



Rudolf Magnus Institute of Neuroscience

Rudolf Magnus Bulletin 44 December 2009

RMI symposium and evening

An impression

This year the Rudolf Magnus symposium and evening took place on the 25th of November. As each year the symposium highlighted exciting research within the institute with four excellent presentations. The program of the symposium was completed by a keynote lecture of Marian Joëls.

The symposium was opened by a lecture of Roel Ophoff, dept. Neuroscience and Pharmacology. During his lecture entitled: molecular studies of schizophrenia, he gave a short introduction on genetic studies and schizophrenia followed by an overview of the research which is done on the topic schizophrenia within the institute. He described the presence of rare variants (CNVs) causing schizophrenia and the more common variants which can lead to schizophrenia. He highlighted the striking fact that CNVs found to be associated with schizophrenia were also found in populations with autism, epilepsy and mental retardation but not with ADHD and bipolar disorder. Whereas on the level of common variants, there seems to be a link between schizophrenia and bipolar disorder. These facts are the input for the four lines of research currently conducted within the research group on schizophrenia.



The second speaker, Jeroen Pasterkamp of the dept. Neuroscience and Pharmacology, took the audience on a tour of his research on neural circuit development and disease. He explained how defects in mechanisms of neural circuits can lead to several diseases and that it is important to study these mechanisms to understand what goes wrong and eventually come to a therapy or cure of

the diseases. He explained how this has resulted in his four main research lines; first gene expression regulation in neurite growth and guidance; second cell biology and proteomics; third molecular control of neural circuit development and last; the neuronal biology of neurodegenerative and developmental diseases, and gave a short overview of the different studies done in these four research lines, from miRNA to functional studies into ALS.

The symposium shifted gear with the next two speakers with research in the field of neuropsychology and patient-orientated research. Leon Kenemans, dept. Psychopharmacology, gave a lecture entitled: working towards attention and inhibition. He focused on his studies to unravel the truth behind the statement that patients with ADHD have a response inhibition deficit resulting in a longer lag time on stop signals in several cognitive tasks. He was able to show that normally there is a direct link between sensory cortex activation and 'inhibition', whereas this lacks in patients with ADHD. This suggests that patients with ADHD might have an aberrant control mechanism when it comes to inhibition control. The final of the four presentations, given by Ludo van de Pol, dept. Neurology and Neurosurgery, showed the importance of patient orientated research. With the aid of some cases he showed the severity of paediatric neuromuscular disorders, currently over 400 disorders are known with virtually no treatment available at the moment. An important step in the research possibilities into this field is the start of the "spieren voor spieren" child centre. Van de Pol explained that this centre helps to study many children from early on and during the development of the disease. This helps in getting closer to early diagnosis, which is important since it gives a relieve to parents and child, it gives the possibility to genetic counselling and participating in experimental treatments.



Marian Joëls and Jan M. van Ree

After a short coffee break it was time for the keynote lecture of this year given by Marian Joëls on the topic: The stressed brain in health and disease. Her presentation consisted of three parts. She started with explaining the general molecular mechanisms/systems of stress and the key molecular players. And that stress improves your memory and in particular your memory for information that is important and linked to the stress-related event that has resulted in the memory. The second part dealt with the action of hormones involved in stress and the activation of the brain resulting in both rapid and delayed genomic effects of stress. She showed that stress changed the plasticity of the brain, the hippocampus, and that after a first stressful event the brain gets protected by the changes in plasticity against new stress event information. The first memory gets a kind of protection. She ended the presentation with telling that although stress is OK to form memories for later it is bad in combination with other circumstances, when stress is repeated/unpredictable/unexpected or when it happens early in life.

the posters lively discussions were taking place, whilst drinking a glass of wine and enjoying some appetizers. The poster session was followed by a dinner buffet with a variety of dishes and a terrific dessert buffet.

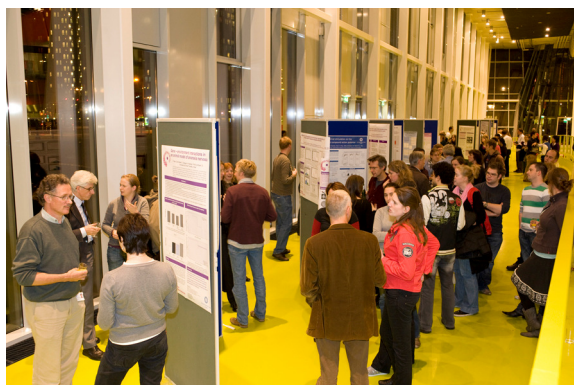


Jan Kimpen, Martijn van den Heuvel and Jan M van Ree

The symposium was closed by the announcement, by Jan Kimpen, of this year's winner of the Rudolf Magnus Research Award. The best publication of this year was chosen by a national jury to be: "Efficiency of functional brain networks and intellectual performance", by Martijn van den Heuvel, published in Journal of Neuroscience June this year. In the article van den Heuvel describes the experiments that show that IQ seems to be determined by the efficiency of the brain rather than the morphology of the brain. His research has gotten a lot of (inter) national attention and has led to a new concept of intelligence.



The grand final of the evening was the announcement of the winners of the Rudolf Magnus Poster awards. Frank Koerselman, one of the poster judges, had the honor to present the prizes. The third price was for the poster of Simone de Jong, the second price was for Marieke Langen, and the first price was for Peter Deschamps.



v.l.n.r. Jan M. van Ree, Marieke Langen, Peter Deschamps and Frank Koerselman

With the ending of the symposium the RMI evening started. Everybody involved in research done in the institute was invited for a nice evening in the 'Kroonluchter' of the Hijmans van den Bergh building. The evening program started with drinks and a scientific poster session. The quality of the posters was very high and at

PhD theses

Many of our PhD students have defended their thesis in the last couple of months. We want to congratulate all of them with their doctorates.

2009-27

November 5, 2009

J.A. Posthumus

Preventive effects and cost-effectiveness of the Incredible Years program for parents of preschoolers with aggressive behaviour

W.C.H.J. Matthys , H. van Engeland

Supervisors

Dept. Psychiatry

Section Psychopathology of developmental disorders

During my thesis work I focused on The Incredible Years (IY) parent program. This program is designed to give parents behavioural training with the aim to prevent the development of conduct problems in at risk children. The parent program appeared to be effective from treatment studies, but evidence for the preventive effectiveness of this program remains inconclusive.

My study aimed to evaluate the effects and cost-effectiveness of the IY parent program for parents of preschool children who were at risk for a chronic pattern of conduct problems two years after termination of the intervention. A population based sample of 144 preschool children with a high level of aggressive behaviour was divided into an intervention group and a matched control group. Results revealed significant improvements in observed and parent rated parenting skills. Furthermore, observed child problem showed significant intervention effects. The change in observed critical parenting from pre to post-intervention mediated the change in child problem behaviour from pre-intervention to two-year follow up. The intervention was most beneficial to children with a high level of initial aggressive behaviour.

With respect to the cost-effectiveness analysis, the intervention appeared to be cost-effective; the IY parent program showed better effects and was cost-saving. In conclusion, the IY parent program appeared to be cost-saving and effective in reducing child problem behaviour. This population based study highlights the potential of the IY parent program as an indicated preventive intervention for preschool children at risk for a chronic pattern of conduct problems.

2009-30

November 5, 2009

R.G. Hoff

Intravascular volume after aneurismal subarachnois hemorrhage

C.J. Kalkman, G.J.E. Rinkel

Supervisors

Dept. Anesthesiology

Section Cerebrovascular disorders

2009-31

November 13, 2009

J. Xiao

Development and evaluation of Monte Carlo-based SPECT reconstruction

M.A. Viergever, F.J. Beekman

Supervisors

Dept. Neuroscience and Pharmacology

Section Behavioural phenotyping and genomics

2009-32

November 13, 2009

J.M.F. Niermeijer

Prognosis and treatment of polyneuropathy associated with IgM monoclonal gammopathy

J.H.J. Wokke, N.C. Notermans

Supervisors

Dept. Neurology and Neurosurgery

Section Neuromuscular diseases

Polyneuropathy associated with IgM monoclonal gammopathy of undetermined significance (IgM MGUS polyneuropathy) is a disabling chronic progressive immune mediated neuropathy with distal sensory disturbances and muscle weakness that usually develops from the age of 55 years onwards.

The Neuromuscular department of the University Medical Center Utrecht serves as a tertiary referral center for this polyneuropathy and has built up experience with this rare disorder over the past 25 years. (head Dr. N.C.

Notermans)

This resulted in the largest group of IgM MGUS polyneuropathy patients followed in one center. It enabled us to develop the first prognostic model of IgM Neuropathy which can be used world wide. A web-based risk calculator was developed, enabling clinicians to inform patients with IgM neuropathy on their risk for disability and assist them to prepare for the future.

<http://www.umcutrecht.nl/subsite/Prognosis-MGUS-Neuropathy>

Optimization of immunotherapy for IgM neuropathy, is an international effort. Immunomodulating therapy directed at lowering of the M protein, and therapy that has a more general immunosuppressive effect were studied in three treatment trials, with different types of immunomodulating therapy. However, still no conclusive therapy of first choice for IgM neuropathy could be determined.

Treatment was successful in individual patients in two open label trials with fludarabine or rituximab, and a placebo controlled trial failed to show benefit of cyclophosphamide with prednisone. The three regimen showed equal response percentages, with the least side effects after rituximab. This supports recent findings in a US study of a similarly sized group.

A novel finding, confirmed by nerve conduction studies, was that treatment earlier in the disease course increases

the chance of effect. We have therefore changed our policy towards starting treatment early in the disease course. This is an important change from the previous policy of waiting for disability to develop.

2009-33

November 26, 2009

A.C. van der Schot

The bipolar puzzle, adding new pieces. Factors associated with bipolar disorder, genetic and environmental influences

R.S. Kahn, W.A. Nolen, M. Vink

Supervisors

Dept. Psychiatry

Section Genetic basis of developmental disorders

2009-35

December 22, 2009

M.J.G. Langen

Repetitive behaviour in autism: Imaging pathways and trajectories

H. van Engeland, S. Durston, W.G. Staal

Supervisors

Dept. psychiatry

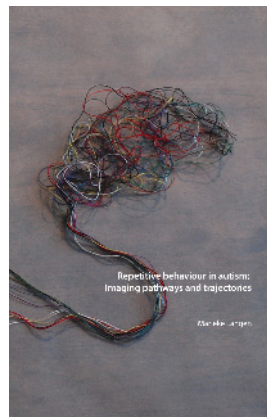
Section Brain changes in developmental disorders

Repetitive and rigid behaviour is one of the core symptoms of autism, a severe and lifelong child psychiatric disorder. Although repetitive behaviour symptoms often form a significant impairment for affected individuals, systematic study of the phenomenology and in particular the neurobiology of repetitive behaviour has been lacking. In her thesis, Marieke Langen, addresses this gap by using neuroimaging techniques (structural magnetic resonance imaging (MRI), diffusion tensor imaging (DTI) and magnetisation transfer imaging) to investigate brain differences associated with repetitive behaviour in autism. She compared groups of individuals (children and adolescents, as well as adults) with and without autism and examined anatomical differences in specific structures and networks of the brain and related these to behavioural measurements. Furthermore, she explored the involvement of differences in developmental trajectories of these structures and networks in autism.

Her studies demonstrate that corticostriatal grey and white matter follow altered developmental trajectories in autism when compared to controls, and implicate corticostriatal circuitry in the repetitive behaviour which characterises the disorder.

In addition to the experimental work, Marieke Langen's thesis includes two reviews on the neurobiology of repetitive behaviour. These theoretical studies emphasise the need for research strategies that take (1) the heterogeneity of autism, and (2) the etiologic overlap with other disorders into account.

In sum, this thesis contributes to our understanding of the neurobiology of autism.



2009-25

December 23, 2009

C.H. Vinkers

The neurobiology of stress-induced hyperthermia

B. Olivier, C.J. Kalkman, L. Groenink, S.M. Korte

Supervisors

Dept. Psychopharmacology

Section Behavioural phenotyping and genomics

The research described in the thesis shows that the change in body temperature in response to stress (stress-induced hyperthermia) can be employed to study the pharmacological, genetic and mechanistic backgrounds of stress and their possible consequences. An important finding of the current research is that the SIH paradigm is suitable to assess the acute and chronic effects of α subunit-selective GABAA receptor agonists. Using novel selective ligands, we show that the SIH paradigm can be used to dissect the contributions of the different α subunits. In particular, we confirm putative anxiolytic effects for GABAA receptor α 2/3 subunit agonists which do not result in the development of tolerance after chronic treatment. Further, our results indicate that the α 1 subunit is involved in hyperthermia and that the α 5 subunit is not directly involved in the anxiolytic or hypothermic effects of benzodiazepines. Together, these data indicate that selective GABAA receptor α 2/3 subunit agonists constitute a promising class of novel anxiolytics.



Nature paper

Maretha de Jonge and Herman van Engeland, department of Psychiatry, are authors on a Nature paper entitled "A genome-wide linkage and association scan reveals novel loci for autism". Weiss *et al.*, 2009, Nature 2009 Oct 8;461(7265):802-8.

FES grant

Eline Lindeman, Nick Ramsey and Sarah Durston have received in total €600.000 for their part, within the theme 'the healthy brain' of the FES project of the NIHC (*Nationaal Initiatief Hersenen & Cognitie*).

Veni grants

Ynte Ruigrok and Aldemar Torres Valderrama both from the department of Neurology and Neurosurgery have received a Veni grant from NWO. Ruigrok for her project entitled: Causes of aneurysms of blood vessels and Torres Valderrama for the project: Human neural interface methods.

Vidi grant

Iris Sommer from the department of Psychiatry has been awarded with a Vidi grant for her project entitled: Experimental treatment for chronic hearing of voices.

ZonMw Parel

The Parel Award is a very prestigious prize and is only rewarded to a few ZonMw projects. The project of Erik Hulzebos is such a project. The UMC Utrecht received the award for the research done on pre-surgery physiotherapy for heart patients.



Erik Hulzebos and Jan Kimpen receiving the award.

Dr. F. Gerritzen-award

Esther van den Berg of the department of Neurology and Neurosurgery received on the 26th of November the prestigious Dr. F. Gerritzen award of the Dutch society for diabetes for her thesis work.



Esther van den Berg

Book on child psychiatry

Prof. Walter Matthys, department of Psychiatry and Prof. John E. Lochman of the University of Alabama, formerly special professor of the Rudolf Magnus Institute, have written and published recently a book on ODD and CD. In this book they give a comprehensive overview of empirical knowledge and associated clinical information on these disorders.

Matthys and Lochman, oppositional defiant disorder and conduct disorder in children, publisher Wiley-Blackwell

Rudolf Magnus Graduate School Certificate

The Director and the Research Training Committee of the Graduate School took pleasure in presenting the Rudolf Magnus Graduate School Certificate to the following Doctors: Jocelyne Posthumus (November 5, 2009), Astrid van der Schot (November 26, 2009), Marieke Langen (December 22, 2009).



agenda and announcements

January 7, 2010 CSCA symposium

'Cognition, the brain, and atypical development'

Amsterdam

more information: <http://www.cscs.nl/>

January 8, 2010 KNAW-congress

'Genomics of gene expression'

Amsterdam

more information: <http://www.knaw.nl/>

January 8, 2010 Helmholtz Lecture

Eli Peli (Harvard University, USA)

'Assistive devices for impaired vision'

16.00-17.00

Ruppert Building, Leuvenlaan 19, Zaal Wit

January 13, 2010 'Congres Neurologie'

'12 maanden neurologie in vogelvlucht'

Jaarbeurs Utrecht

more information: [website Benecke](#)

February 4-5, 2010 IoP-RMI workshop

Joint workshop in London

February 5, 2010 CSCA lecture

Catherine Snow (Harvard University, Cambridge, UK)

Amsterdam

more information: <http://www.cscs.nl/>

March 5, 2010 Helmholtz Lecture

David Fitzpatrick (Duke, USA)

'Imaging experience dependent emergence of functional circuits in visual cortex'

16.00-17.00

Ruppert Building, Leuvenlaan 19, Zaal Wit

March 12, 2010 'Nationaal Autisme Congres'

WTC Rotterdam

more information: www.nationaalautismecongres.nl

March 15-21, 2010 Brain Awareness week

more information: [Brain Awareness Week](#)

March 17, 2010 CSCA lecture

Anne Cutler (Nijmegen)

'Listening to speech'

Amsterdam

more information: <http://www.cscs.nl/>

March 19, 2010 'Nationale Hersenlezing'

Michel Ferrari (Nijmegen)

Topic: Migraine

Utrecht, de domkerk: 17:00-18:00

More information:

<http://www.hersenstichting.nl/actueel/kalender.html>

