Living against the clock: Can a ‘broken’ circadian clock be fixed?

Our bodies are made out of internal biological clocks that regulate our bodily functions and our daily behaviour. Our temperature, blood pressure, and our production of hormones all follow a daily program. Even our organs have a circadian pattern: our liver, for example, shows different activities when we sleep and when we are awake. This circadian regulation helps us adapt to the daily cycle of life by telling us when to sleep and when to eat. For many of us, however, our internal clock is not always synchronized with the clock of our surrounding world. According to Prof. dr. Martha Merrow, it is of vital importance that we decrease the gap between our biological and our social clock, because living against your own clock can lead to physical and psychological problems. In May 2011, Prof. dr. Martha Merrow and her colleagues received a substantial grant in order to examine how these ‘broken’ clocks can be fixed.

Martha Merrow started her career at the Tufts University Medical School in Boston. After receiving her PhD. in Immunology, Merrow specialized in circadian rhythms first at Dartmouth Medical School and then during her habilitation project at the Ludwig-Maximilians-Universität in München. In 2004, she was awarded a Rosalind Franklin Fellowship at the University of Groningen, where she is now a professor in Molecular and Genetic Chronobiology. Initially, she was planning to bring her knowledge of the biological clock back to immunology, but she now considers herself a walking advertisement for chronobiology: ‘I see chronobiology in everything and I believe every cell that evolved on the face of the earth has to have a system to cope with the quite harsh but predictable changing of the environment.’ In May of this year, the Board of Technology Foundation STW has approved funding to the Dutch chronobiologists to conduct applied research into examining the biological clock, and more importantly, how this clock can be fixed when it is broken.

Shift work is the best known example of living against the clock. People who work in shifts have to adapt their daily routine to their work schedule. They suffer from health problems, such as obesity, cardio-vascular diseases, gastrointestinal disorders, and breast cancer at higher rates than the normal population. If you need an alarm clock to wake you up in the morning, as 85% of the people do, you are also living against your own biological clock.
‘Every time we use the alarm clock, we are performing mini shift work,’ says Martha Merrow. ‘Our alarm goes off when our biological clock does not yet expect it to go off and we are getting up and becoming active while we should not yet be getting up. Chronic use of alarm clocks causes a ‘social jetlag’ and we would expect these people to be suffering from similar physical and mental problems as shift workers, although of course on a smaller scale.’

In 2005, after receiving a VICI grant to study the biological clock, Martha Merrow showed that people with a larger social jetlag are more likely to be smokers and that the caffeine and alcohol consumption among this group is higher. Similarly, adolescents also tend to be evening people, and for a long time there seems to be too much space, Merrow was one of the proponents of changing school opening hours. ‘Although I do believe that schools should start later, I also realized that it is very difficult to change this system. If school opening hours would change, the parents’ working schedule would also need to change. Shift work, as well as alarm clocks, are not going to go away any time soon and we better find ways to cope with these circumstances in the most healthy way possible’. In the upcoming 5 years, Martha Merrow and her colleagues will try to find out how people can actually improve their health condition by minimizing the discrepancies between their social obligations and their inner biological clock.

Such a major question demands a variety of projects using different tools and algorithms. There are 14 separable projects within the program. All of them are unified by the biological clock, but each one of them focuses on a different field of research. ‘The idea for the projects arose during one of the meetings of the Dutch Center for Timing Research (CTR). This platform for chronobiology in the Netherlands combines different chronobiology labs and commercial partners. ‘During these regular meetings, we invite several speakers to present their research, but we also talk about grant opportunities. The idea to work together to examine the broken circadian clock is a result of these fruitful meetings’. This is not the only aspect that is special about this program, as Merrow explains: ‘It is actually a very special kind of grant that is part of the ‘STW perspectief programma’. This means that we also had to apply for funding from the industry and the main criterion is that the program has to result in certain applications and products that are useful for the society.’

An example of such a product concerns using light to decrease social jetlag. Light is the strongest cue to synchronize our internal clock, but according to Merrow, we shield ourselves from direct sunlight way too often. ‘During the day, most of us spend at least 8 hours in the office without exposure to natural light. In the Netherlands, the situation is slightly better because many people go to work on their bike and spend at least some time outside, but most people still do not get enough light exposure’. A major challenge concerns the various chronotypes in the population: some people love the early mornings while other people are known to be night owls. ‘Your chronotype is a trait that is genetically determined, but modified by the environment. By changing the environment, you can thus change your chronotype a bit as well. When you are an evening person, you would need to be exposed to light early in the day whereas a morning person would typically benefit from light later in the day.’ The STW project aims to identify interventions with light, but also with nutrition, that can push the circadian clock towards the social one. ‘In shift workers, we will never be able to solve this discrepancy problem, but we can find out how they should expose themselves to light and what they should eat in the middle of the night to keep them alert.’

The project will not only examine possible interventions in shift workers and people suffering from social jetlag: ‘Some of the main challenges of the group include looking at light and food to decrease social jetlag, but they also include examining the clock in relation to insomnia, healthy ageing, and diseases related to a broken clock, such as bipolar disorders, metabolic syndromes, and cancer’. Martha Merrow is hoping to develop recommendations based on answers to simple questions that can be posted on short questionnaires, but also small devices to find out more about your own temporal biology. ‘Using chronotype as a main algorithm, I want to be able to give someone a very simple questionnaire taking into account several different factors such as age, lifestyle (light exposure), chronotype, and social obligations. On the basis of this information as well as what it is that the person would like to achieve, we could give the person feedback. This might be as simple as telling them to sleep with the curtains open or maybe sit in front of a light panel every morning while they drink their coffee. For
What are neurons (not)?

Most neuroscientists consider neurons as the primary elements involved in sensory- and motor- cognitive functions. Whereas the fabulous plasticity of the brain is considered to take place at the level of synapses, at the cellular level our view on brain as a static organ has prevailed for a long time. It is thus generally assumed that after its final development, the brain contains no more stem cells and has lost its capacity for growth and repair. This matches well with the lack of recovery that we observe after injury such as stroke or brain trauma.

Yet the notion that our brain does harbour stem cells has come up every now and then. In the 1960s Joseph Altman showed solid evidence that neurogenesis is taking place in the adult brain. Whereas Altman's findings were largely ignored, in the 1990s the same observations were made by Elizabeth Gould who reported adult neurogenesis in the hippocampus of various animal species. Nowadays the subventricular zone and the hippocampal dentate gyrus are renowned stem cell niches that most likely serve as cellular supply for plasticity in memory and olfactory function. The fact that we failed to see these stem cell niches was resolved by Arturo Alvarez Buylla, who showed that after birth, brain stem cells change their appearance and remain present disguised as glia cells. A salient fact, accompanying his findings is the conclusion that glia cells provide an essential contribution to the origin of the brain and are the mothers of all neurons.

It has also become increasingly clear that the borders between neurons and glia cells are less clear than previously thought. This is illustrated by the abundance of so-called NG2 cells that represent a kind of precursor cell that receives neuronal synaptic input and are likely integrated in neuronal networks. Also mixtures between astrocytic glia cell- and neuronal phenotypes have been reported and distinct transcription factors including PAX6 can convert astrocytes into neurons. These findings suggest that the distinction between neurons and glia is less strict than previously assumed, which is logical as they originate from the same mother stem cell.

Our vision on terminal cell differentiation changed radically when iPSC technology was developed. In a historical publication in the famous journal Cell, Shinya Yamanaka presented technology to genetically reprogram differentiated skin fibroblasts into pluripotent stem cells (iPS cells). Afterwards many groups have followed up on this technology and shown that these skin-derived iPSC cells can be differentiated into neurons. In subsequent publications other groups have presented novel methodology that allows more direct conversion of skin fibroblast to neurons. Evidently, application of the proper neuronal morphogens and neuronal transcription factors converts skin cells into neurons. Regardless of the implications for cell therapy for neurodegenerative disease, these new developments shed a new light on the origin and definition of neurons.
Paul Luiten (The Hague, 1948) is professor of Molecular Neurobiology and Biological Psychiatry. He is specialized in research on the molecular processes that cause Alzheimer’s disease and he has also conducted pioneering research into the role of reduced blood flow in brain tissue at the onset of dementia. In addition, Luiten developed a method of researching neurodegeneration that reduces the number of laboratory animals needed by fifty percent. This method, using one side of the brain as a control for the artificially induced degeneration of the other half, is currently used all over the world. His research is highly regarded internationally, as evidenced by the many times that his work is cited in scientific literature and the many invitations he receives to speak at scientific conferences. Recently, Paul Luiten has been appointed Knight in the Order of the Netherlands Lion.

Interview with Knight in the order of the Netherlands Lion: Paul Luiten

Congratulations on becoming Knight in the order of the Netherlands Lion. How do you feel about this Royal Decoration?

It is a great honour! I was unfamiliar with these kinds of awards, so it came as totally unexpected. It was a very pleasant surprise and it was a really joyful type of event. All the festivities around it made it a great day. Moreover, the reward is not just for me, but also for the work that I am representing. Mainly for the work I have done with several PhD students in the last decades. We all collaborated to come to the final outcome. So I receive the award, but as a representer of the group of coworkers. At least, that is the way I see it. This gives a very good feeling.

I have had a look at your CV and I am really amazed. I did not know one person could do so many things in one life! How do you manage to be involved in many different organizations at the same time?

That is a very good question. Actually, I am also surprised myself, sometimes. These things slowly develop. It is not coming overnight that you start to do everything. I still remember the first time that Diek Duithuis, the director of the BCN at that time, together with Rudy van den Hoofdakker came to ask whether I would like to become a member of the BCN board. I said ‘Ok, let’s do this’. At some point this is part of the job. So after being a member I became chairman. At the same time, they were also looking for someone for the CBN institute. In the course of years you get to know many people, so the communication becomes easier and easier. As soon as you contact someone, he or she already knows who you are, so you do not have to introduce yourself and everything becomes more efficient. You should also remember I was much younger in those days. Let’s say between 40 and 55 years, you are in your heydays, and you are enthusiastic for doing new things. I doubt if I could do all these jobs right now. It takes a lot of energy and concentration, because at the same time you still have to do research, and teaching and organize many other things. Luckily, I did not have to do everything myself; I had some very good collaborators in all the organizations, which is part of the fun. It also gives a very good feeling to do things together.

What is the invention you are most proud of?

Well, an invention or discovery, let me think. The most recent one was a discovery or development together with Marcelo Masman. We were discovering new types of compounds that could counteract the toxicity of the amyloid β peptide (the protein underlying Alzheimer’s disease). This is a very recent finding. In the
years before together with Eszter Farkas, we did a very interesting discovery about how important the blood supply of the brain is. In the normally aging brain, you can see that the microvessels of the brain are deteriorating or degenerating. We then investigated brains of people who died with diseases of the aging brain, such as Alzheimer’s or Parkinson’s disease, and found that they had more than doubled or tripled degeneration of the microvessels. This was much more than we expected, so I think the breakdown of these microvessels is a very important risk factor in the aged brain to develop such serious diseases. This was a very interesting discovery.

I have also read that you came up with the idea of using one hemisphere of the brain as a control for the other. How did you come up with that idea?

That is a good point. Actually, the question was how can we demonstrate if a new drug can protect the brain against degeneration as we know from stroke or Alzheimer’s disease, and discover how these drugs work. What you usually do is give one group of animals a drug and another group of animals the placebo as controls, and you compare the results. We tried to come up with ways to combine this approach within the same animal. At that time we found a neurotransmitter system that was completely bilateral meaning that your two brain hemispheres are independent. Thus, you have one hemisphere to do your experiment and the other is the reference or control side. Since the experimental and control hemispheres are in the same animal the variation between experiment and control is none. That is the idea of the experiment, which means that you can reduce the number of experimental animals by fifty percent. The only thing we had to prove was that the control side was absolutely not changed due to the experimental surgery we did in the other side of the brain. And this we could prove, so we had the ideal animal model to study protective drug effects. We developed this idea already twenty years ago, so for a long time we are now able to reduce the number of animals. This was also an economical factor, because the animals cost a lot of money, but for us the ethical reasons played a very important role as well. We really do want to diminish the number of animal experiments and their suffering, of course. So this is how we developed this animal model. Actually I was surprised to hear about this, because it is an idea from such a long time ago.

**What was the most fun thing to do in your career?**

There are a couple of fun things, but the most fun or rewarding part of my job is to work together with PhD students towards a good thesis. Mainly the final stage of their thesis study is very stimulating, because for a young scientist the PhD thesis is an important step in their career. This is a very joyful thing. At the same time I also enjoy teaching. Explaining students, for instance in the second year course Integrative Neurobiology, how a nerve cell works, how nerve cells communicate with each other and how nerve cells participate in neuronal systems, is basic for understanding the essentials of the brain. It is a very pleasant feeling to be able to convince students that the brain is a very attractive organ to study. This gives me a good feeling. Of course the brain is a very complicated thing, but if you take several hours to explain neuronal functions step by step, in the end the student has gained a basic understanding of the entire organ. The brain is a wonderful topic to teach.

**Did you enjoy being a member and the chairman of the BCN board?**

Yes, absolutely, I will explain why. I came from the faculty of mathematics and natural sciences with its own kind of research and its own particular culture. Then I came to this organization where five faculties were represented. There were people from philosophy, arts and psychology, and medical people, so individuals with all kinds of different backgrounds, with different ideas and different ways of thinking. This surprised me in the beginning, but in the course of years you learn a lot and I started to gain a much better understanding of the research programs in the different faculties. In the end, I really felt like a member of a family. In that sense, it was a really good experience. It broadened my view of science and also of the people who were doing these things. A very good and remaining experience.

**What did you actually do in the board?**

When I started as the chairman of the board, the main thing was setting up an educational system for the PhD students. At that time, there were several rather loose components, so we structuralized the whole PhD training program. That took of course a couple of years. I think we have a set of courses that we can offer to the PhD students who can have very different backgrounds. When a PhD student gathered a certain amount of study points, we also provided a certificate of the BCN training program. This is an additional diploma to their thesis. I think this was my major task at that time. But at the same time, you can imagine that as a chairman you have to deal with all the daily hassles. Basically, the board with their chairman is a sparring partner for the BCN director. The board discussed all issues and ideas with the director; that was (and probably still is) the main function of the board. Now, we always had very good directors, so these were always nice discussions. A very good experience!
**Why do you think the collaboration between biologists and medical people has to be improved?**

Actually, the way that our university is organized is that the faculties have a lot of independence. This is basically a very good idea, but that is not always how science works. Science is crossing these barriers between the faculties, because that is how scientists think. Most faculties like to keep their organization separated and this can be an unnatural scientific barrier. In the scientific sense I am very much against these types of barriers. At the moment I am a member of the faculty of sciences but at the same time I have an appointment at the medical faculty. Also some of my colleagues who teach in the biomedical sciences have appointments in two faculties. This way it is much easier to have contacts with different groups of scientists who may work in different places but who share common interests. It is good for a researcher to not always stay in your own building, but cross the barriers and talk to other people in a more easy way to set up collaborations together. It gives additional value if it is a trans-faculty project. This is the main reason why I am in favour of that.

**Do you still have any research goals for the coming years?**

Yes. My first goal at this very moment is finishing a chapter of a book. This book is an idealistic project called ‘Neuroscience of the 21st century’. This is an undertaking by Springer press to create a textbook that is freely available for students and scientists in developing countries. We were asked to submit a chapter about the aging brain, so together with some of my colleagues here, we are finishing up this chapter. That is one thing. Furthermore, I am busy with a couple of scientific projects. One of the projects is developing potentially promising Alzheimer drugs, which is a major focus at this very moment. We also have a project about the neurobiology of depression, especially late-onset depression in aged persons which is also related to early Alzheimer’s disease. Then, we are starting a project about biomarkers of depression with a lab-on-a-chip approach. The idea of this program is that you put a blood sample on a chip and that is telling you which biomarkers are present in this particular individual giving an indication of the depressive state of the patient. These are the main projects of the following years.

**Because you are an expert in Alzheimer’s disease, I would like to ask you: Why is there still no cure for this disease?**

That is also a good question. I think, if you look at the advancement in Alzheimer research in the last decade, the major progress that is made is in understanding what Alzheimer’s disease actually is. So far, we hardly understood what is happening in the brain of an Alzheimer’s disease patient and we still do not understand it very well. We know some major players like amyloid β protein and we know this protein can be toxic to the nervous tissue, but how this works exactly we still do not know. The point is that if you do not completely understand how it works and how it leads to brain damage, it is very difficult to do something against it. This is the challenge of the coming years, but I am confident that we will find out what exactly causes the disease. Once the molecular causes are revealed, it should be possible to develop good drugs against it. Because of the complexity of the disease, no real cure is yet available. The drugs that have been developed so far work downstream of the toxic cascade that starts with the toxic amyloid β protein and ends with a dying nerve cell. These current drugs were developed to prevent the death of the nerve cell, but meanwhile the toxic cascade is going on. That is why these drugs do not work so well. The idea is now to develop compounds that interfere with amyloid β in a very early stage of this toxic development, but I realize it is a complicated process; otherwise we would have solved it already.

**What are the ingredients for a successful scientific career?**

You have many good questions. In the beginning when you start with science you have no idea of becoming successful; you simply start doing science because you are interested in it. You love what you are doing. It is rewarding to discover things; a very simple process that is the basic stimulus for many or all scientists. At the same time, you should have the feeling that it is fun to do research and do not take it all too serious. Everything is relative, also what you are doing. Also, try to share what you are doing with the people around you; do not take it as your personal thing, be aware that great achievements are the result of a group process. Of course, you know you do your share, but you do it together with other people and so enjoy working with other people. This is the way I think about it, and the way I have been doing it, so I enjoyed my work and it gave me a good feeling. Besides I always have been a kind of free person. There was hardly anyone forcing ideas on me and I had very good people to work with. My ‘old boss’ Bela Bohus, who died far too young unfortunately, gave me all the freedom to do what I thought was best. I had the freedom to develop my own projects but experienced the support of my surroundings.

**Do you think that the freedom is also a characteristic of the university?**

Yes, it is academic freedom. There are two sides of freedom, one in terms of responsibility, meaning that you work for a salary and that you are responsible for students and your environment, the duty part. At the same time you have a lot of freedom to develop things, to come up with ideas. You can share your idea with...
others and convince them it is a good idea. Together you can do something with it. I think having a lot of freedom is an attractive and essential part of working at the university. This is different from working in a company, for instance. In a company they can very easily change the policy and then you have to move on to something else. I have seen several examples of drastic changes in research topics in pharmaceutical industries. So I appreciate the way it is here. Thanks to the University of Groningen.

Do you have anything else you would like to share with the BCN community?

I would like to tell the BCN that I have had a great time with them. I really hope that they will stay together offering stimulating and fascinating scientific and educational activities. I noticed that the BCN has become an institute that has a well appreciated profile in other universities in the Netherlands. Many would actually want what we already have, we should be more aware of that. In particular I hope that BCN will continue to offer the educational PhD program, because I think it is good and let you see over the borders of your basic education. With much pleasure I will continue to do my share in the BCN Research Master program. I wish the BCN a great future! I am sure they will with the fine people working there including Frans Zwarts (for those of you who did not know: Frans was our director before he became Rector, and now he is back and serves as a consultant to BCN). I have found out that Frans made his extensive experience available to the BCN. I think it is great to have Frans as a consultant for the BCN. I suggest the BCN board to invite him for dinner. At such occasions he has the best ideas.

DAFNE PIERSMA

From plants to brains

In March this year I started as the new coordinator of two exciting MSc programmes: the BCN research master and the MSc programme of Biomedical Engineering.

Originally I was born in Hamburg, Germany. I went off to study biology and plant physiology at the University of Göttingen and continued my studies as an ERASMUS exchange student in Helsinki, Finland. Returning to Germany I continued my study programme at the Humboldt University in Berlin before I went to Newcastle upon Tyne, UK and Kiel, Germany for the practical part of my MSc project.

In 2006 I started my PhD project ‘Southern Ocean primary productivity in a high CO2 world’ at the Ecophysiology of Plants group under the supervision of Prof. Theo Elzenga and Dr Jacqueline Stefels. Within this project I focused on the carbon acquisition of Antarctic phytoplankton and how it might be affected by higher atmospheric (and hence oceanic) CO2 concentrations.

My office is located at the Anton Deusinglaan 1 (building 3216, room 120a). As I have to share my time between BCN and BME, you will find me at the office every Thursday and Friday. Should you have any questions or comments, please feel free to contact me at any time (i.a.neven@rug.nl). I am looking forward to meeting you all!

IKA NEVEN, COORDINATOR, BCN RESEARCH MASTER, MSc PROGRAMME, BIOMEDICAL ENGINEERING
Reference Manager, Refworks, Endnote, and now Mendeley. What to use?

As a researcher you have probably scratched your head when the topic bibliography manager comes up. All bibliography manager programs have their strengths and weaknesses, but somehow weaknesses have the tendency to show up in the most inconvenient moments, e.g. just before sending out an article for publication. The university had licenses for Reference Manager and Endnote, but these expired in July. For the moment the university staff is advised to work with RefWorks. However it is important to ask yourself: “Is this really the best alternative?”. No one can answer this question for you, but it is important to keep in mind that it depends on what you are interested in. Taking a few hours to sort these things out can help you in the long run. David Vállez, a BCN PhD student focusing on chronic symptoms after whiplash injury or mild traumatic brain injury, is an advisor for Mendeley. According to him, this bibliography database is one of the most user-friendly programs he has encountered. Besides that, Mendeley has some functionalities that are unprecedented by any of the other programs. He believes so strongly in the group of programmers behind it, that he is willing to put time and effort in spreading the word around the University. He just gave his first Mendeley lecture at BCN, but he has plans to start giving practical courses at the whole university. The BCN newsletter is always interested in ways to help researchers to do their job, so we decided to go for an interview with David.

David how and why did you decide to become an advisor for Mendeley?
Since I started using computers, I have been looking for open-source and free software. The reason is obvious, when you are a teenager there is always a better way to spend your scarce money. Time passed and I faced the beginning of my PhD. So the first thing I did was to look for a good way to keep all the references and papers organized. I found this amazing tool called Mendeley. At that moment it was, and still is, an enthusiastic young company that is trying to offer a software capable to solve the daily problems in bibliography management. To do that they are always looking for advisors: people involved in the research field, inside universities or schools, librarians, etc.; people willing to “spread the word” and serve as feedback, a link between Mendeley developers and the community of users. And then I thought: Why not return some of my time to those who have been feeding me all this time?

Many people have probably just switched to RefWorks. Why should they now switch to Mendeley?
There are several differences between RefWorks and Mendeley, and if someone is interested in knowing them better, I advise them to come to one of my workshops or to just download Mendeley from their website. There are several main characteristics that make Mendeley special. First, it can be used for free. That means that after my PhD I can keep using my built-up bibliography independently from the institution where I will be. Second, the documents management of Mendeley is really nice to work with. It is possible to organize, read, annotate and highlight important passages of all pdf files stored on your computer easily. Third, the bibliography can be organized in private or shared folders. This allows you to collaborate with colleagues when writing an article. Creating your research network is a simple task, that allows you to keep track of your colleagues and helps you to discover people with research interests similar to yours. Last, one of the strengths of Mendeley is that it is really easy to work with and accessible in many ways. You can work with your bibliography from the web (if you have internet access) or from desktop software if you’re offline, regardless of the operating system (for example if you’re using an Apple Laptop at home). The best part is that all these libraries are synchronized automatically. If you already have spent time building your bibliography in RefWorks, don’t worry, you can easily import it to Mendeley.

Mendeley is in principle a free program, but if you want to have more space and more extensive functionalities you need to pay. Is this a clever marketing trick to attract people?
Yes. Free software can be very lucrative; a clear example is Google. In competitive markets the most important thing is to have more people interested
CONTINUATION INTERVIEW DAVID VÁLLEZ

in your product than the competitors’. Obviously, a free version of your software is a clever way to obtain that. Then, if your work is good and people like your product, they get used to it. Therefore, upgrade to premium plans with additional features for a reasonable fee is a logical step for many users.

What are your plans with regards to Mendeley for the future?
In the last months, I was organizing presentations about Mendeley for friends, my department and my colleagues of BCN. But I realized that the best way to let people get acquainted with the capabilities of Mendeley is during workshops. In these “hands-on” events, I expect people will soon start to see the advantages of Mendeley over its competitors. So this will be my aim for the next scholar year. I will try to organize these workshops not only for BCN, but also for the whole university. At this moment, I’m the only official Mendeley advisor in the north of The Netherlands, so I slowly hope to increase my range of action.

INGE RICHÈLLE HOLTMAN
Lost in Building 10

When I came to interview for a postdoctoral position at the National Institutes of Health (NIH) in April of 2007, the overall kindness of the people I interacted with on that day left a lasting impression. After minutes of walking through the hallways of building 10 (known as “B10”) for the first time, I came across a distinguished looking lady who voluntarily walked straight up to me asking if she could help me find my destination. In addition to my impression of how kind she sounded in her enquiry about my destination of interest, I was equally impressed by her ability to read the supposedly uncertain look on my face that might have suggested: help! I am truly lost. So it’s not hard to imagine how relieved I felt when I looked into that helpful lady’s eyes and happily told her that I indeed needed help in getting to the main reception area (atrium) where someone would be picking me up in a couple of minutes.

Within a year in B10 as a postdoctoral fellow at the National Institute of Mental Health (NIMH), one of the 21 institutes of the NIH housed in B10 and surrounding buildings at the Bethesda campus and elsewhere, I came to realize that the lady, who correctly read that ‘help, I am lost’ look on my face and showed me the way to the clinical center atrium on my first day in B10, exhibited a character trait (always ready to help the lost ones find their way) that all veteran B10 dwellers inadvertently acquire through the years. B10 dwellers very quickly become experts in reading the face of a lost person who has never worked and dwelled in such a complex maze-like environment. Thus as big as B10 is, the unwritten code of ‘always help the lost ones find their way’ helpfulness is simply a conditioned response. In other words, working in B10 makes one hardwired (perhaps through all the countless experiences of getting lost in one’s own tracks in B10) to understand the look and to empathise with the sense of being lost in others.

B10 (please see the web link for more on this: http://clinicalcenter.nih.gov/ccc/crc/) is said to be the biggest redbrick building in the world, for whatever that’s worth. Importantly though, the new clinical center (the lower rise section in the foreground) built in 2005 and connected to the older high rise section, makes B10 clinical center by far the biggest hospital in the world dedicated to biomedical research. It houses hundreds (if not thousands) of labs and clinics from many of the NIH institutes. B10 clinical center is the address where many medical milestones have been reached, including cancer treatments, gene therapy, AIDs treatment and many more. And yes, the wave of smoking bans that has captivated the world ‘from public to commercial spaces’ all started here not so long ago.

With its hundreds of meters of corridors/doorless and windowless mazes (windows are a rarity here and most office and lab spaces have none), in addition to the thousands of research projects and labs that utilize the world class facilities, it is not only easy to get lost while navigating the space, but also very easy to get lost in one’s research path with so many possible avenues as well in B10. As a golden rule, postdoctoral fellowship training at the NIH takes five years, with yearly renewals depending on one’s progress (or the lack of it). So when I was told that I would need 1.5 years to find my way and get settled in a really fruitful project, I thought that was an unreasonably long time for adjustment. It took me two years instead to find my way and now I am lost in the act of research itself. We are trying to figure out how a network of human brain regions (the so-called “salience circuitry”) communicates with each other during normal behavioral adaption, such as emotional perception and experience. We try to induce emotional feeling states by using a conditioned paradigm in healthy humans, with the hope of doing the same in psychiatric populations in the future. Trying to understand the temporal dynamics within this network and the inter-network interactions, as well as the neurochemical mediation of these dynamics, is the focus of my current training.

In sum, with its size and inevitable mazelike environment, as well as the exceptionally generous research opportunities the intramural program of the NIH has to offer, B10 epitomises the reality that greater size and possibilities comes with a greater risk of getting lost within those realms; both in terms of navigating one’s way through a complex physical environment as well as finding one’s research bearings when faced with so many possibilities. Like the distinguished looking lady who helped me find my way to the atrium on that day, the multidisciplinary nature of the excellent training I received at the RUG and ultimately BCN, in addition to my current training, is helping me carve out a line of research that I am exceptionally passionate about. So I hope to keep you posted on my progress here in B10!

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How to become a famous scientist

Finally, you are a PhD candidate. You are passionate about your research, you love academia and you love that tingling sound of the title ‘Dr.’ that will appear in front of your name that one day. You would think that passion, love and hard work is all it takes to be a successful researcher. Sadly, at this stage most of us have been faced with the reality of the PhD, where it takes more than brains and hard work to make it.

Nowadays it is a world of combat. Fighting about authorships, self-citing to boost H-indexes, journals flashing their impact factors, pimping curriculum vitae’s to get the grants. All of this because for scientists, keeping up performance is a matter of life or death. How do you stay ahead of your competitors?

This inspired us to dedicate a PhD day to the modern days science. The PhD Day took place on the 25th of May, 2011 and was a joint venture of the graduate schools of BCN and BSS. Our speakers were asked to give tips and tricks on how to become a successful scientist.

The PhD day was opened by James Coyne, Professor of Psychiatry at the University of Pennsylvania and Senior Fellow, Leonard Davis Institute of Health Economics, as well as Professor of Health Psychology at University of Groningen, where he teaches scientific writing. He has been designated by ISI Web of Science as one of the most impactful psychologists and psychiatrists in the world. In 2008, a JAMA article on which he was a co-author was selected by BMJ as one of the 8 top medical papers of the year. The opening talk was entitled “The Low Road and the High Road to Becoming a Top Scientist: Facing the Choice.” He shared observations about the Dutch culture he had made while teaching scientific writing at the University of Groningen.

For such a small country, the Dutch have many more than a normal share of famous scientists and academics. Nonetheless, there are various features of Dutch culture that can pose some difficult dilemmas for junior scientists with serious ambitions for their careers. For example:

1. A “Good Enough” mentality (zesjes mentaliteit) acquired in junior and secondary school, early enough to dispel an irrational fear of doing work that is not good enough, but nonetheless an important brake to major career achievements.

2. The ambivalent assessment of competition and the tendency to see Dutch people who do their best as standing out from the crowd (kop boven het maaiveld uitsteken).

3. Thinking about working on a PhD or having a postdoctoral fellowship as a 9-to-5 job, rather than as a significant contribution to one’s career development.

4. Making sharp distinctions between work and play, and between work time and evenings, weekends, and vacations.

He noted that for many productive scientists, both Dutch and non-Dutch, the blur between work and play is total and irretrievable. The line between work time and playtime or vacation is thoroughly blurred.

5. The “Glass Cliff.” Dutch academic women initially compete well but find themselves falling off a “glass cliff” after childbirth, with lack of practical and cultural support for continued achievement.

Yet he admitted that the Dutch system has several advantages in addition to these disadvantages. For example, that young researchers do not spend all their time on trying to become the best scientists, but also have a life apart from work, and may therefore have a better chance of avoiding a burnout at 30. “A foreigner, no matter how driven, has to begrudgingly admire the balance of Dutch life and wonder if more of it could be attained in their own life without sacrificing drive and ambition,” Coyne said.

He went on “But there are new challenges to becoming a top scientist, one not only has to do great science, but one has to market it effectively. It’s no longer enough to present well conducted research in passable English.” Increasingly, journal editors return manuscripts without review, with only the comment that the manuscripts
are not of sufficient interest. An author has to capture the Editor’s attention with a carefully crafted cover letter, title, and abstract. Otherwise the manuscript can quickly become a lost cause. And the marketing doesn’t stop there: after a paper is accepted, authors are now expected to write press releases, talk to the media in sound bites, and go to conferences with carefully prepared elevator talks that seem to flow spontaneously, conveying great enthusiasm, passion, and knowledge of the subject matter.

Social media, like Facebook and Twitter, have also become crucial tools for drawing visitors to the webpages of labs and for marketing research. PhD students often have to mentor their mentors in the use of these new tools.

Coyne asked “Can good marketing make up for bad research? Sadly, yes.” Many papers are written with press releases and sound bites in mind, even at the expense of scientific accuracy and transparency in presenting and interpreting the findings. In his talk Coyne gave numerous examples of high-profile research in hot areas, such as neuroimaging, mind-body relationships, and gene-environment interactions, that simply did not stand up to scientific scrutiny.

“Hype sells, sometimes more than substance, at least for a while, before the self-correcting forces of science take over.”

Coyne identified the “low road” to becoming a famous scientist as catering to popular prejudices and the media, and writing in sound bites and with a “best foot forward” confirmatory bias.

However, recognition of such a “low road” has given rise to new scepticism about science as it is presented not only in the media, but also in scientific journals. There is a new importance to uncovering the differences between bad science and good science. “Evidence sceptics” are making careers by exposing how much of what we know is not true and by asking “Are most positive findings in the journals false or at least exaggerated?” Coyne gave examples from his work, much of it with colleagues at Groningen, in which he had exposed such myths and biases.

“We showed that psychotherapy and support groups cannot extend the lives of cancer patients, despite persistent claims in the literature. Support groups can improve quality of life, but do not prolong life.”

After the keynote speech, the workshops started. This PhD day contained 4 workshops that covered different and crucial parts of the PhD life. The workshops were scheduled in two sessions, containing two parallel workshops each.

Based on his impressive career, we thought that James Coyne was the right person to tell us how to write high impact papers and what to do when your manuscript is rejected. Scientific writing is undergoing dramatic changes, professor Coyne told us. Many papers are rejected without being sent for peer review and yet other papers appear on PubMed within weeks of submission. There is an increasing need for manuscripts to be immediately engaging and clear in the contribution to the literature that is being made, and writing in clear, grammatically correct English is no longer sufficient to ensure acceptance for publication. Many journals have new policies concerning salami slicing, redundant publications, and self-plagiarism that are enforced with sophisticated web tools and that can trap the unwary. His workshop introduced strategies for coping with these new developments and for writing journal articles so that the process may not be effortless and joyous, but at least less painful and more assured of success. Topics included creative means of using electronic resources, cultivating collaborations, building writing into your lifestyle, writing and rewriting the manuscript, getting your manuscript past the editor and send out for peer review, post-submission responsibilities, and using publicity to increase early citations.

The next workshop was dedicated to grants. The speaker was Dr. ir. M.E. (Ties) Huigens, post-doctoral researcher at the Laboratory of Entomology (Wageningen UR). Since 2008 Ties is involved in the workshop “applying for grants” at the NWO talent days that are organized twice a year for scientists in
the early stage of their career (PhD’s and Post-doc’s). The workshop gave general information about NWO grants, with an emphasis on the Veni grant from the Innovational Research Incentives Scheme. Ties told us about his path to the Veni grant and shared some tips and tricks to increase your chances at being a successful Veni grant winner. What is important for the application? Can I phone NWO for an explanation of the assessment? How should I prepare for the interview? His workshop offered the chance to pose all this questions and more.

The following workshop was entitled ‘Publish or Perish’. Good publications are a mark of a good scientist. However, the field of publishing is highly competitive. In order to have a glimpse of how the masterminds work that decide whether you publish or perish, it is necessary to have an insiders’ view. That is why we asked Jaap Koolhaas to give this workshop. Apart from being a professor in Behavioral Neuroscience at the RuG, Jaap Koolhaas has also been the Editor in Chief of the journal Physiology & Behavior. With 10 years of experience in the field of editing under his belt, he gave a workshop on what happens with your paper after you have submitted it. Questions that were covered were ‘What makes and what breaks a paper?’, ‘What are the common pitfalls?’, ‘What draws the attention to a good article?’, and many more.

All these workshops mostly covered aspects of scientific writing. That’s why the last workshop was all about presenting. This “Giving effective presentations” workshop touched on a few of the key aspects that make a presentation successful. It covered issues such as the Q&A session, which some dread, how to use your voice effectively and some typical presentation language for English presentations.

The PhD day was concluded with a general discussion, during which all groups actively thought along and participated.

The PhD day received positive evaluations from the participants. They liked the set-up, theme and content of the PhD Day, particularly the keynote of James Coyne, whose workshop received a good feedback.

We hope to see you all next time!

EMI SALIASI
PHD COUNCIL

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BCN SYMPOSIUM: EPIGENETICS OF BEHAVIOR

What the “bleep” is epigenetics????

Don’t eat licorice when you’re pregnant!

During the BCN newsletter editorial meeting, my colleagues asked if I wanted to write something about the Epigenetics of Behaviour Symposium, which was held on May 11th at the UMCG. Because epigenetics is an important part in my PhD, I quickly said yes! I subsequently asked my editorial colleagues what they knew about it, and how I should set up such an article, and I noticed some glazy eyes and vague remarks, which suggested to me that they, like many others, are not really familiar with epigenetics. Even for many scientists it is still rather unclear what epigenetics actually is.

Wikipedia describes epigenetics as: “the study of changes produced in gene expression caused by mechanisms other than changes in the underlying DNA sequence – hence the name epi- (Greek: επί- over, above, outer) – genetics”. To put it more simply: epigenetics is about gene switches. Almost all cells in the human body have the same genetic code, but they function quite differently. The difference between, for example, a red blood cell and a liver cell, is that in a red blood cell, the genes that are important for uptake and distribution of oxygen are turned on. In a liver cell these genes are turned off, and other genes, like those for metabolism and breakdown of toxins, are turned on. There is no cell that uses all the genes in the genome. Each cell merely ‘selects’ those genes that are important to fulfil its function.

To come back to the symposium about Epigenetics of Behaviour, accumulating evidence shows that gene expression in the brain is highly flexible. Many aspects of memory formation, adjustment to stress, neurological and psychiatric disorders are related to epigenetic modifications. In the morning session, two cooperating researchers told about their perspective on stress in early life environment and the ability to cope with stress in later life. Prof. Bruce J. Ellis and Prof. Marco Del Giudice have developed a model describing this relation: the adaptive calibration model of stress responsivity. The stress system is crucial for an individual to adapt to physical, psychosocial and environmental stressors. Ellis and Del Guidice’s elaborate model basically states that if a child grows up in a safe and completely stress-free environment, they won’t be good at dealing with stress as an adult. If the child has moderate stress levels, they will be better at this, but if the stress levels during infancy are too high, then the stress-resiliency as an adult will be lower. They believe that epigenetic factors are underlying this relation, but for the moment they don’t have data to back up this statement.

Another important question in the field of epigenetics is: how do cells turn genes off and on? Prof. Bart Eggen gave an introduction to the molecular building blocks of epigenetics. Generally spoken, there are three classes of molecular switches. DNA methylation, histone modifications, and microRNA’s. DNA methylation silences gene expression for a longer time period, and is thought to be quite stable. Genes that are not used by a cell will often become hypermethylated. Histones are important proteins that interact with the DNA. These proteins have long tails and these tails can be modified by molecular “flags”. For example, an important flag is H3K9 acetylation, and this flag helps to increase expression of that gene. There are also flags that do the opposite. So histones modifications can either activate or silence gene expression, depending on the specific flag. Third, microRNA’s, are more like dimmers; they fine tune expression of a gene. Gene expression is not only an on or off situation but also needs to be regulated to a smaller degree. In his lecture, Prof. Eggen gave some nice examples of how these mechanisms come to play in the brain and nervous system, and can predispose individuals to certain diseases.

A fascinating talk was given by Prof. Katri Raikkonen from the University of Helsinki. She addressed how an environmental factor, like eating licorice during pregnancy, can have vast consequences on development of the baby in the long term. Her group showed that children of women who ate a lot of...
licorice during pregnancy had significant decrements in verbal and visuospatial abilities, narrative memory and a significant increase in externalizing behaviours like rule breaking and aggression problems. Licorice seems to exert this effect by influencing gene expression in the stress system of the unborn child. So spread the word: don’t eat (too much) licorice when you’re pregnant!

In epigenetics a long held dogma was that the switches were all reset during fertilization, but this is now seen in a more nuanced way. Certain epigenetic modifications can be transmitted to the next generation and influence the biology of subsequent generations. Prof. David Crews, from the University of Texas, calls this germ line dependent epigenetic changes. Crews’s group showed that toxin administration in one generation can influence metabolic and genomic activity in the brain of subsequent generations in rat. Translated to humans, this means that choices you make in your life, for example drug use, diet, stress, exercise can potentially influence the biology of your grandchildren and the likelihood they will get certain diseases.

Taken together, epigenetics is an extremely interesting field. It combines molecular and evolutionary biology, sociology, epidemiology, developmental psychology and has far fetching implications in all of these fields. Epigenetics has changed our understanding in many ways and led to a more nuanced perspective on many long-standing dogmas. I am certain that epigenetics will become more influential in each of these fields in the future, so hopefully BCN will organize more of these symposia.

Inge Richelle Holton

BCN dinner at Gigi’s

The BCN dinner was organized on Tuesday the 19th of April. BCN staff, PhD student council members and BCN newsletter writers were all present, resulting in an enthusiastic group of 18 people meeting at Gigi’s Culinary Centrum. We started having drinks and bread with pesto in the garden since the weather was very nice. Gigi’s is not a regular Italian restaurant, because the food is cooked by the customers themselves. Thus, after relaxing in the backyard it was time for action. Our group was divided into couples and every couple received a recipe to follow. Bauke Buwalda and I have cooked an oven dish with chicken. We had to make use of many fresh ingredients and I have learned what spices look like before they are cut into pieces and potted. After quite some time of cooking everybody was finished and hungry. We positioned ourselves at a long table and several salads, prepared by a few couples, were served. A very nice start of the meal! The main dish was our chicken and pasta. One couple took care of making the pasta itself while the others cooked the pasta sauce. These dishes were also very much appreciated, but the dessert of Erik Boddeke and Nynke Groenewold was yet to come. This dessert was not easy to prepare and took a lot of effort, time and power. Luckily, the dessert came out well and everyone loved it. Even though most of us were already stuffed, some people still managed to eat a second portion. Then, the BCN dinner came to an end. It was very nice to get to know more BCN people and fortunately they are all well able to cook a delicious dinner! If you are interested in the recipes, please visit http://www.floriansense.com/gigis-recipes/.

DaFne Piersma

>> CONTINUATION HOW TO BECOME A FAMOUS SCIENTIST
The Second Symposium on the Neurobiology of Learning and Memory

Last year the first Memory and Brain Symposium was organized at the UMCG in Groningen and because of the success of this congress, this year it was held again resulting in another great success on the 10th of May.

Candice Coker Morey organized the morning session about mechanisms to remember or to forget. Three speakers were invited to give a talk for 45 minutes. Michael Anderson from Cambridge University (UK) was the first presenter dealing with the inhibitory processes as a cause of forgetting. People are exposed to many experiences but cannot remember them all. Anderson states that this is due to inhibitory processes. Furthermore, he claims that we can actively suppress unwanted memories. Functional MRI during active suppression of a memory shows activity of attention control regions and reduced activity in the hippocampus in comparison to active remembering. This leads to a hippocampal modulation hypothesis predicting that if you want to remember the hippocampus is activated and if you do not the hippocampus is deactivated. The reactive control hypothesis is added to this theory. If you face an unwanted intrusion memory, the reaction is to deactivate both hippocampi more heavily. Anderson concludes that hippocampal modulation is a basis for memory control and we should remember that forgetting is often more active than we realize.

Jeroen Raaijmakers from the University of Amsterdam (the Netherlands) continued after the coffee break discussing the costs and benefits of retrieving information from memory. While studying you try to remember as much as possible. To accomplish this, it is better to practice questions after reading the book than to read the book again. According to Raaijmakers not an active inhibitory process but competition between items leads to forgetting. After practicing item A and ignoring item B, the memory of item A will be stronger or the memory of item B weaker or both. Associated items are remembered more easily, but in some ways cuing does not help because the inter-item-associations of the person are disrupted. Conclusively, Raaijmakers states that memory data can be explained without the theory of inhibitory processes, but Anderson thinks both theories might exist together.

Karl-Heinz Bäuml from Regensburg University (Germany) also travelled to Groningen to show us the two faces of memory retrieval. The question he asked was: Does the retrieval of a specific memory influence retrieval of other memories? Assuming yes, this can be a self-propagating process in which one memory leads to remembering more memories or a self-limiting process in which one memory leads to remembering less other memories. The self-limiting process has been shown with different paradigms and this so-called retrieval induced forgetting is even worse in people with a high working memory capacity. However, the question remains whether the self-propagating process can exist as well. Subjectively, it often seems as if remembering one thing makes us remember another related thing, suggesting a self-propagating process. Usually only recent memories are studied, but studying old memories in a certain context seems to show the self-propagating process in addition. Bäuml concludes that retrieval of a specific memory often attenuates retrieval of other memories, but in some cases not. The self-limiting and self-propagating processes are present at the same time and the circumstances cause one of them to overrule the other.

Now, it was time for lunch and everybody enjoyed socializing while feasting on a large variety of food. The following afternoon session about the aging brain was organized by Eddy van der Zee. Three speakers covered interesting parts of this broad topic. Patricia Reuter-Lorenz from the University of Michigan (USA) started with a talk about the decline and compensation of the aging brain and mind. Older people show a gradual cognitive decline, while only world knowledge, such as vocabulary, does not decline. Atrophy is present in the brains of elderly, mainly due to a loss of synaptic density. Still, many healthy older adults are very successful, how is this explained? Functional MRI of the aged brain reveals underactivation of brain regions in the prefrontal cortex explained by the decline, but also an overactivation of the other hemisphere. The performance of a task is similar in the old and young adults, but the brain activity to achieve this is different. Reuter-Lorenz shows that overactivation can be a typical neural response to
compensate for increasing task demand. The limit of the brain activity in response to increasing task demand will be reached sooner in older adults than in young adults, so it would be wonderful if we could shift this drop-off point to a later stage. Somehow, a decreased reliance on the compensation and an increased efficiency of the task-specific network should be established.

The second afternoon speaker Paul Lucassen from the University of Amsterdam (the Netherlands) covered the topic neurogenesis. For a long time, people believed neurons could only die and no new neurons could be formed in adulthood. Nevertheless, increasing evidence has convinced scientists that neurogenesis does take place in the adult brain. The places of neurogenesis are the subventricular zone and the dentate gyrus of the hippocampus. When the formation of newborn cells is blocked in the hippocampus memory deficits occur, indicating a role for neurogenesis in learning and memory. Many regulators are influencing neurogenesis, age and early life stress being the major negative ones and exercise being a huge positive regulator. An interesting thought is that antidepressants might work via enhancing neurogenesis, because the time line of a clinical antidepressant effect and the time line of integration of new neurons in the brain are comparable. Neurogenesis is important for the adaptability of the brain and it might occur in even more brain areas.

After the tea break, Erik Scherder from the VU University of Amsterdam (the Netherlands) was happily surprised to see his audience consisting of many people at this late time of the day. His talk was about exercise, additionally addressing physical activity, cognition and emotion in the context of dementia. Scherder started with positioning aging in a positive standpoint. Reasoning improves with aging and the older healthy people get, the happier they become. Is wisdom a characteristic of the elderly? A key ingredient of wisdom is impulse control regulated by the prefrontal cortex. Exercise in aged people improves their prefrontal cortex function. However, in demented elderly impulse control is limited and because of that all incoming information seems equally important leading to a chaos instead of selective remembering. Exercise would be a great solution to improve their prefrontal cortex function thereby improving impulse control and moreover reappraisal of emotions. Older people are able to remember positive things better than young adults by making use of their prefrontal cortex. Dementia patients show no initiative to move due to the neurodegeneration, but a part of the prefrontal cortex is still present and the people remain to be able to smile. A positive approach of demented elderly involving exercise and humor would be very beneficial. By exercising and laughing dementia can be prevented or at least the quality of life of the patients can be increased significantly.

With this very convincing and enthusiastic talk the symposium came to an end. All attendees experienced an amusing and fascinating day. Thanks to the organizers Eddy van der Zee, Candice Coker Morey and Benno Roozendaal. Hopefully we meet again on the third Memory and Brain Symposium.

**DAFNE PIERSMA**
**ORATIONS**

**Bouwen aan systemen**

**ORATIE**
A.K. Groen

**TITEL**
Bouwen aan systemen

**LÆROPDRACHT**
Kindergeneeskunde, in het bijzonder de systeembiologie

**DATUM**
17 mei 2011

In zijn oratie gaat prof.dr. Bert Groen in op recente ontwikkelingen binnen de kindergeneeskunde. Hij verwacht dat de nieuwe integratieve systeembiologische benadering kan leiden tot een nieuw soort diagnostiek voor vooraljongen onbegrepen afwijkingen, zoals metabole afwijkingen zonder duidelijke etiologie bij jonge kinderen.

Biologische systemen bestaan uit een groot aantal zeer verschillende componenten. De systeembiologie bouwt niet alleen de functie van de componenten (zoals DNA, lipiden en eiwitten) te doorgronden, maar vooral ook de dynamische interacties die de verschillende componenten verbinden. De gedachte achter een dergelijke holistische benadering is zeker niet nieuw, maar het wachten was op de recente revolutionaire technologische vooruitgang om de holistische benadering ook praktijk toepassen.

De integratie van genomics, proteomics en metabolomics waarmee steeds grotere hoeveelheden genen, eiwitten en stofwisselingsproducten in cellen in kaart worden gebracht, maakt het mogelijk complexe samenhangen te onderzoeken. Deze interacties zijn zo complex dat ze zonder gebruik te maken van uitgebreide computermmodellen niet bestudeerd kunnen worden.

Deze nieuwe integratieve benadering zal in Groningen op een aantal fronten ingezet worden. In het interfacultaire ‘Systems Biology Center of Energy Metabolism and Ageing’ wordt de systeembiologie ingezet om een beter begrip te krijgen over de processen die betrokken zijn bij veroudering. Dit centrum wordt gehuisvest in het in aanbouw zijnde ‘European Research Institute on the Biology of Ageing’ (ERIBA).

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Naast dit fundamentele onderzoek wordt de systeembiologische benadering ook ontwikkeld om tot een nieuw soort diagnostiek te komen voor vooraljongen onbegrepen afwijkingen. In de kinderkliniek presenteren zich vaak patiënten met metabole afwijkingen zonder duidelijke etiologie. Deze groep van afwijkingen wordt zeer waarschijnlijk veroorzaakt door clusters van enzyminsufficiënties, die verstoringen veroorzaken in metabole netwerken. Door de integratieve systeembiologische benadering moet duidelijk worden wat de onderliggende oorzaak is van de metabole afwijkingen waarmee de patiënten zich presenteren en hoe de metabole netwerken weer in balans gebracht kunnen worden.

**PROMOTIONS**

**Self-regulation of learning and the performance level of youth soccer players**

**ORATIE**
M.S. Schmid

**TITEL**
Treacherous Shibboleths: language as an indicator of origin

**LÆROPDRACHT**
Engelse taalkunde

**DATUM**
7 juni 2011

**EVELYN KUIPER-DRENTH, OP BASIS VAN PERSBERICHTEN VAN DE RIJKSUNIVERSITEIT GRONINGEN**

Verband vermogen zelf leerproces te sturen en prestatienniveau jonge voetballers

Het vermogen om zelf hun leerproces te sturen is mogelijk de sleutelfactor voor jonge voetballers om hun top te bereiken. Wat spelers uit hun trainingen halen, lijkt minstens zo belangrijk als het aantal gemaakte trainingsuren. Voetballers op het hoogste niveau van Nederland scoorden het hoogste
Zelfregulerend leren helpt individuen om effectiever te leren. Dit houdt voor voetballers in dat zij moeten weten welke vaardigheden zij moeten verbeteren en hoe ze dat kunnen doen, dat ze gemotiveerd zijn om zich te verbeteren en dat ze actie moeten ondernemen om zich te verbeteren. In haar onderzoek ging Toering na hoe zelfregulerend leren (ZRL) en het prestatieniveau van jeugdvoetballers van 11-17 jaar samenhangen. Ook onderzocht zij hoe dit wordt weerspiegeld in het trainingsgedrag van spelers. Toering keek daarbij naar zes onderdelen: plannen (voor het uitvoeren van een taak een plan van uitvoering maken), monitoren (tijdens het uitvoeren van de taak nagaan of alles goed gaat), evalueren (na het uitvoeren van een taak het proces en resultaat beoordelen), reflecteren (de dingen die zijn geleerd omzetten in gedrag), inzet (de bereidheid zich in te zetten voor het uitvoeren van een taak) en self-efficacy (het vertrouwen dat een taak succesvol kan worden uitgevoerd).

Uit haar onderzoek blijkt dat spelers die bij een betaald voetbalclub op het hoogste niveau in Nederland speelden, hoger scoorden op ZRL dan spelers op amateurniveau. Vooral de onderdelen ‘reflecteren’ en ‘inzet’ zijn bij hen sterker ontwikkeld. Bovendien bleek dat binnen de groep spelers van een betaald voetbalclub de beste spelers het hoogst scoorden op ‘reflecteren’, terwijl het aantal trainingsuren voor alle spelers gelijk was. Hieruit blijkt dat de beste spelers meer van deelname hoeveelheid training profiteren dan andere spelers. Niet zozeer het aantal gemaakte traininguren is beslissend, maar wel wat jeugdvoetballers uit hun training halen.

Om progressie te boeken, adviseert Toering jeugdvoetballers en jeugdtrainers zich te richten op het identificeren van sterke en zwakke punten en het stellen van doelen die daarbij passen. De trainers moeten hun spelers goed kennen, zodat zij hun feedback kunnen aanpassen aan dat wat de speler nodig heeft. Daarbij kan de trainer de spelers aanmoedigen om voor elke training een specifiek doel te hebben en na de training voor zichzelf te evalueren of het doel is gehaald. Trainers moeten de spelers de ruimte geven om zelf na te denken en met oplossingen te komen in plaats van dat de trainer dit telkens doet. Op deze manier creëren zij een leeromgeving die spelers aanmoedigt om pro-actief in hun leerproces te zijn.

Bagatelliseren hun ziekte en zijn niet geneigd de aanwezige symptomen toe te schrijven aan hun psychiatrische stoornis.

Het onderdrukken van je eigen perspectief en het aannemen van dat van een ander, maakt dat je van een afstandje naar jezelf kunt kijken om te proberen jezelf te zien zoals anderen je zien. Met andere woorden, als je de symptomen die je ervaart en de gevolgen van je stoornis vanuit andermans perspectief kunt bekijken, kan dit leiden tot beter ziekte-inzicht. Van de Meer suggereert dat een gebrek aan ziekte-inzicht bij patiënten met schizofrenie mogelijk samenhangt met de vaardigheid om hun eigen karaktereigenschappen en vaardigheden te evalueren.

De twee belangrijkste strategieën die mensen normaalgesproken gebruiken om met negatieve gebeurtenissen om te gaan zijn herinterpreteren (ofwel relativeren) en onderdrukken van het gevoel. Het vermogen om negatieve ervaringen te relativeren wordt gezien als een gezondere reactie dan het onderdrukken van emoties. In haar onderzoek heeft Van der Meer aangetoond dat patiënten met schizofrenie vaker dan gezonde personen gebruik maken van de techniek van hersenonderzoek mogelijk samenhangt met de vaardigheid om hun eigen karaktereigenschappen en vaardigheden te evalueren.

Schizofrenie is een complexe stoornis waarbij vele processen in de hersenen anders verlopen dan bij gezonde personen het geval is. De kennis uit dit onderzoek kan worden ingezet om patiënten met schizofrenie beter te begrijpen en hen te helpen in het omgaan met hun stoornis.

Amplitude integrated EEG. Longitudinal recordings in critically ill newborns

Promotent Prof. dr. A.F. Bos
Promovendus Henk ter Horst
Promotor Dr. Lisette van der Meer (Groningen, 1979)

De aEEG-techniek blijkt een bijdrage te leveren aan het hersenonderzoek bij baby’s die bij de geboorte zuurstofgebrek hebben opgelopen. Maar ook in andere gevallen kan aEEG nuttig zijn, bijvoorbeeld wanneer sprake is van een hartafwijking of een ernstige infectie. Als ook NIRS wordt gebruikt, kunnen artsen een scherpere diagnose stellen en de behandeling mogelijk verder verbeteren.


ASD symptoms in children with ADHD familial and genetic underpinnings

Promotoren
Prof. dr. R.B. Minderaa
Prof. dr. J.K. Buitelaar

Overlap tussen ADHD en ASD nader in kaart

Attention-Deficit/Hyperactivity Disorder (ADHD) en autisme spectrum stoornissen (ASD) worden in psychiatrische handboeken strikt van elkaar gescheiden. Pas de laatste jaren wordt duidelijk dat er overlap tussen beide aandoeningen is. Judith Nijmeijer bracht deze overlap nader in kaart. Kinderen kunnen in de toekomst sneller één heldere (combinatie) diagnose krijgen. Dat scheelt frustratie en verwarring, zeker ook voor de ouders.

Voor haar proefschrift onderzocht Nijmeijer aard en oorsprong van ASD-symptomen bij kinderen met ADHD. Zij deed dat in een grote internationale databank met gegevens over kinderen met ADHD en hun familie. Kinderen met ADHD en hun broertjes en zusjes hebben meer ASD-symptomen dan gezonde controlekinderen, zo blijkt. Niet alleen hebben zij problemen in sociale interactie, maar ook communicatieproblemen en stereotype en rigide gedrag kwamen vaak voor. Ook blijkt dat broers en zussen op elkaar lijken wat betreft de ernst van de ASD symptomen. De kans dat kinderen behalve ADHD ook ASD-symptomen hebben, is groter bij kinderen die bepaalde varianten van risicogenen hebben, maar alleen bij kinderen van wie de moeder rookte tijdens de zwangerschap of die een laag geboorstegewicht hadden. Deze bevindingen laten zien dat de interactie tussen geiten en omgeving belangrijk is bij het ontstaan van ASD symptomen bij kinderen met ADHD.


Inflammation and remodelling in experimental models of COPD. Mechanisms and therapeutic perspectives

Promotoren
Prof. dr. H. Meurs
Prof. dr. J. Zaagsma

Nieuwe mechanismen voor luchtwegontsteking en luchtwegverdikking bij COPD geïdentificeerd

Tonio Pera onderzocht nieuwe potentiële mechanismen voor de pathofysiologie van COPD. Hij ontwikkelde een diermodel waar mee verschillende aspecten die ten grondslag liggen aan luchtwegobstructie en progressieve afname van de longfunctie bestudeerd kunnen worden. Met behulp van dit diermodel toont hij aan dat het geneesmiddel tiotropium, dat als luchtwegverwijderende medicijn bij COPD gebruikt wordt, ook luchtwegontsteking, luchtwegfibrose en verhoogde slijmproductie remt. Deze resultaten bieden een mogelijke verklaring voor de niet-luchtwegverwijderende effecten van tiotropium die in een recent klinisch onderzoek gevonden zijn.

Met het model is ook aangetoond dat de activiteit van het enzym arginase in de long is verhoogd. De studies beschreven in het proefschrift van Pera tonen aan dat inhalatie van een specifieke arginase-remmer de luchtwegontsteking, luchtwegfibrose en verhoogde slijmproductie remt. Daarnaast werd aangetoond dat door behandeling met de arginase-remmer ook de verdikking van het rechterhartventrikel kan worden voorkomen. Verdikking van het rechterhartventrikel is een kenmerk van pulmonale arteriële hypertensie, dat bij een groot aantal COPD-patiënten aanwezig is. Deze bevindingen suggereren dat arginase een potentiële target is voor de behandeling van COPD.
Ten slotte tonen in vitro studies van Pera naar luchtweggladde spiercellen en spierweefsel aan dat het enzym TGF-β-activated kinase 1 (TAK1) een belangrijke rol speelt in processen die celgroei bevorderen en tot afgifte van ontstekingsmediatoren leiden. Omdat die processen kunnen bijdragen aan luchtwegontsteking en luchtwegverdikking bij COPD, wordt hiermee een rol voor TAK1 gesuggereerd in de pathofysiologie van COPD.


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**When we move together: the neural correlates of joint action**

**Promovendus**
I. Kokal

**Promotor**
Prof. dr. C. Keysers

**Promotyp**
Prof. dr. H. Critchley

**Hersenactiviteit tijdens sociale interactie onderzocht**

Promovenda Idil Kokal onderzocht de werking van onze hersenen tijdens sociale interacties tussen twee mensen. Met behulp van functionele MRI (fMRI) werden hersenscans gemaakt tijdens verschillende experimenten, zoals een samenwerkingsspel en samen drummen. De resultaten van het onderzoek wijzen erop dat tijdens dergelijke activiteiten sprake is van activatie van een hersennetwerk dat verder gaat dan het systeem van de spiegelneuronen. Tijdens de drum-experimenten werd activiteit gevonden in de nucleus caudatus wat samenhangt met beloning. De mate van activiteit in de nucleus caudatus correleerde met het aantal potloden dat de proefpersoon oppakte om met de andere persoon mee te drummen. Kokal concludeert dat onze hersenen gesynchroniseerde activiteiten vertalen in beloning, op basis waarvan iemand vervolgens beslist om al of niet verder te gaan met het gesynchroniseerde gedrag.

PHD AND OTHER NEWS

BCN has moved to another building!
The BCN Office has moved! You can find us now in the UMCG, ‘De Brug’ (bldg 3217), 7th floor, room 721 (Diana and Janine) and 731 (Evelyn). This building houses the GSMS, the graduate school to which BCN belongs.

GSMS
The PhD study guide and other information is accessible on the GSMS website: http://www.rug.nl/corporate/onderzoek/graduateSchools/gradSchoolMedSciences
All courses in this guide are free of charge for GSMS members, therefore also for all BCN members. In September you will receive a new edition of the BCN Training Programme. Hopefully all major changes will be completed at that time.

Phd student card
BCN can help you to get your PhD student card. This card can be used as a proof that you are a PhD student, and will give you a discount at conferences sometimes. In order to apply for this card, we need your P-number and a passport photograph. Please bring this to our office, if you are interested in this card.

New item on the BCN website
On the BCN website you can find a new item: BCN-Forms. On this page, you will find application forms for financial support, new PhD students, BCN Accredited events, and financial support for printing costs of theses. Please fill in these forms and send them to:
BCN-Office
Hpc: FA33
Postbus 196
9700 AD Groningen

BCN Buddy System
BCN introduces a Buddy System. The idea is that a new PhD student will be related to another senior PhD student, who is available for practical questions, and will help new students with their social integration in the PhD community.

We are still looking for Buddy’s!! If you are in the 2nd, 3rd or 4th year of your project, and you would like to help a first year’s colleague, please sign in as a buddy. The form can be found on the BCN website (BCN-forms).

Finance of external courses and conferences
The system for applying for financial support of BCN for courses or conferences has changed. On the BCN website, you can find a new item: BCN-Forms. On this page, you will find the application forms. Please use these forms! You do not have to contact me by email, just fill in the form in advance.

At this moment, the exact rules for finance are not clear. I hope that I can inform you in September.

BCN Orientation 2011: start September 9, 2011
The Orientation Course 2011 will start on September 9. Other course dates: September 23, October 7, and 21, November 4 and 18, 2011.

If you would like to participate, please send an email to d.h.koopmans@umcg.nl

Agenda BCN activities
September 9, 2011: Start of the BCN Orientation Course
September 16, 2011: First years BBQ
October 31, 2011: Halloween Party!

Check the website for detailed information.

Diana Koopmans
I am a last-year, actually last-month, PhD candidate in the Neurolinguistics research group of the Faculty of Arts. I have spent the last four years investigating auditory and audiovisual speech perception in both non-brain-damaged and aphasic listeners.

As I have mentioned, my project is almost finished and through the years so many things worth writing about have happened. For example, I could focus on coming to the Netherlands as a German, a thing often underestimated by both Dutch people and other foreigners, who say things like: ‘Ahh, you’re from Germany! So coming here is not really different for you’. But this is not entirely true. Indeed the cultural and language differences are smaller than with other countries, but still it is a foreign country you moved to and adapting is not always that easy. A lot of small things differ. Still, there are situations when I’m surprised about how things are done here.

But moving here and adjusting are already so far in the history that I don’t want to waste the rest of this column by writing about it any more. Besides, I really enjoy living in the Netherlands and intend to stay here, so why bother with those ‘starters’ troubles’. I could use this space better by telling you about the research I was able to do those last four years. I had the opportunity to carry out my own research plan, working with individuals with aphasia, usually people who have suffered from a stroke. I investigated the influence of speechreading (seeing the speaker instead of only hearing him) on their perception. I also learned to carry out research with the EEG technique. So I was able to investigate the neural correlates of audiovisual speech perception. In my opinion, doing a PhD is about more than your research. It is an exciting opportunity to gain other skills as well, e.g. by organizing a conference or being part of PhD candidate representation. I did both and again, I could write pages about it as well. In my faculty there are three research institutes which are all part of the Graduate School for Humanities. There was however hardly any PhD representation at faculty level, when I started. Each institute had one representative in an advisory council, which meets twice a year. As the faculty-level graduate schools now handle a lot of the official matters, we felt a more proper representation was needed. Therefore, the two representatives from the other institutes and I then decided it was time for our faculty to have a PhD council as well and so we set one up. Especially in the beginning this was very exciting, as we had a lot of things to work out for ourselves. Now, more than one and a half years later, the PhD council is a vivid part of the Graduate school.

Organizing conferences, workshops and being part of the PhD representation taught me a lot about the ways a university is run. I got close insights into the bureaucracy and the struggles attached to it. However, while it was frustrating at times to call Facilitair Bedrijf almost daily to make sure that the coffee is served at the correct time and location, I now feel that organizing my own defense and the workshop accompanying it is much easier than it would have been without any prior experience. So now, knowing my way around, things are going very smoothly, which is a big relief after the stressful times of working on the thesis.

Only one struggle is left at the end of my PhD trajectory and that is finding my place for the future. Do I want to stay in research? If yes, how far away am I willing to move, both in terms of geographical distance and flexibility concerning the topic? If not, what does a neurolinguist do outside of academia? So the first part is to take those decisions and then the second part (even more difficult) is to find the kind of job I would like to have. So even though the book has been sent to the reading committee, the biggest struggle seems still ahead.

In retrospect, coming to Groningen to do my PhD taught me a lot, not only about my research topic, but also about life in academia, organizational processes within a university and most importantly about myself. So my advice to starting PhDs is to risk looking further than their own lab or office and grab some of the various opportunities the PhD time offers.

Dörte Hessler, PhD Candidate in Neurolinguistics