Donders Institute Newsletter

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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 Nijmegen 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.

Radboud University

Making sense of sensation

'Food can wait, science can't'

The cerebellum and neural control of movement

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Donders Institute for Brain, Cognition and Behaviour

Tansu Celikel
'I do my research everywhere', Professor Celikel says, and he has the track record to prove it. He received his PhD in Systems Neuroscience in Trieste (Italy) and worked as a postdoctoral researcher at the University of California in San Diego (USA) and the Max Planck Institute for Medical Research in Heidelberg (Germany). From 2008 to 2012, he was a Professor of Neurobiology and Biomedical Engineering at the University of Southern California in Los Angeles (USA). In August 2012 he moved to Nijmegen to establish the Department of Neurophysiology at the Donders Institute.

Making sense of sensation

Although sight is a very important sense for humans, your eyes do not provide you with all the information you use to make decisions. Besides seeing the steam coming from your cup of tea, you also smell its flavour and use your fingertips to feel how hot the cup is. When you then lift up the cup, its weight confirms your expectations of how full it is, allowing your brain to direct the muscles in your arm to bring the cup to your mouth to take a sip. Information from all of your senses is combined in making even simple decisions as well as in generating action.

Professor Tansu Celikel, head of the Neurophysiology Department at the Donders Centre for Neuroscience, studies how our brain processes sensory data and translates them into actions. 'The plasticity of the sensory and motor circuits in the brain teaches us how neural representations of our surroundings lead to action and cognition in an ever-changing world.' Researchers in his department aim to describe the underlying neural circuits in a systematic way.

Internal representation of the external world

When orienting in space you rely on two cognitive systems: the egocentric system, which represents information from your senses with respect to your body, and a second system, which is world-based and relies on cognitive maps constituted by (for instance) cells that encode space. Prof. Celikel: 'In our group we look at both self and world-centric sensory representations, since these systems continuously communicate with each other in order to generate motor action. While sensory systems provide the input needed to make movements possible, the movement of the body alters the dynamics of the subsequent inputs to the sensory system. It's in this infinite loop that sensory information and motor output come together to create a neural representation of space and enable motor action.'

Cells that encode space

The 2014 Nobel Prize in Physiology or Medicine went to the discovery of the brain's own GPS system: grid cells that constitute a neural positioning system. Professor Celikel sees the award as encouragement for systems neuroscientists who are seeking to explain the neural basis of behaviour.

Endless possibilities

Prof. Celikel and his colleagues do a lot of their work with rodents. Experiments in which a mouse explores a confined space may sound simple, but the opposite is true. The animal is incorporating information about its body position, head orientation, centre of mass, sensorimotor and cognitive states – all at the same time – in order to navigate through its environment. 'A fascinating, but also complicating aspect of this navigation is the fact that the amount of information used to reach a decision changes continually. If there is a sense of urgency, for instance when the sensory information is available only for a short time or the animal faces a perceived danger, less information is required to make a decision.' Active sensing – using adaptive control of the motor system to optimize sensory sampling strategies – is one of the solutions that the mammalian brain employs and is one of the processes that Prof. Celikel and his colleagues aim to understand. 'We need to know how active sensing works if we ever want to build a smart robot that can for instance collect empty cups in a restaurant.' This robot needs to be able to scan the room, find a table with cups on it, move over there, scan the table, see which cups are empty and grasp them (instead of the full ones). Just as in humans, robotic motor control depends on sensory information and on a spatial map of the environment, and motor actions are closely interrelated with information that sensors collect from the environment. 'When we can actually model these systems and understand the mechanics of the solutions the mammalian brain provides for similar problems, the end point could be anything: from intelligent systems to robots that work in healthcare. That's what's most exciting about this research for me.'

Optogenetics

To establish the causal interaction between the activity of a group of neurons in the brain and the behavioural outcome, researchers in the Department of Neurophysiology use a technique called optogenetics. After genetically sensitising selected neurons to light, they implant home-made miniature electronic chips, which allow them to wirelessly control the brain using infrared light. This is like using a remote control to zap between TV channels while sitting at home on your couch. These chips can create any colour of light in the visual spectrum, opening specific ion channels in the underlying neurons. This makes it possible to control the activity of single neurons, or populations neurons, even in freely-moving animals. Prof. Celikel and his colleagues can measure the effects of those manipulations very precisely and in real-time by using home-made electrode arrays which are only 3 micron wide (1/7 the size of a neuron). Together with the robotic trainers they develop to train animals in their behavioural tasks, optogenetic neural control and physiological recordings will ultimately generate mechanistic insight into how the brain generates behaviour.

Body heat instead of batteries

The equipment used in optogenetics keeps getting better, and smaller. New prototypes with wireless controlling systems are being developed and one of the Neurophysiology PhD students is working on a chip that replaces the current battery with energy generated from body heat. According to Prof. Celikel, developing novel techniques is a good way to distinguish your own research from that done by others. 'Everybody has smart questions, but what really makes a world player is providing smart techniques to answer these questions definitively. With a group of researchers working at the intersection between synaptic, cellular, systems behavioural, and computational neuroscience, combined with our expertise in autonomous system design, we have a real chance to answer some of the most fundamental questions in neuroscience.'

Staying focused

Since there are many links with other research groups and many options, plus the need to collaborate in this field, it is a true challenge to remain focused. To do this, Prof. Celikel and his colleagues make a clear distinction between exciting research questions and challenging fundamental problems. 'We focus on fundamental problems because the answers, even though they are harder to arrive at, will ultimately provide us with the possibility to make giant leaps. And that's what we want, instead of incremental science, which is based on the status quo.'

'I think this is the best time ever to do neuroscience. Since we are truly multidisciplinary in our approach, we can make a major impact that will hopefully last for generations.'

Iris Kruijen

‘Food can wait, science can’t’

The Italian neuroscientist Giacomo Rizzolatti is the founding father of mirror neurons. In 1992 he by chance recorded peculiar electrical activity from single neurons in the premotor cortex. These were activated by both observing and executing grasping behaviour. Later studies showed that the primate brain has dozens of these so-called mirror neuron clusters, which are mostly found in the premotor cortex, but also in other motor areas and in the parietal cortex. Each cluster is activated in its own way: some only fire as the result of specific actions, others react to more general movements or to specific points of view, auditory stimuli or the subjective value a movement has for the observer. This implies that other brain areas modulate mirror neurons in a top-down fashion. However, studying the functional role of the human mirror system in learning and adaptation during social exchanges remains difficult, mostly due to methodological challenges.

It all started in Parma, more than twenty years ago, in the lab of the Italian neuroscientist Giacomo Rizzolatti. Researchers were eating peanuts out of a jar. A macaque watched it and suddenly a loud noise filled the room. It came from the amplifier connected to an electrode that was implanted in the monkey’s premotor cortex (Rizzolatti had put it there to study how the brain executes movements). But now, this motor area suddenly became active, not while the monkey was grasping something, but while it was *watching* someone grasp something. Rizzolatti was puzzled: how could that be?

Until then, it was thought that brain areas that executed motor actions were totally separate from those that dealt with cognition. However, these neurons apparently fire in response to both motor and perceptual events. Could it be, hypothesized Rizzolatti, that these neurons allow us to mirror somebody else’s action in our brain, and in this way understand the intention of that action via our own motor intentions? In 1998, he gave a speech at the Max Planck Institute for Psychological Research in Munich, which was attended by postdoc Harold Bekkering, who raised his hand after the talk. Could these ‘mirror neurons’ have anything to do with imitation, the topic he was then studying in Munich? Rizzolatti immediately invited him to have a chat, since he was also interested in this potential link. Bekkering first hesitated, as Rizzolatti was about to have dinner with his supervisor, the director of the institute. ‘Food can wait’, replied Rizzolatti, ‘but science can’t’.

In 1999 they published their findings (‘Cortical mechanisms of human imitation’) in the journal *Science*. This contributed to a revolution for neuroscientists and non-experts alike, or, as critics might put it, the most hyped concept in neuroscience. Mirror neurons were considered to form the basis of human empathy and, according to well-known neuroscientists such as Vilayanur Ramachandran, even ‘the origins of human civilisation’. Critics tried to downplay the hype and put the function of mirror neurons into perspective: how can we be sure that mirror neurons have shaped social evolution when we know for a fact that their activity is also modulated by social interactions?

Since their publication 15 years ago, Rizzolatti and Bekkering have developed their own distinct views on mirror neurons. Although both of them are convinced that these cells are crucial to experiencing empathy, Rizzolatti now claims that autism can be attributed to a dysfunctional mirror neuron system. Harold Bekkering, Professor in Cognitive Psychology at the Donders Centre for Cognition at Radboud University, is more cautious. Not only has he revised his own ideas on imitation, but he also has serious doubts about the autism claim. The University invited the Italian neuroscientist, now aged 77, to give a speech on the 50th anniversary of the Faculty of Social Sciences. A nice opportunity to reflect on mirror neurons and find out where neuroscience now stands on this issue. Prof. Bekkering explains why scientists should be careful with their claims.

Is it still generally believed that empathy is based on mirror neuron activity?
'Yes,' confirms Bekkering, 'It's now generally believed that mirror neurons don't act on their own, but rather have a facilitating function. They connect or 'mirror' our internal representation of another person's behaviour to our own higher cognitive interpretations of that behaviour. And, depending on that interpretation, watching somebody else act can cause empathy.'

'For example, consider someone who's who in pain. We know that when we experience pain ourselves, a network of subcortical areas is activated in our brain. But, when we see somebody else suffering, for example, from a large, bleeding wound, this network is also activated. Nevertheless, other factors, such as whether the person we observe is someone close to us or an enemy, will modulate the cognitive experience of empathy with the person in pain.'

Can you develop your mirror system?
'Our whole life is about learning from or adjusting our behaviour to match that of other people. By experiencing the consequences of own actions and watching the effects of other people's actions, you are not only training your perceptual and motor functions separately, but also the connection between them. In other words, you're training your mirror neuron system.'

Prof. Bekkering personally believes that mirror neurons may be the reason that most people aren't violent. 'Suppose you're angry and you punch somebody. You're immediately alarmed by your own action (hurting that person). This unwanted perceptual consequence is integrated within the mirror neuron system and makes it more likely that next time you will not be so inclined to punch. Some people however, do not experience this sensation of alarm. These might be the people who can effortlessly tackle someone in a soccer match, or knock someone down. But this is more my personal view than a scientific theory.'

Rizzolatti claims that autism is caused by a dysfunctional mirror system – an assumption that is poetically called 'the broken mirror'.
'Here I don't agree, it's more likely the other way around. I think children with autism don't pay as much attention to social signals as other children do. They are thus less active in developing connections between their own actions and those of the others, possibly resulting in a less developed mirror system. But again, all theories on mirror neurons and autism are highly speculative.'

Why is that so? Can't we get insights by mapping the connectivity of mirror neurons?
'That's not at all easy. Each method has its own advantages and limitations. Rizzolatti's single-cell measures elegantly identify the functional role of mirror neurons in monkey brains, but this technique can't easily identify larger functional brain networks. Brain imaging techniques such as MEG and fMRI can show these networks in humans but are too imprecise to identify the function of mirror neurons themselves. Nowadays, we have more than a hundred neuroimaging studies which confirm an overlap between activity while observing actions and executing them. But this is still only indirect proof of the causal role of human mirror system activity in understanding actions.'

Is it beyond doubt then, that humans have mirror cells? 'Yes,' says Bekkering. 'The abundant neuroimaging literature – plus a few single cell recordings from neurosurgical patients – provides proof of human mirror neuron activity.' This emphasizes his final point. 'I think it's very exciting to keep theorising on mirror neurons and their potential role in social interaction, but we have to be careful with our claims.'

Anna Tuenter

Donders lecture 12 March 2015

The cerebellum and neural control of movement

Professor Reza Shadmehr

Johns Hopkins University School of Medicine

'I once attended a lecture given by Reza, and wow, I wish we had taken all of our students to it. In just 90 minutes he covered the whole of the history of the internal model of motor control – in other words the importance of predictions in perception and action research – in such a way that it literally saved going through a pile of literature this high.'

Luc Selen uses his hands to show how high that pile is – at least a metre. 'And I was not bored for a single second. He really is a fantastic speaker.' Luc Selen works at the Donders Institute, having graduated in biomedical engineering, just like Reza Shadmehr, who will give the first Donders Lecture in 2015 on 12 March.

For whoever needs further encouragement to attend the lecture after such a warm recommendation: Shadmehr is widely regarded as the leader in the field and he's great at formulating research questions. 'Where Reza is concerned, he'll be writing a formula on the board, but he also has a fantastic way of explaining such formulas.'

'Everything he does is helpful, for example the way in which he disentangles into different components the contributions of the various brain structures with which we perceive the world and react to it. Or the way he makes such a convincing case for the brain being a probabilistic calculator,' explains Pieter Medendorp.

Both researchers regularly meet Shadmehr at conferences and, although they have never published together, their research has a great deal in common. 'At John Hopkins University – where Reza works – clinical and fundamental sensory motor control are tightly interwoven, whereas here at the Donders Institute we focus more on imaging sensory motor processes. These two approaches complement each other extremely well.'

'He steadfastly follows his own path and his vision is original. He introduced the use of a robotic manipulandum – now hugely popular in the field of revalidation – as early as 1994 and it still represents the gold standard in research on motor learning. His research and results often have far-reaching consequences for the field; in September this year he published an article in *Science* about how we learn from our mistakes.'

Donders lecture 12 March Professor Reza Shadmehr

The cerebellum and neural control of movement

The Donders Lectures take place on the University campus at the Linnaeus Building, Heyendaalseweg 137, Nijmegen and they start at 4.00 p.m.

More about the 2015 series at www.ru.nl/donders

Robert Desimone will speak in June, Dorothy Bishop in October, Stephen Faraone in October and Erich Jarvis in December.

Iris Roggema

Meanwhile at www.ru.nl/donders

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

Heineken Prize winner speaks at Radboud University

Prof. Jay McClelland of Stanford University has won the Heineken Prize for Cognitive Science 2014. In the 1980's, McClelland came up with the revolutionary insight that our brain works as a parallel processor rather than as an analogue computer. He gave a public lecture in the main Aula at the University on 1 October.

EU grants for Barbara Franke and Jan Buitelaar

Barbara Franke and Jan Buitelaar, Principal Investigators at the Donders Institute and Radboudumc, each received a € 3.9 million Horizon 2020 EU grant scheme for their Early Training Network proposals on neurodevelopmental disorders. Franke's MiND project and Buitelaar's BRAINVIEW project investigate the cause of attention deficit hyperactivity disorder (ADHD) and autism spectrum disorders (ASD).

Successful Summer School on Stress & Cognition

Each year, the Donders Institute hosts a cognitive neuroscience summer school, bringing together some of the world's leading scientists as well as outstanding MSc students, PhD students and postdocs. The topic of the 2014 Summer School, which was organised by Professor Benno Roozendaal and Dr Erno Hermans was *Stress & Cognition: From basic mechanisms to psychopathology*. Over 75 participants from more than 15 countries attended.

Six Veni grants for Donders researchers

Six researchers at the Donders Institute have received a prestigious Veni grant from the Netherlands Organisation for Scientific Research (NWO): Saskia Haegens, Tessa van Leeuwen, Arnt Schellekens, Guillaume Sescousse, Tineke Snijders and Monique van der Voet. Veni grants allow promising researchers who recently obtained their PhD to conduct research for a period of three years.

Guillèn Fernandez member of the Academia Europaea

Guillèn Fernandez, Director of the Donders Centre for Neuroscience and head of the Memory and Emotion research group, has been elected as a member of the Behavioural Sciences Section of the Academia Europaea,as was affiliated PI Prof. Paula Fikkert. The Academia Europaea is an international, non-profit association of individual scientists and scholars representing all major disciplines, who are experts in their own subject areas as recognised as such by their peers. Membership is by invitation only.

Three talent grants for young researchers

Three young and ambitious researchers in the social and behavioural sciences have received a Research Talent grant from the Netherlands Organisation for Scientific Research (NWO) to pursue a 3-year PhD project at the Donders Institute. The award winners – Jennifer Swart, Lonja Schurmann and Guus van Bentum – will be supervised by Roshan Cools, Christian Doeller and John van Opstal, respectively.

Donders Wonders blog launched

In June 2014, the Donders Institute launched a blog for the general public: Donders Wonders, which can be found at *blog.donders.ru.nl*. The blog features background articles, columns, opinion pieces and science experiments people can try at home, written by a team of enthusiastic PhD students and postdoctoral researchers. For now, the blog is only available in Dutch, but future plans include an English version. See the back cover of this newsletter for more information on Donders Wonders.

OUT OF OFFICE

'Thanks for your message. I regret that I'm unable to answer your e-mail – I'm busy blogging.'

The Donders Institute may be a highly ambitious international research centre, but what do staff get up to after office hours? More research, of course – clearly, it doesn't all get done from nine to five – but lots of other things too. This produces some fascinating out-of-office replies…


The Donders Wonders crew: Julian, Richard, Jeanette, Romy, Piet, Alina, Winke, Susanne and Lieneke (the tenth crew member is Janita)

Brain reading, YouTube videos of dancing animals and encounters with Nobel Prize winners. The *Donders Wonders* blog clearly doesn't disappoint in covering a broad range of subjects (see blog.donders.ru.nl). The brains behind this blog about neuroscience are ten enthusiastic PhD students and postdocs who currently work at the Institute.

Donders Wonders has been online since the summer of 2014 and it already attracts a steady number of readers each month. The bloggers share scientific news but also their personal fascinations, thoughts and doubts on brain and behaviour research. 'I think one of the coolest results up to now was when the science pages of NRC Handelsblad (a major Dutch quality newspaper, red.) mentioned us in a tweet,' blogger Romy says. Her fellow blogger Lieneke adds: 'I'm most proud of the fact that we manage to publish two posts every week, which is pretty intensive alongside our usual research work.'

During editorial meetings all bloggers are asked to pitch at least one but preferably two new ideas. Does beer flow abundantly to improve creativity? 'Well, no. Our meetings are on Thursday mornings! But who knows what will happen in the future, if it becomes harder for us to come up with new ideas…' They all laugh. 'For now, we try to link our blogs to current events, social issues and everyday life as much as possible in order to attract a broad audience,' Susanne says.

The bloggers also experience personal benefits from the project. Julian: 'It's easier to talk about your research when you have had this much practice translating scientific results into information that will appeal to laymen'. 'I also notice it in our lab meetings – our enthusiasm for communicating science seems to be contagious,' Lieneke adds. 'And it's a fun way to get to know the full scope of the Donders Institute,' says Romy. 'I talk to colleagues who I normally probably never would have met.'

So far, the *Donders Wonders* blog is only available in Dutch. But in future we intend to create a bilingual blog. Furthermore, the bloggers aim to incorporate more opinion pieces by senior researchers and more substantive input from Radboudumc.

Do you have any ideas or feedback for *Donders Wonders?* Or do you want to contribute by writing a blog entry yourself? Send an e-mail to blog@donders.ru.nl and one of the bloggers will be in touch soon.

Iris Kruijen

Diary

12 December 2014, **Symposium Clinical applications of smart glasses**, University of Twente (9:30 – 17:30)
16 December 2014, 12:30 – 13:30, **DCC Lecture Walter van Heuven,** University of Nottingham, Research focus: *Monolingual and bilingual language processing, computational models of language processing, and neuroimaging studies of the bilingual brain.* Spinoza SP A -1.54
18 December 2014, **Annual Donders Poster Session**, Radboudumc, Tuinzaal (route 706)
2 and 3 March 2015, **Visit Donders Advisory Board**
Donders Lectures 2015
Location: Linneaus Building, time: 16:00 – 17:00, drinks at 17:00!!
- 12 March 2015, **Rehza Shadmehr**, Johns Hopkins University
  The cerebellum and neural control of movements
- 25 June 2015, **Robert Desimone**, McGovern Institute for Brain research, MIT
  The top-down control of feature and spatial based attention
- 1 October 2015, **Dorothy Bishop**, University of Oxford
  The enigma of cerebral lateralization
- 29 October 2015, **Stepen Faraone**, SUNY Upstate Medical University, *Advances in genetics and neurobiological mechanisms underlying neuropsychiatric disorders*
- 3 December 2015, **Erich Jarvis**, Duke University Medical Centre
  Learned birdsong and the neurobiology of human language

PhD defences

2 September 2014 - **Stolk, A.** *On the generation of shared symbols* (Dondersseries 166)
10 October 2014 - **Krause, F.** *Numbers and magnitude in the brain: A sensorimotor grounding of numerical cognition* (Donders series 167)
3 October 2014 - **Munnike, M.** *Measuring and modulating the brain with non-invasive stimulation* (Donders series 168)
24 October 2014 - **Von Borries, K.** *Carrots & Sticks - a neurobehavioral investigation of affective outcome processing in psychopathy* (Donders series 169)
24 October 2014 - **Leoné, F.** *Mapping sensorimotor space: Parieto-frontal contributions to goal-directed movements* (Dondersseries 171)
26 November 2014 - **Van Kessel M.** *Nothing left? How to keep on the right track - Spatial and non-spatial attention processes in neglect after stroke* (Dondersseries 172)
3 December 2014 – **Oerlemans A.** *Shared underpinnings of Autism Spectrum Disorders and Attention-Deficit/Hyperactivity Disorder. New approaches to tackling phenotypic and genetic heterogeneity*
3 December 2014 - **Van den Abeelen, A.** *In control. Methodological and clinical aspects of cerebral autoregulation and haemodynamics* (Donders series 170)
9 December 2014 - **Vlek, R.** *From Beat to BCI: A musical paradigm for, and the ethical aspects of Brain-Computer Interfacing* (Donders series 164)
16 December 2014 - **Vulto van Silfhout, A.** *Detailed, standardized and systematic phenotyping for the interpretation of genetic variation* (Donders series 173)
12 January 2015 - **Meyer, M.** *Inbetween Modalities combined EEG – fMRI* (Dondersseries 175)
12 February 2015 - **Bralten J.** *Genetic factors and the brain in ADHD* (Donders series 176)

Donders Institute Newsletter

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