The Department of Biological Psychology offers a wide variety of internships, including behavioral genetic and epidemiological topics but also topics related to psychophysiology, or 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(s) 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 INTERNSHIP POSSIBILITIES**

Please find below the internships offered at the Department of Biological Psychology.
**B-thesis**

**Effects of regular exercise and aerobic fitness on physiological stress reactivity: why don’t we see them?**

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 by exercise-induced increases in aerobic fitness 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 either regular exercise or aerobic fitness 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 only using artificial laboratory stressors, but also 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

**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.


**Investigating the relationship between affective states and autonomic nervous system activity**

In your thesis project you investigate the relationship between (positive & negative) affect and various autonomic nervous system (ANS) activity measures. 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 and a wrist watch measuring skin conductance responses under development at Philips. You will use a dataset of a study in which participants performed a variety of task (known to influence ANS activity) at our laboratory while wearing the VU-AMS and the Philips watch. They continued to wear these devices during a 24 hour ambulatory measurement to measure ANS activity in daily life. At the laboratory section participants were asked to report their affect after various tasks, by filling in a short questionnaire. During the ambulatory section participants were asked to report their affect (but also main activity, location and social environment) by filling in a short diary on an iPod hourly. After having gained hands on experience in collecting and handling these ambulatory data, you will perform analyses on the link between emotional affect and physiological reactivity, using both the existing laboratory and the ambulatory data sets.

**Level:** B-thesis

**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 is preferred.

**Supervisors:** prof dr. Eco de Geus, & Denise van der Mee, MSc.
**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 labour 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/full siblings 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. We hypothesize that leisure time physical activity in the weekend, driven mainly by intrinsic motivation, will be more heritable than work-related physical activity during the week, which is more environmentally determined.

**Level:** B-thesis

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

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

**Exercise behavior 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 behavior. This project aims to investigate if monozygotic twins who differ in voluntary exercise behavior display differences in DNA methylation in white blood cells. This study may provide novel insights into the epigenetic effects of exercise behavior. The student will perform statistical analysis of existing DNA methylation data from monozygotic twins and link this to information on exercise behavior to examine the question which locations in the genome show differences in DNA methylation between monozygotic twins who are discordant for exercise behavior. The student will perform basic statistical analyses (paired t-tests, correlations) 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:** Matthijs van der Zee Msc, Dr. Jenny van Dongen, Prof. Eco de Geus

**Modelling the developmental process that leads to educational outcomes**
Educational success is the outcome of a long and complex developmental process in which both cognitive abilities (i.e. what an IQ test measures) and non-cognitive abilities (i.e. perseverance and social skills) play a role. During the process there are possibly mutually reinforcing effects. For example, if I learn to read, this helps me study my math text book, studying math strengthens my reasoning abilities. Experiencing early success in school increases my motivation, which in turn may lead to the grit needed to tackle increasingly complex topics. In this project we will not just describe associations among school achievement and non-cognitive abilities, but we aim to study causal influences. The B-thesis student will select two traits of interest. Options include arithmetic skills, reading and language skills, bullying behaviour (victimisation and/or perpetration), perseverance, and being task-oriented. The student will model the causal influences between these two traits using longitudinal cross-lagged models (see e.g., Abdellaoui et al., 2019) and/or (cross-sectional) direction of causation modelling (see e.g., van Bergen et al., 2018). He/she will use the extensive datasets of the Netherlands Twin Register to model the developmental process that leads and/or follows educational success.

**Level:** B-thesis

**Requirements:** Interest in statistical modelling, interest in child development, experience with the R programming environment

**Supervisors:** Dr. Michel Nivard & Dr. Elsje van Bergen


The causal link between self-control and psychopathology
Children vary a lot in their ability to adopt to rules and control their emotions, behavior and impulses. Children with lower self-control are at increased risk for developing internalizing and externalizing problems. This study will use the large dataset available in the Netherlands Twin Register to get more insight in the association between self-control and different types of psychopathology (e.g. attention problems, autistic traits, anxiety, depressive symptoms). The aim will be 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. We will use the classical twin design to determine if the genes and environments that play a role in self-control also have an effect on psychopathology and the within monozygotic twin pair differences design to investigate if the association between self-control and psychopathology also exists when controlling for confounding due to genes or the home environment.

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

Stress during pregnancy.
Stress during pregnancy may have adverse consequences for the physical and psychological development of children. For example, stress during pregnancy appears to be associated with, among other things, a shorter gestational age and a lower birth weight. With this research we want to answer the following questions: is there a relationship between stress during pregnancy and gestational age, birth weight, motor development and temperament of the children. Another question is whether the heredity of these outcome measures changes due to stress during pregnancy. The questions will be examined on the basis of questionnaire data collected by the Dutch Twin Register, in which we have been asking mothers of twins since 2006 whether they have experienced a stressful event during pregnancy. Encoding stressful events can be part of the b-thesis.

Level: B-Thesis
Requirements: basic statistical skills
Supervisor: Dr. Toos van Beijsterveldt.

Associations between aggressive behavior and brain structure
Differences in aggressive behavior between individuals spark reason to study the (neuro)biological foundations. Interestingly, some recent studies pointed to an association of aggression with volumes of subcortical brain structures (a.o. the amygdala) and neocortex (frontal lobe). In the present study we will further investigate possible relations of aggressive behavior with regions of the subcortex and cortex.

Level: B-thesis
Requirements: Experience with basic statistics and SPSS
Supervisor: Dr. Dennis van 't Ent

The Happiness-Formula
Recently it has been claimed that there is some kind of happiness-formula (see for example Mogawdat’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 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.

**Are optimist 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

**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

**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 to 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 question 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
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 ~800 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: Passed on the RM behavioral genetics course. Good statistical skills, knowledge of SPSS, and ideally R/Matlab; background knowledge on the biology of the ANS.
Supervisor: Prof dr. Eco de Geus

Causal modelling in twins to study the association between social relationships and health behaviors

It is indisputable that high-quality social relationships are correlated with decreased risk for morbidity and mortality from a range of disease outcomes, and that poor-quality relationships or social disconnection are correlated with considerable risk for negative outcomes. For humans, however, strong evidence for causal effects does not exist in this area. High-quality relationships can serve as surveillance indicators of/for good health, but risk indicators alone do not point to causal mechanisms of action. Building an experimental literature in the study of relationships and health is inherently difficult; random assignment to, for example, marital status or having high/low loneliness is not possible. Genetically informed research methods provide a range of design and analytic approaches that can help address gaps in this area. These approaches allow researchers to rule-out causal explanations for phenotypic associations (e.g., between loneliness and smoking or alcohol abuse), and/or to identify effects that may be consistent with a causal influence. Using intrapair regression in MZ twins, the co-twin control method, and you will examine the association between loneliness and and health behaviors (regular exercise, smoking status, alcohol use, sleep duration) in the NTR. Based on the extant literature, you outline a series of confirmatory hypotheses to guide these co-twin analyses. In supplemental analyses, as a means of triangulation toward causal inference, you could also choose to apply Mendelian Randomization, an analytic approach in which the specific genes associated with chronic loneliness are used as instrumental variables to test the causal effects of loneliness on the health behaviors.

Level: M-thesis
Requirements: A motivated student with interest in causal inference using twin data, experience/motivation to learn R programming, interest in the link between social relationships and health behaviors.
Supervisors: Prof dr. Eco de Geus, prof dr David Sbarra (University of Arizona)

Epigenetic prediction of complex traits and environmental exposures
Epigenetic mechanisms such as DNA methylation regulate the expression of genes in cells, and may respond to environmental influences. Recently, epigenome-wide association studies (EWAS) have identified DNA methylation sites associated with a number of traits, diseases, lifestyle factors, and other environmental exposures. This project aims to investigate how well complex traits, such as height, body-mass-index, and aggressive behavior, and exposure to environmental influences and lifestyles, such as smoking and prenatal smoking can be predicted based on genome-wide DNA methylation profiles. The student(s) will apply state-of-the-art analysis tools to existing DNA methylation data from the Netherlands Twin Register. The aim is to apply two new methods. The first is a software package called OSCA (omic-data-based complex trait analysis), which will be used to calculate a methymic relationship matrix (MMR) that contains the pairwise correlations between individuals based on their genome-wide DNA methylation profile, in order to estimate the proportion of variance in a complex trait captured by all genome-wide DNA methylation probes together. This approach is similar to the calculation of SNP-heritability based on a genetic relationship matrix (GRM). The second “DNA methylation score approach” is comparable to the “polygenic score approach”, but applied to DNA methylation data and summary statistics from previous EWAS studies.

Level: M-thesis
Requirements: An interest in the topic, basic experience with R
Supervisor: Dr. Veronika Odintsova, Dr. Jenny van Dongen

Sex differences in DNA methylation
Many complex diseases show sex differences in the etiology. For example, women have a lower incidence of cardiovascular disease before menopause, and a higher incidence after menopause. Such differences might be explained by sex-differences in epigenetic mechanisms and gene expression. A previous study identified many genes on the sex chromosomes as well as genes on the autosomes of which the expression level in blood cells differed between males and females. The expression level of some genes was affected by menopause, and/or the use of oral contraceptives. In the current project, we want to extend these observations to DNA methylation data. DNA methylation is one of the epigenetic mechanisms that regulates genes expression. The questions are: which genomic regions show DNA methylation differences between males and females, what are the causes of these differences, and could they explain sex differences in complex disease? We are looking for a student who can perform statistical analyses of existing DNA methylation data from the Netherlands Twin register in R.

Level: M-thesis.
Requirements: An interest in the topic, basic experience with R
Supervisor: Dr. Jenny van Dongen, Prof. Dorret Boomsma

Modelling the developmental process that leads to educational outcomes
Educational success is the outcome of a long and complex developmental process in which both cognitive abilities (i.e. what an IQ test measures) and non-cognitive abilities (i.e. perseverance and social skills) play a role. During the process there are possibly mutually reinforcing effects. For example, if I learn to read, this helps me study my math text book, studying math strengthens my reasoning abilities. Experiencing early success in school increases my motivation, which in turn may lead to the grit needed to tackle increasingly complex topics. In this project we will not just describe associations among school achievement and non-cognitive abilities, but we aim to study causal influences. The M-thesis student will select two or three traits of interest. Options include arithmetic skills, reading and language skills, bullying behaviour (victimisation and/or perpetration), and grit (i.e., perseverance). These traits will be modelled as latent variables with multiple items as indicators. The student will model the causal influences between the chosen two or three traits using longitudinal cross-lagged models (see e.g., Abdellaoui et al., 2019), longitudinal cross-lagged models with random intercepts (see e.g., Hamaker et al., 2015), and/or (cross-sectional) direction of causation modelling (see e.g., van Bergen et al., 2018). He/she will use the extensive datasets of the Netherlands Twin Register to model the developmental process that leads to and/or follows educational success. The student’s project will be part of a larger project that we will pre-register on Open Science Framework.


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 Register. 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)

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

Introducing polygenic scores in the twins and parents phenotypic assortative mating model: statistical power

The twins and parents phenotypic assortative mating model provide one approach to modeling the effects of assortative mating. Usually this model is fitted using phenotypic data only. The aim of this project is to determine the advantages of including parental and/or offspring polygenic scores in this model to detect phenotypic assortative mating and other effects that are identified in this model, such as cultural transmission.

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

Gene-set analysis to investigate the underlying biological mechanisms across psychiatric
**disorders and related traits.**
Psychiatric disorders and related traits are strongly influenced by genetic factors and the rapid recent increase in sample sizes of 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 psychiatric symptoms. 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 selecting a set of related disorders and traits that will be investigated, data preparation, meta-analysis of GWAS summary statistics, and gene-set analyses, 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

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**A summary statistic-based approach to investigate the relationship between neuroimaging and metabolomics and their role in human aggression**

Hypotheses about the etiology of psychopathologies frequently entail changes in brain structures or neurotransmitter levels. As a result, neuroimaging studies have been conducted for a wide range of psychopathologies. To investigate the role of neurotransmitters, peripheral tissues (such as blood or urine) have been screened for differences in neurotransmitter concentration or metabolites involved in neurotransmitter synthesis or degradation. Another active research topic involves the role of lipids, as lipids have many important functions in the brain, for example they are present in the myelin sheaths and are involved in many cellular processes. With the development of high-throughput metabolomics techniques it is possible to simultaneously measure, and therefore assess the effect of large amounts of small molecules (e.g., neurotransmitters or lipids) on psychopathologies. Both neuroimaging and metabolomics studies of psychopathologies have proven successful. However, as changes in metabolites and brain structures are likely linked, it would be of interest to investigate these together. Especially for human aggression, few studies have combined neuroimaging and metabolomics, primarily due to the fact that studies investigating metabolomics only are limited. Luckily, genome-wide association studies are now available for a wide range of human complex traits and molecular phenotypes. During the internship the student will work with summary statistics from well-powered metabolomics and neuroimaging GWA studies to first investigate their genetic correlations using LD-score regression. Next, the student will use a new method, primo (R-based), to integrate the summary statistics to examine how metabolomics and neuroimaging SNPs affect aggression.

**Level:** Master

**Requirements:** The student has an interest in combining different high-dimensional data types, is experienced in R, and has some familiarity with working in a Linux environment.

**Supervisors:** dr. Dennis van ’t Ent & Fiona Hagenbeek (PhD student)

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**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 to 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 question 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

**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 (rGE) 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 polygenic 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

**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 life 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:** Prof. dr. Meike Bartels, & Margot van de Weijer

**B/M-thesis**

**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.


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**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 effect of parental psychopathology on self-control via the environment that parents create for their children.

**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 discordant MZ twin design vs the discordant MZ and discordant DZ twin design.
The discordant twin design is often used to test causal hypotheses (X causes Y). This involves strong assumptions concerning the absence of unshared environmental effects common to both X and Y. The aim of this project is to determine whether the addition of discordant DZ twins to the discordant MZ twin design can help to relax this strong assumption. The point of departure is the standard bivariate twin model. Based on this model, we consider the MZ discordant twin model and then the addition of DZ discordant twins.

**Level:** B-thesis or M-thesis
**Requirements:** Interest in the classical twin design, causality, statistics and willingness to use R
**Supervisor:** Prof. Conor Dolan

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

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
Genetic and environmental influences on steroid hormone levels in school-aged children
Steroid hormones are involved in metabolism, inflammation, immune functions, and development of sexual characteristics. There are two types of steroid hormones: corticosteroids and sex steroids. Corticosteroids, such as cortisol, are involved in a wide range of physiological processes, including stress response, immune response, but also in behavior. Sex steroids are responsible for the development of sexual characteristics. Androgens, such as testosterone, are the “male sex hormones” and estrogens and progestogens, such as estradiol, are considered the “female sex hormones”. Steroid hormones have often been investigated as biomarkers for various psychological traits and disorders. Particularly, in externalizing behaviors, such as aggression, steroid hormones are hypothesized to play a major role. In the Netherlands Twin Register (NTR) large-scale urine collection was performed in 5- to 13-year-old MZ and DZ twins (N = 1,347), selected for their concordance or discordance on childhood aggressive behavior. With mass spectrometry it was possible to measure multiple steroid hormones simultaneously in these urine samples, resulting in a unique dataset. During the internship the student will investigate the genetic and environmental influences on multiple urinary steroid hormones.

Level: B- or M-thesis
Requirements: The student has some familiarity with the R, specifically the R-packages OpenMx or umx to analyze twin and family data (i.e., completed ‘Genes in Behaviour and Health’ (BSc) and/or ‘Behavioural Genetics’ (MSc)).
Supervisors: prof. dr. Dorret Boomsma, Fiona Hagenbeek (PhD student), Dr. Rene Pool

Multi-omics biomarker discovery for depression in adults
Major depressive disorder (MDD) is globally one of the most prevalent psychiatric disorders, and poses a large burden on patients, their relatives and society at large. Treatment of MDD with traditional antidepressant medications remains difficult, with 15%-50% of patients not properly responding to medication. This is because our understanding of the pathophysiology underlying MDD remains incomplete. Recent advances in high-throughput techniques have enabled researchers to investigate the etiology of MDD with genomics, proteomics and metabolomics techniques. Investigations with each of these types of omics data aim at identifying biomarkers to identify or stratify MDD patients, to monitor therapeutic effectiveness or find new targets for drug development. Integrating multiple omics technologies could help identify system-wide biological processes involved in MDD and thereby identify multi-omics biomarkers. For participants of the Netherlands Twin Register (NTR) several ‘omics datasets are available, including gene expression, genome-wide methylation data, and several metabolomics platforms. During the internship the student will use the mixOmics R-package for multivariate multi-omics modelling to integrate the different omics datasets in the search for MDD multi-omics biomarkers.

Level: M-thesis (possibly also highly motivated B-student, as the actual mixOmics code is not very complicated and well documented)
Requirements: The student is familiar with R, has an interest in multivariate statistics and working with high-dimensional ‘omics data. Some familiarity with working in a unix environment is appreciated, but not necessary.
NB it is also possible for 2 or more students to work on this project and have additional outcomes to MDD.
Supervisors: prof. dr. Dorret Boomsma, Fiona Hagenbeek (PhD student), Dr. Rene Pool

Phenome-wide association study for well-being
A now well-known study design is that of a genome-wide association study: millions of genetic variants across the genome are regressed on a trait of interest in order to identify relevant genetic variants associated with that trait. However, instead of focusing on one trait, and associating this trait with a wide range of genetic variants, one might also think the other way around and associate (a part of) the genome with a wide range of traits. In this project, we want to create polygenic scores (which aggregate the effects of thousands of DNA variants from genome-wide association studies) for well-being and well-being related traits (think: depression, neuroticism, etc.) based on existing genome-wide association studies. Next, we will associate these polygenic scores with a wide range of traits. In this way, we aim to systematically assess the genetic relations between well-being and other behavioral/psychological traits. Additionally, by comparing results from different well-being-related
polygenic scores (e.g. depression), we might find some interesting discrepancies and similarities worth future investigation. Another optional extension we are looking into is to create so-called “poly-environmental” scores, where we aggregate the effect of different environmental factors. In case there is time, this will be an interesting addition to the project.

**Level:** B/M-thesis  
**Requirements:** (basic) R knowledge  
**Supervisors:** prof. Meike Bartels & Margot van de Weijer

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**Sitting too much: effects on well-being**

The Dutch working population spends around nine hours of every working day in a seated position (Bernaards et al., 2016). Especially, higher educated people are more likely to be seated a lot, as they are more likely to perform sedentary work, spending more hours behind a computer (e.g. working in banking or, in our case, science). Sedentary behavior is defined as any waking behavior characterized by an energy expenditure ≤1.5 metabolic equivalents (METs), while in a sitting, reclining or lying posture. Sedentary behavior is not the same as a lack of physical exercise. Even if you exercise vigorously three times a week, too much sedentary behavior can lead to health risks, e.g. increased risk of diabetes, cardiovascular disease or depression. Whereas the relation with health outcomes is well-documented, the relation between well-being and sedentary behavior is not clear. Are people who are sitting less hours per day happier compared to people who are seated more hours?  
Sedentary activity can be measured objectively, using data of an accelerometer worn by participants. Accelerometer data can capture all physical and sedentary behavior over the day, without self-report biases. In this project we will combine accelerometer data on sedentary behavior and data from well-being questionnaires of participants in the Netherlands Twin Register. The accelerometer data will be processed into patterns and measures of sedentary behavior. We will answer the question if objectively assessed sedentary behavior is associated with well-being and happiness, both on a phenotypic and genetic level. Is there overlap in the genetic factors influencing sedentary behavior and well-being? In addition, you will help recruit participants and collect data in a project to measure the fluctuations of well-being over the day and relate this to physical activity and environmental variables. This data will be collected using smartphone applications.

**Level:** B/M-thesis  
**Requirements:** experience/motivation to learn programming in R.  
**Supervisors:** Prof. dr. Meike Bartels, Prof. dr. Eco de Geus, dr. Hidde van der Ploeg (VUmc), & Lianne de Vries.

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**Freaky Happiness: differences in happiness over the day**

Like many complex human characteristics, well-being fluctuates over time and in different contexts. Some people are relatively stable in their happiness and moods, whereas others show more fluctuations. How can these individual differences in well-being fluctuations be explained? Are fluctuations in well-being heritable? Furthermore, not much is known about the effect of the environment on momentary well-being.  
We want to capture the fluctuations of well-being over time and in different contexts. Using smartphone applications and ecological momentary assessment (EMA (Stone & Shiffman, 1994)), we will assess the fluctuations of well-being multiple times a day over time in the daily life of participants and in their natural environment. In addition, we will measure different environmental variables using the sensors of the participant’s smartphone. Variables of interest in relation to well-being are the nature of the environment (Are people happier in a green environment or in the city?), light and noise levels in the environment, but also phone use (how often do people unlock their phone?), physical activity, and the number of people around the individual.  
You will help recruiting participants and collecting data of well-being fluctuations and the environment in the current project. Combining existing data of the Netherlands Twin Register and the new data, we will estimate the heritability of WB fluctuations and relate environmental variables to (momentary) well-being.

**Level:** B/M-thesis  
**Requirements:** experience/motivation to learn programming in R (and maybe Python).  
**Supervisors:** Prof. dr. Meike Bartels, & Lianne de Vries.

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**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 currently hardly differ between men and women. Usually within the original GWAS meta-analysis male and female individuals either have been analyzed separately, or there has been corrected for gender as a co-variante. If there has been corrected for gender, the effect of gender would be absent in the beta’s of the summary stats, and hence we would not find any difference in risk scores. Therefore, we want to ask several consortia (Giant, PGC, MAGIC) for which the male and female analysis was done separately, to get the summary stats separately for each gender (without the NTR). With these stats we can subsequently examine the difference in males and females (if present here) and calculate new gender separate summary stats. Then we could test whether there is no difference in scores, whether the scores predict the individual genders better (or reverse), or if it all does not matter using the Netherlands Twin Register data. Thought will be the use of large genetic datasets and summary statistics, polygenic risk score calculation with various methods and relevant statistics.

**Level:** Master student / Bachelor student.

**Requirements:** Some knowledge of command line work would be appreciated. Basic statistics, basic genetic knowledge.

**Supervisor:** Jouke-Jan Hottenga

### Haplotypic GWAS

In GWAS ‘tagging’ SNPs are associated against a trait /disease /phenotype, resulting in general locations on the genome where a mutation should be present that is affecting the trait. These associated SNPs often have common alleles with a low relative risk, and many people likely also carry the risk allele without having the actual mutation. A clear indication of this problem is also present when examining polygenic scores calculated over several ethnicities using the summary stats of only Europeans. The risks highly fluctuate depending on allele frequencies and linkage disequilibrium (LD).

As a new design I want to test whether we could, instead of using the linkage disequilibrium of genotypes (2 alleles) to correct for this, use the LD based on single parental haplotypes instead from phased data. Another idea is to test whether there are unique haplotypes present, that are better capturing the affecting mutation instead of a single SNP allele, and how these are scattered across different ethnicities. How to test this is and on what trait / phenotype is open for discussion with the student candidate.

**Level:** Master student / Bachelor student.

**Requirements:** Some knowledge of command line work would be appreciated. Basic statistics, basic genetic knowledge.

**Supervisor:** 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.
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

Understanding occupational choice: Why do some choose a military profession, others nursing and again others teaching?

In the past year, a large proportion of the data on occupation, collected by the Netherlands Twin Research, have been coded and made available for analyses. As part of a first internship, the influence of heritability on occupational choice was examined, but many further steps are needed to increase our understanding of occupational choice. For instance, are spouses alike in their professions, what is the role of educational attainment, how is personality related to occupational choice?
The research question you take on during this thesis project will depend on your own interests as well as your expertise in data analysis and data coding may be part of the project.

**Level:** B-thesis or M-thesis

**Requirements:** Experience with SPSS is required. Experience with R-programming and structural equation modelling depending on the focus of the thesis.

**Supervisor:** Prof. dr. Gonneke Willemsen and prof. dr. Conor Dolan

**Assortative mating: to what extent are partners alike?**

Higher educated women marry higher educated men and vice versa: it this true now and has it been true over the last 100 years. As part of a collaborative project with Finland, we are looking into this phenomenon of assortative mating for educational attainment and possibly other related traits. While the twin register in Finland has extensive data, the NTR has an extensive database on the highest education achieved for spouse pairs in the Netherlands, with information available for multiple generations. Over the past 100 year the educational system in the Netherlands changed a lot, and within the project we will explore the effect this may have had on the assortative mating over the years. As the NTR also collects data on parents and spouses of twins, this allows for a greater understanding of the processes involved and allows extension towards other traits, such as health behaviour. Depending on your background, your thesis may take a more epidemiological or behaviour genetic approach.

**Level:** B-thesis or M-thesis

**Requirements:** Experience with SPSS is required. Experience with R-programming and structural equation modelling depending on the focus of the thesis.

**Supervisor:** Prof. dr. Gonneke Willemsen and prof. dr. Conor Dolan

**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

**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