ANNUAL REPORT 2020

SCHOOL FOR MENTAL HEALTH AND NEUROSCIENCE

Maastricht University
Faculty of Health, Medicine and Life Sciences

MH&NS

Maastricht University | Maastricht UMC+

CONTENT

Annexes*:

** Annexes only available on the website.*

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PREFACE
DAVID LINDEN

Photography: Maastricht UMC+

Prof David Linden
Scientific Director

School for Mental Health
and Neuroscience

Few would have predicted that one year on from our last Annual Report we would still be in the grip of the Covid-19 pandemic. My first task is to thank all those members of the MHeNs community who work in patient care at the Maastricht University Medical Centre (MUMC+) and beyond. They have faced a particularly challenging year and did a truly impressive job looking after Covid patients and keeping our hospitals, GP surgeries and ambulatory care facilities running throughout the pandemic. It was also impressive to see how, regardless of these challenges, our clinical departments carried through their important translational research projects, started up new clinical trials and conducted longitudinal assessments in our unique cohort studies.

2020 was also a challenging year for those not directly involved in patient care. Because of the necessary restrictions of access to University buildings most work (with the exception of essential lab work and face-to-face patient research) was done at home, and everyone missed the direct contact with colleagues and students. To make up for this, the divisions set up online social gatherings and moved the regular seminar series to online formats as well. The collaborative work in our different research groups actually progressed well and was, again, recognized and rewarded by a high level of grant capture from both national and international funders (€ 8.4M in new grants in 2020).

Of course, we had to cope with some delays of our research activities, for example because of limited laboratory occupancy or restrictions on patient research in the hospital setting. Those PhD students and postdoctoral researchers affected by these delays are being supported by the School and the Faculty in the necessary adjustments to their projects (and by extensions if needed). However, we have also been able to set up new projects specifically related to Covid-19, for example the NeNeSCo-study (Neurological & Neuropsychological Sequelae of COVID-19 Infection) funded by the Dutch Brain Fonds (Hersenstichting) coordinated by Caroline van Heugten. This project is an example of the intensifying collaboration between MHeNs and the Department of Intensive Care in the areas of neuromonitoring and prevention, treatment and rehabilitation of brain injury.

2020 was again a successful year for our Early Career Researchers. Two researchers started their VENI fellowships awarded by the NWO (Dutch Science Funding Organisation) at MHeNs. Willemijn Jansen (Division 1, Department of Psychiatry and Neuropsychology) is investigating the amyloid model of Alzheimer's disease using a range of biomarkers, with a particular focus on resilience against dementia. Mor Dickman from the Department of Ophthalmology/ University Eye Clinic (Division 3) is starting the project "Light for Sight", in which he will develop a novel treatment for progressive severe myopia. Our former VENI laureate Ali Jahanshahi received a VIDI fellowship that will enable him to develop a new semi-invasive

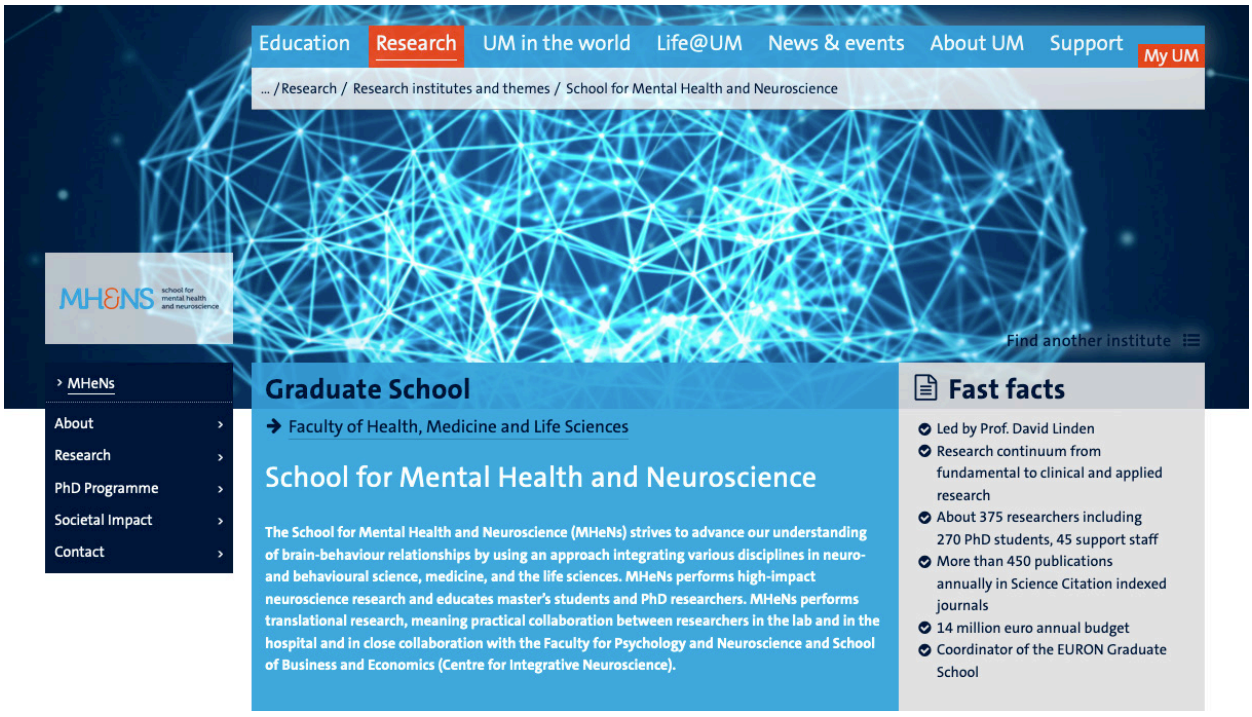
neuromodulation technique for Parkinson's disease based on magneto-electrical nanoparticles.

Two of our academic clinicians, Jacqueline Strik (Psychiatry) and Henny Beckers (Ophthalmology) received professorships. Professor Strik's research focuses on delirium in small children and other aspects of child psychiatry, whereas Professor Beckers is advancing the surgical treatment of glaucoma.
We also welcomed two new clinical professors, Machteld Marcelis and Ingemar Merkies. Machteld Marcelis is a senior psychiatrist at GGZe, a large regional mental health care provider based in Eindhoven. Her professorship is focused on transdiagnostic psychiatry, and her research expertise includes neuroimaging, research in large patient cohorts and ambulatory monitoring. Ingemar Merkies is a senior neurologist at Curaçao Medical Center in Willemstad. Professor Merkies is an expert in clinimetrics, and we look forward to working with him on new assessment tools for clinical outcomes in the broad range of diseases that are within the remit of MHeNs.

Naturally we had fewer teaching and training events than normally, but the 14th MHeNs workshop "Topics in Translational Neuroscience - Neurodegeneration: a vascular perspective", organized by Sebastian Foulquier and Jos Prickaerts, did go

through on 15 September in a hybrid format. In that brief window of relaxation in September 2020 we also managed to have a very productive "mingle day" for academic staff that gave us an opportunity to hear about the research of new faculty members and discuss our strategy for the future in preparation for our 6-yearly evaluation in 2021.

This Annual Report contains highlights of the research in our three divisions as well as updates on our education activities, selected publications and the list of our excellent PhD theses. It is complemented by our recently updated website, which contains detailed information and instructive illustrations of our research at the intersections of the clinical pillars and thematic research lines: https://www.maastrichtuniversity.nl/research/school-mental-health-and-neuroscience. The MHeNs Management Board hopes that you will enjoy reading the report as well as browsing through our new website!



DIVISION I

Cognitive Neuropsychiatry & Clinical Neuroscience

Division Leader:
Prof Frans Verhey

Deputies:
Prof Robert Van Oostenbrugge
Prof Caroline Van Heugten

SUMMARY

The mission of the division Cognitive Neuropsychiatry & Clinical Neuroscience (CNP&CNS) is to generate new insights into mechanisms of cognitive and other neurological or otorinolaryngological disorders, and to improve diagnosis and treatment, and eventually impact the quality of life of people with these disorders positively. 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 therapy.

For its larger part embedded within the Maastricht University Medical Center (MUMC+), the division has an emphasis on clinical research, and includes the departments of Psychiatry and Neuropsychology, Neurology, Radiology, Neurophysiology, General Practice, Internal medicine, Health, Ethics and Society, and Otorhinolaryngology.

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

Goals & results

At the moment that I write this introduction, the COVID-situation is gradually improving and we now can have hope that the crisis that has changed the world for many of us so dramatically will soon be ended. It is too early to see what changes COVID-19 will bring into our daily work, and whether everything will return to the same situation as we had before this pandemic. Will we still make more use of Zoom and Teams for our meetings with our colleagues outside the university, and travel less? Will working from home become more part of our daily work than it was previously, and will we be more cautious to gather in large groups?

It is amazing that anti-Corona vaccines have been developed within less than a year, which at last bring light at the end of the tunnel. This once more underlines the great impact that research can have on society, and that a thorough understanding of the causes of a disease is key to its solution. But in spite of this positive perspective, we must also be fully aware of the huge consequences that the virus has had, not only in terms of the high mortalities and morbidities, but also the long term sequelae related to damage of the lungs and, perhaps, also brains of those who have been affected. The latter is now under investigation, both in the large Maastricht Study and in the multicenter MRI study into brain damage and its consequences after COVID-19, which is led by prof Caroline van Heugten and granted by the Dutch Brain Foundation (NeNeSCo study: Neurological and Neuropsychological Sequalae of Covid-19 infection; Maastricht-Amsterdam-Utrecht)).

These are still challenging times, especially for those at the start of their career. Nevertheless, we still manage to work efficiently and stay productive, and despite all, 2020 has again been a productive year for our division. The research output was substantial, with 16 PhD defenses, 250 scientific WI-1 publications and a total earning power of € 3,7 M. The research of this division is mainly clinically oriented, as most of the staff is appointed to the Maastricht University Medical Center (MUMC+), with close links to the departments of Psychiatry and (Neuro)psychology, Neurology, Radiology, Neurophysiology, Otorhinolaryngology, Internal Medicine and Family Medicine. In line with this development, there is also strong integration of patient care facilities and clinical research into the centers, such as the Alzheimer Centrum Limburg, Center for Movement Disorders, Limburg Brain Injury Center and the Stroke Center. With the further implementation of MUMC+'s Brain Nerve Centre and the integration between hospital and university, there is a firm infrastructure for this more integrative approach.

I want to name a few highlights here. We congratulate Willemijn Jansen, a researcher from the Alzheimer Center Limburg who was successful in obtaining a ZonMw VENI grant for a collaborative project on biomarkers for the diagnosis of Alzheimer's Disease. Marjolein de Vugt and Sebastian Köhler are closely involved as work package leaders in the 5 year national ABOARD project into personalized preventive medicine for Alzheimer's Disease. Research led by Sebastian Köhler into the prevention of cognitive disorders is gaining increasing attention, and has resulted in 2020 in the participation in the international consortium WorldWide-Finger, and the national 7-year project Maintaining Optimal Cognitive function In Ageing (MOCIA). Ron Handels and Lizzy Boots are also to be congratulated for their ZonMw grant into the costs and benefits of the e-health module Partner in Balans, for caregivers of people with dementia. We also congratulate Jaap Jansen and his team for a grant for a new study into the cerebral pathology in diabetes in the Maastricht Study. Furthermore, Walter Backes (Radiology), Julie Staals and Robert van Oostenbrugge (Neurology), and Sebastien Foulquier (Pharmacology) are leading two work packages in the EU-funded CRUCIAL project which intends to identify the role of microvascular rarefaction in cognitive impairment and heart failure by developing innovative imaging instruments and taking advantage of non-contrast and AI methods. The MR CLEAN group including Robert van Oostenbrugge (Neurology) received The Winkler medal of the Dutch Society of Neurology, which is awarded once every five years for the most valuable contribution to research within clinical neuroscience.

In 2021, our division will build further on these collaborations and crossroads and continue our successful work along these research lines.

THE MERITS OF NEUROIMAGING TO STUDY CEREBRAL PATHOLOGY IN DIABETES

How does type 2 diabetes affect the brain?

Type 2 Diabetes Mellitus (T2DM) has a broad range of serious clinical complications, and is often accompanied by cardiovascular risk factors. T2DM is also associated with a higher risk of late-life cognitive impairment and eventually brain diseases such as dementia and depression. The Maastricht Study, which was started by the School for Cardiovascular Diseases (CARIM) at FHML, is an ongoing observational prospective population based cohort study that focuses on the etiology, pathophysiology, complications, and comorbidities of T2DM and other chronic diseases (Schram, Eur J Epidem 2014). Its extensive phenotyping approach is suitable to study the mechanisms and determinants of brain alterations in a population based setting. In a collaborative effort of MHeNs and The Maastricht Study, we aim to highlight the adverse effects of diabetes on the brain to assess contributing pathophysiological mechanisms. In addition to conventional MRI, sensitive to macrostructural cerebral changes (i.e. end-stage effects of impaired tissue), we also apply potentially more-sensitive MRI techniques, such as functional MRI (fMRI) and diffusion MRI (dMRI), which could lead to a better insight into the mechanisms that precede macrostructural abnormalities.

Highlighted Output

In a ZonMW-funded pilot study (VENI Jaap Jansen, 2011-2016), 120 participants from The Maastricht Study were recruited to undergo advanced brain MRI measurements. The hippocampal microstructural and microvascular properties were investigated with a diffusion MRI (dMRI)-based technique, intravoxel incoherent motion (IVIM). It was found that in addition to the parenchymal microstructure, especially the microvascular properties of the hippocampus are altered in participants with both T2DM and memory problems which possibly hints at an underlying vascular mechanism (van Bussel, Diabetes Care 2015[1]). Using functional MRI, we demonstrated that participants with T2DM have altered functional brain networks, and that this alteration is already apparent in the prediabetic stage to a somewhat lower degree, hinting at functional reorganization of the cerebral networks as a compensatory mechanism for cognitive decline (van Bussel, Diabetes 2016). Scaling up over the years to a neuroimaging dataset of more than 2000 participants, we demonstrated using anatomical T1-weighted scans that prediabetes is associated with macrostructural brain abnormalities, with further deterioration in T2DM (van Agtmaal, Diabetes Care 2018). Additionally, we found using dMRI-based white matter tract visualization,

that prediabetes and T2DM are associated with fewer white matter connections and weaker organization of white matter networks, corresponding to 2.3 or 10.4 years of aging, respectively (Vergoossen, Diabetes Care 2020[2]). As of 2020, advanced neuroimaging data is available for more than 5500 participants.

Future plans: cerebral microvascular dysfunction
From 2021 onwards, participants will be approached for a follow-up visit, and it is expected that approximately 3000 participants will undergo a follow-up MRI scan. To match the Maastricht Study's in-depth phenotyping approach on microvascular dysfunction, the new MRI protocol will include quantitative, physiological microvascular brain MRI measurements (arterial spin labeling, ASL and IVIM). By adding functional cerebral measurements to the array of microvascular measurements, for which structural features of cerebral small vessel disease are already included, together with extensive phenotyping of biometrics, lifestyle and cardiovascular risk factors, and co-morbidities, the role of cerebral microvascular dysfunction in the development and progression of various diseases can be studied, prior to the subsequent structural alterations of the small vessels and nearby brain tissue. MHeNs has decided to make a substantial contribution to this follow-up phase of the Maastricht study.

Future plans: combining imaging with genotyping
We furthermore plan to complete genotyping and genotype data processing of the Maastricht Study cohort, and to include the genotype and imaging data (structural MRI and dMRI) in large-scale Genome-Wide Association Studies (GWAS) through collaboration with the international Enhancing Neuro Imaging Genetics through Meta-Analysis (ENIGMA) Consortium. ENIGMA currently comprises nearly 40,000 individuals from ~60 cohorts world-wide. GWAS studies are expected to find new clues regarding the genetic variants contributing to brain white matter microstructure and grey matter phenotypes, and the degree to which these genetic factors overlap with those contributing to T2DM, cognitive impairment, and depression, with the ultimate goal of identifying targets for translational research.

Our research has been widely covered in the media
- Dagblad de Limburger: *"Voorstadium diabetes zorgt voor hersenschade"* | November 9th, 2018
- Dagblad de Limburger: *"Hersenen worden sneller ouder door diabetes"* | October 2nd, 2019
- Elsevier Weekblad: *"Diabetespatiënt heeft oudere hersenen"* | December 2nd, 2019
- Gezond Idee MUMC+: *"Diabetes maakt hersenen sneller oud"* | March 2020

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[2] *Vergoossen LW, Schram MT, de Jong JJ, Stehouwer CD, Schaper NC, Henry RM, van der Kallen CJ, Dagnelie PC, van Boxtel MP, Eussen SJ, Backes WH, Jansen JF. White Matter Connectivity Abnormalities in Prediabetes and Type 2 Diabetes: The Maastricht Study. Diabetes Care. 2020 Jan;43(1):201-208.*

SUMMARY

Crossroad: Neuroimaging - Cognition and Dementia
Advanced MRI techniques are applied to the general population and patients with cognitive decline and neurodegenerative disorders, to obtain a better understanding of the underlying mechanisms of dementia and its comorbidities.

Neuroimaging - Diabetes
A collaborative effort of MHeNs and The Maastricht Study aims to highlight the adverse effects of (pre)diabetes on the brain, for which neuroimaging provides key pathophysiological insights.

INTEGRATED CARE PATHWAY FOR LONG-TERM CONSEQUENCES OF ACQUIRED BRAIN INJURY

Long-term sequelae of acquired brain injury

Each year 140.000 people sustain an acquired brain injury in the Netherlands, of which stroke (cerebrovascular accident: CVA) and traumatic brain injury (TBI) are the most common forms. By now, it is widely acknowledged that not only physical, motor and communicative consequences may follow, but that particularly the cognitive, emotional and behavioral sequelae impact the patient's daily life negatively. It is therefore important to offer long-term care from an integrative perspective.

The 'CVA-stadspoli' is a form of nurse-led stroke aftercare, which is part of the regional stroke service Maastricht-Heuvelland. This facility is a combined effort of the neurology department of the academic hospital and the general practitioners as part of Primary Care Plus ('anderhalve lijnszorg') aimed to reduce healthcare costs by offering specialist knowledge in the primary care setting. We developed the CVA-stadspoli, trained the nurses and evaluated its feasibility and clinical[1] and cost-efectiveness[2]. Currently we are evaluating and improving the regional stroke service along the recommendations of the European Stroke Organisation to become a stroke center. Finally, we are transferring the concept of the CVA-stadspoli to other forms of acquired brain damage such as TBI. This transfer is based on a direct comparison between the long-term consequences of minor stroke and mild traumatic brain injury. Both forms of brain damage have a high impact on psychosocial outcomes in which the cognitive and emotional symptoms play a crucial role. In parallel to case management for people with dementia, we evaluate a similar form of integrative care for people with brain injury, commissioned by the Ministry of Health.

Collaborations

All projects are conducted within the Limburg Brain Injury Center (www.hersenletsellimburg.nl) led by Caroline van Heugten, which is a joint initiative of MHeNs, FPN and MUMC+ in close collaboration with regional health care and patient organizations. The evaluation of the stroke after care is conducted in a collaboration with the department of Neurology, Julie Staals, and the department of Health Services Research (HSR) of the research school CAPHRI, Marielle Kroese and Ghislaine van Mastrigt, and the regional health care partners of the stroke service. For the long-term outcomes comparing stroke to traumatic brain injury, the Limburg Brain Injury Center involves all Limburg hospitals (Maastricht, Sittard, Heerlen, Roermond, Weert and Venlo). The focus on cognitive and emotional con-

sequences after stroke is part of a multicenter project team in which we collaborate with Amsterdam (Jos Slenders, Vincent Kwa and Renske van der Berg-Vos), Utrecht (Anne Visser-Meily, Marcel Post) and Tilburg (Paul de Kort, Britta Nijsse). Psychosocial outcomes after rehabilitation are studied within an international context. We collaborate with the Oliver Zangwill Center and Cambridge University in order to unravel the client's perspective on outcome (Barbara Wilson, Jessica Fish, Jill Winegardner, Andrew Bateman, Leyla Prince). And finally, we have a strong collaboration with Monash University, Jennie Ponsford, to further understand long-term outcomes after mild traumatic brain injury.

Future perspectives

Currently we are designing a new nurse-led aftercare clinic in which not only stroke patients are invited, but also patients with moderate forms of TBI. This elaboration of current care is done with the regional health care partners and health insurer VGZ. Extension to the other stroke services in Limburg is currently in preparation as part of a ZonMw project 'Juiste Zorg op de Juiste Plek'.

In the media, many long-term consequences of Covid-19 infection are mentioned. It is not clear yet whether these consequence result from brain damage and whether structural aftercare for neurological and neuropsychological consequences is needed. Currently, we are conducting the NeNeSCo study (Neurological and Neuropsychological Consequences of Covid-19 infection, funded by the Dutch Brain Foundation) to study long-term sequalae from a biopsychosocial perspective.

Finally, in the coming years we will focus on the post-concussion syndrome (PCS). While people sustaining a concussion are generally expected to recover completely, a minority will develop PCs, which is until now only poorly understood.

Societal Impact

On 13 May, the national telephone service for information on healthcare for people with brain injury 'Breinlijn' was launched. Persons with brain injury, their caregivers, and healthcare professionals can employ this service to come into contact with an independent brain injury expert who can provide information on healthcare services and procedures. The website www.breinlijn.nl has more information.

Caroline van Heugten and colleagues developed an outpatient cognitive rehabilitation programme for people with cognitive problems called 'Niet Rennen Maar Plannen'. This week, the online version of the intervention was released on Jouw Omgeving, an online platform for eHealth interventions. https://www.hersenletsellimburg.nl/nl/niet-rennen-maar-plannen-online
We have also contributed to the national debate on the consequences of Covid-19: Samen het juiste beeld schetsen: onderzoek naar hersenschade na het coronavirus. Interview met Caroline van Heugen en Janneke Horn voor Hersenmagazine, jaargang 18, nr 3, 2020 (blz 12-13)

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2. *Verberne D, van Mastrigt G, Ponds R, van Heugten C, Kroese M. An economic evaluation of nurse-led stroke aftercare addressing long-term psychosocial outcome: a comparison to care-as-usual. BMJ Open2021 Feb 25;11(2):e039201 .*

SUMMARY

Acute medical care for brain damage such as stroke is improving which increases survival rates and functional outcomes. Discharge home is considered earlier and more often. However, even mild strokes have long-term consequences such as fatigue, cognitive and emotional problems, which influence societal participation. Integrated care pathways are needed to ensure people with stroke receive the care they need when they need it. The Limburg Brain Injury Center aims to improve the quality of life of people with brain injury and their families by health care innovation and evaluation: development of outcome measures, and evaluation of clinical and cost-effectiveness of health care solutions in the context of regional, (inter)national collaborations.

DIVISION II

Mental Health

Division Leader:
Prof Thérèse van Amelsvoort

Deputies:
Dr Sinan Guloksuz
Dr Wolfgang Viechtbauer

SUMMARY

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

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

Goals & results

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

One of the core research activities of our Division involves ecological momentary assessments through the experience sampling method (ESM) by using a tool which acquires data in real life allowing the study of real-time and real-world person environment interaction patterns. The Division has 30 years of ESM experience and has established a world leading position in this field (www.esm-maastricht.nl), and the Psymate, the data collection tool, is freely downloadable from iTunes and Android Store. In 2020, we continued increasing our visibility of our Division's ESM expertise in and outside MUMC+, which is illustrated in one of this year's highlights (pages 14-15). The work is mostly represented in the 'monitoring' and 'prevention/ rehabilitation' section of the research matrix of MHeNs, and led by the ESM experts of our division in collaboration with colleagues from the other MHeNs divisions and NUTRIM.

Another key research activity of our division involves translational research activities in collaboration with division 3 aiming to understand the biological and molecular basis of psychopathology. Examples include our research into preclinical models of panic disorders and detecting rare forms of psychosis by for example looking for auto-antibodies. Also, in collaboration with the Department of Bioinformatics a system biology approach to rare genetic disorders is currently being developed and in collaboration with GROW we have started research using iPSCs of patients with rare genetic disorders. This work is embedded in the 'cell biology / genetics' sections of the research matrix, and is further described in one of this year's highlights (pages 16-17).

The combined statistical, epidemiological, genetic and imaging expertise of our Division has ensured continuing high-quality scientific output and participation in, and leading large national and international consortia including EUGEI, PSYSCAN, GROUP, ENIGMA, RTOC. In addition, a NIH funded international collaborative study on CNV disorders has been embedded in the Genes2Mental Health network (genes2mentalhealth.com), our division being the only Dutch partner in this consortium. OPHELIA, a Dutch consortium on treatment of psychosis is a follow-up study to HAMLETT, with the GxE WP being led by our division.

In 2020, the COVID-19 pandemic dominated our lives and this had an effect also on our research activities. Also, in our division several studies relating to COVID-19 were started, both international and local initiatives. Most of our studies could continue remotely, which worked well.

In 2020 we have seen the continuing success of @ease with the first results being published, and with expanding our service with an anonymous chatline since the start of COVID-19 pandemic.

In 2021, we will see the opening of more @ease centers. Also, further integration of our research activities within the BNC will take place in 2021. Furthermore, in 2021 we are expecting the kick-off of a few clinical trials in patients with psychotic disorders, and 22q11.2 deletion syndrome. In addition, a H2020 study on pharmacogenetics, PSY-PGx, coordinated by our division will start in 2021.

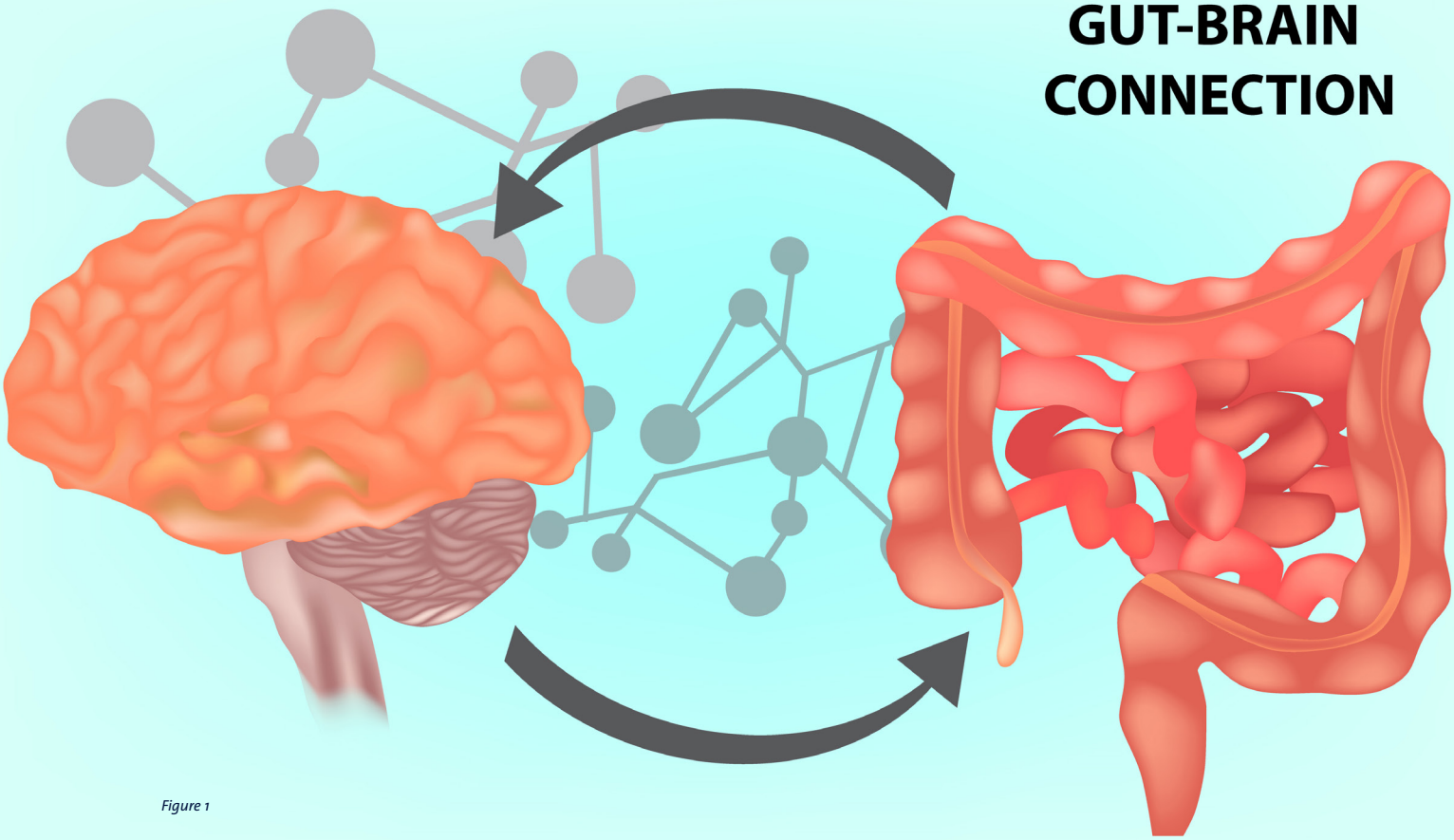

Figure 1

MOMENTARY ASSESSMENT IN PSYCHOSOMATICS - UNRAVELING SYMPTOM FORMATION WITH ESM

Psychosomatic medicine is a multi-disciplinary arena, embracing health care and both fundamental as well as clinical research, where different medical specialties explore the interrelationship between bodily processes and psychosocial factors. Clinical courses of mental processes affecting physical outcomes and, vice versa, somatic processes influencing mental well-being constitute the main field of interest. Attempts to distinguish between purely physical or solely mental disorders have become obsolete since almost all somatic diseases are known to be affected by mental factors, and mental illness is closely associated with somatic pathways. In this arena, mood and anxiety disorders are the two most prevalent mental health conditions, which belong to the leading causes of disability, making a powerful case for joint assessment and personalized management. Patients often have complex clinical presentations resulting in referral to academic hospitals.
At the MUMC+ an established integrated care tradition exists, in particular concerning functional somatic conditions and affective co-morbidities. This integrated care approach combines research expertise from different FHML Schools, particularly MHeNs and NUTRIM (School of Nutrition and Translational Research in Metabolism), and clinical expertise from several MUMC+ departments (e.g., gastroenterology, urology, psychiatry). Functional somatic disorders (FDs) of individual and societal impact are, for instance, overactive bladder, irritable bowel syndrome or chronic pelvic pain syndrome. They are highly prevalent, frequently interrelated and characterized by a chronic course and considerable treatment resistance. Poor treatment outcomes are in part attributable to undetected mental disorders. Co-occurrence of FDs on the one hand, and mood and anxiety disorders on the other, are common and associated with greater symptom severity. A useful framework under which this interaction can be studied is the 'bladder-gut-brain-axis' (BGBA), which postulates that FDs represent a sensitized response, or 'false alarm', to earlier threats (i.e., infections, childhood adversity, earlier trauma), resulting in emotional and bodily distress (the symptoms of FDs – e.g., diarrhea, urgency, pain, anxiety) [Figure 1].

In order to investigate how affective and somatic complaints are interrelated, an ecological momentary assessment (EMA) tool is needed to accurately measure symptoms. Such EMA-research tradition has existed at Maastricht University (UM) for decades. We are pioneers of the Experience Sampling Method (ESM), which randomly measures patients' symptom experiences repeatedly at several time points a day, over a period of several days, in the real world context of a patient's daily life. ESM is a digital device, giving a beep to initiate assessment with a

focus on the subject's in-the-moment physical, behavioural and mental state [Figure 2].

ESM has provided insight in psychotic and affective symptom dynamics in relation to stressors originating from patients' environment and has led to tailored care perspectives. To support personalized health care in psychosomatic medicine, developments have taken off at the UM/MUMC+ in recent years. First, we piloted, together with NUTRIM-investigators, the use of ESM (i.e., MEASURE, Figure 3) in IBS with comorbid panic disorder. This research revealed a peak pain reporting in retrospective questionnaires compared with ESM. Our investigation confirmed recall bias in retrospective somatic questionnaires, based on autobiographical memory, representing a subjective reconstruction of specific moments, rather than a reliable reflection of symptoms over a predefined period of time. Second, we demonstrated the reliability and sensitivity of ESM as trans-diagnostic m-health routine outcome measurement (ROM) at the MUMC+'s psychosomatic outpatient department. At present, several clinical departments are using ESM in clinical research and to document therapeutic outcomes routinely, ranging from ENT to the Pelvic Care collaboration.

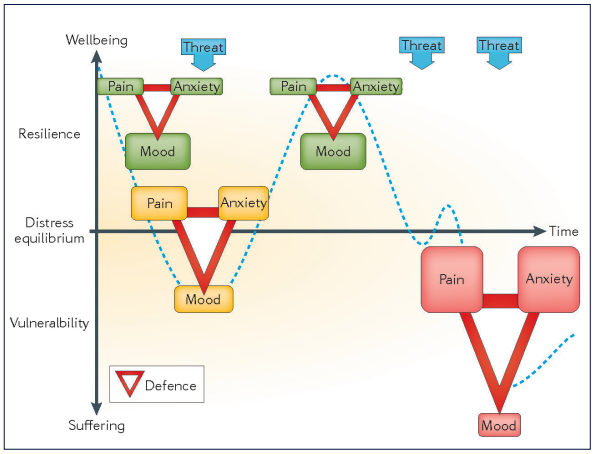

Figure 2: Timecourse of cumulative threat and the consecutive alarm falsification of defence. Defensive behaviour (fight, flight or freeze; voiding; vomiting; diarrhoea; depicted as a red triangle) and corresponding emotional reactions (pain, anxiety, mood) to threat (trauma, childhood adversity, infections) during a timecourse of repetitive cumulative stress show that defensive behaviour and related pain and anxiety levels increase after threat, whereas wellbeing (mood) decreases. Stress-related behaviour and emotions recover after exposure to a single or less-intense stressor (green), but after cumulative stress, pain and/or anxiety increases and related defensive behaviours become bothersome and enduring functional complaints, reflecting a sensitized defence reaction and alarm falsification (red).

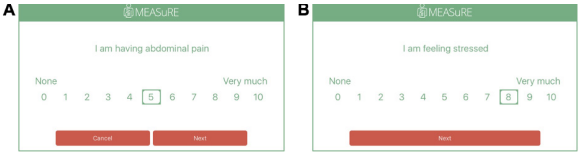

Figure 3 shows the display of the ESM device for somatic (A) and psychological (B) symptom experience.

The main advantage of EMA over retrospective questionnaires is the assessment of symptom formation, i.e., how symptoms have impact on other symptoms in the context of daily life. EMA might answer the question whether anxiety leads to pain, or, vice versa, pain induces anxiety. Hence, ESM may lead us to new insights regarding causal disease models, beyond today's descriptive diagnostic concepts. Because different functional somatic syndromes co-occur in complex patients, ESM-research has spread to different somatic areas. Together with the MUMC+'s Urology department, we introduced the 'Uromate'. The 'Dizzy Quest' was created with ENT-investigators, and the Pelvic Care Centre has involved the department of Gynaecology and the School of GROW (School for Oncology and Developmental Biology) in EMA-research on endometriosis. Future initiatives consist of ESM research in atrial fibrillation, implantable cardioverter-defibrillation and in pain rehabilitation.

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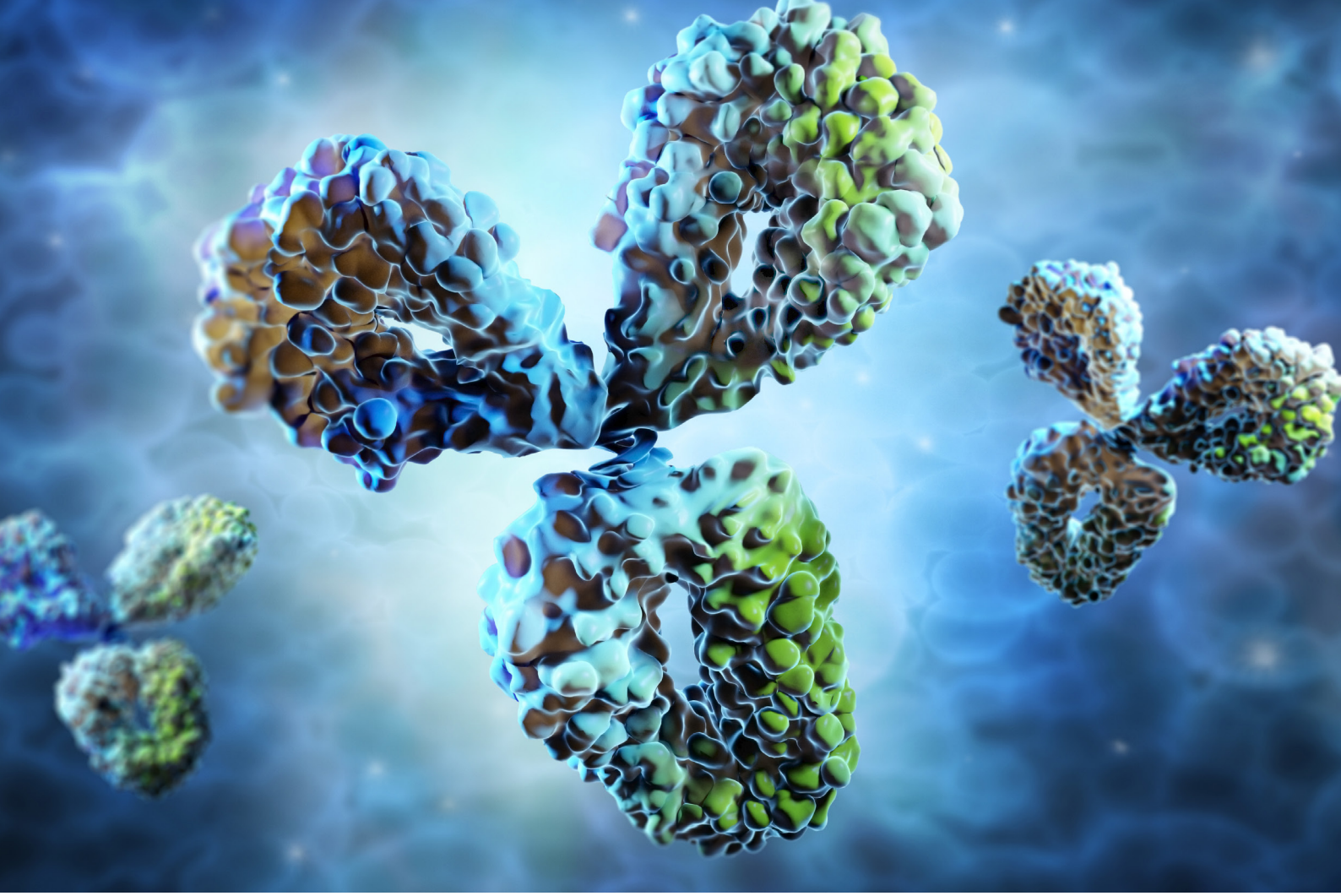
SUMMARY

Since mental health factors are closely associated with somatic pathways, ESM research at MHeNs has developed from a psychiatric enterprise to a transdisciplinary programme in which clinical researchers from a wide range of disease areas join forces in the understanding of mutual influences of psychological and somatic factors on health, illness and recovery.



NEUROPSYCHO-IMMUNOLOGY

What does neuropsycho-immunology mean in the research context of MHeNs?

It focuses on the interactions between the immune system and the nervous system. This brings together different MHeNs disciplines spanning from immunology and neural sciences to basic sciences, including biochemistry and physiology. Under this umbrella, psychosis is an interesting and important subject of study of disturbed immunity. Psychotic disorders are debilitating illnesses associated with abnormalities in various neurotransmitter systems, but the therapies generally have no basis in etiology and pathophysiology, which are mostly unknown. In autoimmune encephalitis several autoantibodies against neuronal antigens are responsible, as they disrupt synaptic transmission within the brain. This results in a wide range of neurologic and psychiatric manifestations which include psychosis. The overlap of symptoms of autoimmune encephalitis with psychotic disorders raised the question as to whether autoantibodies against a number of receptors or ion channels could ultimately be responsible for some forms of psychosis. In the peripheral nervous system, attack by autoantibodies can cause a range of neurological symptoms such as in myasthenia gravis (MG), and while the pathophysiology of this disease is well known, standard treatments are far from optimal in subgroups of patients. In this regard, novel treatment strategies that are immune cell-specific are desirable. Another important area of this research field is the role of lipids in inflammation in neurodegenerative diseases such as Alzheimer's (AD). The metabolism of certain lipids could be disturbed and so be part of the early stage of the disease process. How altered lipid levels or changes in their composition affect the activation of the immune system and trigger a pathogenic response is largely unknown. Hence the importance to study these novel pathways using in vitro and in vivo models with the aim to design novel treatment strategies.

Autoimmunity in Neuropsychiatric Disorders - Improvement of Diagnosis and Treatment. Neuronal surface autoantibodies

Neuronal surface antibodies (NSAbs) are associated with symptoms of psychosis. These autoantibodies are pathogenic by interacting with neurotransmitter receptors, ion channel proteins, ultimately leading to dysfunction of neural signal transduction. Neurotransmitter transporters and receptors are also implicated in the pathology of depression and anxiety and they are targeted therapeutically with anti-depressant drugs. Thus, one might consider that certain NSAbs may be a cause of depression and anxiety. Currently, improved diagnosis and treatment strategies are being investigated for autoimmune disorders of the central nervous system. Our group's work clearly shows that known autoantibodies present in autoimmune encephalitis are not present in chronic patients with psychotic

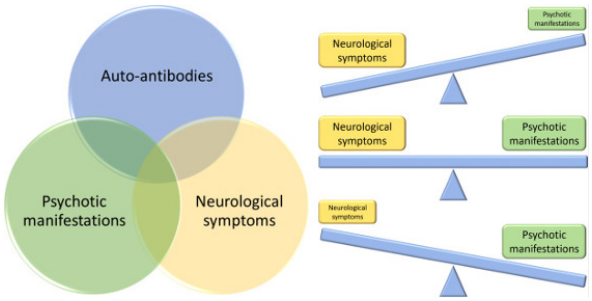
disorders and depression. Importantly, novel NSAbs are being investigated in subgroups of these patient groups, as well as in other mental disorders. A case in point, is a recent patient identified with pre-existing Hashimoto's thyroiditis and progressive cognitive complaints with epileptic abnormalities associated with the novel autoantibodies.

Autoantibodies attacking receptors and proteins at the neuromuscular junction cause a range of neurological symptoms in MG. Some autoimmune pathogenic mechanisms have been elucidated to which we have made important contributions. Novel mechanisms are being investigated in a variant of MG (Musk-MG). Moreover, new strategies in MG are being investigated for personalized, specific immunosuppression.

Structural Lipids and their Transporters in Neuropsychiatric Disorders. Targeting Lipids for Diagnosis and Treatment
The metabolism of certain lipids could be disturbed and be part of the early disease process in AD. We aim to elucidate the role of membrane lipid dysregulation in onset and progression of neurodegenerative diseases. We hypothesize that targeting this pathway with drugs may help to slow down or even stop the neurodegeneration. Several new treatment strategies have been tested that demonstrate that influencing this lipid pathway can change the course of AD in animal models. We plan to clarify the molecular pathways involved for our treatment strategy. Additionally, we are exploring the possibility of using lipids as biomarkers for diagnosis of neurodegenerative/neuropsychiatric diseases.

Ongoing projects and collaborations:

We have investigator-initiated grants in collaboration with the companies Apellis, Argnex and Imcheck and two NIH projects as well as grants from the Dutch Brain Foundation and the INTERREG programme, besides national collaborations. In the area of central nervous system research, collaborations are ongoing with Harald Prüss at the Charité in Berlin, Anne-Katrin Proebstel at the University of Basel and Anna Mané at the Hospital del Mar in Barcelona. Mané is recruiting severe first episode patients for our Psyantib study where screening of serum of the patients for autoantibodies is performed. For MG we have a collaboration with René Hoet, and, additionally, studies are ongoing with Washington University to search for treatment response biomarkers together with Henry Kaminsky and Linda Kusner. Moreover, new animal models of MG are being developed in collaboration with Kevin O'Connor at Yale University. Finally, the role of the thymus in autoimmunity is a focus for the next years since MUMC+ is a center of excellence for thymectomies that are performed by the DaVinci Robotic® System. In the lipid area we collaborate with



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Michelle Mielke at Mayo Clinic, Erhard Bieberich at the University of Kentucky, Tomas Blom from the University of Helsinki and Jochen Walter at the University of Bonn.

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SUMMARY

Our body has two defense systems, inflammation and antibody reactions, that while highly effective against foreign pathogens, sometimes are taking a dramatic turn by attacking our own tissues. In our project we focus on the pathological effects of auto-antibodies against cell surface proteins in the nervous system, which include various forms of psychosis, depression, anxiety and epilepsy and, also, the weakness caused by auto-antibodies on the nerve-muscle system. Our general aim is to improve the diagnostic process and subsequent pharmacological intervention in autoimmunity. This work is a cross operational collaboration between Division 2 and 3 and an interdepartmental collaboration including Psychiatry (Prof van Amelsvoort & Prof Marcelis) and Neurology (Dr Rouhl).

DIVISION III

Translational Neuroscience

Division Leader:
Prof Jos Prickaerts

Deputies:
Dr Mark Janssen
Dr Mario Losen

SUMMARY

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

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

Goals & results

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

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

Our multidisciplinary staff consists of professionals from relevant clinical and basic research disciplines. This allows us to integrate a variety of techniques such as detailed biochemical, cellular and animal experiments, as well as human studies. The division of Translational Neuroscience has state-of-the-art laboratories for electrophysiology, microscopy, molecular biology, as well as biochemistry laboratories for tissue processing, cell culturing, immunohistochemistry, proteomics and genomics. For example, there is access to a light sheet

Photo Jos Prickaerts: Anke Geurts Photography

microscope, confocal microscopes and various stereological microscopy set-ups of the highest standard. There are excellent molecular biology labs for in vitro and in vivo non-viral as well as viral gene transfer experiments including optogenetics and CRISPR/Cas9. The behavioural animal labs meet the latest up-to-date standards for automated assessment of animal behaviour. There is a large expertise in a wide variety of animal models and tests for diseases of the central, autonomic and peripheral nervous systems, muscle diseases and diseases of the sensory systems. The technological expertise in our division is currently centralised in expertise groups that are coordinated by senior staff members and supported by experienced technicians: Molecular and Cell Biology, Microscopy and Imaging, Neuromodulation and Electrophysiology, Stem cells, In Silico and Functional Genomics (established in 2020), and In Vivo and Behaviour.

We have collaborations within worldwide international networks of research offering a strong academic environment. For the upcoming years, we continue to align and integrate our research lines within MHeNs and within Maastricht University. Our research is fully incorporated and integrated into the research lines of the MHeNs research matrix. The Brain and Nerve Center (BNC) within the MUMC+ offers further excellent opportunities as its research lines overlap with those of MHeNs. Next to research lines, the BNC also has clinical research themes (e.g pain, cognition and dementia, epilepsy, movement, vision, hearing and balance), which overlap with the division's research topics and offer excellent opportunities for integrating its preclinical research with the clinical expertise. This translational advantage generates scientific input with clear translational and clinical impact and also increases opportunities for further funding. An additional point of attention is extending our stem cells and iPSC research. This was initially done within the Brightlands e-infrastructure for Neurohealth (BReIN) Institute within MHeNs, and has now been secured by the establishment of the latest two expert groups (Stem cells (2019), In Silico and Functional Genomics (2020)). Linked to this we keep on stimulating more integration with the Institute of Data Science (IDS) and the Institute for Technology-Inspired Regenerative Medicine (MERLN). Also important for the Division in this respect is the start of more integration with M4I (e.g. via the Interreg project EURLIPIDS) and Systems Biology (MaCSBio). The scientific collaboration with the Faculty of Psychology and Neuroscience (FPN) will be continued and intensified within the Center of Intergrative Neuroscience (CIN). Finally, we will keep on focusing specifically on Dutch and international personal grants. Therefore, we are happy and proud to announce that we could welcome a VENI fellowship (Mor Dickman) and a VIDI fellowship (Ali Jahanshahi) in our division in 2020.

TRANSLATIONAL PAIN RESEARCH

The international association for the study of pain (IASP) defines pain as *'An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage'*. Pain is complex and closely associated with co-morbidities like anxiety, depression and stress.
Pain in itself is of fundamental importance for survival and protection of the human body but when it develops and becomes chronic it is a disease and needs treatment.

From a clinical point of view research at the Dept. of Anesthesiology and Pain Management is focussed at: 1. Chronic Postsurgical Pain (CPSP) and 2. Chronic neuropathic pain. Experimental studies in the pain laboratory (Head: Prof Bert Joosten. Embedded in Division 3, MHeNs) are closely matched to clinical test and trials.

1. Chronic Postsurgical Pain (CPSP) or 'pain that develops or increases in intensity after a surgical procedure or a tissue injury and that persists beyond the healing process, i.e. at least 3 months after the initiating event'[1] , is one of the major clinical problems of today. CPSP, depending on the type of surgery, may be observed in over 30% of patients. Multimodal analgesia is key in the acute and chronic postoperative pain management strategy but very often remains suboptimal in the prevention or treatment of CPSP. Research related to CPSP is related to **1. Modulation; 2. Monitoring, 3. Genetics and 4. Imaging** of this disease.
Ad.1. With use of well-defined clinical cohorts (hysterectomy patients) important personal and psychological risk factors for CPSP are defined. In collaboration with FPN (Madelon Peeters) the next step is to develop treatment paradigms aimed to **modulate** pre-surgery psychological risk factors like (ZonMW grant, Anne Lucas)). The "better in better out" principle is being implemented into the clinic of today.
Ad.2. Monitoring of pain and the objective assessment of this disease is still a challenge in clinical research. New apps are developed to accurately monitor pain status and/or provide on-line feedback for optimizing treatment.
Ad.3. Lack of knowledge on **genetic** risk factors and mechanism(s) underlying the development of CPSP have made us decide to start the first Genome-Wide Association Study in this field (based on an interdivisional grant MHeNs, and linked to division 2) and from that, in close collaboration with Radboud University, further pharmaco-genetic analysis and studies are now planned for optimal and accurate identification of patients at risk (NWA-ORC application). For the development of new pharmacological targets the pain laboratory developed genetic screening and drug testing in a nociceptive assay in zebrafish.

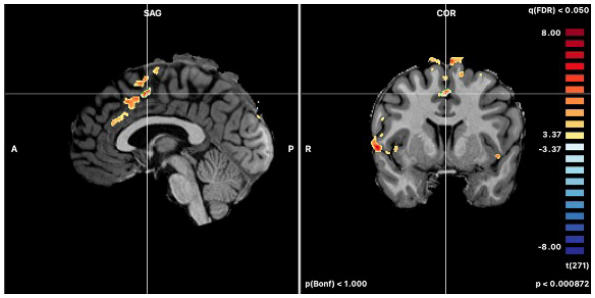

Figure 1: Single subject brain activity for painful electrical shocks vs baseline.

Ad.4. With use of partners at FPN (Amanda Kaas) the pain laboratory and clinic is now implementing **imaging** techniques into the pain field. It is aimed to develop a neurofeedback protocol related to habituation of pain in chronic pain patients using fMRI analysis (collaboration with FPN and Scannexus) (Institutional grant MHeNs with David Linden [Figure 1]).

Staff involved: Clinical: Anne Lucas , Carine Vossen, Andrea Balthasar, Wolfgang Buhre, Dianne de Korte. Pre-clinical: Bert Joosten

2. Neuropathic pain is a complex, heterogeneous disorder that affects approximately 8% of the total adult human population. Despite the development and use of many pharmacological drugs and guidelines for the treatment of chronic neuropathic pain over the years, a substantial amount of neuropathic pain patients remain under- or untreated. Hence, the development of last-resort interventional treatment therapies, like spinal cord stimulation (SCS) is crucial.

Clinical studies and randomized clinical trials performed at the Dept. Anesthesiology and Pain Management were able to demonstrate significant pain relief for spinal cord stimulation (SCS) in selected indications like Complex Regional Pain Syndrome (CRPS) and Painful Diabetic Polyneuropathy (PDPN [Figure 2]). In this context the research at the pain laboratory aims to understand the mechanism underlying SCS in these indications, with emphasis at central sensitization. Here innovative research is related to use understanding mode of action of new SCS treatment paradigms like Burst, and High-Frequency SCS as well as those to related to the use of new locations like the Doral Root Ganglion. The molecular mechanism underlying chronic pain and SCS is further analyzed using mass spectrometry in collaboration with M4I (Ron Heeren).

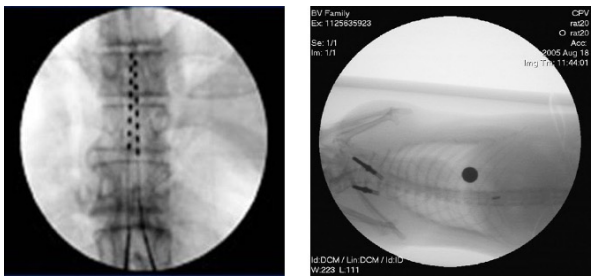

Figure 2: X-ray pictures of implanted Spinal Cord Stimulation electrodes positioned on top of the spinal dorsal columns in spinal cord A: in humanB: in experimental rat model.

This translational research is supported by many grants from world leading companies in this field: Medtronic, Abbott, Boston Scientific, Saluda, and is embedded in many international collaborations.

Staff involved: Clinical: Jan van Zundert, Xander Zuidema, Nelleke de Meij. Pre-clinical: Glenn Franken, Bert Joosten.

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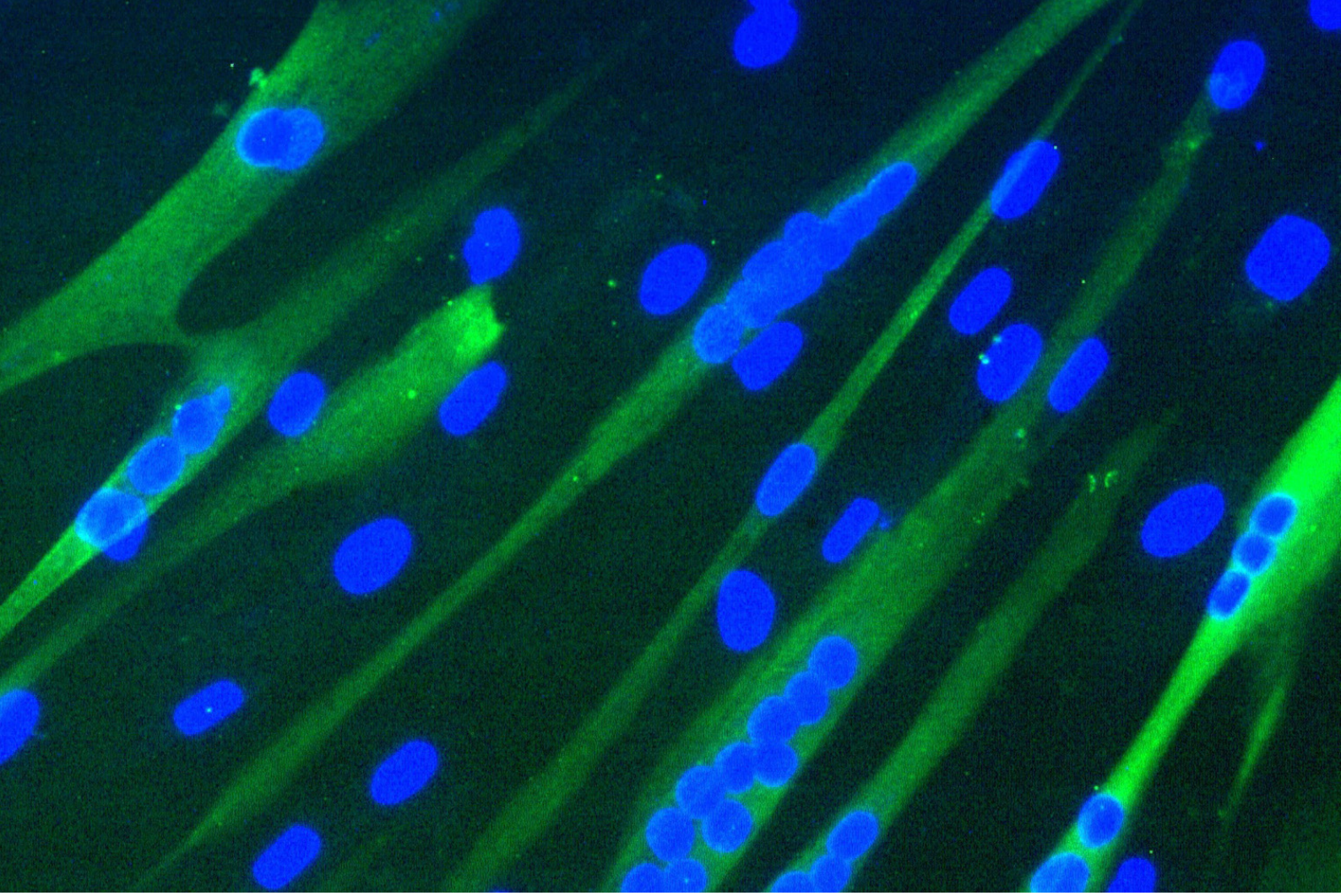
SUMMARY

Translational pain research starts from defining clinical problems and research questions related to diagnosis and treatment of CPSP or chronic neuropathic pain. These research questions are then addressed in the pain laboratory and with use of innovative cutting edge technical, genetic and imaging tools a mechanism based answer is formulated.



MHeNs AND REGENERATIVE MEDICINE

Mitochondrial medicine has been a key research line at MUMC+, initially embedded in a joint expertise center with ErasmusMC (ERN A-1-8), to be continued solely from MaastrichtUMC+. Mitochondrial diseases have a heterogeneous clinical manifestation, generally including, brain, eye, nerve system and/or muscle. The initial focus was on finding the genetic cause in monogenic mitochondrial diseases using next-generation sequencing, which has been successful in 2/3 of the patients. A state-of-the-art sequencing infrastructure was established within MHeNs. The current focus has shifted to studying prevention and pathophysiology, using stem cells and zebrafish models, and to developing novel therapies, based on autologous healthy, adult muscle stem cells. Florence van Tienen and Bert Smeets demonstrated for the first time that patients with a genetic mitochondrial disorder, due to an mtDNA mutation, have muscle stem cells that are largely mutation-free and can be directly used for treatment, enabling the first clinical trial in 2021, using autologous stem cells for neuromuscular disorders[1]. This therapy-driven research obtained funding from 20 organizations and foundations (GYM project: www.generateyourmuscle.com), 5 of them being patient organizations. User groups are closely engaged in this translational research. The chairman of the MDC1A muscular dystrophy patient foundation "Voor Sara" (https://mdc1a.com/) Bram Verbrugge is responsible for the communication workpackage of the GYM project, guaranteeing a direct transfer of project results to "Voor Sara" and other supporting organizations and, vice versa, direct access and input from these organizations to the researchers. Bram creates international visibility and awareness of the general public for the project by using mainstream and social media.
As mitochondrial dysfunction can be a modifying factor in monogenic and complex disorders as well, the research group also analyzes mitochondrial genes and function in other genetic diseases, like myotonic dystrophy and 22q11 deletion syndrome, in common disease, like glaucoma and pain, and in neurocognitive function, including 7T MRI, thereby connecting to key research groups within MHeNs.

Regenerative medicine research in the University Eye Clinic
The University Eye Clinic Maastricht integrates top-quality care with scientific research and is recognized internationally as a center of excellence for innovative surgical treatments in glaucoma, corneal and refractive (cataract) surgery. We complement research that is primarily clinical in nature, with a direct impact for patients (clinical trials, clinical decision models) and society (efficiency research and cost-effectiveness models), with fundamental research in the field of innovative imaging technology, biomaterial applications and stem cells.

On a large scale we collect patient-derived ocular tissue and fluids in the the Eye Tissue Bank Maastricht. These data will allow more detailed diagnosis, which is particularly relevant for the multifactorial and heterogeneous disease of glaucoma. In addition, the biomaterial will be used to generate ocular cells and tissues via iPSC technology. These tissues will enable in vitro modelling needed to study disease mechanisms and test new drugs. Moreover, they provide the cells and tissues for regeneration of cornea, lens and optic nerve, restoring lost vision.

Supported by the EU and the European Society for Cataract and Refractive Surgevy, the department of Ophthalmology established a multinational registry to capture the outcomes of corneal stem cell transplantations (www.ecctr.org) and is currently seeking European Medicines Agency (EMA) qualification. The registry contains information on the recipient, donor and eye bank processing, transplant procedure and two-year follow-up including graft survival and failure, and patient-reported outcome measures (PROMs). With more than 13.000 records the ECCTR is one of the largest databases in the field. In October 2019, almost 60 people from 16 EU countries and representatives from the World Health Organization (WHO) and the European Commission DG SANTE attended the final European Cornea and Cell Transplantation Registry (ECCTR) project conference in Brussels, Belgium[2].

Regenerative medicine holds the promise of restoring vision through a combination of approaches involving stem cells, progenitor cells, and novel materials. Our mission is to perform translational research using stem cell technology. A successful example is the clinical application of ex vivo cultivated limbal stem cell transplantation in Maastricht restoring vision to patients with corneal damage. Our future translational goals are focused on the corneal endothelium.

In the framework of the alliance with the Radboud University Medical Center in Nijmegen, the department of Ophthalmology is exploring CRISPR-based therapy approaches for Fuchs disease. We have established patient-specific iPSC lines from patients with a trinucleotide repeat expansion in the TCF4 gene. Our preliminary results show it is possible to successfully remove the repeat and revert the underlying pathogenic mechanism. Another research line with Radboud on cornea regeneration involves development of transdifferentiation protocols of skin and oral mucosa cells towards limbal stem cells to treat patients suffering from blindness due to bilateral limbal stem cell deficiency that currently have no therapeutic alternative.

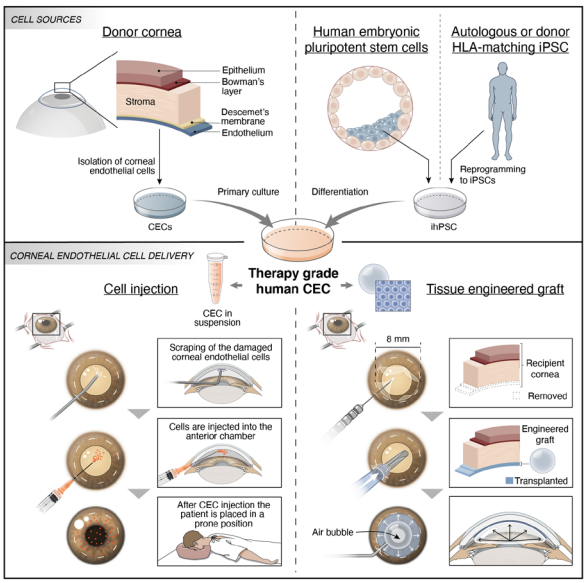


Figure 1: Approaches for corneal endothelial regeneration.

Beyond these examples from mitochondrial medicine and ophthalmology, MHeNs researchers are also actively involved in regenerative medicine approaches to other diseases of the nervous and sensory systems, for example in the areas of neurodegeneration and pre- and perinatal brain injury.

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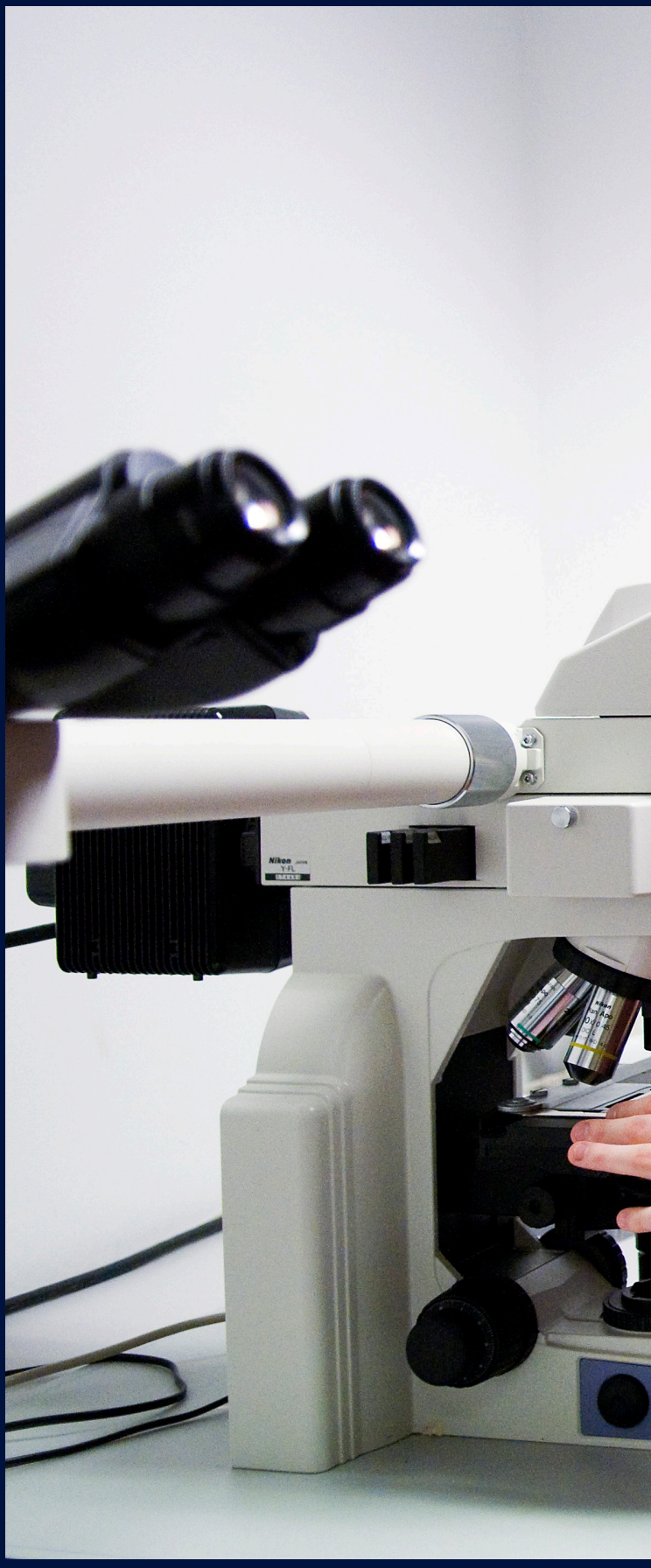
SUMMARY

Regenerative medicine has been identified as one of the 25 routes of the Dutch National Research Agenda and is highlighted in the Topsector Life Sciences and Health Knowledge and Innovation Agenda 2020–2023. In particular, RegMed XB, a public–private partnership aiming to bring regenerative medicine solutions to patients with chronic diseases, is a flagship programme of LSH. The MERLN Institute of FHML, with which we are collaborating, was a founding partner of RegMed XB. We have started initiatives in regenerative medicine particularly in mitochondrial diseases and ophthalmology.

EDUCATION



The training of Master and PhD students in the areas of mental health and neuroscience and related medical and psychological disciplines is a primary aim of MHeNs. The PhD educational programme of MHeNs has a strong multidisciplinary character and is on a European level embedded within the European Graduate School of Neuroscience (EURON). The aim of the programme is to promote a high level of competence in a specific research field, but also in more generic, transferable skills that are important for high level profile careers in research, education, or clinical practice.

PHD PROGRAMME

As of Jan. 2021 MHeNs had in total 290 registered PhD candidates, of whom 103 are employed by Maastricht University as internal (regular) PhD candidates (21 have newly started in 2020). Furthermore, there are appr. 190 external PhD candidates. MHeNs is not only involved in the design, management and teaching of different Master programmes (see below) – graduates of these programmes also make up a significant percentage of MHeNs PhD candidates. For instance, many graduates from the Research Master Programme Cognitive and Clinical Neuroscience (CCN) have joined MHeNs as promovendi.

MHeNs has established educational guidelines, whereby PhD candidates are expected to complete educational activities equivalent to at least 20 European credits (EC/ECTS) to qualify for the MHeNs Certificate. A large part of the PhD training occurs in the context of conducting a research project, supervised by an expert or a group of experts. In addition, all category PhD candidates will engage in more specific or generic educational activities, which may vary based on their category (e.g. different agreements can be made for internal vs. external PhD candidates). The PhD students formulate and regularly update their personal research plan (PRP) and training & supervision plan (TSP) in consultation with their supervisors, based on an assessment of previously acquired competencies, skills specifically needed for the PhD research, more general knowledge and skills, and future career plans. They use the PhD tracking system (TRACK) that enables administrative management of each PhD trajectory, intermediate assessment of progress and student status, and upload of important documents pertaining the progress, such as certificates of participation in courses, TSP and PRP. The school PhD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coordinator (Martin van Boxtel) has access to periodically generated progress indicators in TRACK and acts on projects that are flagged as 'needing attention'.

The PhD student programme of MHeNs has a strong multidisciplinary character and is embedded within EURON. EURON offers an additional EURON PhD Certificate of Excellence, which will be awarded if the PhD candidate fulfils the required criteria in terms of training, networking, international mobility, and scientific publications. The EURON PhD Certificate of Excellence is recognized by the Governing Boards of the participating universities. Since one important requirement for the certificate is mobility, PhD candidates are encouraged to spend a period of at least 3 months abroad to receive international experience. In addition, as part of their training, MHeNs PhD candidates are expected to follow general courses offered by Maastricht University (for example, writing skills, statistics, teaching skills, and career development), in addition to specific, research related courses organized by MHeNs and EURON (Annex 2).

MHENS INVOLVEMENT IN MASTER PROGRAMMES

MHeNs is involved in the curricula of several master programmes of both the Faculty of Health, Medicine and Life Sciences and the Faculty of Psychology and Neuroscience. Many new PhD students of MHeNs are recruited from these programmes. Internships for students are offered on a broad range of topics within the field of mental health and basic neuroscience.

- Research Master Cognitive and Clinical Neuroscience (2 years programme). The master consists of six specialisations and MHeNs staff contributes heavily to four of them i.e.: Fundamental Neuroscience, Neuropsychology, Psychopathology and Drug Development and Neurohealth. In addition, MHeNs is coordinator of the Fundamental Neuroscience specialization (Daniël van den Hove) .
- Master programme Biomedical Sciences (2 years programme). The Master BMS consists of six specializations of which MHeNs staff coordinates the specialisations Inflammation and Pathophysiology (Pilar Martinez) and Neuromodulation (Ali Jahanshahi).
- Master Physician-Clinical Investigator (Arts-Klinisch Onderzoeker – A-KO; 4 years programme). The modules Brein, Beweging and Gedrag are coordinated by MHeNs staff (Rob Rouhl and Janneke Hoeijmakers). A-KO students have several research internships in their program, a short internship in their 2nd year and a combined clinical and research internship in their last (4th) year. Researchers from all MHeNs divisions actively contribute to these internships as mentors.

PROFESSIONAL COURSES

MHeNs is one of the key partners in the INTERDEM Academy for training of early career researchers in dementia, which is connected to Division 1 and the Alzheimer Centrum Limburg (https://www.alzheimercentrumlimburg.nl/interdem-academy). In 2020 MHeNs staff (Frans Verhey, Dorothee Horstkötter, Fania Dassen) have organized the interactive seminar on "Ethical Dilemma's in Research Practice" during the 30th Alzheimer Europe Conference 2020 (online setting). Division 2 staff has a longstanding expertise in the Experience Sampling Method (ESM), a psychological technique for obtaining ecologically valid momentary assessments of mental states and behaviours in daily life through remote communication, for example using smartphone apps. Several courses have been organized (physically and online) in 2020 (see Annex 2). Within the framework of the series of workshops called "Topics in Translational Neuroscience" (organized since 2009) the 14th MHeNs workshop on "Neurodegeneration: a vascular perspective" took place, organized by Sebastian Foulquier and Jos Prickaerts. 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 these 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. For more information on all events see Annex 2.

Website information:
https://www.maastrichtuniversity.nl/research/mhens/mhens-phd-programme

https://euronschool.eu/training/phd-training-programme

https://www.maastrichtuniversity.nl/education/master/research-master-cognitive-and-clinical-neuroscience-specialisation-fundamental

Research Master Cognitive and Clinical Neuroscience: Fundamental Neuroscience (FN) specialisation

This programme is hosted by FPN and FHML. The programme is subject to a strict and highly competitive selection procedure, which only allows a limited number of the very best students to participate. This selection procedure is centered around screening of a student's portfolio consisting of a motivation letter, CV, certified bachelor's transcript, referee reports, and evidence of English proficiency. If deemed of sufficient quality, a student is invited for a 30 min interview with two Board of Admission members to assess the quality of the applicant's academic background , research interests and aptitude, fit with the chosen specialisation, career aspirations, and general social skills. Applicants then complete a 45-minute analytic writing assessment. Approximately 70% of the applicants are rejected and only 24 students are allowed to do a specialization every year.

FN provides students with both the theoretical background and practical experience for research at the interface between neuroscience and psychology, thus offering interdisciplinary cross-integration. The focus is on acquiring the relevant molecular biological (e.g. proteomics, genomics), neuroanatomical (e.g. immunocytochemistry), electrophysiological (e.g. linked to Electroencefalography [EEG], Event Related Potentials [ERP]) and behavioural skills (e.g. linked to rodent and human testing) necessary for preclinical basic research. In addition, the specialisation provides an in-depth study into state-of-the-art knowledge of physiological and pathophysiological mechanisms underlying psychological, psychiatric and neurological disorders (e.g. affective disorders, cognitive disorders, motor disorders). Within this context, the role of the emerging fields of neuroinflammation and pain are also addressed. Main research topics include cell signaling, brain plasticity, neurodegeneration, regeneration, and genetics and epigenetics, all in a translational setting. The specialisation in Fundamental Neuroscience trains researchers to be equipped for investigations into the underlying fundamental molecular mechanisms of psychological and psychiatric disorders in academic as well as industrial settings.

FN started in 2009 with increasing student numbers every year and since 2014 the number of students enrolled in FN has been steadily fluctuating between 21-24. Not reaching 24 students implies that not enough students met the high quality standards. Teaching activities are particularly organised by a multidisciplinary team from division 3, which also offers the main labs for practicals and internships. Jos Prickaerts has been the first coordinator of FN and his position was taken over fully at the start of the academic year in 2020-2021 by Daniel van den Hove. Academic year 2019-2020 served as a transition year for both coordinators.

FN is characterized by a strong social coherence because of the almost one to one ration between staff and student numbers. Every student has a staff member as personal mentor. Many students feel very strongly connected to each other and the programme. The staff encourages and facilitates the students to perform their 8 months internship an international top lab abroad, including the Massachusetts Institute of Technology (MIT), Harvard University, Yale University, the University of Oxford and the University of Cambridge. The international character of FN is also reflected by the fact that students from more than 30 different countries so far studied FN. Students are seen as ambassadors of MHeNs and help to strengthen and extend international collaborations of the staff.

The National Alumni Enquête (NAE) and FPN alumni surveys report 4.9% and 8% unemployment rates among the Research Master graduates 0.5 to 2.5 years after graduation, respectively. Five years after graduating, as the UM Scanner shows, unemployment among Research Master graduates is reduced to 0%. About 15% of the graduates of FN including the graduation in 2020 (cohort that started in academic year 2018-2019) acquired a position as PhD student at division 3. This reflects about 3 PhD students per year, which is also a reflection of the strong imbedding of FN in Division 3. In numerous cases, FN students end up at collaborating institutions abroad, including those listed above (internships) and often accompanying a joint PhD degree programme with MHeNs (e.g. Hasselt University, the University of Würzburg).

The Research Master in Cognitive and Clinical Neuroscience is a "Top Rated Programme" and ranked 1st in the Psychology: Neuroscience research master's category of the 2019 Keuzegids Masters. This programme has been ranked best in its class for 2 years in row. It is important to note that FN is not just a top-programme because it is good, it is also fun! The social coherence was seriously challenged by the COVID-19 pandemic, but FN would not be FN if it did not find solutions to this crisis. Staff members dedicating their spare time to be able to offer extra (COVID-proof) skills trainings and weekly online social gatherings show that FN is not just an educational programme. It represents a family, for better and for worse.

FACTS AND FIGURES

Despite the pandemic and all related measures that could possibly influence the productivity, the MHeNs research output was impressive again in 2020.
Again the amount of new contracts and grants (8.2 M) and especially the number of publications in international journals (626) show an impressive growth. The number of thesis defenses (44) is in line with the 3-year average of the School (45) and is again a great effort taken into account the pandemic restrictions. With a total number of 344 registered PhD's (internal and external) within MHeNs there are a lot of thesis defenses in the pipeline.
This development is a result of strategic investments over the last few years as both direct funding and contract research funding have increased significantly. Due to an increasing number of realized PhD dissertations over the last few years (resulting in an increase of the 3 year average), additional direct funding became available. As a result MHeNs was able to invest in talented tenured and tenure-track staff within all three divisions.

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

KEY FIGURES 2020

ANNUAL BUDGET: € 17.0 M

NEW CONTRACTS AND GRANTS: € 8.4 M

RESEARCHERS: 152 FTE (INCL. 97 FTE INTERNAL PHD STUDENTS)

TECHNICAL AND SUPPORTING STAFF: 35 FTE

DEPARTMENTS/DISCIPLINES: 14 DEPARTMENTS (7 CORE AND 7 NON-CORE)

SCIENTIFIC ARTICLES: 623 (WI-1 PUBLICATIONS)

PHD THESES: 44

PATENTS/SPIN-OFFS: 4

TOP PUBLICATIONS

COGNITIVE NEUROPSYCHIATRY AND CLINICAL NEUROSCIENCE

Stroke Etiology and Thrombus Computed Tomography Characteristics in Patients With Acute Ischemic Stroke: A MR CLEAN Registry Substudy
Boodt, N., Compagne, K. C. J., Dutra, B. G., Samuels, N., Tolhuisen, M. L., Alves, H. C. B. R., Kappelhof, M., Lycklama a Nijeholt, G. J., Marquering, H. A., Majoie, C. B. L. M., Lingsma, H. F., Dippel, D. W. J., van der Lugt, A., van Oostenbrugge, R. J., van Zwam, W. & MR CLEAN Registry Investigators,
Jun 2020, In: Stroke. 51, 6, p. 1727-1735 9 p.

2BALANCE: a cognitive-motor dual-task protocol for individuals with vestibular dysfunction
Danneels, M., Van Hecke, R., Leyssens, L., Degeest, S., Cambier, D., van de Berg, R., Van Rompaey, V. & Maes, L.,
14 Jul 2020, In: BMJ Open. 10, 7, 11 p., e037138.

Association of Markers of Microvascular Dysfunction With Prevalent and Incident Depressive Symptoms: The Maastricht Study
Geraets, A. F. J., van Agtmaal, M. J. M., Stehouwer, C. D. A., Sörensen, B. M., Berendschot, T. T. J. M., Webers, C. A. B., Schaper, N. C., Henry, R. M. A., van der Kallen, C. J. H., Eussen, S. J. P. M., Koster, A., van Sloten, T. T., Köhler, S., Schram, M. T. & Houben, A. J. H. M.,
Aug 2020, In: Hypertension. 76, 2, p. 342-349 8 p.

The presubiculumlinks incipient amyloid and tau pathology to memory function in older persons
Jacobs, H. I. L., Augustinack, J. C., Schultz, A. P., Hanseeuw, B. J., Locascio, J., Amariglio, R. E., Papp, K., Rentz, D. M., Sperling, R. A. & Johnson, K. A.,
5 May 2020, In: Neurology. 94, 18, p. E1916-E1928 13 p.

Early cognitive and emotional outcome after stroke is independent of discharge destination
Slenders JPL, Verberne DPJ, Visser-Meily JMA, Van den Berg-Vos RM, Kwa VIH, van Heugten CM.
J Neurol. 2020 Nov;267(11):3354-3361.

MENTAL HEALTH

DNA methylation in the 5-HTT regulatory region is associated with CO2-induced fear in panic disorder patients
Leibold, N. K., Weidner, M. T., Ziegler, C., Ortega, G., Domschke, K., Lesch, K. P., Van den Hove, D. L. & Schruers, K. R.,
Jul 2020, In: European Neuropsychopharmacology. 36, p. 154-159 6 p.

No boundaries: a 2 year experience in a specialized youth mental health care program in the Netherlands
Leijdesdorff, S., Postma, M. R., van Kersbergen, L., Marchetta, N. & van Amelsvoort, T.,
Apr 2020, In: Early Intervention in Psychiatry. 14, 2, p. 228-234 7 p.

Association of Recent Stressful Life Events With Mental and Physical Health in the Context of Genomic and Exposomic Liability for Schizophrenia
Pries, L-K., van Os, J., ten Have, M., de Graaf, R., van Dorsselaer, S., Bak, M., Lin, B. D., van Eijk, K. R., Kenis, G., Richards, A., O'Donovan, M. C., Luykx, J. J., Rutten, B. P. F. & Guloksuz, S.,
Dec 2020, In: JAMA Psychiatry. 77, 12, p. 1296-1304 9 p.

Glutamatergic and GABAergic reactivity and cognition in 22q11.2 deletion syndrome and healthy volunteers: A randomized double-blind 7-Tesla pharmacological MRS study
Vingerhoets, C., Tse, D. H. Y., van Oudenaren, M., Hernaus, D., van Duin, E., Zinkstok, J., Ramaekers, J. G., Jansen, J. F., McAlonan, G. & van Amelsvoort, T.,
Aug 2020, In: Journal of Psychopharmacology. 34, 8, p. 856-863 8 p., 0269881120922977.

Monitoring risk assessment on an acute psychiatric ward: Effects on aggression, seclusion and nurse behaviour
Florisse, E. J. R. & Delespaul, P. A. E. G.,
2 Oct 2020, In: PLOS ONE. 15, 10, 12 p., 0240163.

TRANSLATIONAL NEUROSCIENCE

The association between genome-wide polymorphisms and chronic postoperative pain: a prospective observational study
van Reij, R. R., Hoofwijk, D. M. N., Rutten, B. P. F., Weinhold, L., Leber, M., Joosten, E. A. J., Ramirez, A., van den Hoogen, N. J., & Italian Pain Group,
Jan 2020, In: Anaesthesia. 75, S1, p. E111-E120 10 p.

Ceramide analog [F-18]F-HPA-12 detects sphingolipid disbalance in the brain of Alzheimer's disease transgenic mice by functioning as a metabolic probe
Crivelli, S. M., van Kruining, D., Luo, Q., Stevens, J. A. A., Giovagnoni, C., Paulus, A., Bauwens, M., Berkes, D., de Vries, H. E., Mulder, M. T., Walter, J., Waelkens, E., Derua, R., Swinnen, J., Dehairs, J., Mottaghy, F. M., Losen, M., Bieberich, E. & Martinez-Martinez, P.,
9 Nov 2020, In: Scientific Reports. 10, 1, 14 p., 19354.

GAT-1 (rs2697153) and GAT-3 (rs2272400) polymorphisms are associated with febrile seizures and temporal lobe epilepsy.
Schijns OE, Bisschop J, Rijkers K, Dings J, Vanherle S, Lindsey P, Smeets HJ, Hoogland G. Epileptic Disord.
2020 Apr 1;22(2):176-182. doi: 10.1684/epd.2020.1154.

Roubroeks, J. A. Y., Smith, A. R., Smith, R. G., Pishva, E., Ibrahim, Z., Sattlecker, M., Hannon, E. J., Kloszewska, I., Mecocci, P., Soininen, H., Tsolaki, M., Vellas, B., Wahlund, L-O., Aarsland, D., Proitsi, P., Hodges, A., Lovestone, S., Newhouse, S. J., Dobson, R. J. B., Mill, J. & 2 others, van den Hove, D. L. A. & Lunnon, K.,
Nov 2020, In: Neurobiology of Aging. 95, p. 26-45 20 p.

Bertens, C. J. F., Martino, C., van Osch, M. C., Lataster, A., Dias, A. J. A. A., van den Biggelaar, F. J. H. M., Tuinier, R., Nuijts, R. M. M. A. & Gijs, M.,
May 2020, In: European Journal of Pharmaceutics and Biopharmaceutics. 150, p. 120-130 11 p.

PHD THESES 2020

Last name	Initials	Theses defence	Promotor(s)	Copromotor(s)	Title Theses
A. Youssef	N.	23–01–2020	Prof. Dr. B. Rutten	Prof. Dr. P. Sienaert (Leuven)	*Epigenetics, resilience and brain stimulation: advances in the mechanistic and therapeutic utility in patients with affective (PTSD and mood) disorders*
Aldheri	M.	07–10–2020	Prof. Dr. Y. Temel	Dr. S. Hescham Dr. A. Jahanshianvar	*Deep brain stimulation, memory functions and mechanisms*
Appaji	A.	30–01–2020	Prof. Dr. C. Webers	Dr. T. Berendschot Dr. N. Rao (Bangalore)	*Retinal vascular features as a biomarker for psychiatric disorders*
Atagun	I.	27–05–2020	Prof. Dr. T. van Amelsvoort	Dr. S. Guloksuz Dr. M. Drukker	*Cognitive neurophsysiology and neurochemistry in bipolar disorder.*
Atcharayam	N.	23–04–2020	Prof. Dr. T. Delhaas Prof. Dr. B. Kramer		*Duchenne Muscular Dystrophy: The NIMHANS Experience*
Bartels	S.	17–09–2020	Prof. Dr. F. Verhey Prof. Dr. M. de Vugt	Dr. R. van Knippenberg Dr. C. Malinowsky - (Karolinska Institutet, Sweden)	*Monitoring Everyday Life in Aging & Dementia - Perspectives from Experience Sampling and Technology Use*
Bennis	F.	13–11–2020	Prof. Dr. T. Delhaas Prof. Dr. B. Kramer	Dr. P. Andriessen (MMC Veldhoven)	*Machine learning in medicine - Big picture require small, but crucial strokes*
Bernas	A.	29–09–2020	Prof. dr. A. Aldenkamp	Dr. ir. S. Zinger (TUE)	*Resting -state fMRI neurodynamics in neuropsychiatric disorders*
Bronswijk van	S.	11–12–2020	Prof. Dr. F. Peeters Prof. Dr. M. Huibers	Dr. L. Lemmens	*Personalized treatment strategies for depression*
Brunings	J.W.	10–12–2020	Prof. Dr. B. Kremer	Dr. L. Baijens Dr. A. Hamaekers	*Concerning Assumptions in Laryngology*
Christie	H.	18–09–2020	Prof. Dr. M. Vugt Prof. dr. F. Verhey	Dr. H. Tange	*The Implementation of EHealth in Dementia Care: Lessons learned*
Damas	M.	16–12–2020	Prof. Dr. P. Martinez	Dr. M. Losen Dr. R. Rouhl	*Autoantibodies in the nervous system: pathophysiology and new therapeutic strategies*
Drenthen	G.	02–07–2020	Prof. Dr. ir. W. Backes Prof. Dr. A. Aldenkamp	Dr. J. Jansen	*Myelin and networks, Magnetic Resonance Imaging in Epilepsy*
Elbatrik	M.	26–08–2020	Prof. Dr. H. Schmidt	Dr. A. Casas Guijarro	*Network pharmacology for mechanistically redefined comorbidities*
Fonseca-Wald	E.	03–06–2020	Prof. Dr. R.J. Vermeulen	Dr. S. Klinkenberg Dr. M. Debeij-van Hall Dr. J. Hendriksen	*Absence Epilepsy and Panayiotopoulos Synrome: Neurocognition and Brain Development*
Franken	G.	03–12–2020	Prof. Dr. E. Joosten Prof. Dr. J. van Zundert	Dr. A.L. Liem (MC Jan van Goyen A'dam)	*Neuromodulation of the Dorsal Root Ganglion in Experimental Chronic Neuropathic Pain: Efficacy and Mechanisms of Action*

Last name	Initials	Theses defence	Promotor(s)	Copromotor(s)	Title Theses
Gorlova	A.	03–05–2020	Prof. Dr. K. Lesch	Dr. T. Strekalova Prof. Dr. L. Bettendorff (Liege)	*Understanding the Molecular Mechanisms of Aggression in BALB/C and TPH2-Deficient Mice*
Gronning	A.	28–08–2020	Prof. Dr. H. Schmidt Prof. Dr. J. Baumbach (University of Southern Denmark)	Dr. R. Rottger	*Big Data Analytics in Bioinformatics*
Gruters	A.	18–12–2020	Prof. dr. M. de Vugt Prof. dr. F. Verhey Prof. Dr. R.P.C. Kessels (Radboud)	Dr. I.H.G.B. Ramaekers	*Neuropsychological Assessment at the Memory Clinic: Innovations in communicating neuropsychological test results in the diagnostics of dementia*
Hagen van	B.	14–09–2020	Prof. dr. J. Prickaerts Prof. dr. H. Schmidt		*Improving Pattern Separation and Cognition: Effects of Pharmacological Interventions on Rodent Behavior and europlasticity*
Haumann	J.	01–08–2020	Prof. Dr. E. Joosten	Prof. Dr. M.H.J. van den Beuken-van Everdingen Dr. S.M.J. van Kuijk	*Prevalence and pharmalogical treatment of pain in patients with cancer; The role of opioids with and without NMDA receptor affinity*
Hoevenaars	J.	20–11–2020	Prof. Dr. C. Webers	Dr. J.S.A.G. Schouten (Radboud)	*Knowledge, adherence and outcome in glaucoma*
Hovinga	K.	02–07–2020	Prof. Dr. Y. Temel	Prof. V. Tabar (New York)	*Angiogenesis Inhibition in Glioblastoma*
Kamps	R.	20–11–2020	Prof. Dr. H. Smeets	Dr. F. van Tienen	*Resolving the Role of Genetic Defects and mtDNA Copy Number in MitochondrialDisease and Development*
Kentheeswaran-Wijesinghe	P.	25–08–2020	Prof. Dr. H. Steinbusch Prof. Dr. R. de Silva (extern) Prof. Dr. D. Shankar (NIMHANS)		*Age-related cytoskeletal pathologies: A study on elderly brains to investigate the extent of neuropathological and cerebrovascular changes at death ad their risk factors*
Kirli	U.	18–11–2020	Prof. Dr. J. van Os	Dr. M. Drukker Dr. T. Binbay (Dokuz Eylul University, Turkey)	*Exploring Psychotic Experiences in the Context of Multidimensional Psychopathology: A Longitudinal Community-based Approach'*
Koetsier	E.	09–02–2020	Prof. dr. E. Joosten Prof. dr. J. van Zundert	Dr. S. van Kuijk	*Dorsal Root Ganglion Stimulation for Pain Relief in Painful Polyneuropathy: Efficacy and Mechanism of Action*
Kucukgoncu	S.	14–12–2020	Prof. Dr. B. Rutten	Dr. S. Guloksuz	*Metabolic Disturbances in Mental Illness*
Meijer	S.	09–11–2020	Prof. dr. R. Ponds	Dr. J. de Jonghe	*Visual Associative Learning in Alzheimer's Disease and Performance Validity*
Montes Diaz	G.	15–10–2020	Prof. Dr. R. Hupperts Prof. Dr. V. Somers (Hasselt)	Dr. J. Fraussen (Hasselt)	*Immune regulation by mimethyl fumarate (DMF) in relapsing-remitting multiple sclerosis patients*

Last name	Initials	Theses defence	Promotor(s)	Copromotor(s)	Title Theses
Mulders	A.	11–05–2020	Prof. Dr. A. Leentjens Prof. Dr. Y. Temel		*Monitoring and Modulating Neuropsychiatric Symptoms in Parkinson's disease and obsessive-compulsive disorder*
Nijsse	B.	09–02–2020	Prof. Dr. C. van Heugten Prof. Dr. J. Visser-Meily Prof. Dr. J. Spikman	Dr. P. de Kort	*Cognition after stroke; various perspectives*
Noij	K.	03–06–2020	Prof. Dr. H. Kingma Prof. Dr. S. Rauch (Harvard)	Dr. R. van de Berg	*Cervical vestibular evoked myogenic potentials; Toward optimizing clinical use*
Oosterloo	M.	11–06–2020	Prof. Dr. R. Roos (Leiden) Prof. Dr. C. de Die-Smulders	Dr. E. Bijlsma	*Controversies and pitfalls in diagnosing Huntingyon's disease*
Pavlov	D.	03–05–2020	Prof. Dr. K. Lesch	Dr. T. Strekalova Prof. Dr. L. Bettendorff (Liege)	*The contribution of CNS inflammation and Glycogen Synthase Kinase-3 (GSK-3)-cascades on adverse memory learning on mouse models of emotional stress*
Pazinato Aguiar	R.	15–12–2020	Prof. Dr. J. Prickaerts	Dr. R. Welfort de Oliveira (State University Maringa, Brazil)	*The contribution of 5-HT1A receptors in improving plasticity and function of the brain*
Pries	L.	11–12–2020	Prof. Dr. B Rutten Prof. Dr. J. van Os	Dr. S. Guloksuz	*The interplay between the genome and the exposome in psychosis spectrum*
Priovoulos	N.	01–09–2020	Prof. Dr. F. Verhey	Dr. H. Jacobs Dr. B. Poser	*Structural and functional imaging of the locus coeruleus at 7T: from methodological to clinical application*
Raghu	R.	07–12–2020	Prof. Dr. Y. Temel Prof. Dr. N. Siraam (Karnataka, India)	Dr. P. Kubben Dr.E. Gommer	*Automated seizure detection for remote monitoring*
Reij van	R.	17–09–2020	Prof. dr. E. Joosten	Dr. N. van den Hoogen	*Genetic Risk Factors in prediction and tratment of Chronic Post-Surgical Pain"*
Riphagen	J.	01–08–2020	Prof. Dr. F. Verhey	Dr. H. Jacobs	*Vascular matters in aging and dementia*
Tilburg van	M.	03–06–2020	Prof. Dr. H. Kingma Prof. Dr. S. Rauch (Harvard)	Dr. R. van de Berg Dr. B. Hermann (Boston)	*Advancement cVEMP's*
Veniaminova	E.	03–05–2020	Prof. Dr. K. Lesch	Dr. T. Strekalova Prof. D. Anthony (Oxford)	*The impact of the 'Western Diet' on Emotional, Social and Cognitive Behaviours as revealed by a study on conventional and serotonin Transporter-Deficient Mice*
Verberne	D.	09–11–2020	Prof. dr. C. van Heugten Prof. dr. R. Ponds	Dr. M. Kroese	*Psychosocial outcome after stroke and traumatic brain injury - Longitudinal perspectives and recommendations for aftercare*
Verhagen	S.	01–10–2020	Prof. Dr. P. Delespaul Prof. Dr. J. van Os (UM/UU)	Dr. C. Simons	*The power of individual landscapes; A clinical exploration of personal experience sampling and new horizons*

Last name	Initials	Theses defence	Promotor(s)	Copromotor(s)	Title Theses
Weijers	J.	08–12–2020	Prof. Dr. J. P. Selten Prof. Dr. E. Eurelings-Bontekoe (Leiden)	Dr. W. Viechtbauer	*Mentalization and psychosis - Trying to understand the "un-understandable"*
Yakkioui	Y.	09–09–2020	Prof. dr. Y. Temel Prof. dr. M. van Engeland		*Molecular biomarkers in skull base chordoma*

Contact information

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