



Rudolf Magnus Institute of Neuroscience

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interview

When the voices are within your head

Healthy people, but schizophrenia patients in particular, may experience auditory hallucinations. Iris Sommer is a specialist in the representation of language in the brain. She now studies the regions of the brain that are involved in hallucinations in healthy individuals to understand and help patients with schizophrenia to overcome this disabling symptom.

Mrs. C. hears whispering voices in the night. She can just make out the words, but she is hardly able to make sense of what is said. She is fully aware of the fact that these voices are not real, and that her mind is playing a trick on her, and she knows that if she ignores the voices they will eventually stop. She experiences what many normal individuals experience, namely auditory verbal hallucinations. Sommer explains the value of healthy hallucinators: "Although auditory hallucinations occur with a lifetime prevalence of 10 to 15% in persons without neuropsychiatric diseases, they are most common in schizophrenia, with an average prevalence of 60%. Therefore, models of auditory hallucinations are based on investigations of schizophrenia patients. Three cerebral deviations have been found by others and us in schizophrenia, which may underlie their tendency to misinterpret inner speech as external. All three mechanisms, altered language representation in the brain, altered connectivity, and structural deficit of the language system, may be predisposing factors for hallucinations. However, these have been

shown to correlate with schizophrenia, which is a complex syndrome consisting of psychotic, cognitive and negative symptoms and not to auditory hallucinations per se."

In order to learn if language activation and connectivity play a causal role in the pathophysiology of auditory hallucinations, Sommer will use MRI to look into the 'pure' form of hallucinations. She will do this by studying healthy subjects who experience hallucinations, without other psychotic or cognitive symptoms or any history of hospitalisation or chronic medication use. A large group of healthy volunteers is asked to answer a short questionnaire (see, <http://www.verkenuwgeest>) on hallucinatory experiences. Fifty persons with high scores and 50 persons with low scores will be invited to participate in the MRI study. A much larger group of healthy hallucinators, as well as a group of healthy subjects with delusion-like phenomena are included for genetic research.

When the regions in the brain that are involved in hallucinations become apparent, Sommer will try to help patients with persistent hallucinations using repetitive Transcranial Magnetic Stimulation (rTMS). Sommer: "In many patients, auditory verbal hallucinations are the central symptom of the psychosis. Secondary to these hallucinations, patients may develop a delusion to explain the origin of the perceived voices. For these patients, the perceived voices often become proof that their delusion is true. As long as the hallucinations are perceived, the patients will not be able to correct their false beliefs. Patients with such hallucinations and subsequent delusions become socially isolated. rTMS may offer an alternative therapy for patients who do not respond to antipsychotic medication. For this group potential effects on health and social functioning are expected to be high, since a decrease in hallucination severity will decrease their fear, delusions and apathy."

Iris Sommer (MD, *Vrije Universiteit*, Amsterdam, 1997) worked as a PhD student in the Department of Psychiatry, Rudolf Magnus Institute in 1997-2002, and received her PhD (cum laude) at Utrecht University (2004) for her thesis '*Language lateralisation in Schizophrenia*'. Since 2002 she is a resident in psychiatry, Department of Psychiatry, UMC Utrecht. She received the Rudolf Magnus Research Award 2004 for an article in *Br.J.Psychiatry*. She presently works on a VENI grant that she received from the Netherlands Organisation for Scientific Research in 2005 to study the origin of auditory hallucinations in healthy individuals.



PhD theses

2006-1

Quality of health care can be 'depressing'

January 17, 2006

Ton (A.)C.M. Vergouwen

Adequate follow-up can't be optional. Improving the management of major depression in primary care

G.F. Koerselman, Th.J.M. Verheij, H. Burger supervisors

Depressive illness is a public health issue of major significance. Despite proven efficacy of antidepressant medication, the quality of depression management in primary care is still generally insufficient. Ton Vergouwen developed a depression care programme, with which he was able to demonstrate that the management of major depression in primary care in the Netherlands can be substantially improved.

Presently, few patients with major depression receive levels of treatment consistent with guidelines. Moreover, effectiveness of antidepressant medication is reduced by patients' non-adherence. This may result in treatment failure, high medical care utilization, and functional impairment. Vergouwen aimed to gain more insight into the possibilities to improve adherence, patients' attitudes towards antidepressant medication, and depression outcome.

Vergouwen developed a depression care programme (DCP) that was feasible in primary care practices in the Netherlands, which consisted of enhanced patient education, enhanced general practitioner education, stimulation of participation of general practitioner and patient in the treatment, patient's self-management support, and discussing the costs and benefits of antidepressants. In a cluster randomized trial, Vergouwen compared the effects of this programme with those of a less complex systematic follow-up programme (SFP) in patients suffering from major depression, who were prescribed selective serotonin reuptake inhibitors. The SFP is in line with what is recommended in most treatment guidelines. Vergouwen demonstrated that adherence was high and depression outcomes were favourable in both conditions. So, it was concluded that SFP is an effective intervention per se.

Vergouwen further developed a prediction rule from collected baseline patient characteristics, which provides the general practitioner with a useful instrument to predict remission of individual patients. Greater illness severity, comorbid anxiety disorder, chronic somatic illness, a PDQ-R total personality-score greater than 26, employment status, and being unfit for work predicted non-remission by week ten fairly good.

Most guidelines on the treatment of depression recommend to evaluate treatment results after four to six weeks, and, if necessary, to change treatment. However, the evidence on which such recommendations are based is rather weak. Vergouwen investigated the relation between initial symptoms change and remission. His data show that treatment with antidepressant medication should be reconsidered if patients still fail to improve or are only partially improved after six weeks. To monitor symptoms change, he recommends the use of a self-administered questionnaire. Many depressed patients have negative

attitudes towards antidepressants, leading to poor adherence and depression outcome. In another study, Vergouwen demonstrated that these attitudes can be ameliorated using DCP. Vergouwen concludes that, "The management of major depression in primary care can be substantially improved. This may result in higher adherence rates, more positive patient attitudes towards antidepressant medication, and better outcome of depression treatment. Since systematic follow-up seems to be as effective as more complex interventions, one might rightly state that systematic follow-up cannot be optional anymore"

Ton Vergouwen (May 6, 1963, Goes). Secondary education (Gertrudislyceum, Roosendaal), 1981; Medicine, *Vrije Universiteit*, Amsterdam, MD, 1989. Specialization in psychiatry, Academic Hospital, *Vrije Universiteit*, Brussels (1992-1996), psychotherapeutic training (Jelgersmakliniek, Oegstgeest). Since 1997 he works as a psychiatrist at the Sint Lucas Andreas Hospital, Amsterdam.

2006-2

Caring and coping in ALS

January 23, 2006

Jan-Paul Van den Berg

Specialised ALS care and quality of life

L.H. Van den Berg, E. Lindeman, S. Kalmijn supervisors

There is still no curative treatment for amyotrophic lateral sclerosis (ALS). The main goal of rehabilitative care for patients and their families is to maintain or improve their quality of life (QoL). Jan-Paul van den Berg demonstrated that a multidisciplinary integrated care approach improved the mental QoL of ALS patients. Also an active coping style of the patient is positively related to the mental QoL in ALS.

New treatments for ALS are likely to be developed, the potential effects of which will need to be communicated carefully, as the expectations of patients are high, leading to disappointment and feelings of failure. The mean life expectancy of patients with ALS is likely to increase in the future, as treatments slow the progression of the disease. This will lead both to an increased prevalence and an increased demand for high-quality symptomatic and rehabilitation care. Van den Berg studied the development and implementation of a Dutch protocol for optimal rehabilitative management in ALS, and advocates that a specialised multidisciplinary ALS team must consist of at least a consultant in rehabilitation medicine, a physical therapist, an occupational therapist, a speech pathologist, a social worker, and a dietician.

Van den Berg studied 208 ALS patients and found that patients with multidisciplinary ALS care had a better mental QoL than patients who were provided with general care. The difference in QoL was most pronounced in the domains of social functioning and mental health, and was independent of the presence of aids and appliances. In addition to the previous finding that multidisciplinary ALS care prolongs survival of patients with ALS, his study provides further support for a beneficial effect of a multidisciplinary approach to ALS care given by experienced professionals. Van den Berg also investigated the relationship between loss of function and QoL. Multivariate linear regression analyses revealed that patients with

bulbar onset had a better physical functioning than patients with a spinal onset. Patients with swallowing dysfunction had a lower mental QoL, which appeared the most important determinant for a reduced subjective QoL. As expected, patients with extremity disorders, especially the patients with lower extremity dysfunction, had significantly worse physical functioning, as compared to patients without extremity dysfunction.

Van den Berg further examined the relation between coping styles and QoL in ALS patients and their caregivers. A passive coping style in both patients and their caregivers appeared to be the strongest predictor for a lower mental QoL. Reassuring thoughts and an active approach were positively related to mental QoL in ALS patients. The physical QoL in ALS was not associated with coping style. Van den Berg: "Results suggest that a passive coping style should be avoided in favour of an active approach and reassuring thoughts. Measuring QoL is multidimensional and QoL should be measured with a health-related QoL scale and an individual, subjective QoL scale. QoL in ALS and their caregivers improve when multidisciplinary ALS care is applied."

Jan-Paul van den Berg (May 6, 1960, Hilversum). Secondary education (Comenius College, Hilversum), 1979; Medicine (Erasmus University, Rotterdam), MD 1986. Specialisation in Rehabilitation Medicine, Academic Hospital Rotterdam and Rehabilitation Centre *De Hoogstraat*, Utrecht. Rehabilitation specialist (1993-1999) *Diakonessen-Ziekenhuis* and *De Hoogstraat*, Utrecht. As of 1999 he is rehabilitation specialist at Meander Medisch Centrum (Amersfoort, Baarn). Since 2003 he works also for the *ALS Centrum Nederland*, Utrecht.

'An Evening with Rudolf Magnus' a success

Following this year's Rudolf Magnus Symposium featuring the Rudolf Magnus Lecture by Michael Gazzaniga and the presentation of the Rudolf Magnus Research Award to Louk Vanderschuren, we organised an Evening with the man himself: Rudolf Magnus.

The late Rudolf Magnus and his wife Traudl visited the Institute that now bears his name, and marvelled at all the advances of neuroscience in Utrecht that he once set in motion (excellent stage play by Ruud van den Bos and Nienke Vulink, both staff of our Institute).

More than 150 of our staff enjoyed the buffet-style diner and drinks. Meanwhile there was ample time to discuss the many selected posters of the staff. The best poster was presented with the Rudolf Magnus Poster Award (see page 4).

Several members of staff were invited to show their artistic talents during three 15-minutes intermezzos. Meg Breuer (vocals) and Reinoud de Jongh (guitar) played several modern rock songs before dinner. After dinner Gert-Jan Geerse (vocals) and Tom Roeling (vocals and guitar) played three Irish-American ballads. In the final performance, Geartsje Boonstra achieved the unthinkable. With her clear (and non-amplified) soprano and with the excellent play of Hugo Schnack (piano) and Maria Boersma (violin) she was able to stop our scientists talking about science for a while and listen in.

Below you will find photographs giving an impression of the 'Evening with Rudolf Magnus'.

(Photographs by Erik van Beers)



Rudolf Magnus Graduate School Certificates

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:

Trynke De Jong (December 1, 2005)
 Marijke Eurelings (December 2, 2005)
 Fabienne Naber (December 20, 2005)

Marjo Zonneville wins Rudolf Magnus Poster Award 2006

For 'An Evening with Rudolf Magnus' (see page 2-3), 36 posters were selected by the section coordinators of our Institute to be presented during the evening poster session. The three-headed jury, with Frank Koerselman as chair, judged the posters especially for their ability to advertise their message. Marjo Zonneville (Child- and Adolescent Psychiatry) won the Rudolf Magnus Poster Award (€ 200 plus a certificate) with her poster entitled, '*Preventive effects of treatment of DBD in middle childhood on substance use and delinquent behaviour.*'



Frank Koerselman presenting the Rudolf Magnus Poster Award to Marjo Zonneville (courtesy of Erik van Beers)

Retirement of Guido Smoorenburg

Guido Smoorenburg (Experimental physics and Applied mathematics, Utrecht University, 1967) received his PhD for his thesis '*Aspects of two-tone perception*' in 1971 working with professor Bouman at the *TNO Instituut voor zintuigfysiologie* in Soesterberg. Since 1983, Guido Smoorenburg was professor of experimental audiology (Dept Otorhinolaryngology, UMC Utrecht); from 1983 till 1995 as extraordinary professor, from 1995 as full professor.

His research approach was multidisciplinary and has involved linguists, physicists, physicians, biologists, and pharmacologists. He was especially interested in inner ear implants in patients with hearing disability, which contributed hugely to the first cochlear implantation in the Netherlands in 1985, in Utrecht. On the occasion of the retirement of Guido Smoorenburg a symposium is organised '*Moving forward in a snail shell*', 20 January 2006, see *agenda*.



January 19, Helmholtz Lecture

Robert Shannon (House Ear Institute, Los Angeles, USA)
 'Restoration of hearing by electric stimulation of the cochlea, brainstem, and midbrain'
 16:00-17:00, Van Unnik Building, Room 00.1, Heidelberglaan 2, Utrecht, contact, v.maassen@fss.uu.nl

January 20, Symposium 'Moving Forward in a Snail Shell'

On occasion of retirement of **Guido F. Smoorenburg**, Professor of Experimental Audiology.
 9:30-18:00, Gertrudiskapel, Conference Centre 'In de Driehoek', Willemsplantsoen 1c, Utrecht, and Academy Building, Domplein 29, Utrecht. Programme, <http://www.rudolfmagnus.nl>
 Registration required, contact, s.klis@kmb.azu.nl

January 26, Psychopharmacology Colloquium

Trynke de Jong (Psychopharmacology) 'Neurobiology of ejaculation, role of serotonin and oxytocin'
 12:00-13:00, Room N017, Went Building, Sorbonnelaan 16, Utrecht
 Contact, k.b.e.bocker@pharm.uu.nl

February 3- March 10, Course Grant Writing

Graduate School ONWA, Amsterdam and the Rudolf Magnus Graduate School are offering a grant writing course for PhD students in the third or fourth year of their research project.
 Information and registration, <http://www.rudolfmagnus.nl>

April 19-27, Course on Neuropsychopharmacology

The course on Neuropsychopharmacology is accredited by the Rudolf Magnus Graduate School of Neuroscience and will be awarded by 7 credits.
 Venue, partly in Amsterdam, Weesp, and Utrecht
 Programme, <http://www.rudolfmagnus.nl>
 Registration, Els Borghols, eam.borghols@vumc.nl

May 4-5, Meeting of the Association of European Psychiatrists - Neuroimaging Section

'Neuroimaging Change over Time in Psychiatry'
 Venue, Academy Building, Domplein 29, Utrecht
 Programme and registration, <http://www.rudolfmagnus.nl>

August 28-29, Rudolf Magnus-Helmholtz Summerschool

Mark your agenda for the joint Summerschool of the Rudolf Magnus and Helmholtz Graduate Schools.
 Venue, Conference Centre Ottone, Kromme Nieuwegracht 62, Utrecht. Programme to be announced, check our website for updates, <http://www.rudolfmagnus.nl>