DONDERS INSTITUTE

Newsletter 32

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How we face our fears

TOWARDS A NEW FREEZE-FLIGHT-FIGHT MODEL

Making sense of everything we see

RESEARCH ON HOW THE BRAIN PROCESSES VISUAL IMAGES

A BIG database

HELPING TO UNDERSTAND THE GENETICS OF THE BRAIN

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How we face our fears: towards a new model

More effective therapy for patients suffering from anxiety, and serious games for police officers. In recent years, Karin Roelofs' multifaceted 'freeze-fight-flight' research has led to numerous applications. Although she's still completing her research projects – with the support of an ERC Starting Grant – Roelofs is already lined up for a new freeze-fight-flight study, funded by an ERC Consolidator Grant. The research will again have benefits for society. "It may seem that my main focus is on increasing the societal value of my work, but in fact the applications are just a natural outcome of my fundamental research interests."

You stand still, your heart rate drops: is that man pulling a gun or a telephone out of his pocket? This so-called freeze reaction helps you to quickly assess the source of danger and to prepare the appropriate response. But not all of us respond in the same way. Some freeze for a long time, others only briefly, and that influences their subsequent decisions to fight or flight.

This defence mechanism is hard-wired in our brains, as Karin Roelofs, Professor of Experimental Psychopathology, first demonstrated in 2010. Since then, her study of 'freeze-fight-flight' behaviour in the brain has yielded not only valuable fundamental knowledge, but also considerable societal benefits.

FOCUS ON BEHAVIOUR

Patients who are anxious tend to avoid challenging situations. As a result, their fears cannot be alleviated and new behaviours cannot be learned. Avoidance behaviour causes significant problems in patients' daily lives. Roelofs: "Our idea is that very primal defensive freeze-and-flight responses underlie these avoidance patterns. Most research in anxiety disorders has focused on cognitive and emotional aspects of the disorders. I believe there should be more emphasis on behaviour: an emotional cue automatically induces an action tendency and we have shown that such tendencies have a strong influence, also on more complex approach and avoidance decisions."

In recent years, funded by an ERC Starting Grant, Karin Roelofs has studied how these primary defensive responses work in our brain and how they're altered in patients who over-engage in social avoidance or approach, such as anxiety and aggressive patients, respectively. "Anxious and aggressive people alike have difficulties controlling their automatic responses. Whereas anxious individuals exhibit excessive avoidance behaviour, aggressive people are more than ready to 'fight.' The forebrain, together with testosterone, plays an important role in this lack of control."

Roelofs also collaborates with developmental psychologists at the Behavioural Science Institute (BSI), observing dozens of children to see how hormone imbalances influence the development of possible socio-emotional disorders. The study began when the children were just 15 months old. "When I arrived in Nijmegen, they were aged 14 and we started scanning them right away. Now they're 20, and we're scanning them for the third time." "Ultimately we aim to predict who is vulnerable to developing socio-emotional symptoms and who is resilient. We can see the effects of early-life events on neural development during puberty and we observe that pubescent neural development is different among aggressive children."

KARIN ROELOFS

Karin Roelofs obtained her PhD at Radboud University in 2002. She was a research fellow at the National Institutes of Health (NIH) in Bethesda, USA and worked first as an Assistant and later as an Associate Professor at Leiden University (2001-2011). She then moved to Nijmegen where she was appointed Professor of Experimental Psychopathology at the Behavioural Science Institute and Principal Investigator, leading the Affective Neuroscience group at the Donders Centre for Cognitive Neuroimaging.

SOCIAL ACTORS SEE THE VALUE OF APPLICATIONS

Although her work mainly involves fundamental research, various interested parties see the benefits of applying the new knowledge. Karin Roelofs: "Our clinical practice partners (such as Pro Persona, -ed.) are very interested in our observations of the effects of testosterone on anxious people. Now they're running a trial to examine whether a dosage of testosterone is a useful addition to their regular treatment, which includes exposure to threatening situations."

The Dutch police have also benefited from the research, in several ways. This led to a joint project within the context of Karin's Vici research. "Police officers regularly find themselves in threatening situations and have to make complex decisions, fast. So, it's useful to know, for example, whether an individual tends to freeze or respond aggressively in a stressful situation." The illustration above, of a man pulling an oblong object from his pocket, is a topical example.

"That in turn led to another new project, in which we're working with various gaming companies, an insurance company and the Netherlands Organisation for Scientific Research (NWO). We are developing a virtual reality game which we can use to train police officers in coping with stressful situations. We know that the police tend to make many more errors when they're confronted with an acute threat. In this training we give real-time biofeedback so that, during acute stress, they can first adopt a freeze-type state, which enables them to make better decisions."

NEW MODEL

Roelofs is developing a computational model designed to predict 'approach' or 'avoidance' decisions under acute threat, based on the transient psychophysiological states of the decision-maker. This project can be used to develop more effective treatment for patients suffering from anxiety. "I'm more interested in understanding the mechanisms, but I think it's wonderful if others want to experiment by applying academic insights in new applications."

Harriëtte Koop

Making sense of everything we see

Take a quick look outside the window or, if you're outside, have a quick look around you. How many people did you see? Was there a car and what colour was it? These may not seem like difficult questions, but how is it that our brain can answer them so quickly? The scene is complex and yet our brain can analyse our surroundings, apparently with little effort. Discovering how the human brain processes naturalistic visual input is the core of Marius Peelen and his team's research.

Marius Peelen began working at the Donders Institute in September 2017. He brought a personal ERC Consolidator grant worth €2 million with him. With it he can head up a six-person research team for five years. Before joining the Institute, he led the Visual Cognitive Neuroscience group at the University of Trento in Italy.

The reason he moved from Italy to the Netherlands was personal. "Once a grant period starts, it's hard to change institutes," Peelen explains. "So, when I was informed that I had won the ERC grant, my Italian wife and I discussed where we wanted to raise our children for the next few years. We felt it was the right time to move to the Netherlands after eight years in Italy. And, in the Netherlands, the Donders Institute was the obvious choice. It has a strong international reputation in neurocognitive research and it has all the top-notch equipment I need to do the kind of research I want to do."

GOOD TEAM SPIRIT

Donders' reputation very quickly paid off for Peelen. "I received almost a hundred applicants for the research positions I advertised. I was in the luxurious position of being able to choose some pretty amazing people." Peelen's team now includes researchers from the Netherlands, India, Australia and Italy. The team also encompasses a wide variety of expertise, including a physicist, an Artificial Intellingence specialist, cognitive scientists and psychologists. "Because we all started at the same time, there's a great atmosphere and a good team spirit. Everyone is smart, enthusiastic and constructively critical of each other's work."

Peelen is also happy with the institute he is now part of. "The support staff are really supportive. Management is smooth and, if there's a problem, they seek solutions rather than put up barriers. The vibe is positive. There's pride without arrogance. I also don't feel any rivalry. Everyone is excited about what they're doing, but also excited about what I'm doing."

FROM BLOB TO BOAT

So, what exactly is Marius Peelen doing? "Impressionist paintings demonstrate what our brain can do," explains Peelen. He grabs a painting hanging in his study. "What may otherwise look like a blurry, black blob on its own becomes a boat when we see it set within an ocean setting. I want to find out how the brain does that."

MARIUS PEELEN

Marius Peelen completed his undergraduate studies at the Vrije Universiteit of Amsterdam. He received his PhD at the University of Wales and completed postdocs at the University of Geneva, Princeton University, and Harvard University. At the University of Trento he started a group and he now leads his own group at the Donders Institute.

Peelen explains how his approach differs from that of his predecessors, i.e. he doesn't reduce a scene to simple elements. "Most previous work was based on a reductionist approach. Subjects were shown, for example, a canvas with several blue lines and one red one and, with the help of fMRI scans, we examined what happens in the brain as someone searches for and then detects the red line. Other studies manipulated other aspects of these simple line elements, such as their orientation and location."

"But these constructed situations don't tell the whole story. In real-life scenes, which are far more complex, our brains can pinpoint objects a lot quicker. For example, show subjects a picture of a cluttered living room and ask them to find a TV and they can instantly find it. Our brain doesn't just process the images it sees from scratch – it relies on knowledge (what a living room is supposed to look like), memory (how other living rooms you've seen look like), context (in a living room most objects have a set position) and attention (when you look for something you overlook other things). All of these aspects influence the efficiency of naturalistic human vision."

COMPUTER VISION AND ARTIFICIAL INTELLIGENCE

Right now, this research is purely scientific: "It's about understanding the system in all its richness," as Peelen puts it. "That isn't to say that it won't have applications. Our visual system helps us navigate and recognize objects, so that we can interact with them. Our findings could be very significant for computer vision. Computers could use artificial neural networks that are based on how our brain works. Self-driving cars could use our research to navigate and robots could use it to recognize human emotions."

Peelen is also working together with AI scientists on campus, such as Marcel van Gerven, to discover how computers can be made to work more like the brain. There is currently no specific collaboration with medical researchers. "But my door is certainly open for them. There are lots of possibilities there, too, I'm sure, as I also study neural processes related to memory and attention."

For now, Peelen is excited to dive further into the brain systems to help detect information that is relevant to tasks. "I hope we can discover how the brain so quickly makes sense of the extremely complex and ambiguous two-dimensional input it receives from the retina every time we move our eyes."

Vanessa Deij

Go to our website to check out the latest news and events

Meanwhile at www.ru.nl/donders

SOME RECENT HEADLINES

- **Eight researchers** of the Donders Institute received a **Vidi grant of NWO** (The Netherlands Organisation for Scientific Research). They are each to receive up to €800,000 to develop an innovative research theme and to build up their own research group.
- **Peter Hagoort** has been elected as a **Foreign Associate of the US National Academy of Sciences** in recognition of his distinguished achievements in original research.
- **Roshan Cools, Guillén Fernández and Antje Meyer (MPI)** have been appointed as **new members of the Royal Netherlands Academy of Arts and Sciences (KNAW).**
- A subsidy of almost **€2.5 million has been awarded to collaborative projects in which science meets business**. Nearly €2 million goes to a project that will deliver faster, easier and better images of the brain. Approx. €500,000 will go to a project designed to develop better images of brain diseases (MR Brain).
- Nael Nadif Kasri and Hans van Bokhoven have been awarded a prestigious **ZonMw TOP grant** (worth **€675,000**) **for their project "Brain on a dish**: developing innovative stem cell technologies for personalized medicine in epilepsy."

SOME RECENT HIGH-IMPACT PUBLICATIONS

- **Meditation has little impact on social behaviour**
  Inti Brazil and his colleagues found that, contrary to what is often claimed, meditation does not make you a better person. The effects established by researchers in twenty publications on various types of meditation turned out to be much smaller than was originally claimed (Scientific Reports).
- **Laser shoes help Parkinson patients to break their freeze**
  Freezing of gait is a debilitating symptom of Parkinson's. With the help of visual cues, patients can overcome blockages during walking. Murielle Ferraye developed shoes that project a line on the floor in the rhythm of footsteps to help trigger patients to walk (Neurology).
- **Top-down expectation effects of food labels on motivation**
  Researchers at the Donders Institute and Wageningen University found that subtle manipulation of written information on food labels leads to approach-bias effects that are strong enough to override goal-directed, instrumental responses and thus obtain reward outcomes (Neuroimage).
- **Using deep learning to predict people's personality**
  Marcel van Gerven and his group developed a deep neural network, which they use to predict the personality traits of people based on short YouTube videos. They showed that the network produced similar personality scores to those recorded by human observers (IEEE Research).

PhD defences

**Donders series number*

- 8 December 2017, DS. 303*. **Vugs, B.**, *Executive functions in children with SLI: A dynamic perspective.*
- 11 December 2017, DS. 304. **Van der Sluijs, B.**, *Oculopharyngeal muscular dystrophy (OPMD) in the Netherlands, beyond dysphagia and ptosis.*
- 18 December 2017, DS. 308. **Sianipar, A.**, *Emotional and semantic meanings of words in the first and second language: Representation, learning and processing.*
- 20 December 2017, DS. 306. **Mecacci, G.**, *Towards a humane neurotechnology: the impact of neuroscience on the human self-image.*
- 2 February 2018, DS. 305. **Kroeze, Y.**, *Effects of serotonin signalling on behaviour and gene transcription. A journey through postnatal brain development.*
- 5 February 2018, DS. 307. **Franken, M.**, *Listening for speaking: Investigations of the relationship between speech perception and production.*
- 8 February 2018, DS. 310. **Janssen, R.**, *Connecting the dots and dotting the connections: novel approaches for improving the sensitivity of graphic statistics in neuroscience.*
- 9 February 2018, DS. 290. **Braukmann, R.**, *Social-cognitive processing and familial risk for autism spectrum disorder.*
- 14 March 2018, DS. 312. **Zwart, F.**, *What have we learned? On implicit learning in ASD and SLI.*
- 22 March 2018, DS. 302. **Hoffland, B.**, *Investigating the role of the cerebellum in idiopathic focal dystonia.*
- 28 March 2018, DS. 317. **Kayhan, E.**, *(A scientist's model of) how young learners adapt to change.*
- 3 April 2018, DS.309. **Barthel, C.**, *Moving beyond freezing of gait in Parkinson's disease.*
- 13 April 2018, DS. 315. **Sikora, K.**, *Executive control in language production by adults and children, with and without language impairment.*
- 24 April 2018, DS. 313. **Bakker, F.**, *Decisions in motion – action plans for reaching under whole body translation.*
- 24 May 2018, DS. 318. **Sheppard, D.**, *Predictability different? Prospective memory in autism.*
- 5 June 2018, DS. 319. **Shitova, N.**, *Electrophysiology of competition and adjustment in word and phrase production.*
- 13 June 2018, DS. 316. **Richter, A.**, *Network-based care for people with dementia: A complex transition*
- 14 June 2018, DS. 314. **Van Rooij, F.**, *Transient neurological attacks. Neuroimaging, aetiology, and cognitive consequences.*
- 15 June 2018, DS. 311. **Van Donkelaar, M.**, *Genetic and neurobiological mechanisms underlying aggression subtypes.*
- 3 July 2018, DS 321. **Knuijt, S.**, *Prevalence of dysarthtia and dusphagia in neuromuscular diseases and an assessment tool for dysarthria in adults.*

Donders Lecture 28 June 2018

What the visual system teaches us about the brain

How does the human brain piece together information from the senses in order to interact with the outside world? That is one of the main questions that Prof. Zoe Kourtzi, a leading researcher at the University of Cambridge, is asking. "Her research is directly linked to the questions that we ask in our own research group," Janneke Jehee says. "How do we learn to see better? And how exactly are the decision processes in our brain influenced by visual information?" Janneke Jehee, Principal Investigator of the Visual Computation & Neuro-imaging group at the Donders Institute, will be hosting Kourtzi during her stay in Nijmegen.
"Zoe Kourtzi is someone who's really interested in the details," Jehee says. "Because she uses advanced analysis techniques and unconventional methods, she's able to make very precise statements in her work. Her approach is something we could definitely learn from."
But, for another reason, Jehee recommends that researchers working in all neuro-related disciplines attend the Donders Lecture: "It's relevant for all researchers, because her story could generate new insights into a large array of research questions about learning in other domains as well, such as: How might the representation of more general forms of knowledge change with learning? How do we learn to better represent certain aspects of language?"
Historically it was thought that the visual system is an unalterable system in the brain. However, researchers have discovered that the structure remains very plastic, even in adult life. Jehee: "By learning we constantly induce changes in the receptive fields in the visual system. And because we know the tuning properties of the neurons in this system, we can investigate how learning works at a very detailed level."
"Because the learning mechanisms in the visual system are probably very similar to learning mechanisms in other brain regions, the visual system serves as an ideal model for understanding other forms of learning in the brain as well," Jehee concludes.

The Donders Lectures take place at the Linnaeus building on the Radboud University Campus, Heyendaalseweg 137, Nijmegen, at 4.00 p.m.
For information about this year's lectures, please go to: www.ru.nl/donders/lectures

Harriëtte Koop

Donders celebrates 200 years of brain science

DONDERS 200 YEARS

On Thursday May 31st, the Donders Institute celebrated the 200th anniversary of the birth of Franciscus Cornelis Donders by organizing a symposium entitled *The Legacy of F.C. Donders*. In addition, guided tours were organised to the Anatomical Museum, where the original Noëmatachograph – the instrument that Donders used for his reaction time experiments – was displayed, together with several of his nineteenth-century eye models. The instrument was on loan from the Utrecht University Museum.

Speakers at the symposium included Dora Angelaki, Marcus Raichle, Pim Levelt, Douwe Draaisma and Jan Keunen. With approximately 120 visitors, the symposium was a great success.

For more information about other Donders 200 activities throughout the rest of the year, go to: www.ru.nl/donders/200

From left to right: Pim Levelt, Dirk Ruiter, Lutgarde Buydens, Marcus Raicle, Dora Angelaki, David Norris, Paul Smits, John van Opstal, Ardi Roelofs.

THE MACHINE

A BIG database to understand the genetics of the brain

To better understand the effects of genes on our brain, researchers in Nijmegen have created a large database that links brain images and genetic data. This will help them analyse how genetic factors influence the brain's structure and the way it functions.

Since 2007, healthy participants who come to the Donders Centre for Cognitive Neuroimaging for a structural MRI scan are asked to participate in the Brain Imaging Genetics (BIG) study. They are also requested to donate saliva. As a result, genome-wide genotyping is currently available for more than 2,500 people.

To further enrich the current data – and thus allow links to behaviour and disease – the BIG subjects are regularly invited to answer questionnaires about things such as their health, background or behaviour. "It has, for example, helped us to discover that risk alleles (alternative forms of a gene that arise by mutation and are found at the same place on a chromosome) for Alzheimer's disease can affect the structure of the hippocampus, even in young healthy individuals," geneticist Barbara Franke, one of the initiators, explains. "Or that the symptoms of ADHD are associated with total brain volume."

Geneticists and neuro-imaging experts interact closely in cognomics, processing large volumes of data, and they help each other interpret the findings from the BIG project. "In the years we've worked together, we've done our best to learn each other's language and understand one another's expertise," says neuroscientist Marcel Zwiers, who is part of the team that tackles the questions posed by researchers. "For example, the geneticists filter the data for a gene variation, while we define the most relevant and interesting regions revealed by MRI."

In 2009, Donders researchers co-founded what is currently the largest international consortium for brain imaging genomics studies: ENIGMA. The ENIGMA database contains genome-wide genetic data and the brain images of over 30,000 subjects. "And this number is still growing," Franke remarks. "The power of ENIGMA lies in the large numbers, which make it possible to identify gene-brain relationships in a brain-wide, genome-wide manner. However, the phenotypic depth of such studies is limited. The hypotheses formed in ENIGMA can be further tested in our rich BIG database."

Vanessa Deij

DONDERS INSTITUTE Newsletter

The Donders Newsletter is published twice a year by the Donders Institute for Brain, Cognition and Behaviour, which brings together research groups at Radboud University and the Radboudumc as well as the Max Planck Institute for Psycholinguistics. Its purpose is to keep you informed of developments within the Donders Institute and the field of neuroscience.

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