Donders Institute Newsletter

Issue 22
15 June 2013

The Donders Newsletter is published twice 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 within the Donders Institute and the field of neuroscience.

Role of genetic makeup in language learning

The power of 3 Tesla

The cognitive neuroscience of remembering

Donders Lecture 5 September 2013, Anthony Wagner

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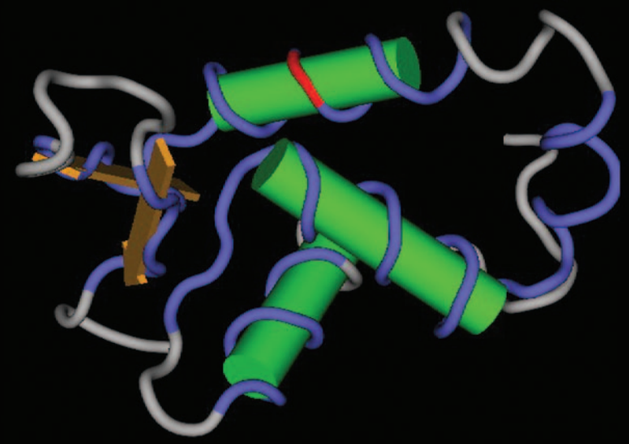
Donders Institute
for Brain, Cognition and Behaviour



Genes as windows into human biology

Which molecular factors underlie human language and how do they explain its origins and evolution? Professor Simon E. Fisher – the co-discoverer of FOXP2, the first gene to have been implicated in this unique aspect of human biology – peers into the genetic 'black box' of speech and language.

Simon E. Fisher is Professor of Language and Genetics at the Donders Institute and director of a new department at the Max Planck Institute for Psycholinguistics. This department was established at the end of 2010 with the goal of using genes to provide insight into the biological basis of speech and language. Prof. Fisher and his colleagues are taking advantage of the latest innovations in molecular methods to discover how our genome helps us learn to speak. 'We want to reveal the DNA variations that affect our extraordinary ability to communicate in a complex way,' he explains. 'This is a novel approach to the enigma of spoken language, but one that can be remarkably effective. We have already gained exciting insights by studying children who mysteriously fail to develop proficiency in this area.'

Despite the extreme complexity of the task, most children learn their native language almost effortlessly, without needing to be formally taught. What role does our genetic makeup play in language learning? 'Initial clues come from pinpointing susceptibility genes that contribute to language impairments,' Prof. Fisher says. 'FOXP2 was the first example of this. We identified the gene in 2001 when I was at Oxford University, and it sparked off a whole new wave of research.'

Family studies

'In the mid-1990s, when I was a postdoctoral researcher at Oxford,' he continues, 'my projects involved gene hunting in families with specific language impairments or reading disabilities. These disorders typically have complex genetic underpinnings involving several – perhaps many – different genes. But then we started working with an unusual family, known as the KE family, which was originally identified by our collaborators in London. Half of the family – 15 people across three generations – were affected by problems which revealed a surprisingly simple pattern of inheritance.' Prof. Fisher and his colleagues tracked the cause of the disorder to part of chromosome 7 and eventually zeroed in on the mutation responsible, which disrupted FOXP2. 'Family members who carry this mutation all have severe problems with learning to make sequences of mouth movements that are important for speech, accompanied by further difficulties in language production and understanding. Just a single letter of DNA is affected, a G mutated to an A. That's enough to change the shape of the protein which FOXP2 encodes in a critical way that prevents it from working properly.'

Could this family be unique – Prof. Fisher and his colleagues wondered – or would mutations of FOXP2 also explain common forms of language impairment? 'We found that it's rather rare to have mutations in FOXP2; we now know of several other families which were similarly affected by vulnerability to disruptions of this gene. So most cases of speech and language problems remain unexplained and this is something we really want to tackle in the new department.' Prof. Fisher is also concerned that language impairments are not sufficiently well understood in society. 'When an individual has a problem in this area, it can make it difficult to function in the modern world, a world which is increasingly dependent on language. One of our goals is to raise awareness of the impact that these types of disorders have on people's lives.'

Sequencing whole genomes

Meanwhile, the technology for tracking down genetic causes of disease has made enormous strides with the arrival of next-generation DNA sequencing. 'It took a large international consortium over a decade and billions of dollars to sequence the first human genome. Now it's possible to determine the DNA sequence of a person's entire genome in a matter of days, at a cost of around several hundred euros.' Prof. Fisher's department has been collaborating with Professors Joris Veltman and Han Brunner as well as colleagues at the Human Genetics Department of Radboud University Nijmegen on sequencing whole exomes (all the protein-coding parts of the genome, comprising around 20,000 genes) in children and families with language-related impairments. But 'while the tools for DNA sequencing have advanced dramatically, our ability to interpret genomic data is lagging behind,' cautions Fisher. 'Each human individual carries a great many DNA variations, most of which are benign; the big challenge in the future is to figure out which variants are functionally important.' These issues become even more pertinent as the researchers broaden their focus beyond disorders to consider natural variations in language performance in the general population. 'We also aim to extend our work to cases of exceptional skills, such as those of simultaneous translators and people who quickly become fluent in numerous languages.'

Simon E. Fisher

Peering into the black box

Simon Fisher's department is not only interested in identifying genomic variants. 'There's a vast gap between DNA on the one hand and features of behaviour and cognition on the other. Speech and language are defining features of the human condition – a fundamental part of what makes us human. Yet, we still know very little about how the genome is able to build a language-ready brain and why even our closest primate 'cousins' appear unable to match human capabilities in this area.' Prof. Fisher believes that genes FOXP2 provide unprecedented opportunities to look into the black box and shed light on the biological machinery that supports speech and language. Researchers in the department analyse the relationship between gene variants and function at multiple levels: in human neuron-like cells grown in the laboratory, in neural circuitry from animal models carrying gene disruptions, all the way to human brain structures and functions. Prof. Fisher was one of the initiators, together with Professors Barbara Franke, Peter Hagoort and colleagues who work in the Nijmegen Cognomics programme, which links the advent of personalised genomics to state-of-the-art brain imaging and other cutting-edge techniques used by modern neuroscientists in studies that include thousands of people.

A Darwinian view

Researchers working on another research line in the department ask how language-related genes have changed in the course of evolution and how variants of such genes spread around the world. 'Again, FOXP2 has proved to be pretty interesting,' he says. 'It's been around for a long time and is in fact one of the oldest genes, which is found in all vertebrates as far as we know. Some years ago – together with Professor Svante Pääbo's team at the Max Planck Institute for Evolutionary Anthropology in Leipzig – we compared FOXP2 in humans to versions found in other primates. Curiously, there was evidence that the gene underwent accelerated change in the line that led to humans, after splitting from chimpanzees, which suggests its functions might have been tweaked during human evolution.' Studies in animal models implicate the gene in motor-skill learning and auditory-motor associations. So Simon Fisher thinks that any role that FOXP2 plays in language must have been built on ancient evolutionary functions such as these. 'It's a Darwinian view of the emergence of language,' he says.

Myrna Tinbergen

The power of 3 Tesla

The new 3 Tesla scanner, which was recently installed at the Donders Institute, enables researchers to do more and better research. Not only do they have an additional machine to use, they can also work faster and more precisely by using it.

To have a scanner is one thing, but to know what you can do with it's another, says David Norris (Professor of MR Physics in relation to applications in cognitive neuroscience, at the Donders Institute). He and his team are developing techniques to enable researchers to get more benefit from the technical potential of a 3T scanner.

The 7T, the extremely expensive crown jewel of scanners, gives better spatial resolution and higher sensitivity than its little brother, the 3T. But generating data on the 7T takes more time. The Donders Institute publishes around 100 articles based on fMRI research every year, says Norris. "So reducing the time spent on research is important." And it has been reduced.

It's now possible to make a three-dimensional image of a brain three times faster than was previously possible. Thanks to that increased speed, researchers can easily filter interference from the data. Norris explains it this way: "If people wriggle in the scanner, the signals that this produces are so different from the pattern you're looking for that you can collect them quite clearly. But breathing and the heartbeat are more difficult to identify. The higher speed means not only that more data can be gathered – the measurements are also more precise. The faster you go, the cleaner the signal."

That's important, especially in resting state research, he says. This is the study of spontaneous correlations between areas of the brain where there is no task-related brain activity. Norris: "In a resting state, there is no a priori way of avoiding physiological noise. But if you make your observation very quickly, you can remove a lot of noise at the source. Thanks to these multiband techniques, which are also being used in the Human Connectome project in the US, we get a better picture of spontaneous activity in the brain." And there's another important consideration: "For a 7T scanner, you need four times as much high-frequency power to do the same experiment."

In the multiband technique, different areas of the brain are scanned at the same time. The technique can be combined with a multi-echo technique, which improves the sensitivity and further enhances the separation of physiological noise from the real signal.

New techniques make it possible to study the cortical layers of the brain on the 3T scanner as well. "It's often thought that this is only possible with a 7T, but we have developed techniques to make it possible with a 3T," says Norris. The cortex consists of six different layers, which together are between 2.5 and 3 millimetres thick. Norris: "Cognitive brain research is no longer about which areas of the brain are active, but about the relationship between them, about the network activity. Particular small areas are activated simultaneously and work together. Some cortical layers are mainly processing input, while others mainly produce output. If you can differentiate the various layers in the network, you can see what the information is indicating and better understand how the network functions."

Norris wants to make tools that researchers can easily use. "These should become standard methods. I'm not so much interested in a proof of principle, of the sort you often find in the literature. You should be able to use them in your work." Twenty-five research groups are now using the methods developed at the Donders Institute.

"The potential of MRI is virtually unlimited," says Norris. "In future the techniques will be even faster and they'll provide even higher resolution. It will be possible to examine not only the cortical layers, but also the cortical columns in the brain." The final goal is to be able to make scientifically valid statements at an individual level.

Norris: "We've been doing fMRI research for twenty years now. It's almost always about the averages in a group. Psychiatric and neurological diseases demand a new approach based on individual medicine and very high-resolution imaging. It's very difficult territory, but that's what we're committed to achieving."

Malou van Hintum

FieldTrip: Donders goes global

In addition to developing imaging tools, the Donders Institute is also working hard on data analysis tools. Senior researcher Robert Oostenveld and his team travel all over the world to explain the MEG/EEG software they've developed to users. This year they will go to Toronto, Birmingham, San Sebastian and Tuebingen, and that's just for a start.

The basis for the FieldTrip software was laid in 2003 because analysing of MEG data started then. The researchers combined two techniques: multitaper spectral analysis and beamformer source reconstruction. Oostenveld: "We found a way to reliably localise very small oscillatory activity. In 2006 we were the first to show that you can measure gamma waves with an MEG system. Until then there were serious doubts that this could be done. Now people around the world have replicated that research and everyone is taking it further."

Oostenveld develops the software by coming up with a methodical solution for an experimental problem. So he doesn't write a dry methodological paper. This has the disadvantage that you can't study everything in detail, but the advantage that the results can be published in journals such as Science, Neuron and the Journal of Neuroscience, he says. "By linking the method to the application, its value is much higher."

Toolkit courses have been given in Nijmegen for the past ten years now. "Because there was a lot of demand, we started to organise workshops outside the Donders Institute as well," says Oostenveld. "We are developing FieldTrip as an open source project. We want to create a community that will encourage people at the Donders Institute and internationally to contribute their expertise. When I have to explain the FieldTrip project to researchers who want to apply it elsewhere, for example in their own institute, I always say: it consists of the software, the documentation that's been developed over the years, and especially of the expertise in the user group. So the project comprises three aspects: two in the computer, and the third in the heads of the users. That's the working method that we use. It reflects how we work together in the Donders Institute: in interdisciplinary teams in which people contribute and share their expertise."

Radboud University Professors Charles de Weert (l) and Peter de Vooijs (r) played an important role in the foundation of the Donders Institute for Brain, Cognition and Behaviour ten years ago. On 2 April 2013 they had the honour of opening the new 3 Tesla scanner. This t[illegible]RI scanner in Nijmegen (Donders co-owns a fourth MRI scanner, a7 Tesla stationed in Essen), will help shorten the waiting list for researchers, and will provide improved image quality.

Put this date in your diary:

Donders lecture 5 September 2013: Anthony D. Wagner

The cognitive neuroscience of remembering

Anthony Wagner combines meticulous experimental design with theoretical depth. I really look forward to meeting him in September,' says Christian Döller after serving giving me a strong espresso in his office at the Donders Institute. Three white boards are totally covered in scribbles – full from edge to edge as silent witnesses of lively research discussions. 'He's one of the big players in the field of memory research and cognitive neuroscience.'

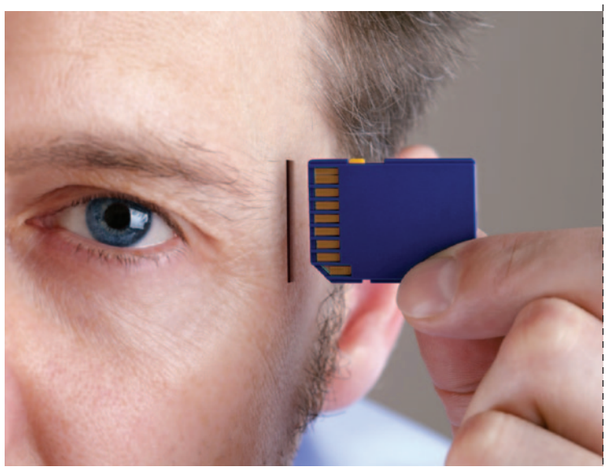
Christian Döller has met Wagner a couple of times at international conferences and always enjoyed the interesting discussions he had with him. 'Wagner pioneered the study of human memory using fMRI. He was the first to demonstrate that activity during the encoding of new experiences hippocampus – a brain structure in the medial temporal lobe – predicts whether participants later remember or forget these episodes.'

Christian Döller heads up the 'Memory and Space' research group at the Donders Institute, which cooperates with the Faculty of Science.Like Wagner he investigates the brain systems which support the transformation of experience into enduring episodic memories and how these networks help us to map and navigate our way through our surroundings.

'A lot of our knowledge about the hippocampus comes from single-cell studies in freely moving rodents. So-called place cells in the hippocampus – in concert with other spatially-tuned cells – provide an internal map of our world, rather like having a satnav in your head or like dots highlights on a tourist map that you use when planning a holiday.'

'At the Donders Institute we combine functional neuroimaging with virtual reality (VR) techniques. Our participants navigate virtual worlds when they are inside the brain scanner. In this way, we are able to link the cellular and systems levels, which we hope will enable us to see how spatial memory (where you were) and episodic memory (what you did) fit together.'

'In his lecture Anthony Wagner will discuss the cognitive neuroscience of remembering. Understanding how the brain recalls episodes and describing the type of information we remember will help us unravel how memories are stored in the brain. In particular, how do neural processes and decisions made in the brain influence access to stored information? And how do these mechanisms interact with memory formation, which is guided by the hippocampus? Novelty might be an important factor. Next year you will probably remember David Norris dropping in during our conversation, even though this event wasn't at all relevant to this article.'



Donders lecture 5 September: Anthony D. Wagner, PhD

Professor of Psychology and Neuroscience and Co-Director of the Cognitive and Neurobiological Imaging Center at Stanford University.

Location: on the campus of Radboud University Nijmegen in the Linnaeus Building, Heyendaalseweg 137, starting at 16:00 on Thursday 5 September.

Meanwhile at www.ru.nl/donders

Go to our website to review the latest news and events.

Rubicon grant
Dr Marlieke van Kesteren has received a Rubicon grant from the Netherlands Organisation for Scientific Research (NWO) for her project entitled 'How schemas influence new learning: Different mechanisms, distinct memories?' The Rubicon programme allows recently graduated researchers to gain valuable research experience at a leading institute abroad. Van Kesteren will study the influence of schemas (prior knowledge) on learning at the Department of Psychology at Stanford University.

Successful Breinfest in local theatre
Breinfest was the festive culmination of BrainGain, the Dutch research consortium consisting of researchers, companies and potential users of brain-computer and computer-brain interfaces (BCI). On Tuesday March 19, the Lindenberg theatre in Nijmegen was filled with almost 400 guests, who attended brain-related talks given by experts on neuroscience and BCI, demonstrations and theatrical performances. Visitors included young and old, experts and the general public.

10th anniversary of MSc programme Cognitive Neuroscience
In August, the Research Master's programme in Cognitive Neuroscience, which is offered by the Donders Graduate School for Cognitive Neuroscience, will celebrate have its 10-year anniversary. To mark this milestone, students and alumni joined forces to organize a one-day symposium and Summer Ball. The symposium took place on May 29. Students and renowned researchers engaged in cognitive neuroscience presented their work in oral and poster presentations.

Vici grants
The NWO's prestigious Vici grants were awarded to Barbara Franke, Professor of Molecular Psychiatry and Principal Investigator at the Donders Institute, and Karin Roelofs, Professor of Experimental Psychopathology at the Behavioural Science Institute and research fellow at the Donders Institute. Prof. Franke will use the €1.5 million grant to study the biological causes of ADHD by combining genetic research, MRI studies of the brain and genetic research on fruit flies. Prof. Roelofs will use the grant to identify neurobiological vulnerability markers for the development of posttraumatic stress symptoms in young police recruits.

Human Brain Project receives €1 billion
The Human Brain Project was selected by the European Commission as one of two FET Flagship projects. Researchers working on this project will use the grant (which is worth a billion euros) to address one of the greatest challenges of modern science: understanding the human brain. Central to the project is the development of ICT platforms for Neuroinformatics and brain simulation as well as supercomputing, which will make it possible to collate neuroscience data from all over the world, integrate the data in unifying models and simulations of the brain, check the models against data from biology, and make them available to the scientific community. The ultimate goal is to allow neuroscientists to connect the dots leading from genes, molecules and cells to human cognition and behaviour. The Human Brain Project, which is planned to last ten years (from 2013 to 2023), will bring together researchers from over 80 European, North American and Asian research institutions. Peter Hagoort and Paul Tiesinga, directors at the Donders Institute, will contribute to this European project. Prof. Hagoort will focus on cognitive neuroscience, while Prof. Tiesinga will work on neuroinformatics. Paul Tiesinga: 'We're going to describe the connections in the brain. This is a gigantic effort: the human brain contains a hundred billion neurons, each of which can be connected to ten thousand others. So far there is no computer that can handle this amount of data. We will start putting together existing brain data to make statistical models of this connectivity.'

OUT OF OFFICE

text

Diary

5 September 2013, 4pm **Donders Lecture by Anthony Wagner** (Stanford University) *Radboud University Nijmegen, Linnaeus Building, Heyendaalseweg 137, Nijmegen*

12 September 2013, 3.45 pm **Inaugural Lecture Asif Majid** *Radboud University Nijmegen, Aula, Comeniuslaan 2, Nijmegen*

26 September 2013, 3.45 pm **Inaugural Lecture Simon Fisher** *Radboud University Nijmegen, Aula, Comeniuslaan 2, Nijmegen*

3 October 2013, 4 pm, **Donders Lecture by Susan Gathercole** (MRC Cognition and Brain Science Unit, Cambridge, UK) *Radboud University Nijmegen, Linnaeus Building, Heyendaalseweg 137, Nijmegen*

28 November 2013, 4 pm, **Donders Lecture by Rainer Goebel** (University of Maastricht) *Radboud University Nijmegen, Linnaeus Building, Heyendaalseweg 137, Nijmegen*

PhD defences

4 february 2013 Böckler, A. Looking at the world together. How others' attentional relations to jointly attended scenes shape cognitive processing. (Dondersseries 115)

7 february 2013 Tesink, C.M.J.Y. Neurobiological [illegible]ts into language comprehension in autism: context matters. (Dondersseries 114)

25 april 2013 Volman, I. The neural and endocrine regulation of emotional [illegible]s. (Dondersseries 117)

15 May 2013 Buchholz, V. Oscillatory activity in tactile remapping. (Dondersseries 118)

17 May van Dongen, E.V. Sleeping to Remember. On the neural and behavioral mechanisms of sleep-dependent memory consolidation. (Dondersseries 116)

11 June 2013 Van Deurzen, P.A.M. Information processing and depressive symptoms in healthy adolescents. (Dondersseries 119)

20 August Whitmarsh, S. Nonreactivity and Metacognition in Mindfulness. (Dondersseries 120)

20 August Vesper, C. Acting Together: Mechanisms of Intentional Coordination(Dondersseries 121)

22 August Eskenazi, T.T. You, Us & Them: From motor simulation to ascribed shared intentionality in social perception (Dondersseries 123)

11 september 2013 Lagro, J. Cardiovascular and cerebovascular physiological measurements in clinical practice and prognostics in geriatric patients. (Dondersseries 122)

Donders Institute Newsletter

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Photography: Donders Institute, Bert Beelen

Graphic design and layout: Hartebeest (www.hartebeest.nl)

Priniting: JP Offset, Duiven

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