

MedNeuro

CNS

# Charité NeuroScience

a newsletter brought to you by the International Graduate Program Medical Neurosciences

September 2012 - Volume 05, Issue 03



engineering  
the brain





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## Best Regards to All of You!

It's time to celebrate! Since the relaunch of the CNS newsletter in May 2010, we have published 10 issues, 172 pages, 192 articles, and a lot of pictures. Our journey has taken us from more general topics – technology transfer, women in science, good & bad scientific practice, funding in science, and open access – to more scientific topics – neuroenhancement, brain stimulation, mental health disorders, and eventually this issue's main theme engineering the brain. We have covered research and fun – articles about Berlin researchers, among them students and professors, paper reviews, conference reports, art and culture, etc. We hope it has always been enjoyable and interesting for all of you.

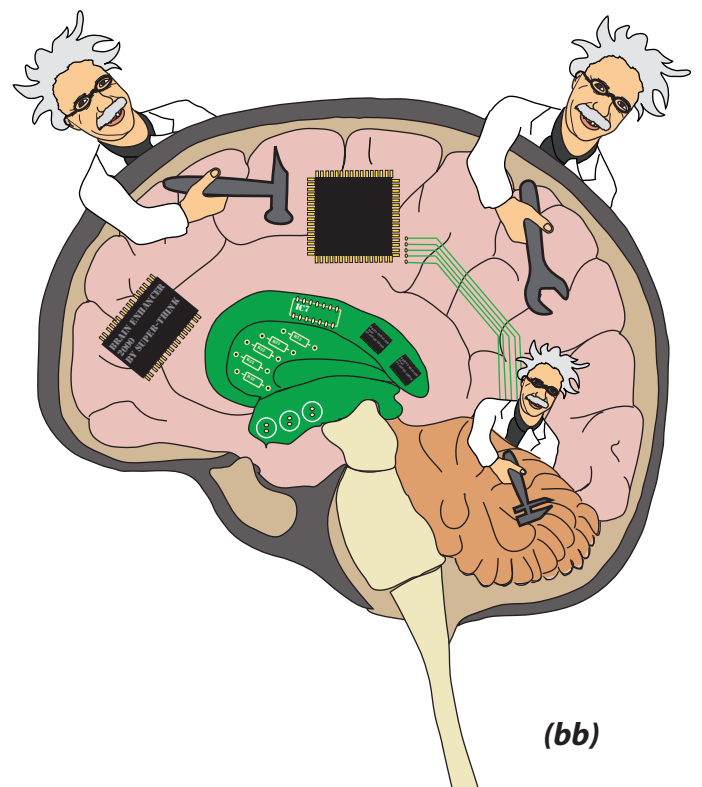
In the course of the ten issues, we saw editors come and go, just as MedNeuro students come and go – that's the life of a researcher. The editorial team grew as the number of external writers increased. We are very happy to see more and more interest in the production of the CNS newsletter. Stay interested, we are thankful for criticism as well as for positive feedback at all times.

For the last six issues, we have a professional layouter. We are very grateful for this as it has made our newsletter much more appealing.

In the current issue, we would like to share with you a broad range of topics under the umbrella 'engineering the brain'. You can read about the pros and cons of cognitive enhancement, adult neurogenesis, stem cell research, and brain-computer interfaces. Learn about Ghana, what's new from the FENS and BNF conferences, and whatever happened to Andriana Fetani, a former MSc student.

Now enjoy reading and let's all see what the next issues will bring.

– Marietta



(bb)

Coverpage: Julia Rummel

# HAPPY ANNIVERSARY CNS

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# Bright Ideas?: The Promises and Perils of Cognitive Enhancement

By Linda MacDonald Glenn, Bioethicist and Counselor-at-Law

In the last few years, the rapid convergence of nanotechnology, biotechnology, information technology, and cognitive science (NBIC) technologies, has fueled a growing debate in the scientific and bioethical arenas about the issues in cognitive enhancement. Nanotechnology is providing research instrumentation for improving knowledge of brain structure and function as well as new means of drug delivery. Neurobiology is developing increased understanding of how brains and associated neural systems work. Information technology provides signal-processing capabilities for neurobiological research and for interfaces among sensors, computers, brains, and prosthetic devices; it also enables modeling and simulation for computational neuroscience. Cognitive neuroscience has extended traditional cognitive psychology into the realm of understanding correlates between brain structure and function and cognition [1].

While cognition-enhancing drugs have received a lot of attention in recent literature, there is another emerging area of research that poses a number of ethical, legal, and social questions: Nano-neural

The ethical, legal, and societal concern is that by merging with technology, we change what it means to be 'human' or a 'person' and change basic human nature. Brain implants that create interfaces between human neural systems and computers will allow for (1) the improvement and augmentation of human capabilities, (2) the advent of 'human' immortality through cloning and implantation of bioelectronic chips with the uploaded emotions, memories and knowledge of the source human, and (3) the possibility that humanity may be replaced by the next stage in guided evolution [2].

As with many other emerging controversial technologies, there is a spectrum of beliefs. At one end of the spectrum, there are people who argue that neuroenhancements should be embraced as freeing and transcendent. At the other end of the spectrum are those who argue that neuroenhancement is an illustration of humanity's hubris and we, as a species, should put the brakes on further technological development. In the center of the spectrum are those who recognize that neuroenhancements are changing and challenging our current definitions of normalcy, as well as our relationships [2].

Most ethicists recognize that new technologies present the challenges of weighing and balancing potential benefits versus potential harms. At least one ethicist has argued that that the knowledge that we have gained about the relationship between our brains and behavior, may allow us to develop 'moral enhancements', a heightened sense of responsibility and empathy for others and our fellow creatures [3].

We will continually incorporate more and more computer technology into our lives, and ourselves, until we become one with it [4]. Even though enhancements and alterations are not likely to be banned, I would argue that it is prudent to advocate a thoughtful, cautious approach, with discourse recognizing public input, as well as a consideration of unintended consequences that may occur. The discussions ethics of cogni-

interfaces. This technology has the potential not only for brain repair or axon regeneration, but the merger of artificial intelligence with human capabilities. Futurist and scientist Ray Kurzweil predicts within the next 25 years, "the union of human and machine, in which the knowledge and skills embedded in our brains will be combined with the vastly greater capacity, speed, and knowledge-sharing ability of our own creations;" and that the merger between human and machine will be so complete that distinctions will be impossible or rendered meaningless.

**The Singularity University** is a new university in California that aims to educate young potential leaders (as well as existing ones) in the "number of exponentially growing technologies that will massively increase human capability and fundamentally reshape our future". They run an 10-week interdisciplinary graduate program each summer and are very interested in applications by enthusiastic, high calibre students with an international background. Scholarships are available.

tive enhancement should not be limited to neuroscientists: A creative multidisciplinary proactive approach that includes thoughtful reflections implications of the nano-neural interfaces is needed to address ethical and moral conundrums.

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- [2] Ethical, Legal and Social Issues in Nanotechnology and Regenerative Medicine: Methods and Protocols, Methods in molecular biology (Clifton, N.J.), v. 811, pp. 303-16, 2012
- [3] <http://www.theatlantic.com/technology/archive/2012/02/why-cognitive-enhancement-is-in-your-future-and-your-past/252566/>
- [4] Case Studies: Ethical and Legal Issues in Human-Machine Mergers (or the Cyborgs Cometh), 21 Annals of Health Law-ASLME edition 75"

## Further Reading

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- Andy Clark Natural Born Cyborgs.
- Martha J Farah Briefing: Brain Machine Interfaces and Non-Pharmacological Enhancement <http://www.neuroethics.upenn.edu/index.php/penn-neuroethics-briefing/non-pharmacologic-enhancement>
- Benedict Carey Brain Enhancement is Wrong, Right? [http://www.nytimes.com/2008/03/09/weekinreview/09carey.html?\\_r=1&pagewanted=all](http://www.nytimes.com/2008/03/09/weekinreview/09carey.html?_r=1&pagewanted=all)

**Linda MacDonald Glenn** is a bioethicist and counselor-at-law currently based in Vermont. She spent a large part of her career presenting pioneering cases in fields such as patient advocacy, genetics (nature vs. nurture) and neuroethics. She now focuses on academic aspects of these topics and is or has been a fellow of several institutions including the Institute for Ethics and Emerging Technologies and the Institute for Ethics at the American Medical Association. She is on the teaching faculty of several prestigious bioethics and scientific writing programs, including the Singularity University in Silicon Valley, California (see further reading box). She is the author of numerous seminal papers on her topics of expertise (for example "Biotechnology at the Margins of Personhood: An Evolving Legal Paradigm" and "When Pigs Fly? Legal and Ethical Issues in Transgenics and the Creation of Chimeras").

## Stem Cell-Based Therapies in Clinical Trials

Name of the Study	Intravenous Autologous Mesenchymal Stem Cells Transplantation to Treat Middle Cerebral Artery Infarct
Disease	Middle Cerebral Artery Infarct
Intervention	Autologous bone marrow-derived mesenchymal stem cells
Aim	There is a pressing need to develop other treatment modalities that can restore cell function, especially in strokes involving large arterial territory, such as the middle cerebral artery, as subsequent disability rates are higher. One of the most promising neurorestorative strategies in ischemic stroke, which has gained importance more recently, is cell based therapy. This study aims to determine the efficacy of intravenous transplantation of autologous bone marrow-derived mesenchymal stem cells in patients with acute middle cerebral artery infarct.
Study Design	Allocation: Non-Randomized
Status	Phase II
Sponsors and Collaborators	National University of Malaysia Cytopeutics Pte. Ltd. Cytopeutics Pte. Ltd.

Name of the Study	Safety Study of Human CNS Stem Cells Transplantation in Patients with Pelizaeus-Merzbacher Disease (PMD)
Disease	Pelizaeus-Merzbacher Disease
Intervention	Human CNS stem cells (HuCNS-SCs)
Aim	The purpose of this study is to determine the safety and preliminary effectiveness of human central nervous system stem cell (HuCNS-SC®) transplantation in patients with Connatal Pelizaeus-Merzbacher Disease (PMD), a leukodystrophy that affects growth of the myelin sheath.
Study Design	Interventional – Single Group Assignment
Status	Phase I
Sponsors and Collaborators	StemCells, Inc.

Name of the Study	Study of Human Central Nervous System Stem Cells (HuCNS-SC) in Patients With Thoracic Spinal Cord Injury
Disease	Thoracic Spinal Cord Injury Spinal Cord Injury
Intervention	HuCNS-SC cells
Aim	The aim of this study is to evaluate the effect of single transplantation of HuCNS-SC into the thoracic spinal cord of patients with sub-acute spinal cord injury.
Study Design	Intervention – Single Group Assignment
Status	Phase I/II
Sponsors and Collaborators	StemCells, Inc.

Name of the Study	Intravenous Stem Cells After Ischemic Stroke (ISIS)
Disease	Cerebral Embolism Stroke
Intervention	Intravenous autologous mesenchymal stem cell transplantation
Aim	The main objective of this study is to evaluate feasibility and tolerance of intravenous injection of autologous mesenchymal stem cells for patients presenting an ischemic stroke (less than 6 weeks).
Study Design	Allocation: Randomized
Status	Phase II
Sponsors and Collaborators	University Hospital, Grenoble Commissariat à l'Energie Atomique Institut National de la Santé Et de la Recherche Médicale, France



## Adult Neurogenesis in the Mammalian Brain — A Question of Methodological Progress and Acceptance of Revolutionary Ideas

By Ana Luisa Piña, PhD, Group Leader at Experimental Neurosurgery

Historically, the structure of the adult mammalian brain has been considered resilient to structural changes. However, it is now clear that the adult brain can respond to environmental and internal challenges with significant structural, biochemical, and even genetic changes, a phenomenon termed neural plasticity. One of the most dramatic scientific advances demonstrating this plasticity was the discovery of adult neurogenesis in mammals, including humans.

Neurogenesis, defined as the process of generating functional neurons from precursors, was traditionally viewed to occur only during embryonic and perinatal stages in mammals. From the beginning of the Neuron Doctrine in the late nineteenth century to the early 1990s, the central dogma in neuroscience established that new neurons are not added to the adult mammalian brain. The main reason why this static idea remained valid for such a long time was the inadequacy of the available methods both for detecting cell division and for determining whether the apparently new cells were glia or neurons.

As the first evidence against this dogma, it was shown that some regions of the adult brain exhibit ongoing neurogenesis demonstrated by DNA labeling by [3H]-thymidine, which is incorporated into the DNA of dividing cells. Therefore, the progeny of cells that have just divided could be labeled, and their time and place of birth determined.

Starting in the early 1960s, Joseph Altman published a series of papers reporting thymidine autoradiographic

evidence for new neurons in the dentate gyrus of the hippocampus, the olfactory bulb, and the cerebral cortex of the adult rat as well as new neurons in the neocortex in the adult cat. Although published in the most prestigious journals of the time, these findings were totally ignored or dismissed as unimportant for over two decades.

Years later and in a series of electron microscopy studies, Michael Kaplan showed that [3H]-thymidine-labeled cells in the dentate gyrus and olfactory bulb of adult rats have the ultrastructural characteristics of neurons, such as dendrites and synapses, rather than those of astrocytes or oligodendrocytes. He also gave evidence for new neurons in the cerebral cortex of adult rats, and mitosis in the subventricular zone of adult macaque monkeys. Again, publication in prestigious and rigorously reviewed journals, was not enough to demand attention from the scientific community.

An important reason for the small impact of Kaplan's work may have been a study presented by the well known Yale University Professor Pasko Rakic, who failed to detect brain neurogenesis in adult rhesus monkeys, thus suggesting that this phenomenon could not occur in primates.

However, the general acceptance of neurogenesis in the adult mammalian brain, as much as the relevance of this phenomenon, came after a series of scientific and methodological developments, which are briefly summarized here:

The discovery of neurogenesis in adult birds, in a series of elegant experiments

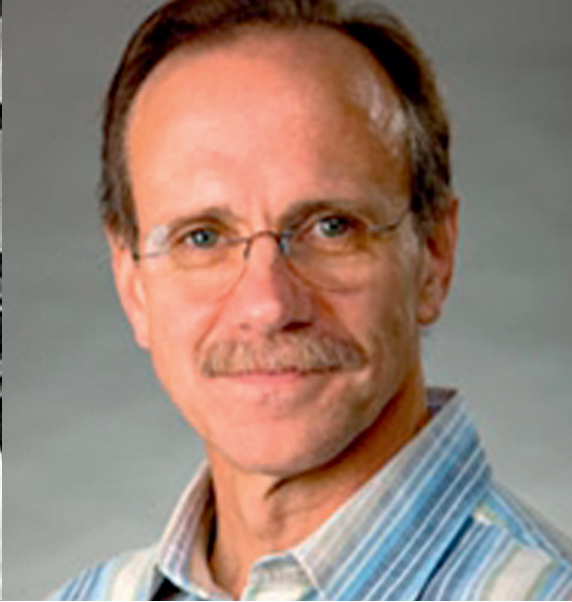
by Fernando Nottebohm and coworkers who showed that, in canaries, the vocal control nuclei of the male brains show seasonal neurogenesis with a dramatic increase in the number of neurons and their functional integration during the singing season.

Next the introduction of new methods for labeling newly dividing cells and for distinguishing neurons from glia came about. BrdU (5-bromo-3-deoxyuridine), a synthetic thymidine analogue, is, like thymidine, taken up by cells during mitosis and is a marker of proliferating cells and their progeny. BrdU labeling can be visualized with immunocytochemical techniques and does not require autoradiography. A further simultaneous key advance was the use of cell type specific markers enabling the immunohistochemical distinction of the newly generated neurons from glia cells.

In the early 90s, the demonstration that cultures of adult mouse brain with epidermal growth factor produce new neurons (Reynolds and Weiss) gave new input to the study of adult neurogenesis, since it gave the possibility for these adult proliferating neurons to be the consequence of the proliferation and differentiation of latent stem cells persisting inside the adult central nervous system (groups of Temple, Alvarez-Buylla, Johansson). This new enthusiasm for the study of adult neurogenesis led to the detection of this phenomenon in the mature brain of a variety of mammalian species, including humans (Eriksson and Gage).

It is now clear that active adult neurogenesis is spatially restricted under





normal conditions to two specific "neurogenic" brain regions: the subgranular zone in the dentate gyrus of the hippocampus and the subventricular zone of the lateral ventricles, where new neurons are generated and then migrate through the rostral migratory stream to the olfactory bulb to become interneurons (group of Alvarez-Buylla), and also neocortical association areas of the prefrontal, inferior temporal and posterior parietal cortex of primates (Gould and co-workers). Neurogenesis in other adult CNS regions is generally believed to be very limited under normal physiological conditions, but could be induced after injury (groups of Gould, Gage and Alvarez-Buylla). It has also been established that significant adult neurogenesis occurs under physiological circumstances and is regulated by

**Pictures from left to right:** Dr. Joseph Altmann and Dr. Arturo Alvarez-Buylla receiving the 'Principe de Asturias' prize for their work in adult neurogenesis (AP Photo/Paco Paredes), Dr. Fernando Nottebohm (photo: National Geographic), Dr. Elizabeth Gould (photo by Denise Applewhite, Princeton University), Dr. Fred 'Rusty' Gage (photo: Christopher and Dana Reeve foundation), Dr. Gerd Kempermann, (©CRTD, photo: Center for Regenerative therapies Dresden)

various experiential, environmental, and pathological regulatory factors. (groups of Gould, Kempermann, Gage). Adult neurogenesis is a dynamic, finely tuned process and subject to modulation by various stimuli. These findings suggest an important biological role for adult-generated neurons, and the persistence of neural progenitors in the adult brain provides hope that the understanding of adult neurogenesis may prove to be of therapeutic significance.

#### Further Reading

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## Adult Neurogenesis and Spinal Cord Injury

Why is NOGO-A different?

CNS plasticity by definition should not be seen as a specific mechanism, but as a global phenomenon of change involving the whole CNS network: the cortex, subcortical regions and the spinal cord. These changes can happen at different levels such as biochemical, and molecular, at the synaptic site or anatomical level.

After an injury, there are multiple inhibitory molecules counteracting neuronal plasticity, sprouting, and regeneration found both in the extracellular matrix, such as inhibitory chondroitin sulfate proteoglycans, and in adult myelin, among others nogo, myelin-associated glycoprotein, semaphorin [1,2]. Once there are many factors playing a role in neuroregeneration, it seems improbable that targeting of a single mechanism would be specific enough to induce functional recovery. Nevertheless, convincing findings were reported in rats and monkeys after spinal cord injury (SCI) associated with the neutralization of NOGO-A.

NOGO-A was identified by Martin Schwab's group in 1998 and purified from mammalian CNS in 2000. It is claimed to be the most potent neurite growth inhibitor in CNS myelin and tissue [3]. In the case of mild lesions, the nervous system has the intrinsic capacity of remodeling through detour pathways, which leads to major, if not total, recovery. However, the severe lesions are the ones that pose the major challenge. In

such cases, the intrathecal infusion of anti-NOGO-A antibody was shown to promote long-range axonal regeneration, increased compensatory growth of intact fibers, spinal midline crossing fibers compared to controls, and sprouting of anatomically spared pathways (e.g. rubrospinal) to compensate for corticospinal tract (CST) damage. This was accompanied by improvements in the hind limb function in rodents after thoracic spinal cord lesions [1,4]. In non-human primates after a cervical lesion, fine movements of a paralyzed hand were recovered associated with corticospinal axon sprouting and innervation of lower cervical segments past the lesion site.

The success of NOGO-A in preclinical trials has warranted its use in humans. Two clinical trials have been started: One in SCI patients and the other in amyotrophic lateral sclerosis, the latter exploring NOGO-A's role in synaptic destabilization during the early phase of the disease. **(ii)**

#### Further Reading

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- [2] Blesch A and Tuszynski MH, *Trends Neurosci*, 2009
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## Adult Neurogenesis and Parkinson's Disease

By Charlotte Klein, PhD Student Medical Neurosciences, AG Neuronal Regeneration and Plasticity

Idiopathic Parkinson's Syndrome (IPS) is the most common neurodegenerative disease. The current available therapeutic strategies are restricted to symptomatic pharmacological substitution of endogenous dopamine with L-DOPA or dopamine agonists, but these do not delay the progression of dopaminergic neuron degeneration in the substantia nigra. Aside from motor deficits, IPS is accompanied by psychiatric symptoms such as depression and cognitive deficits, which cannot be treated sufficiently. Deep brain stimulation and exogenous cell replacement represent alternative, but restricted and risky therapy strategies. Therefore, the idea to functionally replace dead nerve cells by stimulation of endogenous neurogenic or neuroprotective potential is of growing importance. It is well known that the adult brain is capable of generating neuronal progenitor cells and new neurons in certain brain areas, even in older adults. In animal experiments, it has been demonstrated that physiological stimuli, particularly physical activity or an enriched environment, enhance the production of neural progenitors, their differentiation into mature neurons and functional integration into

existing neuronal networks [1]. It is suggested that these new cells play an important role in learning and memory formation [2]. However, to date, it is not known which role these new nerve cells play in pathological processes in the brain. In IPS, physical exercise is usually employed as a symptomatic accompanying therapy, but preliminary experimental studies in humans show that with physical activity or dietary change, a release of neurotrophic factors, an increase of gray matter volume in memory-relevant areas, and improved cognitive functions can be achieved [3]. This opens up noninvasive causal therapeutic options for the treatment of IPS as well as other neurodegenerative disorders and aging processes in general by inducing changes in lifestyle.

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## Adult Neurogenesis and Neuroinflammation

By Petra Huehnchen, MD, Dept. of Experimental Neurology

Many autoimmune diseases of the CNS also lead to neurodegeneration, the most prominent being Multiple Sclerosis (MS). Inflammation not only destroys the myelin sheath of neurons but also targets neurons directly via CD8+ and CD4+ T-cells [1]. Neurodegeneration, however, seems to evoke the brain's potential for self-renewal. As shown in the animal model of MS – experimental autoimmune encephalomyelitis – stem cell proliferation in the neurogenic regions of the adult brain is increased, resulting in higher numbers of newborn neuronal precursor cells (NPCs) [2]. But, myelin-directed inflammation leads to changes in the molecular pathways that regulate neurogenesis, resulting in a shift towards gliogenesis, which is equally observed during acute and chronic phases of the disease [3]. Particularly the type 1-cell subpopulation, the pluripotent stem cells that reside in the neurogenic niches, seem to be susceptible towards pathological stimuli [4]. Chronic inflammation, as evidenced in MS, also leads to an increased inactivation of NPCs [5]. In addition, CD4+ T cells are of special interest as they provide the neuroimmunological link in control of adult hippocampal neurogenesis [6]. Taken together, the brain's restorative potential is disrupted as the initially increased cell proliferation does not translate into a higher number of mature, functionally integrated neurons. An intact microenvironment seems to be crucial for differentiation and mat-

uration of stem and precursor cells. Due to the close proximity to the vasculature, the neurogenic niche is especially prone to immunological changes. In light of this distinctive anatomical feature, soluble factors of the immune response (e.g. chemokines) are believed to be of equal importance in the regulation of neurogenesis as cellular interactions. This hypothesis is further strengthened since impaired neurogenesis was also witnessed in systemic autoimmune diseases like SLE, diabetes type 1 or rheumatoid arthritis, despite an intact blood-brain barrier [7-9]. In conclusion, the immune system plays a large role in regulating adult neurogenesis by modulation of cell proliferation, states of activation, and lineage determination.

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### Contest

We are always interested in including your contributions. You can submit anything you see fit on the topic of neuroscience. Send us your most exciting microscopic pictures, or a creative photo, thoughts on neuroscience or self-written poems – whatever comes to mind! The best contribution will be published and rewarded with a €25 voucher for Lehmanns bookstore. So, what are you waiting for? Start the engine of your mind and get going! Trust us, it is worth participating! Send your contribution to [cns-newsletter@charite.de](mailto:cns-newsletter@charite.de) to **win a €25 voucher for Lehmanns bookstore**. Deadline for submission for the next issue: October 31, 2012.

This issue's winner is Natalia Denisova who contributed to this issue's main theme – engineering the brain – with an awesome article about brain-computer interfaces. Thank you very much for your contribution!



# Brain-Computer Interfaces: Revolutionizing Human-Computer Interaction

By Natalia Denisova, MSc Student Medical Neurosciences

Can you imagine the potential to manipulate computers or machinery with nothing more than a thought? And it is not about convenience – for severely disabled people, development of a brain-computer interface (BCI) could be the most important technological breakthrough in decades. A BCI is a direct communication pathway between the brain and an external device such as a computer or robotic arm.

Research on BCIs began in the 1970s at the University of California, Los Angeles. This field has focused primarily on neuroprosthetic applications that aim at restoring damaged hearing, sight and movement. BCI technologies can significantly improve the quality of life and restore function for people who are totally paralyzed ('locked-in syndrome') or have motor disabilities due to amyotrophic lateral sclerosis, multiple sclerosis, Parkinson's disease or stroke. Simple BCI applications can be configured for basic word processing, accessing the internet, television control or operating a motorized wheelchair. More complex applications such as the operation of a robotic arm or a neuroprosthetic limb are able to provide multidimensional movement to a paralyzed limb.

The main principle behind this interface is the bioelectrical activity of nerves and muscles. When we imagine ourselves doing something, a command is generated from the frontal lobe in form of electric signals, which are different in magnitude and frequency. These signal patterns are not large enough to travel down the spinal cord and cause actual movement; however, they are measurable and can be used to control external devices.

Electrical fields that result from brain activity can be recorded at the scalp as electroencephalogram (EEG), at the cortical surface as electrocorticogram (ECoG), or within the brain by monitoring local field potentials and neuronal action potentials. EEG recording is simple and noninvasive, but has limited signal resolution and is susceptible to contamination from muscle activity. ECoG and intracortical methods have better topo-

graphical resolution, but require invasive implantation of electrode arrays. Issues to be addressed include the risk of tissue reactions and long-term recording stability.

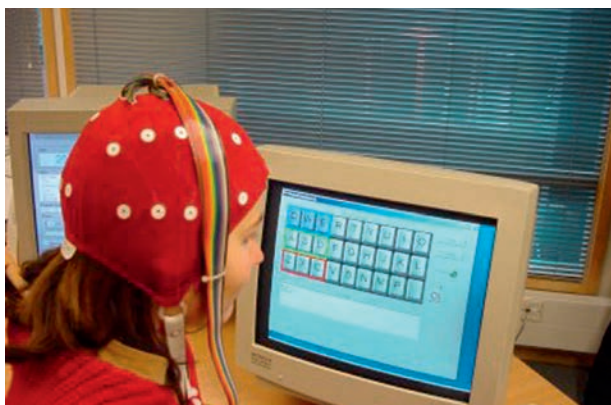
Acquired brain signals are processed in real time to extract information relevant for a particular motor output, e.g.

BCI device depends on principles of neural plasticity. In this case, the learning system consists of two adaptive controllers: the brain and the BCI software. The BCI user produces brain signals that encode his intent and the BCI system translates them into commands that carry out the desired action. For instance, people learning to use EEG-based BCI typically start with using various kinds of motor imagery to modify rhythm amplitudes. As training proceeds, the actual or imagined movements become less important, the use of a BCI system becomes more automatic, similar to conventional muscle-based skills [1].

A recent development in the field of neuroprosthetics is an implementation of proprioceptive feedback in the design of BCIs. In primate studies, an integration of microstimulation of the sensory cortex during execution of specific motor actions closes the normal physiological sensorimotor loop [2]. This effect provides not only real-time control and correction of movement errors, but it also contributes to restoring normal brain plasticity and more efficient learning. This is particularly important in neurological rehabilitation.

While the results are very impressive, there are still many limitations to the current BCI technology. The speed and accuracy of decoding and signal analysis need to be greatly enhanced to permit real-time communication. Even advanced BCIs can hardly control robotic extremities doing small movements in a confined space. The main challenge is to create user-friendly devices that can be operated at home without supervision.

The future for BCI technology is boundless. In addition to restoring mobility to disabled persons, it also offers a potential method to overcome blindness, deafness and other sensory-affected conditions.



Pictures: <http://www.ice.hut.fi/research/css/bci/>,  
<http://www.mpcolleges.in/paathshala/content/ztechvocab/player.php?id=1>

which letter to select for spelling a word or which direction to move a cursor. This signal processing involves fast feature extraction and classification. Typical features can be simple measures, such as amplitude and frequency of specific EEG rhythms or firing rates of individual cortical neurons, while more complex measures include spectral coherences. No matter what features are used the goal is to form distinct set of features for each mental task. Next, they are classified and translated into device commands using a translation algorithm.

The process of learning to operate a

## References

- [1] Daly JJ et al., *Lancet Neurology*, 2008
- [2] O'Doherty JE et al., *Frontiers in Integrative Neuroscience*, 2009

# Fusing Neuroscience with Engineering

By Dr. Markus A. Dahlem, Member of the Collaborative Research Centre 910, TU Berlin

**W**hat does it take to fuse neuroscience with engineering? Various invasive and noninvasive human brain stimulation techniques are available. They alter brain activity through the use of electrical and magnetic stimulation.

Let us look at headaches first. Headaches are not generally considered appropriate for invasive neurosurgical therapy, but when all else fails – preventives, abortives, and pain management – invasive brain stimulation techniques are considered, e.g. occipital nerve stimulation (ONS) or hypothalamic deep brain stimulation (DBS).

Better known examples for deep brain stimulation are treatment-resistant movement disorders, such as Parkinson's disease. Here, thalamic DBS is used, but the difference between the treatment of movement disorders and headaches is not merely the precise stereotactic DBS placement of minuscule electrodes into the brain's target area. In addition to being on target, the stimulation protocol needs to be optimized to modulate the distinct abnormal patterns of neural activity within the particular network. This optimization can be done either empirically or quantitatively with

model-based methods. Simply said, given that the hardware works well with the wetware, what is the optimal software? To answer this, we need models.

Mathematical models of the neural tissue surrounding electrodes are given by integro-differential equations. Network dynamics are investigated with stability analysis, for instance with a formalism called master stability function that allows you to separate the dynamics at the nodes from the network topology. And, finally, the influence of electric fields applied in a closed loop configuration can be described by control theory using these models.

Steven J. Schiff (Director of Penn State Center for Neural Engineering) and author of the recently published book "Neural Control Engineering" (MIT Press) remarks: "It seems incredible that the tremendous body of skill and knowledge of model-based control engineering has had so little impact on modern medicine. The timing is now propitious to propose fusing control theory with neural stimulation for the treatment of dynamical brain disease."

For model-based control, devices need not only to be able to stimulate but also monitor neural activity, either with the electrodes in place or with additional encapsulated microsensors (lab-on-a-chip). Building such combined intelligent devices is the paramount bioengineering task at the emerging intersection between neuroscience and control theory. Mastering this in the future is what it will take to make an impact.

**Markus A. Dahlem** (TU Berlin) is a member of the Collaborative Research Centre 910: "Control of Self-Organizing Nonlinear Systems" and the Bernstein Center. He works together with Steve Schiff on Model-based Control of Pathological Neural Activity in Migraine (BMBF/NIH).

## BrainGate Project

Just by Thinking, you can Control Movement of a Robotic Arm

**R**esearchers at Brown University and their international team of colleagues have made a major breakthrough in spinal cord research. Tetraplegia is the devastating condition where both arms and legs can no longer be moved – often from a spinal cord injury or from a stroke

**"The most hardest thinking brain machine interface has made a milestone"**

that cuts off the neural connections from the brain. Tetraplegics rely heavily on caretakers' help for day-to-day functioning and live with the condition for the rest of their lives. Lochner and colleagues have now shown that it is possible for patients in this debilitating state to control the movement of a robotic arm just with their thoughts.

The system works with what is called BrainGate, a brain-machine interface. A chip containing 100 electrodes is surgically implanted onto the motor cortex, and this sensor then relays signals to a computer that functions as a decoder of the neural signals. The computer serves as the link

between thoughts and the machine (the assisted technology component of the system). Prior to linking the decoding system to a robotic arm, which can move throughout three-dimensional space, considerable work was done on 2D computer screens – moving the cursor of a mouse with thoughts alone. Being able to work with the German Aerospace Center to develop a reliable, well engineered robotic arm to serve the purpose of this study took considerable efforts and careful planning. The recent highlight of their study was watching Cathy, a woman who has been tetraplegic for 15 years control the robotic arm with her thoughts to serve herself a cup of coffee.

The goal of the BrainGate project is to eventually roll this system out to eligible patients and even go wireless – such that the decoding device doesn't have to have a direct physical connection to the patient's head.

BrainGate2 is currently recruiting patients for a pilot clinical trial. (ge)



Picture: Hochberg LR et al., Nature, 2012

### Further Reading

- Hochberg LR et al., Nature, 2012



## Utilizing BCI Technology for Identifying Cortical Network

By Thorsten O. Zander, Leader of the Team PhyPA (Physiological Parameters for Adaptation, TU Berlin)

**H**uman-Machine Systems (HMS) can read aspects of human brain activity if linked to this by means of a brain-computer interface (BCI). This connection can be established by combining methods of machine learning and given knowledge on the interpretation of the electroencephalogram (EEG). The resulting technology allows for automated analyses of brain activity in real-time, and can also be utilized to provide input commands for a technical system. BCI has mainly been investigated for the purpose of defining assistive technology for people with severe disabilities, leading to new channels for communication and control.

My personal research is dedicated to a new endeavor in this field – the application of BCIs in HMS that are operated by users without disabilities. I identified unreliability, limited bandwidth of information transfer, high cognitive effort as well as cumbersome and time-consuming preparation as the main problems BCIs have to face in applications outside the laboratory. To address these problems, I introduced an extension of contemporary BCI systems with the approach of passive BCIs. Contrary to classic BCI systems, these do not aim at directly controlling a system by commands sent intentionally by the user. Passive BCIs access information about cognitive user state, which is hardly inferable from behavior, and makes it available to the machine, with the aim of enhancing the given interaction. Based on this, recent studies have shown that passive BCI technology can indeed be

**Thorsten O. Zander** (TU Berlin) is leading the working group Team PhyPA (Physiological Parameters for Adaptation) which aims at transferring technologies from BCI research into the context of human-computer and human-machine interaction.

valuable for contemporary research in the field of HMS for healthy users.

One major aspect for validating a given passive BCI approach is the identification of cognitive processes underlying the extracted information. A dependency on muscular and ocular artifacts would weaken the reliability of the system, as these are likely to be modulated with changes in context. Several new combinations of methods have been developed to get insight into neural correlates generating patterns in the EEG that are utilized by passive BCI. Recently, these principles have been reversed: The BCI mechanism can be used to identify cortical networks contributing to the examined task. This opens up a new field of analyzing brain processes in complex and more natural experiments, as passive BCIs are inherently designed to work in such environments.

Nevertheless, until now, only a few first steps have been made into this direction; however, this approach contains a high potential.

## How a Robot can Assist Locomotion in Rats after Spinal Cord Injury

**A** so-called robot was conceived by Grégoire Courtine's group as a part of a locomotive rehabilitation program for rats. In addition, they explored the already established concept of neuroprosthesis based on electropharmacological stimulation associated with locomotor training. The aim was to reestablish locomotion in rats after a double hemisection at the levels of T8 and T10 interrupting any connection between the brain and the hindlimbs.

Both the robotic system and the electrochemical neuroprosthesis were shown to be essential for reestablishing locomotion. The treadmill-restricted training in combination with the excitatory serotonergic and dopaminergic cocktail, improved the functionality of lumbosacral circuits and promoted sensory input to modulate stepping, are the source of coordinated, although involuntary, stepping driven by the treadmill belt.

Despite the treadmill-restricted training, only the postural interface provided by the robotic system promoted bipedal locomotion during different tasks. It consists of a positioning system that allows translations of the rat in the horizontal plane, while providing vertical support and rotation. This

postural interface was shown to be essential for initiation of full weight-bearing locomotion towards a reward, the performance of voluntary tasks such as going upstairs, and overcoming obstacles which appear to be a result of a supraspinal command. In contrast, treadmill-restricted training with electrochemical stimulation failed to induce voluntary control of locomotion.

In addition, the examination of anatomical reorganization of the spinal neuronal circuitry confirmed the advantage of a robot-assisted overground training. These rats showed remodeling of intra- and supraspinal projections including corticospinal tract as well as cortical projections mainly from the motor cortex into brainstem locomotor regions.

These findings challenge an old paradigm. In order to achieve locomotion and consequently neuronal plasticity and regeneration, both the reinforcement of spinal interneuronal network as well as the reestablishment of supraspinal axonal connections are essential. **(ii)**

### Further Reading

- van den Brand R et al., Science, 2012



## Brain in Press

### Free data for everyone! EU commission suggests open access as of 2014

For certain, it was due to our last CNS issue that the EU commission decided to suggest their new objective: Open access to all research data that was financed by taxes. Tax-payers should automatically have the right to access the research they pay for, argues the commission. This approach is in line with the recent proposal of David Willets, British Minister for Universities and Science, who plans to provide free access to publications of publicly financed research. The costs for the reviewing and publishing process could be covered by the authors, research institutes, and universities, which in turn would save money on expensive journal subscriptions. Such rearrangements of the publishing companies' business models are supposed to begin as of 2014 and by 2016, it is planned that sixty percent of all research results will be openly accessible. (*jr*)

Source: <http://www.spiegel.de/wissenschaft/mensch/open-access-eu-will-forschungsergebnisse-fuer-jeden-zugaenglich-machen-a-844973.html>

### A pill that fits for everyone! New drug for Alzheimer's, Parkinson's, multiple sclerosis, and traumatic brain injury

A new and likely omnipotent drug for the treatment of Alzheimer's, Parkinson's, multiple sclerosis, and traumatic brain injury was developed at Northwestern University Feiberg School of Medicine. Recently, clinical Phase I was completed by a biotech company.

The common denominator of all mentioned diseases is the development of neuroinflammation. During cerebral inflammation, pro-inflammatory cytokines are excessively produced leading to neuronal misfiring, disconnection of neurons, and — eventually — synaptic malfunctioning. In this way, cytokines can cause the progressive damage seen in these chronic neurodegenerative illnesses. A new class of drug (MW151 and MW189) prevents the overproduction of cytokine proteins and might thereby prevent neuronal damage. The recent study, published in the *Journal of Neuroscience*, focussed on the optimal time-window for drug application in a genetic animal model of Alzheimer Disease. Here, MW151 prevented the full-blown development of AD and previous animal experimental studies showed reduced neurological damage in traumatic brain injury and inhibited development of a multiple-sclerosis-like disease. Watterson, co-author of the study, further proposed beneficial effects for Parkinson's, frontotemporal dementia, and amyotrophic lateral sclerosis. However, more animal studies must be performed before further clinical trials with the new drug can get started. (*jr*)

Source: <http://www.sciencedaily.com/releases/2012/07/120724171302.htm>





# Ghana

By Priscilla Koduah, MSc Student MedNeuro

## Have you got about idea of Ghana?

**G**hana is a beautiful country located in West Africa with a total area of 227,540 km<sup>2</sup> and a population of 24,658,823.

Ghana is bordered by Burkina Faso to the north, Côte d'Ivoire to the west, and Togo to the east. One interesting piece of historical accident (as a result of colonization) about these three neighbouring countries is that they are all French-speaking, while Ghana is English-speaking. The last bordering territory, which of course is not a country, is the Gulf of Guinea to the south.

Ghana is located a few degrees north of the equator. Also, the Greenwich Meridian passes through the eastern part of country, at a busy harbour city called Tema. In terms of terrain, Ghana has both lowlands and highlands. The highest point is 883 meters and about half of the country lies less than 152 meters above sea level.

The coastline comprises mostly of sandy beaches with several intersecting rivers and streams most of which are navigable by canoes. It is a sight to behold children having a free bath in these streams whilst fishing at the same time. Ghana has about six vegetations, the biggest of which is the semi-deciduous forests where most of the country's cocoa, timber and minerals are obtained.

The climate in Ghana is tropical with two main seasons; the wet and dry seasons. The ambient temperature is between 25° to 34°C with an average annual temperature of 26°C. Ghana can boast of many waterfalls and virgin forests which attract tourists into the country all year round.

## Research in Ghana

Most of the common diseases in Ghana include those endemic to other sub-Saharan African countries. The predominant ones are malaria, cholera, pulmonary tuberculosis, infectious hepatitis, typhoid fever, schistosomiasis, meningococcal meningitis, etc. The Ghana Health Service reported in 2011 that malaria was the primary cause of morbidity and as many as 32.5 % of people admitted to most of the country's medical facilities was as a result of malaria.

As a result of the frequency of these diseases, most research institutions fo-

cus on these fields. It is therefore not surprising that they are mostly infectious-disease oriented. The major medical research institutions in the country include the Noguchi Memorial Institute for Medical Research (NMIMR), Mampong Centre for Scientific Research into Plant Medicine, Kintampo Health Research Centre, the Navrongo Health Research Centre, Kumasi Centre for collaborative Research in tropical medicine (KCCR) which co-partner with the Bernhard-Nocht Institute for Tropical Medicine, (BNITM), Hamburg, Germany and the Kwame Nkrumah University of Science and Technology (KNUST). There are other research institutions like the Council for Scientific and Industrial Research and the Cocoa Research institute which research into agriculture and agro-products.

NMIMR researches into diseases of public health and has several departments. One of these departments is the Animal Experimentation where animal models of diseases are made. There are also departments for bacteriology, virology, immunology, electron microscopy and histopathology, nutrition, epidemiology, clinical pathology and parasitology. The various departments in the universities such as the University of Ghana, the University of Cape Coast, the Kwame Nkrumah University of Science and Technology – to mention just a few – also conduct research.

## Neuroscience Research

Although research institutions in Ghana are infectious-disease oriented, efforts have been made to set up a stable neuroscience research centre since some of the death cases reported in the major hospitals are related to neurology. Most of these patients die from stroke and cerebral malaria.

There are also reported cases of other neurological disorders such as Parkinson's disease, schizophrenia, epileptic seizures, or benign familial neonatal convulsions. Apart from the fact that there are very few neurologists in Ghana serving a population of about 25 million, public awareness on neurological disorders is also very low despite the increase in death rates.

Fortunately in 2000, the Korle-Bu Neuroscience Foundation (KBNF) was started by a Vancouver-based neuro-



Cape Coast Castle, Source: private

science nurse, Marjorie Ratel. Korle-Bu Teaching Hospital is the premier health facility in Ghana. The KBNF is a volunteer-based and charitable organization that receives support from donations and contributions from North America and individuals who have interest in saving the people of Ghana from dying needlessly from preventable brain and spinal cord injuries.

It aims at becoming a world-class hospital in Ghana and West Africa by conducting neurological research and providing medical training to doctors, nurses and other health attendants. The foundation is focused on health care for brain and spinal cord injuries. At the moment, there is no on-going research, but effort is being made to generate more funds which will be used for the acquisition of equipment and other infrastructure needed to run the research labs. The research centre will be under the Anatomy Department and will co-partner with North American universities to train students in the field of Neuroscience.

There are also psychiatric hospitals in Ghana, like the Accra Psychiatric Hospital, the Pantang Psychiatric Hospital and the Ankaful Psychiatric Hospital which aim to assist patients with schizophrenia, epilepsy, depression and other neurological diseases. These hospitals work in collaboration with psychologists who try to give some form of treatment to the patients. They also serve as home for people with dementia and other cognitive disorders.

Although most hospitals in Ghana take care of patients with neurological disorders to some degree based on limited infrastructure and neurologists, it is hoped that the KBNF will be able to achieve its goals to help the people of Ghana and West Africa at large.

### Further Information

- Korle-Bu Neuroscience Foundation: <http://kbnf.org>

## Andriana Fetani

A Conversation with Andriana Fetani, MSc Medical Neurosciences



Andriana was a student in the Medical Neurosciences Master's program from 2009 to 2011. Before she joined the program, Andriana studied Biology in Athens and did Erasmus in Freiburg. Now, Andriana works as a key account manager and explains to us why she quit research.

### **MZ: What did you do after finishing the MSc in Medical Neurosciences?**

AF: The truth is that after finishing my Master's degree, I hadn't actually concluded on what to do next. My first thought was to continue my career in research doing a PhD. Science, and more specifically Neuroscience, always fascinated me the most, so it kind of seemed like the next step to take. On the other hand, during my 2<sup>nd</sup> year of studies in Medical Neurosciences, I participated in some of the 'Career Days' organized by the program concerning jobs in industry, such as pharmaceutical companies. From these 'Days' on, I developed a preference for the field of industry too! At the end, I weighed my options, taking seriously into account my future career goals, and decided that an experience in the field of industry would be more suitable for me as a person.

### **The field of industry is huge, what do you do exactly now?**

I was lucky enough to find a position in a multinational company as a key account manager. Key account management by definition is a management approach adopted by selling companies aiming at building a portfolio of loyal key accounts (customers), by offering them a product/service package tailored to their individual needs. So, in short, my responsibili-

ties are to develop relationships, manage the accounts, develop sale strategies, resolving 'day-to-day' problems, reporting and providing two-way information. It's quite a challenging job as you have to communicate with different types of people and find a unique way to cooperate effectively with each one of them.

### **Why did you quit research? What would have made you stay?**

The reason for that, as I mentioned before, was the general picture that I had always imagined for my future! I am quite sociable and communicative as a person and love interacting with other people. I am definitely a team player and a faithful fan of innovative and creative brainstorming! All the above virtues can be met/are required while carrying out your own research! The difference when working in a multinational company is that they promote these ideas even more and most of the time you have to meet, quite quickly, your individual limits! In other words, it is a multiplication of the challenge that you have to face every single day! Plus, in order to succeed, you have to broaden your knowledge in multiple fields, e.g. sales, finance, business administration, and training coordination. It's the angle from where each one sees it! Science is uniquely great! I just felt that I needed something more to complete my sociable personality (laughing). Something where I could exceed myself and meet my limits in multiple different fields!

Science is nice as it is! I don't know if there is something that would have made me change my mind. I had the chance to meet and be influenced by exceptional people in science and this should have been enough for me to stay. So, I guess at the end, it's a matter of who you really are and then comes all the environmental factors!

### **What motivated you to join the Medical Neurosciences Program?**

I performed my Bachelor thesis in a lab that studied dementia syndromes, specifically Alzheimer's disease. Since then, I developed an interest for neuroscience. My love for Germany, after the time I spent in Freiburg as an Erasmus student, was the second factor that solidified my decision to do a Master's in Neuroscience in Germany. I searched a lot about all the Neuroscience programs offered

in Germany. Eventually, the Medical Neurosciences Program scored the highest in my preferences! It combined both a good curriculum and people worth being taught from.

### **How did you benefit from the program?**

Looking back at the past two years, I am grateful for all the people I've met and the opportunities I was offered! Throughout the program, I realized what science is all about, how you should do it properly, and how somebody can harmonize his passion for science with his job! I have to admit that in my new position I meet science issues everyday! I am obliged to follow research news and inform other people about them as well! So knowing how to do it right and effectively counts! Also, some tasks included in the Master's portfolio, like how to do a good and effective presentation, organizational stuff etc, gave us a preview of what would follow in our future jobs, not only concerning science but all jobs! To sum up, Medical Neurosciences was a pretty realistic program that could be helpful not only for people who want to follow a scientific career but in general everyone who wants to be a professional!

### **What are your aspirations in your current position?**

In my current position, I crave to acquire as much knowledge as possible concerning the field of pharmaceutical companies, how they function, what their virtues are, etc., and develop many new skills assisting my current duties. Acquiring new responsibilities day by day and delivering them fast and effectively is my new everyday battle!

### **Where do you see yourself in 10 years from now?**

In 10 years from now, I want to be really into the pharmaceutical industry. Having a job that would ensure the best medication for the patients all over the world is rather appealing to me! Of course, starting a family at some point is also on the table, because creating a family can bring inner peace and satisfaction.

### **What other passions do you follow besides neuroscience?**

Neuroscience remains my No1, but due to my job, I have to follow other fields as well, like business and finance. My 'all-time-classic' passion though, is staying up-to-date with movies! I try to see as many as I can in my free time, no matter the category that they belong to. Sailing is something that I am trying to develop as my new hobby! I hope it works!

Thank you, Andriana. (mz)



## Arina Riabinska

A Conversation with Arina Riabinska, MSc Medical Neurosciences

**A**rina was a student on the Medical Neurosciences Master's program from 2009 to 2011. Before joining the program, Arina studied Biology in Kiev (National University 'Kyiv-Mohyla Academy') and did her Bachelor thesis in the laboratory of Experimental Neurosurgery on brain gliomas. After her Master thesis, Arina chose cancer research as her main focus and she now is a PhD student in Cologne.

### **MZ: What did you do after finishing the MSc in Medical Neurosciences?**

AR: After finishing my Master's, I continued my Master's project in Ana Luisa Piña's laboratory to finish what we started. Now, I am a PhD student at the University of Cologne in the group of Prof. H. Christian Reinhardt.

### **What is the main focus in your new laboratory?**

We are working on DNA damage response in cancer. Current anti-cancer therapy is mostly based on agents that induce robust DNA damage, followed by apoptosis. This is the normal reaction of a cell to such stress. However, in many cases this therapy has transitory effects. Some cancer cells escape the classical scenario, become resistant to chemo and even more aggressive due to mutations in their DNA damage response machinery. Our task is to investigate the key genes driving the DNA damage response, like Ataxia telangiectasia mutated (ATM) kinase and the ataxia telangiectasia and Rad3-related protein (ATR) and their downstream pathways.

### **This has little relation to neuroscience anymore? Why did you change your interest?**

Well, I am still interested in neuroscience! But beside this, I am really keen on oncology and there is only limited cancer research possible in the brain. I also have some ideas about how to link our work to neuroscience. Interestingly, patients with an ATM mutation display a neurologic phenotype, ataxia, and additionally have a high predisposition to cancer. Why these events come together would be one of my questions.

### **What motivated you to join the Medical Neurosciences Program?**

This was for sure my great interest in Neuroscience. The word 'medical' in front of it was a deciding factor to specifically join the Berlin neuroscience community. At that time, I anticipated the program to be either a gate into neuroscience research or a bridge between my education in Biology and possible medical studies, which I took into consideration.

### **How did you benefit from the program?**

This was a very fruitful and interesting experience, partly because the whole educational system was quite different from what I was used to. In Kiev, we had a lot of seminars where our active participation was required as well as small tests during the semester. All this helped us to steadily gain knowledge. Here in Berlin, I only had one large exam at the end of each block, which assumed more independence and self-motivation in the learning process. No doubt thanks to the

**“I had the opportunity to join great research groups during my lab rotations and meet wonderful people“**

program I learned a lot about neuroscience in its multiple aspects. Furthermore, I had the opportunity to join great research groups during my lab rotations and meet wonderful people.

### **Do you miss Berlin?**

Berlin is always in my heart and I will love it forever. It is a magnificent city! As well as the Charité. One of the priceless opportunities the MedNeuro actually gives to you is to feel that you are a part of this great Medical School. For example, you can join medical lectures in a frame of your individual focus, as I did participating in a course given by Prof. Einhäupl! All in all, I am really grateful for being a part of this program. And I'd also like to



give something back. In April, I helped Ana Luisa within the brain tumor lecture, which she gives during Block B. That was a wonderful experience.

### **What are your aspirations in your current position?**

I want to complete an interesting and independent project; just unassuming and ambitious at the same time. While during the master thesis we are thoroughly supervised, now comes the time to be in charge of the project. Of course, this means being in charge of mistakes too, but having not made them, one never gains experience. I think this is an important step in development of a researcher's analytic mind.

### **Where do you see yourself in 10 years from now?**

Doing research. (laughing) Ana Luisa said she would skin me alive unless I get a noble prize.

### **What other passions do you follow besides neuroscience?**

Well, as you can see, I follow the passion of cancer research. I also find the link between development, stem cells, and cancer captivating, so I follow related literature. Otherwise, languages, world cultures, traveling, dancing, and, curiously, programming, fall among my interests.

**Thank you, Arina. (mz)**

## FENS 2012

By Violeta Castelo Szekely, MSc Student Medical Neurosciences

**C**onference Report The Federation of European Neurosciences Societies (FENS) held its 8<sup>th</sup> Forum of Neuroscience in Barcelona, Spain, from July 14<sup>th</sup> to 18<sup>th</sup> 2012. Organized every two years since 1998, the FENS Forum is the largest meeting for neuroscientists in Europe. This year, it gathered more than 6500 scientists from all over the world, who were able to present, share and learn from the latest and most important advances in brain research, in fields like learning and memory, synaptic plasticity, neurodegeneration, neurodevelopment, behavior and emotion, psychiatric disorders, genetics, epigenetics, etc.



**8<sup>th</sup>**  
**FENS**  
FORUM OF  
NEUROSCIENCE

The program was very attractive, with a combination of plenary lectures, parallel symposia, technical workshops and special lectures every day. Poster presentations played a very big role, with four sessions each day and more than 2500 posters displayed during the whole event.

One of the special lectures held at the FENS Forum was dedicated to the winners of the Brain Prize in its inaugural 2011 edition. The Brain Prize is awarded by the Grete Lundbeck European Brain Research Foundation to one or more scientists who have contributed to European neuroscience advance with an outstanding and relevant research. Although nominees can be of any nationality, the prize is aimed at researchers whose work has been carried out in Europe or in collaboration with neuroscientists in Europe.

The prize, consisting in € 1 million, was awarded in Copenhagen, Denmark, on May 2nd, 2011, to Péter Somogyi (Oxford University, UK), Tamás Freund (Institute of Experimental Medicine, Budapest, Hungary) and György Buzsáki (Rutgers University, New Jersey, USA) 'for their wide-ranging, technically and conceptually brilliant research on the functional organization of neuronal circuits in the cerebral cortex, especially in the hippocampus, a region that is crucial for certain forms of memory' [1].

The three awarded researchers are native Hungarians. The prize therefore seeks to also recognize the recent contribution of Hungarians to neuroscience that follows the tradition already started by scientists like Károly Schaffer (who gave name to 'Schaffer collaterals') or Mihály Lenhossék (who introduced the term 'astrocyte'). Somogyi, Freund and Buzsáki have worked together, as reflected in several collaborations and joint publications, with their research focused on the structure and function of complex circuits of nerve cells, particularly in the hippocampus, as unravelling these is important for the understanding of information processing.

During the FENS lecture, Peter Somogyi explained his concept of the unity of time and space in the brain, an idea he has termed 'chronocircuitry'. He presented his latest work

aiming at understanding the functional organization of the brain by identifying the specific neuronal subtypes that make up a given neuronal circuit, their morphology, the particular expression of certain neurotransmitters and receptors and their input-output relationships.

In his talk, Tamás Freund presented how different types of interneurons modulate neuronal oscillation in the cortex and hippocampus and the role of endocannabinoid signaling. To explain it, Freund used a comic, yet very didactic video of an octopus: In the animation the octopus represented the interneuron, holding in its tentacles several swimmers (pyramidal cells) under the water. When the octopus releases the swimmers, they all go and reach the surface of the water at the same time to catch their breath, therefore, representing the role of interneurons in synchronizing pyramidal cells to fire at the same time and frequency. In the same way, release of endocannabinoids by a pyramidal cell inhibits GABA release by the interneuron onto them – thus, avoiding synchronization. This was shown in the video as a Bob Marley-looking swimmer who, by smoking marijuana (the analogue to endocannabinoid release), had escaped from the octopus tentacles and could thus breathe at his own rate.

Finally, György Buzsáki presented his recent work on how brain rhythms coordinate cell assemblies – transiently active ensembles of neurons – to allow them to perform operations like encoding memories or reasoning. The idea behind his research is that hierarchical organization of cell assemblies can be seen as a 'neural syntax', i.e. as a mean of an ordered language construction in the brain.

In addition to the scientific program, a number of social and special events were organized, such as 'Cooking with the brain' about the evolution of food perception, 'Meet the expert' and 'Build your career', giving scientists and industrial partners the chance to meet other scientists in a more informal environment or the 'Jump the FENS Party'. Finally, participants had the opportunity to visit several touristic attractions in the city as well as museums, such as the Museum of Natural Sciences, located next to the FENS venue.

The Forum took place at the International Convention Center of Barcelona (CCIB), right in front of the beach, by the Mediterranean sea, an ideal location to allow everyone to enjoy the warm temperatures and sunshine weather before, in-between and after the daily sessions.

### References

[ 1] Soltesz I, Trends in Neurosciences, 2011

### Further Information on The Brain Prize

- [http://www.thebrainprize.org/flx/the\\_brain\\_prize/](http://www.thebrainprize.org/flx/the_brain_prize/)
- Fens 2012 website: <http://fens2012.neurosciences.asso.fr/index.php>





## Learning to Learn with Action Video Games

By Esperanza Jubera and Luisa A. Hasam, MSc Students Medical Neurosciences

**H**uman learning capacity is astonishing. The most unexpected stimuli can elicit a wide range of learning strategies in order to produce more efficient responses. In one of the plenary sessions at the FENS meeting 2012, Dr. Daphne Bavelier presented her studies on the implications of playing action video games, especially in the visual and learning capacities.

As an example of her work, she explained the methodology followed in one of her more recent studies: a sample of non-ordinary video game players, between 18 and 25 years old, were selected. This sample was randomly divided into two groups, where one played the action video games 'Call of Duty 2' and 'Unreal Tournament', and the other group played 'The Sims 2', a non action video game. The training consisted of playing the assigned game for 10, 30 or 50 hours, over a period of 2 to 10 weeks. Prior to the experiment, subjects were tested on perceptual, attentional, and cognitive tasks. After the training period, subjects were tested again to assess the improvement, if any.

Results from this and other previous studies have shown that playing action video games can enhance different capacities, for instance, spatial-temporal resolution and vision sensitiv-

ity. Cognitive functions, such as short-term memory, spatial cognition, multi-tasking and some executive functions, also improve. Regarding decision making abilities, action game players have shown the ability to extract and integrate information from the surroundings faster, producing more correct decisions per unit of time.

Moreover, the recognition and pattern extraction from the environment is improved, resulting in more efficient task performance by suppressing irrelevant and distracting information. In other words, action video game players are better and faster at learning to learn what is a relevant signal and what is distraction in their environment.

Bavelier points out the importance of these acquired atypical enhancement learning properties in practical applications, such as rehabilitation of patients with vision impairments. Also, playing action video games could be used as a training tool in certain professions, such as surgeons and pilots, or in the field of educational.

### References

- Bavelier D et al., Annu Rev Neurosci, 2012

## German Nobel Laureate at FENS: on History of Modern Electrophysiology

By Pei Zhang, MSc Student Medical Neurosciences

**D**uring the FENS Forum 2012 in Barcelona, I had the privilege of listening to the talk of Prof. Dr. Erwin Neher, who developed the patch-clamp technique and was awarded the Nobel Prize in Physiology or Medicine in 1991, together with Bert Sakmann, for "their discoveries concerning the function of single ion channels in cells".

The Nobel Prize Laureate's talk was preceded by presentations by three other renowned electrophysiologists, Marco Bresadola, Marco Piccolino, and Bernd Nilius. These talks traced back to the first notion of electrical excitation of the nerve-muscle preparation made by Luigi Galvani in the late 18th century, to Julius Bernstein's first recordings of action potentials. After this brief but detailed introduction on the early history of electrophysiology, Erwin Neher led us through his scientific career with a presentation titled "Ion channels: early concepts, single channel recordings and some surprises".

In his unhurried and composed presentation, Erwin Neher explained how they came up with this idea, what the challenges were, and their solutions. He especially mentioned that during his study in Munich, he befriended Dr. Bert Sakmann, who he met again later at the Max-Planck Institute

in Göttingen in 1973 and began a fruitful collaboration with. "Bert Sakmann and myself set out to prove the ion channel concept by measuring ion currents in small membrane patches. With this tool in hand, we were able to observe a variety of surprising properties. Well, they were quite surprising to us at that time, but are now already commonplace", he said, which was greeted with laughter and applause by the audience. Later when faced with questions from the audience, he was also quite frank about their previous false hypotheses and the limitations of this technique.

What is more surprising, after being awarded the Nobel prize 21 years ago, is that Erwin Neher has still had a considerable amount of scientific output in high impact journals in recent years. This makes it clear that he remains fascinated by and is still actively contributing to knowledge of biophysics, with a shift of research interest from membrane channels to the molecular mechanisms underlying short-term synaptic plasticity and vesicle release. I was deeply moved and filled with admiration to hear his everlasting passion for science and the story of the advent of this still powerful and exciting technique.

## Multifaceted Neuroscience

A Review of the Berlin Neuroscience Forum 2012

By Christine Römer, PhD Student Medical Neurosciences

The Berlin Neuroscience Forum provides the opportunity to meet neuroscientists from Berlin ranging from young fellow neuroscientists to professors. This year's meeting took place on July 5<sup>th</sup> to 6<sup>th</sup> at the nature resort Liebenwalde in Brandenburg.

The meeting was opened by Benedikt Grothe (Munich, Germany) who gave an exciting overview of the field of binaural processing and its dynamics. Questions on hearing loss and neuroplasticity as well as neuronal translation regulation were answered in oral presentations from young neuroscientists and students. Later on, Christine Heim (Berlin, Germany) gave an excellent talk on depression and how it links to early childhood abuse. She also gave an insight into genes that protect against the development of depression. Following this, Katharina von Kriegstein took us to the more general neural basis of human communication. The first day of the conference closed with a talk by Istvan Mody (Los Angeles, USA), a well-acknowledged researcher in the field of epilepsy and, more recently, stroke. The necessity for improving functional recovery after stroke rather than targeting very early events (such as cell death) was emphasized.

The second day of the conference focused more on CNS pathology. Britta Eickholt (Berlin, Germany) revealed some novel interactions in the CNS synapse and their role in macrocephaly, autism, and Alzheimer's disease. Imre Vida (Ber-

lin, Germany), continued on the topic opened by Istvan Mody and took us to the world of GABAergic interneuron networks in the hippocampus, explaining the inhibitory control the interneurons establish on each other. During the student and young neuroscientist presentations, we learned about the possible therapeutic uses of human-induced pluripotent stem cells as well as the association of microglia with blood vessels in glioblastoma multiforme.

The poster presentations are the heart of the meeting. They covered very different aspects of neuroscience, ranging from clinical studies and molecular biology, to mathematical models of metabolism. A broad field of pathological conditions of the nervous system as well as healthy CNS function were presented and interactions on various topics were enthusiastic. The poster awards were received by Raul Bukowiecki, Joanna Fedun and Janina Hesse.

The meeting ended with Mathias Jucker's (Tübingen, Germany) talk on a current hot topic, the prion-like aspects of Alzheimer pathology, which induced a heated discussion as to whether or not and to what extent Alzheimer disease can be considered an infectious disease.

The Berlin Neuroscience Forum reminds us how many different facets neuroscience truly has and how complex, yet necessary it is to bring all these together to create a common picture.

## Neuroscience in Your Everyday Life

Why is it again that Hypnosis Works?

Close your eyes... Your eyelids are getting very heavy... You are feeling sleepy...

These words might sound familiar to anyone who has been to a hypnosis show. But you might wonder: Does it really work or is it all a farce? It is often falsely believed that hypnosis is based on a loss of autonomy and will and is, moreover, some form of sleep. However, today with modern imaging technology, scientists are on the trail of how hypnosis works, which brain areas are involved and why some people are more susceptible than others.

Hypnosis can be characterized by three major components: absorption, dissociation and suggestibility [1], meaning perturbation of the plane of attention. The traditional view of hypnosis was based on a strongly focused attention however recent imaging data suggest that control of attention is largely compromised during hypnosis. Hereby, the 'neutral hypnosis' state (inducing a hypnotic state without suggestion) is imaged. This state shows alterations in anterior brain functions, such as selective inhibition, disconnection, and dissociation of the frontal lobe [2]. Hereby, the anterior cingulate cortex (ACC) and dorsolateral frontal cortical areas (LFC) seem to have a predominant function.

More precisely, there is functional decoupling between conflict monitoring (ACC) and cognitive control processes (LFC) of the frontal lobe [3]. This leads to a decrease in spontaneous conceptual thought and an increase in mental absorption. When comparing the level of susceptibility to hypnosis, people with high susceptibility have an increase in neural activity in the ACC, whereas it is reduced in low susceptibility people [2, 4].

As mentioned above, the third characteristic of hypnosis is suggestibility. This is the basis of hypnotherapy, in which hypnosis is usually used to create a posthypnotic state, where certain previous suggestions are acted out. In addition to the frontal lobe, other brain regions which are involved in suggestion (e.g. pain perception) are also highly active [5]. This property of hypnotherapy is applied in the clinics as an adjuvant therapy in many different fields such as pain management (hypnotic analgesia) [5], treatment of irritable bowel syndrome (IBS) [6] and also to explore a wide range of psychological phenomena [3].

...and when I snap my fingers you will wake up feeling refreshed and renewed.

Do you also sometimes wonder about the simple neuroscientific questions in everyday life, but don't really feel like looking them up right away? For questions like this, just mail us your question (cns-newsletter@charite.de) and Dr. Harebrained will give us his explanation in the next issue! Our next issues question: **Why is it again that we dream? (vi)**



### References

- [ 1 ] Spiegel DA, J. Neuropsychiat Clin Neurosci, 1991
- [ 2 ] Egner T et al., NeuroImage, 2005
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- [ 4 ] Gruzelier J. et al., Contemporary Hypnosis, 2002
- [ 5 ] deCharms RC et al., Proc Natl Acad Sci U S A, 2005
- [ 6 ] Whorwell PJ, Nature reviews. Gastroenterology & Hepatology, 2012



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September	
3-8	EMBO Practical Course: Computational analysis of protein-protein interactions for bench biologists ( <a href="http://www.embo.org/events">www.embo.org/events</a> )
4	Einstein Meeting Wendelin Werner, Université Paris-Sud ( <a href="http://www.einsteinfoundation.de/de/meeting-einstein">http://www.einsteinfoundation.de/de/meeting-einstein</a> )
12-14	3 <sup>rd</sup> Leopoldina Symposium on Human Rights and Science ( <a href="http://www.leopoldina.org/en/events">http://www.leopoldina.org/en/events</a> )
13-16	15 <sup>th</sup> International Symposium Signal transduction in the blood-brain barriers, Potsdam-Sanssouci ( <a href="http://bbb2012.fmp-berlin.de">http://bbb2012.fmp-berlin.de</a> )
15-16	Entheo Science Kongress: <i>Bewusstseinsverändernde Pflanzen und Substanzen im Kontext von Forschung Heilung und Ritual</i> ( <a href="http://entho-science.de/">http://entho-science.de/</a> )
17-20	23 <sup>rd</sup> European Students' Conference ( <a href="http://www.esc-berlin.com">http://www.esc-berlin.com</a> )
October	
3-6	German Congress on Addiction 2012
10	Einstein Meeting Nancy Fraser, New School for Social Research New York ( <a href="http://www.einsteinfoundation.de/de/meetingeinstein">http://www.einsteinfoundation.de/de/meetingeinstein</a> )
21-24	World Health Summit 2012 ( <a href="http://www.worldhealthsummit.org/">http://www.worldhealthsummit.org/</a> )
22-28	Open Access Week ( <a href="http://www.openaccessweek.org/">http://www.openaccessweek.org/</a> )
November	
9	Falling Walls: International Conference on Future Breakthroughs in Science and Society ( <a href="http://falling-walls.com">http://falling-walls.com</a> )
21-24	<i>Deutsche Gesellschaft für Psychiatrie, Psychotherapie und Nervenheilkunde</i> (DGPPN) Congress ( <a href="http://www.dgppn.de/dgppn-kongress2012.html">http://www.dgppn.de/dgppn-kongress2012.html</a> )

### Choosing Elective Courses

In addition to merely relying on [neuroscience-berlin.de](http://neuroscience-berlin.de), we also recommend to look for courses the old-fashioned way: browse the course catalogues (*Vorlesungsverzeichnisse*) of the universities in Berlin (HU: <http://bit.ly/S73VEg>; FU: <http://bit.ly/QMgA2s>; TU: <http://bit.ly/y2WRoQ>), or the institutes' websites.

### New Elective Course Documentation

Please find the new elective course documentation on blackboard. It should help you to keep track of your credit point score and give some information on how these credit points can be obtained. More importantly, they also serve as a proof that you have earned these points, so please ensure they are properly signed and keep them safe.

### New MSc Students

In October the new cohort of Master students, including 1<sup>st</sup> and 2<sup>nd</sup> year Neurasasmus students, will dive into the Medical Neurosciences Program. To let them get started as smoothly as possible, we would like to ask MSc and PhD students to help them during their first weeks, either as a tutor or by participating in the organization of the welcome week. Interested students are invited to contact the program office.

### Evaluation — 85 % of the Lectures

Evaluations are not just an important tool to control and improve the quality of our teaching. The program in turn needs evaluations as a formal requirement to be accredited. Since very few students participated in evaluating the lectures in the past couple of months, we would like to stress that 85 % of all lectures of a lecture series or seminar have to be evaluated to be admitted to the final examinations. This is similar to the attendance rate of 85 %, and in fact, in the future, we will assume that if you do not evaluate, you did not attend the lecture.

### SfN Neuroscience 2012 — Call for Assistance

As every year over the past decade, the Medical Neurosciences Program is represented together with other neuroscience programs by the German Graduate Schools of Neuroscience at the SfN annual meeting. Since none of the program staff will be in New Orleans, we are looking for volunteers to take some information and advertisement material to our booth, e.g. flyers, brochures, posters. Please contact the program office if you would like to help.

### PhD Students

Please note that new material regarding the submission of the thesis has been uploaded to the Students' Corner section in Blackboard.

### Graduation 2012

We plan the graduation of the Master students admitted in 2010 to take place during the welcome week. On Friday, October 5, we would like to celebrate with graduates, alumni, current and new students. Faculty, of course, is invited, too!

#### Imprint

Charité Neuroscience (CNS) Newsletter

#### Corresponding Address

Charité - Universitätsmedizin Berlin  
International Graduate Program Medical  
Neurosciences, Charitéplatz 1, 10117 Berlin  
ralf.ansorg@charite.de, t: +49 30 2093-4584  
f: +49 30 2093-4590

#### Contact

[cns-newsletter@charite.de](mailto:cns-newsletter@charite.de)

#### Editorial Staff

Benedikt Brommer (**bb**), Ellie Rea (**er**), Gina Eom (**ge**), Inês Laginha (**il**), Jennifer Flynn (**jf**), Julia Rummel (**jr**), Muhammad Liaquat Raza (**mlr**), Marietta Zille (**mz**), Nicole Hentschel (**nh**), Veronika Lang (**vl**)

#### Design

Viktoria Stoiser

#### Illustrations

Benedikt Brommer (**bb**)

#### Contributors

Markus A. Dahlem, Natalia Denisova, Andriana Fetani, Luisa A. Hasam, Petra Huehnchen, Esperanza Jubera, Charlotte Klein, Priscilla Koduah, Linda MacDonald Glenn, Ana Luisa Piña, Arina Riabinska, Christine Roemer, Violeta Castelo Szekely, Thorsten O. Zander, Pei Zhang