



Rudolf Magnus Institute of Neuroscience

Rudolf Magnus Bulletin 34
September 2007

interview

Third IoP-RMI workshop

The third IoP-RMI workshop took place on June 11th and 12th in London at the Institute of Psychiatry. During two days a selected group of researchers from the Institute of Psychiatry, London, and the Rudolf Magnus Institute of Neuroscience, Utrecht, discussed different topics within the general theme 'Animal and Behaviour Genetics'.

The idea behind the third workshop was to make an inventory on the current collaborative projects between the RMI and the IoP concerning animal and human genetics and discuss new opportunities for collaboration. The new dean of the IoP, Peter McGuffin opened the workshop with an interesting overview on the current research within the IoP. This lecture was followed by Martien Kas of the RMI, who introduced the general theme of the workshop and gave a broad overview on current ongoing collaborations between both institutes.



During the following days we had five sessions addressing specific research using human and animal studies to unravel and understand the background of neurological and psychiatric disorders. The five disorders that were discussed during this workshop were epilepsy, autism, anxiety, schizophrenia and eating disorders. During these sessions data were presented on studies performed in collaboration, like in autism and eating disorders, but also topics were introduced on which collaboration could be initiated, like epilepsy and anxiety.



The scientific program was completed with a very nice and interesting keynote lecture by Avshalom Caspi. Caspi gave a lecture on environmental factors, genetic factors and their combination leading to certain specific endophenotypes. He also addressed how to cope with environmental factors in genetic study designs, a problem most of the researchers in the genetic and behavioural field are struggling with.

Besides the scientific part of the workshop, the IoP also took care of a nice social programme. During the lunches and the wine reception researchers of both institutes could exchange information, establish new collaborations, make plans for writing grants together and discuss data and the writing of papers. During the dinner there was time to relax, to get to know each other better, and to finish up the discussions started during the wine reception.



The third workshop was a great success, with new collaborations start and already existing collaborations more firmly established. Plans have been made for a fourth workshop, which will be held 26 and 27 November in Utrecht.



For those of you taking part in a collaboration between the IoP and the RMI, or those who want to start a new collaboration: remember that there are travel grants available for short exchange visits of staff and PhD-students between both institutes and for 1-2 months' visits for performing experiments at the partners' Institute. More information on these possibilities can be obtained with Mariken de Krom (m.dekrom-3@umcutrecht.nl)

PhD theses

2007-15
July 12, 2007

Sanneke van Vliet

Neuroprotection in Parkinson's disease: modafinil and $\Delta 9$ – tetrahydrocannabinol

B. Olivier, I.H.C.H.M. Philippens
supervisors

Sanneke van Vliet started her PhD in 2003 after she had finished her studies in medical biology. She performed her PhD work in the department of Psychopharmacology of the Pharmaceutical Sciences of the Beta faculty of the University Utrecht and TNO and completed her thesis in the section of Behavioural Genomics. She will start as a postdoc in the group of Gert ter Horst in Groningen (UMCG) where she will work on the neurobiology of panic attacks.

In Parkinson's disease (PD) is the output of the basal ganglia irreversibly affected due to degeneration of the dopaminergic neurons in the substantia nigra pars compacta. This results in manifestation of symptoms including akinesia, postural instability, and rigidity and resting tremors. PD is incurable, since present medications (predominantly with levodopa) do not counteract progression of the disease. Therefore, a better strategy aims to focus on prevention of the neuronal loss in an attempt to stop or slow down the progression of the disease. One way to achieve neuroprotection is via pharmacological interference aimed at crucial steps in the neuronal cell death process to promote neuronal survival.

Sanneke van Vliet investigated during her PhD-project of the neuroprotective effects of the alertness enhancer, modafinil and the psychoactive drug, delta-9-tetrahydrocannabinol (THC). For this purpose an animal model for PD closely related to man was used. In this model systemic injections of the neurotoxin MPTP induced specific lesions of the dopaminergic neurons in the substantia nigra. In this experimental setup, treatment with THC could not protect the neurons against the damaging effect of the neurotoxin. However, modafinil treatment resulted in an increased survival of the neurons and, consequently, reduction of the parkinsonian symptoms. The results show that neuroprotection in general and modafinil in particular could form an effective treatment strategy for Parkinson's disease.

news and other things

Jan Veldink receives 'lichtpad'

Jan Veldink of the department of Neurology and Neurosurgery has been awarded with an Enlighten Your Research grant (20.000 euro) from SURFnet in collaboration with NWO.



Jan Veldink and the other four winners of the 'lichtpaden' competition

The 'lichtpaden' competition, Enlighten Your Research, has been started with the aim to stimulate the use of 'lichtpaden' as tool for scientific research. A 'lichtpad' is a new functionality of the hybrid network SURFnet 6 and is special because of the high speed data throughput and the reliability of the system, a low and constant delay caused by the network and very high security.

These capacities make 'lichtpaden' very useful for scientific research and made Veldink decide to enter the competition. Now that he has received the award, a 'lichtpad' will be installed to make high-volume, genome-wide analyses of Amyotrophic Lateral Sclerosis (ALS) possible between the UMC Utrecht and the University of California Los Angeles, where the genome wide studies are performed. For more information on the 'lichtpaden' competition: <http://lichtpad.surfnet.nl>

Representatives of Psychopharmacology visit the Dutch parliament

Prof. Dr. Berend Olivier, Dr. Lucianne Groenink, Dr. Ronald Oosting and Dr. Mechiel Korte visited two members of the Dutch parliament to discuss the new legislation on animal welfare and animal experiments.

The 21st of June a delegation of the section psychopharmacology of the UIPS and RMI visited members of the Dutch parliament; Ormel and Atsma, who are responsible for animal welfare and animal experiments. This year the new 'Nota Dierenwelzijn' will be announced by the ministry. In this 'Nota' the policy regarding animal welfare will be explained. The visiting scientists have discussed the necessity and usefulness of animal experiments with Ormel and Atsma. Furthermore the effect of the law on animal experiments on the work floor and the functioning of the committees responsible for judging animal experiments (the DEC) were discussed. During the meeting it has been agreed on that also in the future the members of parliament will be given specific knowledge to be able to make a better judgment on the new legislation on animal welfare.



from left to right: Prof. Dr. Berend Olivier, Dr. Lucianne Groenink, Dr. Ronald Oosting and Dr. Mechiel Korte.

Three prizes for researchers of the Rudolf Magnus Institute at international and national symposia.

Frans van der Have of the group of Freek Beekman has received the second price in the Animal co-images of the year competition at the meeting of the Society of Nuclear Medicine, Philadelphia 2007.

Gitte Tiesjema, former PhD student of Roger Adan at the department of Pharmacology and Anatomy has been awarded the GlaxoSmithKline reward (3000 euro) for the best young scientist at the Dutch Endo Neuro Psycho meeting 2007.

Sietske Helder, student of Susanne la Fleur at the department of Pharmacology and Anatomy has won the Gerard Boer poster price (500 euro) at the Dutch Endo Neuro Psycho meeting 2007.

Article on Parkinson published in Development July 2007

Frank Jacobs and Simone Smits of the department Pharmacology and Anatomy have published their findings on pitx3 and Parkinson in the journal Development.

Parkinson's disease is a neurodegenerative disorder caused by the selective loss of dopaminergic neurons in the substantia nigra pars compacta (SNc). A few years ago we demonstrated in mice that the transcription factor Pitx3 is essential for the proper development of a specific dopaminergic subset that resembles the population susceptible to degeneration in Parkinson's disease (Development 2004). In order to identify the mechanism underlying the selective vulnerability of this specific group of dopaminergic neurons, our main focus has been to unravel the molecular pathways controlled by Pitx3. In a recently published study, we identified the aldehyde dehydrogenase gene *Ahd2* as a transcriptional target of Pitx3. Interestingly, we found that *Ahd2* distribution is restricted to the dopaminergic neurons that are affected by Pitx3-deficiency. Indeed, in the SNc region of mice that lacked Pitx3, *Ahd2* expression was completely lost. *Ahd2* is a potent generator of retinoic acid, the active derivative of vitamin A, which is involved in embryonic patterning and neuronal differentiation. Most intriguingly, restoring retinoic acid signaling, thereby bypassing the necessity of Pitx3 and *Ahd2*, efficiently counteracts the developmental defects of the SNc region in Pitx3 deficient embryos. This positions Pitx3 centrally in a developmental cascade involving retinoic acid signaling. This novel mechanism in which retinoic acid is involved in proper development and maintenance of the dopaminergic neurons of the SNc, is currently under further investigation at the department of Pharmacology and Anatomy.

Jacobs FM, Smits SM, Noorlander CW, von Oerthel L, van der Linden AJ, Burbach JP, Smidt MP. Retinoic acid counteracts developmental defects in the substantia nigra caused by Pitx3 deficiency. *Development*. 2007 Jul;134(14):2673-84.

Prof van Gijn decorated

After his farewell lecture on the occasion of his retirement, Prof. Dr. Jan van Gijn was on behalf of the Queen of the Netherlands decorated as Knight of the Order of the Dutch Lion.

Bas Neggers receives grant in Open competition NWO

Bas Neggers from the department of Psychiatry has been rewarded with a grant in the Open competition of NWO MagW. The grant enables him to appoint a PhD student on a fundamental neuroimaging project using fMRI and DTI.

The research project aims at combining several recent neuroimaging techniques, most notably functional magnetic resonance imaging (fMRI) and diffusion tensor imaging (DTI), to follow neuronal activation in healthy volunteers. During fMRI scanning, Transcranial Magnetic Stimulation (TMS) will be applied to selectively disturb brain activation in a safe and reversible manner.

The dynamics of blood flow following neuronal activation in areas along the dorsal stream involved in controlling our movements will be investigated in detail. Recently it has been established in several animal models that massive feedback projections from motor brain areas to the occipital lobe are active during movements, although their function is unknown. The idea is tested whether these connections can reshape visual cortical processing to accommodate the requirements of goal directed actions.

The combination of fMRI, DTI and image guided TMS has never been used before, and might lead to methodological advancements. Especially in combination with realistic mathematical models of brain function this might be a unique and innovating approach, bridging the gap between cognitive neuroscience theory and experimental data in an empirical and quantitative manner.

The proposed new view on visuo-motor processing could lead to an improved understanding of the motor and visual problems that brain-damaged patients experience, and lead to better treatment or regeneration therapies.

The emerging field of applied neuroscience "brain-machine-interfacing", where direct or indirect neural recordings of motor and association areas are used to operate machines, might also profit from a better understanding of visuo-motor control.

agenda and announcements

September 3, 2007 Neuroscience seminar

Jürgen Sandkühler,

'Learning and memory in pain pathways'

ErasmusMC, Rotterdam,

16:00, tea and coffee from 15:45

more information: <http://www.erasmusmc.nl/neuro/>

September 19, 2007 Research Lunch

Research lunch department of psychiatry

Aula Psychiatry, UMC Utrecht

12:30, lunch provided

contact, i.sommer@umcutrecht.nl

September 21, 2007 Swammerdam lecture

Peter Seeburg, (Max Planck Institute, Heidelberg)

'Of mice and memories'

15:00, Amsterdam

more information:

<http://www.onwa.med.vu.nl/pages/lectures/swammerdam.htm>

September 27, 2007 Swammerdam lecture

Pamela J Shaw, (University of Sheffield, UK)

'Mechanisms in motor neuron disease'

Amsterdam

more information:

<http://www.onwa.med.vu.nl/pages/lectures/swammerdam.htm>



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