



Rudolf Magnus Institute of Neuroscience

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interview

Rehabilitation receives four research grants

Prof Eline Lindeman, head of the department Rehabilitation and Sports Medicine, and the researchers within her group have been rewarded with four grants within the ZonMW programs Rehabilitation and Efficiency research (Doelmatigheidsonderzoek). These grants will support four PhD students in her department.

The four grants are all part of the main research focus of the department Rehabilitation and Sports Medicine. The first grant is focusing on child rehabilitation and is a joint project of the rehabilitation departments of the UMC Utrecht, VuUMC Amsterdam, UMC Groningen and Erasmus MC Rotterdam, with UMC Utrecht being the leading party. The project has a main focus on the rehabilitation of children who have suffered brain damage. The idea behind the project is that parents are feeling sorry for their children and in the process stop stimulating their children to try to do stuff themselves. Instead the parents do everything for them and there is no stimulus anymore for the children to learn again. In the project at each center an intervention study will be done with cohorts of children. Each center will study a different age category; UMC Utrecht will study the toddlers. During the intervention study the parents will be thought to stimulate their children and to evoke movements from their children. This way the researchers hope to improve the rehabilitation and learning curve of children with brain damage.

The second project is a multicenter project, in which AMC Amsterdam, UMC Utrecht and Radboud MC Nijmegen are participating, with AMC Amsterdam being the leading party. The main focus of the project is neuromuscular disorders. Since patients with neuromuscular disorders suffer from degeneration of their muscles and with that related loss of physical power and control of movements it is important to develop good rehabilitation programs to help these patients during their disease process. Within this project there is a close collaboration between the departments of neurology and rehabilitation of the participating centers. In each center intervention studies will be done addressing problems in the cognitive field, physical strength and control of movements, each center will address a specific patient group.

The collaboration in UMC Utrecht will be with Leonard van de Berg of the department of Neurology and Neurosurgery, and the main focus will be on patients with ALS.



prof Eline Lindeman

The third project has as main topic CVA. The centers participating are UMC Leiden, VuUMC Amsterdam, UMC Utrecht and Radboud MC Nijmegen. UMC Leiden is the leading party; however, the majority of the project has been designed by Kwakkel of UMC Utrecht. The goal of this project is to evaluate the recovery mechanisms of arm and hand functions after a stroke related event. Each center will in a multidisciplinary team evaluate these mechanisms using a different approach. The idea behind the project is to better understand the recovery mechanisms and with that knowledge improve rehabilitation therapies used with patients recovering from a stroke event.

The evaluation in UMC Utrecht will be done using fMRI techniques in collaboration with Nick Ramsey and Frans Leijten from the department of Neurology and Neurosurgery. The department of Neurology and Neurosurgery will also be involved from the clinical point of view.

The fourth and last project is an efficiency project, which will solely be done at the department in Utrecht. This is a so-called fit-stroke study. It will be an intervention study in which the effect of training of chronic patients after a stroke event will be studied. At the same time a cost-benefit analyses will be done to evaluate the used training procedures.

All four projects are close to the work floor and results of these studies will certainly have an impact on the day to day routine within the rehabilitation centers in the Netherlands.

PhD theses

2007-16
September 27, 2007

Claudine Dietz

The early screening of Autistic Spectrum Disorders

H. van Engeland, J. Buitelaar, S. Swinkels
supervisors

Claudine Dietz started her PhD in 1998 after she had finished her studies in Psychology. She performed her PhD work in the department of Child and Adolescent Psychiatry and completed her thesis in the section of Developmental Disorders. She has already a staff position at the department of Child and Adolescent Psychiatry and will remain working at the department.

Autistic Spectrum Disorders (ASD) are seriously disabling disorders with early onset. Generally, the clinical diagnosis is established years after the first symptoms reveal. The Early Screening of Autistic Traits (ESAT) was developed and tested within a large population of 14-15 months old children, and within an at risk group of children below three years. Results show screening to be inefficient at population level at this young age as many 'cases' were missed and rate of false positives was high. A two-stage screening strategy within at risk children would result in a much higher detection rate of ASD, a lower rate of false positives and in a higher compliance of parents. We would recommend physicians at well-baby clinics to use our "red flags for ASD" to find at risk children, followed by specialist screening with the ESAT. Screen-positive children need a clinical evaluation at a child psychiatric centre.

2007-17
October 10, 2007

Marieke Lansbergen

Impulsivity: A deficiency of inhibitory control?

H. van Engeland, J. L. Kenemans, K.B. E. Böcker
supervisors

Marieke Lansbergen started her PhD in 2002 after she had finished her studies in biological psychology. She performed her PhD work in the department of Child and Adolescent Psychiatry and completed her thesis in the section of Developmental Disorders. She will start as a postdoc at the UMC St. Radboud in Nijmegen.

Impulsivity is a personality trait and varies across the population. Extreme impulsive behavior is one of the major characteristics of several psychiatric disorders such as attention-deficit/hyperactivity disorder (ADHD). Impulsivity can be quantified by self-report questionnaires but also by behavioral paradigms which tax inhibitory control. Previous findings and one part of this thesis have consistently indicated deficient inhibitory control in ADHD. Abnormal baseline brain activity (i.e., high theta/beta ratio) has also been associated with impulsive behavior in ADHD.

The main goal of this thesis was to examine whether 'healthy' volunteers who scored extremely high on self-reported impulsivity might also show deficient inhibitory control and/or abnormal baseline brain activity. Behavioral as well as electrophysiological findings, reported in the present thesis, suggest that high self-reported impulsivity, deficient inhibitory control, and high theta/beta ratios in the normal population are qualitatively different from that in ADHD.



In particular, healthy individuals that report high impulsivity or have high theta/ beta ratios tend to score better in tests of inhibitory control and associated brain-activity correlates. These findings indicate that healthy highly impulsive individuals are inadequate to model pathological impulsivity and increase our insight into neurobiology and possible treatments of pathological impulsivity.

news and other things

VIDI grant for the genetic dissection of psychiatric behavioral traits in mouse and men

Martien Kas of the department of Pharmacology and Anatomy has been awarded with a VIDI research grant (600.000 euro) from ZonMW NWO. This grant will help him to establish and enlarge his research group at the Rudolf Magnus Institute.

Eating disorders are complex psychiatric disorders in which patients display a variety of behavioral traits, including obsessiveness, increased anxiety, hyperactivity and altered appetitive motivation. These traits are also seen in other psychiatric disorders, such as in obsessive-compulsive disorders and depression, which are often comorbid with eating disorders. Family and twin studies have revealed that genetic factors play a major role in eating disorders.

However, novel approaches are needed to deal with both phenotypic and genetic heterogeneity in patient populations and with gene-environment interactions to unravel the mechanisms underlying these disorders.

Martien Kas from the Department of Pharmacology and Anatomy recently received a ZonMW VIDI grant for his proposal to use interspecies genetics in mouse and men to tackle these issues.

With the availability of a large variety of inbred mouse strains and their known genome sequences, mouse genetics offer a challenging way to study complex traits. For example, in contrast to patient populations, mouse strains can be used to control for phenotypic and genetic heterogeneity as well as for complex gene-environment interactions. Interestingly, recent studies have shown that genetic variation associated with psychiatric disorders affect analogous neural circuits and behavioral traits in mice and men, demonstrating that mouse models can contribute to systematic searches for genetic determinants of psychiatric disorders (Chen et al., *Science*, 2006).

Martien's VIDI project aims to identify novel genetic loci and associated genetic pathways regulating mouse behavioral traits related to eating disorders. To establish this, a novel mouse genetic mapping population will be exposed to a comprehensive animal model of eating disorder traits.

These so-called chromosome substitution mouse strains were introduced by Martien some years ago as part of the ABC-neurogenomics program and offer a sensitive approach to further genetically dissect complex behavioral traits. For example, in an initial screen using these mouse strains, specific behavioral eating disorder traits were linked to mouse chromosomes that overlap with human linkage regions for anorexia nervosa and obsessive-compulsive disorders.



Dr. Martien Kas

Further genetic fine-mapping of these chromosomes and genome-wide gene expression profiling will reveal novel genetic loci and associated pathways for these behavioral traits in mice. This then offers the opportunity to test homologous candidate genes in available DNA samples from well-characterized eating disorder patients through various collaborations, such as with Rintveld in Zeist and with the Institute of Psychiatry in London. Gene variants observed in humans that are indeed associated with the disease can subsequently be functionally tested in mouse mutants for these genes. As recently described by Martien and partners from the Institute of Psychiatry in London (Kas et al., *Molecular Psychiatry* 2007), interspecies genetics will offer a great opportunity to translate essential behavioral traits in animals to psychiatric disorders and to further understand the mechanisms underlying these traits.

State of the Art High-Field human MRI scanner to boost Neuroscience at the RMI

The University Medical Center of Utrecht has acquired one of the most advanced MRI scanners. It is a 7 Tesla scanner made by Philips for human applications. A separate building had to be built to house this machine, which happens to be located next to the Psychiatry department. The 7T scanner is a research machine. The hardware is all operational but the scans (which are computer programs) have to be developed because the strong magnetic field changes properties of tissue. To accomplish this, a new MRI research and development team is started under Prof. Dr. Peter Luyten of the Radiology Department, with the goal of developing clinical applications for 7T. The Rudolf Magnus Institute will use the 7T for brain research, and for this purpose contributes three researchers to the team. We expect that the 7T will improve the research on brain anatomy (structural MRI and DTI) and on brain function (functional MRI) that is conducted on patients with psychiatric and neurological disorders, thereby strengthening our international position in neuroscience.

Philips has only 10 of these machines worldwide, of which two in the Netherlands (one in Leiden). To develop scans we will collaborate with the other centers, notably Leiden, Nottingham (UK) and Cleveland (USA). With the 7T acquisition and the new research group, the Rudolf Magnus Institute also expands and intensifies collaboration with the Image Sciences Institute with several MRI-related projects in which researchers from both institutes participate.

Long-lasting collaborations between the two institutes and the Helmholtz Institute are the basis for the current Neuroimaging Research program on the 3 Tesla scanner. This strategic alliance is carried over to the 7T scanner, and is reinforced by the new MRI research team. Utrecht is ready to enter the new High-Field MRI era!

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:
Claudine Dietz (September 27, 2007) and
Marieke Lansbergen (October 10, 2007).

agenda and announcements

October 1, 2007 Neuroscience seminar

Eckart Gundelfinger, (Leibniz Institute for Neurobiology, Germany)

'The brain's extracellular matrix: a 100 year-old structure still in search for functions'

ErasmusMC, Rotterdam,
16:00, tea and coffee from 15:45

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

October 9, 2007 'Congres cognitieve revalidatie'

'Onderzoek in de praktijk en praktijk in het onderzoek'

Hotel Figi, Zeist
contact, Majanka Keijer, KNMG, 030-282 32 10

October 11, 2007 'Publieksdag Hersenstichting'

Beatrix theater, Jaarbeurs Utrecht
more information: <http://www.hersenstichting.nl/hsn.cgi?home>

October 12, 2007 'Congres dag van de verslaving'

'o.a. over alcohol en jongeren'

Jaarbeurs Utrecht
more information: Stichting Zelfhelp Nederland, 020-689 59 89

October 31, 2007 Rudolf Magnus symposium

Keynote speaker: Judith Rapoport

'The state of art of psychiatric developmental disorders'

Pink lecture hall, UMC Utrecht, 16:00
Contact: Krista Poel, k.poel@umcutrecht.nl

October 31, 2007 Rudolf Magnus evening



Rudolf Magnus