ANNUAL REPORT 2018

SCHOOL FOR MENTAL HEALTH AND NEUROSCIENCE

Maastricht University
Faculty of Health, Medicine and Life Sciences

MHeNS

Maastricht University | Maastricht UMC+

CONTENT

PREFACE
DAVID LINDEN

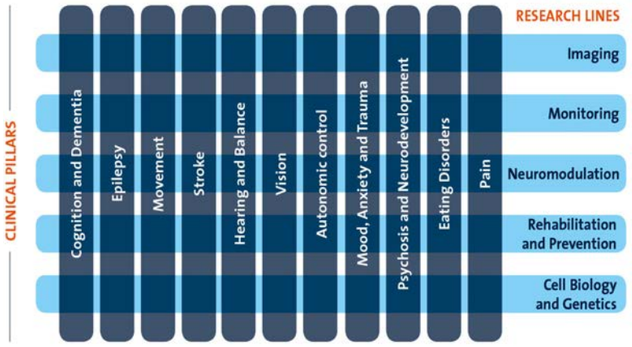
Photography: Maastricht UMC

Prof. David Linden
Scientific Director

School for Mental Health
and Neuroscience

In 2018 we implemented several strategic initiatives that had been conceived in previous years. We had the official opening of the Centre for Integrative Neuroscience (CIN), in which we join forces with the Faculty of Psychology and Neuroscience (FPN) and which is co-directed by Professor Bart Rutten and Professor Alexander Sack from FPN. The CIN currently hosts five joint PhD students, and it was exciting to hear about their cross-disciplinary work at the regular CIN seminars. Another innovative initiative of the CIN was a joint seminar with the behavioural economics group of the School of Business and Economics (SBE), which will join the CIN in 2019.

2018 also saw the launch of the Brain and Nerve Centre (BNC) of the Maastricht University Medical Centre, through which we bundle our clinical research activities. The BNC, led by neurologist Professor Robert van Oostenbrugge, brings together the top-level care in psychiatry and clinical neurosciences (see the eight vertical pillars on the left of the figure below) at the Academic Hospital and our clinical partners and links it with our research strengths in the cross-cutting domains of imaging, monitoring, neuromodulation, rehabilitation and cell biology and genetics. Within the MHeNs matrix this work is extended to the clinical pillars of "Hearing and Balance" (Department of Otorhinolaryngology), "Vision" (Department of Ophthalmology and University Eye Clinic) and "Autonomic control" (Department of Urology).



We also started a series of School-wide seminars, partly in collaboration with FPN and the Maastricht Brain Imaging Centre (MBIC). In January 2018 we organised an event on the auditory system that brought together researchers from MHeNs and MBIC and explored the translational opportunities of research in areas such as vestibular implants and tinnitus. We also started the two-monthly MHeNs lectures with external speakers. In March, Dr Thomas Lancaster from Cardiff University's Neuroscience and Mental Health Research Institute presented neuroimaging and genetic research into risk and resilience in psychiatry. This was followed by a talk on cellular models of rare genetic risk variants for neurodevelopmental disorders by Dr Yasir Syed, also from Cardiff. These rare genetic risk variants, particularly copy number variants such as the 22q11.2 deletion, are a central topic of research within our division 2, and also a field in which MUMC provides national clinical services (coordinated by Professor Therese van Amelsvoort). It was thus very fitting to have another MHeNs lecture on these highly penetrant risk variants, this time more from a clinical perspective, by Dr Erik Boot, an expert on learning disabilities and movement disorders at 's Heeren Loo who also has an academic affiliation with us. The topic of neurodevelopmental disorders was concluded by Professor Grainne McAlonan from King's College London who told us about the exciting developments in neonatal neuroimaging.

To further attest to the success of our educational programme, we had a record number of PhD defences last year - 52 in total. The overview on our website (https://mhens.mumc.maastrichtuniversity.nl/) shows the range of clinical and translational topics covered by our excellent PhD students. A particular success was the award of two cum laude PhDs on the same day to two clinical researchers from the vestibular implant programme of the Department of Otorhinolaryngology, Dr Raymond van de Berg and Dr Nils Guinand. Further on in the academic career path, we had three inaugural lectures in 2018. Professor Marjolein de Vugt was installed as Professor of Psychosocial Interventions in Dementia with a lecture entitled "Goldilocks chair: het gulden midden", Professor Pilar Martinez presented her work on "Lipids and antibodies in neurological and psychiatric diseases" related to her chair in Neuro-inflammation of Neuropsychiatric Disorders, and Professor Jos Prickaerts, chair in Experimental Neurpsychopharmacology discussed "Pharmacology in Translation: Where do we go from here?"

Our international activities have continued through wide-reaching collaborations in research and education. The flagship EURON graduate school was renewed with seven partners in Germany, Belgium, France and Luxemburg and continued with its highly acclaimed annual Human Neuroanatomy course and the PhD Days, which were held at EURON partner University Catholique de Louvain in Brussels. Thus, 2018 was also a very successful inaugural year for Dr Gunter Kenis at the helm of EURON.

MHeNs is very committed to engagement with the public and research activities that benefit the regional and wider communities. A prime example is the Mijnbreincoach project that was launched by the Alzheimer's Centrum Limburg at the museum in Kerkrade, in collaboration with the Province of Limburg. The Mijnbreincoach app (www.mijnbreincoach.eu) has already been used by thousands of people across the Netherlands who want to find out more about lifestyle changes to prevent dementia. This research group also opened the Amsterdam Stock Exchange on 26 November in order to raise awareness of dementia risk and prevention.

Researchers from division 2 are centrally involved in the first @ ease centre in the Netherlands in Maastricht, opened by the Wethouder of Maastricht on March 14, which was also covered by the EenVandaag television program. You will find many more examples of public engagement and research for patient benefit on the pages of this report.

This year's research day had the topic of "Career perspectives in and outside academia". Several alumni and the Mayor of Maastricht highlighted the need to think outside the box when planning one's career – which may then lead to unexpected new opportunities. Our cross-disciplinary research and education programme is designed to prepare our future PhDs for such varied career opportunities. I hope that when perusing this Annual Report and the updates from our divisions and research lines you will get a good impression of this interdisciplinary atmosphere and that you will share our excitement about the opportunities of translational research into mechanisms, treatment and prevention in mental health and neuroscience.

DIVISION I

Cognitive Neuropsychiatry & Clinical Neuroscience

Division Leader:
Prof. F. Verhey

Deputies:
Prof. R. Van Oostenbrugge
Prof. C. Van Heugten

SUMMARY

The Division Cognitive Neuropsychiatry & Clinical Neurosciences (CNP&CNS) performs fundamental and applied clinical research on neuropsychiatric, neurocognitive and other neurological disorders. The name CNP&CNS 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 treatment, and to improve the quality of life of people affected by these disorders.

The research performed in 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 Psychology, Neurology, Radiology, Neurophysiology, Otorhinolaryngology, Internal Medicine and Family Medicine. The division consisted in 2018 of 35 staff members, covering in total 12,1 FTE from 8 MUMC departments. In 2018, the research output was substantial, with 26 PhD theies defences, 284 scientific WI-1 publications and an earning power of € 2.537.000.

With respect to the core topics, the focus is upon neurodegeneration of the central nervous system, more specifically Alzheimer's disease and its prodromal phases, other dementias, Vascular Cognitive Impairment, other related cognitive disorders, Parkinson's disease and other movement disorders, peripheral nervous system disease such as small fiber neuropathy, acquired brain damage such as stroke or traumatic brain injuries, MS and epilepsy.

Traditionally, these disorders have often been studied as separate disease entities (e.g., Alzheimer's disease, Parkinson's disease), thereby reducing complexity but also ignoring the synergistic interaction that exists between different pathologies. Our vision is that a broader approach is needed to really understand the underpinnings of these disorders , taking into account genetics, various neuropathological dimensions, but also the aging perspective, and lifestyle factors (like physical and mental activities and nutrition), including vascular risk factor,s interacting with genetic and age-related processes.

In 2018 the institution of the MUMC's Brain and Nerve Center (BNC) (Hersen + Zenuw Centrum) has further strengthened the integrative and multidisciplinary focus of our division. Most of our research is being conducted in a multi-disciplinary way, with input from the departments of Psychiatry & Neuropsychology, Clinical Neurology, Radiology, Neurophysiology, Otorhinolaryngology and Health, Ethics and Society. There is a strong integration of patient care facilities and clinical research into Centers, such as the Alzheimer Centrum Limburg, Center for Movement Disorders, Brain Injury Center and the MUMC Stroke Center. Therefore, we have strong patient care facilities at our own disposal, providing an excellent infrastructure for clinical research.

Hereunder, the main characteristics of the division are being described, and some examples are being mentioned of activities that typically illustrate the integrative nature of our approach

- Life-long perspective with various long term cohort data, studying the complex interplay between vascular risk factors, lifestyle, environment and age-related changes in the brain. A strong infrastructure is created with close links to the Maastricht Study, the Maastricht Aging Study, and the Biobank of the Alzheimer Centrum Limburg. Dr Sebastian Koehler was installed as a member of the management board of the Maastricht Study. Furthermore, preparations have been made to extend the follow-up of the Maastricht Aging Study up to 25 years, which creates a unique oppertunity for studying cognitive decline from a multidimensional aging perspective.
- Covering the full spectrum from public health approach to biomarker research and neurorehabilitation and caregiver research. In 2018 the Alzheimer Centrum Limburg held an extensive public campaign, which was supported by the province of Limburg, in order to promote Brain Health to prevent dementia. In May we had the installation of Prof Marjolein de Vugt with her inaugural lecture.
- Our division can build on a firm infrastructure with large datasets, with biobanks with DNA, CSF and imaging, combined with data on cognitive and ADL functioning and neuropsychiatric disorders. In 2018 further preparations were being made for a new collaborative initiative in Limburg called BReIN (Brightlands Research Infrastructure for NeuroHealth). This Kennis-As project is supported by the province of Limburg, and will make use of and expand this infrastructure.
- In 2018 we further built our collaboration with the Institute of Data Science, in order to better study these complex interrelationships. One shared PhD was initiated.
- Extensive collaborative networks, both locally with other MHeNs divisions, other Research Schools and on a national and international level. In 2018 we reinitiated our collaboration with division 3, with two shared PhDs and three-monthly scientific meetings.

PRECODE

Prevalence REcognition and Care pathways in young Onset Dementia

2018 marked the start of the PRECODE study (Prevalence REcognition and Care pathways in young Onset Dementia). The PRECODE study is a collaboration between Alzheimer Centrum Limburg (Maastricht University) and the Alzheimer centers of Radboudumc, Amsterdam UMC, Erasmus MC, Alzheimer Nederland, and NIVEL. PRECODE is funded by Gieskes Strijbis Fonds, Alzheimer Nederland, and Stichting Kenniscentrum Dementie op Jonge Leeftijd. Prof. Marjolein de Vugt (Alzheimer Centrum Limburg) is the project leader. Dr. Kirsten Peetoom (Alzheimer Centrum Limburg) coordinates the project together with Dr. Christian Bakker (Alzheimer Centrum Radboudumc).

Why this study?

It is estimated that 12.000-15.000 people have young-onset dementia in the Netherlands. Young-onset dementia denotes dementia with a symptom-onset before the age of 65. Young-onset dementia has profound implications since it affects people in an active life phase. It also has a great impact on the family and financial problems may arise because of job loss.
For people with young-onset dementia, the availability of specialized care is crucial but limited. As a result, they often have to make use of facilities for elderly people with dementia. In order to develop adequate appropriate help for this specific target group, it is essential to have accurate data on how often and which forms of dementia occur at a young age in the Netherlands. Current estimates are based on outdated data. In addition, approximately 45% receive a wrong diagnosis at first, such as depression or burnout. Next, it takes on average of 4.4 years for a dementia diagnosis, while this is 2.8 years in older people. It is therefore necessary to improve the recognition of young-onset dementia in primary care, gain insight into the current access to healthcare after diagnosis and to improve support.

Study objectives

PRECODE is a 4-year study and aims to (1) obtain insight in the prevalence of young-onset dementia in the Netherlands, (2) to improve recognition of young-onset dementia to achieve a timely diagnosis, and (3) to obtain insight in access to care to improve care provision.

Work packages

In addition to coordination, monitoring, quality control of the project and setting up an expert panel (work package 1; Alzheimer Centrum Limburg), the PRECODE study consists of several work packages:

Work Package 2 (Alzheimer Centrum Radboudumc) consists of a Delphi study to reach international consensus on the terminology and definition of dementia at a young age. This is needed since different terms are currently used to indicate the target group and there is also a difference in which disorders are seen as the cause of young-onset dementia. Work package 3 (Alzheimer Center Limburg) consists of a systematic literature review and meta-analysis to gain insight in the international prevalence and incidence of young-onset dementia. Scientific articles are included when population-based prevalence or incidence rates are provided for people under 65 years of age. The literature search yielded over 10.000 articles, which are independently screened by two researchers. The results of eligible studies will be pooled when possible to estimate the incidence and prevalence of young-onset dementia. Where possible, a distinction will be made between men and women, as well as between different ethnic backgrounds. The results of work package 2 and 3 will be presented during the Alzheimer Europe conference in October 2019.

To obtain insight in the prevalence of young-onset dementia in the Netherlands, work package 4 (Alzheimer centrum Erasmus MC) aims to estimate the prevalence of dementia at a young age in a number of defined geographical areas in the Netherlands. In these regions, all general practices, memory clinics, psychiatry and neurology departments of hospitals, nursing homes, home care organizations, and mental health organizations will be contacted to identify people with the diagnosis young-onset dementia. In addition, work package 5 (Alzheimer Centrum Amsterdam) aims to develop an online database for young-onset dementia in order to arrive at a description of the characteristics of these people within memory clinics. The database is set up in collaboration with the Dutch Memory Clinic Network (NGN) and regular exchange with Alzheimer Nederland and NIVEL ensures that the data can eventually be linked to the Dementia Care Register. Pilot testing of the database will start in Fall 2019.

Work package 6 (Alzheimer Center Limburg) focuses on obtaining insight in the early recognition signals of young-onset dementia in general practice and access to care after diagnosis. We will collaborate with the department of Family Medicine (CAPHRI, FHML) to analyze early signals by means of the Research Network Family Medicine Maastricht (RNFM) database. This work package will lead to an update of the early signal list of young-onset dementia for general practitioners. This work package is in preparation.

The final work package (Alzheimer Centrum Radboudumc) focuses on the dissemination of project results.

The multidisciplinary research team in Maastricht consists of Prof. Marjolein de Vugt, Prof. Frans Verhey, Dr. Sebastian Köhler, Dr. Kirsten Peetoom, and PhD student Stevie Hendriks.

More information:
www.precode-project.nl
kirsten.peetoom@maastrichtuniversity.nl

PRECODE

INTERDISCIPLINARY NETWORK FOR DEMENTIA

INDUCT/DISTINCT

INDUCT in Salamanca, Spain for the first INDUCT Summer School.

Building on success: Innovative Training Network DISTINCT follows INDUCT
In 2015, European researchers from the INTERDEM network formed a consortium to answer to the call for a H2020 Marie Skłodowska Curie Actions- Innovative Training Network (ITN) grant. Involving multi-disciplinary experts in the field of dementia from the UK, Sweden, the Netherlands, Belgium, Czech Republic, and Spain, as well as collaborating with international and inter-sectorial partners, their efforts were rewarded.

With a successful rating score of 99,2%, the 'Interdisciplinary Network for Dementia Using Current Technology'(INDUCT), received 3.888.600 euros to conduct the proposed projects and provide fifteen Early Stage Researchers (ESRs) with extensive training and education. Professors Marjolein de Vugt and Frans Verhey are Maastricht University's INDUCT project leads. During the two-day kick-off event in London in May of 2016, they selected two ESRs to conduct their PhD projects as a part of MHeNs: Hannah Christie from Belgium and Sara Laureen Bartels from Germany. Over the past three years, INDUCT has offered Hannah, Sara, and the thirteen other ESRs the exciting opportunity to develop a deeper understanding of the nature of dementia and needs in relation to technology use. Furthermore, the ITN equipped the ESRs with skills needed to work in academia, industry, or policy making. But what exactly does such a training consist of?

Like other PhD students at Maastricht University, Hannah and Sara followed courses offered locally, such as the self-management course or classes at the language centre. In addition, the Maastricht-based INDUCT training managers, Dr. Inge Klinkenberg and Dr. Fania Dassen, organized five INDUCT schools. These schools were held across Europe and provided courses on dementia care-specific skills, such as palliative care, as well as transferable skills, such as grant writing or communicating with journalists. The INDUCT schools were partially open to INTERDEM Academy members and thus facilitated networking with other academics and non-academic partners.

While in Maastricht, Hannah and Sara focused on their own individual research projects. Hannah explored the implementation of eHealth interventions for caregivers of people with dementia through an EU-regional project, while Sara investigated the use of technology (such as the experience sampling method, or 'ESM') to monitor daily life and improve health outcomes for older adults with and without dementia. Additionally, both PhD students completed two three-month secondments, where they spent several months at another INDUCT partner. Hannah visited the Mindtech at the University of Nottingham (Nottingham, UK), as well as Betawerk (Heerlen, the Netherlands), a Dutch company that can help translate research projects into digital concepts and strategies (Myinlife https://www.myinlife.nl/nl; MijnBreincoach https://www.mijnbreincoach.eu). Working at Betawerk gave her insights into the development of business models to implement eHealth interventions. At the same time, Sara explored the world of industry through her secondment at EuMediaNet (Maastricht, NL) and observed the process of implementing technological solutions in Dutch care homes. Spending three months at Karolinska Institutet in Stockholm (SE), she developed an understanding of how occupational therapists work in the field of dementia and everyday technology.

In September 2019, Hannah and Sara will start the final year of their PhD projects. They feel equipped to prospectively work in various settings, including academia, policy making, industry, and clinical settings. Happily, the success story of INDUCT will now be continued, as the INDUCT consortium was successful in once again acquiring funding for an ITN. In October 2019, two new ESRs will start within DISTINCT: 'Dementia: Intersectorial Strategy for Training and Innovation Network for Current Technology'. One ESR (Gulnaz Atefi) will work on technology-assisted Acceptance and Commitment Therapy in daily life for caregivers of people with dementia, while the second ESR (vacancy) will work on improving social participation in dementia with the Geographic Information System-based intervention 'Viamigo' Hannah and Sara are very much looking forward to meeting their DISTINCT successors and guiding them the many new and exciting experiences associated with Maastricht and starting a PhD with MHeNs.

DISTINCT
dementia: intersectorial strategy for training and innovation network for current technology

INDUCT
interdisciplinary network for dementia using current technology

RESEARCH LINES DIVISION I

1. NEURODEGENERATIVE DISORDERS	1.1 MECHANISMS, EARLY DIAGNOSIS AND BIOMARKERS
COORDINATOR:	Prof. F. Verhey
RESEARCH STAFF:	Dr. P. Aalten, Dr. M. Van Boxtel, Prof. R. Van Oostenbrugge, Prof. P. Hofman, Prof. W. Backes, Dr. J. Jansen, Dr. H. Jacobs, Dr. I. Ramakers, Dr. A. Leentjens, Dr. A. Duits, Dr. E. Gronenschild, Dr. S. Köhler, Dr. PJ. Visser, Prof. F. Verhey, Prof. M de Vugt, Prof. R. Ponds, Dr. R. Handels, Dr. S. Vos.
POSTDOCS:	W. Jansen, A. Moonen.
PHD-STUDENTS:	S. Schievink, T. Van der Voort, B. Reijs, E. Zhang, C. Mestres, W. Freeze, J Riphagen, B. Gulpers, L. Müller-Ehrenberg, N. Priovoulos, I. Bos, I. Verheggen, E. Douven, A. Gruters, L. Banning, L. Pagen, R. van Hooren.
EXTERNAL COLLABORATORS:	European Alzheimer's Disease Consortium, Parelsnoer Initiative (PSI) , EMIFAD, ROADMAP, VPH, Neurodegenerative diseases consortium.
FOCUS OF RESEARCH:	Translational research into the early diagnosis and pathophysiology of pathological ageing. A large-scale national biobank, coordinated by MUMC+ and the Erasmus MC, formed the infrastructure for translational research into the early diagnosis of pathological ageing (PSI Neurodegenerative disorders, coordinated by Dr. P. Aalten). Novel diagnostic technology for the early detection of Alzheimer's disease will be examined and evaluated in terms of Health Technology Assessment, i.e., with respect to its added value to existing diagnostic procedures Leiden-Alzheimer Research Nederland Project (LeARN, CTMM).

Description

This research line focuses on biomedical research on mechanisms of cognitive disorders, notably (prodromal and clinical stages of) Alzheimer's disease and other cognitive disorders. Research activities are integrated with patient care facilities in the Alzheimer Centre Limburg (PIs Prof. Dr.F. Verhey, Prof. M. de Vugt); and there is a close collaboration with the Stroke centre (PI Prof. R. Van Oostenbrugge) and Centre for Motor Disorders (PIs Prof. Y. Temel, Dr. A. Leentjens). In 2018, efforts have been made to collaborate between these research centers, and to strengthen their common basis.

We continued in 2018 the National Parelsnoer Initiative (PIs: Dr. P. Aalten, Dr. I . Ramakers), which is a collaboration of 8 Dutch UMCs on several chronic diseases. Maastricht University/ Alzheimer Centre Limburg, together with Erasmus MC (co-coordinator since 2017), is national coordinator of the Pearl "Neurodegenerative diseases", focusing on the early diagnosis and prognosis of Alzheimer's disease.

The European IMI -ROADMAP project started at the end of 2016 (PI: Dr. P.J. Visser; coworkers Dr. S. Vos, O. Janssen, Dr. R. Handels). The aim of the project is to model the progression of Alzheimer's disease across the full disease spectrum and to lay the foundation for a European-wide Real World Evidence (RWE) platform on AD. RWE and Randomised Controlled Trial (RCT) data sources relevant to Alzheimer's disease will be identified, extracted, harmonised, integrated and analysed. Examples of data sources are cohort studies, national registries, trial placebo data, health care registries, electronic medical records and data from general practitioners. Key outcome measures across stakeholder groups will be identified, and guidelines for combining different RWE data sources in AD will be developed. Maastricht is leading a work package on data collection and harmonisation and is involved in several data analyses.
The SNAP-MCI project is a personal grant from ZonMw Memorable Deltaplan Dementia (PI: Dr. S. Vos). The aim of this study is to investigate the underlying mechanisms of individuals with mild cognitive impairment and an atypical Alzheimer's disease biomarker profile, i.e. neuronal injury without amyloid pathology. Existing clinical data, CSF samples and MRI scans were collected from 210 subjects with mild cognitive impairment and cognitively normal individuals from memory clinics in Maastricht, Amsterdam, and Antwerp. We have the first results of targeted CSF proteomics and MRI atrophy and vascular profiles in these subjects.

The Maastricht group also coordinates a worldwide subject-level meta-analysis on the prevalence, risk factors, and clinical correlates of amyloid aggregation in nondemented and demented individuals (PI: Dr. P.J. Visser, coPI Dr. W. Jansen). Several "LOCUS" projects are ongoing (PI: Dr. H. Jacobs), focused on investigating the structural and functional role of specific brainstem nuclei, including the locus coeruleus, for early detection of preclinical Alzheimer's disease. These projects are funded by NWO, Alzheimer Nederland and the Centre for Integrative Neuroscience of Maastricht University. Within these projects, we are collecting longitudinal state-of-the-art MRI methods at ultrahighfield MRI, CSF samples, blood samples and clinical data of healthy persons (20-100 years old) and patients with prodromal Alzheimer's disease. These projects are conducted in close collaboration with the Cognitive Neuroscience department of the Faculty of Psychology and Neuroscience.
Within the "MONA" project, funded by the Deutsche Forschungsgemeinschaft and NWO (PI: Dr. H. Jacobs), we investigate the potential of noninvasive brain stimulation methods (tDCS, tRNS, tVNS) to alter functional brain networks related to memory functioning in healthy older individuals and in patients with prodromal Alzheimer's disease. These projects run at standard 3T and ultrahighfield (7T) MRI scanners and are conducted in close collaboration with the Cognitive Neuroscience department of the Faculty of Psychology and Neuroscience and Massachusetts General Hospital (Boston).
For the INPAD project (PI: Dr. I. Ramakers) that just started, we aim to innovate and improve neuropsychological assessment in early dementia. The objectives are (1) to increase efficiency by the development of a webbased, computerized, cost-effective and user-friendly neuropsychological assessment analysis tool, and (2) to innovate patient communication by the development of a patient and clinicianfriendly visualization of cognitive test performances.
Collaboration with the Departments of Neurology and Radiology was intensified, which has led to a new study on neurovascular mechanisms of cognitive disorders, and the interaction between vascular and neurodegenerative mechanisms. Dr. H. Jacobs and Prof. W. Backes and Prof. F. Verhey continued their study on bloodbrain barrier (BBB) leakage in dementia (funded by an Alzheimer Nederland award), investigating the contribution of increased bloodbrain barrier permeability to Alzheimer disease pathology and cognitive deficits and developed a new dynamic contrast enhanced MRI scan. This project is conducted in collaboration with the University of Edinburgh and Massachusetts General Hospital (Boston). A new grant NWO Top talent was obtained by Mrs I Verheggen to expand this research line.
A second BBB project (funding NWO/Mozaïek) is ongoing to investigate the role of BBB leakage and microvascular impairment in patients with Vascular Cognitive Impairment and Lacunar Stroke (Prof. R. van Oostenbrugge, Prof. W. Backes, thesis E. Zhang). Further research will be continued using advanced MRI techniques into the neuronal correlates of cognitive decrements in a diabetes cohort in collaboration with The Maastricht Study.

1. NEURODEGENERATIVE DISORDERS :	1.2 NEUROEPIDEMIOLOGY
COORDINATORS:	Dr. S. Köhler, Dr. M. van Boxtel.
RESEARCH STAFF:	Prof. F. Verhey, Prof. W. Backes, Dr. J. Jansen, Prof. R. van Oostenbrugge.
POSTDOCS:	Dr. K. Deckers.
PHD-STUDENTS:	M. Wong, L. Berk, I. Verheggen, A. Geraets, I. Heger.
FOCUS OF RESEARCH:	Insight into the prevention, etiology and treatment of cognitive dysfunction by conducting observational, interventional and implementation research in the general adult population.

Research line staff members are active contributors to De Maastricht Studie (DMS), a study to provide more insight into the prevention, etiology and treatment of type 2 diabetes and other chronic diseases in relation to mental health. DMS is a good example of the integrative approach that we aim for, with multidisciplinary input from staff in the Departments of Psychiatry & Neuropsychology, Neurology, Radiology, Ophthalmology and Otolaryngology. Participation in DMS so far has resulted in PhD theses of Dr. F. van Dooren (diabetes and depression, in collaboration with Tilburg University), Dr. P. Spauwen (cognition in diabetes) and Dr. F. van Bussel (multiparametric imaging of cerebral biomarkers of cognitive deterioration). Current projects focus on the relation between depression, cerebrovascular disease and cognition (A. Geraets) as well as lifestyle in relation to brain health (I. Heger).

The Maastricht Ageing Study (MAAS) is a 12-year observational cohort study with repeated assessments of health, lifestyle, cognitive functions and incident dementia spanning the whole adult age range. It continues to be a major source for new studies into determinants and course of cognitive ageing, including studies on positive affect, hypertension, obesity and cardiovascular disease. MAAS has been added to the 'Cohort Studies of Memory in an International Consortium (COSMIC)' harmonisation project, allowing highpowered analyses of population-based studies into cognitive ageing. In 2017, a new MRIsub study was launched to examine the role of bloodbrain barrier function in successful cognitive aging (I. Verheggen).

The FP7 funded 3-year study into preventive strategies to ameliorate the individual dementia risk in middle aged individuals (InMINDD) has produced an evidence-based and well-validated polyenvironmental risk score to estimate individual potential for dementia risk reduction: the 'Lifestyle for Brain Health (LIBRA)' index. This product was implemented in an ongoing multicentre European intervention study in general practice aimed to reduce the dementia risk in middleaged individuals. Preliminary results have shown that the tool is feasible and offers opportunities to be implemented fur use in the general population. Implementation of InMINDD findings is currently ongoing through funding from the Province of Limburg in the 'MijnBreincoach' project. The aim is to create awareness for factors that influence brain health by a dedicated campaign in Limburg and use of eHealth technology to help people in making and maintaining healthy lifestyle choices.

The results of the NWO/FES programme 'Healthy Cognitive Ageing' aimed at the development of internet-based low-level intervention strategies to support the cognitive ageing process in middle-aged and older adults have been implemented as the eHealth module 'Keep your brain fit!', which has been made available for the general public. Other products of this National collaboration with the universities of Amsterdam (VUmc, UvA) and Nijmegen (RUMC) are available at the consortium portal 'BreinWeb.nl'.

New projects explore the role of mindfulness in cognitive ageing and dementia, both in observational and in intervention studies, in part funded by Alzheimer Nederland (L. Berk).

Finally, members of the Neuroepidemiology group provide methodological support for different projects within MHeNs and MUMC+.

1. NEURODEGENERATIVE DISORDERS:	1.3 PSYCHOSOCIAL INTERVENTIONS AND COGNITIVE REHABILITATION
COORDINATORS:	Prof. C. van Heugten, Prof. M. de Vugt.
RESEARCH STAFF:	Prof. R. Ponds, Dr. M. van Boxtel, Prof. F. Verhey.
POSTDOCS:	Dr. C. Wolfs, Dr F. Dassen, Dr. L. Boots, Dr. J. Millenaar, Dr. A. Stiekema, Dr. M. Veenstra, Dr. B. Lenaert, R. van Knippenberg.
PHD-STUDENTS:	B. Dandachi-Fitzgerald, J. Collet, R. B. ter Mors, A. Dam, L. Kerpershoek, E. Tan, B. Appelhof, J. van Duin, Y. van Os, S. Bartels, H. Christie, A. Gruters, E. Janssen, M. Schichel, L. Berk, J. Bruinsma, D. Verberne, F. Domensino, J. Rauwenhoff, F. Rienacker, B. Nijsse, D. Hellebrekers, A. Gerritsen, S. Hendriks.
EXTERNAL COLLABORATORS:	International Interdem network, Horizon 2020 DRS.AITN2015 INDUCT consortium, JPND Actifcare consortium, JPND Rapsody consortium, ZonMw consortium Restore4stroke, ZonMw Nationaal Programma Gehandicapten Gewoon Bijzonder, regional network of the Limburg Brain Injury Center and the Alzheimer Center Lim-burg, Alzheimer Society, Alzheimer centers, Marie-Curie ITN INDUCT con-sortium.
FOCUS OF RESEARCH:	Psychosocial interventions, cognitive rehabilitation and health service evaluation research. Interventions in cognitive and acquired brain disorders such as acquired brain injury (stroke and traumatic brain injury) and (young onset) dementia. In this research line a strong focus is put on evidence-based cognitive rehabilitation, neuropsychological interventions, psychosocial interventions, caregiver interventions, and health service evaluation research. Both clinical and cost-effectiveness and feasibility are investigated. In addition, research is focusing on the implementation of effective interventions, development and evaluation of new instruments to measure outcome of treatment and on investigating factors which influence outcome. Innovative treatment techniques are being evaluated in this programme, such as selfmanagement techniques and ehealth and mhealth interventions.

In 2016 we started a research line with joint initiatives in the field of dementia and brain injury. These clinical areas are linked by the experience of cognitive deficits and life changing consequences of the diseases. Neuropsychological and psychosocial interventions and outcome measures can be shared and common frameworks can be applied such as positive health and social health (Dr. A. Stiekema). Common themes and techniques are ehealth and mhealth, the family-centered perspective and the societal relevance and impact. In 2018 this re-search line was considered an important element of the research line Rehabilitation of the Brain Nerve Center of the MUMC.

The emphasis in 2018 has been on the implementation of the various interventions already developed (www.partnerinbalans.nl www.mylinlife.nl). A new development concerns the collaboration with the Knowledge Transfer Office and the IT company QNH (www.QNH.eu) to arrive at a business model for the 'Partner in Balance' intervention and for a visualization tool for neuropsychological diagnosis, the `INPAD 'project (PhD A Gruters; collaboration with Prof. R Kessels, Radboud University Nijmegen). In the context of this collaboration, a "Memorandum of Understanding" has been signed between QNH and Maastricht University, describing the partnership. Work will continue on the business model and the licensing of both products in the coming period.

The Senior Friendly Communities project (Interreg grant; PhD M Schichel, Postdoc M Veenstra, collaboration with R Kempen CAPHRI), continued with implementation of best practices from the region, including the Ehealth interventions Partner in Balance and Inlife. The implementation of this will take place and will be evaluated in the coming year (PhD H Christie; collaboration with Dr. H Tange CAPHRI). The evidence-based Partner in Balance intervention is now also being made suitable for use in new populations. In collaboration with another line of research within the division focused on Parkinson's (collaboration with Dr. A Duits and Dr. A Leentjens), the modules of the intervention will be adjusted in collaboration with experts and the target group itself (CZ grant; post-doc A. Moonen)In the field

of dementia at a young age, intensive collaboration with the Alzheimer Center Nijmegen has been continued (external PhD students B. Appelhof, A. Gerritsen, J. van Duin) and expanded to the Alzheimer centers in Rotterdam and Amsterdam, National knowledge center for dementia at a young age, Nivel and Vilans. The cooperation takes place, among other things, for the implementation of the dementia care standard at a young age (UNICITY project, ZonMW grant) in which Maastricht is leading a work package aimed at adapting the Ehealth intervention Partner in Balance for other relatives of young people with dementia. A grant was received from the Hersenstichting to adapt this program to the target group of loved ones with Frontotemporal Dementia (PhD J Bruinsma). Prof M de Vugt is also the project leader of a national prevalence study of dementia at a young age in the Netherlands (PRECODE project, grant Gieskes Strijbis fund and Alzheimer Nederland; PhD Stevie Hendriks) (see also Highlight p. 8-9). In the context of the MARIE SKLODOWSKA-CURIE Innovative Training Network INDUCT (https://www.dementiainduct.eu), the training program of 15 early stage researchers (ESRs) was continued from Maastricht (in collaboration with Prof F Verhey, Dr. F Dassen) in the field of technology and dementia in Europe. Two ESRs are being trained from Maastricht (PhD's H. Christie and S. Bartels), with the collaboration between Maastricht, the Karolinska Institute in Sweden and Nottingham University UK being intensified in the past year (see also Highlight p. 10-11).

In 201,5 the development of the Limburg Brain Injury Centre was started. In this expertise centre, researchers of the UM of both FHML and FPN work closely together with psychologists from the MUMC+ and hospitals all over Limburg (Sittard, Heerlen, Roermond, Weert, Venlo). The expertise centre aims to improve the quality of life of brain injured patients and their caregivers by scientific research in combination with health care development and innovation, education and societal activities. In 2018 the MUMC outpatient clinic on brain injury started as part of the Limburg Brain Injury center. The clinic is mostly aimed at people who experience long term neuropsychological consequences after stroke or traumatic brain injury.

In March 2018 the second symposium of the centre was organized during the international Brain Awareness Week. In 2018 the centre expanded with another researcher, Dr. Stiekema, and PhD students D. Verberne, F. Domensino, J. Bruijel (FPN) and J. Rauwenhoff.

In the programme on neuropsychological interventions for patients with acquired brain injuries, the two large national initiatives ZonMw Restore4stroke and NWO HCMI Cognitive Rehabilitation were successfully finished in 2016 while additional PhD students are extending the research output until this day .

2. VASCULAR NEUROLOGY I.E. THE VASCULAR CONTRIBUTION TO NEURODEGENERATION	
COORDINATOR:	Prof. Dr. R. van Oostenbrugge
RESEARCH STAFF:	Prof. Dr. W. Backes, Dr. J. Jansen, Dr. J. Staals, Dr. S. Köhler, Prof. Dr. F. Verhey
POSTDOCS:	Dr. S. Foulquier, E. Douven
PHD-STUDENTS:	S. Schievink, M. Wong, R. Uiterwijk, E. Zhang

The vascular Neurology group has a longstanding research tradition on cerebral small vessel disease (cSVD). Within division 1 the long term consequences of cSVD, specifically cognitive ones, are being studied. A project funded by NWO aiming to determine the role of blood brain permeability in cognitive function in cSVD was started in 2012. At the end of 2015, funding within the framework of HORIZON 2020 was obtained for a collaborative project with several European universities to study mechanisms of disease in cSVD. Furthermore, we participate in the JPND funded project 'Vascular Contribution to Neurodegeneration'. Main aim of this collaboration is to establish a platform holding information about cohorts, relevant to vascular contribution to neurodegeneration (METACOHORTS).
Translational research on cSVD is performed in collaboration with researchers from the School for Cardiovascular Diseases (CARIM). The focus is directed on the interaction of neuroinflammatory responses and blood brain barrier leakage in cSVD.

3. MOVEMENT DISORDERS:	3.1 MOVEMENT DISORDERS IN ADULTS
COORDINATOR:	Prof. A. Leentjens, Dr. M. Kuijf, Dr. A. Duits.
POSTDOCS:	Dr. A. Moonen, S. Michielse.
PHD-STUDENTS:	A. Mulders, A. Wolters, M. Heijmans, S. van de Weijer.
EXTERNAL COLLABORATORS:	- Movement Disorder Center Lille University Hospital, Lille, France (Prof. K. Dujardin and Prof. L. Defebvre); - Department of Neurology and Psychiatry, Johns Hopkins Medical University, Baltimore, USA (Dr. G. Pontone); - Department of Neurology, Radboudumc, Nijmegen.
FOCUS OF RESEARCH:	Clinical subtypes and biomarkers in Parkinson's disease and in specific non-motor symptoms including mood, anxiety, apathy and cognitive decline.

Longitudinal ultra-high field imaging in Parkinson's Disease: Tracking the disease course (Track PD study) (Prof. Y. Temel, Dr. M. Kuijf, Prof. A. Leentjens): a prospective cohort of 135 Parkinson patients and 50 healthy control patients who will be extensively characterized as far as motor and non-motor symptoms are concerned, and undergo a 7T MRI scan at baseline. Longitudinal anatomical and functional MRI changes in PD will be assessed and correlated with clinical characteristics, clinical subtype, genetic characteristics and progression of symptoms.

Cognitive Behavioral Therapy for anxiety in Parkinson's disease (Prof. A. Leentjens, Dr. A. Moonen, Dr. M. Kuijf, Dr. A. Duits). This is a randomized controlled trial of a Cognitive Behavioral Treatment Module especially developed for treatment of anxiety disorders in Parkinson patients. Apart from the clinical response, other outcome measures are the changes in cerebral connectivety (as measured by MRI scanning) and cost-effectiveness of the treatment. Inclusion has finished; treatment of included patients is ongoing.

Cognitive phenotypes in Parkinson's disease (CogPhen study) (Prof. A. Leentjens, Prof. K. Dujardin, Dr. A. Moonen, Dr. A. Duits). A cross-sectional study in which 150 Parkinson patients will be extensively charactized by clinical, neuropsychological and neuropsychiatric examination as well as by 3T structural and functional MRI and high density EEG. The aim is to identify cognitive phenotypes. Inclusion has fished; analyses are ongoing.

Parkin'Play study (Prof. Bloem Radboudumc), dr. M. Kuijf, dr. A. Duits). A randomized controlled clinical trial investigating an online game for training of cognition. Inclusion of pilot phase study finished, analysis finished. Manuscripts submitted for publication.

3. MOVEMENT DISORDERS:	3.2 PAEDIATRIC MOVEMENT DISORDERS
COORDINATORS:	Prof. R.J. Vermeulen.
RESEARCH STAFF:	Dr. S. Koudijs.
CO-INVESTIGATORS:	L. Speth (Adelante, rehabilitation), Dr. K. Meijer (movement sciences, UM) Dr. Janssen Potten (Adelante, rehabilitation), Dr. E. Rameckers (Rehabilitation UM).
PHD'S:	L. Bonouvrie, I. Moll.

Early brain damage leads to movement disorders (spasticity, dystonia and ataxia), which interfere with motor development. We focus upon mobility (i.e. walking) and head use. Therefore, the focus of this research line is upon interventions as treatment for motor disorders. The abnormalities of the brain are the primary cause of the motor disorder and therefore extensively studied in the study populations, using standard and advanced MR imaging.

Currently, a randomized controlled trial with Intrathecal baclofen is conducted in paediatric and adolescent patients with dyskinetic cerebral palsy (IDYS study, sponsored by the Phelps stichting, revalidatie fonds and Johanna kinderfonds). Mobility is investigated with 3D over ground gait analysis (VICON) and treadmill gait analysis with virtual reality (CAREN).
In September 2017 we started a new study with functional electrical stimulation as treatment for children with unilateral spastic cerebral palsy (cosponsored by the "revalidatiefonds). In this study we will look at the effect of functional electrical stimulation on the drop foot in these children and at predictors of outcome (e.g. neuroimaging). We also started a new study on the development of Walking ("Firststeps" study, in collaboration with the VU in Amsterdam). For this project we got a new paediatric treadmill especially for young (small) children (sponsoring Stichting Vooruit).
In collaboration with Adelante rehabilitation we started a new project on improvement of hand function in children with unilateral spastic cerebral palsy. We have a special interest in sensory function in these children. In the next years we will evaluate the effect of motor training on sensory function in relation the underlying brain abnormality.
For the next years we aim at further development of new imaging diagnostics (i.e. advanced MR Imaging) in paediatric movement disorders and further development of neurointerventions such as deep brain stimulation.

4. EPILEPSY:	4.1 EPILEPSY IN ADULTS
COORDINATORS AND RESEARCH STAFF:	Prof. A. Aldenkamp, Dr. R. Rouhl, Prof. W. Backes, Dr. J. Jansen, Dr. G. Hoogland, Prof. V. van Kranen-Mastenbroek, Dr. L. Jacobi, Prof.Dr. J. Wildberger.
PHD STUDENTS:	A. Vinke, K. Bekelaar, F. Schaper, M. Archila Melendez, H. Bernhard, G. Chaitanya, J. van Tuijl, W. van Blarikom, L. Gupta, M. Teunissen, L. Canjels.

The central theme within the research topic of epilepsy is "Chronic Epilepsy", previously already funded by a substantial grant from the National Epilepsy Fund (NEF) for this program (led by Prof. A. Aldenkamp). One of the severest consequences of chronic epilepsy is the impairment of cognitive functioning, including the general thinking, memory, language and problem-solving capabilities. The novel insight today is that epilepsy is more a network disease rather than a single focal abnormality or malfunction. Traditionally, in our epilepsy research we have used different techniques and methods: measurement of brain waves (electroencephalography, EEG), imaging (acquisition of anatomic and functional brain images) and neuropsychological assessment. Continuously ongoing technological developments of MRI methods, in particular functional and diffusion MRI as well as dynamic contrast enhanced MRI, as well as high field imaging 7 and 9.4 Tesla, provide possibilities to obtain new insights in the organization and integrity of cerebral networks, as well as blood brain barrier integrity, which may lead to strategies that prevent chronic epilepsy and cognitive comorbidity. Starting in 2014, as a consequence of a further integration of and novel opportunities within the Academic Centre for Epileptology (ACE), a close collaboration between the MUMC and Epilepsy Center Kempenhaeghe, new focus points for research emerged: special diagnostic methods (immunology (autoantibodies) and genetics (whole exome sequencing)) as well as special therapeutic methods (deep brain stimulation) and intracranial registration. All these research lines led to fruitful collaborations with other research groups within MHeNS divisions 1, 2 as well as 3, but also to cross-disciplinary research together with the Faculty of Psychology and Neuroscience (FPN). External partners for projects within this theme include Massachusetts General Hospital (A. Viswanathan), Centre Hospitalier de Lille (C. Cordonnier), University College London (D. Werring), Twente University (C. Heida), Technical University Eindhoven, Ghent University (P. Boon), Harvard University (M. Fox), and ErasmusMC Rotterdam (M. Titulaer).

4. EPILEPSY:	4.2 EPILEPSY IN CHILDREN
COORDINATORS:	Prof. J. Vles, Prof. A. Aldenkamp.
RESEARCH STAFF:	Dr. S. Klinkenberg, Dr. M. Debeij van Hall, Dr. J. Hendriksen, Prof. H. Majoie, Dr. G. Hoogland, Dr. J. Jansen, Dr. J. Nicolai, Dr. S. Zinger.
PHD STUDENTS:	E. Fonseca Wald, G. Drenthen, C. van den Bosch, /WagenerSchimme, S. Schipper.

Within the Academic Centre of Epilepsy (ACE) collaboration between Epilepsy Centre Kempenhaeghe and Departments of Neurology concerning diagnostic and treatment options augmented. In 2015 preparations were made for a total package of diagnostic and treatment modalities for (refractory) epilepsy within ACE, leading among other things to scientific spin off in various directions: for example the thesis by S. Klinkenberg (VNS in children, a neuromodulation treatment alternative in refractory epilepsy).
Cognition in relation to (interictal) epileptic discharges and functional networks, especially during development in children, is another research focus in ACE. Preparation of the LEES study, a longitudinal follow-up study in children with absence epilepsy, was started.
Benign childhood Epilepsy with Centro temporal spikes is another research theme, resulting in 'The Rolandic care programme', a national recognized expertise centre. This programme covers both diagnostic modalities (clinical, neurophysiological and neurocognitive) and expertise in counselling. Current study provides insight in subtypes and timing of treatment and consequences for later life. Next to these clinical research lines there is an established preclinical research programme on cognition in relation to epilepsy and interictal epileptic discharges among other themes.

5. NEUROMUSCULAR DISORDERS:	5.1 NEUROMUSCULAR DISORDERS IN ADULTS
COORDINATOR:	Prof. C. Faber.
RESEARCH STAFF:	Dr. J. Hoeijmakers, Dr. I. Merkies.
POSTDOC:	R. Almomani.
PHD'S:	B. de Greef, M. Sopacua, I. Eijkenboom, R. Slangen, B. Brouwer, T. Draak, M. Pruppers, I. Joosten.
EXTERNAL COLLABORATORS:	Giuseppe Lauria (Carlo Besta Institute Milan) and Stephen Waxman (Yale University).

Painful (small fibre) neuropathies (PhD students B. de Greef, M. Sopacua, I. Eijkenboom): the research on painful neuropathies focuses on the genetic mechanisms underlying neuropathic pain, identifying molecular targets which may reveal new drug gable sites, and creating the possibility for personalized pain medicine in a collaborative project, 'Probing the role of sodium channels in painful neuropathies (PROPANE Study)', granted by the EU (Health.2013.2.2.15; Understanding and controlling pain. FP7Health2013Innovation1). Furthermore, studies for improving diagnostic techniques and development of new therapeutic strategies, including new trials, are being performed.
Outcome measures for use in neuromuscular diseases (PhD students T. Draak, M. Pruppers) are essential for development of new trials in the upcoming therapeutic era, leading to several PhD theses (S. van Nes, E. Vanhoutte).
M. Pruppers was awarded the Mazawey Fellowship, a 3-year Fellowship ($ 300.000) for the antiMAG neuropathy study proposal.
Myotonic dystrophy is another main research theme. The 'Maastricht Myotonic Dystrophy Register' dates from the early 1980s and contains data on more than 500 DM1 patients. A grant for development of the national registry for myotonic dystrophy was given to the Myotonic Dystrophy Centre the Netherlands (Maastricht UMC+ and Radboudumc), as well as new grant for developing new nutritional approaches (PhD student I. Joosten).

5. NEUROMUSCULAR DISORDERS:	5.2 NEUROMUSCULAR DISORDERS AND/OR NEUROCOGNITION IN CHILDREN
COORDINATORS:	Prof. J.S.H. Vles, Dr. J.G.M. Hendriksen
RESEARCH STAFF:	Dr. S. Klinkenberg
PHD STUDENT:	R.G.F. Hendriksen

Learning problems, attention deficit disorders (ADHD) and autism spectrum disorders are more common among patients with dystrophinopathies (Duchenne muscular dystrophy and Becker muscular dystrophy) and myotonic dystrophy. Knowledge of this dyadic relationship between muscle and brain is important; with prolonged life expectancy these neurodevelopmental disorders may have growing impact and may be highly debilitating. The lack of dystrophin in the brain may be the explaining factor in this dyadic relationship. The possible role of dystrophin in neural excitability is the aim of the PhD study of R.G.F. Hendriksen and also focussed on the role of dystrophin deficiencies in epilepsy with both clinical and preclinical data being published. In collaboration with Leiden UMC a study on brain imaging (MRI and rfMRI) and neurocognition was done in 30 DMD patients and 30 controls. Results have been published in Annals of Neurology and are currently under further investigation for longitudinal follow up. Furthermore, in collaboration with Leiden UMC, Radboudumc, Kempenhaeghe centre of Neurological Learning and Developmental Disorders (CNL) and Maastricht UMC+ (department of child neurology)we acquired a grant of 250.000 Euro for a longitudinal follow up and intervention study of neurodevelopmental disorders in Duchenne and Becker dystrophy and a grant of 100.000 Euro for a study of medical outcome measures and relationship be-tween dystrophin and somatic functioning.
In patients with myotonic dystrophy a prospective follow up study on neurocognitive and neu-robehavioral functioning in collaboration with Prof. K. Faber is under progress.
Another focus of interest within the department of child neurology MUMC+ and Kempenhaeghe Centre of Neurological Learning and developmental disabilities is Neurofibromatosis type 1 and cognition, (a NF1 neurocognition registry). This is in line with the national recognition by NFU as a centre of expertise. (Coinvestigator: Dr. C. Catsman, Erasmus MC).

6. THE SENSE OF HEARING AND BALANCE: ADVANCED DIAGNOSIS AND SUBSTITUTION	
COORDINATOR:	Prof. B. Kremer.
RESEARCH STAFF:	Dr. R. van de Berg, Dr. E. George, Prof. H. Kingma, Dr. Kunst, Dr. I. Maes, Dr. Widdershoven.
PHD-STUDENTS:	J. Debruyne, E. Devocht, T. van Dooren, N. Guinand, M. van Hoof, R. Jansen, L. Lambriks, M. van der Lubbe, F. Lucieer, L. van Nierop, K. Noij, , M. Pleshkov, J. Smit, D. Starkov, J. Stultiens, M. van Tilburg, S. Wagemakers.
CO-INVESTIGATORS:	Prof. B. Kramer (MUMC+), Prof. K. van Overbeeke (MUMC+), Prof. M. Joore (MUMC+, KEMTA).
EXTERNAL COLLABORATORS:	Prof. E. Formisano (FPN), Prof. Y. Temel, dr. L. Riecke (FPN), Dr. B. Sorger (FPN), K. Meijer, R. Peeters, D. Jiang (UK), Dr. D. Kunst (RU Nijmegen), V. Demkin (Russia), Dr. JP. Guyot (Switzerland), D. Zee, (US, Johns Hopkins), S. Rauch (US, MIT), V. Van Rompaey (Antwerp).
FOCUS OF RESEARCH:	Translational research into the etiology, treatment and impact of sensory disorders, and the effect of neuromodulation devices.

Hearing, tinnitus and balance problems are among the most prevalent chronic health problems in our population, and are associated with substantial societal and healthcare costs. Our research activities are divided in three subcategories:

Tinnitus

In clinical care, our team follows a multidisciplinary approach to combine hearing and tinnitus indications, and to assess acceptability, feasability and cost effectiveness of future interventions. Valorisation and further improvement of our current approach forms the basis for the Dutch care standards. We therefore aim at better understanding patient heterogeneity and emerging comorbidities, aiming at an optimized fit between treatment and individual patient's needs. Our earlier experiences with tinnitus implants have lead to

fundamental research aiming to unravel central nervous mechanisms causing tinnitus by using fMRI and animal models. Moreover, the potential of neuromodulation, specifically deep brain stimulation, for tinnitus complaints is assessed.

Hearing

Optimizing the diagnostics of hearing loss at a very young age has been systematically studied, to enable an earlier detection and intervention. Special attention has been given to basic mechanisms causing hearing damage in premature infants. Bilateral deafness treatment by cochlear implantation has been institutionalized at MUMC+. Research efforts are currently focused on optimizing coding strategies, on improving individual electrode placement using advanced fusion imaging, and on optimizing electrical and acoustic (bimodal) bilateral hearing.

Balance

Advanced diagnosis and treatment possibilities of vestibular disorders have attracted many patients to our MUMC+. New medical and surgical treatment strategies became available for balance disorders, for example using the round window membrane as a pathway to the inner ear. However, for an important proportion of these patients, neuromodulator devices remain the sole treatment option. A special balance belt has been developed with IDEE, supported by the Dutch Health Insurance Companies that increase the proprioceptive substitution for patients with severe balance disorders. In collaboration with Geneva, Tomsk, Antwerp and industrial partners a vestibular implant has been developed which substitutes a defect vestibular system and is currently evaluated and developed further.

DIVISION II

Mental Health

Division Leader:
Prof. T. van Amelsvoort

Deputies:
Dr. S. Guloksuz
Dr. W. 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 division

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 Division Mental Health captures a wide range of themes, which can be broadly clustered in 3 different research strategies.

First, 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 2018, we worked hard to increase the visibility of our Division's ESM expertise in and outside MUMC+.

Second, another longstanding important research activity 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.

The combined statistical, epidemiological, genetic and imaging expertise of our Division have ensured also in 2018 a continuing high-quality scientific output and participation in, and leading large national and international consortia including EUGEI, PSYSCAN, GROUP, ENIGMA. In addition, in 2018, our division set-up a new ENIGMA working group on high-risk populations in collaboration with Pittsburgh University. In 2018, the SCRUM Club was launched, initiated from within our division, a Club to Explore and Learn about Tools/Software for Scientific Computing and Research @ UM. The purpose of the SCRUM club is to explore and learn about software/tools for scientific computing and research.

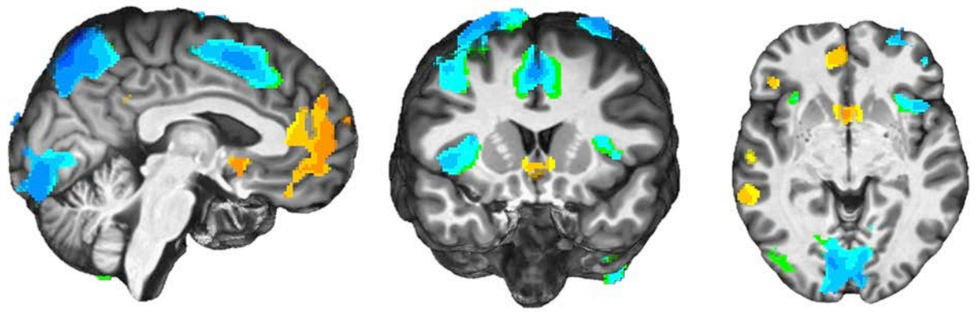
Third, several PIs of our division use experimental mechanistic approaches to study proof of concepts or efficacy of novel interventions. Examples of this work include pharmacological challenge studies in combination with fMRI or 7T-MRS, CO_2 challenge as a model for panic attacks, or an RCT using a transdiagnostic intervention boosting self-esteem. Several of these proof of concepts studies are the first of their kind and warrant replication in larger samples. In 2018, several of these studies led to high-quality scientific output.

Several changes in personnel took place in just before 2018. Two new faculty members came back to UM after spending time as postdocs in the United States (see page 26-29 highlights division 2). In 2018, our division was actively involved in the development of the MUMC+ Brain and Nerve Centre (BNC, HersenZenuw Centrum), in which our Division is taking a leading role in the clinical themes, Psychosis, Anxiety and Mood, and Eating Disorders, along with the research line, Monitoring. Several PIs of division 2 are involved in other clinical pillars and research lines across the matrix of the BNC (see MHeNs website).

One major highlight of 2018 was the National launch of new innovative mental health care developments like @ease (www.ease.nl) and De Nieuwe GGZ (www.denieuweggz.nl). Both are currently being implemented throughout the Netherlands, but their research activities are led by scientists of our Division, in which we collaborate with the department of Health Technology Assessment. @ease is the Dutch version of the successful Australian Headspace, and we were proud that Maastricht opened the first center in the Netherlands in 2018.

In 2019, we will see the opening of another @ease center in the region, in Heerlen. Also, further integration of our research activities within the BNC will take place in 2019. Furthermore, in 2019 we are expecting the launch of the Reward Task Optimising Consortium (RTOC), where research partners from pharma, academia, and SMEs have come together. RTOC is a competitive initiative, which aims to advance the development of clinical tools to measure impaired motivation in people suffering from mental disorders. Maastricht University is the leading center in this multi-center study. Also, the new NIH funded multi-center study on cognition and psychopathology and CNV disorders, led by the University of Pennsylvania , is expected to start in 2019.

USING COMPUTATIONAL MODELLING TO BETTER UNDERSTAND THE MOTIVATIONAL DYSFUNCTION



One example of how computational modelling can reveal the representations of reward prediction errors, choice value, and effort cost.

My name is Dennis Hernaus, and I started a junior faculty position at the School for Mental Health and Neuroscience (MHeNs), division Mental Health, in April 2018. Prior to my appointment at MHeNs I was a post-doctoral fellow at the University of Maryland, School of Medicine (Baltimore, USA).

My aspirations at MHeNs are to work towards a research line that revolves around the study of reward processing (how do appetitive and aversive outcomes affect an organism's actions?) and motivation (willingness to work for a reward) as important drivers of behaviour. Among others, I study the behavioural and neuropharmacological underpinnings of such mechanisms, and how these mechanisms may be altered in individuals who suffer from, or are at risk of, mental illness. The long-term aim of this work is to contribute to formal frameworks explaining how humans optimize behaviour and how a lack of adaptive behaviour or motivational drive can produce motivational dysfunction, such as anhedonia (the inability to enjoy pleasurable activities). Since my arrival I have focussed on initiating this work at MHeNs, which I will describe in more detail below.

The use of computational modelling is central to much of my work. That is, I apply models to empirical data in the service of formally implicating, or ruling out, mechanisms that may drive (abnormal) behaviour in a task or other setting. Importantly, these models can span different levels of inquiry. They can range from more abstract, complex, psychological processes, such as the formation of expectations according to Bayesian probability principles, to highly specific neurophysiological properties of major ascending neuromodulatory systems, for example phasic activity of mesolimbic dopamine neurons that encode the difference between expectation and outcome (also known as "reward prediction errors"). Such models can be applied to test mechanistic hypothesis in virtually any kind of repeated measures data, including experimental behavioural paradigms, functional magnetic resonance imaging, or electrophysiology data.

In summer 2018 I started my first PI project at MHeNS, work that is partly funded by a consumables grant. This study aims to investigate how healthy humans learn to maximize rewards and minimize physical effort, and how such reward and effort-cost computations are affected by stress-induced changes in noradrenaline function. This work is motivated by the idea that stress exposure leads humans to employ inefficient strategies that favour the conservation of energy over the accumulation of rewards, a strategy that could intuitively account for the development of avolition, an impairment in undertaking meaningful, goal-directed, behaviour. In November 2018, prof. Thérèse van Amelsvoort and myself appointed a PhD student, drs. Stella Voulgaroupolou, to carry out these studies. In the future we aim to expand this work to a transdiagnostic sample of individuals experiencing depression, a study that will be conducted in collaboration with dr. James Waltz of the Maryland Psychiatric Research Center.

2018 also marked the year of my first venture into "big data": together with dr. Maria Jalbrzikowsi (U. Pittsburgh) we managed to set up a new Enhancing Neuro Imaging Genetics Through Meta Analysis (ENIGMA) working group. This working group will pool together all available magnetic resonance imaging data from individuals at risk of developing psychosis later in life, and to make these available to others. Our primary goal is to uncover structural and function abnormalities associated with risk for psychosis. Moreover, this large combined dataset may provide a proving ground for the use of prediction algorithms, aimed at making (semi-)individualized predictions about illness or conversion risk. While working on this project, I hope to be able to learn from and collaborate with our "big data" experts within MHeNS, people that have been using these approaches for many years.

In the final weeks of 2018, we were delighted to secure an industry-sponsored grant (with P1vital Products Ltd.) to investigate whether experimental measures of reward learning and effort-cost computations are reliably associated with motivational dysfunction. Initially, the study will collect performance and electroencephalogram data on three candidate tasks in individuals with depression and psychosis, two populations known to often experience motivational impairments. Here, the ultimate goal is to develop clinical assessment tools that do not rely on verbal self-report. Such tools could serve as formal endpoints for the evaluation of novel pharmacological agents, or other interventions aimed at improving motivational deficits. In order to achieve these aims, this initiative involves partnerships with pharmaceutical industry (Boehringer Ingelheim, BlackThorn Therapeutics, Janssen, Lundbeck, and Roche), EEG experts (Biotrial), and academic partners (University Hospital Frankfurt; the Institute of Neuropsychiatry and Addictions (INAD) Barcelona; and the Aristotle University of Thessaloniki). I am happy announce that MHeNS will act as the study Sponsor in this exciting new consortium.

Although the transition from the University of Maryland to Maastricht has made 2018 a busy and hectic year, I am delighted with the progress we have made in the brief available amount of time. In the coming years, I will be motivated to work towards achieving my scientific ambitions, as well as to learn from, and forge new collaborations within, our great MHeNS community.

RTOC
Reward Task Optimisation Consortium

UNDERSTANDING THE (NEURO)BIOLOGY OF EMOTIONS

Photography: Freek Boesten

Nicole Leibold started working as Assistant Professor at Division 2 in April 2018. The overarching aim of her work is to understand the (neuro)biology of emotions such as panic, including the relationship between physiology and subjective experience, and to explore treatment and prevention strategies.

After studying Molecular Life Sciences and Fundamental Neuroscience at Maastricht University I did an innovative interdivisional PhD project in close collaboration with Division 3: I used CO_2 exposure as experimental model to provoke short-lasting panic attacks in healthy participants and panic disorder patients and subsequently established a translational rodent model. This model allowed me to show for the first time that CO_2 exposure causes corresponding respiratory and cardiovascular effects across both species, in addition to triggering a robust fear response in terms of panic symptom ratings in humans and behavior in mice. Thereby I went beyond the traditional behavioral outcome measurements and successfully set up a cross-species model to study the pathophysiology of panic.

Furthermore, in a functional imaging project, we examined which brain region is involved in the response to inhaling CO_2. We showed a primary role of the brainstem and an increased neural sensitivity to CO_2 at the brainstem level in panic disorder patients.

Inspired by this previous work, I endeavoured to examine the molecular mechanisms in the brainstem that are involved in sensing changes in CO_2 and how a (pathological) response is triggered. I managed to obtain competitive grants (Kootstra Fellowship and Niels Stensen Fellowship) to answer my research questions at the University of Iowa in the United States, a world-renowned institute in this field. During these 2.5 years, I focused on brainstem serotonin neurons as attractive candidate for mediating arousal to CO_2 because of their sensitivity to CO_2 and pH changes. To investigate which population of serotonin neurons in the brain, i.e. in the midbrain or in the medulla, is more important in this mechanism, I applied numerous, state-of-the-art techniques in genetically modified mice, from reverse microdialysis to locally change brain pH to optogenetic stimulation in combination with CO_2 exposure. We demonstrated that dorsal raphe nucleus serotonin neurons play an essential role in the arousal response to CO_2 and that their activation is sufficient to cause arousal. This work received widespread media attention and the National Institute of Health (NIH) invited me to present our data at their annual meeting.

To establish my own research line at the interface of biology and psychiatry I returned to Maastricht University in Spring 2018. I further investigate the mechanisms of (pathological) emotions and the relationship between physiology and subjective experience, and envision to translate this knowledge into new therapeutic and preventive approaches.
With a special emphasis on panic as an intense emotion, I have continued using exposure to CO_2 in line with my previous work. My first focus is on using my recently established translational CO_2 model to speed up the search for new pharmacological treatment options. It serves as a novel screening model to evaluate the effectiveness of current and new drugs. As drugs are generally first tested in animals, it is imperative that the model needs to be predictive for the response in humans. This is the case in the CO_2 model: the resemblance of the animal model to the human model could significantly increase the chance that an effective compound in rodents will eventually also be panicolytic in humans. My second focus is on exploring the use of repeated CO_2 inhalations in interoceptive exposure therapy for panic attacks. It has been repetitively shown that inhaling CO_2 provokes the fear and symptoms defined in the Diagnostic and Statistical Manual of Mental Disorders for having a panic attack. In this respect, CO_2 inhalations are superior to traditional methods such as spinning with a chair or breathing through a straw that only induce a small number of symptoms. Yet, this method is not yet implemented as standard treatment in the clinic. Therefore, for the first time I systematically investigate whether patients accept repeated exposure to CO_2 and its effectiveness. In addition, I aim to tap into the involved mechanisms by looking at the changes in emotional reaction over the course of therapy sessions and potentially associated changes in physiology.
I also see great promise in moving to patients' natural environment to unravel the dynamic course of physiological changes preceding spontaneous panic attacks. In contrast to the general belief that panic attacks occur fully out of the blue, research indicates that some physiological alterations occur more than half an hour before the attack is subjectively noticed. This inspired me to make use of the latest technical innovations to obtain more detailed insights into these changes and to come closer to individualized interventions.
On the molecular level, I have a strong interest in epigenetic modifications such as DNA methylation and their role in determining the sensitivity to CO_2, including the contribution of specific brain regions, and in predicting treatment response and relapse.

In the near future, I will go beyond panic as specific emotion of interest. Together with other scientists from Maastricht University I will work on identifying the physiological and other components of emotions to determine targets for neuromodulation in anxiety disorder patients. Another future project is to determine and enhance resilience factors in youth with mental health issues, a group that is highly vulnerable to suffer from chronic problems. I envision that a better understanding of emotions will be a milestone in improving and personalizing treatments, and in developing novel prevention strategies. I am looking forward to the collaborations within and beyond our university.

EXPERT GROUPS DIVISION II

EXPERTGROUP:	1 GENETICS
COORDINATORS:	Dr. S. Guloksuz.
RESEARCH STAFF:	Prof. J. van Os, Prof. B. Rutten, Dr. G. Kenis, Dr. W. Viechtbauer, Dr. G. Blokland, Prof. T. van Amelsvoort, Prof. D. Linden.
POSTDOC:	Dr. C. Simons.
PHD STUDENTS:	L. Pries, B. Klingenberg, O. Cinar.
FOCUS OF RESEARCH:	The design of genetic studies in the field of psychiatry as well as investigating the role of genetic variation and gene-environment interactions in the etiology, severity and course of psychopathology.

The genetics expert group coordinates the design of genetic studies in the field of psychiatry as well as the choice of various genetic methodologies, choice of polygenic scores, pathway scores, epigenetic scores and genes of interest for the different research lines. Furthermore, it offers a platform for bringing together several disciplines in order to conduct adequately designed multidisciplinary and translational research to establish the role of genetic variances and gene-environment interactions in the etiology, severity and course of psychopathology and dimensions of psychological and psychiatric traits.

EXPERTGROUP:	2 EXPERIENCE SAMPLING
COORDINATOR:	Dr. M. Janssens, Dr. C. Simons.
RESEARCH STAFF:	Prof. Ph. Delespaul, Prof. N. Jacobs, Dr. M. Drukker, Dr. W. Viechtbauer.
POST DOC:	Dr. M. Janssens, Dr. N. Gunther, Dr. J. Lataster, Dr. S. Peeters, Dr. C. Simons, Dr. V. Thewissen, Dr. C. van Zelst.
PHD STUDENTS:	S. Bartels, L. Berk, M. Daemen, N. Daniels, E. van Duin, J. Habets, S. Leijdesdorff, C. Rauschenberg, S. Verhagen.
FOCUS OF RESEARCH:	To guard and increase the quality of ESM data collections and analyses, as well as to increase statistical expertise and analytic possibilities.
SUPPORTING STAFF	K. Borkelmans, T. Driesen, N. Volbragt.

The aim of the EXM expert group is to guard and increase the quality of ESM data collections and analyses, to examine the validity of the method and the items used in ESM and report on this in international peer-reviewed journals, as well as to increase statistical expertise and analytic possibilities, such as timeseries analysis in ESM.

EXPERTGROUP:	**3 NEUROIMAGING**
COORDINATOR:	Dr. D. Hernaus.
RESEARCH STAFF:	Prof. T. van Amelsvoort, Prof. K. Schruers, Dr. G. Blokland, Dr. L. Goossens, Prof. D. Linden, Dr. D. Hernaus, Dr. N. Leibold, Dr. D. van der Meer, Dr. S. Gülöksüz, Dr. M. Marcelis.
POST DOC:	Dr. E. Boot, Dr. I. Lange, Dr. C. Vingerhoets, Dr. P. Domen, Dr. C. van der Leeuw.
PHD STUDENTS:	S. Baldi, S. Voulgaropoulou.
FOCUS OF RESEARCH:	Examining brain structure and function in relation to psychopathology and biological and environmental risk factors.

The Neuroimaging Group of Division II: Mental Health uses various neuroimaging techniques (sMRI, fMRI, MRS, PET, SPECT, EEG) and analysis approaches to study structural, functional, and neurochemical alterations in the context of psychopathology. The Neuroimaging Group has two main goals:

1. The study of structural, functional, and neurochemical mechanisms related to psychopathology, and therapeutic effects. Examples include the study of the neural correlates of operant (appetitive/aversive) learning deficits in psychopathology, dopamine dysfunction in psychosis (-prone individuals), and cholinergic and glutamatergic mechanisms linked to cognitive deficits in genetic syndromes (e.g. 22q11.2). In 2018, members of the Neuroimaging Group (dr. Hernaus, prof. van Amelsvoort) initiated an industry-sponsored multi-center collaboration to study how reinforcement learning deficits may contribute to motivational deficits (anhedonia, avolition), and functional outcome using EEG. Prof. Schruers and dr. Goossens successfully started a collaboration with the Faculty of Psychology and Neuroscience (FPN) to use high-field sMRI to improve the efficacy of deep brain stimulation in OCD. The Neuroimaging Group published important fMRI , SPET and PET studies related to cognition and reinforcement learning deficits in psychosis (dr. Hernaus, prof van Amelsvoort), 22q11.2 deletion syndrome (prof. van Amelsvoort), and anxiety disorder (prof. Schruers). Other achievements include published work on cognitive impairments related to acetylcholine, and glutamate dysfunction. The group submitted several national and international competitive grant applications in these domains, and some of these are still under review.
2. A second aim of the Neuroimaging Group is the use of neuroimaging to predict symptom severity and illness risk. The Neuroimaging Group started an Enhancing Neuro Imaging Genetics Through Meta Analysis (ENIGMA) Working Group focusing on individuals at ultra-high risk for psychopathology (dr. Hernaus). The ENIGMA 22q11.2 Working Group based at Div 2 (prof. van Amelsvoort) moreover published seminal large-scale studies on cortical morphology in 22q11.2 deletion. Other published work include the study of white matter changes related to subclinical psychotic experiences (dr. Marcelis) and anxiety symptoms (prof. Schruers). In 2018, the neuroimaging marker research line started to include the use of polygenic risk scores, and several new junior faculty members, including dr. Blokland, have joined the Division to strengthen this line of work.

2018 saw the birth of a number of new initiatives to improve inter- and intra-faculty neuroimaging collaborations. These initiatives include cross-faculty meetings with the School for Business and Economics (SBE) in the context of using neuroimaging to study the neural correlates of value-based decision-making, FPN cross-faculty meetings to optimize neuroimaging data pre-processing, and intra-faculty Brain and Nerve Centre Neuroimaging Theme Groups to foster new collaborations in the domains of PET (lead by Prof. Mottaghy) and MRI research.

EXPERTGROUP:	**4 EPIDEMIOLOGY AND HEALTH SERVICES RESEARCH / CROSS DIVISIONAL EXPERT GROUP EPIDEMIOLOGY**
COORDINATOR:	Dr. M. Drukker.
RESEARCH STAFF:	Dr. M. Drukker, Dr. U. Reininghaus, Dr. S. Koehler, Dr. K. Deckers, Dr. M. van Boxtel, Dr. S. Gülöksüz, Dr. W. Viechtbauer, Dr. E. Pishva, Dr. D. van den Hove, Prof. Ph. Delespaul, Prof. T. Van Amelsvoort.
PHD STUDENTS:	Division 1: I. Bos, O. Janssen, S. Vos, I. Ramakers, L. Banning, D. Verberne, W. Jansen, A. Geraets, M. Schram, S. Hendriks, H. Park, L. Bakker, I. Heger. Division 2: C. Rauschenberg, M. Daemen, S. Leijdesdorff, S. Michielse. Division 3: C. Choe.
FOCUS OF RESEARCH:	To discuss the correct use of research methods.

The proper use of research methods is always important. This group aims to bring together expertise across our divisions. Meetings are planned bimonthly.

EXPERTGROUP:	**5 NETWORKS**
COORDINATOR:	Dr. M. Drukker.
RESEARCH STAFF:	Dr. W. Viechtbauer.
PHD STUDENTS:	A. Klippel, S. Peeters, S. Michielse, L. Hasmi, J. Bakker.
FOCUS OF RESEARCH:	Networks in all their diversity.

The network expert group was founded to exchange knowledge and to make use of each other's expertise rather than to re-invent methods. The group read and discussed important network literature. This group aims to include all colleagues working on networks. In 2018, several members finished their PhD and left the department. For this reason, meetings were not frequent. In the future, with the start of new PhD students this group will become more active again.

SCRUM Club: A Club to Explore and Learn about Tools/Software for Scientific Computing and Research @ UM
The purpose of the SCRUM club is to explore and learn about software/tools for scientific computing and research. For example, most of the research conducted at MHeNs involves the collection of data, requiring appropriate statistical software for its analysis. We therefore cover software such as R (a free and open-source software environment for statistical computing and graphics) and Python (a general-purpose programming language with extensive support for data analysis), but also other tools that are useful when conducting research. In 2018, the club had 12 meetings, where we covered various topics, including R, version control (with Git/GitHub), reference managers (EndNote and alternatives), data visualization using Tableau, LaTeX, command line interfaces, remote computing, and computational notebooks for literate programming (in particular JupyterLab).

DIVISION III

Translational Neuroscience

Division Leader:
Prof. J. Prickaerts

Deputies:
Prof. P. Martinez-Martinez
Dr. M. Janssen

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, Toxicogenomics, Clinical Neurophysiology, and Genetics and Cell Biology.
The mission of Division 3 is to significantly improve the understanding of the biological 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.

The 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 senior scientific staff in the Division embody common methodological concepts that cut across these research lines. The coordination and development of methodological expertise is organized into expert groups, which are coordinated by senior staff and technicians.
The Division has one main laboratory that is shared by all its scientists. The different sections of the laboratory are based on the methodologies used, i.e. in vivo experiments, electrophysiology, molecular and cellular biology, and quantitative immunocytochemical microscopy.

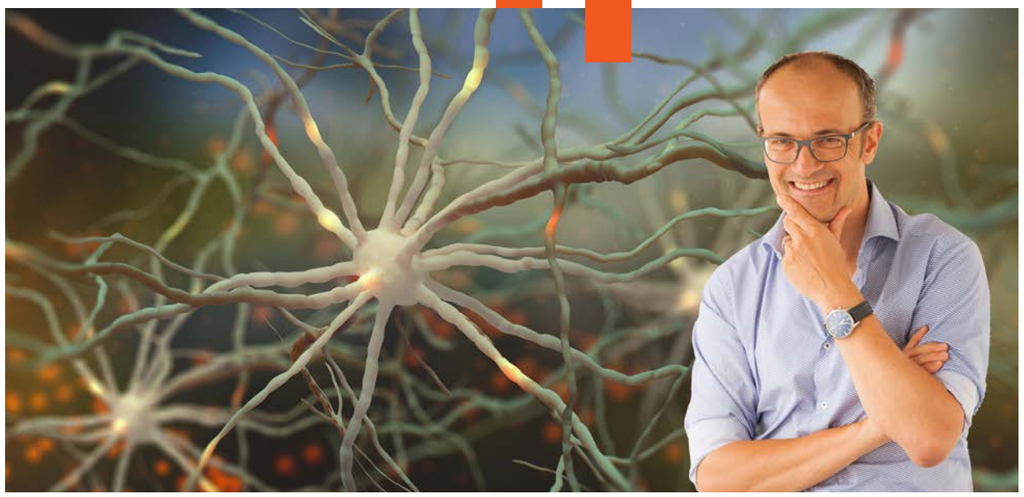


Photo Jos Prickaerts: Anke Geurts Photography

Goals & results division

In short, the Division Translational Neuroscience performs fundamental and translational neuroscience research on the mechanisms related to neuroplasticity, neurodegeneration and regeneration in health and disease across the life span. Currently the division has converged the activities of the different research lines into the following thematic research lines:

1. Neuroepigenetics
2. Neuropsychopharmacology
3. Neuroinflammation
4. Neuromodulation

Thus, we aim to gain knowledge of physiological and pathophysiological mechanisms underlying in particular affective, cognitive and motor functions and disorders thereof and to develop strategies for improving healthy living, as well as preventing and treating neurological and psychiatric disorders.

Our main research lines converge on regulation of neurotransmitter functioning, cell signalling, brain plasticity, biological mechanisms mediating gene-environment interactions (such as epigenetic control of gene expression), and neuroinflammation including autoimmunity in a lifetime perspective. Our neuroscience studies combine fundamental, preclinical and clinical expertise and interests on developmental programming (including prenatal and perinatal life), as well as experience- dependent plasticity during sensitive time windows and age-related changes of the nervous system. Technological expertise in our division is currently centralised in four expertise groups that are coordinated by senior staff members and supported by experienced technicians: molecular and cell biology, microscopy and imaging, neuromodulation and electrophysiology, and in vivo and behaviour.

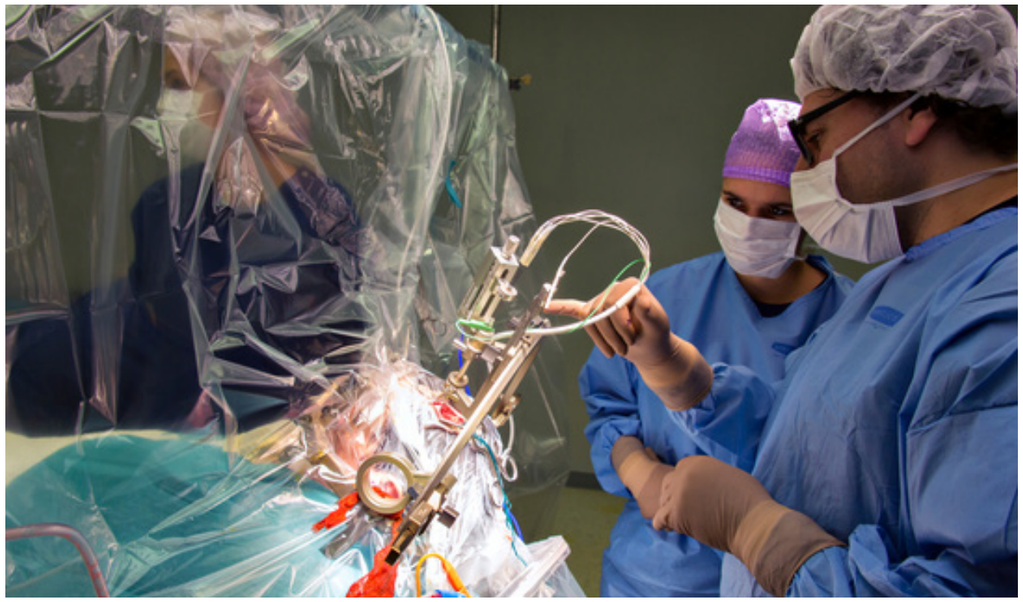
In addition to investigations on overt dysfunctions involving the central nervous system including depression, dementia, Parkinson's disease, psychosis and epilepsy, we also investigate peripheral mechanisms mediating central control of peripheral bodily function such as pain, auto(immunity), vision and neuro-urogenital functioning.

Our researchers conduct specific study paradigms to answer clinically relevant research questions, typically by combining a range of techniques and approaches such as detailed cellular work, experimental animal studies as well as observational human studies and clinical trials.

The multidisciplinary staff consists of professionals from relevant disciplines within research and clinic. There are collaborations within worldwide international networks of research offering a strong academic environment. By doing so, we attempt to improve scientific knowledge on healthy functioning of the brain and on the aetiology of disorders. At the same time, we translate relevant scientific findings swiftly into biomarkers development as well as new neurotherapeutical applications including lifestyle interventions, pharmacological and antibody-based therapies, or neuromodulative treatments.
For the upcoming years we first strive to align and integrate our research lines. The thematic research lines of the Brain and Nerve Center (BNC), in particular Modulation, Monitoring, and Cell Biology and Genetics, offer an excellent opportunity in this respect. Next to research lines the BNC also has clinical pillars (e.g pain, cognition and dementia, epilepsy, movement and vision, hearing and balance), which offer the division excellent opportunities for integrating its preclinical research with the clinical expertise. This translational advantage will generate scientific input with clear translational and clinical impact and also increase opportunities for further funding. A second point of attention has been extending our stem cells and iPSC research. This will be done within the recently established Brightlands e-infrastructure for Neurohealth (BReIN) Institute within MHeNS. Linked to this we will stimulate more integration with the Institute of Data Science (IDS) and the Institute for Technology-Inspired Regenerative Medicine (MERLN).

WEIJERHORST STICHTING RESEARCH PROJECT 2018

THE UTAP- STUDY



Photography: Maastricht UMC+

The UTAP-study consists of three multidisciplinary work packages (WPs) which are interconnected. WPs 1 and 2 use precision and individualized medicine approaches and WP3 uses an E-and M health approach. This combination is unique and creates a powerful approach to generate essential knowledge to improve the management of patients with PD.

Demographic changes: The rise of the Parkinson-Problem

Neurological disorders are becoming one of the greatest threats to the public health (www.who.int). The main reason is ageing. In the Netherlands, approximately 650.000 people suffer from a neurological disorder (www.hersenz.nl). One of the most prevalent neurological disorders is Parkinson's disease (PD). The cost of this disease in the Netherlands is approximately €300 M per year (www.volksgezondheidenzorg.nl). The prevalence of PD is expected to increase by 60% in men and 40% in women in the next 10 to 15 years. This will cause a serious socioeconomic burden for our society. Clinically, the disease is characterized by a trias of motor symptoms, consisting of rigidity, hypokinesia, tremor and postural instability. Besides, disabling cognitive and autonomic symptoms can occur throughout the disease course. Different combinations of these symptoms determine the clinical phenotype of the patient. The most frequently seen phenotypes are the tremor-dominant and akinetic-rigid type.

Current concepts are not future-proof

The two main breakthroughs that have led to better care for patients with PD are the introduction of levo-dopa as drug therapy in 1969 and Deep Brain Stimulation (DBS) in 1993 as a surgical therapy. Currently, these treatments form the cornerstones of the medical management of patients with PD. In addition, these treatments represent the classical viewpoints how PD is generally approached.

1. The neurochemistry viewpoint: The levo-dopa and related drug-based treatments are largely based on replacing the mono-aminergic cell dysfunction. Namely, in PD cell death occurs in the monoaminergic systems, and mainly the nigrostriatal dopaminergic system is prominently affected. To this histopathological concept, the theory of Braak and Braak has been added. This theory suggests a caudo-cranial distribution of the PD pathology.
2. The neuroanatomy viewpoint: The DBS therapy is based on the viewpoint that there is a dysfunction in neural circuits such as the cortico-basal ganglia-thalamocortical circuit, resulting in motor and non-motor symptoms. The direct, indirect and hyperdirect pathways are the main circuits which have been investigated for a long-time in PD. Dysfunction of these circuits have been linked to the clinical symptoms of the patient.

Innovations to tackle the Parkinson-Problem: the UTAP-study

Unfortunately, these treatments and concepts in their current forms will not be able to provide solutions to the Parkinson-Problem as described above. They cannot explain how dysfunction in brain's connections result in clinical symptoms in PD (precision medicine), do not incorporate the individual differences between patients (individualized medicine), and do not include the innovative approaches (E-, and M-health). As a consequence, we have critical gaps in our knowledge. To provide solutions and add value to the lives of PD patients and ultimately to contribute to a sustainable society, we need to enhance our knowledge of how PD influences the brain.

Photography: Maastricht UMC+

In the Understand-Track-Adjust Parkinson's disease- study (UTAP-study), we aim to overcome the critical gaps in knowledge by combining the latest views on neurological medicine (precision medicine and individualized) with cutting-edge technologies (ultra-high field magnetic resonance imaging and Electronic- and Mobile-health applications). We will add to this the strongest research lines of our group (>20 years experience in Neurosciences) and our network in PD management.

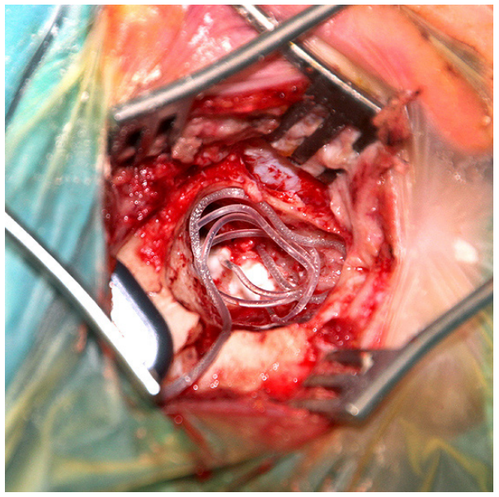
GRANT FOR THE DEVELOPMENT OF AN ARTIFICIAL BALANCE ORGAN

Photography: Maastricht UMC+

Severe and chronic hypofunction of the vestibular system, bilateral vestibulopathy, is very disabling. Patients suffer from imbalance and with each head movement they experience a sensation of dizziness and disorientation. This strongly influences their daily functioning, with big socio-econimic consequences like reduced participation in social activities and society. Approximately 75% of the patients are not able to work, and they have a 30-fold increased risk of falling. This not only leads to a reduced quality of life, but also puts a socio-economic pressure on society. The estimated amount of patients suffering from severe vestibular hypofunction is approximately three million worldwide, but this is very like to be an underestimation.

Unfortunately there is no treatment yet for loss of vestibular function. Therefore, the team from Maastricht UMC+ and the University of Geneva have built a strong collaboration to develop an artificial balance organ. This has resulted in the first surgically implanted artificial balance organs in humans in the world, and feasibility was demonstrated in two cum laude PhD-defenses (Dr. R. van de Berg (Maastricht UMC+) and Dr. N. Guinand (University of Geneva). Until now, this team has still the biggest patient population with implanted artificial balance organs in the world (13 patients). The last couple of years, this has attracted the attention of international, national and local media, including radio, television, newspapers and social media.

The artificial balance organ is a bio-electronic prosthesis, that replaces the failing vestibular organ. Gyroscopes capture motion and these motion signals are converted by a processor into electrical pulses. These electrical pulses are then transferred by surgically implanted electrodes to the vestibular nerve. By this, the brain of the patient is able to recognize motion again. Now that feasibility has been shown, it is important to further investigate all factors necessary to facilitate fast clinical availability on the market. The team of Maastricht UMC+ and the University of Geneva have therefore extended their collaboration with, among others, the faculty of physics of the university of Tomsk (Russian Federation), the department of otorhinolaryngology of the university of Antwerp (Belgium) and the manufacturer Med-El (Austria). This has resulted in obtaining several grants (including multiple international grants from Russia) and PhD positions with each their own specific research domain. First, the patient group will be characterized more in detail, to develop a diagnostic pathway and implantation criteria. Core members of the team of Maastricht UMC+ are already strongly involved in international cooperations regarding development of criteria. Secondly, additional outcome measures will be developed, including the use of Psymate (cooperation with Prof. Delespaul, Prof. Peeters, Dr. Leue and the European Dizziness network “Dizzynet”), to complement the current outcome measures with improved subjective and objective parameters. Thirdly, the surgical technique and electrode design will be fine-tuned, to improve safety and efficacy of surgery. By this, surgical implantation can be safely performed in multiple centers in the world. Fourthly, the settings of the implant will be optimized (optimizing stimulation paradigm by investigating the transfer function) and tested, to ensure the most optimum stimulation by the artificial balance organ. Finally, a new PhD student will start end of 2019 to run the trial funded by ZonMw and Heinsius Houbolt Fonds. This creates the opportunity to extend the patient group with eight additional patients, and to implant them with the newest version of the artificial balance organ. These patients will be chronically stimulated with the implant in a controlled setting, outside the laboratory. In addition to investigating safety and efficacy of chronic stimulation, a rehabilitation program will be developed to get patients home as fast as possible to use their implant in daily life. Patient participation in the development and execution of the trial is crucial. It will be attempted to increase their capabilities and functionalities in a personalized manner.



Photography: Maastricht UMC+

After successful completion of the studies mentioned above,we aim to have the artificial balance organ clinically available on the market within five to ten years. Maastricht UMC+ is currently the only “center of expertise” in The Netherlands for this disorder, and therefore has already many patients waiting for this treatment.

RESEARCH LINES DIVISION III

1. NEUROEPIGENETICS

COORDINATOR:	Dr. D. van den Hove.
FACULTY:	Prof. B. Rutten, Dr. G. Kenis, Prof. KP. Lesch, Dr. L. Eijssen, Dr. L. de Nijs, Prof. J. Prickaerts.
POSTDOCS:	Dr. E. Pishva.
PHD-STUDENTS:	G. Al Jowf, M. Ali, K. Bassil, M. Bustelo, K. Choe, P. Koulousakis, A. Ning, D. Paes, R. Riemens, J. Roubroeks, C. Snijders, A. Thomson, M. Weidner, R. Lardenoije, A. Iatrou, J. Zöller.
EXTERNAL COLLABORATORS:	Prof. J. Mill, Dr. K. Lunnon (University of Exeter, UK), Prof. T. Haaf (University of Würzburg, Germany), Prof. M. Wagner, Dr. A. Ramirez (University of Bonn/Cologne, Germany), Dr. T. Sesia (University of Cologne, Germany), Dr. R. Delgado (IDIBELL, Spain), Prof. A. Del Sol (Luxembourg Centre for Systems Biomedicine, Luxembourg), Dr. T. Vanmierlo (BIOMED, University of Hasselt, Belgium), Prof. L. Lanfumey (University Pierre & Marie Curie, France), Dr. C. Lemere (Harvard Medical School, USA), Prof. P. Coleman, Dr. D. Mastroeni (Arizona State University, USA).
FOCUS OF RESEARCH:	Understanding the role of gene-environment (GxE) interactions and associated epigenetic mechanisms during development and aging, with a particular focus on the pathophysiology of psychiatric and neurodegenerative disorders.

The organization of DNA into chromatin enables the cell to use powerful regulatory mechanisms broadly defined as epigenetics. Epigenetic changes are reversible and responsive to environmental influences, unlike genetic mutations, which represent rare events with permanent consequences on genes. Research on Neuroepigenetics and environmental epigenetics aims to characterize the molecular basis that underlies sensitivity to environmental exposures and associated gene-environment (GxE) interactions in (neuro) psychiatric and neurodegenerative phenotypes and disorders, with a particular interest in epigenetics.

This program examines several aspects of epigenetic regulation, such as DNA methylation at promoter sites, chromatin modifications, gene silencing induced by miRNAs, and other novel epigenetic mechanisms, for their roles in disease and dysfunction consequent to environmental conditions. The ultimate goal of this program is to identify molecular and cellular pathways that are causally involved in the etiologies of psychiatric disorders, to identify biologic markers that predict disease onset and course, to determine the reversibility of neurobiological changes, and to find novel preventive and therapeutic strategies.

Neuroepigenetics focuses on two main research themes/questions. First, what are the neurobiological underpinnings of neuropsychiatric and neurodegenerative phenotypes? Second, what is the role of epigenetic mechanisms in mediating gene-environment interactions in and long-term consequences of (developmental) environmental perturbations? These research themes/questions are applied to Alzheimer's disease, mood and anxiety disorders, schizophrenia and epilepsy. State-of-the-art technologies (e.g. ranging from epigenome-wide association studies [EWAS] to single cell methylation profiling) are being employed to analyze the

epigenetic changes in single genes, signaling pathways or the entire genome. Research involves various innovative, translational projects using in vitro cell cultures (e.g. in vitro epigenetic editing), in vivo animal models (e.g. in vivo epigenetic editing), and human tissues and/or biologic samples to examine (epi)genetic modifications and to determine the precise mechanism responsible for these changes.

Of note, the Neuroepigenetics group is part of a broader initiative at Maastricht University, bringing together all divisions within MHeNs in a collaborative approach to further investigate the neurobiology of psychiatric disorders in a translational setting.
As such, these lines of research are supported by grants from the Internationale Stichting Alzheimer Onderzoek (ISAO), Alzheimer Netherlands (AN), the European Union (e.g. EU-GEI [FP7], see http://www.eu-gei.eu; EPI-AD [H2020-JPND], see http://www.epi-ad.eu), NWO-Veni, NWO-Vidi and Hersenstichting Nederland.

2. NEUROPSYCHOPHARMACOLOGY; SIGNAL TRANSDUCTION

COORDINATOR:	Prof. J. Prickaerts.
RESEARCH STAFF:	Prof. Y. Temel, Prof. F. Verhey, Prof. R. van Oostenbrugge, Prof. M. De Baets, Dr. P. Aalten, Dr. I. Ramakers, Dr. D. van den Hove, Prof. B. Rutten.
POSTDOCS:	Dr. P. Heckman, Dr. N. van Goethem.
PHD-STUDENTS:	B. van Hagen, E. Argyrousi, D. Paes, M. Schepers, S. Caldenhove, M. van den Berg, R. Pazinatto Aguiar, L. Sales Kanazawa.
EXTERNAL COLLABORATORS:	Dr. A. Blokland, Dr. A. Sambeth, Prof. J. Ramaekers (FPN), Prof. H. Schmidt, Dr. T. Vanmierlo, Prof. N. Hellings (BIOMED, University of Hasselt, Belgium), Dr. P. Wieringa (MERLN), Dr. R. Havekes (GELIFES, University of Groningen), Prof. O. Bruno, Dr. E. Fedele (University of Genoa, Italy), Dr. D. Puzzo (University of Catania, Italy), Dr. L. Wennogle (IntraCellular Therapies, New York, USA), Prof. O. Arancio, (Columbia University, NY, USA), Dr. R. Weffort de Oliveira (State University of Maringá, Brasil), Prof. R. Adreatini (State University of Paraná, Brazil).
FOCUS OF RESEARCH:	Cellular signal transduction in affective and cognitive processes in health and disease.

The focus of research is on signal transduction and plasticity. In particular the role of phosphodiesterases (PDEs), specific neurotransmitters (e.g. serotonin) and growth factors (e.g. BDNF) in this respect is being studied. The major aim is to unravel the mechanism of action of signaling pathways both in health and disease (mainly Alzheimer's disease, depression and Multiple Sclerosis), while at the same time exploring the therapeutic potential of key players in the affected signaling pathways. Research involves working with animal models and tests in a translational context up to testing drugs in clinical trials. There is also a substantial collaboration with pharmaceutical companies to develop and test new cognitive enhancers.

As shown by us, phosphodiesterase (PDE) inhibitors, which inhibit the degradation of cAMP and/or cGMP by PDEs, improve signal transduction and memory processes in monkeys and rodents. This is of major importance since this indicates that these second messengers can be targets for new drugs to improve memory function directly. Therefore, the biological mechanism of action of specific PDE inhibitors to improve memory is investigated in depth in collaboration with international academic partners (e.g. University of Genoa, University of Columbia, State University of Maringá) and pharmaceutical companies. Part of this research is also conducted in close collaboration with Hasselt University and funded by Alzheimer Nederland. PDEs are being explored at the isoform level as therapeutic targets for the treatment of Alzheimer's disease. A proof of concept study funded by a grant from ZonMw showed the memory improving potential of the PDE type 4 inhibitor roflumilast in human subjects with age-associated memory impairment. This was done in collaboration with Division 1 of MHeNs and the Faculty of Psychology and Neuroscience (FPN). In addidtion, parallel preclinical and clinical studies are ongoing on new therapeutic targets besides PDEs to stimulate signal transduction. One example is the project within the Centre for Integrative Neuroscience (CIN; both FHML and FPN) in which the focus is also on miRNA as biomarkers of drug induced changes in neural integrity and cognition.

Finally, besides using pharmacological interventions, signalling is manipulated in mouse models of Alzheimer's disease or multiple sclerosis via gene transfer techniques including CRISPR/Cas9 and a micro electroporation approach. The results of all our studies will eventually help us to find new therapeutic targets for affective and cognitive disorders.

3. NEUROINFLAMMATION; NERVOUS SYSTEM NEUROINFLAMMATION: IMMUNOTHERAPY AND AUTOIMMUNITY

COORDINATORS:	Prof. P. Martinez & Dr. M. Losen.
RESEARCH STAFF:	Prof. B. Rutten, Prof. M. De Baets, Dr. P. Molenaar, Dr. R. Rouhl, Prof. T. van Amelsvoort.
POSTDOCS:	Dr. C. Hoffmann.
PHD-STUDENTS:	M. Mané-Damas, S. Crivelli, S. Zong, D. van Kruining, L. Quian, C. Giovagnoni; X. Zhang.
FOCUS OF RESEARCH:	Understanding neuro-inflammation in neurodegenerative diseases and nervous system autoimmunity.

Our team is studying neuroimmunological mechanisms of the innate and adaptive immune response in the peripheral and central nervous system, with the focus on antibody-mediated autoimmune diseases. We are working on various diseases, including myasthenia gravis (MG), Alzheimer's disease (AD), schizophrenia and depression.

An important goal of our work is the development of new methods to diagnose psychosis with autoimmune origin (projects funded by ZonMw and the Hersenstichting) in order to enable specific (immunosuppressive) treatment of patients.

Additionally, we study the role of lipids and their transporters in the early inflammatory process of neurodegenerative diseases. In particular, we investigate the function/dysfunction of danger signal molecules e.g., serum amyloid P component and the ceramide transporter. This work is supported by the Internationale Stichting Alzheimer Onderzoek (ISAO). Additionally, a Weston brain institute grant from Canada, and European grant Interreg, and a Memorabel/ZonMw grant support the work on sphingolipids in AD.

Finally, we are working on the development of relevant experimental CNS autoimmune models of mental illness, work funded by an Aspasia grant and industry initiated grants.

In MG, we are investigating the possible use of proteasome inhibitors for targeting autoimmune plasma cells. Long- living plasma cells are resistant against broad-range immunosuppressants and are therefore a major problem in the current treatment of MG and other antibody-mediated autoimmune diseases. Plasma cells depend on their proteasome to sustain high rate protein synthesis. Consequently, proteasome inhibitors have the capacity to kill plasma cells by inducing the terminal unfolded protein response.

With support from the AFM Telethon (France) and an NIH grant, we are investigating disease pathology in a rare form of MG with muscle specific kinase antibodies. For this purpose, we are generating monoclonal autoimmune B cells from these patients. The cell lines are used to define fine antigen-specificities of individual patients' antibodies and to develop an animal model that can be used for testing future therapies. Finally, several collaborations with industry in these related topics are ongoing.

4. NEUROMODULATION:	4.1 EXPERIMENTAL NEUROSURGERY
COORDINATOR:	Prof. Y. Temel.
RESEARCH STAFF:	Dr. L. Ackermans, Dr. G. Hoogland, Dr. A. Jahanshahi, Dr. M. Janssen, Dr. P. Kubben, Dr. M. Kuijf, Dr. K. Rijkers, Dr. O. Schijns, Prof. Y. Temel.
POSTDOCS:	Dr. S. Hescham, Dr. S. Michielse, Dr. C Herff, Dr. J-P Frimat.
PHD-STUDENTS:	A. Smeets, T. Bouwens van der Vlis, M. Aldheri, L. Huawei, R. Haeren, F. Schaper, F. Alosaimi, S. Pol, M. Roet, J. Smit, M. Bos, F. Almasabi, G. van Zwieten, J. Habets, M. Heijmans, A. Wolters, M. Alahmari, R. Assmann, C. Vanderheijden, F. Gubler, B. Isaacs, A. Mulders, Y. Yakkioui, J Boonstra, G. Son, R. van Lanen, M. Zhang, M. Raijmakers, J. Sloekers, J. Kellenaers, M.Ottenhoff (sep 19), R. Siddha.
RESEARCH INTERESTS:	Neuromodulation, Basal Ganglia, Epilepsy, Neural circuits, Neurodegeneration, Neurogenesis, Neuroanatomy, Brain-on-a-chip, Blood-brain barrier, BCI, cost-effectiveness.

The experimental neurosurgery group has developed over the last decades. Currently, more than 20 PhD students are trained under the guidance of several senior researchers. These experts are neuroscientists with different backgrounds, ranging from neurobiologist and neurophysiologists, to clinical neurophysiologists, neurologists and neurosurgeons.
The focus of the research group is to make progress in neuromodulative treatments of neurological and psychiatric disorders, and in neurosurgical treatment of drug-refractory epilepsy. Several lines of investigation are conducted. This research is conducted in both human and preclinical studies.
These lines of research are supported by grants from the ZonMw, NWO, transnational University Limburg, Prosensa BV, Medtronic, Hersenstichting Nederland, Stichting Weijerhorst, Stichting St. Annadal, and Saudi Ministry of Health.
The research is organized in three themes within the experimental neurosurgery group, namely the Fundamental Neuromodulation, Clinical Neuromodulation and Epilepsy.
The fundamental neuromodulation line focuses on investigating the mechanisms behind the effects and side-effects of neuromodulation therapies using experimental animal models. Moreover, this line aims to develop novel neuromodulation approaches, as well as modifying and optimizing the effectiveness of existing neuromodulation approaches.
The focus of the **clinical neuromodulation** research line is to make progress in neuromodulative treatments in neurological and psychiatric disorders. Several lines of investigation are conducted: 1) Novel neuromodulative techniques are tested in early phases of development. 2) New applications are investigated. 3) Novel DBS paradigms are developed, like adaptive or closed loop DBS 4) Optimization of the DBS target is investigated by ultrahigh field MR imaging and electrophysiological techniques. 5) Development of new paradigms for brain computer interfacing, e.g. to decode speech or to restore motor function using invasively recorded brain signals.
Finally, the **epilepsy** research line aims at improving the selection and treatment of drug-refractory focal epilepsy patients who are eligible for neurosurgical treatment. To this end, histopathologic, genetic, neurophysiologic and imaging techniques are applied. This line includes research on intraoperatively collected human brain specimesn (biobank) as well as animal models of epilepsy. Evaluating cost-effectiveness of DBS and resective epilepsy surgery are also part of this research line. Finally, we are developing an animal-free, translational model for physiological experiments in the human 3D brain.

4. NEUROMODULATION:	4.2 MODULATION OF CHRONIC PAIN
COORDINATOR:	Prof. B. Joosten.
RESEARCH STAFF:	Prof. W. Buhre, Prof. J. van Zundert, Dr. M. Sommer; Dr. H. Gramke, Prof. M. van Kleef, Dr. D. de Korte, Dr. N. de Meij, Prof. D. Linden.
POSTDOCS:	Dr. N. van den Hoogen, Dr. A. Balthasar, Dr. C. Vossen.
PHD-STUDENTS:	A.R. de Kort, R. van Reij, M. Mons, G. Franken, P. Douven, E. Koetsier; P. Maino, L. Heijmans, A. Lucas, V. Wintraecken, T. van Neste, A. Tottungal, M. Homberg, M. Bos.
EXTERNAL COLLABORATORS:	Prof. S. Eldabe (University Hospital, Newcastle, UK), Prof. Chi Wai Cheung (HKU, Hong-Kong); Prof. D. Tibboel and Dr. S. Simons (Sophia Hospital and Erasmus University), Prof. B. Linderoth (Karolinska , Stockholm, Sweden), Dr. T. Trang (Hotchkiss institute, Calgary, Canada), Prof. G.J Scheffer and Prof. K. Vissers (Radboud University).
FOCUS OF RESEARCH:	Line 1: Neuromodulation and Interventional Pain Management in Neuropathic Pain (Prof. J. van Zundert, Prof. B. Joosten; research coordinator: Dr. N. de Meij). Line 2: Perioperative Management (Prof. W. Buhre, Prof. B. Joosten; researchcoordinator: Dr. D. de Korte).

Line 1: Neuromodulation and Interventional Pain Management in Neuropathic Pain. Research focused at further insights into mechanisms of pain relief of interventional techniques like spinal cord stimulation (spinal cord stimulation, SCS) or pulsed radio-frequent lesions (PRF). This research is both fundamental and translational and a close interaction between the Pain Clinic (Prof. J. van Zundert) and the Laboratory Exp. Anesthesiologie and Pain Management of the Dept. Anesthesiologie (PI: Prof. B. Joosten). It is aimed to improve treatment of chronic neuropathic pain based on mechanism related insights of interventional treatments. Fundamental, preclinical insights are immediately implemented into clinical studies. Focus is on peripheral neuropathies. Fundamental research is embedded within the NeuroIntervention Centrum (NIC) where collaboration between Exp. Anesthesiologie and Pain Management (Dept. Anesthesiologie), Dept. Surgery and Dept. Urology started in 2017 (PhD project P. Douven).

Line 2: Perioperative Management. Research within this line deals with the prediction and/or treatment of perioperative complications with focus at pain treatment and chronification of postoperative pain. This is part of the care path Pain (conveners: Prof. K. Faber (Dept. Neurology) and Prof. B. Joosten (Dept. Anesthesiology)) as defined within the research school of Mental Health and Neuroscience (MHeNS) and the Brain Nerve Centre (BNC).

Within this line cross-sectional research is developed between the research theme Pain and the following research-lines in the BNC:
1. Genetics. Subject: Chronification of postoperative pain and genetics (R. van Reij; with Dept. Psychiatry; Prof. B. Rutten))
2. Modulation. Subject: Prediction and treatment of postoperative pain (A. Lucas and Dr. N. van den Hoogen; with FPN, Prof. M. Peeters)
3. Imaging. Subject: Neurofeedback in treatment of postoperative pain (C. Vossen; with Prof. D. Linden; with FPN, Dr. A. Kaas)
4. Monitoring. Subject: Perioperative pain monitoring (Dr. A. Balthasar; with FPN Prof. F. Peeters; with Dept. Neurology, Prof. K. Faber)

The lab. Exp. Anesthesiology and Pain Management further extends and focusses research on implementation and development of promising new techniques like spinal electrophysiology (Dr. T. Trang, Calgary, Canada), pain brain analysis using full-brain mass spectrometry (M4I, Prof. R. Heeren), new operant pain tests for rodents (Noldus, Wageningen) or zebrafish modelling for nociception and development and screening of new pain medication (with Prof. B. Smeets).

4. NEUROMODULATION:	4.3 FUNCTIONAL NEURO-UROLOGY
COORDINATOR:	Prof. G.A. van Koeveringe.
RESEARCH STAFF:	Prof. Ph. van Kerrebroeck, Dr. D. Vrijens.
POSTDOCS:	Dr. S. Schipper, Dr. M. Rahnama'i.
PHD-STUDENTS:	R . Jairam, J. Drossaerts, D., P. Douven, M. de Rijk, M. Reekmans, A. Herrewegh.
FOCUS OF RESEARCH:	Neuro-Urology: Lower urinary tract signalling, control mechanisms and neuromodulation.

The research focus is directed towards fundamental understanding of bladder and lower urinary tract physiology, pharmacology and the origins and treatment of lower urinary tract dysfunction. Four project lines are ongoing in order to study different levels of bladder dysfunction in a translational research programme based in the Research School for Mental health and Neuroscience, The Brain and Nerve Centre (BNC), the MUMC+ profile Neurosciences and in close association with the clinical urology department and the Pelvic Care Centre Maastricht.

Line 1: Basic research line on the connection between Bladder and Brain. Using neurophysiological, neurochemical and tracing techniques the connection between bladder, lower urinary tract and the brain is studied.
Line 2: Functional Imaging of the bladder brain connection. Using high-field MRI imaging facilities in Scannexus, both brain and spinal cord areas are studied in relation to stimuli in and disorders of the lower urinary tract.
Line 3: Neuromodulation as treatment of lower urinary tract disorders: both for under and overactive bladder and sphincter disorders. To improve the techniques of neuromodulation basic research using animal models is done in a multidisciplinary fashion as well as clinical research is done to improve stimulation techniques and devices. Care pathways and specialized diagnostic approaches are also studied in this research line in close collaboration with other partners in the BNC.
Line 4: Psychological, psychiatric and behavioural aspects in relation to disorders of urinary control and sensory aspects of the pelvic organs. In this research line aspects to improve detection and diagnosis of Lower urinary tract disease for example using Momentary assessment tools are studied. In addition, disturbed sensation in the pelvis and lower urinary tract due to psychological and psychophysiological comorbidity or effects such as alarm falsification and catastrophizing behavior are studied in collaboration within MHeNS and with external partners in basic research with animal models. Translational research links are studied in the clinical situation.

4. NEUROMODULATION:	4.4 OPHTHALMOLOGY
COORDINATOR:	Prof. C. Webers.
RESEARCH STAFF:	Prof. R. Nuijts, Dr. H. Beckers, Dr. T. Berendschot, Dr. T. Gorgels.
PHD-STUDENTS:	A. Tan, M. Elshout, M. Dickman, L. Wielders, J. Hoevenaars, H. Römkens, N. Makhotkina, S. Zhang, S. Jonker, W. Hubens, C. Bertens, R. Simons, P. Mokhles, V. Webers, J. Brekelmans, I. Liesenborghs, S. Dunker, F. van der Heide, L. Spekreijse, N. Pahuja, A. Mohan, P. Sarbanja, M. Francis, S. Mohan, N. Shetty, K. Nagpal, Z. Pradhan, R. Battu, R. Teja, A. Abhishek.
FOCUS OF RESEARCH:	Scientific research focuses on glaucoma, corneal diseases and cataract and ocular neurodegenerative changes in diabetes and other chronic diseases.

Research is primarily clinical in nature, with a direct impact for patients (clinical trials, clinical decision models) and society (efficiency research and cost effectiveness models). Research results contribute directly to sustainable care by preventing diseases and by controlling growth in care costs thanks to cost effective solutions. Further, abnormalities of both neural and vascular tissues are directly measurable in the living eye.

Research is concentrated along the following lines:
Glaucoma: Modelling (identification of risk factors for disease progression), imaging (anterior chamber morphometry, nerve tissue analysis) and the development of new treatment strategies (glaucoma filtration implant). In addition, basic studies on retinal ganglion cells, trabecular meshwork and aqueous humour aim to discover the molecular pathology of glaucoma and to design new (neuroprotective) treatments. Omics research and systems biology are used to integrate findings.

Cataract and Refractive Surgery: Development of innovative cataract surgical technologies such as femtosecond laser assisted cataract surgery. Development of biomaterial applications for sustained release of drugs. Improvement of presbyopia correction using adaptive optics and toric (multifocal) intraocular lenses, intracorneal inlays and scleral implants.
Corneal Transplantation: Optimizing lamellar corneal surgery for diseases of the cornea and development of regenerative medicine models using corneal stem cells and biomaterial technology.
Prevention: Development of retinal vascular analysis for early detection and monitoring of diseases such as diabetic retinopathy, age related macular degeneration and Alzheimer's disease and research into the influence of diet in these diseases.

The Maastricht study: In a large epidemiological cohort study diabetes patients and controls are measured with state of the art measurement modalities to study causes and consequences of diabetes and other chronic diseases. Imaging techniques of the optic nerve, cornea and retina will provide new insights into neurodegenerative changes in these syndromes.

4. NEUROMODULATION:	4.5 NEONATOLOGY, DEVELOPMENTAL NEUROSCIENCE, MITOCHONDRIAL DISEASE
COORDINATORS:	Prof. B. Kramer, Dr. A. Gavilanes, Prof. B. Smeets
RESEARCH STAFF:	Prof. H. Steinbusch, Prof. L. Zimmermann, Prof. J. Vles, Dr. D. van den Hove, Dr. T. Wolfs, Dr. Markus Müller, Prof. B. Rutten.
PHD-STUDENTS:	M. Seehaase, J. Heiter, L. Klein, M. Cetinkaya.
EXTERNAL COLLABORATORS:	D.r Florence van Tienen, Dr Jo Vanoevelen.
FOCUS OF RESEARCH:	Asphyxia and inflammation.

The department of Paediatrics continued its research line on perinatal hypoxia-ischemia in newborn rats and preterm sheep and in patient studies. Multiple approaches to treat brain injury were studied (and discussed in invited reviews):
In the past years, we have developed an understanding of the effects of hypoxia-ischemia on the immune system of the exposed foetus with profound modulation of inflammatory responses. We studied the effects on isolated astrocytes in a cell culture model of hypoxia and glucose deprivation. We published two key papers in the pursuit of translating the identified mechanisms of disease into clinical care. We tested a clinical grade stem cell product which is already in clinical trials in our model of hypoxia-ischemia in preterm lambs where we could show a neuroprotective effect on brain function and baroreceptor reflex. These findings substantiate the possibility of stem cells in the treatment of brain injury after hypoxiaischemia. We also investigated the possibilities of a postnatal treatment for neuroprotection by administering propofol after hypoxia-ischemia. Propofol protected the newborn brain against hypoxic ischemic brain injury. Two new aspects were recently developed when we studied the innervation of the fetal gut after antenatal exposure to inflammation. We hypothesize that the innervation of the gut is impaired after antenatal inflammation. The second aspect is epigenetic changes that antenatal inflammation induces in the fetal brain, which we explore in vivo and in vitro.

Due to rapid developments in next-generation sequencing and other -omics technologies it has become much easier to define the genetic cause in monogenic mitochondrial diseases. A joint diagnostic and research effort identified by whole exome sequencing (WES) the genetic defect in 2/3 of a selected mitochondrial disease cohort. Although we were able, based on two gene defects identified, to develop a life-saving treatment (SLC19A3 – Thiamine, ACAD9 – Riboflavin), this is not the case for the majority of patients. Therefore, we aim to develop a generic stem-cell-based strategy to treat the common myopathy of mtDNA patients. We use autologous muscle stem-cells, called mesoangioblasts, which proliferate well in culture, can be injected in the blood stream and migrate out of the blood vessel to repair damaged muscle. Patients with the m.3243A>G mtDNA mutation in muscle have mesoangioblasts, which are largely mutation-free and ready to be used for therapy. A phase I/II clinical trial in this patient group is in the preparation phase. Our approach can be extended to patients suffering from atrophy from disuse or ageing or as comorbidity from stroke or cancer, and to patients with nuclear genetic muscle disease following CRISPR/Cas9 correction of the gene defect. The central role mitochondria play in many physiological processes and ageing, combined with the availability of patient material with defects in different mitochondrial pathways allows us to study the role of mitochondrial deficiencies in common disease and traits, like glaucoma, pain, cognitive dysfunction, including 7T MRI, and radiation induced lung toxicity, We combine iPSC technology to study tissue-specific manifestation in humans with zebrafish as a vertebrate model.

EDUCATION

The training of Master and PhD students in the area of neuroscience and related medical 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.

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):

- Research Master in Cognitive and Clinical Neuroscience
- Research Master Physician-Clinical Investigator (AKO)
- Master Biomedical Sciences (BMS)

MHeNs is the coordinator of the International Master of Affective Neuroscience, a postgraduate joint degree master program from the Universities of Maastricht and Florence (Italy).

Personnel for these programs is provided by the complementary educational capacity granted by the FHML Educational Institute, which is awarded by departments to qualified staff members. In 2018 in the dept. of Psychiatry and Neuropsychology alone, almost half of the educational activities were associated with the master programs, particularly with the Research Master in Cognitive and Clinical Neuroscience.

PHD PROGRAM:

In 2018 (reference date 25 Nov.) MHeNs had in total 305 registered PhD candidates, of whom were employed by MHeNs as regular PhD students. Furthermore, there are 206 external 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 receive a MHeNs educational certificate. The PhD students formulate and regularly update their personal research and training & supervision 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. The PhD student program of MHeNs has a strong multidisciplinary character and is embedded within the European Graduate School of Neuroscience (EURON).

SUMMARY

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). 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 annually the theoretical and practical 4 days course on "Human Neuroanatomy to Psychopathology" in which many staff members of MHeNs are involved. 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 MHeNs and EURON certificates. Many of these collaborations concern mutual PhD projects and often result in a joint or double PhD degree.

History of the MHeNs course "Human Neuroanatomy to Psychopathology"

The MHeNs course "Human Neuroanatomy to Psychopathology" started 11 years ago (2008) as a 5 days meeting initiated by Prof. Harry B.M. Uylings (visiting Professor) and organized in collaboration with Prof. Harry Steinbusch, Prof. Jos Prickaerts and Dr. Nicole Senden. This first course was entitled "Course on Functional Human Neuroanatomy and Cognition: From Development to Aging".
Currently, the workshop is a 4-day course but has expanded in content and in involvement of experts from MHeNs and EURON. The course introduces the basic concepts of neuroanatomy, functional neuroanatomy and neuropathology and links this knowledge to the neurobiological underpinnings of neurological, neuropsychiatric and neurodegenerative disorders.
Since the first course, the hands-on dissection of a human brain has been a pivotal aspect of the workshop, and has been very well evaluated by the participants throughout all editions.
Next to the macroscopical hands-on training, a microscopical practical was integrated in combination with a visit to the M4I Division of Nanoscopy (FHML), and theoretical and practical experience with functional and structural MRI methodologies became an intensive part of the 4 days program ever since. The course program is focused on linking human neuroanatomy to the clinical expression of brain disorders and their treatment.
Since 2019 an important part is to show the anatomy in health and disease (through microscopy) directly linked to imaging.
Since 2013, each year a renowned keynote speaker has been invited to provide a lecture on a relevant topic.
After the guidance of Prof. Uylings for two years, MHeNs staff took over its organization. During the period 2010 – 2015 the organizers Prof. Jos Prickaerts, Prof. Bart Rutten, Dr. Pauline Aalten, Prof. Harry Steinbusch and Dr. Nicole Senden involved experts and multidisciplinary teaching staff from MHeNs (researchers as well as clinicians) and the Faculty of Psychology and Neuroscience. In addition, the teaching cacacity was boosted by collaborating with the Dept. of Anatomy, Dr. Ulrike Von Rango and Prof. Andreas Herrler and by involving experts in histology and anatomy from the EURON participating universities RWTH Aachen University, Hasselt University and UCLouvain. As such, the course benefits from involving leaders in the field, recruited from the broad MHeNs network.
In 2016 another organizing committee took over the responsibilities (Dr. Heidi Jacobs, Dr. Ali Jahanshahi, Dr. Jörg Mey). Since 2017/2018 the responsible persons are Dr. Jörg Mey, Dr. Ali Jahanshahi, Prof. Boris Kramer, Dr. Gunter Kenis, Dr. Nicole Senden and Prof. David Linden. The course is since 2018 one of the basic courses of the EURON educational program.

Overview of past TTN workshops

2010	1. Psychiatric and somatic comorbidity– Prof. Jim van Os; Prof. Brian Leonard
	2. Schizophrenia: from Gene to Behaviour – Prof. Jim van Os; Prof. Brian Leonard
2011	3. Pain and Pain Modulation – Prof. Bert Joosten
2012	4. Lifelong Ageing – Dr. Pauline Aalten; Dr. Martin van Boxtel
	5. Approaches to studying gene-environment interactions – Prof. Koen Schruers; Dr. Marjan Drukker; Dr. Ruud van Winkel
2013	6. Controlling Brain Function – Prof. Jos Prickaerts; Dr. Daniel van den Hove; Prof. Yasin Temel
	7. Blood Brain Barrier: a key player in the etiology and treatment of mental and neurological disorders – Prof. Robert van Oostenbrugge; Dr. Saartje Burgmans
2014	8. Waking up the brain: Mechanisms of aurousal in health and disease – Prof. Koen Schruers; Dr. Daniel van den Hove
2015	9. When the brain is under attack: Auto-antibodies and neurotransmitters as key player in neurological and psychiatric diseases – Prof. Pilar Martinez; Dr. Carolin Hofmann
2016	10. Recovery after stroke: a translational perspective - Prof. Carolien van Heugten; Dr. Martin van Boxtel
2017	11. Studying Experience and Behaviour in Neuroscience: Methods and Challenges – Prof. Jim van Os, Dr. Gunter Kenis
2018	12. Stress, depression and Alzheimer's Disease – Dr. Daniel van den Hove
2019	13. Pain and Comorbidities – Prof. Bert Joosten; Dr. Nynke van den Hoogen; Roel van Reij (PhD candidate)

History of the MHeNS Workshops "Topics in Translational Neuroscience (TTN)"

MHeNs has set up the framework of a series of workshops called "Topics in Translational Neuroscience" since 2009. The motivation for organizing these integrative workshops is to continuously improve the cohesion and interdisciplinarity of research training across the three MHeNs divisions (Cognitive Neuropsychiatry and Clinical Neuroscience, Mental Health, and Translational Neuroscience).
With the TTN workshops, MHeNs aims: (1) to broaden the theoretical perspective of young scientists in the three MHeNS divisions, going beyond their own research topics; (2) to stimulate interdisciplinary research approaches and collaborations and (3) to stimulate interaction among PhD students with diverse backgrounds
The initiators in 2009 were Dr. Nancy Nicolson, Prof. Harry Steinbusch and Dr. Nicole Senden. Since 2016 Dr. Martin van Boxtel took over the responsibilities from Nancy Nicolson and since 2018 Prof. David Linden is involved. The different workshops are organized alternately in collaboration with staff members of one division. Over the years, the course set-up has evolved to offer the most optimal teaching experience from a PhD student perspective. Currently, the established framework is as follows:

- frequency: optimal twice a year.
- format: full-day workshop, given entirely in English, with interactive lectures by experts in the morning and small-group projects plus plenary presentations and discussion in the afternoon.
- topics: research areas that should interest beginning and advanced level PhD students across all three MHeNS divisions. Each workshop should highlight translational research approaches, i.e. "from bench to bedside" and back.
- instructional approach: participants study assigned literature in advance and prepare for small-group projects. On the day of the workshop, expert lecturers present new information during interactive presentations. Participants then integrate material from provided readings, the lectures, and their own scientific background by working in sub-groups on an assignment. Expert "moderators" are available throughout the day to guide and assist the workgroups. The last part is reserved for short presentations by the subgroups, followed by plenary discussion led by the moderators.
- credits: participants who are adequately prepared, show active participation and attend the entire workshop receive one credit (28 hours) towards their PhD educational requirement for the MHeNs and EURON certificate.

FACTS AND FIGURES

The year 2018 was again a very successful for MHeNs in terms of scientific output.
In addition grant income, number of PhD theses and number of high impact publications are all showing a trend upwards.
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, additional direct funding became available.
As a result MHeNs was able to invest in talented tenured and tenured-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.
The increasing level of external grant capture is promising and sets amibitions for 2019 and further.

KEY FIGURES 2018

ANNUAL BUDGET: 13.063 K€

NEW CONTRACTS AND GRANTS: 6.036 K€

RESEARCHERS: 136,4 FTE (INCL. 84 FTE INTERNAL PHD STUDENTS)

TECHNICAL AND SUPPORTING STAFF: 22,7 FTE

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

SCIENTIFIC ARTICLES: 518 (WI-1 PUBLICATIONS)

PHD THESES: 52

PATENTS/SPIN-OFFS: 4

TOP PUBLICATIONS

COGNITIVE NEUROPSYCHIATRY AND CLINICAL NEUROSCIENCE

High-resolution in vivo imaging of human locus coeruleus by Magnetization Transfer MRI at 3T and 7T
Priovoulos, N., Jacobs, H. I. L., Ivanov, D., Uludag, K., Verhey, F. R. J. & Poser, B. A.,
Mar 2018, In : Neuroimage. 168, p. 427-436 10 p.

Course of Social Participation in the First 2 Years After Stroke and Its Associations With Demographic and Stroke-Related Factors
Verberne, D. P. J., Post, M. W. M., Köhler, S., Carey, L. M., Visser-Meily, J. M. A. & van Heugten, C. M.,
Sep 2018, In Neurorehabilitation and Neural Repair. 32, 9, p. 821-833 13 p.

Association of Cerebral Amyloid-β Aggregation With Cognitive Functioning in Persons Without Dementia
Amyloid Biomarker Study Grp, Jansen, W. J., Ossenkoppele, R., Tijms, B. M., Fagan, A. M., Hansson, O., Klunk, W. E., van der Flier, W. M., Villemagne, V. L., Frisoni, G. B., Fleisher, A. S., Lleo, A., Mintun, M. A., Wallin, A., Engelborghs, S., Na, D. L., Chetelat, G., Molinuevo, J. L., Landau, S. M., Mattsson, N. & 31 others Kornhuber, J., Sabri, O., Rowe, C. C., Parnetti, L., Popp, J., Fladby, T., Jagust, W. J., Aalten, P., Lee, D. Y., Vandenberghe, R., de Oliveira, C. R., Kapaki, E., Froelich, L., Ivanoiu, A., Gabryelewicz, T., Verbeek, M. M., Sanchez-Juan, P., Hildebrandt, H., Camus, V., Zboch, M., Brooks, D. J., Drzezga, A., Rinne, J. O., Newberg, A., de Mendonca, A., Sarazin, M., Rabinovici, G. D., Madsen, K., Kramberger, M. G., Verhey, F. R. J. & Visser, P. J.,
1 Jan 2018, In : JAMA Psychiatry. 75, 1, p. 84-95 12 p.

Baseline Vascular Cognitive Impairment Predicts the Course of Apathetic Symptoms After Stroke: The CASPER Study
Douven, E., Kohler, S., Schievink, S. H. J., van Oostenbrugge, R. J., Staals, J., Verhey, F. R. J. & Aalten, P.,
1 Mar 2018, In : American Journal of Geriatric Psychiatry. 26, 3, p. 291-300 10 p.

Quality of Life, Care Resource Use, and Costs of Dementia in 8 European Countries in a Cross-Sectional Cohort of the Actifcare Study
ActifCare Consortium, Handels, R. L. H., Skoldunger, A., Bieber, A., Edwards, R. T., Goncalves-Pereire, M., Hopper, L., Irving, K., Jelley, H., Kerpershoek, L., Marques, M. J., Meyer, G., Michelet, M., Portolani, E., Rosvik, J., Selbaek, G., Stephan, A., de Vugt, M., Wolfs, C., Woods, B. & 3 others Zanetti, O., Verhey, F. & Wimo, A., 1 Jan 2018, In : Journal of Alzheimer's Disease. 66, 3, p. 1027-1040 14 p.

MENTAL HEALTH

Neuroendocrine stress responses predict catecholamine-dependent working memory-related dorsolateral prefrontal cortex activity
Hernaus, D., Quaedflieg, C. W. E. M., Offermann, J. S., Santa, M. M. C. & van Amelsvoort, T.,
1 Jan 2018, In : Social Cognitive and Affective Neuroscience. 13, 1, p. 114-123 10 p.

Relationship between muscarinic M-1 receptor binding and cognition in medication-free subjects with psychosis
Bakker, G., Vingerhoets, C., Boucherie, D., Caan, M., Bloemen, O., Eersels, J., Booij, J. & van Amelsvoort, T.,
1 Jan 2018, In : NeuroImage: Clinical. 18, p. 713-719 7 p.

Prescription and Underprescription of Clozapine in Dutch Ambulatory Care
van der Zalm, Y. C., Termorshuizen, F., Schulte, P. F., Bogers, J. P., Marcelis, M., Sommer, I. E. & Selten, J. P.,
11 Jun 2018, In : Frontiers in Psychiatry. 9, 7 p., 231.

Evidence That Environmental and Familial Risks for Psychosis Additively Impact a Multidimensional Subthreshold Psychosis Syndrome
Pries, L-K., Guloksuz, S., ten Have, M., de Graaf, R., van Dorsselaer, S., Gunther, N., Rauschenberg, C., Reininghaus, U., Radhakrishnan, R., Bak, M., Rutten, B. P. F. & van Os, J.,
6 Jun 2018, In : Schizophrenia Bulletin. 44, 4, p. 710-719

The Relative Impact of Traumatic Experiences and Daily Stressors on Mental Health Outcomes in Sri Lankan Adolescents
Ponnamperuma, T. & Nicolson, N. A.,
1 Aug 2018, In : Journal of Traumatic Stress. 31, 4, p. 487-498 12 p.

TRANSLATIONAL NEUROSCIENCE

Neuronal Activation in the Periaqueductal Gray Matter Upon Electrical Stimulation of the Bladder. Meriaux, C., Hohnen, R., Schipper, S., Zare, A., Jahanshahi, A., Birder, L. A., Temel, Y. & van Koeveringe, G. A., 18 May 2018, In : Frontiers in Cellular Neuroscience. 12, 18 p., 133.

Long-term Outcomes of Repeated Corneal Transplantations: A Prospective Dutch Registry Study. Dickman, M. M., Spekreijse, L. S., Dunker, S. L., Winkens, B., Berendschot, T. T. J. M., van den Biggelaar, F. J. H. M., Kruit, P. J. & Nuijts, R. M. M. A., Sep 2018, In : American Journal of Ophthalmology. 193, p. 156-165 10 p.

Assessing spatial pattern separation in rodents using the object pattern separation task. van Goethem, N. P., van Hagen, B. T. J. & Prickaerts, J., 1 Aug 2018, In : Nature Protocols. 13, 8, p. 1763-1792 30 p.

Longitudinal analyses of the DNA methylome in deployed military servicemen identify susceptibility loci for post-traumatic stress disorder. Rutten, B. P. F., Vermetten, E., Vinkers, C. H., Ursini, G., Daskalakis, N. P., Pishva, E., Nijs, L., Houtepen, L. C., Eijssen, L., Jaffe, A. E., Kenis, G., Viechtbauer, W., van den Hove, D., Schraut, K. G., Lesch, K-P., Kleinman, J. E., Hyde, T. M., Weinberger, D. R., Schalkwyk, L., Lunnon, K. & 8 others Mill, J., Cohen, H., Yehuda, R., Baker, D. G., Maihofer, A. X., Nievergelt, C. M., Geuze, E. & Boks, M. P. M., 1 May 2018, In : Molecular Psychiatry. 23, 5, p. 1145-1156 12 p.

Severity of Neuropathy Is Associated With Long-term Spinal Cord Stimulation Outcome in Painful Diabetic Peripheral Neuropathy: Five-Year Follow-up of a Prospective Two-Center Clinical Trial. van Beek, M., Geurts, J. W., Slangen, R., Schaper, N. C., Faber, C. G., Joosten, E. A., Dirksen, C. D., van Dongen, R. T., van Kuijk, S. M. J. & van Kleef, M., 1 Jan 2018, In : Diabetes Care. 41, 1, p. 32-38 7 p.

PHD THESES 2018

Last name	Initials	Theses defence	Promotor	Copromotor	Title Theses
Altinbas	K.	22–03–2018	Prof. Dr. J. van Os	Dr. I.S. Guloksuz	*Reconstructing The Diagnostic Framework of Bipolarity*
Bakker	J.	24–05–2018	Prof. Dr. I. Myin-Germeys (KU Leuven), Prof. Dr. M. Wichers (UMCG)	Dr. L. Goossens	*On the bumpy road of happiness: mechanisms of daily life reward processing and how it can be changed*
Balthasar	A.	23–03–2018	Prof. Dr. M. van Kleef	Dr. G-J. van Geffen (RUMC)	*Eyes of the needle; Spectral tissue sensing, an innovative technology for detecting various tissue types during percutaneous needle-based procedures in locoregional anesthesia and pain medicine*
Berg van de	R.	20–09–2018	Prof. Dr. H. Kingma	Dr. J.-P. Guyot (Universite de Geneve, Swi)	*The Vestibular Implant: Feasibility in humans*
Bos	I.	10–12–2018	Dr. P.J. Visser, Prof. Dr. F. Verhey	Dr. S. Vos	*Biomarkers of Alzheimer's disease: Relations with vascular factors and cognition in the pre-dementia stages*
Breuer	L.	22–11–2018	Prof. Dr. A. Aldenkamp, Prof. Dr. P. Boon (UZ Gent)	Dr. A. de Louw (Kempenhaeghe), Dr. Ir. S. Zinger (TUE)	*Accelerated Cognitive Ageing in Epilepsy' Does it Exists?*
Chaitanya	G.	26–02–2018	Prof. Dr. A.P. Aldenkamp, Prof. Dr. P. Satishchandra (NIMHANS, India)	Dr. J. Jansen, Dr. S. Zinger (TUE)	*Epilepsy: A network disorder*
Dam	A.	25–10–2018	Prof. Dr. M. de Vugt, Prof. Dr. F. Verhey	Dr. M. van Boxtel	*INLIFE; An innovative online social support intervention for caregivers of persons with dementia*
Diniz	G.	18–12–2018	Prof. Dr. H. Steinbusch, Prof. Dr. J. Bittencourt (ICB/USP)		*Weaning-induced alterations on neuroeptidergic populations of the rat hypothalamus*
Duin van	E.	15–11–2018	Prof. Dr. T. van Amelsvoort, Prof. Dr. J. Booij (UvA)	Dr. D. Hernaus	*Dancing in the (B)rain'; neurobiology of reward, stress & Information processing in 22q11.2 deletion syndrome*
Fabbri	C.	14–11–2018	Prof. Dr. K. Schruers, Prof. Dr. A. Serretti (Bologna)		*Pharmacogenomics of anti-depressant drugs: perspectives for the personalization of treatment in depression*
Freeze	W.	28–06–2018	Prof. Dr. F. Verhey, Prof. Dr. Ir. W. Backes	Dr. H. Jacobs	*Microvascular contributions to dementia: Exploring the role of blood-brain barrier leakage in cerebral small vessel disease and Alzheimer disease*
Guinand	N.	20–09–2018	Prof. Dr. H. Kingma	Dr. J.-P. Guyot (Universite de Geneve, Swi)	*The Vestibular Implant: a more stable horizon for patients with a bilateral vestibular deficit?*

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Gupta	L.	03–08–2018	Prof. Dr. Ir. W. Backes, Prof. Dr. P. Hofman	Dr. J. Jansen	*Inhomogeneities in spontaneous brain fluctuations*
Haeren	R.	26–10–2018	Prof. Dr. Y. Temel	Dr. K. Rijkers, Dr. G. Hoogland	*Vascular ventures; Analysis of vascular structures and function in epilepsy*
Hoffmann	C.	20–04–2018	Prof. Dr. P. Martinez, Prof. Dr. B. Rutten, Prof. Dr. J. van Os		*The Brain under Attack: Autoantibodies in Psychotic Disorders*
Hoofwijk	D.	09–05–2018	Prof. Dr. W. Buhre, Prof. Dr. E. Joosten	Dr. H.-F. Gramke, Dr. A. Fiddelers	*The way to understanding Chronic Postsurgical Pain; From clinical and psychological predictors to incorporating genetics*
Hoogen van den	N.	04–06–2018	Prof. Dr. E. Joosten, Prof. Dr. D. Tibboel, Erasmus	Dr. J. Patijn	*Repetitive painful procedures in the neonate: treatment and adult pain sensitivity*
Iatrou	A.	07–12–2018	Prof. Dr. B. Rutten	Dr. D. van den Hove, Dr. G. Kenis	*Epigenetics in mental and neurodegenerative disorders; The unusual suspects*
Jayadev	C.	16–03–2018	Prof. Dr. C. Webers	Dr. N. Bauer, Dr. A. Vinekar	*Impact of imaging the pediatric retina*
Jong de	M.	18–05–2018	Prof. Dr. F. Peeters	Prof. Dr. D. Mischoulon	*Between mood and matter; studies on the interface between mood disorders and physical conditions*
Kemna	M.	07–05–2018	Prof. Dr. J. Cohen-Tervaert	Dr. J. Damoiseaux, Dr. P. van Paasen	*Predicting relapses in ANCA associated vasculitis*
Kerpershoek	L.	12–07–2018	Prof. Dr. F. Verhey, Prof. Dr. M. de Vugt, Prof. B. Woods (Bangor University)	Dr. C. Wolfs	*Access to formal dementia care; A European perspective*
Klippel	A.	21–03–2018	Prof. Dr. I. Myin-Germeys (KU Leuven), Prof. Dr. M. Wichers (UMCG)	Dr. U. Reininghaus	*Navigating through complexity; processes and mechanisms underlying the development of psychosis*
Leenen	L.	09–07–2018	Prof. Dr. H. Majoie, Prof. Dr. mr. S. Evers, Prof. Dr. C. van Heugten		*Self-management in Epilepsy; The Goal is: "Live with a Z(s)mile"*
Mehnert	U.	13–12–2018	Prof. Dr. G. van Koeveringe, Prof. Dr. Ph. van Kerrebroeck, Prof. Dr. S. Wachter (Antwerpen)	Prof. Dr. E. Chartier-Kastler (Paris)	*The management of urine storage dysfunction in the neurological patient*
Meij de	N.	06–07–2018	Prof. Dr. G. van der Weijden, Prof. Dr. M. van Kleef	Dr. A. Koke	*Quality indicators for the assessment of pain clinic care: A step forward? Quality from professionals and pain patients' perspective (QiPPP)*
Mentzel	T.	06–07–2018	Prof. Dr. P. van Harten, Prof. Dr. H. Daanen (VUA)	Dr. Mr. O. Bloemen (GGZ Hilversum)	*Capturing the cacophony of movement*
Mestres Gonzalvo	C.	04–12–2018	Prof. Dr. F. Verhey, Prof. Dr. P. van der Kuy, Erasmus MC Rdam	Dr. R. Janknegt, Zuyderland MC	*Medication optimisation; Methodological aspects and new strategies*
Michielse	S.	19–10–2018	Prof. Dr. J. van Os	Dr. M. Marceli	*Road work ahead; cerebral pathways mediating Psychological mechanisms underlying the psychosis spectrum*
Niemczyk	J.	23–10–2018	Prof. Dr. L. Curfs, Prof. Dr. A. von Gontard (Saarland University, Homburg)		*Incontinence in individuals with genetic syndromes associated with intellectual disability*
Paravil Sankaran	B.	21–09–2018	Prof. Dr. H. Smeets, Prof. Dr. A. Taly (NIMHANS)		*Brain MRI in Mitochondrial Disorders: Correlating the Phenotype with Genotype*
Peila	C.	09–12–2018	Prof. Dr. D. Gazzallo (Alessandria Ita/ MUMC+), Prof. Dr. G. Visser (UU), Prof. Dr. E. Bertino (Alessandria Ita.)		*Effects of Pasteurization and Refrigerated Storage on Human Milk Neurobiomarkers Concentrations*
Pilz	W.	29–03–2018	Prof. Dr. B. Kremer	Dr. L. Baijens, Dr. V. Lima Passos	*Shedding light on oropharyngeal dysphagia in myotonic dystrophy type 1*
Rajendrarao	S.	27–02–2018	Prof. Dr. B. Kramer, Prof. Dr. H. Steinbusch	Prof. T. Raju (NIMHANS, India)	*New Insight into the Multifaceted Pathogenic Mechanisms of Sporadic Amyotrophic Lateral Sclerosis*
Rao	H.	09–02–2018	Prof. Dr. C. Webers, Prof. Dr. R. Weinreb (UoC, San Diego)		*Revisiting the vascular theory of glaucoma using optical coherence tomography angiography*
Ravindra Battu	R.	21–12–2018	Prof. Dr. C. Webers	Dr. J. Schouten (CWZ Nijmegen), Dr. T. Berendschot	*Inherited Retinal Diseases: New Imaging and Molecular Genetics*
Reijs	B.	21–02–2018	Prof. Dr. F. Verhey	Dr. P.J. Visser, Dr. I. Ramakers	*Cognitive correlates ofcerebrospinal fluid biomarkers for Alzheimer's disease*
Roggeveen	S.	02–03–2018	Prof. Dr. J. van Os	Dr. R. Lousberg	*Interference of mobile phones with electrophysiology and emotions; results from short-term experimental studies*
Schievink	S.	10–05–2018	Prof. Dr. F. Verhey, Prof. Dr. R. van Oostenbrugge	Dr. S. Köhler	*Vascular cognitive impairment; at the heart of the matter*
Schoretsanitis	G.	22–10–2018	Prof. Dr. K. Schruers	Dr. M. Bak	*Risperidone-based therapeutic regimens; Drug interactions and adverse drug reactions*
Skowron	M.	06–07–2018	Prof. Dr. G. van Koeveringe, Prof. Dr. P. Albers (Dusseldorf)	Dr. J. van Roermund, Dr. A. Romano	*Cisplatin resistance in urothelial carcinoma; Understanding and targeting inherent and acquired mechanisms*

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Slangen	R.	21–02–2018	Prof. Dr. M. van Kleef, Prof. Dr. C. Dirksen, Prof. Dr. C. Faber		*Spinal cord stimulation in painful diabetic peripheral Neuropathy. Clinical- and cost-effectiveness*
Smeets	A.	06–01–2018	Prof. Dr. Y. Temel	Dr. L. Ackermans, Dr. A. Duits	*New insights in deep brain stimulation for Tourette syndrome*
Smit	J.	21–09–2018	Prof. Dr. R. Stokroos, Prof. Dr. Y. Temel	Dr. A. Jahanshahianvar	*Exploring deep brain stimulation as a treatment for tinnitus*
Steen van der	Y.	15–06–2018	Prof. Dr. I. Myin-Germeys (KU Leuven), Prof. Dr. R. van Winkel (KU Leuven)		*Dissecting the psychosis continuum; risk factors along the pathway from experiences tom disorder*
Steinhart	H.	12–12–2018	Prof. Dr. I. Myin-Germeys (KU Leuven)	Dr. U. Reininghaus	*Same Same but Different; Psychological Interventions and how to Mind the Knowledge Practice Gap*
Vaessen	T.	13–06–2018	Prof. Dr. I. Myin-Germeys (KU Leuven)		*Stress sensitivity in psychosis: assessment, mechanism & intervention*
Verdonschot	R.	15–11–2018	Prof. Dr. B. Kremer	Dr. L. Baijens, Dr. S. Vanbelle	*Oropharyngeal dysphagia and its psychiatric Comorbidities; The prevalence of affective symptoms and the unmet clinical need for integrated care in medically unexplained symptoms*
Vossen	C.	27–06–2018	Prof. Dr. E. Joosten, Prof. Dr. J. van Os	Dr. R. Lousberg	*Cortical processing of pain; the role of habituation*
Walter	M.	03–05–2018	Prof. Dr. Ph. Van Kerrebroek, Prof. Dr. G. van Koeveringe, Prof. Dr. A. Curt (Zurich, CH)		*Multi-methodological approaches to investigate lower urinary tract function in health and disease*
Weidner	M.	20–06–2018	Prof. Dr. H. Steinbusch, Prof. Dr. K.P. Lesch	Dr. D. van den Hove	*Brain serotonin throughout development - for better and for worse*
Wielders	L.	30–08–2018	Prof. Dr. R. Nuijts	Dr. J. Schouten (CWZ Nijmegen), Dr. B. Winkens	*Prevention & Treatment of Cystoid Macular Edema after Cataract Surgery*
Winkel van	M.	02–02–2018	Prof. Dr. F. Peeters, Prof. Dr. I. Myin-Germeys (KU Leuven), Prof. Dr. M. Wichers (UMCG)		*Lonely at heart and stressed in company of Others; the influence of daily life social experiences and emotions on depression*
Wong	S.	30–01–2018	Prof. Dr. W. Backes, Prof. Dr. R. van Oostenbrugge	Dr. J. Jansen	*Advances in Microvascular MRI Techniques: Breaking the Pathophysiological Barriers in Cerebral Small Vessel Disease*
Zare	A.	19–06–2018	Prof. Dr. G. van Koeveringe	Dr. A. Jahanshahianvar	*Unveiling the sensory connections between the bladder and the brain that involve the preaqueductal gray matter*

Contact information

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