Interview with Ronald Boellaard

Recently, the Department of Nuclear Medicine and Molecular Imaging was pleased to welcome a great new addition to the team: Prof. Dr. Ronald Boellaard. His research focuses on quantitative analysis of Positron Emission Tomography (PET) imaging, image reconstruction and processing. He has obtained several grants and is a member of a number of international societies and committees. He is also the principal author of the Netherlands and the European guidelines for standardization and harmonization of FDG-PET and PET-CT studies.

As a PhD student from the same department, I am having the opportunity to work under his supervision, and now I will also have the pleasure of sharing with you an overview of the reach of his research and the importance of his work:

Since no one knows your career better than yourself, could you give us your version of a short professional introduction to your career so far?
I will try to do it in a nutshell. My name is Ronald Boellaard and my career started with a Masters in both Biology and Physics at the University of Amsterdam. After that, I started as a PhD student in the Radiotherapy Department at the Netherlands Cancer Institute, working on a topic related to medical imaging. My PhD project was on portal imaging, a technique that basically measures the transmission of radiation through a patient during the radiotherapy treatment. Those images were primarily used to determine the correct positioning of a patient relative to the treatment beam, but in my project I also used them to verify the right radiation dose delivered to patients.

Once I finished my PhD, I moved to the VU University Medical Center (VUMC) in Amsterdam and started my training to become a Clinical Physicist. Later on in the training, I became more and more involved with research (although I still had some clinical duties) and, in particular, with quantitative molecular (PET) imaging.

What attracted you to join the Nuclear Medicine team in Groningen?
Including the time I spent on my training to become a Clinical Physicist, I have worked in the VUMC for 17 years. I thought it would be good to see how things are done elsewhere, as well as get exposed to a new environment and get some new inspiration, to learn new faces and a different research group.

Besides VUMC Amsterdam, UMCG Groningen is one of the few centers in the country with a very good infrastructure for Nuclear Medicine and, in particular, for PET imaging. There is new instrumentation here, a relatively young team, a strong preclinical imaging section, and an excellent chemistry team.
and laboratories – all of these characteristics made Groningen an interesting place for me to go to. I believe this is the place where I can perform the same research and/or expand it compared to what I have done in Amsterdam.

**What exactly is the research you do at the Nuclear Medicine department? And what do you think is the most exciting part of what you do?**

My line of research is in quantitative PET imaging, partly focused on data analysis (such as kinetic modeling, quantification and validation of radiotracers and/or imaging biomarkers) and also partly on acquisition and image reconstruction (i.e., how the data are generated and how that would affect image quality). Last, but not least, I also perform research on hybrid imaging (the combination of PET/MR or other datasets) and how to use both types of imaging to support image reconstruction as well as combined or multiparametric data analysis. Basically, it is all about quantification and validation of imaging biomarkers, making sure we can properly use them. What I like most about my research is that it is a nice mixture between biology and physics. This is no surprise: I did study both and that was because I always had an interest in working with more applied physics with a link to biology or medicine.

The link to the clinic is also something I enjoy. Although I do like to do “fancy things” for academic research, I enjoy doing things that are a little bit more simple from a technical or mathematical perspective but can be more easily translated to the clinic. In fact, kinetic modeling studies (the “fancy things”) are often complicated, but they can help in finding an optimal and simple way of data collection or analysis. We often look into simple methods that can be used as alternatives for full quantification but are practical enough to be applied to larger patient datasets and in the clinic.

**Although PET is mainly known for its application in oncology, your work is certainly also related to brain imaging. Most of the BCN community makes use of other imaging techniques, such as fMRI and EEG. What do you think is the added value of PET for studying the brain? Can you give an example?**

I believe there are a lot of opportunities in PET brain imaging, mainly in studying neuroreceptors and metabolism. Brain PET imaging can provide opportunities for a more precise differential diagnosis, for example, in dementia. Here in Groningen, for instance, there is a project called GLIMPS, of which I am a part of despite it having started before my arrival. It is a project based on [18F]-FDG brain studies, and it uses the metabolic pattern of [18F]-FDG in the brain to support differential diagnosis for patients with Parkinson’s Disease. But, the same methodology could be used in neurodegenerative diseases such as Alzheimer’s Disease. The study and diagnosis of those diseases also profit from other types of tracers, such as the ones that can image amyloid or tau deposition. There are many other tracers developed here in Groningen (most of them in a pre-clinical stage) that can be used to study the pathophysiology of diseases. With those, we can gain more understanding on which processes go on in a diseased state.

Imaging of the brain with PET also has a lot of room to grow and assist in drug development. With PET, we can study and directly measure whether a drug interacts with the target of interest. It is also possible to explore the target occupancy as a function of the administered dose, which gives us insight in optimal dosing or administration schedules in order to achieve the necessary occupancy of a receptor or target over time. Therefore, such brain PET studies can be helpful to speed up the development of new drugs, taking a drug to either Phase II or Phase III studies more quickly.

**As I understand, you are also well known for your work towards standardization and harmonization of imaging protocols and data analysis in PET. Could you briefly tell us what is that work about and why it is important?**

The most important aspect of this is making PET measurements repeatable and reproducible. Repeatable means that you can replicate the data yourself, and reproducible means it can be replicated by others, in other institutes and with other systems. Personally, I think that precision (which is repeatability and reproducibility) is at least as important as accuracy. That is because if you are not able to generate your data in a reproducible way, then it is basically useless.

Working towards standardization is important for the translation of the academic research to clinical practice. The developed techniques and the way you collect data in research must be replicated elsewhere, which means you have to develop imaging procedures and scanner calibration methods such that data becomes as comparable and exchangeable as possible. This is where standardization and harmonization enters: we really focus on making data comparable between different studies and imaging sites, such that it can be reused and pooled and finally used clinically.

Standardization and harmonization are also very important for the clinical use of PET, especially if you derive criteria (quantitative or visual) for patient classification or response assessment. For example, if a
center defines that the tracer uptake needs to exceed a certain value or threshold in order to determine malignancy or whether a brain is affected, it only makes sense to use that value if the way you collect your data is consistent with the way those criteria were established. This also means that if, for some reason, we have a higher/lower performance system or differences in image quality than the one used to define the criteria, our numbers will be different and those criteria become meaningless.

**For some people, such a line of research is still very distant from society. You now just mentioned the importance of translating academic work to practical clinical use. What else do you believe is the impact your work can have in society?**

Some of the impact of the developments in PET is more indirect. For example, we increasingly see pharmaceutical companies showing interest in research with PET imaging. Together with them, we are evaluating and developing more specifically targeted drugs. In PET, we can label these drugs with a radioisotope and directly evaluate their kinetics because we make them visible in the body. In that way, we can see where the drug goes to and whether the uptake in a tumor is high enough, but we can also explore in much more detail how the kinetics of a drug change as a function of drug dose. In fact, we will set up here in Groningen a Molecular Image Core Lab. This lab will assist pharmaceutical companies in performing PET imaging research for the evaluation of new drugs. Eventually, some of those new drugs will become available and patients will benefit from such developments.

There is also a strong emphasis on what we call precision medicine. We are moving towards precisely identifying which patients have a reasonable chance to benefit from a certain treatment and/or which patients will not benefit from these treatments. One of the easy examples of that scenario would be developing a radiotracer that can identify the presence of a target for a specific drug, for instance a receptor expressed in a tumor. In addition, we can determine if those targets are indeed accessible by the drug and which amount of mass/dose needs to be administered in order to reach a sufficient level of drug uptake to become effective.

New radiotracers and new methods for the evaluation and analysis of PET images can always assist in patient diagnosis, making it more precise, and thereby also tailoring or managing patient treatment. Even further, the knowledge we gain in the pathophysiology of diseases can subsequently help in identifying treatment targets, and I think PET is also useful in that direction.

**Last, but not least, I would like to be able to better connect young and senior researchers. Often PhD students see their professors and supervisors as perfect researchers whose careers are only a series of achievements and successes. To counteract this feeling, there has been a current trend for senior researchers to share their so-called “CV of failures”. What do you think about this and could you maybe share a story of a “failure” of yours?**

To some extent, I think a career is partly built on your own achievements, but also partly determined by luck or chance. After my PhD, I just happened to be able to become part of a group that was being started in Amsterdam. This meant I was able to grow with the group, and I also had some very good mentors and scientists there who helped me to get a career. It is also true that with time and experience, everything becomes easier. Once you have written five papers, the next one will not require as much from you – you will have learned how to better structure and communicate your ideas.

About the failures, of course I made some, but I actually needed to think about it. (I try not to dwell for too long on failures.) Naturally, I did have some applications that were not awarded (or even not selected to be submitted), but I believe that is part of the game. I don’t see that necessarily as a failure, and you can certainly learn from it. But, like everyone, I also made some scientific failures in the beginning. For example, when I started working with image reconstruction, I implemented a method and used the wrong filters for it - actually, I probably have one abstract with data that is at least suboptimal (if not wrong). But these things happen when you are starting a new line of research, and you learn from those mistakes. Actually, the only way of not making mistakes is doing nothing at all, but that is not an option.

Also, I think it is important to notice that almost everybody (including myself) relied on a senior investigator during their early career. Everyone at that point builds on the success of somebody else – but that is part of the traineeship, and you should have some more experienced researchers around you to help you develop your own career.
Interview with a BCN board member:
Berry Kremer

You’re the Head of Neurology at UMCG. Was that something you wanted to do?
I became a professor in 1999 in Nijmegen, where I spent 15 happy years involved in patient care and research. Then around 2008 I was asked to fill the vacancy here at UMCG. At the time I was 52 and I thought to myself, “if there’s anything that I still want to do in my career, what is it?” Being a department head gave me the opportunity to implement some of my thoughts about how a neurology department should be run.

Were you able to achieve this?
To some extent, yes. Reality is always more difficult to change than you think.

How do you strike the right balance between your administrative function, the research, and being a practitioner?
That’s a difficult question. Of course, now I do less research and patient care, but I’m still very much involved in all three. One thing that helps is that clinical research is very connected to the patients you see, so basically this is where you get your inspiration from and where the scientific questions originate.

Your first publication was 28 years ago… what was that time in your life like?
As a PhD student, I got interested in Huntington’s disease, and I did research on its associated neuroendocrinological changes. Through that, I wanted to look at the neuropathology in the hypothalamus.

When I was almost finished, I got the opportunity to go to Vancouver in Canada to work in a group devoted solely to Huntington’s. It was a very stimulating environment and a time when people were hunting for the genes responsible for the disease. We were very close, but were ultimately outrun by an American-British team.

What’s the latest in the field?
One of the fundamental challenges is, of course, to find neuroprotection, a cure.

We have nothing that fundamentally delays the progression of the disease or stops it. And, that’s what everyone is looking for, though it’s much more difficult than anticipated. When the gene for Huntington’s disease was found in 1993, everybody thought that in 10-15 years we would have a cure based on the unraveling of the molecular mechanisms of neurodegeneration. It turned out not to be the case. The same can be said for other neurodegenerative diseases like Parkinson’s or Alzheimer’s. It’s very hard to find the right leverage point. None of them have a cure. It’s quite frustrating.

But, we do have effective symptomatic treatment. One of the major manifestations of Huntington’s is involuntary movements, and we have drugs that ameliorate the rate of them. Unfortunately, we’re unable to suppress the clumsiness and degeneration of fine motor skills. Another thing is mood changes, irritability, sometimes aggression – we are able to work on those. Also, physiotherapy is quite effective; speech therapy works quite well too.

> Everybody thought that in 10-15 years we would have a cure. <
You mentioned psychiatry, physiotherapy, and a couple others. Is this where the idea of BCN comes in?
Multidisciplinarity, yes, certainly. For our work on spinocerebellar ataxias, we’re currently collaborating with a number of experts, combining neuroimaging and other techniques.

Taking that idea even further, I saw a few science literacy videos on YouTube where you explain some controversial scientific issues. What was that project about?
Those videos in particular were about the difference between comatose and brain dead. They were made in association with the Dutch Transplantation Society.

I am really fascinated with the concept of brain death, because you can think about it from a biological perspective, but it also has very profound legal and ethical implications. What is a person? When are they dead? Is that when the heart irreversibly stops beating, or is it when the brain stops functioning? I think it is the brain that makes us who we are, what we are. If we don’t have a working brain, we stop being who we are. So, to me it’s perfectly acceptable to consider someone whose brain is irrevocably gone as dead. But, is that what other people think as well, and how can I convince them? How can this be translated into legislation?

Going back to the beginning, how can we establish that the whole brain is irreversibly gone? It’s quite an intricate issue.

To finish, I wanted to go back to mobility in academics… What advice would you have for the up and coming generation of scientists?
For me, going to Vancouver was a very stimulating, wonderful opportunity. One day, I still want to live and work in Australia. But, these decisions are never just about your career. It becomes a very practical issue when you have children, for example. Young scientists should take into account not just where they want their career to be, but also their personal life. Think broadly!

How do we know?
If somebody comes to the hospital in a coma but we see a structurally intact brain, we can’t say this person is brain dead. But, in somebody who suffered a severe accident or a hemorrhage that is impossible to treat, we know that this is an irreversible process. We also need to establish that there is no brain activity wherever it can be measured. By combining all these different kinds of evidence, we reach a level of specificity that warrants declaring the patient brain dead. In establishing the diagnosis, one should always err on the side of caution.

BY ALEXANDER PIETRUS-RAJMAN
PHOTO BY THE DUTCH TRANSPLANTATION SOCIETY
Fast on track: Interview with Dick de Waard

When I entered a well-structured office, containing a packed toga and traffic board on the wall, I knew I was at the right spot: an interview with a young professor in Traffic Psychology, Dick de Waard (1964). Throughout his career Dick has always been interested in traffic and applied research in this context. In the last 10 years, he also became very motivated to extend mobility of older adults. These interests provided him with experience in both the fundamental and applied fields of Traffic Psychology. Technological advancements to move safely by car or bike are expanding, but the applicability of these advancements in daily life still requires a lot of scientific insights from Traffic Psychology to be translated towards effective and safe interventions. Recently, Dick became a professor on ‘Traffic Psychology and the Retention of Mobility’ in the Department of Clinical and Developmental Neuropsychology of the faculty of Behavioural and Social Sciences of the University of Groningen (RUG), and on May 10th 2016, he gave his inaugural lecture. I talked to him about the opportunities and challenges that he experienced on his move towards professorship.

The road to professorship

Dick’s main research interest has been, and still is, the measurement of driver mental workload. It was also the topic of his PhD thesis (University of Groningen (RUG), 1996). Actually, he never specifically intended to write a PhD thesis, but he enjoyed working at the university, where a PhD was very useful if not required. After his PhD, Dick continued working as a research fellow at the RUG, combined with a brief freelance position at ITS Advies, a scientific research and consultancy company in the area of Intelligent Transport Systems (ITS), and part-time employment at the Faculty of Technology, Policy, and Management at Delft University of Technology. As a result of his growing knowledge and expertise on mobility, he began a Tenure Track position at the RUG in 2009. That position now resulted in his professorship. Dick really values working at the RUG and living in the northern Netherlands, because of, amongst other reasons, the nice colleagues and outstanding opportunities for collaborations.

Information processing in the real and virtual traffic environment

Drivers’ inadequate (either too low or too high) mental workload may lead to imperfect perception, insufficient attention and inadequate information processing. In the past years, Dick has been active in the applied fields of information processing in the traffic environment. Study topics have included the detection of impaired driving, behavioural effects of advanced driver assistance systems, and driver training. These studies were carried out in both real and virtual traffic environments, which allow for empirical and controlled behavioural observations. Empirical research requires flexible adaptations of the researcher to real life situations.

When observing behaviour, you cannot control weather conditions, where cars park, and how many individuals will pass your observation spot. Dealing with these uncertainties is what fascinates Dick; it’s one of the skills that he likes to pass on to students.

According to Dick, observing how car drivers behave ‘in the wild’ is just as important as studying their behaviour in a driving simulator to understanding driving behaviour. For example, Dick investigated mobile phone use while riding a bicycle. Whereas cyclists were mainly calling in 2008, he observed a shift towards screen operation such as texting in 2012. After the first observation, he also performed controlled experiments, such as having participants ride their own bicycle that had been instrumented with a GPS to measure speed while they performed tasks on a mobile phone. They had to type text messages or listen to music. The ethical
I enjoy working at the university and contributing to the retention of mobility through applied science.

Besides behavioural observations in real traffic environments, Dick investigates mental workload in a driving simulator using physiological measures such as brain activity and heart rate. A driving simulator is a suitable research environment to study mental workload because it’s safe, flexible, and allows for good control of specific traffic situations. One example of a task used in the driving simulator is the Gap Acceptance Task. Using this task, the researcher can investigate a driver’s perception of the gap sizes in a moving stream of traffic and the fine coordination mechanisms to synchronize the onset of movement with the approaching gap. Understanding how drivers decide that a gap is crossable, and how they time their crossing in relation to a moving stream of traffic, is critical for understanding how people make decisions on higher levels and the risks they accept. Studies of Brookhuis and De Waard using the Gap Acceptance Task have shown that after the use of the recreational drug MDMA (ecstasy), low-level control remained intact (people do not start swerving, for example). However, those drivers did accept smaller gaps, which reflects increased risk acceptance.

Besides studying the effects of drug use on driving performance, Dick also studies the mobility issues of older adults with and without mild cognitive impairment or dementia. Losing mobility has severe effects on people’s well-being, and very often people can retain mobility and drive safely, even with mild cognitive impairments (MCI). To evaluate fitness to drive, only an on-the-road test under supervision of a CBR driving examiner could be used in the past. Dick and his colleagues are now working on a battery of neuropsychological tests, in combination with heteroanamnesis and a ride in the simulator, to filter out those who do not need the on-the-road test, i.e. people who perform very well and very badly. A validation study showed that over 95% of the predictions of fitness to drive on the basis of test battery, heteroanamnesis, and simulator ride coincide with the outcome of the evaluation of the examiner of the on-the-road test that followed these tests.

Moving abroad – a requirement to become a professor?

Paradoxically for a professor of Traffic Psychology, Dick feels ‘moving abroad’ is a bit overrated with respect to its effect on academic promotion, in particular, if people do not see much more than the four walls of a lab while abroad. However, he values the advantage of international collaborations, for example in European projects. Working with experts from different countries in and outside Europe provides him with an extensive network. For example, Dick collaborates with researchers from JARI, Japan Automobile Research Institute. Together, they have performed studies on the accidents that are common in the rice fields: two cars on a collision course that can see each other but still collide because no motion is detected, as the angle of perception remains constant. In Japan this is a serious problem! They also considered solutions, first evaluated in the simulator and later on site: blocking the view at intervals in order to let vehicles “pop up”. This turned out to be a simple and effective solution. Notwithstanding ample difficulties in written and verbal communication, it is the mutual interest in Traffic Psychology that binds individuals from all over the world. Apart from international European projects, Dick has coordinated and contributed to national projects. For example, the Traffic Psychology staff works together and has close contacts with TNO Human Factors, NLR Dutch aerospace, Visio, and several engineering consultancies. Altogether, (inter)national collaborations, instead of working abroad for a longer period of time, provided Dick with relevant experience and expertise to become a professor.

The future of Traffic Psychology

Dick is most inspired by colleagues who are optimistic and possess the ability to look for opportunities. While moving along the academic ladder, it became more important to use these capabilities not only to develop himself, but also to guide a team of researchers and other collaborators towards a better understanding of drivers’ mental workload. Recently, a new master programme named ‘Traffic Psychology and Sustained Mobility’ was launched at the Faculty of Behavioural and Social Sciences, to make new students develop into experts in the applied and research field. In the Netherlands, this master programme is unique to the University of Groningen. As technology advances, real-life usage of technological advancement ultimately depends on the response of drivers. For this reason, understanding information processing in traffic environments is essential. We hope to hear more about the work of Dick de Waard soon.

Video Master: https://youtu.be/mzzfB79qxcw

BY HELEEN HOOGVEEN
The Wandering Mind

Last April, I could celebrate my second doctoral lustrum: on the 21st of that month, it was precisely ten years ago that I earned my title. Although, actually, because I studied in the era that preceded the Bachelor/Master system, I extended my pre-existing title to “dr. ir.”. It is not very likely that it will grow any further, as I find my life’s thread diverging further and further from academia. I used to be a fairly avid researcher, I tell myself, but I did not fall in love with the funding system that academics enjoy. I did a few post-docs here and abroad, but failing to cash in any of the lottery tickets that are handed out by the various agencies, and not being able to land a permanent position that was compatible with how I saw my future, I opted out. The above extensive lettering in front of my name still may prove useful in the context of job application letters, though.

I had almost overlooked that it was ten years ago that I had to defend my thesis. I had totally forgotten the anniversary, which almost seems like an academic birthday judging from the gravity of the occasion. The sole reason why I was able to announce it just in time on my Facebook timeline at eleven o’clock in the evening was because a perceptive aunt texted me to remind me of the after-party she had so much enjoyed. I graduated from Maastricht University, so immediately after the evening dinner “en petit comité”, I had booked a party-boat loaded with food and drinks. Thus, we navigated our way up the river Maas between 8pm and midnight, if I remember correctly. Not that I got much of a chance to enjoy the view. Those of you who have gone through the same ritual will have noticed that most of your time is spent shaking hands of guests when they arrive, attending a number of comedic presentations that highlight accomplishments that you wish to remember or forget, and then soon again shaking those same hands as they prepare for their way back home. I do have lots of fond memories though, and it is nice to let them pass by my mind’s eye as I write these sentences.

One of the reasons why the special meaning of the 21st of April had completely escaped me this time was the untimely death of Prince Rogers Nelson, i.e. His Royal Badness. Should you already have forgotten, he was of course better known succinctly as Prince, and is now more than ever deserving his self-endowed nickname “The Artist Formerly Known As Prince”. (I am still awaiting the addition of his symbol to the unmanageably growing list of emojis, which might even allow it to sneak it’s way into the Unicode registry.) I do not consider myself particularly attached to his music or style, but I do recognize his position as an influential innovator in music. Unfortunately, we seem to be losing quite a few of such idols this year, as the late David Bowie preceded him in January already (and we may optionally include Keith Emerson, who left behind Lake and Palmer last March). Invariably, these artists’ demises are commemorated by the radio playing their discography for an entire day. If not their genes survive, then surely their memes!

In science, we do not really have many idols, I would say. We respect scientists who have made their mark, but respect is rarely transformed into admiration, and – at least ideally – even the most respected scientist still has to provide evidence or a compelling argument for his or her ideas. Take sir Isaac Newton for instance, to whom I largely attribute perhaps the greatest intellectual framework in science: he also produced many works that would now be classified as occult studies, involving alchemy, Biblical interpretation, and Atlantis, among other things. And if that was too long ago for your taste, Watson and Crick, of DNA-fame, both entertained some pretty loony ideas that may be fun to read up on.

So, what is the highest honor we might achieve, being modest scientists? The Nobel prizes pop into mind, but although many will have had a childhood dream that this might just be within grasp, most of us aim lower than that. The IgNobels may put you in the limelight, but the honor is dubious. I have attended a few conferences, usually organized by scientific societies, that dedicated a session to the memory of some influential colleague: more realistic, but it does not lead to widespread popularity. Perhaps my best bet would be to go for a Darwin award: more easily within my control, but I’ll save that for later in my career. Morituri te salutant!

■ BY DAVE LANGERS
Now what? Life after the defense:
A double interview with Arnoud Potgieser and Kashmiri Stec

One of the decisions after your PhD will be whether you stay close to home or create a new home abroad. While Arnoud Potgieser continued to work at the UMCG, Kashmiri Stec decided to move to Denmark. Both their projects were about the importance of movement. Arnoud researched the involvement of the premotor cortex in Parkinson’s disease and Kashmiri’s project was about non-verbal behaviour during communication. They talk about how important it is to plan your PhD and to be in control of your own project.

What were your projects about and how did you end up in that field of research?

Arnoud: I did an MD/PhD project in the departments of neurology and neurosurgery. My research focussed on the function of the premotor cortex, which is a brain structure involved in the preparation of movements. We performed behavioural and MRI studies in healthy subjects, patients with Parkinson’s disease and patients with primary brain tumours to study the functional and anatomical specialization of the premotor cortex.

Kashmiri: I worked on a Vidi project at the CLCG in the Arts Faculty, focusing on the nonverbal behaviours (gaze, facial expression, posture/body movement, and manual gestures) accompanying certain kinds of spoken quotative utterances. We wanted to understand the extent to which the entire body is used during communication, what role each of the body parts plays, and how they work together with speech to evoke certain aspects of the quoted character. I worked on ‘side’ projects focused on American Sign Language, and took a lot of inspiration from signed languages when working through my spoken language data.

What are you currently doing?

Arnoud: Currently, I am working as a resident at the department of neurosurgery of the UMCG. My current work has no direct link with my PhD project, but I think doing research has helped to develop a systematic way of thinking, which is helpful for clinical problems.

Kashmiri: A couple of days after my defense I moved to my (Dutch) boyfriend’s place in Denmark. I’m now looking for work here, mostly outside of academia. In the meantime, I’ve been getting more involved in some non-governmental organizations (NGOs) that I started volunteering with during my PhD period. Right now one of them has started collaborating with UN Women and UN-NGLS, and I’m right in the middle of it, which is kind of exciting.

What are the fun parts of a PhD?

Arnoud: For me the formulation of a research question and actually doing the experiment that gave an answer to the question was very rewarding. Furthermore, we had a very nice group of PhD students in our department, which created a fantastic work environment, and also friendships and social activities.
KASHMIRI: The feeling of being in control of your project, stretching (exercising?) your brain as you try to discover the best way to answer a question or analyse data, meeting interesting people from around the world – at conferences or your own back yard, and coming to understand just how ... human science and scientists are. In the public sphere, I think there's still a lot of mystique around who we are, what we do, and how we work, but at the end of the day, we're just as human as everyone else.

Did you experience any problems or high workload during your PhD and how did you cope?

ARNOUD: At times there was a high workload. During the MD/PhD project you have a shorter time to obtain your PhD. For me, it worked best to just work hard and tackle problems one by one.

KASHMIRI: Yes. To put it lightly, the first year of my project was hell and I'm grateful to the people who jumped on board and helped me steer towards friendlier seas. Once that was past, the hardest part for me was managing periods of intense work with periods of 'intense' waiting. I picked up a lot of fun side projects during the waiting periods, and the results of those projects ended up shaping the way I approached my primary PhD work.

What skills and life lessons did you learn during your PhD?

ARNOUD: Probably the best lesson is that your PhD confronts you with your own weak points. You have to do your PhD and no one else will do it for you. Therefore, you will quickly learn what your weak points are. I also think that you learn to approach problems from many different angles, which is helpful for me in my clinical work.

KASHMIRI: I agree with Arnoud – it’s your PhD project, and you’re the only one who can see it through to the end and receive the paper from the Dean. The sooner you realize that and take control, the better. I would also add insights into human nature – how you work, how your colleagues and supervisors work, and how to use everyone’s strengths and weaknesses in complementary ways so that you end up with a strong team.

Do you have any tips for starting PhD students?

ARNOUD: Make sure that there is a good plan to start with in your PhD. Otherwise, you will lose a lot of time just figuring out what it is that you have to do. Furthermore, it is very helpful to plan all your projects from the start and begin with the projects/tasks in which you depend on other people to proceed. Find nice colleagues to work and drink with. This gives you the opportunity to talk about the difficult parts of your projects and makes you see that everyone has problems during their PhD. Remember that your PhD is a time when you have freedom and are able to plan your own time. This freedom will probably never come back.

KASHMIRI: Whatever time you think a task will take, double it – then you can be happily surprised with extra time, instead of frustrated at having missed a deadline (even your own). Take charge of your project and make bold decisions. Learn as much as you can, and diversify your knowledge and skillset as much as you can. Talk to people outside of your department and faculty. And remember to take breaks from your RUG email.

> Whatever time you think a task will take, double it – then you can be happily surprised with extra time. <

> BY MANON VAN ASSELT
> PHOTO KASHMIRI BY JOHANNES BODE
> PHOTO ARNOUD BY A.E. EENHUIS
Mindwise: Doing research and the unexpected

Curiosity and deep interest in a topic drive research. My research is no exception to that rule. Could I have foreseen how my career would develop? For example, I could have finished school, gone to university and studied dentistry, and then could have been a dentist with a more than proper income for the rest of my life. As a boy I was determined to become a farmer. I also dreamt of being an explorer of unknown land, a famous architect, or astronomer, and make discoveries at the frontiers of physics. What would I have been without such dreams? Life is about opportunities: some you get, some you don’t, some you don’t see, and some don’t concert with one’s (limited) capacities.

What happened since? I studied astronomy, which was great for two years until I had to admit that the advanced courses became too highly theoretical. Time for plan B. Medical physics was the opportunity I came across, which brought me a PhD.

Running through the newspaper, during an intermezzo in writing the last chapter of my PhD thesis, I came across this odd vacancy in Groningen – Psychology? Children? Developmental disorders? I hardly knew anything about it. But the keywords experimental, movement disorder and EEG raised my interest. Why not apply? They took me on, even though I forgot to change trains in Amersfoort on my way to Groningen. This was 1983.

The Department of Psychology was both more interesting than I had expected as well as a disaster. Back then, some members of the staff had never published a research paper and I remember seeing a request to attend a conference on some vague alternative treatment, including a personal training...
session of walking through burning coal. At the same time, I worked in a newly established, well-motivated research group and learned so much about how to study the fuzzy topic of psychology, as opposed to the clear-cut, theoretically founded physics I was trained in. I discovered that psychologists have developed lousy theories and great experiments using many of the techniques developed in physics and medical research.

What about unexpected main results of a study? How to deal with that? One of my PhD students ran a longitudinal study to explore how the growth spurt in puberty would temporarily hinder the development of motor skills in clumsy boys. After 3 years of data collection, against our prediction, it turned out that most clumsy boys improved their motor skills more than controls during the growth spurt. Fortunately, after much thought, we came up with a plausible explanation: the maturation of the nervous system of these boys was speeded up during puberty. Although the whole research was on boys, guess what a newspaper signaled: Girls not affected by growth spurt!

And the unexpected continues: A few years later I happened to get involved in a really interesting project on lateralization for which we received funding from the NWO, the Dutch Organization for Scientific Research. While preparing the grant proposal, we had the wild idea to study handedness and evolutionary selection in a pre-industrial society. My colleague in the Biology department knew a German anthropologist who was willing to introduce us to the Eipo tribe in the heart of New Guinea. As one of the PhD students unexpectedly had to withdraw, I jumped in. Nine months later I had learned Bahasa Indonesia and found myself living between these friendly people to collect data by means of interviews, observation, and simple measurements of handedness. No electricity, plenty of fresh vegetables, a place to sleep, and the most reliable recording system ever developed: paper and pencil.

As a boy I dreamt of becoming an explorer; now it turns out I have been one my whole life. Wonderful and… unexpected.

**BY REINT GEUZE**

**Relevant publications**


Tracking my steps

With a psychology undergrad degree under my belt, I initially applied for the C-track (Cognitive Neuroscience and Cognitive Modeling) of the BCN ReMa. This seemed like a natural continuation to what I've done before. Ultimately, I made the decision to do a career switch and start the Animal Behaviour track instead. With the support received from the C- and B-track coordinators, this couldn't have been a better decision.

Although not many people seem to make the call (I was the only person without any background in biology in my year), I highly recommend it. This is an excellent chance to broaden your skills and competence, and go outside of your learning comfort zone. It helps that it still is, at the end of the day, a neuroscience degree. So in a general sense, you still study the same field. For me, it was an invaluable experience to learn about animal experimentation and evolutionary sciences, and connect that to what we know in cognitive science.

It is noteworthy that within this programme there’s still plenty of room to further explore your native interests. The idea of the BCN school is to inspire collaboration within different fields, and it’s certainly true for this MSc degree. I’ve recently done a colloquium – a 20-minute talk and literature study – with a supervisor from the psychology department.

The two research projects (first and second year thesis) are a chance to delve even deeper into the notion of multidisciplinarity. I’m doing my first one at the UMCG, exploring yet another type of scientific environment. The second year gives you a chance to take non-track courses and build your scientific network by going abroad and finishing your thesis there (we basically have the freedom to choose any place in the world). I know I can’t wait, but that being said – I will miss Groningen. The master’s degree is the best choice I could have made for my education.

BY ALEXANDER PIETRUS-RAJMAN
PHOTO BY SANDER MARTENS
BCN Retreat 2016 - March 17-18

BCN retreat feedback

BCN retreat held at Odoorn was my first PhD meeting outside Groningen. I had never heard about this place before, and I presumed it was a big city with lots of noise, buildings, restaurants, and shops around. To my surprise, it was the opposite. We were in a beautiful small village, and the environment was so nice and quiet. It was so well arranged and organized by the BCN people. The place where we stayed was amazing and the food was really good. I met many other students doing their PhD in different fields. The presentations given by PhD students were good. They tried to keep it simple so that everyone could understand without having any particular background knowledge. We got some time to interact with each other and discuss our research in one-to-one talks. Although, it was a little overwhelming, and in my opinion the time was too short to remember anything about their research. The outdoor activities were also fun. I took part in go nuts with nuts, and we went into the woods, which were really awesome. The rest of the people went mountain biking. So, there was a good balance of events. In the evening, there was pub quiz, another highlight of this meeting, for social interaction. Overall, it was nice and these kinds of workshops should be encouraged by every university. It could be a little better if we could go for more than two days. I am already looking forward to the next meeting.

BY CHAITALI PAUL
PHOTO BY R. K. CHAUHAN
An impression

On March 17 and 18, BCN once again organized its annual retreat at Hotel “De Oringer Marke” in Odoorn. It was my first time to attend the two-day event, but I soon learned that this year’s format was different from previous editions’. BCN’s PhD students would now give shorter, less technical talks, allowing for better communication between speakers and their heterogeneous audience. Probably a wise change, since the vastly different contexts and jargon of our research here at BCN can easily obscure not just how closely related our projects may really be, but also how we can help each other come to new ideas. Judging from the lively discussions following the talks, it seems like the new approach paid off quite well.

Of course, BCN retreats are not just meant to facilitate the exchange of scientific ideas; they are also nice occasions to get to know or reconnect with fellow BCN members. In this respect, the food, drinks, and the mountain biking activity did wonders (for the latter, it certainly didn’t hurt that the weather was perfect). My personal highlight of the retreat was the pub quiz that I organized on behalf of the BCN PhD Council with the assistance of Isa and Andrea. The quiz’s questions were as frustrating as intended, the team names were funny (special shout-out to The Soggy Bottom Boys), and the shame on people’s faces when they recognized songs by Justin Bieber and Britney Spears but couldn’t identify The Beatles’ “Come Together” in the music round was priceless. Looking forward to the next one!

BCN retreat was a treat!

For me, the BCN retreat was a perfect combination between science and social events. The presentations from different fields of science created a nice overview of all the research that is being performed. Presentations were nicely augmented by social events, creating an informal atmosphere. I think this was an important aspect for the success of the retreat, since the low threshold created opportunities for lively discussions. It is nice to see that we can all contribute, with the knowledge from our different fields.

BY RENSKE LOK
PHOTO BY JELMER LOK

BY STEVEN GILBERS
PHOTO BY RICK SLAGTER

RETREAT PHOTOS BY MICHIEN HOOIVELD
New staff writers wanted!

Do you enjoy reading the Newsletter? If so, why not join our enthusiastic editorial team and make it even better? Regardless of whether you’re a master student or PhD student, it’s a great way to expand your network, improve your English writing skills, and be actively involved in BCN.

Interested? Send an e-mail to Sander Martens, sander.martens@gmail.com!
Exhibition “Gehirn”
From April 12th till July 4th, a number of wooden statues representing the human brain will be on display in the “Blauwe Patio” of the UMCG. The statues have been created by Reinier van den Berg for the book “Brein & Zijn”, which also contains columns by Marije van Beilen and sonnets by Hans Broekhuis (also see issue 99). Bookstore Daan Nijdam UMCG will offer the book at a discounted price during the exhibition.

BCN student wins Dutch FameLab prize
First year BCN student Timothy Sondej has won the audience prize of the Dutch edition of the FameLab prize, an international competition to explain one’s passion for science.

Check out his pitch https://www.youtube.com/watch?v=4Pm7MtrCoZs

For more info http://dekennisvannu.nl/site/special/FameLab-2016/43#!//

Large-scale research into ADHD supported by EU
A consortium of 17 research institutes from 8 countries has received EU funding for a large-scale investigation into ADHD. UMCG researcher Catharina Hartman is one of the project leaders. LifeLines will provide part of the data.

For more info https://www.umcg.nl/NL/UMCG/Nieuws/Persberichten/Paginas/Groot-Europese-onderzoek-ADHD.aspx

Subsidy for methods detecting psychosocial problems
Prof. Marieke Timmerman (Psychology Department) has received a ZonMW grant for developing research methods to detect psychosocial problems in 12-17-year-olds.


Ds. Visscher prize
Former BCN PhD student Kirsten van den Bosch (Orthopedagogy) has won the 2016 Ds. Visscher prize for her dissertation on “Safe and Sound Soundscape research in special needs care”. The prize consists of € 10,000.


7 Million for eye disease research
The EU, UMCG, the RUG and other partners will fund 25 PhD projects investigating glaucoma. Fifteen of those projects will be carried out at the UMCG under supervision of Frans Cornelissen and Nomdo Jansonius (Ophthalmology, UMCG), who both obtained H2020 Marie Curie grants.

For more info http://kennisinzicht.umcg.nl/Paginas/7-miljoen-euro-voor-onderzoek-naar-Glaucoom.aspx
KHMW appoints new members
The Royal Dutch Society of Sciences (KHMW) is a Dutch scientific society initiated in 1752, with the aim to support science in various ways and to build bridges between society and science. Six professors have been appointed as new members, including Prof. Rineke Verbrugge (Artificial Intelligence Department).

Martijn Wieling wins prestigious European Yong Researchers Award
He will receive his prize on July 25 in Manchester during the EuroScience Open Forum (ESOF). Since 2010 the European Young Researchers Award (EYRA) is given to researchers with excellent research results and leadership. The goal of the prize is to inspire young researchers to add a European dimension to their research. This year is the first time that the prize is being awarded to researchers who work in behavioural and social sciences.

VIDI grant for Sarthak Misra
Sarthak Misra (Department of Biomedical Engineering) has been awarded a VIDI grant for his project: SAMURAI (Steering Actuated Probes for Targeted Interventions). Probes are often used in diagnostics and for the delivery of medicines. Often, these generally inflexible instruments miss their target, resulting in complications. SAMURAI will develop flexible, robot-controlled probes to reach difficult locations in the body, thus enhancing both patient comfort and clinical results.

For more info
www.surgicalroboticslab.nl

Petra Hendriks has been appointed a member of the Royal Netherlands Academy of Arts and Sciences (KNAW)
Petra Hendriks is Professor of Semantics and Cognition at the Faculty of Arts of the University of Groningen, and the Director of the Center for Language and Cognition Groningen (CLCG). Hendriks is an internationally influential researcher in the discipline of linguistics, combining theoretical analysis and psycholinguistic methods in her work. She researches how language comprehension normally develops, but also how its development can deviate from the norm in specific groups, such as children with autism, ADHD or hearing impairments. She also focuses much attention in her research on how speakers take into account how listeners hear and understand them.

Early Career Award 2016 for Marie-José van Tol
The Early Career Award is given every two years by the ‘Nederlandse Vereniging voor Neuropsychologie’ (Dutch Association for Neuropsychology) to a scientist who contributed significantly to the field of neuropsychology within the first six years after obtaining a PhD. Dr. Marie-José van Tol was chosen unanimously by the jury because of her excellent scientific achievements, including the publication of over 40 peer-reviewed articles and having obtained two large grants (NWO-VENI and a Hersenstichting Fellowship).
Dear BCN community

This is your PhD Council

We are a direct connection between you and BCN. We represent you at the Education Committees and at the Graduate School of Medical Sciences (GSMS). We also promote educational events such as the PhD lunch.

We are very happy that one new member just joined our team (yay!). This means, the following PhD students are now part of the council (see pictures!).

After the summer, a number of us will be graduating and will be leaving the council. This means we need more support! Are you also interested in joining the council? Contact us at bcnphdcouncil@list.rug.nl.

See you at our next PhD lunch,
Your PhD Council.

Claire Kos
COGNITIVE NEUROPSYCHIATRY, NEUROIMAGING CENTER

Joana Carvalho
LABORATORY OF EXPERIMENTAL OPHTHALMOLOGY, UMCG

Florian Sense
PSYCHOMETRICS AND EXPERIMENTAL PSYCHOLOGY, GMW

Isadora Lopes Alves
NUCLEAR MEDICINE AND MOLECULAR IMAGING DEPARTMENT, UMCG

YOU?

Steven Gilbers
NEUROLINGUISTICS AND LANGUAGE DEVELOPMENT, LET

Stefan Huijser
(NEW MEMBER) ARTIFICIAL INTELLIGENCE & COGNITIVE ENGINEERING, FWN

Enja Jung
DEPARTMENT OF OTORHINOLARYNGOLOGY (AUDIOLGY), UMCG
> PHD AND OTHER NEWS

New course: Writing for General Public

In an earlier edition of the newsletter, you were informed about a new course: Writing for General Public. The course is scheduled for September. As soon as I know the details, I will send out an email about it.

Courses offered by the Graduate School of Science

One of the advantages of being a BCN PhD student is that you can also take courses offered by the Graduate School of Science. This Graduate School organises courses like Teaching for PhD students, Introduction to Bayesian statistics, Integrating R and C++ and a lot more. Check out their current courses on http://cursus.webhosting.rug.nl/gss/courses/
Note that you will have to pay for their courses. Up to 600 euro per year will be reimbursed by BCN, see below.

Reimbursement of external courses and conferences

If you would like to receive a contribution from BCN, use the application form from the BCN website. Sending the form beforehand isn’t necessary unless you’re not sure about the amount you can count on. Please send the form (signed!) to Diana and add (to the fullest extent possible, the original) receipts or proofs of payment, together with an overview of the costs, by snail mail!

Agenda BCN Activities

September 9, 2016
Start BCN Orientation Course.
Application (for all courses): http://cursus.webhosting.rug.nl/gsms

Please check the website and online registration system for detailed information.

Diana Koopmans
(D.H.KOOPMANS@UMCG.NL)
The PhD survey and METC related delays

Together with the GSMS PhD Council, your BCN PhD Council has recently surveyed PhD candidates regarding project delays related to METC applications. The survey resulted in many responses, and the general assessment was that a great number of PhDs encounter considerable delays when applying for a METC approval to start their projects. In order to follow-up on the results of the survey, a representative of the GSMS PhD Council, together with a representative of the GSMS Education Committee (EC), arranged a meeting with the chairman of the METC.

The representatives present at the meeting report that the METC was cooperative and open to suggestions for improvement. In fact, the METC was already working on a new website, designed to provide a clearer set of instructions for the application process. The new website is expected to be up and running in May, and the METC will also host a FAQ session to help address applicants’ doubts.

The METC believes that most delays take place due to insufficient documentation. It was suggested that in many cases the more experienced senior researchers/promotors should better support the PhD candidates in the process of preparing the METC applications. In fact, when an application is considered complete, the committee claims that it provides researchers with a reply within two weeks’ time. Therefore, the new website is expected to help solve most of the problems. The METC would appreciate feedback about the new website.

However, the GSMS EC would like to ensure the expected improvement does take place – for that reason, as soon as the new website is in place, applicants are encouraged to contact the GSMS EC if they still encounter delays. The GSMS EC will communicate these points to the METC, since only then will they be able to provide the METC with a more specific and detailed assessment of the reasons for delays. Two EC members volunteered to help in such cases and can be contacted via email: r.sanderman@rug.nl (Prof. R. Sanderman) and b.wilffert@rug.nl (Prof. B. Wilffert).

■ BY ISADORA L. ALVES

Cool links

www.sciencebasedmedicine.org
> Science-Based Medicine: Exploring issues and controversies in the relationship between science and medicine
http://goo.gl/DZdAsF
> The Magic of The TED talk: Revealed! (Forbes review of TED founder Chris Anderson’s new book)
http://goo.gl/4Fw4xs
> Life Is Chill When You Believe Science Will Solve Death (A Vice/Motherboard documentary investigating the growing popularity and scientific validity of cryonics)
http://hackthebrain.nl/
> “Hacking the brain is both challenging as well as doable, both philosophical as well as practical, both artistic as well as business, both scientific as well as futuristic.”

http://www
“You have come a long way” is an example of a chunk, a relatively fixed combination of words that English speakers regularly use and that has a particular meaning in a certain context. One could also say “You have traveled far” or “You should be proud of what you have accomplished”, but even though these expressions are grammatically correct, they do not convey the same message. Spoken language consists of approximately 60% of such combinations and to sound fluent and authentic second language learners should learn especially these kinds of expressions. However, there is very little room in current language teaching approaches for chunks as an analysis of course books and classroom observations in the Netherlands shows. Instead, teachers spend a relatively long time to teach grammar rules and testing grammar knowledge. It has proven very difficult to convince teachers of the need for a different approach. The reason is probably that there is a deep-rooted conviction that rules exist and forms the basis of language. If you know the grammatical rules, you master the language! In her paper, Verspoor argues that language is not a complex system driven by systematic rules, but a complex, dynamic, self-organizing system that is meant to convey meaning and grammar is just epiphenomenal. To express meaning, language users often use similar expressions over and over again, and some of these have regularities that are similar to rules and linguists describe as such, but they do not form the basis of language. Language Teachers must therefore make of the idea that grammar teaching is the most important. It is better to spend a lot more time on these phrases by listening to spoken and written language authentic material.

EVELYN KUIPER-DRENTH, ON BASIS OF PRESS REPORTS OF THE UNIVERSITY OF GRONINGEN
PHOTO BY JENNE HOEKSTRA
Serotonin manipulations and social behavior: Studies in individuals at familial risk for depression

**PHD STUDENT**
K. Hogenelst

**THEESIS**
Serotonin manipulations and social behavior: Studies in individuals at familial risk for depression

**PROMOTORS**
Prof.dr. P.J. de Jong
Prof.dr. R.A. Schoevers

**CO-PROMOTOR**
Dr. M. aan het Rot

**FACULTY**
Behavioural and Social Sciences

Changes in the availability of serotonin in the brain can lead to changes in social behavior. Interactions with others affect our mood, and vice versa. Unsurprisingly, people with a mood disorder such as depression often have difficulties in their social relationships. Depression is often thought to be associated with a decreased availability of serotonin, a signaling molecule in the brain that enables the processing of social and emotional information. Therefore, a decreased availability of serotonin could also have an adverse effect on social behavior and mood during interactions with others.

However, Hogenelst and colleagues showed that a temporary decrease of serotonin (over several hours) has little impact on mood or social behavior as measured in the lab. The results were similar in study participants with and without an elevated depression risk.

In a second study in people with an elevated depression risk, the researchers increased the availability of serotonin over several days. They examined the effects on mood and social behavior in everyday life. As expected, mood improved with increased serotonin availability. Unexpectedly, however, the participants also became less friendly. This behavioral effect was only seen during interactions at home. It is possible that when serotonin availability was increased, participants stood up for themselves more. This in line with the idea that people who are prone to depression experience little control over their social lives.

As most medications for depression aim to increase the availability of serotonin, an important next question is how these medications affect the social behavior of depressed people.

Koen Hogenelst (1985) followed the research master Behavioral and Cognitive Neurosciences (Molecular and Clinical Neuroscience). He did his research, financed by TNO, at the Research School of Behavioural and Cognitive Neurosciences. He was promoted on February 4, 2016.

Taste and flavor liking: Neurobiological correlates and behavioral diversity

**PHD STUDENT**
J.R. Dalenberg

**THEESIS**
Taste and flavor liking: Neurobiological correlates and behavioral diversity

**PROMOTORS**
Prof.dr. G.J. ter Horst
Prof.dr. M.M. Lorist

**CO-PROMOTORS**
Dr. R.J. Renken
Dr. A.K.L. Reyners

**FACULTY**
Medical Sciences

Different people prefer different foods. This can be problematic for the food industry as researchers often study the “average individual”. However, when it comes to taste, this person does not exist. Taking inter-individual differences into account is crucial to the enhanced prediction of a profitable food product. Furthermore, food preference may be strongly related to emotions evoked by food consumption.

In his PhD project, Jelle Dalenberg implemented a research method to take inter-individual differences into account. By breaking down a large group of people into smaller groups with similar responses, he was able to develop a better understanding about which people prefer which types of foods.
Dalenberg showed that emotions evoked by food consumption are a good predictor of what foods a person will choose for consumption. The relation between taste and emotion is apparent from functional brain imaging. Dalenberg asked people to taste different drinks while brain function was visualized in an MRI scanner. After tasting each drink, participants were instructed to indicate how much they liked it. Dalenberg demonstrated that tasting and taste preference are mainly processed in brain areas involved in emotional processing. Inter-individual differences in taste preferences can also be found within these brain areas.

Jelle Dalenberg (1984) obtained his master title Human-Machine Communication (HMC) at the University of Groningen. He did his research at the Neuroimaging Centre and within the research institute BCN-BRAIN of the University Medical Center Groningen. The research was funded by Top Institute Food and Nutrition (TIFN). Dalenberg continues his career as a postdoc researcher in the UMCG. He was promoted on February 10, 2016.

The influence of genes and environment on the development of bipolar disorder: A twin study

PHD STUDENT
R. Vonk

THESIS
The influence of genes and environment on the development of bipolar disorder: A twin study

PROMOTORS
Prof.dr. W.A. Nolen
Prof.dr. R.S. Kahn

FACULTY
Medical Sciences

Bipolar disorder (or manic-depressive disorder) is a severe mood disorder in which episodes of (hypo)mania (e.g. elevated mood en hyperactivity) and depression (e.g. decreased mood and reduced activity) alternate with periods of normal mood and functioning. Genetic factors as well as environmental factors play a role in the development of bipolar disorder. A serious problem in bipolar disorder is a delay of several years between the first mood episode(s) and the diagnosis. Following diagnosis, it can take several years before the right treatment is started. This twin study shows that the genetic vulnerability for bipolar disorder can appear in several ways and in several phases of life.

- During early intrauterine life, between the 10th and the 17th weeks of gestation, an abnormal development of the embryonal ectoderm tissue can lead to changes in palmar dermatoglyphics, which are associated with structural brain abnormalities in adult life.
- MRI scans of the brain of the adult bipolar twins show white matter abnormalities.
- In early adolescence, (temporary) underperformance in school can be a marker of genetic vulnerability to develop bipolar disorder.
- There is genetic overlap between the development of bipolar disorder and a thyroid auto-immune disease.

This auto-immune thyroiditis can be seen as an endophenotype of bipolar disorder. Endophenotypes can be useful to identify people at higher risk for developing bipolar disorder, early diagnose and starting treatment as soon as possible, maybe even as preventive measure.

Ronald Vonk (1961) was trained as psychiatrist in the former Delta Psychiatric Hospital in Portugal, now part of Antes. He did his research with Professor Emeritus Willem Nolen of the University Medical Center Groningen. The research was financed by the Stanley Medical Research Institute in Bethesda (United States). Vonk works as a psychiatrist in the GGZ-institution Reinier van Arkel in ’s-Hertogenbosch. He was promoted on February 10, 2016.
Ensuring patient privacy in image data sharing for clinical research: Design and implementation of rules and infrastructure

**PhD Student**
K.Y.E. Aryanto

**Thesis**
Ensuring patient privacy in image data sharing for clinical research: Design and implementation of rules and infrastructure

**Promotor**
Prof.dr. M. Oudkerk

**Co-promotor**
Dr. P.M.A. van Ooijen

**Faculty**
Medical Sciences

The protection of personal data has become an important yet challenging process when patient data are distributed among health institutions. Regulations and rules have been issued to govern the protection of the privacy of personal information. To conform to these rules and regulations, data de-identification must be executed properly to ensure the elimination of identifying patient data within the DICOM header. From this, several issues arise when dealing with this data sharing and de-identification process where many factors may influence the success rate.

A set of de-identification rules based on the existing guidelines and regulations has been provided to determine the identifying elements within the DICOM header that should be eliminated to provide the clarity of the effort of the patient data protection. Various toolkits are available that provide procedures to perform the actions to ensure identity protection, and several of them are available freely. However, we found that those free DICOM toolkits should be used with extreme care to prevent the risk of disclosing personal health information, especially when using default configuration. Furthermore, we proposed one toolkit to be used when optimal security is required. Digitalisation of medical data scans has introduced several issues regarding data storage, migration and distribution methods. Distribution over portable media is gradually replaced by more automated approaches to media handling in combination with installation and acceptance of network based sharing using XDS between hospital enterprises. However, data sharing over networking technology has raised the question of where data should be de-identified to provide optimal protection of a patient’s protected health information. We have provided a solution to this problem.

In summary, we have described the important key factors to provide proper imaging data sharing and de-identification to ensure the protection of patient’s personal data in accordance to the existing rules within the European Union.

Kadek Aryanto (1978) did his research at the department of Radiology and the research institute BCN-BRAIN of the University Medical Center Groningen, which also financed the research. Aryanto now works as a teacher and researcher at the Ganesha University of Education in Singaraja (Bali, Indonesia). He was promoted on February 17, 2016.

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**Individual differences in temporal selective attention**

**PhD Student**
C. Willems

**Thesis**
Individual differences in temporal selective attention

**Promotor**
Prof.dr. A. Aleman

**Co-promotor**
Dr. S. Martens

**Faculty**
Medical Sciences

At every waking moment we are bombarded with large amounts of information. Given the limited ability to process this information at a conscious level, some sort of selection for further processing is required to identify the most relevant information (e.g., other road users) while ignoring irrelevant information as much as possible (e.g., a commercial billboard). Our attentional system plays a crucial role in this selection process. When attention is allocated at specific moments in time, we typically refer to this as temporal selective attention, which can be studied using the attentional blink paradigm. The attentional blink is the inability to identify relevant information when it is...
shown within half a second of earlier presented relevant information. By studying the origin of this inability we hope to better understand how our brain selects and processes information over time. Our research specifically focused on addressing the question of how people differ in their ability to rapidly select and process relevant information. We show that individuals who have little difficulty in identifying information in close temporal proximity allocate their attention earlier in time and more precisely than individuals who have more trouble performing such a task. Furthermore, the individuals who perform well seem to chop the incoming information into smaller pieces, leading to less confusion regarding the order in which the information was presented. Finally, we demonstrate a number of ways in which individuals can be trained to improve their ability to process rapidly presented information.

Charlotte Willems (1989) studied Psychology at the University of Groningen. She did her research within the research institute BCN-BRAIN of the University Medical Center Groningen. This research institute also funded the research. Willems is now working as a junior business intelligence consultant at Ordina in Nieuwegein. She was promoted on February 24, 2016.

The molecular neuropathology of spinocerebellar ataxia type 23

PHD STUDENT
C. Smeets

THESIS
The molecular neuropathology of spinocerebellar ataxia type 23

PROMOTOR
Prof.dr. R.J. Sinke

CO-PROMOTOR
Dr. D.S. Verbeek

FACULTY
Medical Sciences

The cerebellum (Latin for “little brain”) is a region of the brain that plays an important role in regulating the coordination, precision and timing of voluntary movements, and lets you know where your limbs are without looking. A malfunctioning cerebellum usually leads to ataxia. Patients with ataxia suffer from the inability to walk in a straight line, imbalance, and loss of control over speech and eye movements. Currently, there is no therapy available for any of the 44 subtypes of this progressive incapacitating disorder. A particular subset of nerve cells is affected in ataxia, namely the Purkinje cells. The Purkinje cells are the sole output of the cerebellum and as such incorporate signals from many cells in order to properly coordinate movement. They play a crucial role in the normal functioning of the cerebellum. We have modelled an ataxia subtype, spinocerebellar ataxia type 23 (SCA23), in mice. The mice contained the human SCA23 disease gene and reproduced the disease symptoms of patients. In order to determine how these symptoms arise, we studied the underlying causes in the cerebella of these mice in great detail and found that mice suffering from ataxia display small but significant changes in the cerebellar circuitry. Additionally, we observed changes in important biological routes that reduced the communication of nerve cells leading to cell death. In this thesis, we describe these changes in detail and offer a possible strategy for drug development.

Cleo Smeets (1985) studied Molecular Life Sciences (BSc) and Clinical Molecular Sciences (MSc) at the University of Maastricht. She did her research within the research institute BCN-BRAIN of the University Medical Center Groningen. The research was financed by U4 Network Ageing Brain. She was promoted on March 2, 2016.

Concurrent multitasking: From neural activity to human cognition

PHD STUDENT
M. Nijboer

THESIS
Concurrent multitasking: From neural activity to human cognition

PROMOTOR
Prof.dr. N.A. Taatgen

CO-PROMOTORS
Dr. H. van Rijn
Dr. J.P. Borst

FACULTY
Medical Sciences

Multitasking has become an important part of our daily lives. This delicate juggling act between several activities occurs when people drive, when they are working, and even when they should be paying attention in the classroom. While multitasking is typically considered as something to avoid, there are instances where we are perfectly capable at performing multiple activities concurrently. It is therefore important that we understand how multitasking works, so that we can predict when engaging in multitasking is a good or bad idea. In this dissertation we examine how our brains are able to multitask, and how multitasking affects task performance. Through a series of behavioral and neuroimaging experiments, we investigate what the cognitive mechanisms of
CONINUATION PROMOTIONS

Digital technology plays a crucial role in today’s radiology department. This means that the job performance of radiologists is determined to a large extent by how well they can interact with computer systems. It is therefore vital that the user interfaces through which this interaction takes place are of high quality, and allow radiologists to perform their jobs with maximal effectiveness, efficiency, and satisfaction.

In this thesis, we aimed to study the interaction between radiologists and computer systems, and to identify ways to improve the quality of this interaction. We focused on usability evaluation, interaction techniques, user interface customization, computer-aided diagnosis, and structured reporting.

While the topics of the studies described in this thesis varied greatly, and all of them produced meaningful results on their own, they have one overarching message: in addition to studying digital technology in itself, it is vital to study the way humans interact with it. In order to design high-quality user interfaces for radiological computer systems, we have to understand how radiologists interact with them.

Wiard Jorritsma (1989) studied Artificial Intelligence (BSc) and Human-Machine Communication (MSc) at the University of Groningen. He did his research at the department of Radiology and within the research institute BCN-BRAIN of the University Medical Center Groningen, by which the research was financed. Jorritsma now works as a ‘usability/human factors engineer’ at Philips. He was promoted on March 16, 2016.

Research on atomoxetine in Dutch ASD/ADHD children: The RADAR study

PHD STUDENT
M.A. Harfterkamp
THESIS
Research on atomoxetine in Dutch ASD/ADHD children: The RADAR study
PROMOTORS
Prof.dr. P.J. Hoekstra
Prof.dr. J.K. Buitelaar
FACULTY
Medical Sciences

Symptoms of attention deficit/hyperactivity disorder (ADHD) are frequently present in children with an autism spectrum disorder (ASD). In this study, which was sponsored by Eli Lilly, atomoxetine appears to be a promising treatment of ADHD in children and adolescents with ASD. Atomoxetine was superior to placebo after a treatment period of 8 weeks and appeared to have positive effects on both attention deficit and hyperactivity-impulsivity symptoms according to clinician-based ratings, with clearly larger improvements on hyperactivity-impulsivity. There were no beneficial effects of atomoxetine on the core ASD symptoms. However, some indication of benefits through atomoxetine on stereotyped behaviours, inappropriate speech, and fear of change were found. Of note was the observation of further improvement in ADHD symptoms beyond 8 weeks of treatment, even when there was minimal or less response after the first five weeks. This has clear clinical implications in that clinicians should allow sufficient time before
On the cause of multiple sclerosis: molecular mechanisms regulating myelin biogenesis

**PHD STUDENT**

M. Bijlard

**THESIS**

On the cause of multiple sclerosis: molecular mechanisms regulating myelin biogenesis

**PROMOTOR**

Prof.dr. D. Hoekstra

**CO-PROMOTOR**

Dr. W. Baron

**FACULTY**

Medical Sciences

Myelin, the fatty insulation layer around nerve cells, sustains damage in patients suffering from multiple sclerosis (MS) due to inflammation. Importantly, eventual regeneration of myelin fails. To understand the underlying mechanism of regeneration, it is important to know how the myelin membranes are formed under ‘normal’ conditions. This knowledge is imperative to develop novel molecular tools for ‘rebuilding’ the protective myelin coat in MS lesions.

This research project revealed new insights as to how the two major myelin proteins, MBP and PLP, can be affected in the process of myelin assembly. For example, when the production of syntaxin 4, a well-known anchor protein in transport processes, is blocked in the precursor cells of oligodendrocytes, the production of MBP halts. We also found that the transport of PLP changes when in more mature oligodendrocytes, MAL protein – a transport-regulating protein – is expressed. Furthermore, factors from outside the cell may also affect the production of myelin. For example, the inflammation mediator TNFα, present in MS lesions, influences the cytoskeleton in such a way that MBP fails to reach the myelin.

This study provides new and detailed insight into molecular mechanisms regulating the localization of the main myelin components and hence, the assembly of myelin. These results will be beneficial in the development of new therapeutic treatments for MS.

Marjolein Bijlard (1983) received her masters degree Medical and Pharmaceutical Drug Innovation at the University of Groningen. She did her research within the research institute BCN-BRAIN of the University Medical Center Groningen. Stichting MS Research funded the research. She was promoted on April 4, 2016.

Rescue strategies in Drosophila models of neurodegenerative diseases

**PHD STUDENT**

M.B. Baratashvili

**THESIS**

Rescue strategies in Drosophila models of neurodegenerative diseases

**PROMOTORS**

Prof.dr. O.C.M. Sibon

Prof.dr. H. van Goor

**FACULTY**

Medical Sciences

In the past decades advances in medicine have...
led to an extended life span of the general population, which, as a negative consequence, increased the occurrence of age-related neurodegenerative diseases. The necessity to improve the quality of life, together with the urge to decrease the economic burden related to patients with neurodegenerative diseases, brings focus to the development of novel treatment strategies for these disorders, as the current medical interventions are mostly symptomatic and do not slow down the progression of the diseases.

In this thesis, we study neurodegenerative diseases in a fruit fly, which is widely used for these kinds of experiments. Our hypothesis was that neurodegeneration could be treated using different approaches: either focusing on the cause of this particular disease or using a general treatment. We show that both of these therapies can be efficient in the example of two diseases, Spinocerebellar ataxia type 3 and pantothenate kinase-associated neurodegeneration. In the case of a general therapy, we show how production of hydrogen sulfide inside the body positively influences neurodegeneration. In the case of the specific treatment, we supplement a substance called coenzyme A to organisms that lack it and we observe a partial rescue of the disease. Further, we demonstrate how these therapies work on the molecular level and create a new fly model for a more efficient study of pantothenate kinase-associated neurodegeneration.

Madina Baratashvili (1987) studied Pharmacy at the Volgograd State Medical University (Rusland). She was promoted on April 25, 2016.

**Communication abilities of children with ASD and ADHD: Production, comprehension, and cognitive mechanisms**

**PHD STUDENT**
S.J.M. Kuijper

**THESIS**
Communication abilities of children with ASD and ADHD: Production, comprehension, and cognitive mechanisms

**PROMOTOR**
Prof.dr. P. Hendriks

**CO-PROMOTOR**
Dr. C.A. Hartman

**FACULTY**
Arts

Children with autism spectrum disorder (ASD) often have communication problems. Children with ADHD may also have communication problems, but little is known about this.

For successful communication, it is crucial that the listener understands what the speaker means. Therefore, as a speaker you need to take into account the listener, and vice versa. As a speaker, you must constantly decide how specific to be when referring to someone. For example, you can refer to “the singer” (specific) or the personal pronoun “he” (less specific).

I tested the performance of children with ASD and with ADHD in language production and language comprehension tasks. I investigated whether or not they took into account their conversational partner’s perspective. I also examined whether their perspective-
taking skills, working memory capacity, and impulse control contributed to successful communication.

In the structured tasks, the children with ASD and with ADHD were able to take into account the perspective of their conversational partner equally well as typically developing children. The better their perspective-taking skills and impulse control, the better able they were to take into account their conversational partner. Their working memory capacity was particularly important in complex situations where much information needed to be remembered.

Despite children’s ability to take into account different perspectives in language, I observed several language problems in children with ASD and with ADHD. They had difficulties with telling cohesive stories and with formulating grammatically complex sentences. This shows that language can be challenging for children with ASD and with ADHD.

Sanne Kuijper (1981) studied Psychology. She did her research at the Center for Language and Cognition Groningen, as part of the NWO Vici-project ‘Asymmetries in Grammar’. She was promoted on April 28, 2016.

**Pieces of the puzzle: Empirical studies on the diagnosis Dissociative Identity Disorder**

**PhD Student**
E. Vissia

**Thesis**

Pieces of the puzzle: Empirical studies on the diagnosis Dissociative Identity Disorder

**Promotors**
Prof. dr. A. Aleman
Prof. dr. D.J. Veltman

**Co-Promotor**
Dr. A.A.T.S. Reinders

**Faculty**
Medical Sciences

Dissociative identity disorder (DID) is a psychiatric disorder that, among others, is characterized by the presence of two or more distinct personality states that recurrently take control of a person’s behaviour. DID was included in the DSM in 1980. Since then, an ongoing debate regarding the etiology of the disorder is taking place between holders of the trauma and fantasy models. This thesis aims to explore the etiology of DID in a design that acknowledges both the trauma and fantasy models.

Based on psychological measures, we showed that individuals with DID had the highest scores on trauma measures, followed by individuals with posttraumatic stress disorder (PTSD), and then controls (HC). On measures of fantasy proneness and suggestibility, group differences were less pronounced, which is in contrast with the fantasy model’s hypothesis.

Using structural brain imaging, we found that individuals with DID had a smaller hippocampal volume as compared with PTSD and HC. Furthermore, a negative relation was found between childhood traumatization and hippocampal shape and volume.

The first functional neuroimaging study showed that different personality states can be distinguished in DID during a working memory task, with the trauma-related personality state revealing worse task performance and limited activation of the prefrontal-parietal working memory network. The second study showed that when comparing individuals with DID with DID-simulating controls, differences in brain activation were found and actresses’ working memory performance was better. Overall, the thesis predominantly provides empirical support in favour of a trauma-related etiology for DID.

Eline Vissia (1986) studied psychology at the University of Groningen and then followed the training to become a GZ-psychologist. She did her research at the research institute BCN of the University Medical Center Groningen. The research was funded by NWO, the UMCG and BCN. Vissia now works as a GS-psychologist at the Top Referent Trauma Centrum of ‘GGz Centraal’. She promoted on May 2, 2016.

> Evelyn Kuijper-Drenth, based on the press reports of the University of Groningen
> CHEEKY PROPOSITIONS

The current focus in social neuroscience is like the Rolling Stones’ song: “I just want to see his face.”

> Koen Hogenelst

“De term “bitterbal” is vlees noch vis.”

> Jelle Dalenberg

“If you do not believe you can do it then you have no chance at all.” - Arsene Wenger

> Kadek Yota Erminda Aryanto

“I’m so clever, that sometimes I don’t understand a single word of what I’m saying.” - Oscar Wilde

> Cleo Smeets

“Promoveren en een schouwburgabonnement is geen goede combinatie.” - Pieter Hoekstra

> Myriam Harfterkamp

“Always have your radio on while driving; it is worth the risk of looking silly when you sing along.”

> Menno Nijboer

“Just because you cannot find it, does not mean it is not there.”

> Marjolein Bijlard

“Modern day medicine has changed the concept of evolution from ‘survival of the fittest’ to ‘survival of the sickest’.”

> Marjolein Bijlard

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> COLOPHON

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BCN Office (FA30), A. Deusinglaan 1, 9713 AV Groningen, 050 363 4734

Editorial Staff
Sander Martens, Editor-in-chief, s.martens@umcg.nl
Michiel Hooveld, m.h.w.hooveld@umcg.nl
Evelyn Kuiper-Drent, Copy Editor, BCN Office, 050 3634734, e.t.kuiper-drent@umcg.nl
Terrin Tamati, Copy Editor, t.t.tamati@umcg.nl

Staff writers
Isadora Alves, i.alves@umcg.nl
Manon van Asselt, manonvanasselt13@hotmail.com
Sanne Brederoo, sannebrederoo@gmail.com
Heleen Hoogeveen, h.hoogeveen@umcg.nl
Wouter Huiting, wouter.huiting@hotmail.com
Stéphanie Klein Tuente, s.klein.tuente@umcg.nl
Louise Koops, l.e.koops.1@student.rug.nl
Alexander Pietrus-Rajman, alexander.pietrus-rajman@hotmail.com
Anouschka Ramsteijn, aramsteijn@yahoo.com
Anne de Rechteren van Hemert, anne.recht@gmail.com
Peter Roemers, p.roemers@rug.nl
Ihabara Lopes Alvez, i.alves@umcg.nl

Contributors
Kadek Aryanto; Madina Baratashvili; Marjolijn Bijlard; Ronald Boellaard, r.boellaard@umcg.nl; Kirsten van den Bosch; Joana Carvalho, j.c.de.aliveira.carvalho@umcg.nl; Jelle Dalenberg; Reint Geuze, r.h.geuze@rug.nl; Steven Gibb, s.s.k.gibb@rug.nl; Myriam Harfterkamp; Petra Hendriks, p.hendriks@rug.nl; Koen Hogenelst; Stefan Huijser; Wielard Jorritsma; Enja Jung, d.e.jung@umcg.nl; Diana Koopmans, d.h.koopmans@umcg.nl; Claire Kos, c.kos@umcg.nl; Berry Kremer, b.h.kremer@umcg.nl; Sanne Kuiper; Dave Langers, dave.langers@rug.nl; Jelmer Lok; Sander Martens, www.sandermartens.com; Cameo Misiadjan; Barbara Nordhjem; SDC; Rick Slater; Cleo Smeets; www.phdcomics.com; RUG.nl; rug.nl/gmw/

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