

Content

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Before you lies the 10th volume of the Journal of Neuroscience and Cognition. Over the years a lot has changed, especially the look of the journal. It went from being printed and stapled together to a high quality professionally printed piece. What has also changed is the supervision of the editorial boards. In the previous issue, I already introduced myself as the new senior advisor, replacing Pierre.

This issue is the first that was made under my supervision, and I am incredibly proud of it. Furthermore, I hereby refrain from any praise for this issue, because it was really the board who did all the work. I am quite impressed by how much I was not needed during the entire process. Everyone worked hard, meetings were frequent, structured, and efficient. I did give my opinion

when asked (and sometimes, when not asked). It was taken into consideration, but all decisions were made by the board as a group.

On top of making the journal, the board took the “old and new” theme quite seriously and even managed to redo the entire website of the journal, which, considering the amount of work, is quite impressive. Please have a look at www.journal.neuroscience-cognition.org to see the results.

I am sure that you will enjoy this issue, and I personally cannot wait to see what the board has in mind for the next one!

Anouk Keizer

Senior advisor Journal of Neuroscience and Cognition

Editorial

Experience is generally defined as the knowledge gained in time through direct and subjective involvement. If this definition is applied to science, it can be argued that experiments are the experience on which we base our knowledge. As to celebrate this year's 10th volume, we stopped to wonder: how do the past experiences of neuroscience influence its future?

To address this question, we asked four principal investigators to elaborate on how the past 10 years will influence their future work. We asked about the breakthroughs (and fiascos) of their specific field, and their participation in creating new knowledge (page 4). Extending this past-and-future concept to a more personal level, we approached the editorial board of the very first edition of the journal and asked them about their present lives, what their expectations were, and how these changed (or not) through time (page 46): a sneak peek of our future? Also, a story by Prof. Burbach offers light-hearted and passionate suggestions on career perspectives by melting together past, present, and future direction of his own career (page 61). Interestingly, the two interviewees – neurosurgeon and researcher Marike Broekman (page 52), and psychiatrist and author of 'Haperende Hersenen' Iris Sommer (page 55) – shared Burbach's same suggestion: “the key to success is...”. Read them to know more!

Next to these 10th volumeversary special features, the old beloved components of the journal could not be missing. Read the stories of Milou Sep and Jeroen Verharen (page 61 and 62) to see whether a PhD is something for you. Widen your methodological horizons by looking through virtual reality or a two-photon microscope (page 49 and 50). Be entertained by two book reviews (page 65 and 66), by what your fellow

students think about neuroscience and ethics (page 68), and by an opinionated piece about studying abroad... in the Netherlands (page 64).

Concerning the academic content, a special mention to the quality of the submitted articles: the decision of which ones to select was a difficult yet thrilling task. The topics of the here published research articles range from experimental to clinical neuroscience: individual differences in alcohol addiction (page 8), spatial memory in mild cognitive impairment patients (page 38), the role of dopaminergic neurons in impulsivity and attention (page 19), and diet effects on brain development (page 31). Moreover, we integrated an outstanding writing assignment of the *Fundamentals* course, which successfully developed into a published article (page 57).

Lastly, we would like to thank the numerous submissions of both academic and non-academic content, without which this journal would not be possible. Additionally, I especially thank this year's editorial board for its hard work and creativity. Despite the difficulties, working together has been a pleasure and a means of both personal and professional growth. The numerous achievements so far are a demonstration that team work is a winning weapon. The accomplishments are not limited to the journal, but also extend to our brand new website. Please take a look at www.journal.neuroscience-cognition.org and let it convince you further.

Wishing you an instructive yet pleasant and entertaining read,

Valeria Bonapersona

Editor in Chief

10 years back and forward

The focus of my research is on the neurobiological and cognitive mechanisms underlying schizophrenia and bipolar disorder. My aim is to understand abnormal social functioning by applying social cognitive paradigms and obtaining structural and functional brain scans to associate abnormal behaviour to deficits in information processing and brain abnormalities.

“It will become increasingly important to link behaviour to cognition and the brain.”

I started my career investigating longitudinal changes in the structure of the brain, which is still a hot topic of debate in the field. The work of our lab made an important contribution by showing that schizophrenia patients lose more brain tissue with increasing age as compared to healthy individuals. We were particularly interested in confounders that are associated to this tissue loss, such as illness outcome, antipsychotic medication intake, cannabis use, and familial risk for schizophrenia. While I am still involved in this type of studies, I became more and more fascinated in one of the aspects of the illness that patients suffer from most, i.e. problems in social communication and in how to define self in relation to others (e.g. self-disturbances). In recent years, poor cognition is increasingly defined as a crucial feature of schizophrenia. Interestingly, studies show that social cognition and neurocognition are relatively independent, and poor social cognition has been identified as an important predictor for future functional outcome.

One of the understudied social cognitive phenomena is abnormal self-processing. This is not surprising, as it is a complicated concept to translate into experimental paradigms. However, new paradigms and definitions are emerging from social & experimental psychology and from social & affective neuroscience, which are ready for us to apply in the field of schizophrenia research.

It will become increasingly important to link behaviour to cognition and the brain, and to investigate combinations of different imaging modalities or cognitive



paradigms. Simply comparing two or three groups on one measure is no longer sufficiently informative. Applying combinations of techniques, tasks, questionnaires, and interviews to patients with different symptom profiles or diagnoses will increase our understanding of differences between affected individuals.

I predict that in 10 years' time, measures that are already available or that are currently being developed are being used to predict illness onset or future outcome for an individual patient in the clinic. This perspective fits with the current trend to involve the patients in our health care system. Their participation and ideas are valuable, may give direction to research, and motivate us to push harder. However, there always remains a pressing need for fundamental and innovative research projects, that may be difficult to explain, but will potentially lead to a (maybe unexpected) breakthrough.

- Dr. Neeltje E.M. van Haren
Department of Psychiatry, Brain Center Rudolf Magnus,
University Medical Center Utrecht

My research focuses on brain development in developmental disorders, such as ADHD and autism. In the last ten years, the field has increasingly recognised that the brain is a network. Instead of focusing on individual brain areas and their function, we are now considering how they work together. For example, in ADHD it has long been recognised that attention systems are important. However, five years ago, it was suggested that it was not attention systems *per se* that were affected, but rather that intrusions from the default mode network might cause fluctuations in attention. The default mode network is active when we are involved in self-referential thought, such as day-dreaming, and it is easy to see how intrusions from this system might interfere with attention. Indeed, there have been studies since then supporting this hypothesis in ADHD.

A second advancement has been the idea that symptoms of developmental disorders may not always reflect the same brain changes. For example, attention problems in ADHD may be primarily related to problems in attention systems for some children, but may be secondary to default mode intrusions for others. One result from our group that I am proud of is that we showed that there may indeed be differing brain systems affected between individuals with ADHD. Furthermore, these differences permit the segregation of affected individuals into different subgroups, confirming the idea that ADHD does not have the same neurobiological basis for everybody.

“I think the focus on individuals, and the promise of identifying which brain system is involved in an individual case holds great promise.”

These findings have important implications for treatment: if the neurobiological basis of developmental disorders differs between affected individuals, then this implies that treatments targeting only one system will not be effective for everybody. I think that the next ten years will give rise to studies focusing on predicting



which treatment will work for whom, and even tailoring interventions to target specific brain systems.

I think the focus on individuals, and the promise of identifying which brain system is involved in an individual case holds great promise. However, there is also a flip side: we are ‘brain chauvinists’ in psychiatry research (myself included). However, the brain of course does not function in isolation but interacts dynamically with the rest of the organism. There are more holistic interventions that may not affect one individual brain system, but rather impact the whole organism. For example, yoga seems to be effective for managing symptoms of ADHD, but we know nothing of the biological pathways. One thing I would like to happen in the next ten years is for us to also take a more holistic approach to individuals, while not losing sight of the importance of (the balance between) different (neuro-) biological systems.

- Prof. Dr. Sarah Durston
Department of Psychiatry, Hersencentrum,
University Medical Center Utrecht

10 years back and forward

The field of vision has changed dramatically, as we no longer consider vision to be a passive process, in which the visual world just automatically comes to us. We now realize that vision is an active process in which humans use eye movements to interact with their environment. Although this makes the oculomotor selection process crucial for successful vision, this change in focus has opened a whole new set of questions. One of these questions is how we perceive a stable visual world despite the almost continuous movements of our eyes. This question has united previously separated concepts, like visual attention, visual perception and visual working memory. More than ever, we recognize that our perception of the world is an interplay between the content of visual working memory and the basic building blocks at the lowest level of the perceptual system.

“The search for the neural mechanisms of active vision has only just begun.”

Our lab has contributed to these questions by discovering the crucial role that the content of visual working memory plays in determining which element receives priority for visual awareness. In the future, this development will continue and the search for the neural mechanisms of active vision has only just begun. One of our hypotheses is that patients with parietal lesions experience problems in their perception of a stable visual world. Because we have to remap important objects with every eye movement that we make, problems with spatial remapping will result in a diminished experience of visual stability. These patients experience problems in maintaining the location of important objects while they actively explore their environment. We are examining the crucial lesion location that results in these remapping problems and investigating to what extent these patients experience problems in daily life activities.



Although you might have the impression of a rich visual world, we now know that your brain only represents very little of this visual world at each individual moment in time. Current memory models are lacking an important property of the human brain: our brain is an energy-efficient system which aims to minimize its load. Instead of using the expensive internal memory, our brain can rely on the information in the ‘external’ visual world to maintain important visual information. Our lab is testing the novel idea that the default modus of our brain is to rely on external information and we should embrace an embodied view which embraces the external visual world as an actual memory system.

- Dr. Stefan van der Stigchel
Department of Experimental Psychology,
Helmholtz Institute, Utrecht University

Neuroscience research has been exciting and rapidly evolving over the last 10 years. Technological developments in neuroscience help the transition from observing and describing what is going on in the brain to making specific alterations and studying how the system responds. I am very excited about these developments, because it means neuroscientists can now make and test(!) specific hypotheses about the function of certain neurons in particular tasks. Such studies profit from a combination of molecular techniques (e.g. using virus injections to manipulate specific proteins in certain cell types) and the increasing knowledge about genetic differences of cell types (e.g. using the Cre-Lox system in combination with transcription factors). In addition, imaging technology is getting more and more advanced, which allows following (intra)cellular processes with high spatial and temporal precision *in vitro* and *in vivo*, or measuring the activity of large numbers of neurons during behavioural tasks and learning. I am pretty sure that the technological advancements will only continue in the next 10 years and I am looking forward to the new research possibilities it will create.

In my own research, I made the transition from being a rather independent postdoctoral researcher to being a principal investigator (PI). Since 2012, I am leading a small group of enthusiastic young scientists here in Utrecht. Our research focuses on interactions between inhibitory and excitatory synapses within dendrites. We study mechanisms of inhibitory synapse formation and plasticity and how these processes are tuned by neuronal activity or molecular signals. Our most important contribution is that we discovered that inhibitory synapses are highly dynamic structures that can assemble and disassemble rapidly (over the course of tens of minutes). This allows inhibitory axons to rapidly respond to changes in activity or molecular signals, rendering neuronal circuits highly adaptive. We believe that these processes play an important role during development and in neurodevelopmental disorders. We are currently investigating underlying molecular mechanisms and exploring behavioural consequences.

One of the great things about science is that you can never predict what is coming next. It is therefore impossible to predict the scientific breakthroughs for the next 10 years. Yet, I do expect that neuroscientists (hopefully including me) will significantly advance our understanding of the brain. I expect that in the coming years our understanding of functional anatomy of the brain will greatly improve. It is extremely important to determine how different brain regions or cell types are connected to each other and under which circumstances



these connections get activated. One important aspect is to understand how this connectivity emerges during development and how it is maintained during life. Enhancing knowledge on these processes will contribute to a better understanding of the function of brain areas and the neurons that are involved in different aspects of information processing and specific behaviours. I also see that a lot of effort is put into studying pathological processes in diseases of the brain. I expect (and hope!) that these efforts will greatly improve our understanding of many brain diseases in the coming years.

Together with the stronger emphasis on applying existing neuroscience knowledge to the study of particular diseases, I hope there will also be a renewed appreciation for fundamental (neuro)science knowledge. When studying diseases, too often it becomes clear that the function of certain proteins or cells under normal circumstances is actually not well understood. Sometimes fundamental research is necessary for the success of applied or translational studies, but the gain is bidirectional: fundamental insights in brain function can also come while testing new drugs. In my opinion, it will be important to continue to switch back and forth between applied and fundamental neuroscience approaches and not give priority to one over the other.

- Dr. Corette J. Wierenga
Department of Cell Biology,
Faculty of Beta-sciences, Utrecht University

Old board

In honour of the 10th volume of this journal, we decided to reach out to the group of people that started it all. The first board of the Journal of Neuroscience and Cognition was active in 2007-2008 and have been graduated for several years now. With changes over time playing such a fundamental role in our current issue, we approached them with the question to write a short contribution about themselves covering three topics. First and foremost, we wanted to see what kind of work they ended up doing and how it compares to what they originally expected as students. Additionally, we asked them if they had any tips for those readers currently considering their career prospects. We know how stressful these decisions can be and did not want to let this resource go to waste. Finally, we were also curious what changes they expect in the future of their respective fields. As up and comers in the field, they have a unique perspective between new perspectives and established practices.

Do Tromp - Layout

I am currently a neuroscience graduate student at the University of Wisconsin in the United States. My interest is focused on understanding the neural substrates that underlie normal and abnormal brain functioning, and specifically the connectivity that underlies affective processing in the brain. I use state of the art imaging methods, like diffusion tensor imaging (DTI), to examine alterations in white-matter structure in humans and non-human primates in relation to anxiety. I work closely with colleagues in my lab that assay behaviour, genetics, cellular and molecular data. As a master student I hoped to end up in this field, but I never anticipated how much I would still learn, and how far I would come.

Aim high; you can learn more and do more than at first you might imagine. Connections are everything; get yourself out there and meet new people, learn about what they are working on, get to know them. Which takes me to the next point; conferences. They are invaluable and offer scientists important opportunities to be inspired, travel and hang out with the aforementioned science friends. Collaborate. Collaborate. Collaborate. You cannot do this alone, good science is team science. That said, there is a world outside of academia with excellent and challenging industry jobs, do not dismiss them out of hand. Most importantly, try to figure out what drives you and what keeps you motivated. It is easy to move from one project to the next and lose your focus. Do not lose track of your own goals.

Our lab works with non-human primates and faces much scrutiny from animal rights organizations. Although the ethical treatment of research animals is obviously an important consideration when doing research, it is also very important to see the context in which this research is done. Mental illness takes a huge toll on global health, as neuropsychiatric disorders are the number one cause of disability in the United States, and rank third globally. Despite this, US research funding for mental health greatly lags behind other fields. This is likely



“I hoped to end up in this field, but I never anticipated how much I would still learn, and how far I would come.”

due to a continued stigma that surrounds psychiatric illness. These issues are exemplified when our primate research is targeted by institutions like PETA. Animal research into the biological underpinnings of anxiety and mood disorders often receive a greater level of scrutiny compared to other fields. This is unfortunate as non-human primate models are proving essential in delineating the etiology of psychopathology, beyond what we will be able to achieve in rodent models. It is my hope that this stigma will reduce in the future as we gain insights in this field.

Marianne van Leeuwen – *Layout*

I wanted to become a researcher after hearing an exhilarating talk by a scientist when I was seventeen. So after a bachelors in Biomedical Sciences, I started with the master Neuroscience and Cognition in 2007. During the 2 internships I found out that, as expected, working in a lab was really challenging and varied. What I did not realise was that hard work does not always guarantee results and that the work is never finished. I had to conclude that I did not want to pursue a career in fundamental research after all. But what did I actually want then?

I talked to a lot of different people about other career options. One of those options was the most basic default option you always hear about: becoming a clinical research assistant (CRA). At first I was not very enthusiastic since it is hard to imagine what a job is really like on a day to day basis. So I took a leap of faith and applied for a CRA traineeship at resourcing agency DOCS. After this internship I crossed over to the “dark side” and worked for 2 big pharmaceutical companies (GlaxoSmithKline and Boehringer Ingelheim) until I switched to the VUmc and back to the academic world in March 2015.

“I wanted to become a researcher after hearing an exhilarating talk by a scientist when I was seventeen.”

In the VUmc I, together with 3 other colleagues, monitor all the investigator initiated research. We come into contact with all the different departments ranging from neonatology to the Alzheimer Centre and from complex phase 1 oncology studies to the simple withdrawal of 1 extra tube of blood. This job allows me to stay in close proximity of the field of biomedical



science but rather than conducting experiments myself I guide other researchers, many of them being PhD students, to successfully complete their research while abiding to the complex world of rules and regulations concerning research with humans. And this is something I find very rewarding.

Monitoring investigator initiated research has only been around for a few years, so there is a steep learning curve for the researchers as well as us. We try to find a middle ground between practicality and the ever increasing amount of rules and regulations. I do not know what my career will look like in a few years' time. Realising that I did not want to be a researcher taught me that you cannot know what you want to be doing in the future. I think the most important thing is that you keep enjoying what you do no matter where it takes you. It may be a cliché, but it is very true.

Two-photon glutamate uncaging

Hai Yin Hu¹

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Neurons communicate with each other through the release of neurotransmitters and their binding to the corresponding receptors. This occurs at specialised connections between the pre- and postsynaptic neuron. By bypassing the neurotransmitter release, glutamate uncaging allows us to directly stimulate the postsynaptic terminals. Combined with fluorescence microscopy, this has granted us new structural insight into their mechanics. This technique has made it possible to map the glutamate sensitivity of synapses (Matsuzaki *et al.*, 2001), induce LTP at a synapse of choice (Harvey and Svoboda, 2007), and has even shown that glutamate can induce new postsynaptic terminals (Kwon and Sabatini, 2011).

Caged glutamate (Fig. 1) is obtained by attaching a specific photosensitive molecular group to the major excitatory neurotransmitter glutamate, rendering it inactive. Through photo-stimulation, this additional group can be cleaved off, resulting in active glutamate. Activating it on a local scale makes it possible to stimulate single synapses. This can be achieved by using a highly focused light source, e.g. as in a laser microscope system. In addition, a fluorescent marker in the neuron of interest is necessary to visualise the uncaging targets (Fig. 2A). The two-photon laser microscope has significantly less out of focus activation and deeper tissue penetration, making it the ideal choice for local stimulation in thick brain samples. To validate the uncaging, the induced synaptic responses can be recorded using patch clamp (Fig. 2B), an electrophysiological technique. By recording these responses, the researcher can directly observe whether the uncaging produces responses in a physiological range. If necessary, the response strength can be varied by changing the laser power.

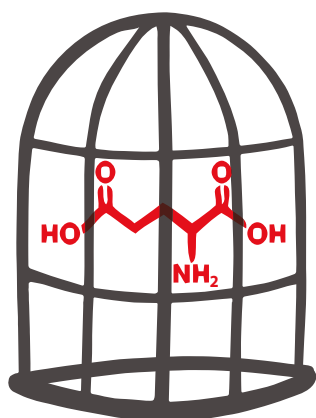


Figure 1. Caged glutamate.

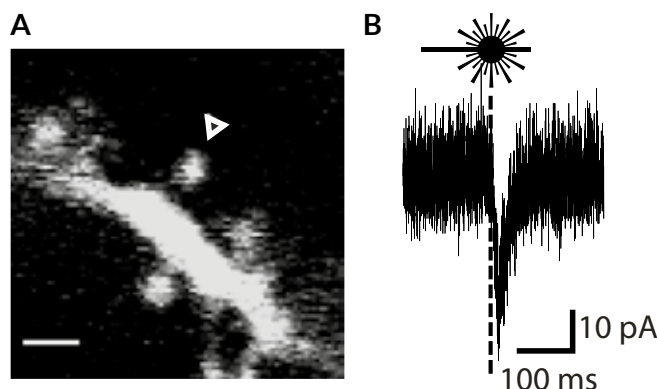


Figure 2. Excitatory response to uncaging stimulus. A) Dendrite visualized by Alexa 568 fluophore. Target of uncaging at triangle. 1 um scale. B) Electrophysiological response measured using patch clamp.

Often, caged glutamate is not completely inert; for instance MNI-Glutamate acts as a strong antagonist for inhibitory transmission. This is frequently bypassed by adding TTX, which blocks all firing activity. However, for certain studies, such as those that investigate inhibition, this may present a severe limitation. More recent caged compounds have increased sensitivity towards two-photon light, making it possible to use it at lower concentrations and partly avoiding this problem, thus opening up for new possibilities (Fino *et al.*, 2009; Chiovini *et al.*, 2014).

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Iris Sommer is a professor in psychiatry at the UMC Utrecht. In 2006 she started the 'Voices Clinic' to investigate hallucinations and schizophrenia. Recently, she published 'Haperende Hersenen' (EN: 'Malfunctioning Brains', 2015), a book describing personal stories of people with neurological and psychiatric disorders. In addition, it explains the causes, symptoms, diagnostic processes, and treatment of these disorders. 'Haperende Hersenen' has been received positively by the media and has been complimented on its clarity and accessibility. We sat down with Iris Sommer to ask her some questions about her book, research, as well as about the psychiatric world, schizophrenia, and the future of neuroscientists.

When did your facination for the brain start?

I think it was a long time ago. I remember that when I was a child, about the age of 10 or 12, I used to go to the library. There I was allowed to borrow a certain amount of scientific books and I always took the maximum of 6 with me. My fascination for science was very broad. I liked the stars and the universe and things like black holes, but dinosaurs were not that interesting to me. Although I liked evolution and molecular science, the brain was one of my favourite topics and I tried to read about it as much as possible.

How did you decide to go into the direction of neuroscience instead of astronomy?

When you study the human body, the brain is by far the most interesting organ. I find it quite astonishing that some people devote their lives to urinary tracts or to the ear. Why not study the brain, if you have the chance? For me, it has never been difficult to choose anything but the brain. After my medical education, I did have to face a difficult decision. There are two brain specialists: a neurologist and a psychiatrist.

How did you decide between becoming a neurologist and a psychiatrist?

Well, I thought that I was going to be a neurologist because I'm highly interested in Parkinson's disease, although I was also fascinated by people with schizophrenia describing their symptoms and complaints. When you start to study the symptoms, it is astonishing to see how all these symptoms occur and it makes you wonder how the normal brain works. How do perception and normal thoughts evolve without these disturbances? For me that was the most fascinating thing and that's why I chose psychiatry. I still miss the aspects of neurology and I wish these two specialisations would come together at one point.

At the moment, what is the most intriguing research question that is driving you? And if you could have the answer to a specific research question right now, what would it be?

For me, there is a difference between what you are most curious about and what is most needed in patient care. In my perspective as a doctor, I think we desperately need



treatments for cognitive dysfunction in brain disorders. This is definitely the case for patients with schizophrenia, but it is also the case for people with all other brain disorders. The society we live in demands people to be cognitively strong. Many people with brain disorders are not cognitively strong enough - that is why they often cannot compete. The most urgent research is not always the most fascinating research. If I could do research only for my own curiosity, I would maybe do something with the gut-brain axis or how the role of the immune system is involved in different types of brain disorders. Although this would stimulate my own curiosity, I do feel the urge for clinical practice driven research

In a previous interview with the Rudolf Magnus Brain Center, you mention that it has been known already for 50 years that the immune system is involved in schizophrenia. How did this point of view evolve over time?

I think it has been known even longer - at least an association between schizophrenia and the immune system. Henry Maudsley was the first to mention it about one hundred years ago. He noted that people

Interview

with schizophrenia more often had type 1 diabetes, which is an autoimmune disorder. Very recently this was replicated for almost all autoimmune disorders. So when you have an autoimmune disorder, let's say diabetes in your family, then the chance for getting another autoimmune disorder, like chronic colitis, thyroid inflammation, or a skin disorder is always increased. Schizophrenia and bipolar disorder also group into that category. One hundred years ago there were quite a lot of syphilis patients and many cases of psychosis were actually caused by syphilis. It was not strange to treat people with psychosis for infectious diseases. Since then we have had a period of brainless psychiatry, meaning all disorders with a known brain base were the domain of neurology and what remained was put into psychiatry. Sometimes it was even thought that there would not be a brain base at all. Of course there is a brain base for psychosis, but we didn't have the means to find it without the many sophisticated measurements that exist today, such as functional MRI, PET scans and MEG. Although nowadays we acknowledge a brain base for psychiatric disorders, we still don't know the complete routes. So, there is still a lot to investigate how exactly these disorders emerge.

In the same interview you also mentioned your fascination for the complexity of schizophrenia. Is 'complexity' something that is characteristic for schizophrenia, compared to other mental illnesses?

That is a good question and perhaps schizophrenia is not

more complex than for example obsessive compulsive disorder. I think what fascinates me about schizophrenia is that many of the symptoms are not experienced by healthy people. We have all gone through some depressive moments, anxiety, or maybe some obsessive behaviour, but only a few have gone through psychosis. That is quite something else. It makes you marvel of what the brain is capable of.

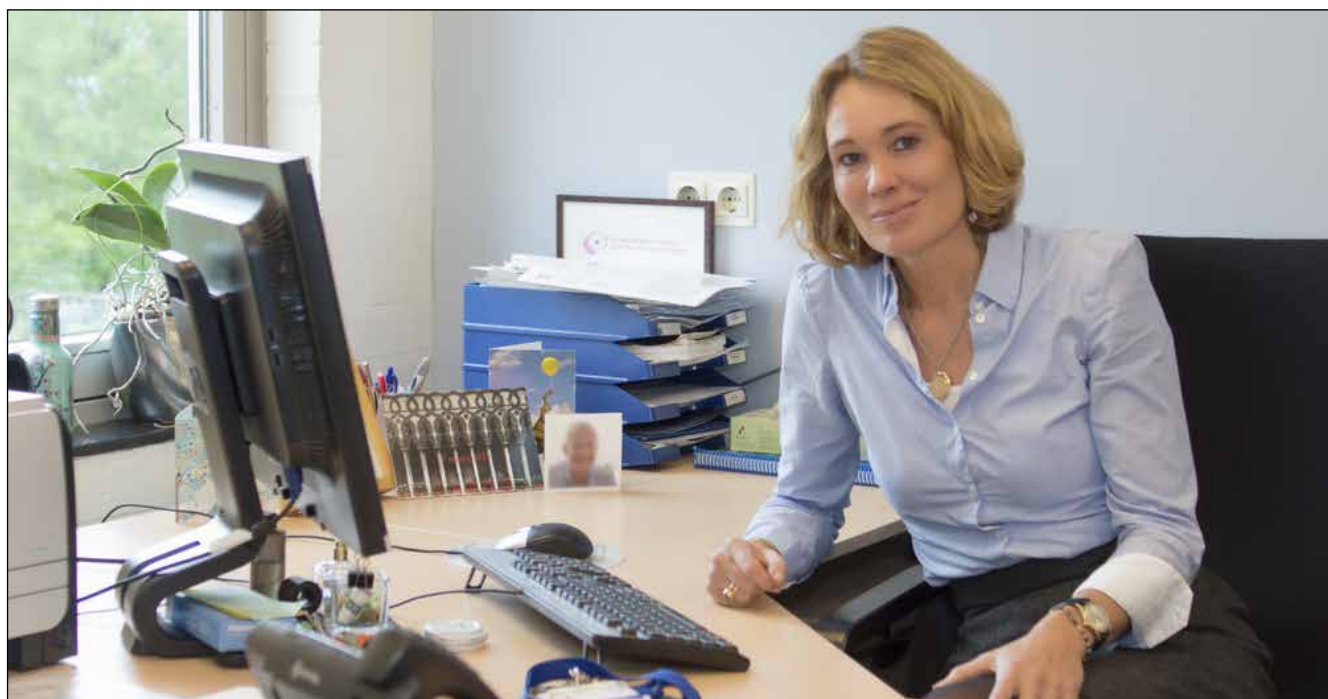
“Why not study the brain, if you have the chance?”

Similarly, would you say that not everyone has experienced hallucinations?

Almost everyone has experienced one or two hallucinations. For example, I have heard my name called out loud, while there was no one present. Sure that is a hallucination, but it is not that interesting. When I listen to my patients and they tell me they are constantly hearing three or four voices, telling them all kind of frightening messages. That is quite a different symptom, in my opinion.

Let's talk about your book. I can imagine writing a book involves time and effort. How did you decide to write a book, where did the idea start?

I like writing! I don't mind writing in the evenings and weekends and I actually like it much better than



watching television. So the motivation to write the book was purely personal. I didn't need funding, all I needed was a laptop. I did collaborate with the Dutch Brain Foundation, because they have more or less the same message as I do.

“If your job is your hobby, it will be very easy to keep up long working days.”

We tried to convey an optimistic perspective on how psychiatry can change in the future. Psychiatry hasn't changed much over the past 20 years. My education was roughly the same as what I teach my students now. For long, psychiatric treatments have been at a standstill, while other medical professions have evolved rapidly. This lack of change made many people quite pessimistic. They assume that we will never understand the brain, that we will never understand psychiatric disorders, and that we will never evolve the current therapies. On the contrary, research has not been on a standstill at all: there have been spectacular breakthroughs in understanding psychiatric diseases. I think it won't be that long before we can use that knowledge to create new and more sophisticated interventions. Interventions not based merely on trial and error, but on the knowledge that we have gained about the brain base of psychiatric disorders. I wanted to share this optimism with patients and their family who are suffering from brain disorders.

When you receive a lot of attention, people might criticise your work. Have you ever felt offended or threatened by other researchers or patients?

A more or less funny aspect of my publicity is that

patients with different types of disorders now tend to visit my clinical hours. Sometimes I am asked for medical advice about for example Parkinson's disease, but I am only a specialist in schizophrenia. Then, I have to ask other colleagues to tell me about Parkinson's disease or for example multiple sclerosis, because I can only do so far.

I receive many positive emails. The only criticism I have had is directed towards the selection of disorders I presented in my book. Sometimes patients are disappointed that what they are suffering from is not in the book. I think I have to write another one!

Will you write another book?

Sure! Maybe not about brain disorders again, but I will certainly start writing again.

As a final question, do you have any career advice for us – students of Neuroscience & Cognition – to become a successful scientist?

Do what you like most. If your job is your hobby, it will be very easy to keep up long working days. Just follow your curiosity, the methods and topics that you like best. Try not to settle down for something that 'maybe pays better' or 'is more important' in any way. You will have to work hard as a brain scientist: it is really competitive and there are many people like us. It will be easier to keep up if your job is your hobby.

REFERENCES

Brain Center Rudolf Magnus. Interview with Iris Sommer. Visited on 25-01-2016, from <http://www.umcutrecht.nl/en/Research/Research-programs/Brain-Center-Rudolf-Magnus/Research-psychotic-disorder/Interview-with-Iris-Sommer>

Interview

Marika Broekman started her career with a double degree in law and medicine. Currently, she is working as a neurosurgeon and researcher in the field of neuro-oncology. She recently moved to Boston and agreed to a casual Skype-interview about her career, her future plans, the difficulties but also the beautiful aspects of combining both research and being a doctor, and we get some insight in her own research regarding the tumour microenvironment.

What made you choose to combine your profession as a neurosurgeon with research? Are both professions what you expected it to be?

I've always liked challenging myself. During my six years in medical school, I noticed that – although I found it extremely fascinating to learn about the human body – the focus was on practical actions. I was, however, always wondering about underlying mechanisms. When I had to choose a place for my medical research internship, I applied to several foreign labs, and ended up in the same lab as where I am now, actually. And I loved it! I was working on a specific neurological disease and a possible new therapy; it was all very biological. In spite of my everlasting motivation to help people, which drives me every day as a doctor – even when I am 60, I think I will still have this motivation to jump out of bed to help my patients – I am convinced that the cure for brain cancer comes from the lab. That's why I decided to combine my job as a neurosurgeon with research; to also be part of that process. Is it what I expected it to be? I don't know, it is difficult to recall the expectations you have in the beginning. It is also always more difficult, more intense than you anticipated, but at the same time it is so much more as well.

“The first time I came to Boston as a MD student, I didn't know anything; I had never even held a pipette!”

You recently started in Boston, what are your experiences so far? Do you see large differences between the research world here in the Netherlands and over there?

To be honest, I am really just settling in. A transatlantic move with the whole family, as you can imagine it is quite an adjustment. Other than that, I really like the stimulating environment over here. Every week, there are talks by Nobel Prize winners, for example. Also, there are a lot of experts in the field who are very approachable for you to talk to. I think that this is quite similar to the situation in Holland, but the main difference is that it is much more concentrated here; it is like a big magnet for talent! Especially if you want to learn a lot, what I



like doing myself, then I think this is a really good environment to be in. Also for you as students, if you get the opportunity to go abroad to a highly recommended place, such as Boston, dream big and just go there!

What are your plans for the upcoming year in Boston?

That is top secret! No, at the moment I am supervising a couple of students, three in the lab and two in the clinic. One of the things we are focusing is the role of the immune system in brain tumours. What we mainly try to figure out is how they react with each other; how they communicate. Extracellular vesicles might play an important role in this process. There are some real experts in the field here, so I think that we will make some progress, definitely. At the same time, we will be looking at more clinical data, in order to find out the impact of certain therapies that we have always been using; to look for possible improvements clinically as well. So, for the upcoming year I hopefully will be doing the same as I was doing in Utrecht: to work with great people to try to answer some of those questions.

What is your opinion about the existing gap between the research world and the “hospital world”? How would you like to see this improved, if possible?

I don't feel that there is a gap for me personally, I can switch between lab and hospital real quick. But I realize, that is not normal for most people. It would be nice if it were normal, and I think it would be great if more medical students would have the possibility to experience the lab as well, so that they first of all understand that it is not scary and that it is hard work. I think that improving the understanding for what we are all doing is really important. Also, I think it is also good for not-medical students, like you, to work at least a bit together with a doctor. This is mainly because you gain some insight in what a doctor exactly does, which is the same as you are doing, namely improving the life of patients.

I can imagine that by being both a researcher and a neurosurgeon, you might encounter difficulties or conflicting issues between a protocol and your acquired knowledge about underlying mechanisms for example. Do you think this is a problem or do you see it as an advantage?

Ultimately, it is an advantage. Knowledge about underlying biological processes of the proceedings you need to perform as doctor, I think that it will make you a better doctor! Of course, sometimes it is difficult. For instance, as a brain surgeon it is possible that you have to deal with emergencies; you have to take out a haemorrhage for example. On one side you are thinking about the function of the brain region that you are operating on, or about the changes you are making on cellular level by performing such an operation. But on the other side, if you don't do the operation, your patient will die. In these cases, it is important that you are able to switch off your underlying knowledge and just perform the operation. But in the long term, I definitely think that it is beneficial if you as a doctor understand a bit more about molecular mechanisms, mainly because you are able to improve the quality of the care that you are providing.

But wouldn't it be frustrating that you have all this knowledge, and still have to follow the protocol?

Perhaps, yes. But the reason why I still have to follow a protocol, is that we don't have the solution to the problem we identified. So, yes, I find it extremely frustrating that I have this knowledge about possible side-effects of some of the proceedings I have to perform, but precisely this

knowledge drives me in my research to find a solution for those problems so that – hopefully one day – we can change that protocol, that is my ultimate goal our own research – concerning glioblastomas, extracellular vesicles, and the tumour microenvironment – is very innovative, and anti-cancer therapies can possibly be realized based on those vesicles.

Do you think this is a near-future perspective or still a long-term goal?

That really depends. These extracellular vesicles can be used in two ways as therapeutic targets. First of all, they can be employed as delivery vehicles to the tumour or the microenvironment, and some groups are actually pretty far on that. Before we can incorporate them into the protocol, a lot must first be accomplished, but for being tested in the clinic we are getting close. Regarding the other technique, stopping the shedding of the vesicles, I think that although the preclinical work is very promising, thus far we have not identified something that we can actually use in the clinic. I think, that this illustrates very well how it works in science; perhaps tomorrow someone comes up with an amazing idea and suddenly it all goes very smoothly. It is not a long-term goal, but a mid-term goal, I would say.

Do you have any advice for us students? Are there any professional skills that you think are important to become a successful scientist?

I think that being a good scientist requires a lot of good skills. But don't worry, the majority of the people I meet, have them. First of all, I think that is important that you can communicate. For example, the first time I came to Boston as a MD student, I didn't know anything; I had never even held a pipette! But people are so nice around here, just by asking questions and helping others with their experiments, you learn a lot. And by learning things, you not only acquire more knowledge but you also found yourself falling more in love with science. Also, be curious, always wonder about the why, the how... Most important: don't ever give up! In research a lot of things can go wrong, you always have those well-known 'grey days' in which nothing works, and then you are like depressed for another month. There will be times that funding is hard, that your experiments don't work, that you have to do it all over again, but just don't give up. Keep in mind that there always will be a time that things do work out for you!

A climate change in science careers

Comparing career steps taken by young scientists currently and in the past provides an interesting view on changes in environmental factors that influence success. Looking back to my years as a starting scientist, I realise that these changes are so extensive that they may be reminiscent to a climate change. I would like to share my personal view here.

I started my career by accepting a PhD position in a project concerning the biochemistry of neuropeptides in 1977, based on my sheer interest and fascination, and not the idea that this was my first step on a planned journey. At that time a career rather happened than was planned. I would describe the climate in which science careers developed then as that of a tropical rain forest: lots of greens and fruits, plenty of water, no eye on the horizon, surprises around the corner, finding your way over short distances only. Science careers were mainly put into effect by supervisors and mentors, as I experienced it. If you did a top job, they didn't want to let you go.

“The science encountered in this climate is more exciting and powerful than ever.”

Consequently, young scientists continued along the lines that they had developed in the place where they did their PhD. So did I. The staff positions were largely taken by scientists who had entered the institute as a student. Doing a post-doc abroad was far from required as a career step. It was granted to you, if you wanted the adventure. An important factor setting this climate was funding. Positions were mainly paid by primary sources of universities. A granting system was in place at 'ZWO' (Zuiver Wetenschappelijk Onderzoek, now Zorgonderzoek Nederland Medische Wetenschappen) with a success rate of about 20%. There was room for bottom-up ideas and fundamental interests. Many things that set the climate of today were not in place: there were no personal grant support programs, journal impact factors didn't play a role and author H-indices had not been invented, there were no Top-sectors or societal-driven science. Quite a comfortable climate to thrive in.

Presently young scientists have arrived in a steppe climate. The outlook is tremendously wide, safe havens are on a long distance and hard to



recognise, it is hot and there is not much drinking water to find on a prolonged trip to the next oasis, and there is serious competition by peers on the same track. Not an easy environment to thrive in. Back in 1977 we were not provided by necessity with survival skills to flourish in a tropical rain forest climate. Now in 2016 students have to be more foreseeing. They must be aware that the essential first step is thorough preparation and constant monitoring, if they successfully want to lead their career through the steppe of science (Yewdell, 2008). Therefore, it is not surprising that many students think that you need to be a 'die hard' to take this trip. But mind you: the science encountered in this climate is more exciting and powerful than ever. Look at the papers in top journals. They contain Experiments more complete than ever, of which the supplements are complete studies themselves. Science is on a speedy flow. This means that those who are ready for it can find themselves to be comfortable with this climate too. There is much to enjoy on your journey!

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Yewdell, J. W. (2008). How to succeed in science: a concise guide for young biomedical scientists. Part I: taking the plunge. *Nature Reviews Molecular Cell Biology*, 9(5), 413-416.

- J. Peter H. Burbach
Department of Translational Neuroscience,
Brain Center Rudolf Magnus, UMCU

I moved from Italy to the Netherlands at the end of August, just a couple of days before classes started. It was a warm sunny day, which would have fooled any newcomer into believing wind and rain are not a big deal here. A week went by and it was pretty clear that raincoats and struggling to cycle into a headwind would be an almost daily event for the next couple of years. It does not take long for you to get used to these small things and get into the real daily life experiences. You meet up with friends, go out, attend classes, get familiar with the city centre, and you know where to go if you and your friends want to have a *biertje* alongside the canals.

“It was a warm sunny day, which would have fooled any newcomer into believing wind and rain are not a big deal here.”

I decided to come to Utrecht because the university provides its students with education at a high academic level and is well-inserted into the world of scientific research. However, I had no idea it would be so different from Italian universities, for example with respect to facilities, research opportunities, and teaching methods. Practice and hands-on experience are a big part of this Master, and they definitely contribute to making it more fun, interesting, and stimulating for students. Even more so for foreign students who, like me, come from countries where most time is spent on studying books and passively listening to a teacher speak.

I would definitely recommend anyone to enroll



in a Master abroad or to participate in an exchange programme. It is a fun, exciting, and very useful experience, both for your personal growth and your CV. I got to meet amazing friends, I am gaining useful skills for my future scientific career, and I am experiencing a new level of independence. Of course preparations have to be made before moving, such as enrollment, documents, money, renting a room, and mentally getting ready to move to another country for at least two years. However, I promise the experiences and memories you will gain are worth it!

- Claudia Amboni
Master student Neuroscience & Cognition

Advice for a young investigator

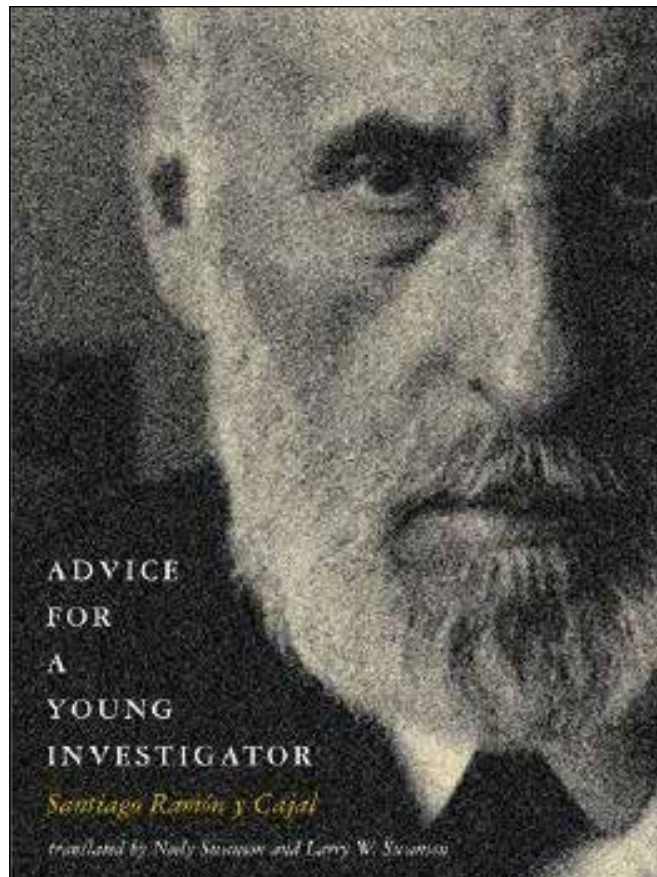
by Santiago Ramón y Cajal

Written by Santiago Ramón y Cajal (1852-1934), 'Advice for a young investigator' summarises the advice he wishes to have had at the beginning of his career. Ramón y Cajal is a Spanish neuroscientist and Nobel laureate, famous for his detailed neuroanatomical drawings, who wrote the first edition of this book in the late 19th century. Despite being over a hundred years old, the advice given by Ramón y Cajal remains surprisingly applicable to the present time.

The book is divided into 9 chapters, and it provides practical instructions on topics such as how to choose your area of research, create hypotheses, and set up a laboratory (which he strongly recommends to setup independently at one's home). In addition, the importance of being up-to-date about the literature within your field of research, the advantages of attending international scientific congresses, and how to write a scientific article are covered. Ramón y Cajal's text is precise, concise, without nonsense, and entertaining at the same time. Also, the author does not restrain himself from ironic comments. For example, when describing types of people to avoid in science he states: "Our neurons must be used for more substantial things".

"Despite being over a hundred years old, the advice given by Ramón y Cajal remains surprisingly applicable to the present time."

While surprisingly translatable to modern times, the sections regarding money, patriotism, and the social life of a scientist seem outdated. Despite being Spanish, he does not have high regard for the research performed by his fellow countrymen and therefore he suggests that all scientists should learn the language of modern science, German. The section that makes the reader cringe is when Ramón y Cajal reveals his thoughts about the ideal partner suitable for a scientist. Although female scientists were not unheard of at the beginning of the 20th century, Ramón y Cajal fails to consider the option that a Young Investigator could be a woman. Therefore, as an answer to his question "What qualities should grace the young woman



chosen by the man of science?" he concludes that the scientist is best off with one of the four types: the intellectual, the rich heiress, the artist, or the professional woman. However, he states that the two latter types usually mean never-ending streams of difficulties and that the goal is to have a wife where the "husband, free of anxiety, may occupy himself in the great things".

The out-dated parts, however, do not detract from the value of the book as a whole. Ramón y Cajal provides great insight into the world of science without the need for self-censorship. He warns the beginning scientist to be aware of distractions such as admiration for authority, excessive theorizing, and preoccupation by valorisation. His book assures that passion for science, perseverance, and a meticulous approach to research are enough for anyone wishing to succeed. 'Advice for a young investigator' is a quick read with practical advice from one of the pioneers in neuroscience offering an interesting view on the struggles faced by scientists then and now.

- Anu Meerwaldt
Master student Neuroscience & Cognition

Tales from both sides of the brain: a life in neuroscience

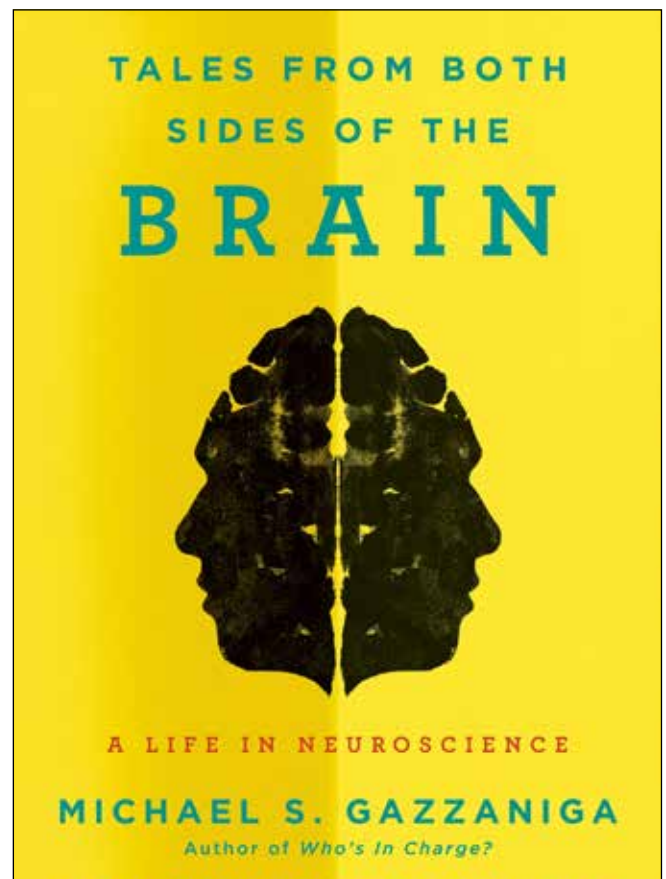
by Michael S. Gazzaniga

"How on earth does the brain enable mind?" This question is both the scientific quest leading the career of Michael S. Gazzaniga for more than 50 years, as well as the starting point of his latest book: *Tales from both sides of the brain: A life in neuroscience*. Gazzaniga, who coined the term "cognitive neuroscience" in the late 1970s, has been a major driver of this field since its birth. Co-founder of both the Journal of Cognitive Neuroscience and the Cognitive Neuroscience Society, he is currently in charge of the SAGE Center for the Study of the Mind at University of California, Santa Barbara.

Cognitive neuroscience - or, generally speaking, the study of the brain mechanisms underlying mental processes - is rooted in the first neuropsychological tests carried out on patient W. J., who had previously suffered from severe epilepsy. In order to palliate the symptoms of this condition, W. J. underwent callosotomy, a surgical procedure in which the corpus callosum is dissected, thus depriving right and left brain hemispheres of their main communication pathway. Gazzaniga was lucky to be the first to realize that callosotomy does not simply split the brain in two differentiated and virtually isolated hemispheres, but that it also gave rise to two differentiated mental systems, each one with its own capacities and distinctive consciousness.

"The book is a careful attempt to show the human face of science."

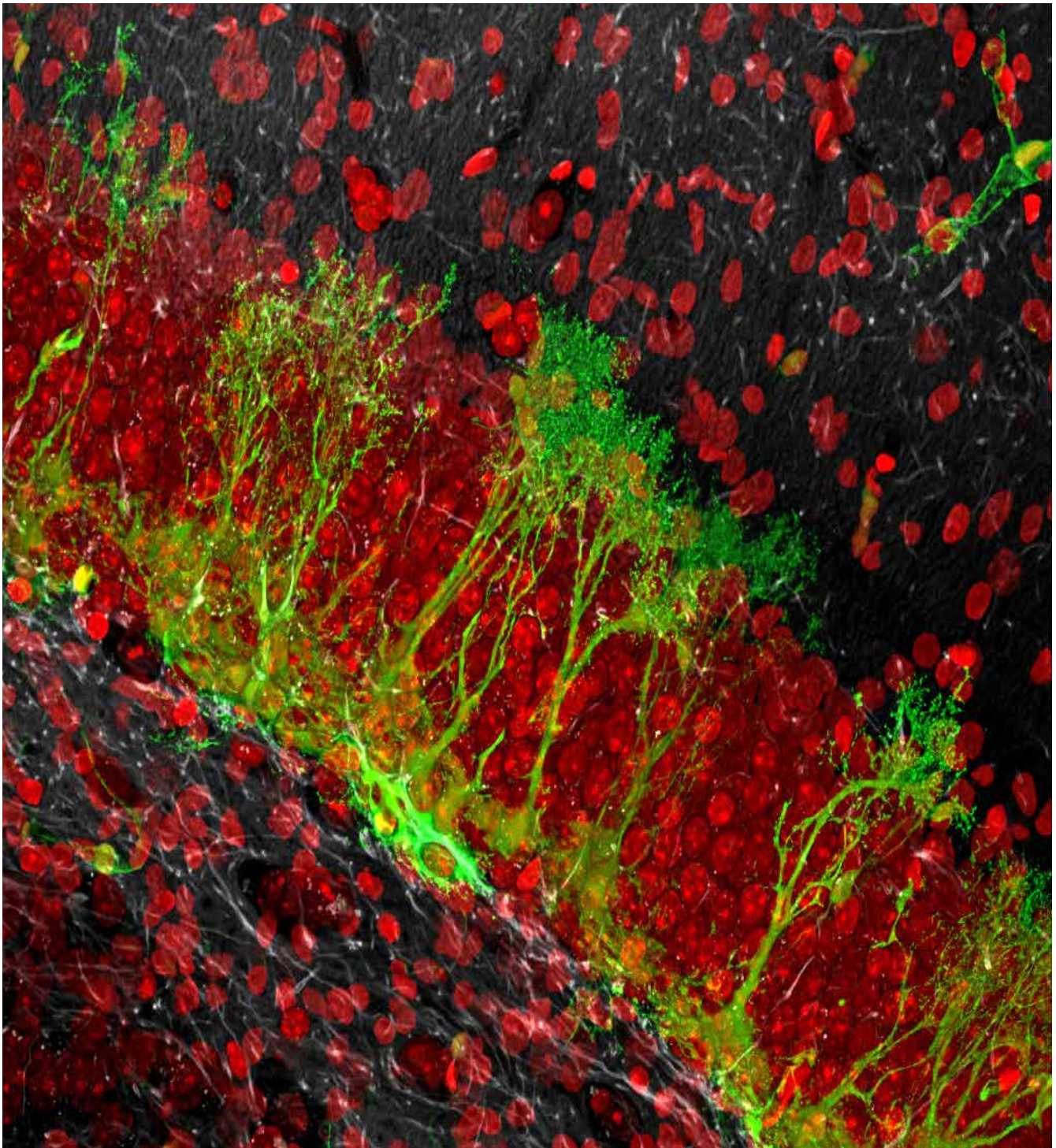
Tales from both sides of the brain: A life in neuroscience chronicles the history of the split brain research since this initial breakthrough, and does so from the behind-the-scenes viewpoint of its most representative figure. The several case studies and experimental results presented along the book will engage anyone curious about the brain-mind relationship, as they show



the dramatic consequences of a relatively simple neurosurgical procedure in domains such as language, consciousness, or self.

Even more remarkable, the book is a careful attempt to show the human face of science, and it constitutes a window to see what the scientist's life really looks like, as well as to what extent factors such as chance, politics, or friendship play an important role in it. Even if it might be argued that the stellar career in science portrayed here is not a representative picture of what careers in science usually are, this book is worth reading. It will encourage any young brain researcher to carry on with his or her own scientific journey and, ultimately, it leaves us in charge of the endeavor to answer one of the greatest questions science has ever asked, namely: how on earth does the brain enable mind?

- Luis Cásedas Alcaide
Master student Neuroscience & Cognition

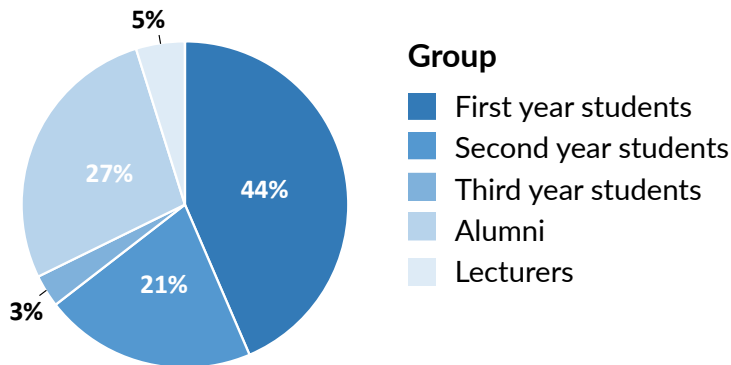


Neural stem cells

Mouse hippocampus section, imaged with the confocal microscope with a 40x C-Apochromat water immersion-objective lens at 62x magnification. Neural stem cells are visualised in green and their progeny, the granule neurons, in red. When neural stem cells are activated by extrinsic stimuli, they enter mitosis and generate neuron progenitor cells, which eventually mature into granule neurons that migrate to the granular zone of the hippocampus.

Picture by Ann-Shyn Chiang and Grigori Enikolopov of National Tsing Hua University (Taiwan).

Scientific research strives to gain knowledge relevant for society, yet their approval is strictly regulated by ethical considerations: the human gain must outweigh the value of the losses, e.g. because it jeopardises animal welfare, or has economical consequences. We created an online questionnaire about current neuroscience-related (ethical) debates. The 62 respondents, ranging from fellow students to alumni and lecturers, were asked to either agree or disagree with 10 motions that are naturally far more complex and nuanced. However, participants could elaborate on their answers by adding a comment, aimed to clarify why they think their opinion could not be restricted to either of the two presented categories. Check out the results to see where you stand compared to the others.

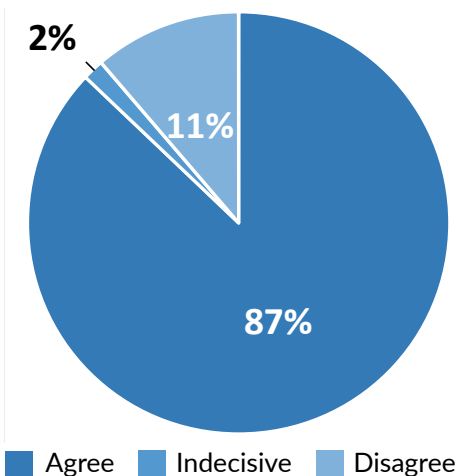
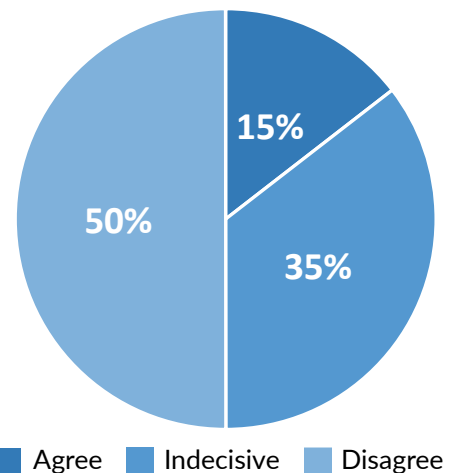


Fundamental research is generally more important than applied research.

"Fundamental research is important, with no direct implementation in mind one cannot say - a priori - how important."

"The strongest combination is when the two meet each other. Both fields can complement each other, none of them is more important than the other."

"There should be a close collaboration between the two in order to come to great discoveries and advancements that can be applied in the clinic."

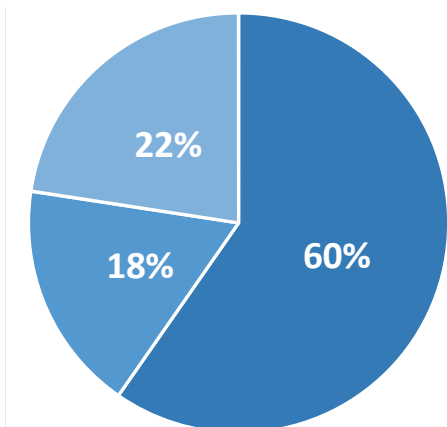


Researchers should be allowed to use human embryonic stem cells for research.

"With the development of induced pluripotent stem cells and the optimization of this human embryonic stem cells can be replaced for those specific research purposes."

"Yes, with stringent control measures in place."

Questionnaire



■ Agree ■ Indecisive ■ Disagree

Researchers should be allowed to use primates for research.

"Only when the research methods are non invasive."

"Only if no alternatives are available and the research is of extreme value. Also no apes should be used as they are highly intelligent."

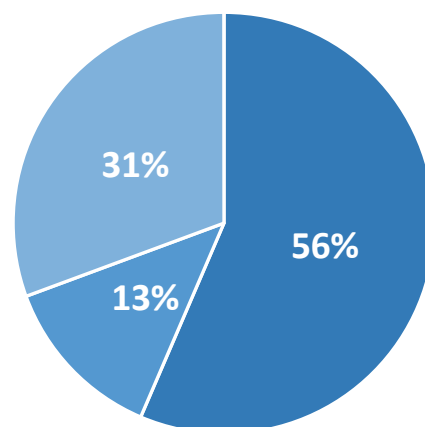
"It really depends on the question. For testing drugs before they go into the clinic, it is a necessary evil. For very fundamental research (e.g. vision), I am very skeptical."

Should neuroscience transform our understanding of criminal responsibility?

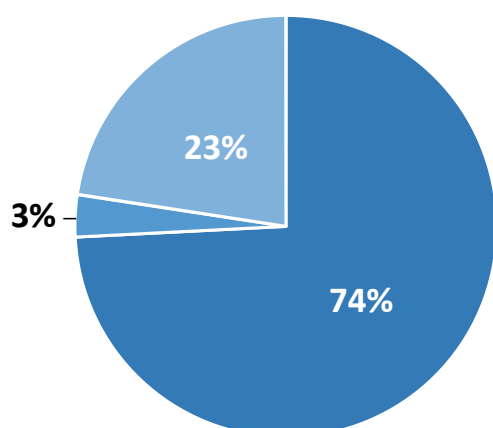
"Yes, but so should our understanding of 'innocence.'"

"Criminal responsibility means that you consciously understand that you are committing a crime, not that you can do otherwise. If a person comprehends the criminal nature of his actions, then he or she is responsible for them. That can be a person with or without any neurological impairments."

"Although we should be cautious with our conclusions. Research results should only be applied in law when there's extensive research evidence."



■ Agree ■ Indecisive ■ Disagree



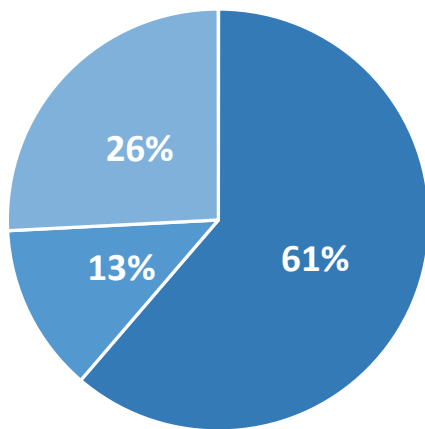
■ Agree ■ Indecisive ■ Disagree

Using neuroscience for commercial interests by making use of neuromarketing should be allowed.

"Yes, is it currently solid science? NO!"

"Even though most (if not all) of neuromarketing is bollocks, companies should be free to do whatever they want within the limits of the law."

"Yes, neuromarketing is a product on itself, sold to marketers - like ice to inuit - for a little bit of logically misplaced reassurance with regard to the effectiveness of techniques they've already been using for decades." Although we should be cautious with our conclusions. Research results should only be applied in law when there's extensive research evidence."



Neuroscience researchers should work in closer contact with industry.

"Yes, knowledge derived from research should be applied as much as possible."

"Depends on the field. Dependencies on industry money might lead to biased results."

"Only if very well monitored to avoid conflicts of interests."

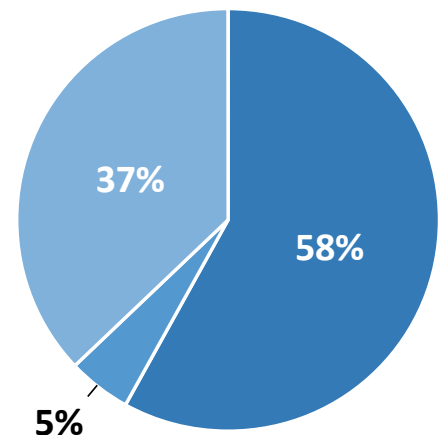
■ Agree ■ Indecisive ■ Disagree

The field of neuroscience should receive more attention in the media.

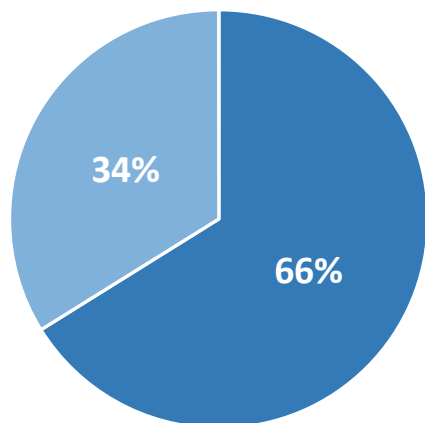
"Yes, as long as this attention is balanced and appropriately represents the research."

"No, it's being hyped enough as it is. I'm sure there are other fields who deserve more media attention."

"Mixed feelings. Fundamental research is very easy to misinterpret or at least to generalise when communicating to the public."



■ Agree ■ Indecisive ■ Disagree



The field of neuroscience should receive more attention from politicians.

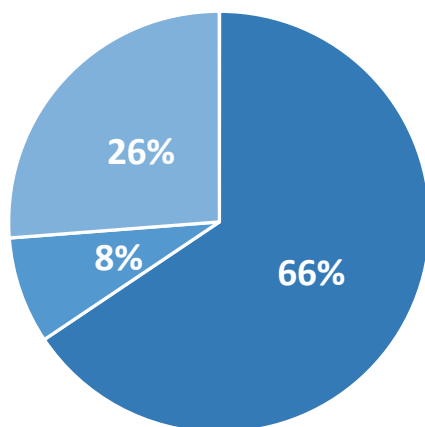
"It should be the other way around. Science should reach out to society more, explain things properly."

"Hopefully, we don't get too embroiled in the politics. Good publicity for fundraising can be important."

"I'm not entirely sure if knowledge about the field of neuroscience is an added value to politicians compared to for example law, physics and basic biology?"

■ Agree ■ Disagree

Questionnaire



■ Agree ■ Indecisive ■ Disagree

The mind is a byproduct of the brain.

"The mind is the brain. This question is posed from a dualistic point of view."

"It is the 'emotional, conscious' component of the brain."

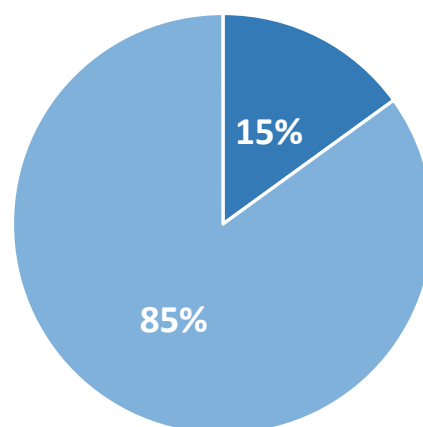
"I don't think it can be simplified to a 'byproduct'."

Given the observation that the human body has more bacteria than human cells, are humans involucre of bacteria?

"We co-exist in the habitat called the human body."

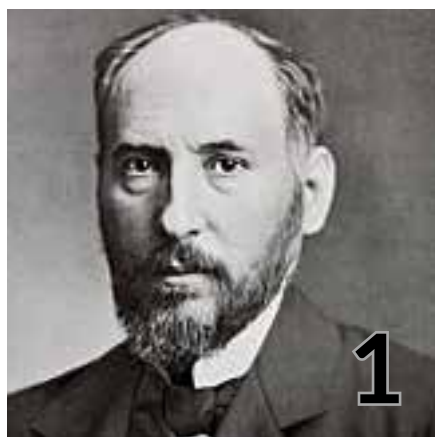
"Bacteria are not that what make us humans, that are the human cells exerting all its unique functions."

"The human body arguably does not have more bacteria than cells. In fact, it is hypothesised that everytime you go to the toilet you have less bacteria then cells."

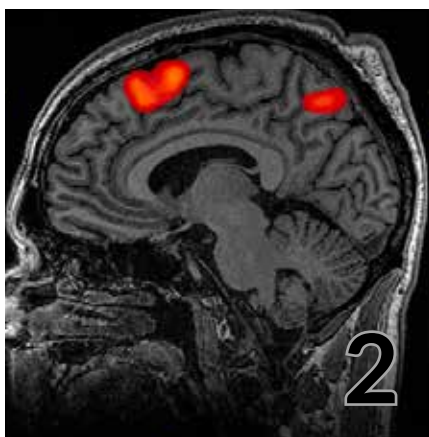


■ Agree ■ Disagree

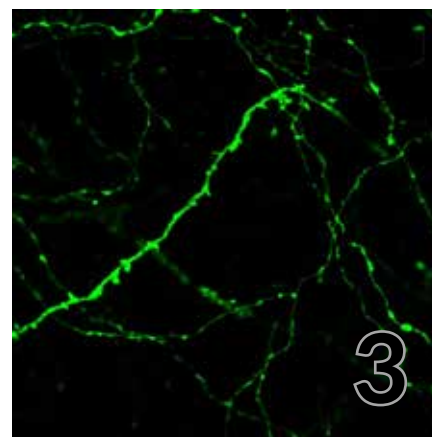
The greatest discovery in neuroscience of all time is...



Investigations of the microscopic structure of the brain by Santiago Ramón y Cajal (~1890)



Discovery of the principle underlying fMRI by Seiji Ogawa (1990)



Discovery and development of GFP (~1960)

19 May 2016
16:00

Towards precision medicine in neurology

David Goldstein, Columbia University Medical Center

Life Sciences Seminar, Utrecht

27 May 2016
16:00

Neural mechanisms of conscious and unconscious visual processing

Philipp Sterzer, Charité University Medicine Berlin

Helmholtz Lecture, Utrecht

02 June 2016
09:00

Synapsium 2016

o.a. Christian Keysers, Netherlands Institute for Neuroscience

Donders Institute, Nijmegen

14 June 2016
09:00

SUMMA Symposium 2016

o.a. George Chrousos, University of Athens Medical School

UMC Utrecht

16 June 2016
09:00

Pathogenicity vs. opportunism in medical fungi, an ecological perspective

Sybren de Hoog, CBS-KNAW Fungal Biodiversity Centre

Life Sciences Seminar, Utrecht

17 June 2016
16:00

Dysregulation of hypothalamic neural-microglial network in obesity and diabetes

Chun-Xia Yi, Academic Medical Center

Amsterdam Brain and Cognition Colloquium

07 July 2016
16:00

Implicit Social Cognition

Mahzarin Banaji, Harvard University

Donders Institute, Nijmegen

05 Sep 2016
17:00

STIM1/TRPC3 in the cerebellum - from synaptic function to behavior

Jana Hartmann, Technische Universität München

Erasmus MC Lecture, Rotterdam

30 Sep 2016
16:00

Synaptic signalling in the input layer of the cerebellar cortex

Angus Silver, University College London

Swammerdam Lecture, Amsterdam

30 Sep 2016
16:00

The Hippocampus as a Cognitive Map: Past, Present and Future

John O'Keefe, University College London

Donders Institute, Nijmegen

Additional information and seminars can be found at:
www.journal.neuroscience-cognition.org

