# ANNUAL REPORT 2019

SCHOOL FOR MENTAL HEALTH AND NEUROSCIENCE

Maastricht University
Faculty of Health, Medicine and Life Sciences

MH&NS

Maastricht University | Maastricht UMC+

# CONTENT



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# PREFACE
# DAVID LINDEN

*Photography: Maastricht UMC+*

Prof. David Linden
Scientific Director

School for Mental Health
and Neuroscience

We are producing this Annual Report 2019 in the middle of the Covid-19 crisis. One of the main effects of this pandemic and the measures that are necessary to contain it has been the almost complete stop of other research, including clinical trials. We are, of course, planning for the restarting of this important research work and are developing strategies to minimize delays. The effects of Covid-19 on our research and education activities, as well as the exciting new projects that are being developed on neural mechanisms and psychological consequences of Covid-19 and new strategies for tackling SARS-CoV-2 by MHeNs researchers will be a topic of the 2020 Annual Report.

2019 was a particularly successful year for our Early Career Researchers. Three researchers started their VENI fellowships awarded by the NWO (Dutch Science Funding Organisation) at MHeNs. Sarah Hescham (Division 3, Department of Neurosurgery) is investigating the use of nanotechnology for the treatment of Parkinson's disease in rodent models. Christian Herff, also from the Department of Neurosurgery, decodes information from brain activation patterns recorded with multiple electrodes directly from a patient's brain during the diagnostic workup for epilepsy surgery. One potential application of such "brain reading" techniques might be communication devices for people who are otherwise unable to speak. The third VENI went to Marlies Gijs (Division 3, Department of Ophthalmology) who is investigating the use of tears as source of biomarkers for Alzheimer's disease, and more broadly the use of this easily accessible but often neglected bodily fluid for diagnostic purposes.

Two further MHeNs researchers received personal fellowships in the area of dementia research. Kay Deckers (Division 1, Department of Psychiatry and Neuropsychology) started his ZonMW Memorabel fellowship on risk models of dementia and ways of incorporating them into prevention programmes. This project is closely linked to the Mijnbreincoach app that I highlighted in last year's introduction. Our other ZonMW Memorabel fellowship went to Ehsan Pishva (Division 3, Department of Psychiatry and Neuropsychology) who researches mechanisms of Alzheimer's disease using post-mortem brains and biomarkers.

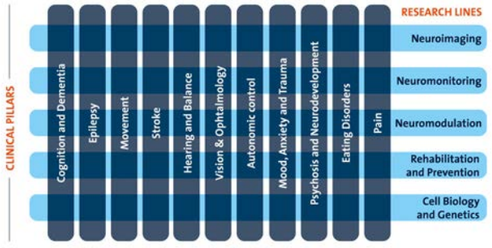
We also welcomed two new clinical professors, Jan van Zundert, an expert in chronic pain research and treatment (Division 3, joint appointment between Department of Anaesthesiology and the Multidiciplinary Pain Centre at the Hospital of East Limburg in Lanaken, Belgium) and Dirk Kunst, an expert in skull base surgery (Division 1, joint appointment between Department of Ear, Nose and Throat Surgery and the respective department at Radboud UMC in Nijmegen). Furthermore, Albert Leentjens (Division 1, Department of Psychiatry and Neuropsychology) was promoted to a clinical chair in neuropsychiatry.

2019 was also a very active year for our programme of workshops and conferences hosted by MHeNs researchers. The 13th Translational Neuroscience workshop, organized by Prof Bert Joosten, Dr Nynke van den Hoogen and Roel van Reij (Division 3, Department of Anaesthesiology) had the topic "Pain and Comorbidities". It covered a wide range of topics of clinical and translational research, ranging from psychological models of development of chronic pain to mechanistic research into spinal cord plasticity in animal models. The EURON workshop "Drugs and the Brain: from Laboratory to Clinic" was held in Crete in collaboration with the University of Crete, Heraklion and the Hellenic Society for Neuroscience. It featured many speakers from EURON partners and from our wider network of collaborators from across Europe. Prof Bert Smeets, jointly with a group of Honours students and with the support of the "Stichting voor Sara" charity, organized an international expert meeting on merosin-deficient congenital muscular dystrophy type 1A (MDC1A), which is closely linked to his ongoing work in clinical trials and highlights the translational research agenda of MHeNs. This rare muscle disease was also the topic of a companion piece in the Volkskrant, a leading national newspaper.

And, finally, in December we hosted the 4th International Real-Time Functional Imaging and Neurofeedback conference (https://www.rtfin2019.org/107020), jointly with FPN (Prof Rainer Goebel and Dr Bettina Sorger) and colleagues from the University Hospital in Aachen (Prof Klaus Mathiak and his team). This conference explored the potential of using functional magnetic resonance imaging signals, analysed in real time and made visible for the patient, for self-regulation of brain circuits. This line of research creates an interface between neuroimaging and neuromodulation and thus brings together two of our main research themes.

Many members of MHeNs were again very active in the dissemination of mental health and neuroscience research both to professional audiences and the general public. We regularly update on these activities in our newsletter and the space of this introduction does not allow me to do full justice to them. I am therefore mentioning a couple of events that I attended myself. Jos Prickaerts (Leader of Division 3) was the chair of the 2019 meeting of the Dutch Neuroscience Association, which again had an excellent programme with both Dutch and international speakers and provided ample opportunity for discussions between PhD students and senior researchers. In the area of public engagement, Professors Therese van Amelsvoort (Leader of Division 2) and Bart Rutten (Head of the Department of Psychiatry and Neuropsychology) talked at the Jonge Brein College about stress, resilience and mental health of young people.

As every year, the highlight of our event cycle was the Annual Research Day, which had the topic "New Technologies in Mental Health and Neuroscience". We heard from three innovators from our own MUMC about new sequencing technologies in clinical genetics (Prof Han Brunner), regenerative medicine (Prof Pamela Habibovic) and advanced optical microscopy (Prof Marc van Zandvoort). Our external keynote speaker was Prof Richard Dobson from the Institute of Psychiatry, Psychology and Neuroscience at King's College London. He provided an exciting overview of new opportunities for data integration in mental health, which is also a very active area of research and clinical development for MHeNs. At this Research Day we also conducted two sessions on specific clinical areas (epilepsy and Parkinson's syndrome) which were guided by individual patient journeys. These sessions reminded us of the importance of aligning clinical research with patient needs and expectations. This link will also be one of the guiding principles of the highlights from the divisions that we have selected for this Annual Report, and which I hope you will find interesting and inspiring.



# DIVISION I

**Cognitive Neuropsychiatry & Clinical Neuroscience**

Division Leader:
Prof Frans Verhey

Deputies:
Prof Robert Van Oostenbrugge
Prof Caroline Van Heugten

## SUMMARY

The mission of the division Cognitive Neuropsychiatry & Clinical Neuroscience (CNP&CNS) is to generate new insights into mechanisms of cognitive and other neurological or otorinolaryngological disorders, and to improve diagnosis and treatment, and eventually the quality of life of people with these disorders. The name CNP&CNSS expresses the MHeNs-wide translational nature of the research program, and the multidisciplinary perspective. CNP&CNS mission is to generate new insights into mechanisms of these conditions, with the final aim to improve diagnosis and therapy.
Embedded within the Maastricht University Medical Center (MUMC+), the division performs mainly clinical research and includes the departments of Psychiatry and Neuropsychology, Neurology, Neuroradiology, Neurophysiology, General Practice, Internal medicine, Health, Ethics and Society, and Otorhinolaryngology.

The vision of CNP&CNS is to embrace a broad perspective on the disorders being studied, and not to see these as neuro-reductionistically defined entities. Embracing the complexity of these conditions, we have broadened our focus towards in the last five years with more emphasis on prevention, e-health technology, data science, and ecological validity.

In CNP&CNS there is a strong integration between research and patient care, into several centers like the Alzheimer Center, Stroke Center, Brain Injury Center and the Center for Movement Disorders. These centers are well aligned with the Brain Nerve Center of the MUMC+.

### Goals & results

When I write this introduction, we are in the middle of the corona crisis that has changed the world for many of us so dramatically. While several colleagues have been working hard at the frontiers of the care for corona patients, most of us were forced to stay at home. It feels weird to work without having contact with the patients included for our clinical studies, and without the possibility of seeing and talking with our colleagues in real life. Zooms, Teams and Skypes have replaced the real intrapersonal meetings that are so important for every group to function. This is a challenging time for us all, but especially for the junior researchers who are more vulnerable at the start of their career. It is great to see that despite these difficulties, we still manage to work efficiently and stay productive. Digital social events, like the Friday afternoon e-drinks and Pub quizzes are organized to keep up the good spirit. Clearly, there is a solid social capital available that makes the teams work even under these circumstances, and this makes me really feel proud.

Looking back to 2019, it was again a productive year for our division. The research output was substantial, with 16 PhD defenses, 252 scientific WI-1 publications and a total earning power of 3.8M. The research of this division is mainly clinically oriented, as most of the staff is appointed to the Maastricht University Medical Center (MUMC+), with close links to the departments of Psychiatry and (Neuro)psychology, Neurology, Neuroradiology, Neurophysiology, Otorhinolaryngology, Internal Medicine and Family Medicine. In line with this development, there is also strong integration of patient care facilities and clinical research into the centers, such as the Alzheimer Centrum Limburg, Center for Movement Disorders, Brain Injury Center and the Stroke Center. With the further implementation of MUMC+'s Brain Nerve Centre and the integration between hospital and university, there is a firm infrastructure for this more integrative approach.

We congratulate prof Albert Leentjens on this appointment as a chair of Neuropsychiatry, which is a great stimulus to expand his work at the interface between movement disorders and mental health disorders, such as the Deep Brain Stimulation for Obsessive Compulsive Disorders. Dr Marlies Gijs, a researcher from the department of Ophthalmology was successful in obtaining a ZonMw Veni grant for a collaborative project with division 1 and 3 on the use of tears for the diagnosis of Alzheimer's Disease. In addition, Kay Deckers was not only granted with the prestigious Young Outstanding Researcher Award of Alzheimer Nederland, but also acquired a Memorabel grant to continue his successful work on a public health campaign for the prevention of dementia. In 2019 a collaborative initiative in Limburg called BReIN started up (Brightlands Research Infrastructure for NeuroHealth). This so called 'Kennis-As' project, which is supported by the province of Limburg and led by Prof Jos Kleinjans, will bring many different disciplines and areas of expertise together. A national multisite project on the epidemiology and early diagnosis of young onset dementia called PRECODE, led by Prof Marjolein de Vugt, has started and will lead to new exciting data in the years to come. A shared PhD with the Institute of Data Science (Michel Dumontier) was also initiated in 2019, in order to better understand the complex interrelationships between different kinds of pathologies that characterize the disorders that we study. Our collaboration with division 3 was also further strengthened, with two shared PhDs and three-monthly scientific meetings. Finally, we are involved as WP lead and coordinating center in a H2020 Marie Sklodowska Curie DISTINCT and the INTERDEM Academy, for which we will organize a comprehensive training program for early stage researchers.

In 2020, our division will build further on these collaborations and crossroads and continue our successful work along these research lines. In addition, we will be participating in two new consortia on the prevention of neurodegenerative disorders, and intensify collaborative activities between clinical departments in the MUMC+.


*Photography: Zuiderlicht*

# MAKING LIMBURG BRAIN HEALTHY!

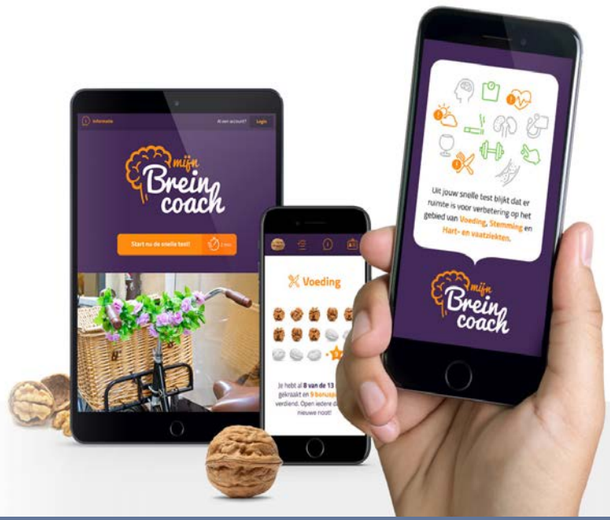
After two years of preparation, the Alzheimer Centre Limburg launched a public health campaign in March 2018 to increase awareness on dementia risk reduction among inhabitants of the Province of Limburg. This campaign aimed at motivating the general public to engage in a brain-healthy lifestyle by means of an eHealth platform called MijnBreincoach (see below). The campaign was developed in collaboration with the Dutch Municipal Health Services and the Department of Health Promotion of Maastricht University. To maximize acceptance in the relatively young target population aged 40-75 years, a positive phrasing was chosen with respect to the slogan ("We are our own medicine"), terminology (e.g. "room-for-improvement" instead of "risk", "brain health" rather than "dementia"), and campaign material visualizing the three campaign themes: "eat healthy", "exercise regularly", and "stay curious". Difference in awareness before and after the campaign was assessed by an online questionnaire in two independent samples of more than 1200 adults. Overall, awareness of dementia risk reduction did not change over time. However, one out of five random persons in Limburg had heard of the campaign, and these people were significantly more aware of dementia risk reduction and the three campaign themes. Further, almost 40% of the respondents expressed to have become more aware of their brain health, and 30% stated to have engaged in a brain-healthy lifestyle during the last 12 months. Currently, several (inter)national parties engaged in health promotion have shown interest to adapt the campaign and/or the eHealth platform for local roll-out.

## The MijnBreincoach eHealth platform

The MijnBreincoach eHealth platform (or app) uses the well-validated "LIfestyle for BRAin health" (LIBRA) score to give people insight into their own dementia risk profile and flags individual room for lifestyle improvement. The LIBRA index consists of 12 modifiable risk and protective factors for dementia. Users start with a 12-item "quick test" that assesses the LIBRA factors and which flags personal room for improvement based on self-reported data on the presence and/or absence of specific LIBRA factors. Next, a user can create an account and complete the more comprehensive administration that assesses the twelve LIBRA factors with follow-up questions on the "quick test" by validated questionnaires. People can get insight and feedback on their personal risk profile, identify areas of healthy behaviour (to facilitate maintenance), areas of unhealthy behaviour (to facilitate change), and identify chronic vascular/metabolic conditions (to facilitate appropriate management). Users can choose a lifestyle topic or health condition of interest and receives daily notifications (cracking the "Nut of the day") on how to improve brain health by improving their score on that factor. The daily notification contains a short text message providing information, a quiz, or a behavioural challenge. At present, the quick LIBRA test (kiosk version) is already available in English, Norwegian and Flemish. Other language versions will follow soon.

Link to the campaign website: www.wezijnzelfhetmedicijn.nl
Link to the eHealth platform: www.mijnbreincoach.eu
More information on LIBRA:
https://www.alzheimercentrumlimburg.nl/sites/alzheimercentrumlimburg/files/development_of_libra.pdf






*Photography: Betawerk*

# MAIN ACHIEVEMENTS DURING THE CAMPAIGN

(March 2018 - January 2019)

**LOCAL ENGAGEMENT AND SUPPORT**

- More than 140 stakeholders (municipalities, schools, health care centres, companies) committed to this campaign by distributing campaign material/messages and/or organizing public events
- Distribution of 35.000 campaign leaflets and more than 1.000 campaign posters (at more than 400 locations within the Province)
- Organization of more than one public event per week (n=52; lecture, workshop or other community activities)
- 400 billboards with the campaign message were visible for throughout the Province of Limburg.

**CAMPAIGN WEBSITE (www.wezijnzelfhetmedicijn.nl)**

- More than 10.000 website visits
- Online campaign posters are downloaded more than 5.500 times in total

**MEDIA**

- Over 65 media outlets (e.g. newspaper item, radio-interview)
- Campaign tweets reached 200.000 people
- Facebook messages reached more than 15.000 people

**EHEALTH PLATFORM (www.mijnbreincoach.eu)**

- 9.000 downloads MijnBreincoach app
- The Dutch Municipal Health Services and the Ministry of Health, Welfare and Sport in The Netherlands promote the app on their website on innovations in health care



# IN VIVO MRI OF THE BLOOD-BRAIN BARRIER

## Historical prelude

It would be interesting to gaze at Paul Ehrlich's face and listen to his opinion on the current advances of magnetic resonance imaging in living humans to detect disruptions of the blood-brain barrier (BBB). The concept of the BBB has often been attributed to Paul Ehrlich (1854-1915)*, a Prussian physician, who performed many experimental studies on the tissue penetration properties of various dyes, but who actually denied the special function of the capillaries in the brain.
The BBB refers to the tight lining of the endothelial cells in walls of blood vessels in the central nervous system which serves to protect the brain cells from toxic substances and to maintain the internal milieu of the brain's tissue by selectively exchanging biomolecules. For its protective mechanism, the barrier function makes it unfortunately extremely hard for therapeutic drugs to enter the brain. In certain diseases the BBB is widely open, for instance malignant tumours and inflammatory hot spots in multiple sclerosis. Today's view is that BBB breakdown is an initiating process for various brain pathologies leading to strokes, epileptic seizures, Alzheimer's disease and other types of dementia. Therefore, the BBB seems to be an attractive target to direct early treatment to and to prevent further escalation of the pathology.

## Maastricht approach

In 2011 Prof. Walter Backes, a medical physicist at the Medical Imaging department of the Maastricht UMC+, started a novel research line on the permeability of the blood vessels of the brain, extending on his previous research experiences in various types of extracranial tissues and disorders. Initial responses from other sites were skeptical due to unsuccessful previous and on-going attempts. One missing link seemed to be how to deal with weak and very noisy signals, a topic close to the heart of a physicist.

By following over time the internal blood circulation and distribution of an administered MRI contrast medium, a magnetic dye serving as a surrogate small biomolecule, MRI measurements were designed to detect contrast leakage in brain tumors and, most importantly, in remotely located normal appearing brain tissue. After an initial demonstration provided pilot results, the Alzheimer Foundation recognized the potential and granted two projects to determine the role of BBB impairment in patients with early signs of Alzheimer's disease. This project was made possible by the multidisciplinary setting created with prof. Verhey and co-workers (division 1) of the Alzheimer Center Limburg and the researchers of the Leiden University Medical Center.

## Intertwining

Around the same time, extending this topic to small vessel disease was made possible in a collaborative effort of the departments of Neurology and Radiology through funding from NWO & Health Foundation Limburg. Small vessel disease is a condition of the smallest brain vessels, a regressive disorder that often manifests itself in patients with cardiometabolic risk factors and also ageing individuals. And this financial injection allowed us to put a novel collaboration into position, using a so-called 'twin model' PhD project. In this model, we coupled two PhD students, one with a technical engineering and one with a medical background, to collaboratively perform research on the same topic. Apart from the technological challenge to measure subtle BBB leakage, such a collaboration involves not only the management of completely different fields of knowledge and skills, but also putting aside differences in expectations, approaches, thinking, and culture. The approach turned out successful and provided novel insights on the relations between brain damage, BBB breakdown, and detriments in cognition and produced multiple publications in a highly ranked journals with praising editorials. Also the connection to the Horizon 2020 project SVD@target led by the University of Edinburgh in collaboration with many European sites has great potential to provide new insights in the role of BBB impairment in several types, including genetic variants, of small vessel disease of the brain. Novel initiatives on BBB imaging have recently been funded, for instance on post-stroke epilepsy led by dr. Jaap Jansen (ZonMw & Epilepsiefonds) and the H2020 project (CRUCIAL) led by prof. Robert van Oostenbrugge on microvascular rarefaction in collaboration with the universities of Leuven, London, and Pamplona.

*Multidisciplinary PhD duo: May Wong (biomedical engineer) and Eleana Zhang (medical doctor).*

The twin approach for this theme was actually resonating on multiple levels, from PhD students with different educational backgrounds, to supervisory teams with different expertises to the research schools MHeNs and CARIM, who embraced the fruitful collaboration. Where in former days a strict border was established for intravascular and extravascular matters, today interdisciplinary research is stimulated in the context of the alliance between MHeNs and the Brain Nerve Center (HZC, Hersen Zenuw Centrum).

## Breaking even more barriers

A currently on-going project that started in 2019 aims to further raise the detectability of the BBB breakdown by down-scaling the noise level with the utilization of the ultra-high field MRI systems at the Scannexus facility and the expertise of the physics group at the faculty of Psychology & Neuroscience. Currently, the scientific interest in BBB research, in particular for in vivo imaging, is growing and expectations for medical applications are high. Though the encouraging results have been confirmed recently by multiple research sites around the world, we should remain modest as standardisation for further improvement of the sensitivity of the technique is still required before it can be spread out widely in clinical research settings. As we reflect on Paul Ehrlich's early efforts we have to realise that we are just at the beginning to re-discover the functioning and the thus far hidden entry & exit routes of the ageing and impaired human brain, and regain step by step novel pathophysiological insights and hopefully prepare for future medical applications.

**Paul Ehrlich performed many experiments with dyes to study the oxygen uptake of various organs. He never actually subscribed to the view that the lack of staining of the brain could be ascribed to some special property of the cerebral endothelial cells. He proposed the brain had the most finely porous tissue of all organs. Actually, the proper naming of the BBB concept ('Blut-Hirnschranke') and the recognition of its basic restrictive function took many experiments and considerations of multiple researchers years afterwards (Saunders et al, Frontiers in Neuroscience 2014).*

# DIVISION II

Mental Health

Division Leader:
Prof Thérèse van Amelsvoort

Deputies:
Dr Sinan Guloksuz
Dr Wolfgang Viechtbauer

## SUMMARY

Division 2 is embedded within the Department of Psychiatry and Neuropsychology and characterized by clinical and epidemiological research on Mental Health performed in affiliation with several regional health care organizations. The mission of Division 2 is to promote mental health, prevent mental disorders and enhance its treatment by using state of the art research methodology in combination with clinical expertise and lived experience. The Division's strategy is to carry out highly innovative clinical science involving both clinical and non-clinical populations across the lifespan and translate and implement its results to the broader community.

The methodological expertise of the Division is organized in several different expert groups, each coordinated by a senior scientific staff member. The overall research infrastructure of the Division is formed by a large support team of experienced research coordinators, research assistants, and ICT staff that provide the basis for the planning, monitoring and execution of the studies that are performed within our Division and which is available to, and used by all scientists of the Division. Finally, several experience experts are embedded within the Division who are involved in dissemination of the Division's research.


## Goals & results

The division Mental Health aims to understand the etiology of mental disorders by using dimensional and transdiagnostic approaches applied to ecological, psychological and biological systems. In addition, the work performed in division Mental Health offers opportunities to develop more individualized treatments and accurate predictive markers that could improve a patient's quality of life, taking into account the daily context of the patient. The research carried out in the Division Mental Health captures a wide range of themes, and making use of different methodologies. This is clearly visible in the School's research matrix on the new MHeNs website.

One of the core research activities of our Division involves ecological momentary assessments through the experience sampling method (ESM) by using a tool which acquires data in real life allowing the study of real-time and real-world person environment interaction patterns. The Division has 30 years of ESM experience and has established a world leading position in this field (www.esm-maastricht.nl), and the Psymate, the data collection tool, is freely downloadable from iTunes and Android Store. In 2019, we continued increasing our visibility of our Division's ESM expertise in and outside MUMC+. The work is mostly represented in the 'monitoring' and 'prevention/ rehabilitation' section of the research matrix, which is led by the ESM experts of our division.

Another key research activity of our division involves risk and resilience prediction by employing large datasets of the general population, high risk and specific clinical samples, including those of rare genetic disorders. This work is embedded in the 'imaging' and 'cell biology / genetics' sections of the research matrix, and is further described on 14-15 and 16-17.

The combined statistical, epidemiological, genetic and imaging expertise of our Division has ensured continuing high-quality scientific output and participation in, and leading large national and international consortia including EUGEI, PSYSCAN, GROUP, ENIGMA, RTOC. In addition, a new NIH funded international collaborative study on CNV disorders was started in 2019, our division being the only Dutch partner in this consortium. OPHELIA, a Dutch consortium on treatment of psychosis started in 2019, with the GxE WP being led by our division.

In 2019, the development of the MUMC+ BNC (Hersen Zenuw Centrum) has taken further shape, and PIs from our Division have presented healthcare pathways on the clinical themes, Psychosis, Anxiety and Mood, and Eating Disorders, and future developments on research line Monitoring to the directors of the MUMC+.

In 2019 we have seen the continuing success of @ease *(www.ease.nl)*, an innovative youth mental health care development with the opening of Heerlen and several media appearances including the visit of the live National Radio Bus *(https://www.nporadio1.nl/nieuws-en-co/onderwerpen/495784-bus-luisterend-oor-jongeren-in-de-knel-deel-1; https://www.nporadio1.nl/nieuws-en-co/onderwerpen/495785-bus-luisterend-oor-jongeren-in-de-knel-deel-2)*. Also, @ease took part in the development of the Global Youth Mental Health guidelines in 2019, a collaborative project of Orygen Melbourne and the World Economic Forum.

In 2020, we will see the opening of more @ease centers in Rotterdam, Groningen and a 2nd one in Amsterdam. Also, further integration of our research activities within the BNC will take place in 2020. Furthermore, in 2020 we are expecting the kick-off of a neuromodulation study in patients with affective disorders in collaboration with MUMC+, and an innovative CIN (Centre for Integrative Neuroscience) project on cost/benefit based decision making in humans in collaboration with FPN (Faculty of Psychology and Neuroscience ) and SBE (School of Business and Economics).

# MOOD, ANXIETY & TRAUMA: AT THE INTERSECTION WITH NEUROIMAGING & NEUROMODULATION

At the end of 2018, we reached the successful completion of the large longitudinal project 'Self-Management of Altered environmental Reactivity Treatment SCANning' (SMARTSCAN) in which we examined the mechanisms of person-environment interaction, functional and structural brain changes after therapy and the risk to develop more severe psychopathology in youth with mild anxiety, depressive and psychotic symptoms. The emphasis in 2019 has been on the analysis of this dataset. Six publications resulted from this database at the intersection between mood, trauma & anxiety, and neuroimaging & -modulation.

Functional imaging data from this project allowed us to investigate the implication of classical fear conditioning, fear generalization, and extinction learning for the development of anxiety disorders. Results indicate that specific phobia may be characterized by enhanced differential fear retention and altered brain activation patterns during fear acquisition and extinction recall. This is a different pattern than usually seen across other anxiety disorders, in which mainly reduced differential fear learning has been reported, and hence emphasizes the importance to differentiate between disorders characterized by more focal fears (specific phobia and discrete traumatization) versus broad distress (general anxiety disorder, major depressive disorder, and complex PTSD) when disentangling the nature and extent of fear conditionability and extinction learning across anxiety disorders.
Furthermore, the randomized-controlled trial set-up in SMARTSCAN enabled us to add important insight into the mechanisms underlying exposure therapy. Exposure therapy is regarded as one of the most effective treatments for anxiety disorders with a large effect size. Yet, non-response and relapse occurs in about half of the patients.
Although extinction learning has long been assumed to represent a core mechanism underlying exposure therapy, empirical evaluation of this assumption was largely lacking. Our data show that exposure therapy response was specifically predicted by prediction-error related ventromedical prefrontal cortex activation during early extinction. Prediction errors are thought to drive the extinction learning process. In addition to extinction learning, reward sensitivity might also represent a predictive factor for exposure therapy outcome, as this therapy promotes positive experiences and involves positive comments by the therapist. Our results confirmed that neural reward-related mechanisms can be specifically associated with exposure therapy outcome in specific phobia. Results indicate that exposure therapy may rely on neural circuitry involved in attentional and cognitive processes during reward anticipation and reward consumption, and that individual differences in engagement of these processes may predict who will best respond to exposure therapy.
On the Mood side, SMARTSCAN was able to relate the neural underpinnings of reward learning to real-life behavior by combing Experience Sampling Method (ESM) in daily life and imaging. It was shown that striatal Reward Prediction Error signals were disrupted along the depression continuum. They were associated with reward-related behaviour in real-life, suggesting that real-life coupling of reward anticipation and engagement in rewarding activities might be a relevant target of psychological therapies for depression.

Another line of research focusses on optimal target selection for DBS and TMS for each patient individually in the treatment of obsessive-compulsive disorder (OCD). This transdivisional (div. 1: A. Leentjes; div. 3: Y. Temel and L. Ackermans) and transfaculty project (FPN: A. Sack, T. Schumann) project combines ultra high-field MRI and neuromodulation. An initial proof-of-concept study has been set up to investigate the individual propagation patterns of TMS-evoked activity in response to stimulation of an individually-defined cortical region, anatomically connected to current OCD-DBS target nuclei. The foundations to extend collaboration to the KULeuven to pool data and knowledge on neuromodulation in OCD have been made in 2019. Concrete plans to streamline treatment/study procedures will take form in the following years.

## SUMMARY

The clinical pillar 'Mood, Anxiety & Trauma' aims to identify factors that contribute not only to affective psychopathology, but also to resilience. The objective is to nurture future development and optimization of (preventive) intervention and treatment strategies in affective symptomatology. Research within this pillar applies and combines a wide range of methodologies (e.g., neuroimaging, experimental models, Experience Sampling Method in daily life) and uses this integrative approach in clinical populations, subclinical populations, and in individuals with no mental health problems.
At the intersection with neuroimaging and -modulation, we add insights to the field of affective neuroscience by exploring the brain mechanisms underlying emotional behavior. We employ various imaging methods to determine brain structure, activity and connectivity, and combine these with neuromodulation techniques such as deep brain stimulation (DBS), transcranial magnetic stimulation (TMS) and neurofeedback.

# PSYCHOSIS AND NEURODEVELOPMENT: AT THE INTERSECTION WITH CELL BIOLOGY AND GENETICS

With a top-down approach, we bridge the gap between epidemiology and molecular genetics & biology to investigate the role of genetic and environmental causes of psychosis spectrum disorder by following transdiagnostic, multidisciplinary, and multimodal framework. Our research group has access to large and diverse population cohorts who have been followed up over many years. We lead the ongoing national and international collaborations with several partners involving the projects European Network of National Networks studying Gene-Environment Interactions in Schizophrenia (EU-GEI), Genetic Risk and Outcome of Psychosis (GROUP), The Netherlands Mental Health Survey and Incidence Study (NEMESIS), and TwinssCan to identify and validate the sources of genetic and environmental vulnerabilities associated with psychosis. Our recent series of work in the EUGEI provided the first molecular evidence for gene-environment interaction in psychosis spectrum disorder (https://doi.org/10.1002/wps.20629). To advance gene-environment research, we pioneer exposome research in psychiatry and generated a composite score of environmental liability for schizophrenia (analogous to polygenic risk score) (https://academic.oup.com/schizophreniabulletin/article/45/5/960/5537033). In the next phase of this work, we will integrate exposome, genome, and epigenome data to execute the next phase of gene-environment interaction research in psychosis spectrum disorder.

Members of Division II are involved in various large-scale neuroimaging collaborations. A large international effort is the Enhancing Neuro Imaging Genetics Through Meta Analysis (ENIGMA) Consortium. Dr. Hernaus co-leads the Clinical High Risk for Psychosis Working Group, Prof. van Amelsvoort is an active member of the ENIGMA 22q11.2 and Schizophrenia Working Groups and the EU FP7 Psyscan Study, Prof. Linden is involved in several ENIGMA CNV (Copy Number Variant) collaborations,and Dr. Blokland is an active member of the ENIGMA Diffusion Tensor Imaging (DTI) Working Group. These ENIGMA Working Groups aim to uncover reproducible markers of illness vulnerability, progression, and resilience, as well as identify the genetic underpinnings of various imaging markers. Further, Dr Blokland leads the GENUS Consortium, a large international collection of schizophrenia case-control datasets with genome-wide genotype (GWAS), cognitive, and neuroimaging data, aiming to evaluate the effect of schizophrenia genetic risk variants on brain-based phenotypes, as well as finding clues for explaining the extensive sex differences observed in risk, presentation, and prognosis of psychiatric disorders. Dr. van der Meer leads an ongoing collaboration with the University of Oslo, whereby they are developing several novel, powerful, multivariate GWAS tools to boost discovery of the genetic variants underlying brain morphology in large population samples and systematically map genetic overlap between these measures and disorders.

With a bottom-up approach, we investigate genetics of psychosis in well-identified genetic syndromes. In a recent NIH-funded project: "Dissecting the effects of genomic variants on neurobehavioral dimensions in CNVs enriched for neuropsychiatric disorders", we collaborate with the International Consortium on Brain and Behavior to understand the convergence and specificity of the impact of CNVs on neurobehavioral dimensional phenotypic measures (http://www.22q11-ibbc.org/home/).

To inform clinical practice and provide insight into illness course, we investigate the role of gene and environment interplay in a first episode psychosis cohort. In a recent ZonMw-funded project: "Outcome of Psychosis: Heterogeneity Explained by Long-lasting Individual Attributes (OPHELIA)", we lead the Workpackage Gene-Environment Interaction (https://www.zonmw.nl/nl/onderzoek-resultaten/geneesmiddelen/contentpaginas-geneesmiddelen/behandeling-op-maat-voor-mensen-met-psychosegevoeligheid/).

## SUMMARY

Psychosis spectrum disorder has marked consequences for those affected, their families and their social- and work- related environments. Our research focuses on identifying genetic vulnerability underlying psychosis spectrum and aspires to predict risk and resilience by employing large datasets of the clinical samples, general population cohorts, as well as specific samples such as rare genetic syndromes. By applying genome-wide association (GWA) and related approaches, we study the effects of genetic variants on neuroimaging, clinical measures, and environmental vulnerability.

Staff involved: Thérèse van Amelsvoort, Lotta-Katrin Pries, Gabriëlla Blokland, Dennis van der Meer, Dennis Hernaus, Sinan Guloksuz, Bart Rutten.

# DIVISION III

Translational Neuroscience

Division Leader:
Prof Jos Prickaerts

Deputies:
Dr Mark Janssen
Dr Mario Losen

## SUMMARY

Division 3 is home to fundamental and translational neuroscience research of scientists affiliated within the departments of Psychiatry and Neuropsychology, Neurosurgery, Anaesthesiology, Neurology, Ophthalmology, Otorhinolaryngology, Paediatrics, Urology, BioMedical Engineering, Toxicogenomics, Clinical Neurophysiology, and Genetics and Cell Biology. The mission of the division Translational Neuroscience is to improve significantly the understanding of the mechanisms mediating normal and aberrant functioning of the nervous system, and to innovate clinical care at the levels of prevention, diagnosis and treatment for patients with disorders of the nervous system.

Our strategy is to embark on this mission by performing high-quality translational and back-translation neuroscience, with a bidirectional roadmap from fundamental via preclinical to clinical neurosciences, and in a life span perspective. The research lines of the scientific staff embody common scientific and methodological concepts that cut across these clinical indications. The coordination and development of methodological expertise is organized into expert groups, which are coordinated by senior staff. The different sections of the laboratory are based on the methodologies used, i.e. in vivo experiments, stem cells, neuromodulation and electrophysiology, molecular and cellular biology, and quantitative immunocytochemical microscopy.

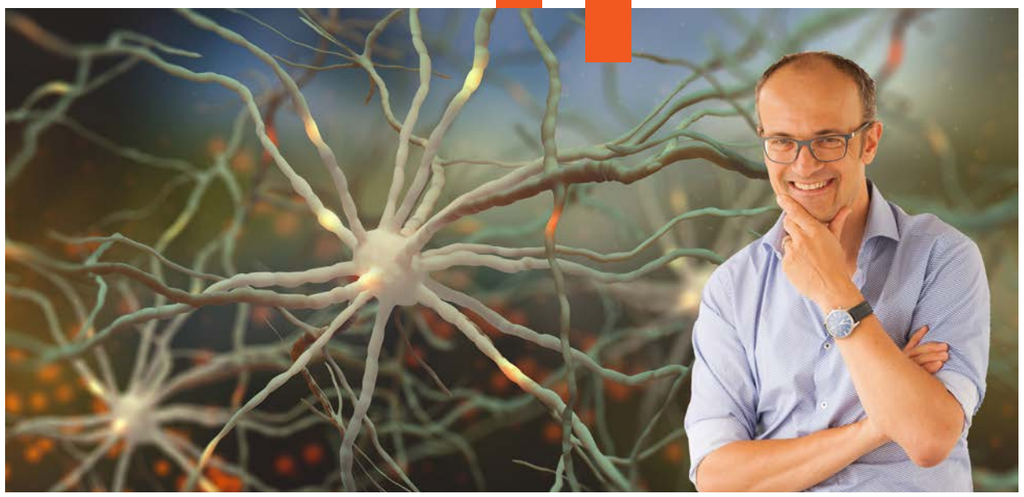


*Photo Jos Prickaerts: Anke Geurts Photography*

### Goals & results

We aim to gain knowledge of physiological and pathophysiological mechanisms underlying diseases of the nervous system including mental and motor disorders and sensory system disfunctions and to develop strategies for improving healthy living, as well as preventing and treating such diseases. In particular we aim to:

- Gain insight into the (epi)genetic, molecular and cellular mechanisms in disease areas of the central nervous system including Dementia, Depression, Psychosis, Post-Traumatic Stress Disorder, Epilepsy, Movement Disorders, Multiple Sclerosis, as well as mechanisms mediating central control of peripheral bodily functions such as Pain, (Auto)Immunity, Ophthalmological and Vestibular and Neuro-Urogenital functioning. There is also an interest in developmental programming including prenatal and perinatal life.
- Translate relevant scientific findings into biomarker development as well as new therapeutic applications including lifestyle interventions, pharmacological and antibody-based therapies, or neuromodulative treatments.

Our multidisciplinary staff consists of professionals from relevant clinical and basic research disciplines. This allows us to integrate a variety of techniques such as detailed biochemical, cellular and animal experiments, as well as human studies. The division of Translational Neuroscience has state-of-the-art laboratories for electrophysiology, microscopy, molecular biology, as well as biochemistry laboratories for tissue processing, cell culturing, immunohistochemistry, proteomics and genomics. For example, there is access to a light sheet microscope, confocal microscopes and various stereological microscopy set-ups of the highest standard. There are excellent molecular biology labs for in vitro and in vivo non-viral as well as viral gene transfer experiments including optogenetics and CRISP/Cas9. The behavioural animal labs meet the latest up-to-date standards for automated assessment of animal behaviour. There is a large expertise in a wide variety of animal models and tests for diseases of the central, autonomic and peripheral nervous systems, muscle diseases and diseases of the sensory systems. The technological expertise in our division is currently centralised in expertise groups that are coordinated by senior staff members and supported by experienced technicians: Molecular and Cell Biology, Microscopy and Imaging, Neuromodulation and Electrophysiology, Stem cells (established in 2019), and In Vivo and Behaviour.

We have collaborations within worldwide international networks of research offering a strong academic environment. For the upcoming years we strive to align and integrate our research lines within MHeNs and within Maastricht University. Till last year the research within the division was organized along the research lines Neuroepigenetics, Neuropsychopharmacology, Neuroinflammation, and Neuromodulation. These lines are incorporated and integrated into the research lines of the MHeNs research matrix. Thus, Modulation now incorporates Neuromodulation, Neuroinflammation and Neuropsychopharmacology. Neuroepigenetics is being incorporated into Cell biology and Genetics. The Brain and Nerve Center (BNC) within the MUMC+ offers further excellent opportunities as its research lines overlap with those of MHeNs. Next to research lines, the BNC also has clinical research themes (e.g pain, cognition and dementia, epilepsy, movement, vision, hearing and balance), which overlap with the division's research topics and offer excellent opportunities for integrating its preclinical research with the clinical expertise. This translational advantage generates scientific input with clear translational and clinical impact and also increases opportunities for further funding. An additional point of attention is extending our stem cells and iPSC research. This is done within the recently established Brightlands e-infrastructure for Neurohealth (BReIN) Institute within MHeNs and by the establishment of an expert group Stem Cells. Linked to this we will stimulate more integration with the Institute of Data Science (IDS) and the Institute for Technology-Inspired Regenerative Medicine (MERLN). An expert group In Silico and Functional Genomics is planned to facilitate this. Also important for the Division in this respect is the start of more integration with M4I (e.g. via the Interreg project EURLIPIDS) and Systems Biology (MaCSBio). Finally, we will keep on focussing specifically on Dutch and international personal grants. Therefore, we are happy and proud to announce that we could welcome three VENI fellowships (Marlies Gijs, Sarah Hescham, Christian Herff) and one memorabel ZonMW fellowship (Ehsan Pishva) in our division in 2019.

# MILD COGNITIVE IMPAIRMENT, STROKE, AND MULTIPLE SCLEROSIS

Phosphodiesterases (PDEs) were first identified about 50 years ago, and it was demonstrated that PDEs hydrolyze the phosphodiesteric bond of the intracellular second messenger molecules cAMP and cGMP. Caffeine is a nonselective PDE inhibitor as it inhibits cGMP- and cAMP-specific PDEs. PDEs have been classified into 11 families (PDE1-PDE11) based on several criteria such as subcellular distributions, mechanisms of regulation, and enzymatic and kinetic properties. Most of these families have more than one class of gene products (e.g. PDE4A, PDE4B, PDE4C, PDE4D). In addition, each gene product may have multiple isoforms (e.g. PDE4D1-PDE4D9). It has been estimated that more than 100 specific human PDEs exist.

PDE inhibitors have been suggested as a suitable tool for the treatment of a variety of cognitive deficits related to CNS disorders. They can stimulate intracellular signal transduction directly, thus enhancing neurotransmitter signaling. They can also exert neuroprotective effects via stimulating synaptogenesis, remyelination, or even been found to have the potential to alleviate amyloid and tau aggregation. Finally, some PDE inhibitors have anti-inflammatory properties.

In Maastricht we focus on PDE4. This type of PDE degrades cAMP, and there are 4 gene products (A-D), each having multiple isoforms. One of the main issues with developing PDE4 inhibitors are the adverse side effects, mainly nausea and vomiting. Prof J. Prickaerts and Prof A. Blokland (FPN) have recently shown that the non-selective PDE4 inhibitor roflumilast has beneficial effects on memory in healthy adults and elderly without having clear adverse side effects. Roflumilast is already on the market as an anti-inflammatory drug under the name of Daliresp or Daxas as a treatment to reduce the risk of chronic obstructive pulmonary disease (COPD) exacerbations in patients with severe COPD. The pro-cognitive effect was found to be at low doses and has resulted in a patent (WO2015022418), which repurposes this drug for cognitive impairment (e.g. in MCI and Alzheimer's disease).

Especially PDE4D inhibition is notorious for its side effects, while this is actually the best target for cognitive enhancement. Therefore, in collaboration with Genova University (Italy) and Columbia University (NY, USA) new PDE4D inhibitors have been developed without emetic effects. The PDE4D enzyme has 9 different long, short and supershort isoforms (see Figure). The PDE inhibitor binds to the catalytic domain (in blue), and through possible interactions with the N- and C-terminus of the enzyme, selectively for a specific isoform can be obtained. We assume that we have created inhibitors with a higher selectively for 'cognitive' PDE4D isoforms over 'vomiting' PDE4D isoforms. The preclinical data is very promising and these inhibitors have been patented for the treatment of Alzheimer's disease (WO20151212).


In 2019 a grant has been obtained from ZonMW. The aim of the project is to validate the effect of chronic treatment with roflumilast on cognitive function in patients with MCI due to AD. The duration of this phase II study is 4 years. It is a collaboration between Division 3 (Prof Jos Prickaerts; PI), FPN (Prof Arjan Blokland) and the memory clinic/division 1 (Prof Frans Verhey and Dr Inez Ramakers).

In 2019 we also obtained a grant from the Dutch Brain Foundation. The aim of the 4 years project is to test if chronic treatment with roflumilast can improve cognitive functioning and daily life activities in patients suffering from a stroke. This 4 years project is a collaboration between FPN (Prof Arjan Blokland; PI), division 1 (Dr Ieke Winkens) and division 3 (Prof Jos Prickaerts).

There is an intensive collaboration between Division 3 (Prof Jos Prickaerts) with BIOMED (Hasselt University, Belgium; Prof Niels Hellings) focusing on the role of PDE4 in demyelination and cognitive decline in Multiple Sclerosis. The linking pin in this respect is Dr Tim Vanmierlo who has a dual appointment at both institutes, focusing on the role of oligodendrocytes in neurodegeneration and CNS repair. MERLN is also implicated (Dr Paul Wieringa,) and all preclinical studies have resulted in a successfully approved PCT patent on PDE4D inhibitors against demyelinating diseases in 2019 (WO2019193091). This patent made it possible to attract additional VLAIO funding for a post-doc to further develop these PDE4D inhibitors in collaboration with the Biotech Rewind Therapeutics (Leuven, Belgium). In addition, two FWO PhD students grants were obtained by Dr Tim Vanmierlo on PDE4 and MS or Alzheimer's disease, respectively. The PhD students working on joint degree projects between Hasselt and Maastricht.

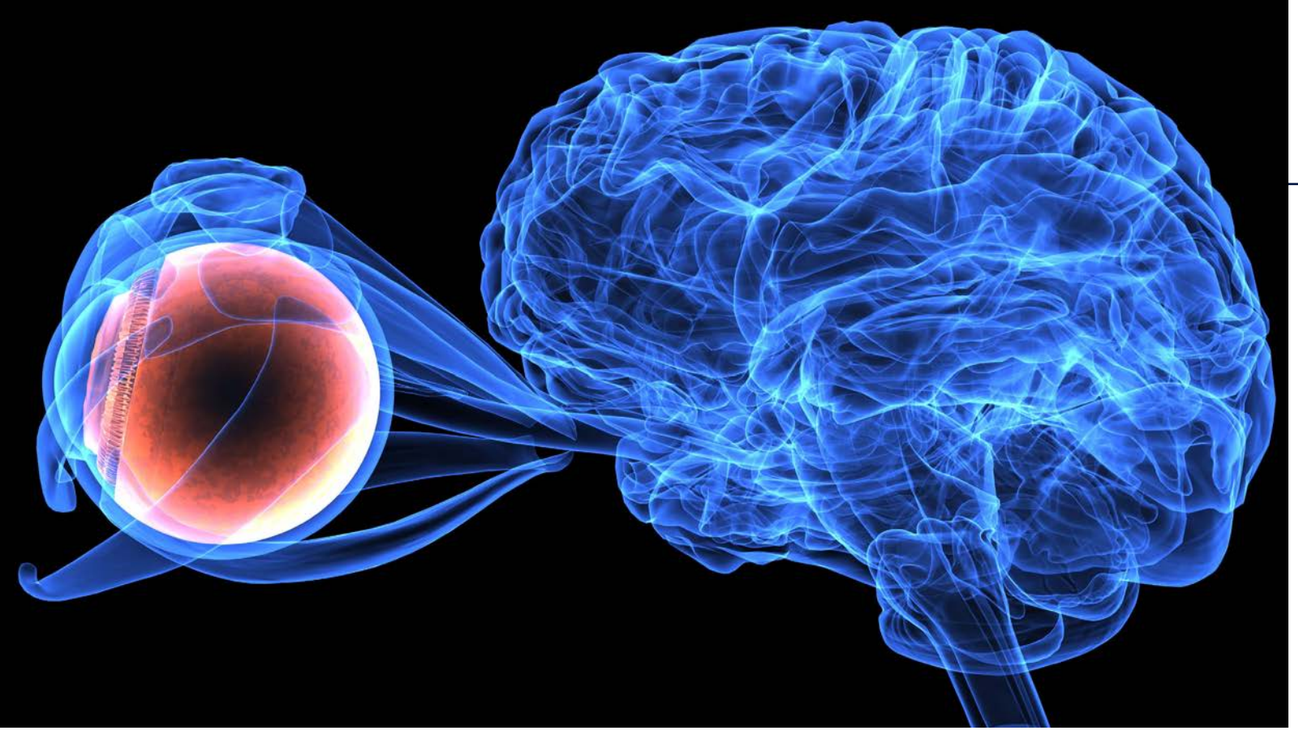
We focused on PDE inhibitors as the obtained grants will facilitate the essential preclinical and clinical studies to show proof-of-concept for these drugs as cognitive enhancers. Even so importantly, there are patents which can facilitate valorization both for the patients (new treatment) as well as research (new funding). Though we only focused here on PDEs, we would like to emphasize that many more exiting research is ongoing in this node. An excellent example is the obtained VENI fellowship by dr. Sarah Hescham to establish a proof of concept for magnetothermal and/or magnetoelectric DBS as a superior alternative to classical DBS.

## SUMMARY

The focus of research is on mechanisms of intracellular signal transduction and cellular plasticity underlying cognitive processes. The major aim is to unravel these mechanisms both in health and disease, while at the same time exploring the therapeutic potential of key players in the affected signaling pathways. Research involves working with in vitro and in vivo models in a translational context up to testing drugs in clinical trials.

Target identification starts mostly in human tissues using genomics (GWAS, eWAS) and transcriptomics (mRNA, miRNA). In parallel, signalling is manipulated in models using pharmacological interventions, optogenetics, (epi)genetic editing including CRISPR/Cas9, or deep brain stimulation (DBS). Based on the target validation experiments, most promising drugs and extracts to improve signal transduction and plasticity are tested in healthy volunteers and patients. There is also a substantial collaboration with biotech and industry to develop and test new neurostimulation applications, cognitive enhancers or neuroprotective compounds. Funding is secured from governmental grants (e.g. NWO, ZonMW, ENW, FWO, VLAOI), foundations (e.g. Alzheimer Netherlands, Charcot Stitching Belgium) and industry. There is strong valorisation potential with own and shared intellectual property.

The major staff at MHeNS involved at this interdivision crossroad are Prof Jos Prickaerts, Dr Tim Vanmierlo, Prof Daniël van den Hove, Prof Frans Verhey, Dr Inez Ramakers, Dr Sarah Hescham and Dr Ali Jahanshahianvar.

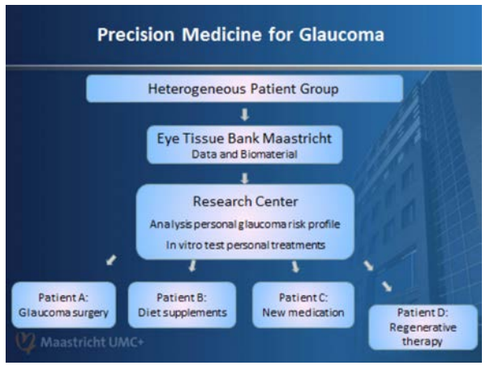


# UNIVERSITY EYE CLINIC MAASTRICHT: RESEARCH TO PREVENT AND CURE BLINDNESS

Vision is the sense we value most. The eye captures light, extracts the information of the world around us, and sends this to the brain for visual awareness. The University Eye Clinic Maastricht studies diseases which threaten this sense. We focus both on diseases of the anterior segment, which affect the light capturing properties of the eye, and on glaucoma which affects the transmission of visual information from the eye to the brain. Our research projects have their origin in the clinical contact with our patients and aim to return to these patients the revenues with regard to prevention and cure of vision loss. As an example, we here show our approach in glaucoma at the crossroads with Cell Biology and Genetics.

Glaucoma is characterized by pathology of the optic nerve. The neurons of the optic nerve degenerate and no longer send the visual information from the eye to the brain. Current treatments aim to reduce the pressure in the eye, since high intraocular pressure is an important risk factor. Yet, this often does not stop glaucoma progression. Glaucoma causes blindness in 7 million people worldwide. At the end of life, 10% of glaucoma patients are blind, also in the Netherlands.

Our research aims to find new treatments. We focus on the neurons, whose axons form the optic nerve: the retinal ganglion cells. We aim to find ways (drugs or dietary supplements) to prevent their death in glaucoma. It is not known exactly why and how these are lost. There are many risk factors, including increased eye pressure, age and hereditary predisposition. Variations in more than 150 genes influence the risk of glaucoma. The latter finding suggests that the disease is heterogeneous and that it is unlikely that we will find one treatment that is effective in all patients. Rather we need to study each patient individually to determine his or her specific glaucoma type and select the appropriate treatment. This requires an integration of patient examination, research, diagnosis and treatment in the future glaucoma care as illustrated in the Figure.




For the glaucoma care of the future, we founded the Eye Tissue Bank Maastricht. Upon informed consent of the patient, we collect and store the clinical data, blood (cells) and tissue. First of all, this biomaterial should make it possible to determine the detailed personal glaucoma profile of the patient. To achieve this, our PhD students currently analyse the clinical images aided by artificial intelligence, search for biochemical biomarkers in blood, aqueous humor and tears, and for glaucoma risk polymorphisms in the genes.

An important extension of this patient characterization is the creation of *in vitro* glaucoma models using the cells of the proper patients. To make the most realistic *in vitro* glaucoma models, we need 1) a genuine glaucoma trigger and 2) retinal ganglion cells of the patient.

To induce glaucoma we focus on two risk factors. First: High intra ocular pressure. In collaboration with the Institute for Technology-Inspired Regenerative Medicine (MERLN, Prof Jan de Boer, Prof Lorenzo Moroni) we made two devices: one, applying pressure to cells in culture, and the other, applying both pressure and stretch to cells in culture, which more closely mimics the circumstances that occur in the eye when ocular pressure is raised. Second, we aim to challenge the mitochondria in these cultures, since mitochondrial dysfunction is implicated in glaucoma (with Prof Bert Smeets, MHeNs). Finally, together with Prof Chris Reutelingsperger (CARIM, Biochemistry), we study the exact cell death machinery in the neuronal cells in order to detect ways to stop and reverse the cell death process.

The work on these glaucoma models currently is done mostly with neuronal cell lines (e.g. PC12). To make patient-derived retinal ganglion cells we collaborate with Dr Florence van Tienen and Prof Bert Smeets (MHeNs, Genetics and Cell Biology) to turn blood cells into induced pluripotent stem cells and then stimulate these cells to develop into a retina. Our technician Iris Boesten recently succeeded in generating retinal organoids containing retinal ganglion cells. Efforts are now directed towards further maturation of these retinal ganglion cells. As soon as well-differentiated retinal ganglion cells are generated, we will isolate them for use in our glaucoma models.

With the use of patient derived neurons in the glaucoma models we will be able to measure patients' sensitivity to specific glaucoma risk factors and, importantly, to screen in this model for drugs that protect the nerve cells of this patient. Moreover, the generation of human retinal ganglion cells will also enable us to start research on transplantation of retinal ganglion cells and regenerating the optic nerve. So finally we can start working on a real cure for glaucoma, restoring the vision that has been lost.

## SUMMARY

Eye and brain work together to achieve vision. The research of the University Eye Clinic Maastricht focuses on the optic nerve (involved in glaucoma) and the anterior segment of the eye (cataract, corneal dystrophies). Cell Biology and Genetics are employed in order to better diagnose and characterize patients, develop new, personal treatments, and restore function by transplantation or regeneration. In addition, brain diseases are studied in the eye, for example in the VENI project of Dr. Marlies Gijs on biomarkers for Alzheimer's in tears.

Staff involved: Carroll Webers, Rudy Nuijts, Henny Beckers, Tos Berendschot, Mor Dickman, Marlies Gijs, Theo Gorgels.

# EDUCATION

The training of Master and PhD students in the areas of mental health and neuroscience and related medical and psychological disciplines is a primary aim of MHeNs. In addition, MHeNs coordinates the European Graduate School of Neuroscience (EURON) and has an internationally recognized PhD educational program.

## PHD PROGRAM

In 2019 MHeNs had in total 318 registered PhD candidates, of whom 108 were employed by Maastricht University as regular PhD students (23 have newly started in 2019). Furthermore, there are 210 external promovendi. MHeNs is not only involved in the design, management and teaching of different Master programs (see below) – graduates of these programs also make up a significant percentage of MHeNs PhD students. For instance, many graduates from the Research Master Program Cognitive and Clinical Neuroscience (CCN) have joined MHeNs as promovendi. MHeNs has established educational guidelines, whereby PhD students with a 4-year contract are expected to complete educational activities equivalent to at least 20 European credits (EC/ECTS) in order to qualify for the MHeNs Certificate. The PhD students formulate and regularly update their personal research and training & supervision (TSP) plan in consultation with their supervisors, based on an assessment of previously acquired competencies, skills specifically needed for the PhD research, more general knowledge and skills, and future career plans. They use the PhD tracking system (TRACK) that enables administrative management of each PhD trajectory, intermediate assessment of progress and student status, and upload of important documents pertaining the progress, such as certificates of participation in courses, TSP and personal research plan (PRP). The school PhD coordinator (M. van Boxtel) has access to periodically generated progress indicators in TRACK and may act on projects that are flagged as 'needing attention'.

The PhD student program of MHeNs has a strong multidisciplinary character and is embedded within EURON (see below). As part of their training, PhD candidates are expected to follow general courses offered by Maastricht University (for example, writing skills, statistics, teaching skills, and career development), in addition to specific, research related courses organized by MHeNs and EURON (Annex 2).

*Summer School on Affective Neuroscience | 2018*

To improve the cohesion and interdisciplinarity of research training across the three MHeNs divisions, the "Topics in Translational Neuroscience" PhD workshops are offered once or twice per year. Furthermore, MHeNs is organizing the theoretical and practical 4-day annual course on "Human Neuroanatomy to Psychopathology" in collaboration with EURON. In addition, PhD candidates have opportunities to follow courses and workshops of the EURON program. There is a continuous exchange of PhD students between MHeNs research groups and international collaborating partners, within and beyond EURON. PhD students are stimulated to perform part of their research in international labs as these visits are mandatory to obtain the EURON Certificate of Excellence. Many of these collaborations result in a joint or double PhD degree.

EURON is a consortium of eight European universities. MHeNS is the coordinator of EURON and organizes the EURON office and appoints the director (G. Kenis) and the program coordinator (N. Senden). The partner universities are from Belgium (Université de Liège, UC Louvain and Universiteit Hasselt), Germany (RWTH Aachen and Universität zu Köln), France (Université de Lille) and Luxembourg (Université de Luxembourg). By combining the expertise of these partners, EURON forms a multidisciplinary and complementary network with a perfect background to educate and train PhD students in the field of basic and translational neuroscience. EURON offers a training program consisting of interactive courses, workshops and an annual symposium. The course topics range from neuroanatomy, molecular neurobiology and electrophysiology to animal and human behaviour and imaging. On top of these, advanced workshops offer a more in-depth study of specific topics. Our annual EURON PhD-Days (in 2019 organized in conjunction with the Life Sciences Days of the Université de Luxembourg) is the ultimate platform for students to present their work and forms an excellent networking opportunity. In addition, we have incentives to encourage exchange of PhD students between EURON research groups, and facilitate the organization of joint PhD doctorates. All activities of EURON are also aimed at enhancing the networking skills of our PhD students. Successful completion of the program is awarded with the EURON Certificate of Excellence. This broad training by a multidisciplinary staff in an international context will equip a new generation of neuroscientists with a unique skills set in contemporary science.

## MASTER PROGRAMS

MHeNs is involved in the curricula of several Master's programs of the Faculty of Health, Medicine and Life Sciences (FHML) and the Faculty of Psychology and Neuroscience (FPN) and these programs form an important source of new PhD students for the MHeNs School.

- *Research Master (RM) in Cognitive and Clinical Neuroscience (2 years program)*
  The RM consist of 6 specializations and MHeNs staff contributes heavily to 3 of them e.g. Neuropsychology, Psychopathology, Drug Development and Neurohealth and is coordinator of the Fundamental Neuroscience specialization (J. Prickaerts).
- *Master Biomedical Sciences (BMS – 2 years program)*
  The Master BMS consists of 6 specializations of which MHeNs staff coordinates the specialisations Inflammation and Pathophysiology (P. Martinez) and Neuromodulation (A. Jahanshahi).
- *Master Arts- Klinisch Onderzoeker (A-KO – 4 years program)*
  The modules Brein, Beweging and Gedrag are coordinated by MHeNs staff (R. Rouhl and J. Hoeijmakers). A-KO students have several research internships in their program, short internship in their 2nd year and a combined clinical and research internship in their last (4th) year. Researchers from all MHeNs divisions actively contribute to these internships as mentors.

## PROFESSIONAL COURSES

MHeNs has a longstanding expertise in the Experience Sampling Method (ESM), a psychological technique for obtaining ecologically valid momentary assessments of mental states and behaviours through remote communication, for example through the smartphone. We have a well-established course program in the area of ESM and in related statistical techniques, run by Division 2. Two ESM courses were run in 2019. Division 2 also coordinates the longstanding series of training courses in clinical psychiatry and psychopharmacology on the Dutch Wadden Islands that are particularly popular as CPD events for psychiatrists (https://www.wadcursus.nl/). MHeNs is also a key player in the INTERDEM Academy for training of early career researchers in dementia, which is connected to Division 1 and the Alzheimer Centrum Limburg (https://www.alzheimercentrumlimburg.nl/interdem-academy). Researchers from Division 3 were, amongst other training activities, heavily involved in the EURON workshop "Drugs and the Brain: From Laboratory to Clinic" that was held in Crete in October 2019.

# History of the Summer School on Affective Neuroscience

*In the late eighties at the initiative of the laboratory for Experimental Psychiatry, Maastricht University, Prof. Griez launched the first course of the "European Certificate in Experimental Pathology and Pharmacology of Anxiety Disorders", in collaboration with the Universities of Caen (FR) and Oxford (UK). This postgraduate, advanced, research-oriented teaching program focused on anxiety disorders and aimed to give a rational understanding of the pathogenesis and the responsible use of pharmacological and psychological treatment strategies. The program was a one-week residential intensive training, bringing together junior attendees and leading scientists in an informal atmosphere. Twenty-nine selected students from seven different European Union member states attended the very first session in April 1989. Due to the high number of applications each following year, the board of directors decided in 1995 to establish the program as a regular trans-European activity and extended the scope to the field of affective disorders. As such, the training scheme included one course on anxiety disorders and one on mood disorders leading to the establishment of the European Certificate in Anxiety and Mood disorders in 1997. The program provided a thorough and updated overview of the most recent scientific developments in the field of affective disorders.*

*Over the years, the scope of the program has broadened even more. Virtually all psychiatric disorders are characterized, or at least accompanied, by some degree of emotional disturbance. However, the underlying mechanisms of emotions are also the least understood by modern science. This illustrated the need for interdisciplinary and translational approaches to come to a deeper understanding of emotions. Hence the program evolved into the Summer School on Affective Neuroscience studying brain mechanisms underlying emotional behavior and getting closer to understanding the mechanisms behind human psychopathology. The Summer School aims to spread current concepts and practices in Affective Neuroscience across disciplines, countries and cultures. The faculty as well as the participants come from diverse professional backgrounds including psychiatry, psychology, behavioral sciences and neuroscience. These different perspectives are the basis for the interdisciplinary approach that is essential to the program.*

*Currently, the Summer School includes two one-week intensive residential courses. The topic of the courses alternates every year; each course being organized biennially. The Summer Course on Mood aims at an in-depth analysis of the latest developments in the field of depressive and bipolar pathology, including phenomena that are related to Mood such as aggression and addictions. The Summer Course on Fear, Anxiety, Obsessions & Trauma aims at an in-depth analysis of the latest developments within the field of anxiety at large, including related phenomena such as obsessions and compulsions, and post-traumatic stress*

*The teaching format is a challenging combination of lectures and small group workshops where participants discuss current hot topics. This format offers valuable opportunities for face-to-face contact between the participants and leading scientists in the field and also a fostering ground for international collaborations between participants and faculty, or a first step towards a PhD. Affective Neuroscience. The Summer School is residential and organized in an informal atmosphere to encourage participants to take advantage of this experience.*
*Upon completion of both summer courses the participants are assigned the European Certificate in Affective Neuroscience awarded by Maastricht University in collaboration with the University of Florence.*

*Since 2014, Prof. Dr. Koen Schruers, Professor of Psychiatry (Chair: Affective Neuroscience) has been the Executive Director of the program on Affective Neuroscience whose executive office is led by the academic coordinator, Dr. Lies Goossens, Ass. Prof., Dept. Psychiatry & Neuropsychology. They both have the major role in the annual organization of the program and make the greatest efforts to maintain it at a high level of excellence. In addition, their work is supported and inspired by the Board of Directors consisting of international experts in the field of affective neuroscience coming from various renowned universities: University of Leuven, University of Western Australia, University of Oldenburg, University of China (Chengdu), Humboldt-Universität zu Berlin, University of Bristol, Caltech, Imperial College London, Humanitas University of Milan and Tel- Aviv University. Besides these, the University of Florence holds a privileged position since, on basis of an agreement of 2004, the Summer School is a joint program of the Universities of Maastricht and Florence.*

# FACTS AND FIGURES

MHeNs had another very successful and productive year in terms of research output. The positive trend over the last few years continued in 2019.
Especially the amount of new contracts and grants (8.2 M€) and number of publications in top journals (568) show an impressive growth. The number of thesis defenses (40) shows a small decrease but is not worrying at all. With a total number of 318 registered PhD's (internal and external) within MHeNs there are a lot of thesis defenses ahead of us.
This development is a result of strategic investments over the last few years as both direct funding and contract research funding have increased significantly. Due to an increasing number of realized PhD dissertations over the last few years (resulting in an increase of the 3 year average), additional direct funding became available. As a result MHeNs was able to invest in talented tenured and tenure-track staff within all three divisions.

The additional means were and are being used to set up and further strengthen collaborations with our academic and clinical partners in the university and hospital (Brain and Nerve Centre (BNC) and Centre for Integrative Neuroscience (CIN)), shaped by joint PhD projects.
Obviously the corona crisis in 2020 puts a few initiatives on hold, but we are making contingency plans to cover for the backlog in research and new initiatives will be set up.

## KEY FIGURES 2019

ANNUAL BUDGET: 14.5 M€

NEW CONTRACTS AND GRANTS: 8.2 M€

RESEARCHERS: 143 FTE (INCL. 92,5 FTE INTERNAL PHD STUDENTS)

TECHNICAL AND SUPPORTING STAFF: 29,1 FTE

DEPARTMENTS/DISCIPLINES: 14 DEPARTMENTS (6 CORE AND 8 NON-CORE)

SCIENTIFIC ARTICLES: 568 (WI-1 PUBLICATIONS)

PHD THESES: 40

PATENTS/SPIN-OFFS: 4

# TOP PUBLICATIONS

### COGNITIVE NEUROPSYCHIATRY AND CLINICAL NEUROSCIENCE

*In vivo imaging of the nucleus of the solitary tract with Magnetization Transfer at 7 Tesla*
Priovoulos, N., Poser, B. A., Ivanov, D., Verhey, F. R. J. & Jacobs, H. I. L.,
2019, In : Neuroimage. 201, 7 p., 116071.

*Modifiable risk factors explain socioeconomic inequalities in dementia risk: evidence from a population-based prospective Cohort Study*
Deckers, K., Cadar, D., van Boxtel, M. P. J., Verhey, F. R. J., Steptoe, A. & Köhler, S.,
2019, In : Journal of Alzheimer's Disease. 71, 2, p. 549-557 9 p.

*Optimal Detection of Subtle Gadolinium Leakage in CSF with Heavily T2-Weighted Fluid-Attenuated Inversion Recovery Imaging*
Freeze, W. M., ter Weele, D. N., Palm, W. M., van Hooren, R. W., Hoff, E., Jansen, J. F. A., Jacobs, H. I. L., Verhey, F. R. & Backes, W. H.,
Sep 2019, In : American Journal of Neuroradiology. 40, 9, p. 1481-1483 3 p.

*Blood-brain barrier impairment and hypoperfusion are linked in cerebral small vessel disease*
Wong, S. M., Jansen, J. F. A., Zhang, C. E., Hoff, E. I., Staals, J., van Oostenbrugge, R. J. & Backes, W. H.,
9 Apr 2019, In : Neurology. 92, 15, p. E1669-E1677 9 p.

*Mindfulness-based intervention for people with dementia and their partners: results of a mixed-methods study*
Berk, L., Warmenhoven, F., Stiekema, A. P. M., Van Oorsouw, K., Van Os, J., de Vugt, M. & Van Boxtel, M.,
24 Apr 2019, In : Frontiers in Aging Neuroscience. 11, 10 p., 92.

### MENTAL HEALTH

*The predictive value of neural reward processing on exposure therapy outcome: Results from a randomized controlled trial*
Papalini, S., Lange, I., Bakker, J., Michielse, S., Marcelis, M., Wichers, M., Vervliet, B., van Os, J., Van Amelsvoort, T., Goossens, L. & Schruers, K.,
8 Jun 2019, In : Progress in Neuro-Psychopharmacology & Biological Psychiatry. 92, p. 339-346 8 p.

*Examining the independent and joint effects of molecular genetic liability and environmental exposures in schizophrenia: results from the EUGEI study*
Guloksuz, S., Pries, L-K., Delespaul, P., Kenis, G., Luykx, J. J., Lin, B. D., Richards, A. L., Akdede, B., Binbay, T., Altinyazar, V., Yalincetin, B., Gumus-Akay, G., Cihan, B., Soygur, H., Ulas, H., Cankurtaran, E. S., Kaymak, S. U., Mihaljevic, M. M., Petrovic, S. A., Mirjanic, T. & 31 others, Bernardo, M., Cabrera, B., Bobes, J., Saiz, P. A., Paz Garcia-Portilla, M., Sanjuan, J., Aguilar, E. J., Luis Santos, J., Jimenez-Lopez, E., Arrojo, M., Carracedo, A., Lopez, G., Gonzalez-Penas, J., Parellada, M., Maric, N. P., Atbasoglu, C., Ucok, A., Alptekin, K., Saka, M. C., Arango, C., O'Donovan, M., Rutten, B. P. F., van Os, J., Alizadeh, B. Z., van Amelsvoort, T., van Beveren, N. J., Bruggeman, R., Cahn, W., Myin-Germeys, I., van Winkel, R. & Genetic Risk and Outcome of Psychosis (GROUP) Investigators,
Jun 2019, In : World Psychiatry. 18, 2, p. 173-182 10 p.

*Changes in physical and psychiatric health after a multidisciplinary lifestyle enhancing treatment for inpatients with severe mental illness: The MULTI study I*
Deenik, J., Tenback, D. E., Tak, E. C. P. M., Rutters, F., Hendriksen, I. J. M. & van Harten, P. N.,
Feb 2019, In : Schizophrenia Research. 204, p. 360-367 8 p.

The impact of adverse childhood experiences on EMG reactivity: A proof of concept study Marsman, A., Luijcks, R., Vossen, C., van Os, J. & Lousberg, R.,
9 May 2019, In : PLOS ONE. 14, 5, 14 p., 0216657.

Measuring within-day cognitive performance using the experience sampling method: A pilot study in a healthy population
Verhagen, S. J. W., Daniëls, N. E. M., Bartels, S. L., Tans, S., Borkelmans, K. W. H., de Vugt, M. E. & Delespaul, P. A. E. G.,
2019, In : PLOS ONE. 14, 12, p. e0226409

## TRANSLATIONAL NEUROSCIENCE

*Confocal Raman spectroscopy: Evaluation of a non-invasive technique for the detection of topically applied ketorolac tromethamine in vitro and in vivo*
Bertens, C. J. F., Zhang, S., Erckens, R. J., van den Biggelaar, F. J. H. M., Berendschot, T. T. J. M., Webers, C. A. B., Nuijts, R. M. M. A. & Gijs, M.,
30 Oct 2019, In : International Journal of Pharmaceutics. 570, 9 p., 118641.

*DNA methyltransferase isoforms expression in the temporal lobe of epilepsy patients with a history of febrile seizures*
de Nijs, L., Choe, K., Steinbusch, H., Schijns, O. E. M. G., Dings, J., van den Hove, D. L. A., Rutten, B. P. F. & Hoogland, G.,
19 Aug 2019, In : Clinical epigenetics. 11, 1, 14 p., 118.

*Characterization of the thymus in Lrp4 myasthenia gravis: Four cases*
Koneczny, I., Rennspiess, D., Marcuse, F., Dankerlui, N., Hamid, M. A., Mane-Damas, M., Maessen, J., Van Schil, P., Saxena, A., Zisimopoulou, P., Lazaridis, K., Woodhall, M., Karagiorgou, K., Tzartos, J., Tzartos, S., De Baets, M. H., Molenaar, P. C., Marx, A., zur Hausen, A., Losen, M. & 1 others, Martinez-Martinez, P.,
Jan 2019, In : Autoimmunity Reviews. 18, 1, p. 50-55 6 p.

*Alzheimer's disease-associated (hydroxy)methylomic changes in the brain and blood*
Lardenoije, R., Roubroeks, J. A. Y., Pishva, E., Leber, M., Wagner, H., Iatrou, A., Smith, A. R., Smith, R. G., Eijssen, L. M. T., Kleineidam, L., Kawalia, A., Hoffmann, P., Luck, T., Riedel-Heller, S., Jessen, F., Maier, W., Wagner, M., Hurlemann, R., Kenis, G., Ali, M. & 9 others, del Sol, A., Mastroeni, D., Delvaux, E., Coleman, P. D., Mill, J., Rutten, B. P. F., Lunnon, K., Ramirez, A. & van den Hove, D. L. A.,
27 Nov 2019, In : Clinical epigenetics. 11, 1, 15 p., 164.

*Inhibition of Experimental Tinnitus With High Frequency Stimulation of the Rat Medial Geniculate Body*
van Zwieten, G., Janssen, M. L. F., Smit, J. V., Janssen, A. M. L., Roet, M., Jahanshahi, A., Stokroos, R. J. & Temel, Y.,
Jun 2019, In : Neuromodulation. 22, 4, p. 416-424 9 p.



# PHD THESES 2019

| Last name | Initials | Theses defence | Promotor(s) | Copromotor(s) | Title Theses |
|---|---|---|---|---|---|
| Albella Anton | R. | 16–09–2019 | Prof. Dr. D. Gazollo<br>Prof. Dr. L. Zimmermann<br>Prof. Dr. J. Vles | Dr. D. Gavilanes | *Cardiac Surgery Biochemical Monitoring in Congenital Heart Diseases Infants* |
| Ali | M. | 30–08–2019 | Prof. Dr. J. Kleinjans | Dr. D. van den Hove<br>Dr. E. Pishva | *Integrative network-based approaches for modeling Human disease* |
| Argyrousi | E. | 21–02–2019 | Prof. Dr. J. Prickaerts | Prof. Dr. O. Arancio (Columbia, NY) | *Dissecting the role of cyclic nucleotides in memory processes* |
| Banning | L. | 20–12–2019 | Prof. Dr. F. Verhey | Dr. P. Aalten<br>Dr. I.Ramaekers | *Neuropsychiatric symptoms in Alzheimer's Disease; Associations with biomarkers* |
| Berk | L. | 22–03–2019 | Prof. Dr. J. van Os<br>Prof. Dr. M. de Vugt | Dr. M.P.J. van Boxtel | *MINDFULNESS AND AGING: Exploring Mechanisms and Interventions* |
| Brouwer | B. | 12–12–2019 | Prof. Dr. C. Faber | Dr. I. Merkies<br>Dr. J. Hoeijmakers | *Painful Small Fiber Neuropathy; Symptoms, assessments and interventions* |
| Collet | J. | 19–12–2019 | Prof. Dr. M. de Vugt<br>Prof. Dr. J. Schols<br>Prof. Dr. F. Verhey | | *Specific Care on the Interface of Mental Health and Nursing home 'SpeCIMeN'* |
| Crivelli | S. | 14–11–2019 | Prof. Dr. P. Martinez<br>Prof. Dr. E. de Vries (VU) | Dr. M. Losen<br>Dr. M. Mulder (R'dam) | *Sphingolipid metabolism in the pathophysiology and treatment of Alzheimer's disease* |
| de Greef | B. | 15–03–2019 | Prof. Dr. C. Faber | Dr. I. Merkies<br>Dr. J. Hoeijmakers | *Small fiber neuropathy: from underlying conditions to treatment* |
| Debruyne | J. | 28–11–2019 | Prof. Dr. B. Kremer<br>Prof. Dr. Ir. T. Francart (Leuven) | Dr. Ir. J. Brokx | *Cochlear implantation in adults with early-onset deafness* |
| Deenik | J. | 22–05–2019 | Prof. Dr. P. Harten | Dr. D. Tenback (CTP Veldzicht)<br>Dr. I. Hendriksen (Living Active) | *Thinking inside the box: Changing lifestyle to improve the health status of inpatients with severe mental illness* |
| DeVocht | E. | 07–03–2019 | Prof. Dr. H. Kingma | Dr. E. George | *Combining a cochlear implant and a hearing aid in opposite ears: The best of both worlds* |
| Dickman | M. | 12–04–2019 | Prof. Dr. R. Nuijts | Dr. T. Berendschot<br>Dr. F. van den Biggelaar | *Practice patterns and outcomes of corneal transplantation* |
| Draak | T. | 21–06–2019 | Prof. Dr. C. Faber | Dr. I. Merkies | *Peripheral Neuropathy outcome measures Standardisation (PeriNomS) study part 3: Capturing the patient's voice* |
| Durand | G. | 05–09–2019 | Prof. Dr. B. Rutten | Dr. J. Lobbestael | *The adaptive side of psychopathy. Investigating adaptive characteristics associated with the psychopathic personality* |

| Last name | Initials | Theses defence | Promotor(s) | Copromotor(s) | Title Theses |
|---|---|---|---|---|---|
| Elshout | M. | 16–05–2019 | Prof. Dr. C. Webers | Dr. J. Schouten (CWZ Nijmegen) | *Neovascular Age-Related Macular Degeneration in the Era of Value-Based Health Care* |
| Eerd van | M. | 17–01–2019 | Prof. Dr. van Kleef | Dr. J. Patijn<br>Dr. M. Sommer | *Diagnosis and Interventional Pain Treatment of Cervical Facet Joint Pain* |
| Geurts | J. | 11–12–2019 | Prof. Dr. C. Dirksen<br>Prof. Dr. M. van Kleef | Dr. P. Willems | *Chronic Pain; Impact of Chronic Pain on a Societal, Personal, and Treatment Level* |
| Gil Martinez | A. | 24–06–2019 | Prof. Dr. H. Steinbusch<br>Prof. Dr. Marina-Trinidad Herrero Ezquerro (University of Murcia) | | *Neuroprotection in neurodegenerative processes associated with Parkinsonism and aging. Correlation between dopaminergic neuronal death and glial activation* |
| Gulpers | B. | 26–06–2019 | Prof. Dr. F. Verhey<br>Prof. Dr. R. Oude Voshaar | Dr. S. Kohler | *Anxiety in older adults; Correlates, comorbidities and prognosis with lifespan perspectives* |
| Gussenhoven | R. | 16–12–2019 | Prof. Dr. B. Kramer<br>Prof. Dr. L. Zimmermann | Dr. T. Wolfs | *Antenatal inflammatory insults and preterm brain injury: Pathophysiology and therapeutic strategies* |
| Henatsch | D. | 06–09–2019 | Prof. Dr. R. Stokroos (UMCUtrecht) | Dr. J. Briede | *Honey: A Novel Treatment in Chronic Ear Infections* |
| Janssen | E. | 10–01–2019 | Prof. Dr. F. Verhey<br>Prof. Dr. M. de Vugt | Dr. M. Schram | *Depression in the elderly: focus on high risk groups* |
| Janssen | N. | 15–11–2019 | Prof. Dr. F. Verhey<br>Prof. Dr. mr. S. Evers | Dr. R. Handels | *Patterns and pathways. Indicators for potential improvements of dementia care* |
| Kallewaard | J. | 06–11–2019 | Prof. Dr. M. van Kleef | Prof. Dr. H. van Santbrink<br>Dr. P. Willems | *Diagnosis and minimally invasive treatment of chronic discogenic low back pain* |
| Khamar Mayur Raksha | P. | 15–11–2019 | Prof. Dr. R. Nuijts | Dr. R. Shetty (Bangalore) | *Clinical, Molecular and Biomechanical outcomes of SMILE (small incision lenticule extraction) and other refractive surgery techniques* |
| Kicken | C. | 17–01–2019 | Prof. Dr. W. Buhre | Dr. B. de Laat<br>Dr. M. Lance (Qatar) | *Extreme blood coagulation; investigating the influence of physiological extremes on thrombin generation and platelet activation* |
| Koizumi | T. | 28–08–2019 | Prof. Dr. H. Steinbusch<br>Prof. Dr. T. Mizuno (Japan) | Dr. S. Foulquier | *Genetic and neuroinflammatory components of familial and sporadic cerebral Small Vessel Disease* |
| Kruythoff | P. | 29–03–2019 | Prof. Dr. A. de Grip<br>Prof. Dr. T. van Amelsvoort | Dr. S. Schinkel (Sigma Research) | *Loopbaanadvisering een vak apart: op weg naar een professie?* |
| Maatman | R. | 05–08–2019 | Prof. Dr. M. van Kleef | Dr. R. Roumen<br>Dr. M. Scheltinga (MMC Eindhoven)<br>Dr. S. van Kuijk | *Anterior cutaneous nerve entrapment syndrome (acnes): an analysis of various subtypes and alternative treatment modalities* |
| Maino | P. | 06–12–2019 | Prof. Dr. E. Joosten<br>Prof. Dr. M. van Kleef | | *Implantable Intrathecal Drug Delivery in Treatment of Chronic Intractable Pain and Spasticity11/8/2019 Improvement of Safety and the Use of Imaging techniques* |
| Mansueto | G. | 26–11–2019 | Prof. Dr. K. Schruers | Prof. Dr. F. Cosci (Florence)<br>Prof. Dr. R. van Winkel (Leuven) | *Childhood adversities and Psychosis: investigation of the potential aetio-pathogenetic mechanisms* |
| Melles | R. | 20–09–2019 | Prof. Dr. M. Peters | Dr. M. ter Kuile (LUMC)<br>Dr. M. Dewitte | *Vaginal penetration: pain or pleasure? The role of fear and sexual arousal* |
| Meuwissen | K. | 05–12–2019 | Prof. Dr. E. Joosten<br>Prof. Dr. M. van Kleef | | *Burst Spinal Cord Stimulation in a rat Model of Chronic Neuropathic Pain: Spinal and Suprspinal Mechanisms* |
| Muller-Ehrenberg | L. | 05–12–2019 | Prof. Dr. F. Verhey<br>Prof. Dr. A. Sack | Dr. H. Jacobs | *Episodic memory in ageing and AD: a possible target for electrical stimulation?* |
| Nigim | F. | 20–12–2019 | Prof. Dr. Y. Temel<br>Prof. Dr. S. Rabkin (Harvard) | Dr. H. Wakimoto (Harvard)<br>Dr. L. Ackermans | *Glioblastoma and Meningioma Biology, Targeted Therapy and Oncolytic Virus Therapy* |
| Ool van | S. | 09–01–2019 | Prof. Dr. A. Aldenkamp | Dr. J. Hendriksen | *Diagnostic and neuropsychiatric considerations in epilepsy and intellectual disability; Psychological perspectives.* |
| Pahuja | N. | 15–11–2019 | Prof. Dr. R. Nuijts | Dr. R. Shetty (Bangalore) | *Etiopathogenesis, advanced imaging and treatment outcomes in Asian Indians with keratoconus* |
| Ponnamperuma | T. | 18–04–2019 | Prof. Dr. M. de Vries | Dr. N. Nicolson | *Mental Health Problems in Sri Lankan Adolescents Exposed to the Tsunami and Other Traumatic Events* |
| Pruppers | M. | 16–10–2019 | Prof. Dr. C. Faber<br>Prof. Dr. N. Notermans (UU)<br>Dr. I. Merkies (ius promovendi) | | *Peripheral Neuropathies: Standardizing Functional Assessment* |
| Snoeijen-Schouwenaars | F. | 09–10–2019 | Prof. Dr. A. Aldenkamp | Dr. H. Schelhaas (SEIN Zwolle)<br>Dr. J. Hendriksen | *Diagnostic, neuropsychiatric and therapeutic considerations in epilepsy and intellectual disability - medical perspectives -* |
| Townend | G. | 07–04–2019 | Prof. Dr. L. Curfs | Dr. P. Marschik (Graz, Austria) | *Rett Syndrome: Recognising the Communication Challenges, Needs and Potential Of Individuals Living with a Rare Disease* |
| Zong | S. | 06–11–2019 | Prof. Dr. P. Martinez | Dr. M. Losen<br>Dr. R. Rouhl | *Autoantibodies in disorders of the brain: expanding the spectrum* |

**Contact information**

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