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How RUGged is your learning?

In this interview with Hedderik van Rijn, the principal investigator of the SlimStampen/Rugged Learning computerized learning system, we talk about the principles behind this adaptive learning algorithm, its development during the past 10 years, and the challenges encountered in the process of transferring a product like SlimStampen from the lab into broad use by more than 300,000 Dutch students in secondary education.

What is SlimStampen and how does it work?
SlimStampen (or RUGged Learning) is a method that we’ve developed to optimize fact learning, such as the learning of vocabulary items, topography, or other type of knowledge that you should know from the top of your head without thinking about it. It is based on two very simple premises. The first one is that it’s better to learn information in a spaced way. We’ve all been told that you shouldn’t wait to study for a test until the very last evening, but, rather, you should spread out your learning sessions. That doesn’t just hold for spreading it out over multiple sessions, but it also holds in terms of spreading out the information within one studying session. The other principle is the testing effect, according to which it’s much better to test yourself on the information you’re studying than to passively read over it. The testing effect only works if you can still retrieve the information from memory. Actively retrieving an item strengthens its memory representation. In this context, a potential problem arises: the spacing effect requires to spread out the information as much as possible, while the testing effect results in improved learning if the testing occurs before the information is forgotten. Therefore, initially, it’s better to repeat the items at a faster rate and decrease their rate of presentation over time by increasing the spacing intervals. The challenge with that is that every learner will have a different rate of forgetting for every item. A way to assess the forgetting rate would be to look at the accuracy of responses to particular items (a correct response would indicate a slower forgetting rate for the corresponding item, while an incorrect response would indicate a faster forgetting rate). However, incorrect responses result in forfeiting the testing effect, which makes this way of estimating the forgetting rate counterproductive. What you want to do, then, is wait as long as possible (spacing effect), but still present the item when the learner can answer correctly. A way to assess the forgetting rate while benefiting from both the testing and spacing effects is to look at the reaction times of different responses. Fast responses would suggest that an item is well-encoded, while slow responses suggest less well-encoded items. That is the principle behind SlimStampen: using the reaction times related to different answers in order to figure out the best time for an item’s next presentation.

How are these principles implemented through the computerized learning system?
The algorithm tracks the rate of forgetting for each item. There is a mathematical model based on human memory theories which assumes that information fades away over time. What we assume is that this information can decay faster or slower for different items and for different participants. We assess the rate of forgetting by looking at the reaction times, because the reaction time...
will be higher if an item has decayed a lot, and lower if the activation of an item is high. Using this mathematical model, we can adapt the rate of forgetting.

**What is the story behind SlimStampen?**

SlimStampen is strongly based on the ideas that were around in literature for quite some time, such as the work by John Anderson and Phil Pavlik, who explore, using the same kind of equations, optimizing learning. However, they only look at the accuracy information, and use much longer learning sessions. In many contexts, such as in high school, the learning sessions are much shorter. When we started with SlimStampen, about 10 years ago, we mainly had versions of SlimStampen that were implemented to run experiments, and with each study the algorithm was slightly adjusted. Over the years, various students have helped me to develop it into a platform-based system. About three years ago, I got an e-learning grant from RUG to develop a system that can be used in the context of Nestor as a stand-alone app. Thus, the first milestone in the development of SlimStampen was seeing that the algorithm really worked. One of the main questions we had was whether we can use reaction times to adapt the forgetting rate, since the reaction time is a noisy signal. The major breakthrough that we have achieved is that we managed to find ways to get this memory signal out of the noisy reaction times. We managed to do that about 10 years ago, showing that the SlimStampen method outperformed the alternative methods that used only the accuracy information based on a flashcards algorithm.

**Has studying the algorithm throughout these years resulted in findings that have fed back into the knowledge base of cognitive psychology?**

In this context, it’s relevant and interesting to mention the work of Florian Sense, who did his PhD on this

> I think that e-learning definitely has a place in any educational program, because it can provide adaptiveness even if you have hundreds of students.
What are the main SlimStampen projects that you work on at the moment?

One project we're working on is based on using the data we already have. Right now, the system starts from scratch in trying to figure out a learner's learning characteristics at the beginning of each 20-minute learning session. It would potentially be much better if the system would already know how good a learner is, and how difficult an item is. For that, we need a lot of data, which we get through the Nestor environment, and the online environment on www.slimstampen.nl.

We use a form of Bayesian optimisation on these data to estimate which items will be difficult and which ones will be easy already at the beginning of a session. This could be achieved in two ways. One of them is using learner characteristics (educational level, experience with learning). We've decided to go with a second way, which is a more data-driven approach. If one has learned two or three different sets of items using the algorithm, we can already predict what the rate of forgetting will be in a new set of data. Similarly, item difficulty could be estimated. In this sense, it becomes more relevant to figure out what, for example, someone's native language is, because depending on that, different sets of words in another language may be perceived as either difficult or easy. Other projects that we are working on are directed towards trying to improve the signal-to-noise ratio. We are searching for other ways, apart from reaction times, to figure out how well a learner knows an item. For example, we have considered skin conductance, heart rate, pupil size, or EEG measures, and there is a number of different projects testing those ideas. In this context, you have to find a balance between practically-applicable and informative ways of attaining this goal. Of course, even if MRI data would be most informative, it is never practically-applicable. We are starting a project now using EEG, with the idea that low-cost, gaming EEG sets could be used to improve learning. If we can show that the signal that we get out of the noise increases two- or four-fold, then it might be useful for people to put this gaming EEG cap when they start learning. A third line of research that we're working on has to do with finding out whether there are neural signatures of individual fact-learning capabilities. Given what I said before about the forgetting rate being an intrinsic property of a learner, there may be other such signatures. Some colleagues at Washington State University in Seattle have shown that a certain power band in EEG resting-state recordings correlates with learning a secondary language. In our project, we are trying to see whether resting-state EEG activity correlates with certain properties of the rate of forgetting data that we collect. We're looking into whether different frequency bands correlate with the rate of forgetting. The general idea is that certain frequency bands are associated with hippocampal function and getting these signals would suggest efficient hippocampal functioning associated with a lower rate of forgetting. Finding such a neural signature would show that what we measure in this kind of applied and pragmatic system has a very close link to something that we would measure in fundamental neuroscientific experiments. That would mean that we don't only have a pragmatic explanation in terms of our model being able to predict how people learn, but also a functional explanation of how it would happen in the brain.

How do you see SlimStampen evolving?

What I didn't expect at the beginning is how happy I would be visiting a high school where they use SlimStampen, and seeing that the students are actually enthusiastic about something that we've made. It's great to get a paper accepted, and it's great to have all sorts of academic achievements, but that can't really be compared to knowing that there are pupils that are
Suddenly, you realise that it’s a specific art to generalise the kind of experiments that we do in the labs to a system that can be used broadly.

We’re setting up these online versions of SlimStampen. There are a lot of challenges involved in that. It’s not easy to set these things up. We have a very good collaboration with Noordhoff publisher of secondary school educational materials. There are half a million Dutch students that have access to their system which is based on SlimStampen. Not all of them are using it, of course, but the ones that do use it keep coming back to the system, and that’s just very nice to see. My goal would be to make it available for more people. At the moment, any teacher at RUG can create SlimStampen units in the Nestor environment, and many teachers have indicated that they are very interested in it. However, the hurdle of actually getting the data in is substantial for many. I’m not really sure how to solve this problem. I can relate to this problem being a teacher myself. There are a lot of great initiatives, but they all cost me time. In that sense, I think it would be great if we could set SlimStampen up in such a way that students could help teachers with creating the materials to be uploaded. Another option is using the online version of SlimStampen where people can create their own materials, so that if someone created a unit, it is automatically open for everyone. A different way of sharing materials through the online version would be providing the person who has created the unit an unique url, which can be shared with others. Another caveat with setting up such systems is the need to check the validity of materials that are being posted. The best solution remains having students create lists of materials, which would subsequently be uploaded by teachers.

What are the challenges of transferring a product such as SlimStampen from the lab into broad use?
The Noordhoff collaboration wasn’t problematic because SlimStampen was embedded in their online system. We helped them develop their online system in such a way that it adheres to the SlimStampen equations and principles. With the website version, there are, of course, issues associated with what I have said before, like materials that you don’t want on such platforms, and issues about copyright and privacy. Suddenly, you realise that it’s a specific art to generalise the kind of experiments that we do in the labs to a system that can be used broadly.

What type of feedback do you get on SlimStampen?
We get two types of feedback. Some students hate it, and some students love it. That’s also what we get from high schools. For example, in the case of a student who is already really good at English, every time they would start to learn vocabulary, the system will start out with a pretty low estimate of their learning strength. Some good learners find learning with the system a bit boring because it takes time for the algorithm to estimate their forgetting rate, resulting in presenting materials they may already know too often and leading to increased study time. We’re now improving the algorithm to make it more sensitive to high-performing learners. The other type of feedback is that some students truly love the current version, and it seems to be nicely aligned to their current needs in studying. I think that if you get feedback about the two ends of the normal distribution, you’re probably doing pretty well. The fact that we see students coming back to the system must mean that they find it useful.

How do you see the role of e-learning in education?
I hope that e-learning and other changes in educational systems will only make it better. I hope we can use e-learning to make learning more attractive and make students more involved. But you need to define the components of e-learning in order to be able to answer this question. I think that e-learning definitely has a place in any educational program, because it can provide adaptiveness even if you have hundreds of students. At the same time, there is a lot to be gained by getting classes or workgroups from motivated, interested and interesting teachers. It’s the same way with reading a book. We can have a book about a certain topic that’s just fascinating, even though the topic may seem boring to some. It has a lot to do with how the material is presented. A combination of good teachers and e-learning is probably the best way to go. The first step we can take is to use e-learning for those things that are easily automatised, like fact learning, or math tutors. In order to transfer passion and interest you need to have very good writers and authors of e-learning materials, or you need to have actual people involved. Even if you have very good writers, it still may be much nicer to attend a lecture. In education, it’s very important to have a direct experience with interaction and communication.

BY VALERIA CERNEI
PHOTOS BY SANDER MARTENS AND PETER VAN DER SIJDE
Philosophy & Neurosciences: An interview with Dr. Felipe Romero

Dr. Romero is Assistant Professor in the Faculty of Philosophy at the University of Groningen. He holds an interdisciplinary Ph.D. in Philosophy, Neuroscience, and Psychology from Washington University in St. Louis. He has been a postdoctoral researcher at the University of Tilburg and the University of Turin. He has organized the “Perspectives on Scientific Error” workshop series, which had its second iteration in Groningen this fall. His research interests are in philosophy of science (especially cognitive science) and social epistemology with a recent focus on the replicability crisis in science.

Welcome Prof. Felipe Romero. To get a closer insight into your persona, can you please tell us where does your interest of Philosophy and Neurosciences come from? What are the questions that you want to answer?

Since very early in my studies, I had an interest in various fields. As an undergraduate (in Bogota, Colombia, where I am originally from), I studied computer science and philosophy. When I decided to pursue an academic career, it was clear to me that I would do interdisciplinary work. When I moved to the United States to do my graduate work, I took courses in Neuroscience and Psychology, and I became interested in two sets of philosophical questions. One set of questions concerns the connections between the multiple disciplines that fall under the umbrella of “cognitive science.” One way of describing what these disciplines do is to say that they investigate different “levels,” e.g., a social level, psychological level, a neurological level, a biological level, and so on. I’m interested in understanding how these different levels fit together, whether reality is layered, or the talk of levels is only a useful fiction. The second set of questions concerns the “social epistemology of science,” that is, the study of the relation between the social structure of science and scientific progress.

As a teenager, philosophy for me was about reflection about who I am and what the world around me was, and trying to understand it with questions and discussions to expand the limits of my knowledge without using any tools. Even if science and philosophy try to expand our knowledge, I have the preconception that philosophy can go further in thinking because it doesn’t have the limitations of tools or computational analysis that scientific methodology requires. Do you agree? And, how is philosophy of neuroscience done?

There are many different views about what philosophy is and how it should be done, and even within the same philosophy department, you will find people who have very opposite opinions on the matter. In my view, philosophy of science is best done in an empirically-informed and formally-grounded fashion, and this perhaps makes philosophy of science less “free” than the more traditional branches of philosophy. The empirical constraints are essential if you are doing philosophy of neuroscience: for instance, if you want to understand what a good explanation in neuroscience is like (a classic problem in the philosophy of neuroscience), then you need to pay close attention at how the tools and methods of neuroscience work. In this respect, being in an environment in which we can interact with scientists is great. At the same time, if you want to express your philosophical ideas rigorously, you will benefit significantly from using formal tools (e.g., mathematical and computational models). In this approach to philosophy, you can still be highly creative.
An important tradition in philosophy of science regards science as self-corrective and the scientific record as generally trustworthy. For this tradition, error is exceptional and not a philosophical but a practical problem. But the replication crisis shows that this tradition is perhaps too optimistic, at least when it comes to some subfields in the social, behavioral, and biomedical sciences. These days, I study how the wrong sort of social structures (e.g., the publish or perish culture) lead scientists to produce non-replicable research and what kind of interventions we can do to address this problem and make science more replicable.

In neuroscience research, we need to use brain-related data to build models and answer our “scientific question.” As a psychologist, I am always afraid of becoming reductionist in my views and unknowingly contributing to an epistemology of academic exclusion towards the construct of mental health or cognition, and discriminating behaviors outside the “new normal.” How does philosophy of science address this issue in neurosciences?

It seems to me that the problem that you describe is one of those instances in which having a hammer makes you think that everything is a nail. This is a common concern that philosophers of science have about the use of some tools in many fields, not only cognitive science research. In the case of neuroscience, the imaging tools that neuroscientists have been developing to study the brain/mind in the past decades raise such a concern. These tools have given us tremendous insights, but given their success, we can get carried away and overestimate what they
can do. In general, looking at the brain exclusively through the lens of a single tool might lead us to dismiss as unimportant what we cannot detect with the tool. The lesson here from the history of science is to rely on methodological triangulation and evidence from various sources (e.g., multiple tools and even multiple disciplines) for building robust theories. Some philosophers of science try to understand how methodological triangulation works and when it is necessary. Nonetheless, about this topic, there are also philosophers who would say “well, it is true that not everything is a nail, but if you have a hammer, hit the nails.”

One of the fundamental topics in philosophy is ethics, and in the past, we could have philosophical discussions with thought experiments like the trolley problem. Today, neurosciences and artificial intelligence have become closer than ever, and with this, they have animated what used to be a metaphysical experiment. I am referring to self-driving cars and the creation of their AI algorithm to “decide” who lives or who dies. Could we say that from a computational neurosciences point of view the AI algorithm tries to mimic the moral decision of an ethical person to “script” and model such attributes?

As an outsider to these debates, when I hear that AI researchers are trying to solve problems like the one you describe in self-driving cars, I experience both curiosity and concern. My curiosity comes from me being enthusiastic about the power of computational methods. But my philosophical concern is that there is a risk of not acknowledging that, at the end of the day, a human being is making the hard decisions. Take an example: should the car save as many people as possible or save its passengers when one course of action excludes the other? The question in the background is one that philosophers have struggled with for centuries: “what is the right moral theory?” This question does not have a technical answer. The system designer has to take a stance on the answer, and the system will reflect such a stance. Notice also that the designer’s position that the right thing to do is to build a system that would mimic real human behavior is a philosophical position that you can disagree with. (After all, a lot of work in moral psychology shows that we are inconsistent and susceptible to arbitrary contextual factors when we make moral decisions.) I believe that we shouldn’t conflate philosophical and technical problems. Even so, at the same time, I find the technical problem fascinating, and I am curious to see what researchers will develop.

With that last question, we have finished our interview. Professor Romero, I thank you for enlightening me on how significant the epistemologies are in neurosciences and for updating my view on how philosophers work: from a picture of thinkers debating in a contemporary agora, to using complex mathematical computations and empirical models as exemplary evidence to deliberate, analyze and critique the making of scientific knowledge. A refreshing look into a new kind of philosophers that are undertaking the oldest question of human kind, about meaning and logic.

For more information about Prof. Romero’s work, you can visit www.feliperomero.org.

You can contact Prof. Romero at c.f.romero@rug.nl.

By Sebastian Balart Sanchez
From the boardroom

The next BCN Winter Meeting will take place in Enschede on Thursday, February 7, 2019 and will be organised by Bart Koopman from the University of Twente together with the BCN Office. In the morning, there will be presentations by our colleagues from Twente. The afternoon is reserved for BCN poster presentations from the BCN PhD students and BCN Research Master students, several lab tours and a keynote lecture by Richard van Wezel, professor of visual neuroscience at the Donders Institute for Brain, Cognition and Behaviour in Nijmegen and professor of neurophysiology at the Technical Medical Centre of the University of Twente.

Within the framework of U4, a collaborative network consisting of the Universities of Ghent, Göttingen, Groningen, and Uppsala, Erik Boddeke, Maarten Postma, Jochem Mierau and Michiel Hooiveld visited Ghent on October 19 to discuss, among other issues, the creation of a U4 cluster Public Health. This initiative fits in well with the recent establishment of the Aletta Jacobs School of Public Health at the University of Groningen and the University Medical Centre Groningen. During the next U4 meeting in Göttingen on November 22 and 23, Erik Boddeke will look for additional Public Health partners in Uppsala and Göttingen. The main topic of the meeting, however, will be the creation of a so-called European University involving the members of U4. The EU expects a total of 30 applications, six of which will be given a grant. The status of European University would be particularly beneficial to the BCN Master programme.

Robert Schoevers and Michiel Hooiveld have talked with members of Campus Frýslan, also known as the eleventh Faculty of the University of Groningen, about future collaboration, including joint presentations in Leeuwarden.

In early 2019, Berry Kremer will resign as director of BCN-BRAIN. Iris Sommer will be his successor.

BY FRANS ZWARTS
PHOTO BY ELMER SPAARGAREN
Ever since I was little, I was fascinated by the working mechanisms of everything around me. As a child, I wondered why the butterflies always sat on that one bush while there were so many others and why people started crying when something happened they were really happy about. When I got older, I became interested in the underlying mechanisms of psychiatric diseases. After my bachelor’s in Psychology, I started the BCN Research Master. For my master’s thesis, I worked together with Marie-José van Tol and Marieke van Vugt on a very interdisciplinary project. We examined whether thought content can be manipulated using stress and positive affect induction techniques in individuals varying in susceptibility to negative affect. As a positive affect induction technique, participants were asked to fantasize about a positive belief they could hold. Interestingly, the positive affect induction technique both increased positive affect and decreased negative affect. Additionally, the content of thoughts changed after positive fantasizing compared to after stress induction. As a PhD student, I am now extending this project investigating how different potent clinical techniques (i.e. preventive cognitive therapy, mindfulness and fantasizing) affect spontaneous thought processes and their neural correlates in individuals vulnerable to depression. We combine cognitive neuroscience with clinical psychology to gain insight into the mechanisms of what is needed to alter depressive vulnerability. Driven by my curiosity, I will continue learning about working mechanisms of the things around me. As a new staff writer for the BCN newsletter, I hope to meet new people who can teach me something about the working mechanisms in their field of research.

To me, the human body is a beautifully crafted machine where every behaviour is an external manifestation of a biological process. I moved to Groningen from India, as a master’s student of the BCN program, in the hope of pursuing my career in the field of neuroscience. Working with underprivileged children for the last two years as a teacher got me wondering about how we are capable of learning new skills and storing information. Young children show tremendous plasticity, but I wanted to understand how nutrition and trauma could influence these cognitive processes. I am also interested in studying emotional regulation in the brain. Every day, we express myriad emotions to convey our thoughts and feelings. I want to explore the evolutionary significance behind empathy, apathy and role of emotions in mate selection. Ultimately, using my knowledge from my bachelor’s studies, I want to merge psychology and biotechnology to explore the cognitive mechanisms of the brain through a molecular perspective.

Apart from my academic interests, I enjoy discussing self-growth, evolution and theory of mind. I am also an advocate of health and fitness and enjoy long distance running and hiking. Through the newsletter, I hope to meet people from the BCN community that inspire and blow my mind with the amazing work that they do.
The book “Math for Scientists: Refreshing the Essentials” by Natasha Maurits and Branislava Ćurčić-Blake was born out of the need to explain mathematics in an accessible way to a broad scientific community, ranging from undergraduate students to junior scientists to professors. Both authors not only utilize their firm mathematical backgrounds (i.e. Prof. Maurits a mathematician and Dr. Ćurčić-Blake a physicist), but also provide tangible scientific examples that allow the reader to understand the concepts explained in each of the seven chapters that make up the book. The book is both didactic, as the authors include exercises, but also pragmatic, as the practical applications of these mathematical principles at the end of the chapter help to consolidate the learning objectives of each chapter.

The story about how the book was conceived takes us back to the BCN Mathematics course for Neuroscientists, which is given every two years to GSMS PhD students, specifically members of the BCN community. The chapters involve the topics presented in the course, including: 1) numbers and mathematical symbols, 2) equation solving, 3) trigonometry, 4) vectors, 5) matrices, 6) limits and derivatives, and 7) integrals. Each chapter is didactically constructed since the objectives are clearly stated in an introductory box, followed by the background context, continuing with a gradual immersion of the reader into the topic and finishing with the scientific applications of the concept presented. Each chapter not only progressively engages the reader but also reinforces each concept by providing examples and exercises. Each chapter ends with a glossary, a list of symbols introduced, an overview of the rules and equations, references and further reading, and, most importantly, the answer to the exercises.

This book serves as a refresher high school mathematics course, while at the same time it provides insight into the underpinnings of concepts that we use in our research, like principal component analysis or Fourier transform. Both authors provide further insight into their book in the following book review. The answers to the following questions are a blend of a series of conversations with the authors Natasha Maurits and Branislava Ćurčić-Blake.
What is the target audience for this book?
The initial target group was the PhD students at the Cognitive Neuroscience Center for whom the course was given to. However, as we started to plan for the book project, it was clear from the feedback of our colleagues that a reference book where one could easily look up a certain concept and within a few pages be able to refresh that concept would optimally extend its reach. The target audience of the book is as many scientists as possible, hence the name Math for Scientists and not math for neuroscientists. In other words, the target audience for the book is essentially people who know math but are not practicing it and will use it in their research.

What is the overall message of the book? How does the structure and design of each chapter deliver this message?
Each chapter starts with the basics and slowly builds up in complexity. Each chapter provides scientific examples that provide insight and aid the reader in further understanding the concept presented. The examples were chosen with the interest of the audience in mind. We chose broad and interesting examples, or at least what we considered our reader would be interested in. We tried to keep the bigger picture in mind, but always explained the concepts in different ways in order to reach a wider audience.

What are the strengths and weaknesses of this book?
One of the strengths of the book is how it is written. On one hand, the reader can read the book like a story where we take them along and progressively build on each concept. On the other hand, the book can be used as a reference book, where it is not necessary to take the course to use the book, since the reader can do the exercises and find the answers at the end of each chapter. The book is compact enough to serve as a quick reference book, but long enough to engage the reader in the story being told. Another strength of the book is the choice and length of the examples, as they put the concept in context and explain why certain mathematics are used in certain problems.

In an attempt to provide examples that were new, we stayed away from examples that have been used in other mathematics books for neuroscientists that use examples in electrophysiology, for example. Another book from the same editorial house, Mathematical Methods in Biology and Neurobiology by Jürgen Jost (2014), provides examples from molecular to evolutionary and ecological levels. While some might consider that the scope of the examples chosen might be a weakness of this book, in reality, the examples chosen reflect the decision-making process where some information had to be edited out. Another limitation of this book, due to the extension limits, is that concepts like wavelets and differential equations, which could easily be integrated into another chapter, could not be incorporated.

The chapters have a narrative perspective to them. What inspired you to tell a story in each one of these chapters?
One of the strengths of the book is that it takes the reader along. This is done by introducing the concept, then by providing examples and concluding with
problems that can be worked out and checked for each concept. Mathematics, from an applied mathematics point of view, can be seen as a toolbox. But it is only a good toolbox if you understand which tool to use for a specific problem. What this book attempts to do is to help the reader develop an intuitive understanding of why certain mathematics are used to solve certain problems. This book attempts to not only explain the “how” but also the “why” behind certain problems in science where mathematics serve as a tool to solve them.

What role do the illustrations and examples play in each chapter? How do they assist in the telling of the story?
The examples were chosen in different ways. Some examples we had been working with for a long time to explain concepts in our courses. Other examples were chosen because they fit very well the idea being explained, and other examples we went looking for them. While the examples and illustrations guide the reader through a story, the examples reinforce the knowledge refreshed or acquired. However, all of these resources are intended to assist the reader to grasp the concept by the end of the chapter.

In the chapter about equation solving, you mention that “solving an equation may be fun, if you look at it as solving a puzzle”. Could you further elaborate on this idea?
Looking at a complex equation or at complex integrals, such in mathematical or physics dynamics can be intimidating. That is why we propose an approach to break down one component at a time in these equations. People have different ways of solving a puzzle. While some like a more structured and generalized process and start by linking the edges, others start in the middle and work their way out. Essentially it is the same process, but a different approach. One of the consistent themes of this book is that different approaches can lead you to the same solution.

Concluding remarks
Beginning with the next course, tentatively scheduled for 5 February 2019 to 21 March 2019, the book will serve as the reference text for the course. However, the classes are tailored to the needs of the attendees, which provides a personalized and individualized learning environment. The book, as well as the course, are targeted at the entire BCN community. This book and course are designed for anyone who encounters math in their research. This book fills the gaps that time has eroded in our memory. Personally, this book explains some of the concepts that I use today but learned about 17 years ago. It serves as a safety net to a neuroscientist with a medical/biological background leaping into problems in neuroscience that require an in-depth understanding of math concepts.

> Solving an equation may be fun, if you look at it as solving a puzzle… People have different ways of solving a puzzle. While some… start by linking the edges, others start in the middle and work their way out. <
**Young women can change the World**

*‘Find what you love and let it kill you’*

Life is not about chasing the best job with the highest package. It is about enjoying the journey and the little things that make each day special. The academic field can be excruciatingly difficult with drawbacks in publishing and research, but what will keep you going is your motivation for your research project. I was fortunate enough to meet professors who inspired me with their work and passion, and I try to live by this philosophy that they taught me.

I grew up in Slovakia and lived in London for a few years. For my bachelor’s, I moved to France to study biology and physiology. During my time, I seized the opportunity to intern in Munich for three months. Through the Erasmus program, I also spent some time at the Roosevelt University Utrecht in Middelburg. All these experiences have shaped me into a true international person. For holistic growth, I believe it is important for cultures to intermingle.

The interdisciplinary aspect of the BCN Research Master was what attracted me to apply to the program. I like the flexibility the program offers through the three different tracks and the choice of electives in the second year. My main academic interest lies in neurodegeneration but I want to combine it with other fields like: neuropharmacology and sensory-neuroscience. After looking at the groups in UMCG and Zernike, I wanted to know what it is like to work with the people here and now I am eagerly looking forward to my minor thesis during which I will join the group of Ody Sibon and focus on the role of dDPCK enzyme in drosophila neurogenesis.

The broad variety of topics this program covers will help me narrow down a topic to research in the future. Moreover, I am interested in diverse interlays of the gut microbiome and the brain, and I want to use my background in molecular biology to collaborate with people from other fields. BCN is the perfect platform to do this as I get to interact with people from so many different disciplines. In addition, I am happy to work as a program committee representative and secretary of the student council since I can bring real impact to the program and education.

Apart from my academic interests, I enjoy cooking and painting. I sell jewellery with my boyfriend in a nearby town. I used to play professional handball for the Slovakia national team and even played in France at a national and international level. I am now a part of the Circle Tigers in Groningen, where I train and play matches every week. We are a team on the field and off the field, and we celebrate and organize dinners together. I try to keep myself as busy as possible and in the little free time I get, I like to travel with my friends and explore different cultures.

The only way I am able to balance work and play is to not think about how unbalanced my life is. When I am sad, an ice cream with friends can cheer me up. I have the support of friends and family and talk to them if I ever need anything. I do not know if my chosen path will lead to the academic or private sector. On one hand, the private sector pays better and has better equipment, but there are restrictions on the type of research you want to do. On the other hand, the academic field is more flexible and offers stability, which I want when I start a family. I also want the opportunity to grow up and inspire young minds, which I will get through the academic field.

One day, I hope to open a neuroscience research centre in Bratislava to provide similar opportunities to young minds that I received thanks to my supportive professors, mentors and family. Due to lack of proper facilities, many either have to move to other countries to pursue their careers or are unable to due to financial limitations.

The term “hysterectomy” is used to describe the removal of the uterus. However, the word is derived from “hysteria” that was once believed to be a mental disorder solely attributable to women characterized by extreme excitability and emotional overflow. The source of overexcitement and excitability was believed to be the uterus. We now know that this is not true but the term still remains. As a feminist, I could not let this happen. With the guidance of my Professor, Ger Rijkers, I wrote a letter to a journal and I am happy to say the article is published in the journal: Frontiers of Womens Health. This experience taught me to fight for the things that matter to you, even if it is small. That is what I will strive to do everyday.

*‘Always question, always wonder’*

**BY NAD’KA MAJERNIKOVA**
Mindwise: Trip your mind

The 2018 Mindwise poster is out! It’s intended to stimulate a sense of wonder about the beauty of Psychology and the workings of the human mind, manifest this wonder in an image that is worth placing on your own wall, and promote a community of local artists. Last year, Mindwise released its first poster, illustrating the neural underpinnings of human behavior. This time, the poster’s trippy theme combines more than twenty perceptual illusions. The poster’s artist is Douwe Dijkstra, a graduate of the Minerva Academy of Visual Arts in Groningen.

Can you discover all the illusions on your own? They are not all easy or as obvious as they first appear! Click through to see the poster in its full splendour, see how it was made, and get a copy for yourself.

http://mindwise-groningen.nl/poster/
The art of science: Kinetic art, a cornucopia of sensory inputs

Lights flashing in rhythmic patterns, rings dancing as cords vibrate, optical illusions that fool your vestibular system and make you think twice if the room is moving. Kinetic art places not only motion but also how we perceive the world through all our senses at the center. The exhibition “Action ↔ Reaction” at the Kunsthal in Rotterdam, now open until 20 January 2019, presents the work from some of the most famous artists in the kinetic art field. The exhibition celebrates 100 years of kinetic art by assembling artwork that stimulates the viewer visually as well as through their other senses. The exhibition is divided into sections titled: cosmos, force field, instability, light, motion, non-materiality, radiation, rhythm, space, structure, vibration, and vortex. The exhibition begins with the phrase, “the spectator is part of the work of art, because it cannot be experienced without a viewer” (Victor Vasarely, 1955). The interaction between the viewer and the art piece is a central theme of this exhibition.

The artist captures not only motion but also recreates it, and, by doing so, immerses the viewer into experiencing motion itself. It is also very interesting to see how a natural phenomenon like light becomes the subject of the piece of art presented to the viewer. Throughout the exhibition, the viewers are interacting with the art pieces, not only visually but also perceptually through all the senses. Kinetic art stimulates the aesthetic experience and bombards the viewer with sensory inputs that make the imagination run wild. Kinetic art is a cornucopia of sensory inputs. In classical mythology, Amalthea, the foster-mother of Zeus, is represented as a goat. In this mythical tale, Amalthea breaks off one of her horns and fills it with flowers and fruits. Taken together, the horn is regarded as the symbol of inexhaustible riches and abundance. As the mythical tale of Amalthea, the exhibition “Action ↔ Reaction” is filled with inexhaustible riches of sensory inputs.
On a personal level, I was taken by how most people interacted with the art pieces, at times forgetting that art was in front of them. It was very interesting to see people interact with what stood in front of their senses. This interaction was more than the usual introspective exercise that most experience at a typical art museum. At times, the exhibition reminisced of a carnival, where children were both amazed and confounded with what was in front of their eyes. It was pleasant to see so much life in a place where solemnity is usually the norm. The exhibition not only challenges our senses but also invites the viewer to reflect on what it is really in front of their senses.

■ BY JAIME MONDRAGON
■ PHOTOS BY SANDER MARTENS
The Art of Science

Doing science requires a lot of creative thinking, and thus a creative mind. We noted that for many scientists creativity doesn’t stop at designing clever experiments or writing exciting papers. Take Tess Beking, for example, who has not only written and defended her dissertation, but also did all the illustrations herself. Pretty awesome, don’t you think?

“*You can’t connect the dots looking forward, you can only connect them looking backwards. So you have to trust that the dots will somehow connect in your future*” – Steve Jobs
NIC changes its name

On September 26, 2018, the Neuroimaging Center (NIC) celebrated its 15th anniversary with a symposium at DOT, which featured four world-renowned speakers. An audience of about 150 people enjoyed the lectures as well as the cake. Former director Gert ter Horst was given a sculpture by the new director André Aleman. Last but not least, André revealed the new name of the research facility: the Cognitive Neuroscience Center (CNC). The new name indicates that the center offers a range of techniques (e.g., EEG, TMS, microTMS, tDCS, NIRS, eye-tracking, pupil dilation deconvolution) and expertise to the BCN research community that goes beyond just fMRI.

■ PHOTOS BY SANDER MARTENS
On September 27th, the BCN PI meeting, organized by Jacolien van Rij and Simone Sprenger, took place. This year’s meeting had the theme “Let’s talk: BCN research on language and the brain”. Speakers consisted of Etienne Gaudrain and Terrin Tumati (UMCG), Roel Jonkers (Faculty of Arts), Jelmer Borst and Rineke Verbrugge (Faculty of Science and Engineering), Sebastiaan Mathôt (Faculty of Behavioural and Social Science), and Carel ten Cate (University of Leiden, biology) as keynote speaker.

PHOTOS BY MICHIEL HOOIVELD
Dear Fellow BCN students,

On Thursday, September 27, 2018, the BCN PhD Council organized a workshop about how to introduce your ideas in a well-crafted manner with the technique “Elevator Pitch”. An essential skill that offers the possibility to connect with others in a short amount of time.

During the workshop, the structure of an elevator pitch was discussed, and the opportunity for the attendees to craft and practice their own ‘elevator pitch’ in front of the participants was provided. The workshop objective at the end was how to transform your scientific speech to establish a powerful introduction that connects with the audience.

For a greater appreciation of the topic, we had a word with the speaker Rodrigo Moraga, who is also a PhD candidate at the UMCG: “Communicating science is a very important skill that we scientists should all take into account. It is very likely that at some point of our career we will have to be able to tell people about what we are doing. This can be very useful when you are applying to a position or a grant, patenting a product, and for many other reasons. One of the main goals of this workshop was to show people that you are able to think outside the box, and you are able – with practice – to create a clear/short message to make it easy to understand”.

BY SEBASTIÁN BALART
PHOTOS BY STEFAN HUIJSER
The Technical Medical Centre at the University of Twente

What’s in a name?
The University of Twente has a very distinctive slogan: “High Tech, Human Touch”. It shows that not only is the technology considered important, but also the context in which technology is applied. One of the most important application areas of new technology is the health domain. However, as it happens, the university does not have a Faculty of Medical Sciences. Although the university has a lot of collaborations with various hospitals, and the hospital in Enschede (MST) is one of the largest non-academic hospitals for top-clinical care in the Netherlands, there is not something like a University Medical Centre. To focus our efforts in this area and to stress the importance of health-related education and research for the university, we developed the Technical Medical Centre, which is already being abbreviated often as TechMed Centre.

Facts and figures
There are three healthcare related educational programs at the University of Twente (BSc and MSc level): Biomedical Engineering, Technical Medicine and Health Sciences. The programs focus on roughly the same health domain, but from different perspectives and starting points: engineering, medicine and society respectively. These programs are therefore quite complementary. Together, they have about 15% of the total student population. Furthermore, we train about 500 healthcare professionals each year in post-graduate and lifelong learning programs, and this number is increasing rapidly. The healthcare related PhD and PDEng programs are located in the faculties and the Twente Graduate School.

All five faculties of the university contribute to research in the health domain. In recent years, about 40% of all externally funded research had a focus on healthcare, and about 50% of the University of Twente’s spin-off companies are dedicated to healthcare. Often, the most interesting research is done at the cross-section of established disciplines. So the trick is to bring people together and “seduce” them into working in multidisciplinary teams. This means that we encourage looking across the boundaries of faculties. By the way, this multidisciplinary approach is already implemented in the project-based educational system of the university, the so-called TOM-model. So for our students, this comes naturally.
The TechMed Centre is designed to bring research and education together, to stimulate the exchange of expertise and to invite external parties to join our efforts.

**The TechMed Centre**
The TechMed Centre aims to improve healthcare by personalised technology. In order to achieve this, we provide education and training, we execute research and development and we stimulate innovation and collaboration. The new centre provides modern engineering based educational programs covering the healthcare value chain and addressing societal needs, delivering future professionals needed for innovation in healthcare.

The core of the research is formed by the former MIRA institute, complemented by several new relevant research chairs. Together, we provide scientific impact in the domains of Medical Physiology, Biomedical Imaging & Diagnostics, Bioengineering Technologies, Biorobotics & Health, and Wellbeing & Technology. With these domains we deliver knowhow and technology for healthcare. We aim to make a social impact by improving personalised diagnosis and treatment, thus increasing the quality of life and enhancing independent living.

For this purpose, the TechMed Centre has a strong focus on actually implementing new technological solutions in healthcare. We do so by stimulating innovation and collaboration. We foster partnerships and collaboration within the regional TechMed Twente Ecosystem up to the global hub-and-spoke network with (academic) medical centres and the medtech industry/SME’s. We connect real medical challenges to the expertise and knowledge of the university’s research groups in order to develop new solutions for patient care, in close collaboration with the right partners.

**Future perspective**
Often in politics the strategy is to divide and rule. Here we try to do the opposite: combine and rule. By physically placing students and research at the same location, we make them benefit from and stimulate each other. The TechMed building (see pictures) will house lecture theatres and project rooms, together with the offices for the TechMed staff. There will be shared research facilities, like imaging equipment (MRI’s, CT’s, etc.), e-Health and robotics labs, equipment for training surgical skills (e.g. endoscopy, operating theatre of the future, also for practicals and the development of new equipment), with plenty of room for PhD students to have a working place and to share experiences.

We expect the TechMed building to become operational during the summer of 2019, and hope to have a royal opening somewhere at the end of 2019. In the meantime, the TechMed Centre organization is already functioning, as shown on the website if you google it. If you have research ideas where we may be able to contribute, please let us know!

■ **BY BART KOOPMAN**
(BCN BOARD MEMBER)
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, and organize social activities, such as borrels (drinks) and the pub quiz at the BCN Retreat. We are always happy to hear from you about what kind of educational events or activities you want. Also, when you have suggestions for new activities, for speakers you want to attract (for seminars or master classes), or in case of general concerns about current policy, don’t hesitate to send us an email: bcnphdcouncil@list.rug.nl.

Currently, we are working on providing more transparency about the statistics requirement of your PhD training. We have created a list of courses that you can follow as an alternative to the BCN Statistics course. This list will be provided to you shortly.

We are also working on the next BCN Lunch workshop. This time, we will invite an expert on how to properly use graphics in papers and posters. We will make sure that the BCN Lunch is in time for the BCN Winter Meeting, so you can use this workshop to prepare your poster for the winter meeting.

See you at our next activity!

Your PhD Council.

Stefan Huijser (Chair)
Artificial Intelligence &
Cognitive Engineering, FSE

Nafiseh Ghazanfari
Nuclear Medicine and
Molecular Imaging, UMCG

Mayra Bittencourt
Villalpando
Neurology, UMCG

Sebastián Balart Sánchez
Neurology, UMCG

Rodrigo Moraga Amaro
Nuclear Medicine and
Molecular Imaging, UMCG

Mila Roozen
GELIFES – Groningen Institute for Evolutionary Life Sciences, FSE
> PHD AND OTHER NEWS

BCN Poster Presentation
The BCN Poster Presentation will take place on February 7, 2019 in Enschede! The course is available in the online course registration system, see link below, for those who would like to participate with or without a poster. The BCN Poster Presentation is embedded in the BCN Winter Meeting.

BCN Winter Meeting
The BCN Winter Meeting will take place at the University of Twente on February 7, 2019! BCN organizes the Winter Meeting every year in the surroundings of one of the participating faculties. This time, the University of Twente, also participating in BCN, will open her doors for BCN members, and will give them the possibility to go on lab visits and guided tours. Four researchers from the University of Twente will give presentations on Exoskeletons, Neuromodulation and EMG-driven hand orthosis. “Brain on a chip” is the intriguing title of the final presentation. Please block the entire day in your agenda. Busses will bring you to Enschede!

Hora Finita
Did you already see the new facelift of Hora Finita? It looks nicer, and we hope that the changes have made it better.

Statistics
The BCN PhD council drew up an inventory of statistics courses offered by the GSMS and other graduate schools, and courses in the curriculum of master’s programs. The list is almost finished; it will be made available to you by mid-December.

Agenda BCN Activities
February 7, 2019
BCN Poster Presentation, BCN Winter Meeting in Enschede
March 21 & 22, 2019
BCN Retreat
Odoorn

Course application: http://rug.nl/gsms
Please check the website for more detailed information.

■ BY DIANA KOOPMANS
Life hack for troubleshooting or Zen of Sorting

It was one of those days when I decided to write at home instead of the office, opting for the comfort and cosiness of the sofa while drawing inspiration from others’ work. At least I planned it that way, except it turned out differently.

I was sitting and staring at my article for more than half an hour already, and my mind was blank. Well, it wasn’t literally blank. I had millions of thoughts, but I had no clue how to proceed with the review. It just happened. First I was writing, and then – bam! – I got stuck at a dead end, or rather in the informational mess. I lacked order and regularity – thoughts were swarming randomly and I saw no way to put them nicely together.

There are tasks that you don’t feel comfortable with, and writing reviews is one of those for me. For some people it is natural to structure various sources of knowledge and to derive clear and critical conclusions from the bunch of articles. I get stuck quite often, seeking out order and structure. Not a very pleasant feeling. Have you ever found yourself in a comparable situation? Have you found a solution for it? I did. And it is in our brain.

I stopped staring at my laptop screen and made myself some tea. It was time for me to put something physical, tangible in order. Luckily, I had a bunch of stuff from my post box that I had to sort out. I spent the next five minutes enjoying sorting out this bunch in a calm and relaxing manner. I separated paper and plastic covers, dividing everything into potentially useful and spam piles. I finished my sorting activity as well as the tea with the satisfying feeling of order, and returned to my work. The decision was already there, thoughts were lined up and it was clear how to rewrite those problematic parts of the review.

The way our brain stores information is remarkably complex. We collect experiences, and when we create something new, we are actually smashing the bits and pieces of previous experiences together. Independently of the preserved experience, be it sensation of fear, experience of a yellow colour or taste of the chocolate cookie, in its essence it is all the same – an association between a group of neurons: one fires and others follow creating a certain pattern. When this synchronous firing is repeated enough times to bind neurons together (if one is triggered, the whole company fires), we create a memory.

Our skills are no exception. Moreover, many of them bear “universal nature”, applying both to physical and mental experiences. You can be lost in a physical forest or in your thoughts, or get tired of multitasking, whether carrying out different physical actions (making food, cleaning, talking on the phone, watching over a kid) or mental tasks (checking emails, facebooking, writing code, surfing for references).

Thus, to help myself out I used that knowledge. I needed to systematize things – I activated the neural network that is responsible for the skill. The activated network will automatically get involved in the task you need to get done. You can try it out for many things! Want to see the bigger picture? Climb a mountain/building with a view. Do you need to make a big and important decision? Start with a small one, change your hairstyle. :-)
Martijn Wieling: new professor by special appointment of Low Saxon/Groningen Language and Culture

On 1 July 2018, Dr Martijn Wieling was appointed professor by special appointment of Low Saxon / Groningen Language and Culture. Wieling, born in Emmen in 1981, is also an associate professor in Information Science at the University of Groningen. In his new role, he will be devoting one day a week to researching Low Saxon in general, and the variants of Low Saxon spoken in Groningen in particular. The appointment is initially for four years, and is based at the new Centre for Groningen Language and Culture (CGLC) at the Faculty of Arts, to which Jan Glas, Theo de Groot, Henk Scholte, Patricia Ottay and Goffe Jensma are also affiliated.


The Young Academy

Marie José van Tol has been admitted to the Young Academy, part of the Royal Society (KNAW). The Young Academy is a dynamic and innovative group of top young scientists and scholars with outspoken views about science and scholarship and the related policy. It organises inspiring activities for various target groups focusing on interdisciplinarity, science policy, and the interface between science and society. The Young Academy has fifty members. All are between 25 and 45 years of age and received their doctorates less than ten years before their appointment to the Academy. They represent a broad spectrum of scientific and scholarly disciplines and work at Dutch universities and a wide range of research institutes.


Researchers Hanneke Wigman and Marie José van Tol in VIVA400

BCN-BRAIN researchers Marie José van Tol and Hanneke Wigman are both nominated for the #VIVA400. This is a list of 400 inspiring women who excel in their fields, which are separated into six different categories. Marie-José and Hanneke are nominated in the “Clever Minds” category.

University Center Psychiatry (UCP) and Cognitive Neuroscience Center (CNC) on television

Robert Schoevers and Marie-José van Tol were both featured on the television show “Dokters van morgen” (“Tomorrow’s Doctors”), talking about how ketamine can be helpful in treating depression.

https://www.umcg.nl/NL/UMCG/Afdelingen/Universitair_Centrum_Psychiatrie/Nieuws/Paginas/dokters-van-morgen.aspx

Two NWO ORA projects faculty GMW

Elkan Akyurek (Psychology) and his international research team is receiving a contribution from the Open Research Area for the Social Sciences funding program (ORA). ORA is an European programme in which Dutch NWO participates. A total of 17 million euros was awarded to sixteen research teams, including fourteen teams from the Netherlands. With this programme, academics in Europe and Japan can collaborate on various projects in the social sciences.


Computational linguistics too cautious in sharing research data and self-written software

Researchers in computational linguistics are insufficiently willing to share their research data and required self-written software and commands with other researchers. This was the conclusion of RUG researchers Martijn Wieling, Josine Rawee and Gertjan van Noord in a study into all scientific papers published between 2011 and 2016 as full papers of 8 pages in the Proceedings of the ACL Annual Meetings (almost 400). This situation has improved over the years. While data was shared relatively often (2011: 76%, 2016: 86%), computational linguists were still reluctant to share their developed, self-written software (2011: 33%, 2016: 59%).
Cool links

> In a parallel universe, Dr. Mantleray (Netflix’s Maniac) invents an experimental treatment consisting of only three pills that can fix a broken mind and replace traditional therapy. Pill A singles out a person’s most significant trauma, pill B analyses the person’s defence mechanisms, and pill C promotes confrontation and acceptance. In this universe, MDMA together with therapy might be a new treatment for PTSD. https://www.inverse.com/article/49274-is-there-a-real-life-version-of-the-experiment-in-maniac

> A different, though no less science fiction-y approach to potentially treating PTSD is being developed by scientists using a camera to identify neuronal ensembles coding for a specific memory. This technique could help in either silencing a traumatic memory or reviving a lost one. https://www.scientificamerican.com/custom-media/mount-sinai/watching-memories-being-made/

> The majority of individuals who go on to develop a neurodegenerative disease have not inherited it from their parents. New findings shed light on how their disease also originates in embryonic development. https://neurosciencenews.com/genetic-mistake-alzheimers-10026

> Luckily (or unluckily), what is around us is just as important as the genes we are made of. https://tmrwedition.com/2018/10/16/its-the-environment-stupid/

> The human intestine is home to up to 500 bacterial species. Recently, the microbiota has been implicated in mental and neurodegenerative disorders. Via the gut-brain axis, the gut seems to be doing much more than just helping us follow our instincts. https://www.straightfromascientist.com/the-microbiota-gut-brain-axis-from-eubiosis-to-dysbiosis-and-back-useful-biomarkers-for-clinical-treatment/
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!
ORATION J. VAN DER NAALT

T I T L E

The consequences of traumatic brain injury in perspective

C H A I R

Neurotraumatology

F A C U L T Y

Medical Sciences

D A T E

September 18, 2018

The impact of traumatic injury on daily living is high, as more than 50% of patients have an impairment that interferes with the resumption of work and daily activities. Each year, 85,000 people are admitted to the hospital with traumatic brain injury. Traumatic brain injury is associated with high social costs and healthcare related costs.

The main field of interest of the chair of “Neurotraumatology” is the prediction of outcome after traumatic brain injury with advanced neuroimaging in order to develop early interventions to prevent incomplete recovery. The role of the frontal cortex for development of behavioral disturbances and executive dysfunction is another research focus.

The topic of Neurotraumatology fits within the UMCG themes of Healthy Ageing and Acute Care.

Often the consequences of traumatic brain injury are underestimated, in particular for mild traumatic brain injury. The challenge for research is to view the consequences of traumatic brain injury from a multilevel perspective. Cellular injury causes brain dysfunction and the integrity of brain networks determines whether patients experience complaints. Personal factors determine whether adequate reintegration into society is possible. In a multicenter cohort study (UPRONT) initiated by the UMCG, not only the extent of temporarily brain network dysfunction as depicted by fMRI was found to be important for outcome, but also personality characteristics like coping and emotional distress.

Regarding the care for traumatic brain injury, it is recognized that patients with behavioral impairments are in need of appropriate care; this category of patients fail to integrate into community since there is lack of adequate care in the current health system. Multidisciplinary care and research is necessary for the early identification of at risk patients in order to provide personalized treatment aimed at improving recovery.

ORATION W. VELING

T I T L E

A different world - psychosis in the social context

C H A I R

Psychosis in the social context

F A C U L T Y

Medical Sciences

D A T E

October 2, 2018

Research on the social context of psychosis is urgently needed to improve treatment of psychotic disorders and to prevent psychosis in youth. Psychosis cannot be understood nor treated well if the social context is not taken into account. The social context has different levels, including living environment, family, friends, sociocultural group and society. Wim Veling investigates the impact of these levels on risk, development and course of psychotic disorders. He uses Virtual Reality as a tool to study social interactions of people with psychosis in complex, dynamic social environments. Also, he is searching for different social contexts for psychosis research, such as Schilderswijk in The Hague, east Groningen, South Africa and Iran. In these settings, the influence of extreme social circumstances can be investigated. Finally, the first signs of emerging psychotic disorders develop in adolescence. In order to prevent psychosis, early identification and care should be delivered in the social context of adolescents and young adults. Based on this research, Wim Veling develops new treatments for (the prevention of) psychosis, such as Virtual Reality therapy. During the oration, the audience collectively experienced the power of Virtual Reality, see https://bit.ly/2y98FHz.
The two sides of the coin of psychosocial stress: evaluation by positron emission tomograph

PHD STUDENT
P. Kopschina Feltes

THESIS
The two sides of the coin of psychosocial stress: evaluation by positron emission tomograph

PROMOTOR
Prof.dr. R.A.J.O. Dierckx

COPROMOTORS
Dr. E.F.J. de Vries
Dr. J. Doorduin
Dr. C.M. Moriguchi-Jeckel

Faculty
Medical Sciences

Major depressive disorder (MDD) is considered to be one of the most burdensome diseases to society, due to the high healthcare costs, loss of productivity, high rates of disability and suicide. It affects approximately 350 million people worldwide, with a lifetime prevalence of 15-20%. Despite considerable efforts, the complete mechanisms underlying depression remains unknown. A recent hypothesis implicates involvement of neuroinflammation in MDD. One of the main risk factors for the development of depression is stress. Therefore, further investigation of the biological pathways related to stress and neuroinflammation might help to understand this disease. In the present study, we observed that activation of the stress system in the well-validated social defeat animal model could induce (neuro)inflammation and depressive symptoms. We also demonstrated in this animal model that a stressful event early in life had a significant impact on the individual behavioural and inflammatory response on a recurrence of the stressful situation later in life. Moreover, we found that exposure to winning aggressive confrontations in the social defeat animal model alters receptors in the brain linked with the pleasure/reward system, suggesting a possible habit-forming effect that increases violence and aggression. In our studies, positron emission tomography (PET), a non-invasive functional imaging technique, was applied to investigate the possible pathways underlying MDD and aggression. Since the same methodology can be applied in humans, PET has the potential to provide useful information regarding alterations in the brain of depressed and aggressive patients and thus, contribute to future personalized diagnosis and therapy for patients. Keywords: PET, major depressive disorder, aggression, stress, neuroinflammation.

Paula Kopschina Feltes (1989) studied pharmacy at the Pontifical Catholic University of Rio Grande do Sul, Brazil. She did her research in the Department of Nuclear Medicine and Molecular Imaging at the University Medical Center Groningen (UMCG). She now works as a staff advisor and project manager in the same department. Her research was financed by the Abel Tasman Talent Program (ATTP) of the UMCG. She was promoted on July 11, 2018.

Feasibility of cardiovascular population-based CT screening

PHD STUDENT
M. Vonder

THESIS
Feasibility of cardiovascular population-based CT screening

PROMOTORS
Prof.dr. M. Oudkerk
Prof.dr. R. Vliegenthart

Faculty
Medical Sciences

The prevalence of cardiovascular disease (CVD) is high in The Netherlands, with an annual incidence of 123,200 (only coronary heart disease). There is an urgent need for large-scale population-based randomized-controlled trials showing the impact of CVD screening followed by treatment in high risk individuals, according to their CVD risk based on classical factors and/or based on coronary calcium quantified with CT. The goal of CVD CT screening is to determine the amount of coronary calcium of an individual and to stratify individuals with high levels of coronary calcium, and to reduce the morbidity and mortality by offering these individuals treatment at an early stage to stop or delay progression of subclinical CVD.

One of the challenges in CVD CT screening is to secure the validity of coronary calcium quantification to perform proper risk stratification on one hand, while screening large populations at a radiation dose as-low-as-possible on the other hand.

The results described in this thesis show that cardiovascular population-based CT screening is feasible with a standardized and validated imaging biomarker (in this case coronary calcium) protocol. This protocol was applied in the ROBINSCA trial in which 13,000 participants were screened. Combining screening protocols, optimizing scan parameters and using latest generation of dual-source CT can significantly reduce the radiation dose. An imaging biomarker profile including quality control guidelines for coronary calcium is needed to ensure proper use of dose-reduced protocols in population-based screening in the future.
Marleen Vonder (1989) studied technical medicine at the University of Twente. She did her research at the Center for Medical Imaging of the University Medical Center Groningen (UMCG) in cooperation with the Department of Social Healthcare at the Erasmus MC Rotterdam. Amongst others, the research was financed by the European Union by ERC scholarships. Also, after her thesis defense, Vonder will stay at the UMCG as a researcher. She was promoted on September 5, 2018.

Insight into light: The influence of luminance on visual functioning in glaucoma

**PHD STUDENT**
R.A.J.M. Bierings

**THESIS**
Insight into light: The influence of luminance on visual functioning in glaucoma

**PROMOTORS**
Prof.dr. N.M. Jansonius
Prof.dr. F.W. Cornelissen

**COPROMOTOR**
Dr. G. Bocca

**FACULTY**
Medical Sciences

Glucoma is a progressive eye disease in which the visual field is permanently damaged but which remains without symptoms until a late stage. Visual field loss in one eye is compensated by the other eye and also the brain fills in missing parts. However, many glaucoma patients indicated that they experienced difficulty with seeing in extreme (low, high and rapidly changing) luminance conditions – complaints that are not typical for glaucoma. Therefore, the aim of this thesis was to unravel the effect of luminance on the visual function of glaucoma patients. With a questionnaire, we confirmed that glaucoma patients had much more difficulty seeing in extreme luminance conditions, especially in...
PETimaging of P-glycoprotein at the blood-brain barrier with new 18F-tracers

H.A. Savolainen

PETimaging of P-glycoprotein at the blood-brain barrier with new 18F-tracers

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The brain is protected from the molecules circulating in the bloodstream by the blood–brain barrier (BBB). Transporter proteins at the BBB, especially P-glycoprotein (P-gp), have been found to be important in regulating brain entry of several compounds by removing them out of the brain. Decreased or increased P-gp function is linked to several neurological diseases, such as epilepsy and Alzheimer’s disease. We developed novel radiotracers for measuring P-gp function with PET. PET scanner locates and measures radioactive tracers that have been injected into the body. We used fluorine-18 to label our P-gp imaging tracers. Fluorine-18 has a half-life of 110 min, optimal radionuclide properties for imaging, and permits transport to other imaging centers. These new radiotracers were evaluated in cells assays and in several animal models. A compound called [18F]MC225 was identified as a weak P-gp substrate. In the normal situation, it has a low uptake in the brain since it is transported out by P-gp but when P-gp function is inhibited, the brain uptake increases. In addition, [18F]MC225 had good selectivity to P-gp and moderate metabolic stability. Therefore, [18F]MC225 is a suitable tracer for measuring P-gp function with PET.

Heli Savolainen (1986) studied chemistry at the University of Turku (Finland). She did her research in the Department of Nuclear Medicine and Molecular Imaging at the University Medical Center Groningen (UMCG) and is financed by the NWO-Veni-grant 723.108.009. She was trained as a radiopharmacist at the Radiation Therapy Institute of the University Medical Center Utrecht (UMCU) and at the University of Utrecht. In 2018, she did her PhD at the University of Utrecht and worked with Prof. dr. B.J.L. Eggen in the Department of Nuclear Medicine and Molecular Imaging at the University Medical Center Groningen (UMCG). In 2019, she was promoted as a radiopharmacist at the Radiation Therapy Institute of the University Medical Center in Utrecht. She was promoted on September 5, 2018.

Long-term regulation of microglia: Role of epigenetic mechanisms, inflammatory events and diet

W. Schaafsma

Long-term regulation of microglia: Role of epigenetic mechanisms, inflammatory events and diet

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The central research question in this doctoral dissertation is what the effects are of acute, but especially the long-term effects of microglia activation on microglia themselves and its effect on the brain. Microglia are immune cells in the brain that are capable of recognizing and clearing damaged or dead cells or harmful microorganisms in the central nervous system. With these activities, immune functions of the cells are activated and inflammation occurs. Also, microglia are involved in mechanisms that support neurons and produce factors that are favorable to neuronal function. This begins well before birth, during embryonic development, which means that early changes in the functioning of these cells can lead to serious implications later in life. An important note related to the central question of this thesis, which is the long-term effects of microglia activation, is that microglia are cells that normally are not replaced by cells from other locations in the body. They can replace themselves through cell division, but under normal circumstances, this does not happen on a large scale. Because of this, some microglia can be decades old. Both short-term and chronic neuroinflammation can leave behind sort of a fingerprint in microglia, which can change the properties, the response and the normal functioning of these cells in future disease or during normal aging. In this thesis we investigated (epi) genetic regulation of neuroinflammation, as well as the effect of inflammation, diet and maternal inflammation on microglia functioning.

Wandert Schaafsma (1984) studied biomedical sciences at the University of Groningen. He did his research in the Department of Neurosciences, section Medical Physiology of the University Medical Center Groningen.
Reliability of diagnostic measures in early onset ataxia

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Reliability of diagnostic measures in early onset ataxia

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Ataxia is characterized by the loss of smooth goal-directed movements. The cerebellum and its networks are crucial for these smooth goal-directed movements. Any disruption in these pathways will result in ataxia. Ataxia starting before the 25th year of life is referred to as Early Onset Ataxia (EOA).

EOA concerns a large group of rare disorders with a wide variety in clinical presentation. This hampers uniform recognition and clinical assessment of EOA. The clinical assessment of EOA is also hampered by concurrence of normal, immature motor behavior, which could resemble ataxic features.

For adequate surveillance of the severity of ataxia, different quantitative ataxia rating scales are applicable for children. These scales are reliable biomarkers in adults, in whom it was indicated that the scales are only influenced by the severity of ataxia. In children however, the reliability of ataxia rating scales has never been tested before.

The studies in this thesis revealed that quantitative ataxia rating scales are reliable applicable in children. However, in children, the ataxia rating scales are also influenced by the normal development of the nervous system, other movement disorders and muscle weakness. This implies that the interpretation of ataxia rating scales depends on the clinical presentation of the child.

This thesis also reveals that the reliability of the clinical assessment of EOA patients remains difficult, illustrated by a moderate inter-observer agreement. To increase the diagnostic yield in EOA, a diagnostic algorithm focusing on genetic testing is provided to guide the clinician in the diagnostic work-up.

Chapter 2 describes the presentation of VAH in a single patient, highlighting the diagnostic and co-morbidity issues involved. Functional MRI (fMRI) revealed activation of the primary auditory cortex, speech areas (Broca, Broca’s homologue and Wernicke), basal ganglia, anterior cingulate gyrus and dorsolateral prefrontal cortex; these results are in line with earlier studies (for a meta-analysis see Jardri et al. 1). In this particular patient, VAH were in full remission after treatment with repetitive transcranial magnetic stimulation directed at Wernicke’s area, together with remission of a range of metamorphopsia and depressive symptoms. Although current knowledge on the pathophysiology of VAH on a neural level is still at an early stage, the studies presented here show the potential of fMRI to guide novel treatment. These studies also indicate that the brain is an integrated network within which local influence can spread across different brain functions.

The study in Chapter 3 investigated whether neurophysiological differences exist between internal VAH and external VAH. This is highly relevant because the clinical tradition generally considers internal VAH to be less pathological and atypical for psychotic disorders. According to this tradition, internal VAH are often referred to as ‘pseudohallucinations.’ Our hypothesis is that the difference between internally perceived versus externally perceived VAH is limited to additional activation in the auditory ‘where’ pathway, i.e. a network of brain regions dedicated to locating sounds in our environment. Results from fMRI show increased activation of the right-sided medial frontal gyrus and the left-sided planum temporale in persons experiencing external VAH. This indicates that the ‘where’ pathway could indeed play a substantial role in the projection of hallucinated voices into external space. Correspondingly, internal VAH are neurophysiologically distinguished from external VAH by their lack of activity within the ‘where’ pathway. Considering that a small amount of auxiliary activation can explain the difference between internal and external VAH, we suggest that caution is required when applying the term ‘pseudohallucinations.’ This recommendation is in line with clinical studies reporting that there is no evidence for a differential impact or effect in patients experiencing either internal...
or external VAH. Chapter 4 steps back from the phenomenological level of studying VAH. The increasing amount of research on schizophrenia and psychotic symptoms has identified a range of factors suggested to be causal to the psychotic state. Although these explorative studies are highly valuable (providing data on, amongst others, genetics, neurodevelopmental trauma, altered brain connectivity, and/or social factors), they should be viewed within a larger context. In our work, an integrative model is proposed for psychosis based on network theory. This model states that the human brain is a ‘scale-free’ structure in which the multilevel and (complex structural/functional) organization contributes to the formation of hallucinations. Within the scale-free biological network, functional brain dysconnectivity is viewed as an intermediary scale level, under reciprocal influence from microlevel and macrolevel states. This ‘integrated network model of psychotic symptoms’ (INMOPS) is described, together with various possibilities for its application in clinical practice.

Based on our INMOPS theory (Chapter 4), an exploratory study was conducted in Chapter 5 to investigate the occurrence of VAH from the perspective of the multilevel and complex (functional) organization of the human brain. The aim was to develop a mechanistic account of the way in which the interaction of multiple functional networks leads to VAH in schizophrenia spectrum disorder. An Independent Component Analysis (ICA) of fMRI data was performed for a large group of persons experiencing frequent VAH, decomposing the overall general function of the brain of these patients into a set of constituent functional subnetworks. The interaction between these functional networks was further studied using network analysis to estimate the flow of activity in the brain circuits that subserve VAH. Firstly, it was found that our rigorous procedure for denoising the data in combination with ICA, decomposed the data into a fine-grained system of 98 functional networks in which 7 higher-level modules could be identified mathematically. These modules constituted plausible functional networks which, in an unsupervised layout produced by a force-directed orientation algorithm, neatly positioned themselves according to global brain anatomy. These so-called large-scale networks of the brain, i.e. default mode network (DMN), central executive network (CEN), and salience network (SN), decomposed into several subunits, each with their own interaction profiles and degrees of correspondence with hallucinatory activity as reported by the patients. These findings show that the commonly reported large-scale networks should not only be studied in their entirety, but also that their constituent parts serve important subfunctions that contribute differentially to the global psychotic phenotype. These results also fit our INMOPS theory by showing that multiple levels of (functional) organization indeed contribute to the formation of hallucinations. Interestingly, several subparts of the global cerebellar network contributed differentially to the experience of VAH, indicating a more
complex pathogenesis of VAH than previously thought. The functional networks showing the most direct involvement with VAH experience were the bilateral anterior cingulate cortex, the right anterior insula, the cerebellum, and the homologue of Broca's area. Based on the causal structure of their mutual connections, we hypothesize that the right-sided insula and Broca's homologue are responsible for the production of preconscious linguistic constructs ('error') to which superfluous importance is assigned by the salience network, producing a conscious experience that matches this disproportionately high level of salience.

Jasper Looijestijn (1983) studied medicine at the University of Leiden. He did his research at the NeuroImaging Center of the University Medical Center Groningen (UMCG), in collaboration with UMC Utrecht, Parnassia Groep and financement of the Parnassia Groep Academie. He now works as a psychiatrist at PsyQ in Rotterdam. He was promoted on September 17, 2018.
and their gender identity). This offered us an experimental approach to study the effects of hormone administration in humans. In the second part of the thesis, we investigated the influence of sex hormones before birth and in puberty on gender role behaviour and gender identity from childhood to adolescence.

Although the asymmetrical distribution of the brain and gender role behaviour and identity are very different output measures, there are several parallels in the effects sex hormones have. The main overarching conclusions are:

1. Exposure to sex hormones before birth affects the influence of sex hormones in puberty.
2. Not only testosterone is important but estradiol plays a major role as well.
3. The effect of sex hormones depends on the phase of development, the cognitive task, and the sex of the participant.

Tess Beking (1988) was promoted on October 11, 2018.

For more illustrations from Tess Beking’s dissertation, see The Art of Science on page 18.
Sjoerd van Belkum (1986) studied medicine at the University of Groningen. He did his research in the Department of Psychiatry and the Department of Neuroscience at the University Medical Center Groningen (UMCG). He now works as a medical doctor in training to be a psychiatrist at the UMCG. He was promoted on October 17, 2018.

Driving slow motorised vehicles with visual impairment: An exploration of driving safety

P H D S T U D E N T
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T H E S I S
Driving slow motorised vehicles with visual impairment: An exploration of driving safety
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F A C U L T Y
Behavioural and Social Sciences

Independent mobility is important for social participation. Many people with visual impairment are dependent on the use of slow motorised vehicles. These vehicles are defined as motor vehicles with a maximum speed of 45 km/h (e.g., microcars or mobility scooters). Legal visual standards for the use of these vehicles do not exist. Yet, it is unclear to what extent people with visual impairment can use slow motorised vehicles safely and responsibly.

In her PhD research, Christina Cordes investigated the visual and cognitive factors that influence safe traffic participation in microcars and mobility scooters. Driving performance was investigated using a real mobility scooter as well as a mobility scooter and microcar driving simulator in both normal sighted controls and visually impaired participants with very low

PHOTO BY AIDAN VEY
visual acuity (from 0.01) and/or visual field defects. In addition, a neuropsychological test battery was administered.

Most participants were able to acquire the skills necessary to drive mobility scooters safely after short instruction and supervised practice in only a short time. Although visually impaired people were evaluated as worse on the mobility scooter on-road test compared to normal sighted participants, their evaluation indicated that they are still able to safely participate in traffic. Participants with visual field defects appeared to have more difficulties in traffic than people with low visual acuity. The driving simulator tasks further revealed that small obstacles with low contrast posed the greatest risk of collision for visually impaired drivers.

It can be concluded that visual impairment by itself cannot determine if someone can safely participate in traffic using slow motorised vehicles. However, individual advice is needed, especially for people with visual field defects. People can be specifically trained by professionals to compensate for their visual impairments in order to use slow motorised vehicles safely and responsibly, despite their limitations.

Christina Cordes (1986) was promoted on October 29, 2018.

**Clinical assessment of motor behaviour in developing children**

**P H D S T U D E N T**

M.J. Kuiper

**T H E S I S**

Clinical assessment of motor behaviour in developing children

**P R O M O T O R S**

Prof.dr. M.A.J. de Koning-Tijssen

Prof.dr. A.F. Bos

**C O P R O M O T O R**

Dr. D.A. Sival

**F A C U L T Y**

Medical Sciences

In this thesis, we clinically assess the motor behaviour of healthy and brain damaged children with movement disorder rating scales. By doing this, we aim to elucidate the influence of age on movement disorder rating scales, which leads to better application of rating scales in children with a movement disorder. In the first part of the thesis, we assess the motor behaviour of healthy children (0-16 years). From newborn age, we observe motor patterns that show similarities with features of movement disorders (dystonia, chorea and myoclonus). From 3 months of age, these features change to mainly ataxic and dystonic features. During childhood, the features become less clear and disappear after puberty. The similarities between motor features and movement disorders can be explained by the incomplete maturation and development of the nervous system. During brain maturation, networks between motor regions of the brain are formed and optimized. This results in better coordination of motor behaviour. With the present insights, the motor behaviour of children who are at risk for developing a movement disorder can be better interpreted. In the second part of the thesis, we implement the insights from the first part to two different groups of children who are at risk of developing a movement disorder, namely 1. children who are at a higher risk of brain damage due to oxygen deprivation during birth and 2. children who were chronically exposed to lead pollution. Outcomes show that the majority of the children in both groups show favourable, but not completely optimal, motor behaviour. Future research is needed to see whether the motor behaviour at adult age is normal, or not.

Definition of movement disorders:

> Dystonia: sustained or repetitive muscle contractions resulting in twisting and repetitive movements or abnormal fixed postures
> Chorea: jerky involuntary movements affecting especially the face and limbs
> Myoclonus: brief, involuntary twitching of a muscle or a group of muscles
> Ataxia: lack of voluntary coordination of muscle movements

Marieke Kuiper (1989) studied human movement sciences (BSc) at the University of Groningen. She started her doctoral research during her master’s studies, which she did in the Department of Neurology and the research institute BCN-BRAIN of the University Medical Center Groningen (UMCG). She now works as a physician’s assistant at the St. Antonius Hospital. She was promoted on October 31, 2018.
> CHEEKY PROPOSITIONS

“If pursuing a PhD degree can be compared to running a marathon [PhD students’ common knowledge], following a double PhD programme is comparable to competing in the Ironman triathlon [personal experience].”
> Paula Kopschina Feltes

“Je hoeft niet ziek te zijn om je ziek te voelen. Je hoeft je niet ziek te voelen om ziek te zijn. Je hoeft niet ziek te zijn om beter te worden.” (You do not have to be sick to feel sick. You do not have to feel sick to be sick. You do not have to be sick to get better.)
> Ronald Bierings

“The hurrier I go, the behinder I get.” – The White Rabbit

“Een man die het heel druk heeft, verandert zelden van mening.” – Friedrich Nietzsche
> Jasper Looijesteijn

“Creativity is connecting and extrapolating ideas. This creativity is needed for science, but could also be used to communicate science in a more appealing way.”
> Tess Beking

“The prescription that PhD students should wear muted colours during their own PhD ceremony is outdated.”
> Tess Beking

“Oan de ein fan de fûke fangt men de fisk.” – Frisian proverb
> Sjoerd van Belkum