Newsletter 16
24 September 2010

The Donders Newsletter is published three times a year by the Donders Institute for Brain, Cognition and Behaviour, which consists of research groups at Radboud University Nijmegen and the Radboud University Nijmegen Medical Centre as well as the Max Planck Institute for Psycholinguistics. Its purpose is to keep you informed of developments and important news in the field of neuroscience.

Newsletter
Donders Institute
for Brain, Cognition and Behaviour

Welcome to another edition of the newsletter of the Donders Institute! In this issue we feature the research of Paul Tiesinga. Paul has rapidly made an impact in Nijmegen, and in addition to building up his research group he is also the speaker for Theme 4, Brain networks and neuronal communication, within the Institute. It is an especial pleasure to commemorate the tenth anniversary of the famous Nijmegen baby lab by interviewing Sabine Hunnius: and the importance of this lab will be further emphasised in the near future by the publication of a book on the baby brain. One of the loyal and dedicated workers without whom this Institute could not succeed is Yvonne Schouten, who will be well known to those working at the DCC and many of the Masters students, and is featured in the 'backbone' section.
Finally a brief reminder of one imminent highlight: the Donders lecture of Matthew Rushworth, on the role of the prefrontal cortex in changing behaviour, which will take place on 7th October.

With best wishes,

David Norris

Radboud University Nijmegen

www.ru.nl/donders

“It still feels special to do an EEG on a baby”

In 1999, Professor Anne Cutler won the Spinoza award, the highest scientific award in the Netherlands. She used the grant to found the Baby Research Center, which opened in 2000. This is an exceptional laboratory, even by international standards. Sabine Hunnius explains the results of ten years of innovative research.

On the day of the World Cup final, there’s a party in the forest at the edge of the Nijmegen campus. While children have fun in the inflatable castle, their parents listen to short lectures about the research performed over the past ten years at the Baby Research Center (BRC), a partnership between the Max Planck Institute for Psycholinguistics (MPI) and Radboud University Nijmegen.

Parents who registered their baby in Nijmegen or Arnhem received a phone call from the Center soon after, asking them to take part in research, with their babies. No less than 3500 parents have been willing to come to the Center once – or more often – and sometimes they are also prepared to be observed at home. Initially the BRC focused on language development, but now prelinguistic development and social cognitive development are also included. Right now, the Centre’s work includes cross-cultural differences in upbringing and development.

Fast development

Although the party is being held at the MPI, where the BRC was founded ten years ago by linguist Anne Cutler, the actual research is now conducted a little further away: in the basement of Montessorilaan 10, and sometimes at the Donders Centre for Neuroimaging. The research rooms are welcoming and contain lots of children’s books, posters and toys. “Last week we had fifty babies,” says Sabine Hunnius, psychologist and Director of the lab. “At first we had no more than two a day.”

This shows that the BRC is an efficient lab that always manages to recruit new test ‘subjects’. The multidisciplinary team now comprises twenty researchers.

The continuity of the lab sets it apart from others, and so does the advanced equipment that is used. “It still feels special to do an EEG on a baby,” says Sabine. “Over ten years of research, I’ve seen a shift from studying behaviour only to an interest in the underlying neuropsychological processes. That’s why we increasingly use EEG equipment. We also use eye-trackers now, which accurately track the eye movements of babies. This can tell us a lot about how babies perceive their environment and what they understand.”

New methods

“We would like to incorporate new methods into our research to tell us more about where brain activity takes place. FMRI is done with babies in the United States, but we prefer not to use that technique. You have to lie very still in the MRI machine – small children would need to be sedated, which we don’t like to do. We favour research that is fun for the children and their parents. Besides, how do you study the behaviour of a sleeping child? A far more practical technique called near-infrared spectroscopy (NIRS) can measure a BOLD signal (blood-oxygenation level-dependant signal), just like FMRI. The practical objection to NIRS – that some skulls are too thick for the signal to pass through – is fortunately not applicable to babies and toddlers. MEG (magneto-encephalography) could also be suitable.”

New questions

Besides the technological developments and the increased interest in neuropsychology, Sabine sees another growing trend. “Baby researchers have long been trying to prove that very young babies are very smart and can learn a great deal. But really the question of what they can do at six months – or six and a half months – is not that interesting. How they learn, and how the developmental stages follow each other, are what fascinates us more now. If we comprehend the development of babies, how they understand others, how they interact and how they process language, we can gain a whole new insight into how the adult mind works. And finally, understanding the normal course of development will eventually lead to a better understanding of what goes wrong in children whose development is impaired.”

IR

Sabine Hunnius, Psychologist and Director of the lab. Photo: Erik van ‘t Hullenaar

Ten years of baby research

Anne Cutler founded the Baby Research Center in 2000 as a lab dedicated to investigating language acquisition. Since then three distinct lines of research have been developed:
• Early language development
• Communication before language
• Social-cognitive development

Here’s a selection of experiments carried out at the lab:

Universal index finger
Before children learn one of the 6,000 languages in the world as their mother tongue, they point with their index finger to draw their parents’ attention to an object. A cross-cultural study in eight countries by Ulf Liszkowski and colleagues around the globe revealed the universality of this way of communicating.

More or less non-verbal communication
Another cross-cultural study showed that the frequency of gestures in pre-lingual children reflects the frequency of gestures made to them. Mayan parents do not interact with their children very much, whereas Chinese parents interact intensely with their children. Europeans are somewhere in between. As a result Mayan children do not gesture very often, but Chinese children do.

The climbing frog game
Although children as young as 18 months are interested in working together and trying to cooperate with adults, it takes a lot of learning before they can actually do so. Turn taking during joint actions for example is a social skill that 2½-year-olds do not yet master, but 3-year-olds do, as Marlene Meyer and Sabine Hunnius demonstrated with a funny game involving a frog, a ladder and a piglet.

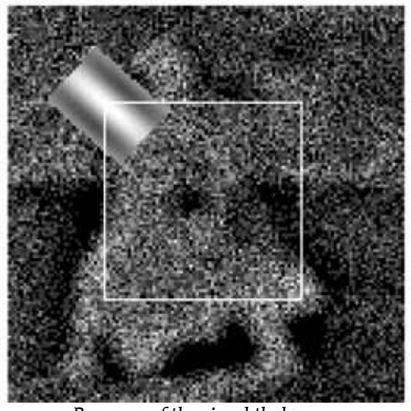
Imitating action
Ten years is long enough to review your own results. In a 2002 paper in Nature, Prof. Bekkering and colleagues presented evidence that even babies reason about the logics of other people’s actions. They made babies look at an adult switching on a lamp with her head. In one condition the adult’s hands were free; in the other condition, she was holding a blanket. Babies who had observed the hands-free condition were more likely to imitate the head switch than babies who had seen the hands-occupied condition. Previously, it has been concluded that babies reasoned about why the adult might have used her head and that they imitated the head action based on whether the adult’s behaviour appeared rational.

So in the case in which the model was holding a blanket, the babies might have thought ‘well, the task is to switch on a lamp and, since I’m not holding anything, I’ll do it just with my hands’. Whereas, in the hands-free condition, they might have thought ‘she could do it with her hands, but she doesn’t, so it might be better to use your head’ and therefore imitated the head action more frequently. However, recent research at the BRC indicates that these conclusions might have overestimated the social-cognitive skills of these 14-month-olds: it may well be that physical constraints have a much stronger impact on whether the babies imitate the head action than reasoning about the logic of the observed action.

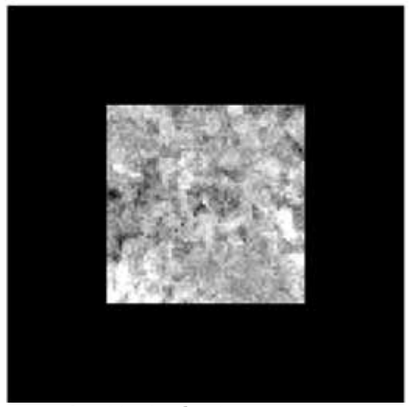
Stops and fricatives
Paula Fikkert discovered that the phonological contrasts children can produce indicate which contrasts they perceive. Children often produce fricatives (f, v, s, z and g) as stops (p, b, t, d and k) but not the other way around. For example, they say tis instead of fish, but they almost never produce val instead of bal. A phoneme perception experiment showed that in the 14-month-old babies’ mental dictionary the distinct property ‘fricative’ is recorded, whereas the property ‘stop’ is not. This, in turn, suggests that their word knowledge is more abstract than was previously thought.

A luminous idea

Image on the retina



Response of the visual thalamus



Input to visual cortex neurons

Many researchers say they 'want to shed light' on whatever their field of research might be, but few take it literally. Paul Tiesinga does. This young professor in neuroinformatics at the Donders Institute for Brain, Cognition and Behaviour is dreaming of using an optogenetic method to cure failing circuits in the brain. Creating a light switch for a brighter mind.

It's quite a challenge to describe the responses of a population of neurons to a real visual stimulus. When we watch a movie, an image is projected on the retina (above, left panel), which turns it into a set of electrical pulses that are processed by the lateral geniculate nucleus (middle panel). The output, consisting of electrical impulses, is recombined, providing inputs to neurons in the primary visual cortex (right panel), at which point the stimulus is no longer recognizable. We show the activity of neurons in the middle and left panel in terms of a gray scale; bright pixels correspond to neurons firing at a high rate. At the Donders Institute, we develop new techniques for modelling the response of the visual cortex to visual stimulation and analyzing the corresponding neural responses obtained in experiments. For these studies a new generation of quantitatively trained neuroscientists are required, which is where Track 4 of the Cognitive Neuroscience Research Master's programme comes in.

The simulations were performed by Paul Tiesinga & Calin Buia and the underlying model is described in Buia & Tiesinga, *Spatial attention in area V4 is mediated by circuits in primary visual cortex.* **Neural Networks** 22:1039-1054 (2009).

It was journalism that introduced him to neuroscience. Paul Tiesinga (1970) was a PhD student in theoretical physics and interested in condensed matter physics, when he joined a journal club. Reading popular science articles he discovered an appetite for biological systems. 'It was then that I bought Francis Crick's book on consciousness - The astonishing hypothesis. I was immediately hooked and lent the book to Jorge José, a Boston-based physicist.' José was equally enthusiastic and created a postdoc position for Paul in computational neuroscience. This was the start of a career that gave him a solid foundation in neuroscience and led to a second postdoc at the Salk Institute. Now he's a professor at Radboud University Nijmegen.

'When you start working in a new field as an outsider, the hard part is getting a good problem to work on. The danger is that you repeat what's already been done. In Boston we started working on gamma oscillations – the brain waves that are active when you're really focused on a task. We discovered that the voltage fluctuations between two action potentials – referred to as noise – weren't irrelevant at all, as was previously thought. This noise does matter when you look at groups of neurons: it can kill oscillations and thus numb out the signal. So, to understand attention, you need to look at groups of neurons, not single ones.'

What neurons do together

At the Salk in San Diego he got submerged in a large, lively neuroscience group built around the famous Terrence Sejnowski, which focused entirely on systems, i.e. what groups of neurons do. 'Here I learned real neuroscience and got acquainted with experimental work, studying slices of rat brain and making the neurons in them act as if they were alive. I found out that this maybe wasn't the best way to spend my time, but it is very helpful that I now know the experimental side of neuroscience. '

Paul remains dedicated to the subject of attention and keen to extend the frontiers of the field. 'Visual attention has been studied for thirty years, resulting in models of firing rate dynamics and the synchrony of groups of neurons, but such models are still correlative. Whatever it is that changes in the neuron (or in a group of neurons) and thus causes the attentive state is not yet fully understood.'

Modern genetics can be used to help fill in the gaps. It provides robust ways of introducing channels, pumps and fluorescent proteins into specific cell types, thus changing their firing ability. One of the most exciting developments is the expression of Channelrhodopsin-2 channels, which are opened by blue light and trigger a depolarizing current. More recently their counterpart, the Halorhodopsin pump – Halo for short – was inserted in neurons, which then produce a hyperpolarizing current when stimulated by yellow light. This makes it possible to switch the firing of neurons on and off with a simple light source. 'My ultimate goal is to test my hypothesis about how the computations underlying selective attention are implemented at the level of the local circuit,' Paul says.

The optogenetic method

'Please keep in mind what I'm telling you now is closer to my dream than reality,' Paul Tiesinga says after explaining his ideas about using an optogenetical method to cure failing brain circuitry. 'But you need a goal to give your work a sharp focus.'

So what is he dreaming of? 'Optogenetics is already feasible, using mouse models, where it's easy to express the necessary proteins using knock-in approaches. The step to non-human primates and then to humans is difficult because viral transfection is required, which often results in less effective expression. But when we understand and manage the method very well, we can start to think about ways of curing human brain diseases, for example schizophrenia. There are deficiencies in the oscillation patterns in patients'brains, which in turn leads to information processing impairments. Using viral transfection we could install genes to repair their neural circuitry by selective strengthening synaptic connections or by shining a light on their cortex. This will literally brighten up their lives!' *IR*

Paul Tiesinga, Professor at the Donders Centre for Neuroscience

'Optogenetics may be used as a tool to cure failing brain circuitry'

Donders graduate school: Brain networks and neuronal communication

The Donders Graduate School offers students a high-quality educational programme at both Master's and PhD level. The school is intended for the best international students in biology, physics, psycholinguistics, behavioural studies and medicine who are strongly motivated to do research in cognitive neuroscience. This year a fourth theme was added to the education programme so that from now on the school can work in parallel with the research themes at the Donders Institute. Track 4 is completely dedicated to networks. The overall theme is the interaction between and within groups of neurons, and with the outside world. Paul Tiesinga: 'People with a mathematical background, informatics, physics, mathematics or engineering who can handle the volumes of data neuroscience generates are much in demand in this field. We've already recruited four Master's students with such a strong quantitative background. They'll have a lot of freedom to identify their own research questions and thus tackle neuroscience issues from a computational angle. '

Please, make up your mind!

In the Donders lecture series outstanding researchers in the field of brain and cognition present their work and ideas to a broad audience of scholars with a wide range of backgrounds – from neuroscience to psychology and linguistics. It is one of the ways that the Institute develops links with the global scientific community.

Ivan Toni, head of the Donders' research group Intention and action, invited Prof. Matthew Rushworth to give a lecture. Why?
'He's a specialist in decision making, i.e. studying how the brain does this trick. Many studies have been done on binary decisions, for example asking subjects to choose between an English or a continental breakfast a hundred times and then averaging the brain responses. He's been able to move the subject forward to a more realistic approach that takes the current circumstances of the subject into consideration. Often, when you have to make a choice, you're not sure about the outcome. How does the brain weigh up such factors? Matthew has operationalized the temporal and conceptual complexity of research on decision making.'

How does Rushworth inspire you?
The way he has been able to simplify a very complex matter – without destroying the complexity to such an extent that it loses all meaning – should be an example to us all. Research can all too easily become trivial by over-simplifying reality. Matthew shows us how to avoid that. The broad basis of his research is exemplary. He's not easily satisfied and his claims are made on the basis of a variety of domains: imaging, animal research and computational models.

What is Matthew Rushworth's main contribution to neuroscience?
Matthew is breaking new ground in the field of the connectivity of the brain. As long as we study the functioning of brain areas without addressing the way these areas connected to each other, our understanding will be limited. Matthew has developed techniques for predicting changes in behaviour due to changes in the connectivity of brain.

Donders Lecture: "The role of the prefrontal cortex in changing behaviour"

Matthew Rushworth (Decision and Action Laboratory , University of Oxford)
Thursday 7 October 2010; 16:15; Linnaeusbuilding , Heyendaalseweg 137, Nijmegen

Meanwhile at Donders

Pay a regular visit to our website *www.ru.nl/donders* to keep up to date on our news and events.

Women and shoes: celebrities really do help sell products

When celebrities are associated with certain products the brain recruits memory systems more than when ordinary people are associated with them. A significant correlation was found by Mirre Stallen, a PhD student at the Donders Institute. She tested her hypothesis by showing shoes and pictures of either celebrities or ordinary people and then measuring the response subjects in an MRI scanner. The pictures of celebrities seemed to trigger retrieval of a specific happy memory episode related to the celebrity. This happy feeling is then transferred to the product associated with the celebrity. These findings have been published in the Journal of Economic Psychology.

Most brain and cognition-related grants go to Nijmegen

Radboud University Nijmegen has been awarded funding worth €4 million for new brain research programmes. Eight research teams will be working on projects designed to shed new light on how the brain works during various tasks, how different areas of the brain work together, the role of genes in the development of ADHD, how we learn words, the impact of anti-depressants on an unborn child, and how envisioning movement can be used to help rehabilitate children with motor disabilities.

The research funding, which comes from the National Initiative for Brain and Cognition, is intended for integrated interdisciplinary research in the field of the brain and cognition. This will hopefully provide new insights into the link between the cognitive functions of humans and neural substrates (the brain and nervous system). Eight of the fourteen national project proposals that won funding were submitted by researchers from Nijmegen – thus underlining the strong position the University has in interdisciplinary research on the mind and brain. Five projects will be based at the Donders Institute.

If you're interested in learning more about specific grant topics, please go to www.ru.nl/donders

Three Veni grants for powerful Donders talent

Three young Donders researchers obtained a prestigious Veni grant from the Dutch Organization for Scientific research (NWO). Guido van Wingen will investigate how we control our emotions, Ali Mazaheri will investigate how brain regions fail to work together in ADHD, and Luc Selen will investigate how we learn to grasp and reach when our body moves fast. The Veni-grant (€250,000) offers researchers who have only recently completed their doctorates the opportunity to develop their ideas for three years.

Review of rare disease published in Brain

Tyrosine hydroxylase deficiency (THD) is an autosomal recessive disorder resulting from cerebral catecholamine deficiency that has been reported in fewer than 40 patients worldwide. Most patients with THD can be successfully treated with l-dopa, stressing the need for early recognition and diagnosis of this rare metabolic disorder. In a collaborative study with colleagues around the world, researchers from the departments of Paediatric Neurology, Human Genetics and Laboratory Medicine reviewed all available evidence on clinical phenotypes and rational diagnostic and therapeutic approaches for this devastating, but treatable neurometabolic disorder. Based on neurological features, the researchers divide THD in two phenotypes: an infantile onset, progressive, hypokinetic-rigid syndrome with dystonia and a complex encephalopathy with neonatal onset. They found marker molecules in the cerebrospinal fluid which concentrations correlate with the severity of the phenotype. The study was published in Brain.

Researchers Night in LUX

Live brain research in down-town Nijmegen and lively debates with the general public in the LUX Researchers Night on September 24. Brain implants, the effects of Transcranial Magnetic stimulation and hopes and worries about the growing control on the human brain were discussed.

Strategic research agenda presented

On the occasion of the Researchers Night the IT Innovation Platform Brain and Cognition presented its Strategic Research Agenda. With two of its members – Stan Gielen and Peter Desain – the Donders Institute is well represented in this platform. The Innovation Platform was established to encourage economic and societal innovation by creating an 'eco-system' of private and public organizations operating at the intersections between the fields of ICT, Brain, and Cognition.

Donders backbone: Yvonne Schouten, 'problem solver'

Due to its academic nature and high ambitions, staffing at the Nijmegen-based Donders Institute is extremely dynamic. Postdoctoral researchers and PhD students fly in from around the globe. Technicians, lab workers and research assistants form the much-needed constant, the backbone of the institute.

Yvonne Schouten is a secretary at the Donders Centre for Cognition, a subdivision of the Donders Institute for Brain, Cognition and Behaviour. She deals with everything involved in the Research Master Cognitive Neuroscience. As of Autumn 2010, she will also work for the Donders Graduate School.

According to her colleagues, Yvonne is the "social hub" of the department. "That's all part of the job as a secretary," she says. "You're the contact, the listening ear. Everyone should be able to come to you." That is how she sees her contribution to the research at Donders and to the teaching in the research master: "As a secretary, you play your part mostly by helping other people, either by finding the solution yourself, or by referring them to the right person. Sometimes I see and hear things that make me think: 'something is going wrong here, that could cause a hold-up soon.' So I take the initiative to contact someone who can prevent it."

Yvonne Schouten

Yvonne speaks with pride about the students in the research master, which she helped establish in 2003. In the beginning she handled everything herself – and with no half measures. For instance, there was a student from India whose accommodations were not quite ready when he arrived. "I took him home." She would also sometimes help other students find rooms. "And sometimes I would say: 'your mother would not like it, if she knew you were living here.' Those were fun times. But it's a good thing a coordinator joined us after two years. The downside of handling everything yourself is that you have to come up with all the answers."

The sailing weekends Yvonne organizes each year are well known. Last June, forty people participated. Most were staff at the Donders Centre for Cognition and students from the research master, but there were also former colleagues and a few people who had nothing to do with Donders. "This sailing weekend is really quite separate from Donders: it's a private activity that I organize, and many colleagues and students happen to attend." A coincidence? "Well, maybe not entirely. Suffice to say there are a lot of people who, like me, are keen to promote social cohesion in the workplace. And it surely does that!"

AvK

Agenda

24 September 2010
EU Researchers' Night: Night of the Brains
Lux Theatre, Marienburg 38, Nijmegen

7 October 2010, 16:15
Donders Lecture by Matthew Rushworth (Oxford Centre for Functional Magnetic Resonance Imaging of the Brain, University of Oxford)
Linnaeusgebouw, Heyendaalseweg 137, Nijmegen

19-20 October 2010
IRUN Autumn School for Transferable skills
Forum de Ganzenheuvel, Ganzenheuvel 56, Nijmegen

21-22 October 2010
Donders Discussions
Forum de Ganzenheuvel, Ganzenheuvel 56, Nijmegen

27-28 October 2010
Workshop the Embodied Mind: Perspectives and Limitations
Aula, Comeniuslaan 2, Nijmegen

2 December 2010, 16:15
Donders Lecture by Tobias Bonhoeffer (Max Planck Institute of Neurobiology, Martinsried)
Linnaeusgebouw, Heyendaalseweg 137, Nijmegen

PhD defences

25 August 2010 - **van Dijk, H.P. (2010).** The state of the brain, how alpha oscillations shape behaviour and event related responses.

29 October 2010 **- van Elk, M. (2010).** Action semantics: Functional and neural dynamics.

11 November 2010 **– Qin, S. (2010).** Adaptive memory: Imaging medial temporal and prefrontal memory systems.

20 December 2010 **- Meulenbroek, O.V. (2010).** Neural correlates of episodic memory in healthy aging and Alzheimer's disease.

Donders Institute Newsletter

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