmental variable at time t+1. Specified as a within twin phenomenon, this is hard to detect, due to lack of information. How does A to E transmission fare, where there is a direct relationship between the additive genetic variable at time t and the environmental variable at time t+1? How does A to E transmission fare given a weak polygenic score?

Level: M-thesis

Requirements: Interest in statistical modelling of twin data, experience with the R programming environment (and the OpenMx library)

Supervisor: Prof. dr. Conor Dolan

Are we programmed before birth to respond more or less to stress?

Some people respond strongly to stress, others remain physiologically calm. It has been suggested that our stress response may be determined by our experiences in the womb. This would result in an association of the stress response with birthweight and gestational age. One way of studying this association is to examine the difference within twin pairs, who share many of the same experiences, but can differ in birth weight. Within the Netherlands Twin Register twins and family members (N~1400) underwent 24-hour ambulatory monitoring of heart action and provided cortisol samples across the day. For most of these individuals information on gestational age and birthweight is also available. You will explore the association between prenatal circumstances, as indexed by birth weight and gestational age, with physiological stress profile, making full use of the fact that with the inclusion of (monozygotic) twin pairs control for genetic and environmental factors is possible.

Level: B or M-thesis

Requirements: This project requires statistical skills and knowledge of SPSS (or similar software).

Supervisors: Prof dr. Gonneke Willemsen

What makes you decide on the type of job you want? The effects of genes and environment on career choice

We often choose similar careers as our parents. This may be due to our familiarity with the work our parents do, but it may be also driven by genetic factors. In this study you will use data collected in adult twin family members to study the influence of genes and environment on job choice.

As part of the project you will score job description data collected in the Netherlands Twin Register. These scored data you will use to conduct twin-family analyses. You may also explore assortative mating for career choice, depending on B or M thesis level.

Level: B or M-thesis

Requirements: This project requires statistical skills, knowledge of SPSS, and knowledge of twin modelling

Supervisors: Prof dr. Gonneke Willemsen & Dr. Conor Dolan

Why do some monozygotic twins differ in socioeconomic status?

Intelligence is one of the most heritable traits and strongly associated with the level of education and occupation that one achieves. Despite this high heritability, there are still twins pairs who differ in their educational or occupational level. Since they both grow up under the same family circumstances, and share the same genes, the question is what factors explain this difference in socioeconomic status? You could think for instance of history of disease (e.g. one of the two could have had an accident) or life events (one of the two had young a relationship or children). Your task is to think of plausible and testable explanations for these differences within monozygotic twin pairs and test these using the large scale data from the Netherlands Twin Register.

Level: B or M-thesis

Requirements: This project requires statistical skills and knowledge of SPSS (or similar software).

Supervisor: Prof dr. Gonneke Willemsen

Eating behaviour and overweight in a Dutch twin family population

In 2008 Maruyama showed for a Japanese population that overweight was related to two simple questions about eating behaviour ("Do you continue eating when you feel full?" and "How quickly do you eat?"). These questions were included in the NTR survey of 2009. The answers of the twins and their family members to these questions can be used to determine whether the same associations are found in a Dutch population, and whether there are age or gender differences. Via genetic behaviour studies, you can also determine the heritability of eating behaviour, while the relation between the genetic risk profile for BMI with eating behaviour can also demonstrate the role of genes for BMI in eating behaviour. Other questions that you can think of: is there assortative mating (to what extent are partners alike), are there social factors like educational attainment or living circumstances that may be important?

Level: B or M-thesis

Requirements: This project requires statistical skills, knowledge of SPSS, and knowledge of twin modelling

Supervisor: Prof dr. Gonneke Willemsen

The effect of work stress and family situation in working women

As part of an international study, 160 women who worked at the VU and surrounding areas provided saliva samples to determine cortisol and alpha-amylase, during a working day and a weekend day. During these two days, participants also underwent 24-hr ambulatory monitoring during a working day and a weekend day. In addition, they completed a survey about work stress, family situation, depression and lifestyle. These data can be used to determine the effect of work stress and family situation on physiological parameters and depression. Dependent on the nature of your thesis (Bachelor or Master) you will choose one or more aspect to examine. To answer your research question(s) you will need to combine and check the data, before starting the analyses. In the analyses you will also take age, educational attainment and number of working days into account.

NB. For a large number of variables we also have data from London and Budapest. If you are interested, you can also compare the outcomes for the project in Amsterdam with the outcomes in those two cities.

Level: B or M-thesis

Requirements: This project requires statistical skills and knowledge of SPSS (or similar software).

Supervisor: Prof dr. Gonneke Willemsen

Can we relate the cell specific transcriptome of brain cells to specific psychiatric and neurological disorders?

In this project you use 2 large data resources: 1. Public genome wide association result for 12 psychiatric and neurological disorders 2. The RNA expression profiles of individuals brain cells (e.g. Neuron, Microglia, Astrocytes etc. etc.), obtained from either fetal of adult tissue and from 2 brain regions From this last resource we can determine which genes are specifically overexpressed in certain cell types, during a certain phase in live, or in a specific brain region. Subsequently we test where sets of genes associated with a specific cell type are differentially enriched in their effect on psychiatric and neurological disorders.

Level: B or M-Thesis

Requirements: This internship requires knowledge of R.

Supervisor: Dr. Michel Nivard

Using the liability threshold model to address scale dependency in tests of GxE interaction in the moderated classical twin design.

The classical twin design has been extended to include moderations effects, where the genetic and environmental effects of one phenotype (Ph) are a function of a measured moderator (M). This approach to the detection of moderation is known to be scale dependent. That means that the detect moderation may is a function of the (non-normal) distribution of the data, and not of true moderation. The liability threshold model does not rely on the observed distribution of the data, and therefore may provide a useful model to investigate moderation. Is this a viable approach to semi-scale independent moderation analysis?

Level: B-thesis

Requirements: Interest in statistical modelling of twin data, experience with the R programming environment

Supervisors: Prof. dr. Conor Dolan, Dr. Michel Nivard

Gene-set analysis to investigate the underlying biological mechanisms across psychiatric disorders.

Psychiatric disorders are strongly influenced by genetic factors and the rapid recent increase in sample sizes for psychiatric genome-wide association studies (GWAS) have led to an immense increase in the identification of significantly associated genetic variants. Based on these GWAS findings, multiple studies showed strong genetic overlap between psychiatric disorders and related traits. However, the biological underpinnings of this shared risk are not yet fully uncovered, and the identification of the underlying biological mechanisms is crucial for the progress in treatment of

these disorders. Within this project the student will apply gene-set analysis to identify sets of genes that are involved in the etiology of multiple psychiatric disorders and related traits. The student will make use of publicly available summary statistics of GWAS and gene sets that are available in public online databases. The work involves data preparation, meta-analysis of GWAS summary statistics, and gene-set analysis, which all will be performed within a linux environment (cluster computer).

Level: M-thesis

Requirements: Some experience with basic statistics and working in a command line environment. Motivation to learn to work on a cluster computer.

Supervisors: Dr. Anke Hammerschlag

Two different kinds of well-being?

Current research on well-being is generally divided into two perspectives: subjective well-being (SWB) and psychological well-being (PWB), shaped by the philosophical concepts of hedonism and eudaimonism, respectively. How these different views relate to each other and to well-being as a whole has not yet been clearly defined, leading to difficulties in interpretation and analysis. For this project we would like to investigate how these two forms of well-being relate to each other on a) a phenotypic and b) a genetic level. On a phenotypic level, we will correlate the items from SWB and PWB questionnaires with items from a series of known external correlates (depressive symptoms, personality traits, self-rated health, loneliness). Our aim is to take a hypothesis-free approach and observe whether the correlational pattern between well-being and these external correlates is in line with the traditional distinction between subjective and psychological well-being. Similarly, on the genetic level, we will assess to what extent the two forms of well-being are genetically associated with external correlates. The B-thesis student will be able to make use of the extensive datasets of the Netherlands Twin Register to answer these fundamental questions regarding the nature of well-being.

Level: B-thesis

Requirements: Basic statistical skills in SPSS/R

Supervisors Prof. dr. Meike Bartels & Margot van de Weijer

Gene-environment interplay in well-being

Research looking at the genetic and environmental influences on well-being has been relatively separate in the past. For this project, we want to integrate these different levels of explanation and test for gene-environment interplay in well-being. To identify gene-(social) environment interplay, we will test for genetic similarity in various groups of people. Group assignment will be based on several (social) environmental variables identified by psychological studies as relevant to well-being. For example, we will compare the genetic similarity of people that live within the same postal code area (postal code group) to a random group of people (random group). If in this example the genetic similarity is higher in the postal code group versus the random group it is implied that there is a gene-environment interplay between the genetic predisposition for WB and the area people live in. These same analyses will be repeated for all other social-environmental variables regardless of expectation of an effect. By examining this gene-environment interplay, we can identify risk factors for well-being for specific groups of individuals with the ultimate goal of targeting these factors for the improvement of well-being.

Level: M-thesis

Requirements: Experience/motivation to learn R programming, SPSS

Supervisors: Dr. Bart Baselmans, Prof. dr. Meike Bartels, & Margot van de Weijer