



The Maastricht Brain Imaging Center is located on the Southern campus of the city's university.

"We Will Increasingly Come to Understand the Mind in Biological Terms"

Using ultra-high field magnetic resonance imaging systems, which are currently under investigation at just a few centers in the world, cognitive neuroscientist Professor Rainer Goebel examines the functional microstructure of the cerebral cortex at Maastricht University – and hopes to decode essential mental processes. Professor Goebel explains how the image of the healthy human brain as well as the knowledge, diagnosis, and treatment of many neuropsychiatric illnesses could change in the next few years.

Text: Martin Lindner
Photos: Thomas Steuer



Professor Goebel, you began your scientific career studying psychology. How does a psychologist end up doing brain research with an MRI scanner?

Professor Goebel: I have always wanted to understand how our minds and our brains are interrelated. How do emotions, memories, and perceptions develop? These are the basic questions of psychology, but no one could offer me any good answers when I was in school. It was only since the 1990s, with the development of functional magnetic resonance imaging (fMRI), that we've been able to measure brain activity and study mental processes with a live and ▶

Right: Neurocognitive research is one pillar of Prof. Goebel's work – passing his knowledge onto his students is the other.



About Rainer Goebel

Rainer Goebel, PhD, is a German-born professor for Cognitive Neuroscience at Maastricht University in the Netherlands and is the founding director of the Maastricht Brain Imaging Center. After his studies in Psychology and Computer Science, he became a fellow at the Max Planck Institute for Brain Research in Frankfurt, Germany. Since the mid 1990s, he has continued to develop "BrainVoyager," an internationally esteemed software tool for the analysis and visualization of functional neuroimaging data. Besides his position at Maastricht University, Dr. Goebel is team leader of the "Neuroimaging and Neuromodeling" group at the Netherlands Institute for Neuroscience in Amsterdam. In 2014, he was selected as a member of the Royal Netherlands Academy of Arts and Sciences.

completely non-invasive method using the scanner. And, it's something that has fascinated me ever since.

Have you ever gone through the scanner yourself?

Professor Goebel: Hundreds of times.

What is it like to look inside your own skull?

Professor Goebel: I was nervous the very first time. Would they discover a small tumor? Was something not right? Now that I know everything is normal, I enjoy looking at my brain.

Do the images arouse a feeling of grandeur?

Professor Goebel: Absolutely, I have a great deal of respect – along with the desire to see even more detail, because, initially, the fMRI scans were somewhat disappointing. For example, you want to know how feelings are represented in the brain – and then you see a few colored spots in the images that merely show that the emotional centers are active, but not whether I am sad or happy. Or you see that the language center is active, but not what words are being spoken.

And those are the kind of details you now want to identify?

Professor Goebel: That is one of the main objectives. The current MRI scanners that work with magnetic-field strengths of 1.5-tesla or 3 tesla

have achieved a spatial resolution of two to three millimeters. In our Brain Imaging Center, we now also have two ultra high-field scanners with magnetic-field strengths of 7¹ and 9.4¹ tesla. Simply put, you get a strong image signal with higher field strengths. You can zoom deep into the brain and measure activity in areas that are tiny. Only few have ever seen brain images like the ones we're getting with our ultra-high field scanners.

Do you expect a qualitative leap in research?

Professor Goebel: Yes, we are profiting from a lucky fluke of nature. The cerebral cortex has characteristic functional units called the cortical columns. These modules contain approximately 10,000 nerve cells that all do the same thing – for instance, they react the same way to a certain sensory input. This represents a kind of redundancy principle in the brain. We are familiar with the column architecture, particularly in the perceptive areas of the cortex², but there are probably comparable functional modules in most – if not all – areas of the brain. The main point is now that with the new ultra high-field scanners we may not be able to detect the activity of individual neurons, but we can detect individual functional modules since they are in a detectable range of the scanner. This means, for the first time, we might be able to improve our understanding ►



Train your Brain

Patients can learn to control their own brain activity using real-time signals from a 3-tesla brain scanner. This neuro feedback opens up new ways of treating, for example, chronic pain, Parkinson's, strokes, or depression.

When around 150 internationally recognized experts in neuronal imaging met in Zurich, Switzerland, in February 2012, it marked a milestone in the development of an emerging therapeutic discipline: brain-scan-based neuro feedback. Back then, the scientists discussed – at the first-ever international conference on the subject – the state and prospects of the methods in which patients learn to control their brain activity.³

The principle involved is simple: While lying in a magnetic resonance imaging (MRI) scanner, the patient views a monitor that shows in real time how active a certain area of the brain is, for example, an activity “thermometer.” Just as it is possible in other forms of bio feedback to control one’s heartbeat and blood pressure, the patient learns to decrease or increase brain activity in the respective region using various mental tasks and imagery – and can immediately see the success of their efforts in the scanner signals. Special software analyzes and visualizes the scanner data.

The idea of neuro feedback is not new. Neuro feedback based on electrical brain activity measurements (EEG) has been used for a long time, for example, to train people with epilepsy to suppress their seizures or to mitigate an attention deficit hyperactivity disorder (ADHD). However, the scanner-based process permits

a deeper look into the brain and a much more precise analysis of activity patterns, which expands the spectrum of potentially treatable illnesses. Neuro feedback training is typically performed in several sessions in MRI machines with a field strength of 3-tesla.

The innovative approach has been developed over the past decade by a relatively small number of international specialists – including Rainer Goebel, who conducted basic research on scanner-based neuro feedback in close cooperation with German neuro researchers Niels Birbaumer and Nikolaus Weiskopf. Interest in the method has since grown considerably. Pilot studies by various teams show that self-regulation of brain activity can alleviate chronic pain, reduce motor deficits in Parkinson’s disease, or even improve rehabilitation after a stroke.⁴

The results in patients with depression are especially promising. A Phase I randomized clinical trial, which examines the benefits of scanner-based neuro feedback in regulating the emotional centers of the brain, is almost finished.⁵ There are more clinical trials on other diseases to follow as part of “BrainTrain,” an international collaborative research project supported by the European Commission.⁶

³ Sulzer J, Haller S, Scharnowski F, Weiskopf N, Birbaumer N, et al. (2013). Real-time fMRI neurofeedback: progress and challenges. *Neuroimage* 76:386-99

⁴ Weiskopf N (2012). Real-time fMRI and its application to neurofeedback. *Neuroimage* 62:682-692

⁵ <http://clinicaltrials.gov/show/NCT01544205> (accessed 19/10/2014)

⁶ www.braintrainproject.eu (accessed 19/10/2014)

of the code with which a sensory input is represented in the cortex.

Can you give us an example?

Professor Goebel: Take facial recognition. What we already suspect from current experiments is that specific facial features – such as the distance between the eyes, the hairline or the position of the eyes in relation to the mouth – are coded by the activity of individual cortical columns. The brain breaks down (so to speak) the sensory input at the columnar level into different aspects, into a distributed code. Based on a specific column pattern, it might be possible that the scanner has the ability to – in principle – discern whether you are looking at your partner's face or the German Chan-

cellor's face. It makes a detailed reading of the brain activity possible. Cortical column patterns probably also explain how the brain registers new faces and recognizes them again later.

Part of your research focuses on not just measuring these processes in the scanner, but also modeling them with a computer.


Professor Goebel: That's right. The models help us generate and test new hypotheses. We can simulate which macroscopic areas of the brain and neuronal networks would have to be active during a cognitive process, all the way to the level of the cortical columns. In the process, we also make up new, hypothetical ►

Risks and Limitations of Ultra High-Field MRI

There are safety limitations when using ultra high-field MRI. These include higher power radiofrequency pulses and the potential for tissue heating or coil burns, stimulation effects from stronger, faster-switching gradients and moving within a higher magnetic field and, most prominently, the potential dangers associated with the main magnetic field, such as ferromagnetic projectiles in the scan room and effects on implanted medical devices. As of 2003, the U.S. Food and Drug Administration specified the criteria for significant risk in humans from the main field to be 8-tesla for adults and infants older than one month and 4-tesla for neonates.

7T MRI is labeled as an investigative device and cannot be used for clinical diagnosis. Instead it can be used for clinical research under the approval of an institutional review board and with informed consent.¹



A man with grey hair and a goatee, wearing a dark suit, light blue shirt, and striped tie, stands next to a Siemens MRI machine. He is smiling slightly and looking towards the camera. The MRI machine is white and has a large circular opening. The background is a plain, light-colored wall.

*“The great
hope is to
achieve indi-
vidualized
treatments.”*

Rainer Goebel, PhD,
Professor of Cognitive Neuroscience,
Maastricht University, The Netherlands



columns, for example, because we assume that the brain interprets two vertically stacked lines coded in V1 as the letter “T” in a higher visual area and this is coded in its own cortex column. We then have to compare these models with actual data measured in the scanner in order to correct and further develop them. This is a lengthy process that will take years, but could further the field of neuroscience and eventually medicine enormously.

Are there already tangible effects?

Professor Goebel: One example we’re currently working on is reading disabilities in children, also known as dyslexia. Thanks to the improved scanner resolutions, we hope to determine why and where letters are mixed up in the cortex through incorrectly coded column patterns and what kind

of training can best influence this – in other words, how the brain’s plasticity can be used for treatment. But we also expect significant advances in our understanding of depression or schizophrenia.

In what way?

Professor Goebel: Today it is really clear that there is not just one form of schizophrenia or one form of depression. Using genetic data, for example from population studies, as well as using brain scan data, we hope to be able to define new subtypes within the next few years – in other words, get away from simply relegating them to one drawer and develop more refined disease concepts. We need to learn how to understand individual brains. For example, it is possible that different forms of depression can be clearly differenti-

ated from a neurobiological standpoint. The great hope is to make disease diagnoses more multifaceted and to achieve better adapted, more individualized treatments through more detailed imaging.

Are there similar perspectives for neurodegenerative diseases such as Alzheimer’s?

Professor Goebel: With Alzheimer’s, we believe that it will at least be possible to make an impactful assessment – because the ultra-high field scanners will probably be able to detect signs of degeneration in the fiber connections of the brain. The high scanner resolution can also help with Parkinson’s when, for example, a patient is supposed to receive what’s called a “brain pacemaker” and precise neurosurgical planning is required for the surgery. However, the advantages of imaging

Left: At the Faculty of Psychology and Neuroscience, international research teams are working together to better understand the human brain.

for treatment do not depend only on a maximum image resolution, but also on the possibility of having scanners that are integrated into new treatment concepts. For instance, for many years we have been examining the possibility of targeted neuro feedback with a 3-tesla scanner in which patients can learn to control the activity levels of individual areas in the brain using signals from the scanner (see box on page 9 entitled “Train your Brain”). This opens up completely new treatment paths for a wide range of illnesses, such as phobias or depression.

Do the modern images of the brain also change how we see ourselves?

Professor Goebel: We hope, in ten years, people may say: “Doctors determined in a brain scan that my left

amygdala in the limbic system is overstimulated. That’s why I am going to neuro feedback therapy to be less afraid of spiders.” Overall, how mental processes work in detail may be much better understood and might even be included in textbooks. We may learn to talk much more concretely and realistically about our brain and ourselves. We will increasingly come to understand the mind in biological terms.

Are we losing our mystique due to fMRI?

Professor Goebel: No, because the images do not provide information about the subjective experience, the experience of our own consciousness. The I-perspective remains a mystery, even for us. ■

Dr. Martin Lindner is an award-winning science writer based in Berlin, Germany. After his medical studies and a doctoral thesis in the history of medicine, he went into journalism. His articles have appeared in many major German and Swiss newspapers and magazines.

¹ MAGNETOM 7T and 9.4 T are ongoing research. All data shown are acquired using a non-commercial system under institutional review board permission. MAGNETOM 7T and 9.4T are still under development and not commercially available yet. Their future availability cannot be ensured.

² http://www.nobelprize.org/nobel_prizes/medicine/laureates/1981/press.html

The outcomes achieved by the Siemens customers described herein were achieved in the customer’s unique setting. Since there is no “typical” hospital and many variables exist (e.g., hospital size, case mix, level of IT adoption), there can be no guarantee that others will achieve the same results.

Brains Unlimited

An interdisciplinary platform for neuro researchers, clinicians, and entrepreneurs

Brains Unlimited is housed in a brand-new building complex close to Maastricht University Medical Center, near the historical center of the Dutch city. It is a center for the interdisciplinary exchange of ideas for neuro researchers, clinicians, and entrepreneurs. The platform, which was officially opened by the Dutch king in 2013 and is supported by Maastricht University and financed by the European Union, among others, will help scientists and companies discover fundamentally new insights into diseases such as Alzheimer’s, Parkinson’s, or multiple sclerosis to hopefully make them clinically and commercially viable.

The key to the project is an ultramodern scanner lab that is equipped with three Siemens MRI scanners with high and ultra-high magnetic field strengths. Only a few centers around the world currently have such powerful equipment. Scientists from the Department of Psychology and Neuroscience at Maastricht University work closely with the imaging unit. *Brains Unlimited* also has a business start-up center that helps companies develop scientific business models.

Brains Unlimited originated from an initiative of the Maastricht Brain Imaging Center under the leadership of Professor Rainer Goebel, PhD. Since then, the project team, who works closely with the Center of Magnetic Resonance Research in Minneapolis, USA, the Jülich Research Center in Germany, and Siemens Healthcare, has built up a network with many national and international research groups. For more information, please visit www.brains-unlimited.nl.

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