# DONDERS INSTITUTE

## Newsletter 33

December 2018

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Radboud University Radboudumc

# *Empowering dementia patients*

## *Research results that underpin practical advice*

**Memory training can prevent cognitive decline. Right? When it comes to dementia, there's a lot of well-intentioned information out there. But how much of it is based on sound research? And how can the research that is reliable help dementia patients in their daily lives? How can it provide help today as well as tomorrow. Researchers at the Donders Institute cut through the hype to give advice that can benefit patients and their families.**

Geriatrician Jurgen Claassen and clinical neuro-psychologist Roy Kessels at Radboudumc co-authored an informative book on dementia. "We started with the questions our patients and those close to them often ask," Kessels explains. "The book is based on scientitfic evidence as well as our own clinical experience. We noticed that there are methods that work in theory but don't work in day-to-day situations for this group."

"We apply the theory," Claassen adds. "We emphasise the fact that research cannot be all-encompassing. General advice may not fit people's personalities or their daily lives. If you like doing crossword puzzles, that could be of benefit, but if you're being made to do it, it may be counterproductive."

"It's all about empowering people with dementia," says Joukje Oosterman, a Donders researcher who specialises in normal cognitive ageing: "I link cognition to changes in the structural integrity of the brain to explain why people age as they do. What accounts for the differences? We see that the amount of experiences people have had during their lives can build up a reserve that protects them from the effects of ageing." Understanding what healthy ageing is helps us understand the challenges that confront people with dementia, or other ageing-related conditions, in their daily life.

## HYPES INFLUENCING BEHAVIOUR

Probably one of the best known misconceptions when it comes to dementia is that memory training will reduce the risk or slow down the process if you already have it. "For example, some patients will not keep written reminders for fear it will make them deteriorate faster," says Kessels. "That may be doing them more harm than good. Using external prompts to remember things can help them make fewer errors and thus boost confidence."


Besides working in the clinic, Kessels also does research on cognition and behaviour. Instead of studying what a person cannot do due to their cognitive impairment, he examines which functions are intact and how they could compensate for those that are impaired. Among other things, he is studying errorless learning, which involves storing information correctly in our memory, without first making mistakes while learning.

"Family members try to keep their loved ones' memory alert by reminding them on everybody's name. The constant failures influence a patient's wellbeing and hamper their performance. We try to show the family methods that focus on what patients can still do."

## GETTING ACTIVE

According to the geriatrician Claassen exercise also influences cognition and the ageing process. He is researching how the vascular system contributes to dementia, and in particular Alzheimer's. High-blood pressure affects the blood flow to the brain and functional thinking requires more blood. So how are the two related?

"We advise our patients to get up and do something – anything. Any extra exercise is beneficial for the vascular and cognitive systems," Claassen explains. "But again, we stress that it needs to fit into their lives. If they don't want to, so be it." "We try to give nuanced advice," Kessels adds. "And not to assign blame by suggesting that a lack of exercise causes their dementia." Claassen points out to patients that even athletes can get dementia. "But, if people are motivated to become more active, we want to give them options."

Oosterman stresses that the problem with advice based on research is the risk of generalising. "Something may work for a majority, but it may not work for you. Each patient is different, and everyone has different needs. So, the challenge is to find out what works best for whom. It comes down to personalised approach." "And that's the major challenge for research," says Kessels. "Personalised healthcare is our goal, but far from easy."

## CONTACT WITH PATIENTS CRUCIAL

Claassen and Kessels' research and work done by others affect the advice they give patients. "But contact with patients also influences our research," Claassen says. "Their questions trigger ideas. Also, when you've seen a lot of patients, you see differences, and that some patients decline faster. You start to see patterns in those differences, and this suggests which areas to research."

They are very aware that their research can have direct benefits for patients. "That's not to say we aren't interested in the science for science's sake," Kessels says. Claassen agrees: "I've been working on a fundamental research topic and it's only recently – after 14 years – that I've been able to demonstrate how it could be applied clinically."

"Patients aren't guinea pigs," Kessels adds. "As researchers we must be realistic and formulate informed research questions. We need to understand how much a patient is capable of doing. You can't expect a dementia patient to perform a computer task for an hour."

Oosterman remarks that a lot of research involves highly educated test subjects. She's discovered that, when it comes to dementia, higher educated people react differently. "They're able to compensate for their impairment and are thus diagnosed later; then they tend to deteriorate faster. That's why it's important that research covers a wide range of subjects."

For all three researchers, the potential benefits for patients will continue to be the primary motivator.

*Vanessa Deij*

# *From building memories to und*

## *Eight Vidi grants for eight research topics*

**How varied can brain research be? Eight promising researchers at the Donders Institute were awarded a Vidi grant this year. This means funding for eight new projects in different fields of expertise. In the years ahead the researchers will study the way our brain processes words and sounds, what happens when we sleep and dream, and how to combat dementia and rare genetic disorders.**

ANDREA MARTIN: **COMBINING WORDS WHEN SPEAKING AND LISTENING**

Human language allows us to combine words in an infinite number of structures and meanings. This ability to combine words into larger meanings is key when we speak or listen. Andrea Martin will develop a computational model for the combinatorial processing used when speaking and listening that functions in a brain-like way and draws on core principles from neurophysiology and network computation. In the second phase of the project she will test the model's predictions by conducting neuroimaging experiments on human participants engaged in producing language.

EDO RICHARD: **TREATMENT OF HIGH BLOOD PRESSURE TO PREVENT DEMENTIA**

High blood pressure increases the risk of dementia. In this project Edo Richard will investigate how personalised treatment of hypertension can prevent dementia. Richard will study data from thousands of people around the world who have been followed for decades. He will also study their brains post-mortem.

MARTIN DRESLER: **PARADOXICAL SLEEP STATES**

REM sleep is a paradoxical state: we are sound asleep, but our brains are highly active; we experience a vivid simulation of reality, but memory and thinking skills are severely restricted. In this project Martin Dresler, together with his fellow researchers, intends to elucidate the neurobiology of REM sleep and explain how typical dream experiences are based in the brain.

BERNHARD ENGLITZ: **LISTENING IN THE WILD**

Hearing is an important sense for humans. Bernard Englitz will study which specific parts of the brain respond to natural sounds and how different types of neurons in the auditory brain respond. The results of this work will shed further light on our understanding of how humans hear in a world of complicated sounds.

# erstanding the disordered brain

TJITSKE KLEEFSTRA: **UNDERSTANDING THE DISORDERED BRAIN IN PATIENTS WITH RARE GENETIC SYNDROMES**

The possibilities for diagnosing rare genetic syndromes have increased tremendously in recent years. The next challenge is to understand the natural course of the diseases and to create tailored interventions. Tjitske Kleefstra will carry out a longitudinal follow-up and intervention study in order to improve care for patients with neurodevelopmental disorders as well as those with significant psychopathology.

SASKIA HAEGENS: **BRAIN RHYTHMS, THE BUILDING BLOCKS OF THE BRAIN**

Every day, our brains receive an enormous amount of information, which needs to be filtered and processed. To accomplish this, the right brain areas must be connected at the right moment. Through this project, Saskia Haegens will study how rhythmic activity in the brain helps to organize these connections.

MARK DINGEMANSE: **ELEMENTARY PARTICLES OF CONVERSATION**

Just below our awareness, interjections such as 'mm', 'huh?' and 'oh' streamline our conversations and make complex language possible. Yet we don't know where they come from, how they get their shape, or whether they are universal. In this project, Mark Dingemanse will use recordings of conversation and computer models to study these elementary components of conversation.

LISA GENZEL: **SLEEP ON IT!**

To retain information in our long-term memory, we need to sleep. Lisa Genzel and her colleague researchers will focus on the communication between two brain areas – the hippocampus and the prefrontal cortex – during sleep. She will investigate how sleep selects and strengthens memories for long-term retention.

**What is a Vidi grant?**

Vidi is a research grant within the NWO Talent Scheme, alongside the Veni and Vici grants. It is awarded to talented scientists who have carried out excellent research for a number of years after obtaining their PhD. The value of the grant is up to €800,000 and it allows a laureate to conduct innovative research for a period of five years. Researchers can use the money to build up their own research group.

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

# Meanwhile at www.ru.nl/donders

## SOME RECENT HEADLINES

- **5 Veni grants for Donders researchers**
  Five researchers at the Donders Institute were awarded a Veni grant from NWO. They each received up to €250,000, which will allow them to develop their own research line.
- **Researchers and industry join forces to unravel and treat autism**
  A subsidy of €110 million has been awarded to AIMS-2, a large public-private project that was established to gain new insights into autism and develop treatments. Christian Beckmann and Jan Buitelaar at the Donders Institute are important partners in this project.
- **10 million to improve healthcare for those suffering from Parkinson's disease**
  The Parkinson Center received €10 million to implement a new model of healthcare that focuses on the wishes and needs of people with Parkinson's disease. The model will be monitored for five years to evaluate health improvements among patients and the implications for health care costs.
- **New collaboration with Ruhr-University Bochum to unravel how stress affects memory quality**
  A new collaborative project involving the Donders Institute and Ruhr-University Bochum will investigate how stress hormones alter the course and the quality of the formation of long-term memories. The project has received €1 million in funding from the Netherlands Organisation for Scientific Research (NWO) and the German Research Foundation.

## SOME RECENT HIGH-IMPACT PUBLICATIONS

- **Very few similarities between brains of schizophrenia patients**
  Thomas Wolfers and Andre Marquand quantified brain structural heterogeneity in adults with schizophrenia. They found little overlap among individual patients, suggesting that the average patient is a non-informative concept in psychiatry and we should work towards personalised diagnosis (JAMA Psychiatry).
- **70 genes linked in search for treat ments of rare movement disorders**
  Researchers in at Human Genetics and Neurology found that over 70 genes that are known to carry genetic defects that can result in cerebellar ataxias have common cellular processes. This finding raises the possibility of treating different diseases with the same medication or with similar intervention strategies (Cell).
- **Auditory feedback serves as quality control system during speech production**
  Peter Hagoort and colleagues carried out a study on the neural underpinnings of auditory feedback processing during speech production. They found that participants responded to small shifts in pitch, of which they were not consciously aware by adjusting the pitch of their vocalisation (Neuroimage).

# PhD defences

**Donders series number*

July 2018,

- **Ruiz Euler, H.**, *Particle smoothing and latent process estimation in Neuroscience. DS 329*
- **Knuijt, S.**, *Prevalence of dysarthtia and dysphagia in neuromuscular diseases and an assessment tool for dysarthria in adults. DS 321*
- **Vesseur, A.**, *Cochlear implantation in deaf children with complex needs.*
- **Manfré, G.**, *Pheno-ratting: towards the characterization of motor and psychiatric phenotypes in the BACHD rat model of Huntington disease. DS 324*

September 2018

- **Heil, L.**, *The predictive social brain: On the processing of other people's behaviour. DS 331*
- **Bakker-Huvenaars, M.**, *Severe aggression in male adolescent boys. The role of genetic, cognitive and hormonal factors. DS 342*
- **Otworowska, M.**, *Computational demons of an adaptive brain. DS 335*

5 October 2018

- **Vermeulen, K.**, *Neuropsychiatry and cognition in genetic developmental disorders: The emblematic of Kleefstra syndrome. DS 333*
- **De Jong, D.**, *Regulation of cerebral perfusion in Alzheimer's disease. DS 327*
- **Fu, L.**, *The ups and downs of episodic memory in older adults: The role of individual differences. DS 336*
- **Collin, S.**, *Mapping memory space: episodic memory organization in the hippocampal- cortical system. DS 323*
- **Karel, P.**, *The role of serotonin trans porter genetic variation in the cause and cure of cocaine addiction. DS 340*
- **Kung, C.**, *Speech comprehension in a tone language: The role of lexical tone, context, and intonation in Cantonese-Chinese. DS 320*
- **Longo, A.**, *Variation in upper body motions. Novel assessment techniques and implications for work-related injuries. DS 348*
- **Barsingerhorn, A.**, *The need for speed: visual development and visual impairment in children beyond visual acuity. DS 338*

November 2018

- **Van Middelaar, T.**, *Integrated primary care for the frail elderly: Implementation, effects and costs. DS 334*
- **Den Besten, C.**, *An assessment of contemporary bone conduction devices.*
- **Wohlgemuth, M.**, *A family-based study in Facioscapulohumeral Muscular Dystrophy. DS 346*
- **Van Mourik, T.**, *On the analysis of layer-specific FMRI. DS 344*
- **Lüttke, C.**, *What you see is what you hear: Visual influences on auditory speech perception. DS 350*
- **Van Leijsen, E.**, *Unraveling the heterogeneity of cerebral small vessel disease – from local to remote effects. DS 345*
- 20 November 2018, *Adiposity and the brain: The adiposity-brain-axis in mice and men. DS 347*
- 26 November 2018, **Suwartono, C.**, *The development and psychometric properties evaluation of the Indonesian version of the Wechsler Adult Intelligence Scale – fourth edition (WAIS-IV). DS 341*
- 30 November 2018, **Ooms, S.**, *Sleep well, age well? Assessing sleep disruption as a player in Alzheimer's disease pathogenesis. DS 343*
- 14 December 2018, **Dupan, S.**, *From man to machine – neural control of fine hand movements. DS 339*

# *Who's afraid of neuroscience?*

Reading our thoughts and dreams might sound like science fiction, but at a crowded public event in September Marcel van Gerven showed that this may be possible. Initial results are already revealing an ability to recognise letters and faces in our mind using brain scans. And vice versa with so-called 'brain writing' as an aid for the blind. Visual information can be written directly into a blind man's brain.

During *Who's afraid of neuroscience?* last September Donders researchers and Radboud Reflects explored answers to this question. Well, are we? *Not really*, according to this audience.

This was confirmed by the answer to a question from Roshan Cools. "Suppose you are easily distracted and imagine there's a medicine to fix that. Would you use it?" Yes, replied most people in the audience. Cools discussed Ritalin, which is widely used nowadays. But increased concentration comes at a price, she warns: it often reduces cognitive flexibility and creativity.

What about bad behaviour? Can we identify a criminal brain? Robbert-Jan Verkes explained that a certain combination of characteristics can be explosive, but that this is not easy to trace back to our brains. Research does reveal that the amygdala, the part of the brain that controls social inhibitions, shows few signs of activity in psychopaths. "Of course, childhood experiences and the environment also play an important role."

How afraid are we of memory manipulation? "We forget things we once remembered clearly, our memories change and sometimes they can be completely false," says Marijn Kroes. This demonstrates the flexibility of our memory, which can certainly be manipulated. This could be useful, for example, in the

treatment of anxiety disorders. Kroes explained how memories and anxiety can be erased with electric shocks and medication.

Last but not least: Nael Nadif Kasri explained that we are able to grow a mini-brain in a lab, from a single stem cell. This makes it possible to test medication without the use of lab animals or patients. Should we be worried about this? "We know that mini-brains don't suffer any pain. But how many brain cells are required for consciousness? Three hundred? Twenty thousand?"

*Roeland Segeren*

Donders Lecture

# *We decide ourselves, or don't we?*

**We've learned to smile when meeting colleagues. To take shelter when it rains. To drink when our throat is dry. It makes us feel liked, keeps us dry, and makes us feel better. Gives us a small reward for every decision we make.**

'Reinforcement learning' refers to our ability to learn to make decisions that maximise reward, with dopamine as a central player. The neuroscience behind it has often focused on simple forms of conditioning, where decisions reflect our experience of reward for those decisions. In the real world however, many decisions are based on knowledge about task rules and expected rewards, even if we've never experienced them. Yael Niv of Princeton University will visit Nijmegen in February to discuss this.

Donders lead researcher, Roshan Cools, who invited her: "Clearly, we are more than a victim of our past. We have access to the 'rules of the game', which we use to plan novel actions." Niv is one of the key drivers of the shift towards understanding how we use representations of our surroundings to make decisions. This relates directly to Cools' research. "Her work inspires much of our current quest for extending dopamine's well-known role in reward-based learning to higher order cognition."

A better understanding of how we learn to make decisions can also ultimately help psychiatry. Cools hopes to pick up some new insights into what goes wrong in tormented brains. "This may inspire novel mechanistic approaches to diagnosis and treatment of mental disease."

*Donders Lecture by Yeal Niv: Carving the world into useful task representations. Thursday 14 February 2019, 16.00-17.00.*

*Roeland Segeren*

THE MACHINE

# *Porcupine gives brain researchers a kick-start in clean coding*

From vague ‘brain blobs’ to sensible conclusions: in order to make sense of raw brain scanning data, neuroscientists use numerous computer programs and scripts. As each research question is unique, most researchers write these scripts themselves - which often makes them very complicated and therefore hard to decipher by colleagues. To help researchers write clean code, Tim van Mourik developed Porcupine to improve the quality of brain science.

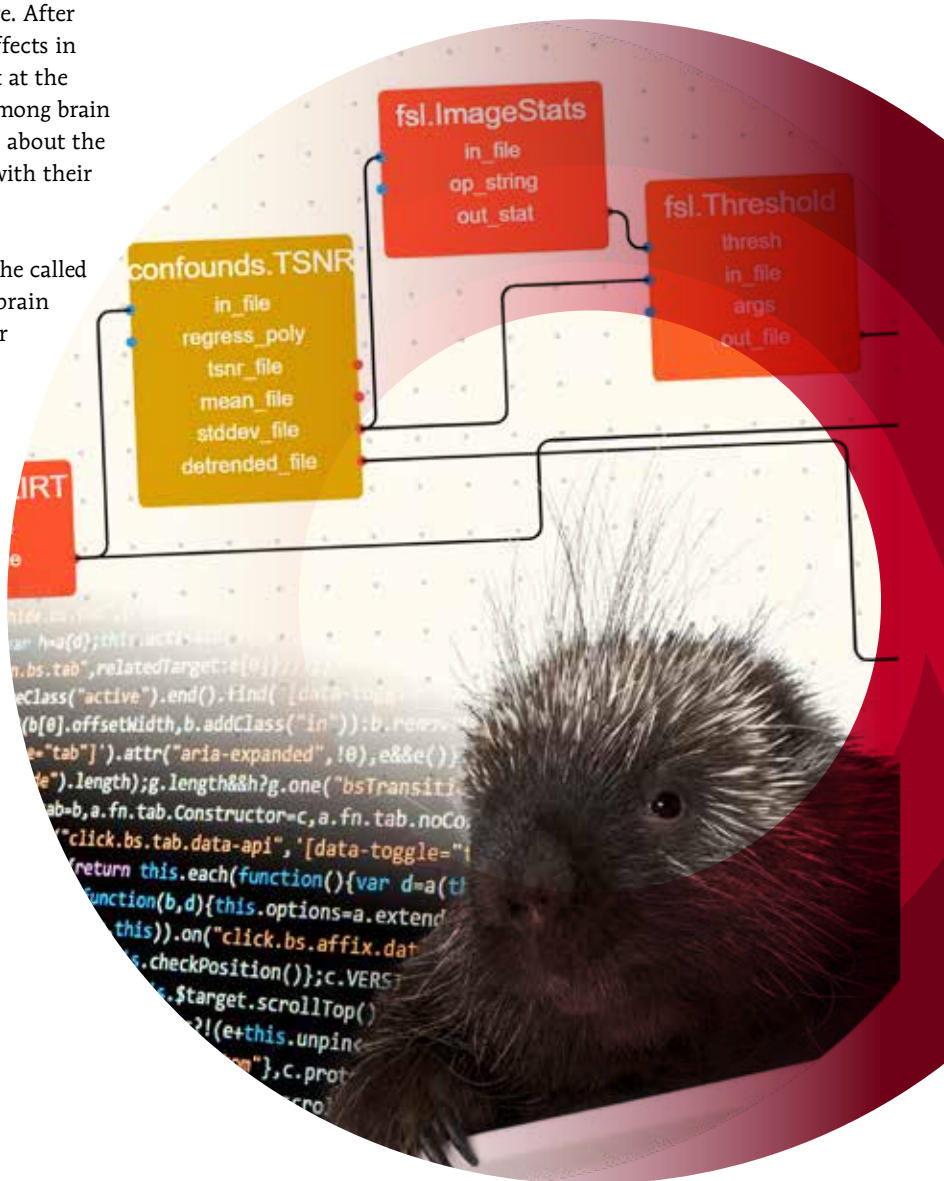
“Programming yourself has the advantage that as a young brain researcher you’re able to learn precisely what you’re doing,” explains Van Mourik. “But the disadvantage is that the quality of analyses of this data can be compromised, compared to the work of an experienced programmer. It also often makes it harder to replicate the studies.”

Van Mourik graduated on 13 November with his thesis *On the analysis of layer-specific fMRI*. While working on his PhD, he developed custom-made software. After studying Computer Animation and Visual Effects in the UK, he started working as a PhD student at the Donders Institute: a computer programmer among brain scientists. “I actually had to learn everything about the brain,” he says. He often helped colleagues with their data analysis.

Van Mourik developed novel software, which he called Porcupine. This program is designed to give brain researchers a head-start when analysing their fMRI data. “If you indicate what you want to know from your data, the program writes the corresponding script for you,” says Van Mourik. “You can intuitively follow what you’re doing and the scripts are written correctly, so you won’t constantly be bothered with error messages.”

The reason why this software has not been developed before is that many scientists believe that writing scripts manually helps you understand the analysis. Making it too easy could therefore reduce good understanding of the data. Van Mourik is not really worried about this: “I think it’s good if PhD students do a lot of the analysis themselves, but in my opinion we should help them get started. Moreover, this software provides more transparency: you can see exactly how someone has done his or her analysis. This leads to greater understanding and makes it easier to reproduce fMRI studies.”

*Roeland Segeren en Harriëtte Koop*




**DONDERS** INSTITUTE Newsletter

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