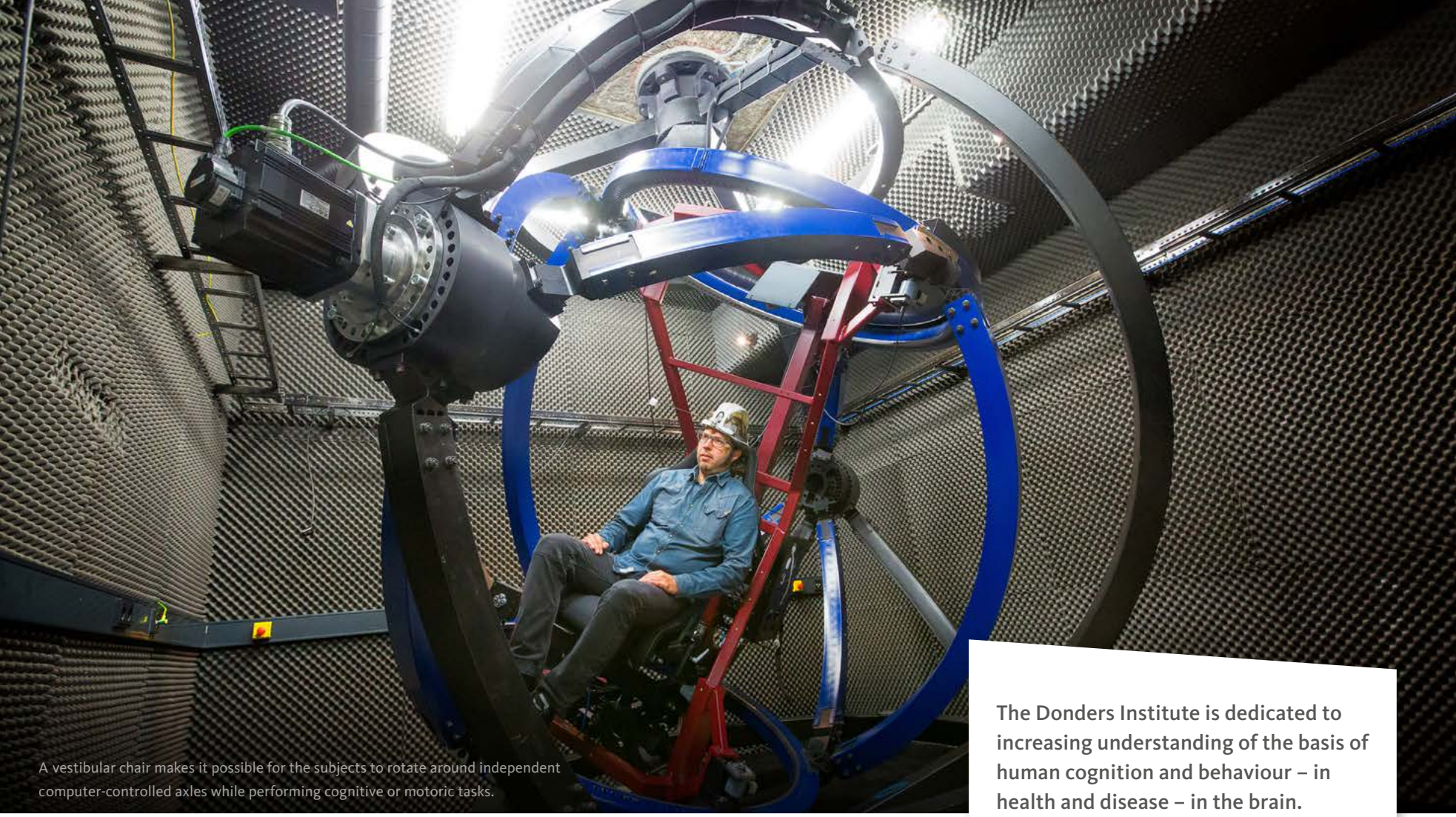


A vestibular chair makes it possible for the subjects to rotate around independent computer-controlled axles while performing cognitive or motoric tasks.

The Donders Institute is dedicated to increasing understanding of the basis of human cognition and behaviour – in health and disease – in the brain.

Donders Institute for Brain, Cognition and Behaviour

Comprehending the brain and how it enables our thoughts, emotions and actions has sparked curiosity for centuries. It is also essential if we are to be able to answer fundamental questions about human beings. Recent technological and theoretical advancements are delivering unprecedented insights into the way the brain works, also making it possible to answer more applied questions.

The Donders Institute is home to more than 700 researchers from more than 35 countries who share the common goal of contributing to advancing brain-, cognitive- and behavioural sciences through investigator and curiosity-driven research, and improving health, education, nutrition, and technology by applying advances in this field. The DI's mission is to be a leading international research centre in the field of systems level cognitive neuroscience. This includes conducting excellent interdisciplinary research at the unique interface between genetic, molecular and cellular processes at one end of the spectrum and computational, system-level neuroscience with cognitive and behavioural analyses at the other end. Within this wide interdisciplinary range the Institute focuses on four research themes:

- Language and Communication
- Perception, Action and Control
- Plasticity and Memory
- Brain Networks and Neuronal Communication

Established researchers head Principal Investigator (PI) groups of varying sizes, composed mainly of young upcoming scientists. They tackle research projects both at the level of the single PI group and by forming highly interactive, collaborative cross-faculty projects and by international networks. They are thus able to answer research questions that are too complex to be answered by single groups.

This interdisciplinary, cooperative culture – combined with excellent multidisciplinary research – is also at the core of the Donders Graduate School, which integrates an internationally recognised Research Masters programme with ambitious PhD training. The Masters programme is structured in four tracks that are fully aligned with the four research themes of the Donders Institute, thus integrating young students optimally in the research. The PhD training programme supports young scientists by providing general academic skills while helping them move towards their own independent lines of research.

Research facilities

The Donders Institute has access to state-of-the-art equipment and highly competent technical staff, which allows researchers to carry out the most advanced work.

To understand human brain function and dysfunction at the cognitive and behavioural level a large number of laboratories are used, with set-ups for baby and toddler studies, an artificial intelligence laboratory, and numerous sensorimotor facilities, including a fall simulator, a vestibular sled and chair, 'reach-in' 3D visualisation and force-feedback virtual reality equipment.

To measure human brain function with precision while individuals perform specific cognitive tasks, the Institute employs a comprehensive set of neuroimaging tools comprising four research-only MRI scanners, including a joint-venture high-field system that is housed at the Erwin L. Hahn Institute, a whole-head MEG system, several multi-channel EEG and near-infrared spectroscopy systems. These neuroimaging facilities are complemented by equipment enabling modulation of human brain function such as several transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) laboratories.

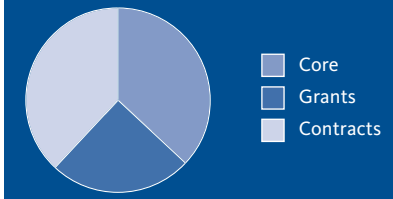
Tenured

Full professors	29.59 FTE
Associate professors	13.39 FTE
Assistant professors	29.57 FTE
Researchers	24.63 FTE

Non-tenured

Researchers	139.02 FTE
Doctoral candidates	226.56 FTE

Research staff funding



To decipher underlying biological mechanisms the Institute also uses a broad range of other laboratories on campus, covering all levels from molecular biology to animal behaviour. State-of-art techniques are available that are at the forefront of sequencing technology developments, including large data sets of patient cohorts and neural stem-cell cultures. The central animal facility provides animal MRI, PET, CT/SPECT and a great variety of behavioural tasks for rodents. In 2016 a light-sheet microscope was installed, which makes it possible to image a whole brain without cutting it open. In addition, several other technologies are available, such as 2-photon microscopy, multi-unit *in vivo* electrophysiology and optogenetics – just to mention a few – and these are being further developed locally within the context of the Radboud Research Facilities and Radboudumc Technology Centres.

These experimental tools are complemented by high-performance computing facilities, which enable advanced data analyses, data modelling and simulations for which the Institute is well known. This computer infrastructure also supports very large-scale studies, creating large databases of several thousands of individuals for brain-imaging genetics and patient cohorts.

Prizes and awards (selection in alphabetical order)

- Harold Bekkering was elected as a member of the Royal Netherlands Academy of Arts and Sciences (KNAW).
- Han Brunner was awarded the Carter Medal of the Clinical Genetics Society Great Britain.
- Han Brunner and Joris Veltman were awarded this year's King Faisal International Prize in medicine.
- Roshan Cools was elected as a member of the Academia Europaea.
- Peter Desain and his team have been awarded First Prize in the Assistive Technology Challenge. He also was elected as a member of the Netherlands Academy of Technology and Innovation.
- Christian Doeller was elected as a member of the Memory Disorders Research Society (MDRS) and he received the Radboud Science Award.
- Jason Farquhar and his team made it to the second position in the BCI race of the Cybathlon at ETH in Zurich.
- Guillén Fernández received the 2016 Hermesdorf Award International. This award is granted to Radboud University researchers whose work has received special attention in the media.
- Corina Greven received the Kramer-Pollnow Young Investigator's Award.
- Nanda Lambregts Rommelse was awarded the Kramer-Pollnow Prize.
- James McQueen was elected as a Fellow of the Association for Psychological Science.
- Sina Radke was awarded with the Heinz-Heckhausen Jungwissenschaftler-Preis by the Deutsche Gesellschaft für Psychologie.
- Johanna van Schaik received the NRO award for promising researchers in education sciences.

Grants

- NWO Veni grants were awarded to Marisa Casillas (MPI), Koen Haak, Rick Helmich, Joost Rommers and Tessa Verhoef (MPI). Linda Geerligs joined the Donders Institute after receiving an NWO Veni grant.
- NWO Vidi grants were awarded to Andre Marquand and Sharon Unsworth (Affiliated Research Fellow, CLS).
- John van Opstal received an ERC Advanced Grant.
- Christian Doeller received an ERC Consolidator grant.
- Janneke Jehee received an ERC Starting Grant.
- José Marques received a grant from FOM projectruimte.
- Mariya Manahova obtained a Research Talent grant from NWO.
- Johan Kwisthout received an NWO EW TOP grant.
- Janny Stapel was awarded a Rubicon grant.
- Rick Helmich and Alex Garanto both received a ZonMw Off-Road grant.
- Adjmal Sarwary was awarded an STW Take-off grant.

Collaboration

Research carried out at the Donders Institute is conducted in a collaborative national and international setting. In Nijmegen the Centre for Language Studies at the Radboud University and the Max Planck Institute for Psycholinguistics are affiliated institutes. In Germany the Institute collaborates with the University of Duisburg-Essen on the operation of a joint research centre for high-field MRI, the Erwin L. Hahn Institute, in Essen. The Donders Institute also signed collaboration agreements with two other preferred partners: with the Brain and Mind Institute of the Western University Ontario (Canada) and with the Brain Mind Institute of the Ecole Polytechnique Fédérale de Lausanne (Switzerland).

Furthermore, the Institute collaborates in research consortia with leading institutes, industrial partners and other potential users of its research. Joining forces in this way extends research beyond the Institute and increases the societal impact of research results. The Institute participates in a large number of high-quality, innovative consortia, including:

- An NWO Gravitation Grant *Language in Interaction*, which is coordinated in Nijmegen, brings together 50 researchers from eight universities and one research institute in the Netherlands.
- Large EU consortium grants, including: Matrics, PREPARE and Eat2BeNICE. Eat2BeNICE is a consortium of 20 partners that investigates links between nutrition, the microbiome, and impulsive and compulsive behaviour. This is an EU Horizon 2020 project in the field of Nutrition (€12 million).

- Several EU (Marie Curie) training networks, such as Healthpac (led by the Donders Institute), Childbrain, MiND and BrainTrainMat.
- Regionally and nationally funded projects that bring together Dutch universities and private- sector partners. Examples are BriteN, NeuroCIMT and NESTOR. The NESTOR consortium will develop a prosthesis that stimulates the brain of blind people via micro-electrodes which will be connected to a camera. It has been selected as part of the financing programme Perspective for Top-Priority Sectors.
- Other consortium projects: BIG and Cognomics, with the Donders Institute, the Radboudumc, and the Max Planck Institute for Psycholinguistics as initiating partners.
- The Institute is a collaborating partner in the Human Brain Project, which was selected by the EU as one of two flagship projects, and it contributes to the US Human Connectome Project.
- An agreement between the Radboud University and Wageningen University and Research for collaboration in the field of Cognition and Nutrition.
- The Parkinson Precision Project, a major public-private partnership between the Donders Institute, Radboudumc, Radboud University and Verily Lifescience.

See the Institute's website for more details about all of these collaborations.

Societal impact

The research carried out at the Institute has considerable potential for benefiting society in five areas: Health & Healthcare, Food & Cognition, Learning & Education, Neurotechnology & Big data and Public & Policy. A key aim is to disseminate expertise and knowledge to a wide range of stakeholders.

- To inform the *general public*, Donders researchers appear regularly on national television, in numerous national and international newspapers, on radio at large festivals and on many websites. In the blog 'DondersWonders', researchers at the Institute write non-specialist articles on neuroscientific topics for the general public. With two blogs per week in Dutch and English, and over 150,000 views in 2016, this clearly has considerable impact. Furthermore, to educate a wider public about the latest research done at the Donders Institute and increase awareness about how neuroscience works, an Open Day was organised in September. With over 2500 visitors from Nijmegen and surroundings, the Donders Open Day was a great success. Finally, the public is informed about research news and events at the Institute through various social media.
- To inform the *scientific community*, Donders researchers took the active lead in workshops and in organising international conferences.
- Donders scientists disseminate new findings and knowledge to *industry*, mostly through numerous mutually beneficial collaborations with commercial partners varying from smaller companies that manufacture technical devices (such as Noldus and Otticon) to large multinationals (*e.g.* Philips, Siemens, Heinz and Danone). The institute is a member of 'ICT for Brain, Body & Behaviour' (i3B), a European network of ICT companies and knowledge institutes in the field of brain, cognition, physiology and behaviour that aims to connect business and encourage innovation through joint R&D projects. The Institute is also involved in Radboudumc Technology Centres and 'Radboud Research Facilities'. The latter is an initiative by the province Gelderland to stimulate the regional economy through innovation by small and medium-size enterprises that apply scientific knowledge and access these facilities.

Director Professor David Norris

Prof. Norris has been Director of the Donders Institute's Centre for Cognitive Neuroimaging since January 2009. In July 2001 he was appointed Principal Investigator of the research group MR Methods for Cognitive Neuroscience at the Donders Institute and in 2003 he became Professor of MR Physics for Cognitive Neuroscience at the University. He is also an external scientific member of the Max Planck Institute for Psycholinguistics (2014). His research interests include improving brain imaging techniques, fMRI of cortical layers and spectroscopy of brain metabolites. Prof. Norris is also one of the directors of the Erwin Hahn Institute in Essen and a member of the medical faculty at the University of Duisburg-Essen.

- Donders researchers are actively involved in several *spin off initiatives*. In 2016, several new initiatives led to new spinoff companies, including Neurant and Mind Trace. These initiatives enhance knowledge transfer to society and enable close collaborations with various societal stakeholders.
- Five vouchers, each worth €5000 were made available to support Donders scientists in working out a creative innovative idea that specifically contributes to the societal relevance of the Donders Institute. With these vouchers, the Institute encourages researchers to engage in innovation and increase the societal impact of their research.
- Research is well embedded in *clinical care* within the Radboudumc and beyond. Implementing new findings in clinical practice is part of the daily work of Donders clinicians, as is the education of peers, patients and patient organisations through lectures, meetings and forums. Donders researchers are actively engaged with patient organisations and participate in developing diagnostic and treatment guidelines and standards of care. Clinical Donders researchers not only strive to translate fundamental insights into advance care, they also innovate the way care is delivered, *e.g.* through e-health applications (example: the project 'Depression treatment at distance' that is part of the INTERREG programme Germany-Netherlands).
- Donders researchers actively participate in *educational development*. In 2016 the Donders Education Hackathon was organised as was as the conference 'Donders meets education 2016: Focus & Flow in the classroom' in collaboration with RadboudCSW.
- Through participation in public debate Donders researchers contribute to *regional and national policies* by discussing the impact of neuroscientific insights on economic and social development. They also play a key role in guiding and organising platforms for the ethical thinking needed to apply new neurotechnologies, for example regarding robotics. At the national level, researchers at the Institute serve on committees of research policy organisations such as the Netherlands Organisation for Scientific Research (NWO), the Royal Netherlands Academy of Arts and Sciences (KNAW), the National Initiative Brain and Cognition, and the Rathenau Institute. Researchers at the Institute collaborate with *external partners* in areas such as psychiatry (*i.e.* those working in the Pompe Clinic in Nijmegen), with the Netherlands Forensic Institute (NFI) the Police Academy, and the Dutch Department of Education. <

Donders Institute for Brain, Cognition and Behaviour

Postal address
P.O. Box 9101, hp204
6500 HB Nijmegen
The Netherlands

Visiting address
Kapittelweg 29
Nijmegen

T: +31 (0)24 365 32 76
E: info@donders.ru.nl
I: www.ru.nl/donders

THEME 1

Language and Communication

Prof. James McQueen (speaker)

Dr Vitória Piai (post-doc, Aspiring Principal Investigator) focuses on language function in healthy and neuropathology patient populations, such as those suffering from stroke, brain tumour, epilepsy and neurodegenerative disorders (*e.g.* dementia, Parkinson's). She applies a range of behavioural and neuroimaging methods and pays special attention to the intersection of language and other functions, such as executive control, (semantic) memory, and motor control relation to speaking.

The goal of the Language and Communication theme (LC) is to understand the uniquely human capacity for language. The LC theme is therefore strongly interdisciplinary, combining research in neuroscience, psychology, linguistics, genetics and computational cognitive science. This approach is necessary to get to grips with the human language faculty in all of its complexity. Explanations are thus sought at multiple levels (linguistic, behavioural and neurobiological), and ultimately at the interfaces between these levels.

LC research focuses on three objectives: *a)* to understand core processes of language and communication (*e.g.* how we speak, understand speech and learn language), and to determine how these processes relate to other cognitive domains (*e.g.* our abilities to perceive and remember); *b)* to determine how language is rooted in the 'language-ready' human brain; and *c)* to understand the balance between the universality and the variability of language and language processes (*i.e.* to determine to what extent abilities are the same across all the world's languages and across all speakers of any given language).

An important feature of this theme is the substantial involvement of the two affiliated institutes: the Max Planck Institute for Psycholinguistics and the Centre for Language Studies.

Research results

A study on neuroimaging genetics used a biology-driven strategy to relate variations in genomic loci, which were previously identified as being active in early embryonic development, to the structure of subcortical brain regions. In a study on >13,000 healthy adults, significant associations were found between targeted single nucleotide polymorphisms and hippocampal volume. This biology-driven approach generates testable hypotheses related to the functional biology of identified associations.

Another study linked previous phonetic, behavioural and neuroscientific work by examining the electrophysiological signatures of speech recognition. Behavioural research has shown that fully-realised forms ("yesterday") have a processing advantage over reduced forms ("yeshay"). Greater oscillatory power in the alpha (8–12 Hz) band, reflecting increased cognitive load, was observed for reduced forms. Greater oscillatory power in the gamma (30+ Hz) band, reflecting a spread of activation through the semantic network, was observed for full forms. These results confirm the processing advantage for full forms and open the door for further research on the oscillatory processes underlying language processing.

Related work explored oscillatory dynamics in the beta and gamma frequency ranges, measured during sentence-level comprehension. A magnetoencephalography experiment compared comprehension of Dutch subject- and object-relative clauses. The results support the view that beta oscillations reflect the maintenance of the neural network configuration responsible for representing sentence-level meaning.

Two studies illustrate work of the theme on prediction. In one, participants listened to incomplete sentences and provided the final word by naming a picture. Pictures were named faster when they could be predicted from the sentence than when they could not. When naming trials were interwoven with trials where sentences had to be read, reading times were faster for predictive than for non-predictive sentences. This suggests that encouraging prediction in production encourages the use of predictive contexts in comprehension. In the other

Staff

Prof. A.F.J. Dijkstra (p)
Prof. S.E. Fisher (e)
Prof. P. Hagoort (o)
Prof. J.M. McQueen (p)
Prof. A.S. Meyer (e)
Prof. A.P.A. Roelofs (p)
Prof. H.J. Schriefers (o)

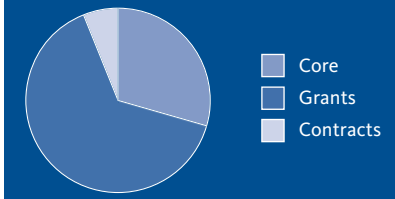
Tenured

Full professors	2.65 FTE
Associate professors	0.47 FTE
Assistant professors	0.83 FTE

Non-tenured

Researchers	6.98 FTE
Doctoral candidates	12.39 FTE

Research staff funding



KEY PUBLICATIONS

- Becker, M., Guadalupe, T., Franke, B., Hibar, D. P., Renteria, M. E., Stein, J. L., Thompson, P.
- M., Francks, C., Vernes, S. C., & Fisher, S. E. (2016). Early developmental gene enhancers affect subcortical volumes in the adult human brain. *Human Brain Mapping, 37*(5), 1788-1800.
- Drijvers, L., Mulder, K., & Ernestus, M. (2016). Alpha and gamma band oscillations index differential processing of acoustically reduced and full forms. *Brain and Language, 153-154,* 27-37.
- Hintz, F., Meyer, A. S., & Huettig, F. (2016). Encouraging prediction during production facilitates subsequent comprehension: Evidence from interleaved object naming in sentence context and sentence reading. *Quarterly Journal of Experimental Psychology, 69*(6), 1056-1063.
- Lewis, A.G., Schoffelen, J.-M., Schriefers, H., & Bastiaansen, M. (2016). A predictive coding perspective on beta oscillations during sentence-level language comprehension. *Frontiers in Human Neuroscience, 10*(85).
- Willems, R.M., Frank, S. L., Nijhoff, A.D., Hagoort, P., & Van den Bosch, A. (2016). Prediction during natural language comprehension. *Cerebral Cortex, 26*(6), 2506-2516.

Dissertations	**8**
Academic publications	**71**
Professional publications	**1**

study, a computational model first determined two measures of word prediction (entropy and surprisal) in three stories, which participants then heard in an MRI scanner. Sensitivity to entropy and surprisal was reflected in different brain regions in the language network, suggesting that prediction during comprehension can occur at multiple levels of processing. This study demonstrates the power of combining computational linguistics with cognitive neuroscience.

Future research

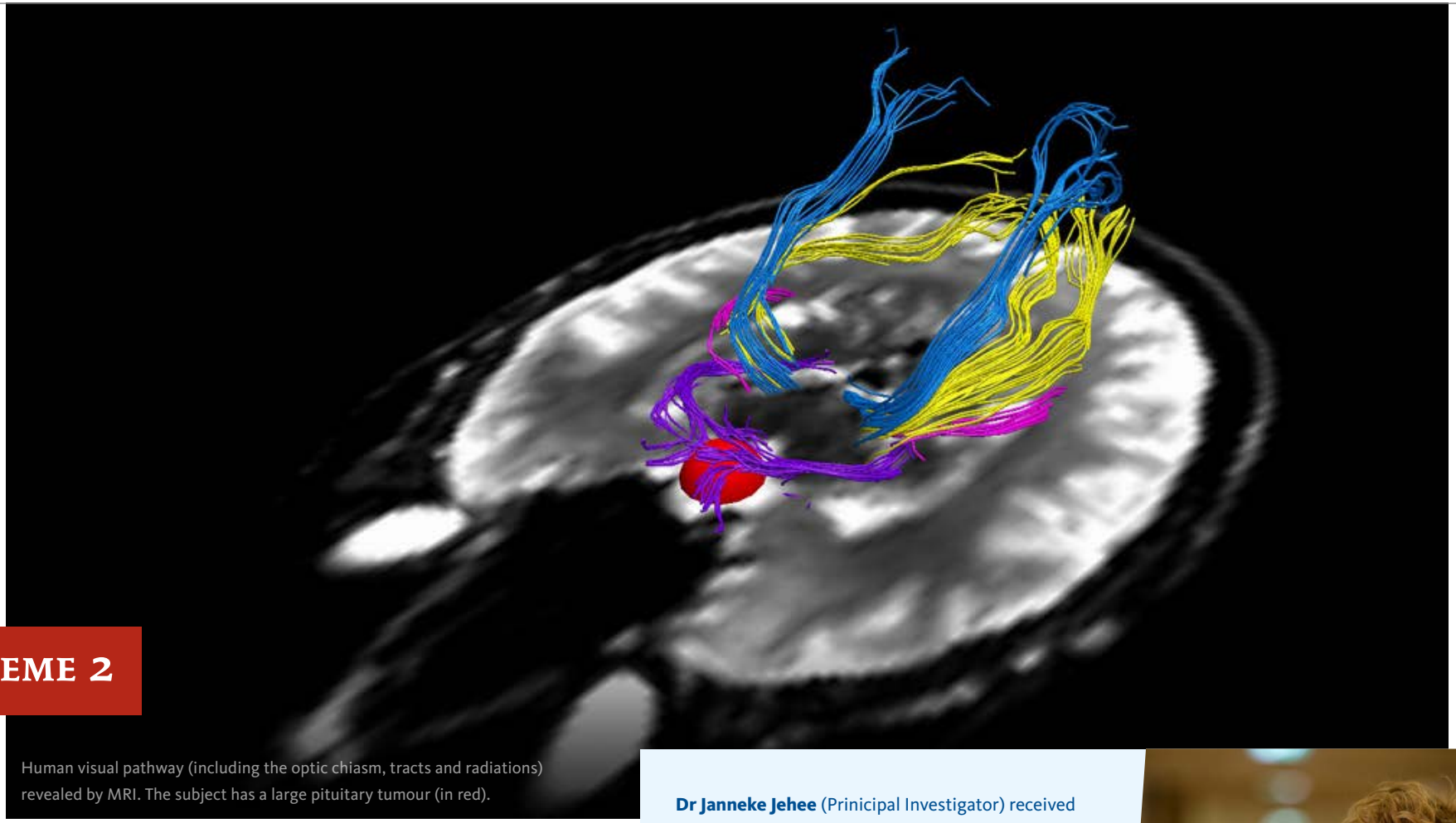
Researchers working on the LC theme will continue to pursue its key objectives in 2017. An important vehicle for this is the NWO 'Language in Interaction' Gravitation grant, which supports a national consortium of researchers including many LC members. PhD and postdoctoral projects already funded by the grant will continue next year. The consortium has recently identified five fundamental questions about language science. New projects designed to answer these questions will begin in 2017.

Donders Institute for Brain, Cognition and Behaviour

Postal address
P.O. Box 9101, hp204
6500 HB Nijmegen
The Netherlands

Visiting address
Kapittelweg 29
Nijmegen

T: +31 (0)24 365 32 76
E: info@donders.ru.nl
I: www.ru.nl/donders



Human visual pathway (including the optic chiasm, tracts and radiations) revealed by MRI. The subject has a large pituitary tumour (in red).

THEME 2

Perception, Action and Control

Prof. Alan Sanfey (speaker)

Dr Janneke Jehee (Prinicipal Investigator) received an ERC Starting Grant. She investigates how visual information is represented in the brain, and how visual representations are adjusted to better serve behavioural demands. She uses both theoretical (modelling) and experimental approaches, including functional brain imaging (fMRI), neural decoding techniques and visual psychophysics.

The mission of the Perception, Action and Control (PAC) theme is to understand the relationship between the brain and the cognitive mechanisms of perception-action integration across a variety of domains, namely perceptual inference, sensorimotor functions, cognitive control, decision-making and social interactions. The following topics are broadly investigated: initial integration between perception and action (during sensorimotor integration), how it is regulated (during decision-making) and how it is exploited (during social interactions), in both health and disease. For sensorimotor integration, researchers examine how sensory processing and motor performance interact within the perception-action cycle. At the level of decision-making, researchers study how the perception-action cycle is regulated on the basis of cognitive, motivational, and emotional factors. During social interactions, researchers study how perception and action are integrated when people are directly interacting with others. Across each of these levels, research also focuses on understanding neurological and psychiatric populations, as well as on the potential social implications of this research. PAC researchers address these issues at the system level; from genes to neuromodulators, from single neurons to brain circuits, and from individual organisms to multiple interacting agents. Multiple techniques are combined, from electrophysiological and neuroimaging methods to clinical and psychopharmacological studies, from genetic and neurobiological methods to developmental and psychophysical studies, and from computational modelling to theoretical analyses. This multidisciplinary and multi-level approach creates the opportunity for a variety of analytical and theoretical perspectives, providing a fertile ground for effective interactions between fundamental and clinical neuroscientists.

Research results

Researchers working on this theme were very productive in 2016. Summarising some important representative findings in the perceptual domain, a study showed that during saccadic eye movements, the image on the retinas is – contrary to subjective experience – highly unstable, outlining how the brain distinguishes the image perturbations caused by saccades and those due to changes in the visual scene. Another publication demonstrated that that true binaural hearing integration in bimodal listeners is only possible when there is sufficient spectral overlap. Using high-field fMRI, another group showed, in collaboration with researchers working on theme 4, that feedback signals evoked by a visual illusion selectively activate the deep layers of the primary visual cortex, demonstrating the potential for non-invasive *in vivo* recordings of neural activity with laminar specificity in humans. Examining learning, a study provided the first behavioural and electrophysiological evidence for influencing reversal learning with exogenous oscillatory electric field potentials. In terms of higher order processes, in a large longitudinal study it was found that puberty shifted emotional control from subcortical brain structures to the prefrontal cortex, with testosterone playing a key role. Finally, researchers developed a suite of tools to quantitatively compare the organisation of brains across species, making it possible to identify homologs of human brain areas for language and social cognition in the macaque brain. On the clinical side, research demonstrated the feasibility of wearing smart glasses for improving gait in people with Parkinson's Disease. Other studies showed that balance capacity in stroke patients can be improved by targeted dynamic balance training, shedding light on the learning potential of

Staff

Prof. H. Bekkering (o)
Prof. B.R. Bloem (o)
Prof. J.K. Buitelaar (o)
Prof. R. Cools (p)
Prof. F.P.M. Cremers (p)
Prof. R. van Ee (e)
Prof. B.G.M. van Engelen (o)
Prof. A.C.H. Geurts (o)
Prof. A.I. den Hollander (o)
Prof. C.B. Hoyng (o)
Prof. J.E.E. Keunen (o)
Prof. B.J. Klevering (o)
Prof. C.J.M. Klijn (o)
Prof. J.M.J. Kremer (p)
Prof. H.F. de Leeuw (o)
Prof. W.P. Medendorp (o)
Prof. R.G.J. Meulenbroek (p)
Prof. A.J. van Opstal (o)
Prof. K. Roelofs (o)
Prof. A.G. Sanfey (p)
Prof. ir. A.F.M. Snik (e)
Prof. I. Toni (p)
Prof. R.A. Wevers (o)
Prof. R.J.A. van Wezel (p)
Prof. M.A.A.P. Willemsen (o)

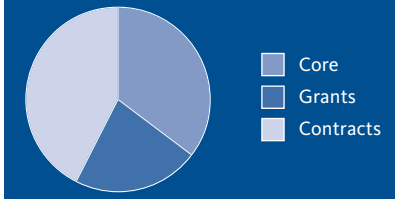
Tenured

Full professors	13.36 FTE
Associate professors	8.57 FTE
Assistant professors	11.73 FTE
Researchers	12.66 FTE

Non-tenured

Researchers	73.48 FTE
Doctoral candidates	103.72 FTE

Research staff funding



KEY PUBLICATIONS

1 Zhao, Y., Nonnekes, J., Storcken, E.J.M., Janssen, S., van Wegen, E.E.H., Bloem, B.R., Dorresteijn, L.C.A., van Vugt, J.P.P., Heida, T., & van Wezel, R.J.A. (2016). Feasibility of external rythmic cueing with the Google Glass for improving gait in people with Parkinson's Disease. *Journal of Neurology, 263*(6), 1156-1165.

2 Kok, P., Bains, Lauren J., van Mourik, T., Norris, David G., & de Lange, Floris P. (2016). Selective activation of the deep layers of the human primary visual cortex by top-down feedback. *Current Biology, 26*(3), 371-376.

3 Stolk, A., Verhagen, L., & Toni, I. (2016). Conceptual alignment: How brains achieve mutual understanding. *Trends in Cognitive Sciences, 20*(3), 180-191.

4 Saksens, N. T. M., Krebs, M. P., Schoenmaker-Koller, F. E., Hicks, W., Yu, M., Shi, L., den Hollander, A. I. (2016). Mutations in CTNNA1 cause butterfly-shaped pigment dystrophy and perturbed retinal pigment epithelium integrity. *Nature Genetics, 48*(2), 144-151.

5 Tyborowska, A., Volman, I., Smeekens, S., Toni, I., & Roelofs, K. (2016). Testosterone during puberty shifts emotional control from pulvinar to anterior prefrontal cortex. *The Journal of Neuroscience, 36*(23), 6156-6164.

Dissertations	**31**
Academic publications	**753**
Professional publications	**20**
Patents	**1**

stroke patients. Donders Institute researchers demonstrated for the first time the *in vivo* potential for splice modulation therapy for a retinal disorder, and in other work used morphological studies in mice to describe mutations in alpha-catenin as a novel cause of macular dystrophy. Finally, the first stem-cell centre-facilitated paper, showing the molecular genetic defect for the most frequent variant in Stargardt disease, was published in 2016.

Future research

Researchers will continue to focus their work as described in the mission. There will be greater emphasis on efforts to align the work of the basic and applied scientists in order to generate and test models of normal and abnormal function, as well as efforts designed to examine the potential relevance of PAC research to public policy.

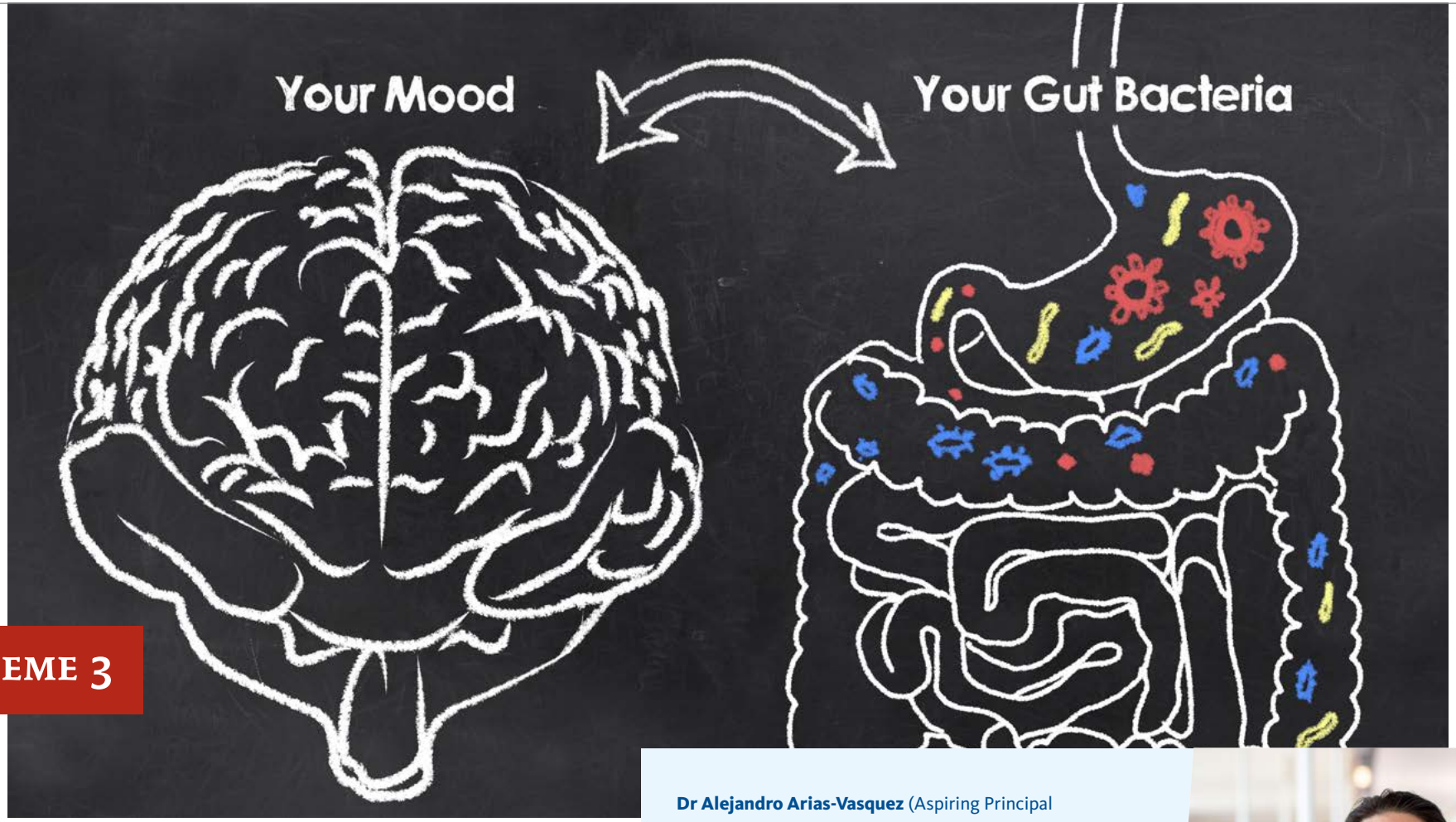
Other studies will test the neural development and predictive value of defensive stress reactions among children who develop typically, as well investigate the long-term effects of perceptual learning treatment in children. Another group will examine how different learning processes enable the dramatic developmental changes young children display in their action performance and in their understanding of others. Research will strongly focus on connecting different levels of analysis to increase understanding of how various top-down factors (expectation and attention) modulate sensory processing. There will be efforts to extend the comparative neuroscience programme, which was established to study the organisation of the great ape brain (gorillas and chimpanzees). Finally, the first gene therapy trials for inherited retinal dystrophies will commence, laying the basis for RetinaNET. ‹

Donders Institute for Brain, Cognition and Behaviour

Postal address
P.O. Box 9101, hp204
6500 HB Nijmegen
The Netherlands

Visiting address
Kapittelweg 29
Nijmegen

T: +31 (0)24 365 32 76
E: info@donders.ru.nl
I: www.ru.nl/donders

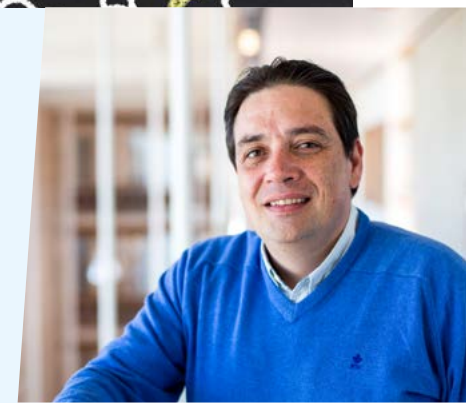


THEME 3

Plasticity and Memory

Prof. Indira Tendolkar (speaker)

Dr Alejandro Arias-Vasquez (Aspiring Principal Investigator) is searching for genes involved in the variation of brain traits as well as for genes involved in the risk of complex neuropsychiatric diseases. He participates in the world's biggest brain imaging genetics consortium, the ENIGMA consortium (enigma.loni.ucla.edu). His group has detected, for instance, an association between the SORL1 gene (a candidate gene for Alzheimer's disease) and hippocampal volume in healthy young adults.



Researchers within the Plasticity and Memory (PM) theme tackle the mechanistic underpinnings and behavioural consequences of long-term changes in neural structure and function. More specifically, the mission is to unravel how neuroplasticity supports adaptation to external and internal challenges, as well as learning and memory throughout the life span. The theme combines a focus on major mental health problems across the life span with the ability to have an impact on other areas such as education.

Research is closely integrated with the Radboudumc research themes 'Neurodevelopmental disorders', 'Stress-related disorders', and 'Alzheimer disease'. It is divided into three subthemes: *a)* development, studying the mechanisms and consequences of normal and abnormal neurodevelopment, including neurodevelopmental disorders and intellectual disability; *b)* adaptation, focusing on the neurobiological effects of external and internal challenges, such as environmental factors, stress and brain damage, as well as their behavioural and emotional consequences, with a clinical focus on affective disorders; *c)* learning and memory, investigating the neural and cognitive mechanisms underlying normal and impaired learning and memory as well as translating these mechanisms into clinically and educationally relevant constructs. The clinical focus of this subtheme is cognitive disorders.

Researchers working on this theme have created powerful networks – making it possible to use state-of-the-art genetic, epigenetic and genomics techniques – and translating them to a variety of animal models as well as human functional neuroimaging approaches, experimental psychology and neuropsychological research. Finally, fundamental research at the human system level is combined with clinical applied research, both in fine-tuned mechanistic as well as large-scale patient cohort studies.

Research results

In a study that received major attention in the international press (Guillén Fernández received the Hermesdorf Award International for this work), researchers have shown that physical exercise performed four hours after learning improves memory retention and increases hippocampal pattern similarity during retrieval. A multi-centre study dissected the system-level machinery underlying this effect in rodents, while a study involving humans revealed that the release of catecholamines related to physical exercise after learning has the same memory stabilising effect in humans. In a large genome-wide association study, meta-analysis researchers showed that early-onset bipolar disorder (≤21 years old) has a significant genetic covariation with attention-deficit/hyperactivity disorder. Further, with respect to developmental neuroplasticity, researchers showed that perinatal reduction of functional serotonin transporters results in developmental delay.

Future research

Alejandro Ariez Vásquez will extend his work on the human microbiome and he has recently received funding from two large EU grants. Hans van Bokhoven and his colleagues will start compound screens using multi-electrode arrays applied to neurons derived from induced pluripotent stem cells from patients with specific neurodevelopmental disorders. Guillén Fernández will continue to tackle two directions of memory, one focusing on knowledge acquisition with special attention paid to the developing brain and another one designed to create clinical tools that reveal individualised assessment of the pathophysiological mechanisms underlying mood and anxiety disorders. Funded by a larger EU-grant, Judith Homberg will continue to investigate whether d-Cycloserine (DCS), a partial NMDA receptor agonist, can facilitate the extinction of drug-related memories. Roy Kessels will establish a network dedicated to

Staff

Prof. J.H.L.M. van Bokhoven (o)
Prof. H.G. Brunner (o)
Prof. J.I.M. Egger (p)
Prof. L. Fasotti (e)
Prof. G.S.E. Fernandez (o)
Prof. B. Franke (p)
Prof. R.P.C. Kessels (o)
Prof. R.T.C.M. Koopmans (o)
Prof. L.T. Kozicz (o)
Prof. E.L.J.M. van Luijtelaar (o)
Prof. G.J.M. Martens (o)
Prof. M.G.M. Olde Rikkert (o)
Prof. B. Roozendaal (o)
Prof. A.H. Schene (o)
Prof. A.E.M. Speckens (o)
Prof. J.A. Veltman (o)
Prof. G.J. van der Wilt (o)

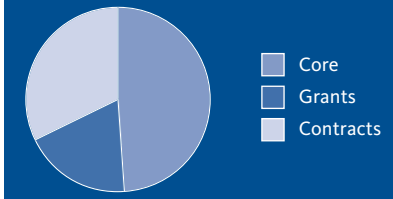
Tenured

Full professors	9.26 FTE
Associate professors	3.83 FTE
Assistant professors	12.51 FTE
Researchers	9.66 FTE

Non-tenured

Researchers	38.30 FTE
Doctoral candidates	63.80 FTE

Research staff funding



KEY PUBLICATIONS

1 Benevento, M., Iacono, G., Selten, M., Ba, W., Oudakker, A., Frega, M., Keller, J., Mancini, R., Lewerissa, E., Kleefstra, T., Stunnenberg, H.G., Zhou, H., van Bokhoven, H., &. Nadif Kasri, N. (2016). Histone methylation by the Kleefstra syndrome protein EHMT1 mediates homeostatic synaptic scaling. *Neuron, 91*(2), 341-355.

2 Kroeze, Y., Peeters, D., Boulle, F., van den Hove, D. L. A., van Bokhoven, H., Zhou, H., & Homberg, J. R. (2016). Long-term consequences of chronic fluoxetine exposure on the expression of myelination-related genes in the rat hippocampus. *Translational Psychiatry, 5*, e642.

3 van Uden, I. W. M., van der Holst, H. M., van Leijsen, E. M. C., Tuladhar, A. M., van Norden, A. G. W., de Laat, K. F., Claassen, J.A., van Dijk, E.J., Kessels, R.P., Richard, E., Tendolkar, I., & de Leeuw, F.-E. (2016). Late-onset depressive symptoms increase the risk of dementia in small-vessel disease. *Neurology, 87*(11), 1102-1109.

4 Thapar, A., Martin, J., Mick, E., Arias Vásquez, A., Langley, K., Scherer, S.W., Schachar, R., Crosbie, J., Williams, N., Franke, B., Elia, J., Glessner, J., Hakonarson, H., Owen, M.J., Faraone, S.V., O'Donovan, M.C., & Holmans, P. (2016). Psychiatric gene discoveries shape evidence on ADHD's biology. *Molecular Psychiatry, 21*(9), 1202-1207.

5 Takeuchi, T., Duszkiewicz, A.J., Sonneborn, A., Spooner, P.A., Yamasaki, M., Watanabe, M., Smith, C.C., Fernández, G., Deisseroth, K., Greene, R.W., & Morris, R.G. (2016). Locus coeruleus and dopaminergic consolidation of everyday memory. *Nature, 537*(7620), 357-362.

Dissertations	**26**
Academic publications	**569**
Professional publications	**40**

communicating new insights into the neural and cognitive underpinnings of Korsakoff patients.

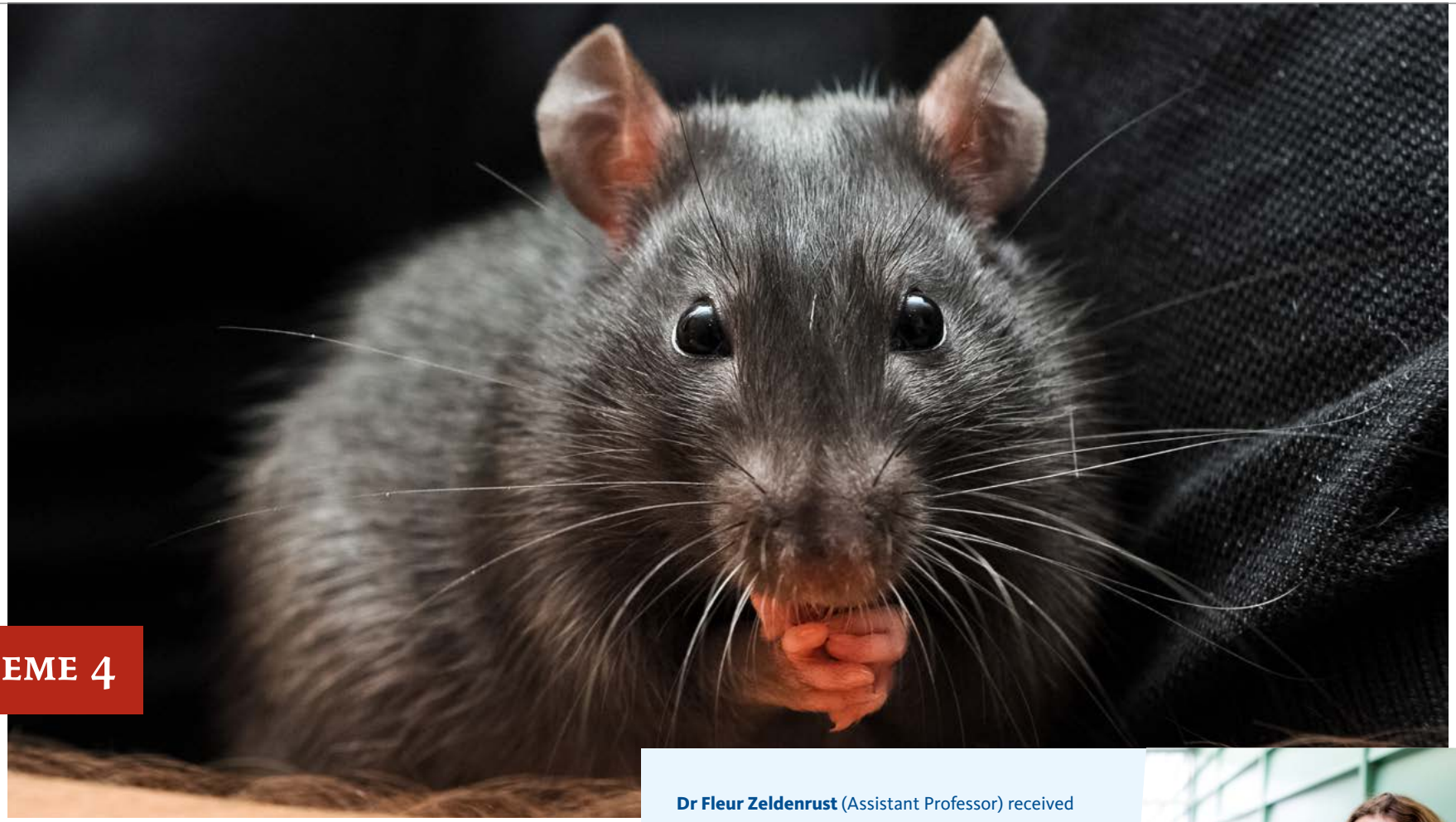
An international imaging consortium working on the effects of electroconvulsive therapy used to treat resistant depression will be coordinated by researchers from Bergen and UCLA as well as Indira Tendolkar. She and her colleagues have received funding from the INTERREG V programme' to develop e-based cognitive intervention for people suffering from depression, in collaboration with partner clinics in Kleve and Essen in Germany. ‹

Donders Institute for Brain, Cognition and Behaviour

Postal address
P.O. Box 9101, hp204
6500 HB Nijmegen
The Netherlands

Visiting address
Kapittelweg 29
Nijmegen

T: +31 (0)24 365 32 76
E: info@donders.ru.nl
I: www.ru.nl/donders



THEME 4

Brain Networks and Neuronal Communication

Prof. Tansu Celikel (speaker)

Dr Fleur Zeldenrust (Assistant Professor) received an NWO Veni grant. She studies the mutual influence of body movements and previous experiences. In her research on these interactions she uses mathematical models and computer simulations, which she compares with measurements on rodent whiskers.

The mission of researchers working on the Brain Networks and Neuronal Communication (BNNC) theme is to characterise and understand how groups of neurons interact and which mechanisms are involved in influencing behaviour and cognition. The research focuses on the network perspective, with the aim of understanding neural coding and communication at various levels. Vertical integration is approached experimentally by applying and developing state-of-the-art methodologies, spanning the full range from recording individual neurons in animals to human imaging of brain networks. The experimental methods are complemented by developing advanced analysis techniques, which also embrace the various levels. Theoretically, computational principles for neuronal coding and communication are developed using computational models ranging from synaptic communication to network dynamics.

It is becoming increasingly clear that cognition and behaviour need to be understood at the level of dynamic network interactions that involve several brain regions. Likewise, it is now also recognised that pathologies in neural communication may underlie neurological and psychiatric disorders. Researchers working on the BNNC theme are therefore involved in numerous clinically-related projects.

The aim of researchers working on this theme is to make theories, method developments and state-of-the art techniques available to the wider community. This is achieved through various proactive dissemination and educational initiatives, including making toolboxes and databases publically available.

Research results

With the increased accessibility of high throughout sequencing, the statistical properties of gene sets now make it possible to study biological processes as molecular networks, from genes to macromolecular complexes. A novel framework now provides a statistical backbone for any gene-set analyses, from single neurons in the brain to the tissue level across the body [1].

Information processing in the brain starts in single neurons, where each neuron generates action potentials based on the input they receive from other neurons. New research now shows that this transformation is dynamically controlled by the recent activity in each neuron, as neurons represent the recent memory of their aggregated synaptic inputs in the form of electrical charges [2]. Experiments *in silico* show that this form of adaptive control of spiking ensures robust information transfer in the brain [2].

The information transferred to the receiving neurons could be excitatory or inhibitory, thus it might either activate or inhibit the neurons that receive the synaptic communication. New research shows that inhibitory synaptic communication might play unique computational roles in the auditory system [3]. Specifically, adaptive control of inhibition might perform gain control, ensuring high fidelity representation of the auditory signals, independent of how loud the stimulus is.

Correlated changes across inhibitory and excitatory neuronal populations contribute to the emergence of oscillations in neuronal activity. Recent research now provides novel insights into how sensory information modulates the timing of oscillatory synchronisation and its informative power in predicting the arrival of sensory information in the near future [4].

One of the ways cortical layers differ from each other is the rhythm of the local neuronal activity. New research provides novel insight into how the functional and electrical signatures of these oscillations vary across

Staff

Prof. C.F. Beckmann (o)
Prof. T. Celikel (o)
Prof. P.W.M. Desain (o)
Prof. P. Fries (e)
Prof. C.C.A.M. Gielen (p)
Prof. M.N. Helmstädter (e)
Prof. O. Jensen (p)
Prof. H.J. Kappen (p)
Prof. D.G. Norris (p)
Prof. B.E.R. de Ruyter (e)
Prof. P.H.E. Tiesinga (o)

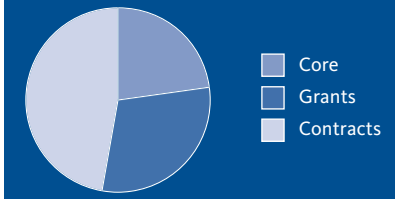
Tenured

Full professors	4.32 FTE
Associate professors	0.52 FTE
Assistant professors	4.50 FTE
Researchers	2.31 FTE

Non-tenured

Researchers	20.26 FTE
Doctoral candidates	46.65 FTE

Research staff funding



KEY PUBLICATIONS

1 de Leeuw, C. A., Neale, B. M., Heskes, T., & Posthuma, D. (2016). The statistical properties of gene-set analysis. *Nature Reviews Genetics*, 17(6), 353-364.

2 Huang, C., Resnik, A., Celikel, T., & Englitz, B. (2016). Adaptive spike threshold enables robust and temporally precise neuronal encoding. *PLoS Computational Biology*, 12(6), e1004984.

3 Keine, C., Rübsamen, R., & Englitz, B. (2016). Inhibition in the auditory brainstem enhances signal representation and regulates gain in complex acoustic environments. *Elife*, 5, e19295.

4 Meijer, D., Te Woerd, E., & Praamstra, P. (2016). Timing of beta oscillatory synchronization and temporal prediction of upcoming stimuli. *Neuroimage*, 138, 233-241.

5 Scheeringa, R., Koopmans, P. J., van Mourik, T., Jensen, O., & Norris, D. G. (2016). The relationship between oscillatory EEG activity and the laminar-specific BOLD signal. *Proceedings of the National Academy of Sciences*, 113(24), 6761-6766.

Dissertations	**9**
Academic publications	**217**
Professional publications	**7**

different cortical layers in the human brain [5]. This fundamental knowledge will help bridge animal and human experiments, ultimately extending the study of neural communication from local populations to whole brain networks.

Future research

The focus will continue to be on developing data acquisition techniques while combining methods. MRI combined with laminar resolution will be further improved and complemented by developing a statistical model to complement multi-unit recordings in freely behaving animals. Analysis approaches will be scaled to accommodate large, high-dimensional datasets, promoting strategic collaborations to enable vertical data integration.

The findings involving humans and animals will be integrated, with the aim of providing a system neuroscience perspective on neuronal communication and dynamics. Collaborations on clinical research will be extended to understanding neurological and psychiatric disorders at the network level. Brain-computer interfacing will be further developed, with the aim of improving communication – and device control – for disabled patients. ‹

Donders Institute for Brain, Cognition and Behaviour

Postal address
P.O. Box 9101, hp204
6500 HB Nijmegen
The Netherlands

Visiting address
Kapittelweg 29
Nijmegen

T: +31 (0)24 365 32 76
E: info@donders.ru.nl
I: www.ru.nl/donders