

'Colour looks nicer than color'

With the help of national television, researchers at the Donders Institute and the Max Planck Institute for Psycholinguistics (MPI) in Nijmegen held a large national survey on synaesthesia and language skills. Tessa van Leeuwen was one of the initiators of this 'Groot Nationaal Onderzoek'. She is now analysing the results.

Four out of every hundred people have synaesthesia, which means that for them, sensory input can evoke unusual sensory responses. For example, a person may smell words, see sounds, or associate letters with colours.

Tessa van Leeuwen was a biology student in Utrecht when she accidently discovered that she was a synaesthete. Not that she wasn't aware of the colours she perceived when naming the days of the week, or looking at letters, numbers and music notes - she had compared her personal colour scheme with her brother's many times. But that it had a name? And might be of scientific interest? This discovery was the trigger for her academic career... Van Leeuwen wrote her master's thesis on the subject and subsequently moved to Nijmegen to pursue it further

as a PhD student. The next stop was Frankfurt, were she carried out MEG studies on people with synaesthesia and schizophrenia. Finally she came back to the Donders Institute with a Veni grant in her backpack.

NATIONAL SURVEY

The Groot Nationaal Onderzoek (GNO) is a large-scale national survey conducted via an easy-to-use website (see www.gno.mpi.nl). It helps people find out how

well their senses work together, using a range of short, simple tests for investigating crosssensory associations in the general population. Subtests of the GNO are designed to help people discover if they have synaesthesia. A total of 15,000 people did one or more tests on the GNO website (30,000 completed tests). Tessa van Leeuwen - who set up the survey with Mark Dingemanse from MPI - estimates that about a thousand participants are synaesthetes in one or more ways (while this article was being written, the statistical analyses were still being carried out).

Synaesthesia is an interesting phenomenon for brain researchers

because the association between the senses provides information on the organisation of the brain and the way sensory information is processed. "One of the hypotheses is that synaesthesia is caused by aberrant connections or altered connectivity in the brains of synaesthetes – going

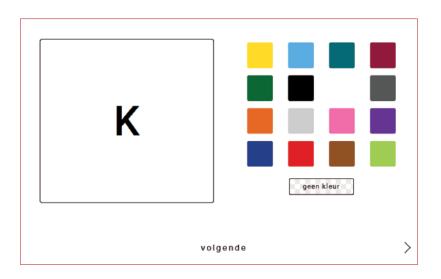
A POOL OF SYNAESTHESIA SUBJECTS

The participants in the large survey who prove to be real synaesthetes will receive a personal invitation to participate in future research. This large group of new people who are willing to engage in experiments is a treat for the synaesthesia research in Nijmegen as a whole. Take Tessa van Leeuwen's colleague Simon Fisher, Professor in Language and Genetics at the Max Planck Institute. For his study of the genetics of synaesthetes large cohorts are needed.

Mixing graphemes with colours is the most common form of synaesthesia while mirror-touch synaesthesia may be the rarest. In case you know someone who involuntarily feels a tap on their own shoulder when observing someone being tapped on theirs, please refer them to Van Leeuwen!

GRAPHEME-COULOUR

The most common form of synaesthesia is letter/number-colour association. It's not only the synaesthetes who completed the tests that provided valuable information. The controls revealed that there are several common trends in colour-letter combinations. Letters that are used more often tend to be associated more with vibrant and primary colours. A is red to most non-synaesthete people, while X – not such a common letter – is perceived as grey. Colour-number trends are less evident in the control group, while synaesthetes generally perceive one and zero as black and white.





back to early childhood. Speaking for myself, I only see music notes in colour that I learned to read very early on,"

Like most synaesthetes, Van Leeuwen doesn't consider her affliction to be problematic. On the contrary – it is actually quite pleasant and it helps her remember ("I choose my PIN codes in cheerful colour combinations") and check for spelling errors. For example, "Colour looks nicer to me than color."

This may be different for people who are extremely sensitive to sensory input, for example those who suffer from an autism spectrum disorder. "In autism it is not only social skills and information processing that are altered; these patients are quite often hypersensitive to sensory input. Hyposensitivity is also common. Altered sensory processing is so common that it was added to

the diagnostic criteria for autism in the new edition of DSM, the handbook for psychiatric diagnosis."

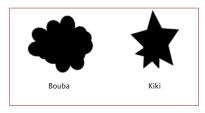
Given these observations, perhaps it comes as no surprise that synaesthesia is much more

common in those with autism than in the general population. Twenty percent perceive that their senses are mixed up. "In the years ahead I will study this special link. One of the hypotheses about autism is that altered connections in the brain arise because of hypersensitivity of the primary sensory cortices. Hyperexcitability of the visual cortex has also been found in synaesthetes. So there is a shared explanation. I want to explore that further, and I will start EEG experiments with young children in the near future. It may be that the sensory cortices of potential synaesthetes are already altered before synaesthesia has emerged. I'm also curious to test whether people with dyslexia experience less synaesthesia, since MPI and Donders colleagues have recently shown that people with dyslexia have a weaker form-meaning association."

Iris Roggema

KIKI-BOUBA TEST

Sound-form associations were tested with the kika-bouba test. The subject hears a sound and is asked to choose a matching picture – either a round or a sharp form. Speech sounds such as /g/ or /i/ tend to be linked to sharp forms, while /m/ and /o/ are connected to rounder forms. The hypothesis is that we perceive sound as sharp or round based on what we do with our mouth and tongue when pronouncing them.



JAPANESE IDEOPHONES

The GNO website was designed not only to diagnose synaesthesia in a playful way; it also tests the hypothesis that synaesthetes may be better at cross-sensory associations in general, also those related to language. Some languages use so-called ideophones: sound-meaning associations. For example, would "bukubuku" mean chubby or lean? What did you think?

All participants who completed the Japanese ideophone test (read a word and choose from two possible meanings) scored far above chance level (~74%), but synaesthetes were even better. Without any prior knowledge of Japanese they matched the words with the correct meaning in 77 percent of the cases.

FUNDING & SUPPORT

The GNO was funded by Dutch Science
Foundation NWO, with financial
support from the Max Planck Institute
for Psycholinguistics and the Donders
Institute at Radboud University. Media
partners include NTR, the Radboud science
communication department and the popular
science journal Quest. Tessa van Leeuwen
and Mark Dingemanse (MPI) set up the GNO.

'Cognition is woven into every step we take'

An uneven sidewalk, a slippery street or a staircase that's steeper than expected: the world is full of hidden dangers that could lead to a fall. For people who are challenged when walking – think of the elderly or people recovering from stroke – these hazards are accidents just waiting to happen. Movement scientist Dr Vivian Weerdesteyn is interested in the cognitive aspects of staying upright – and falling down.

She is trained as a physiotherapist and a movement scientist and her fall prevention programme is highly successful. Scientifically, Vivian Weerdesteyn focuses on the more fundamental aspects of falling. "Something that still fascinates me is that the cortex was long seen as unimportant in walking and mobility," she says. 'People used to say "What does the cortex have to do with it?". Whereas I would rather say: "The cortex has everything to do with it." Cognition is woven into every step we take. Every second, you are taking your surroundings into consideration and, in addition to specific knowledge about your own body, for example previous injuries, you also need knowledge about the context of each situation. There is a degree of redundancy in the sensory information coming from our eyes, ears, and muscles, requiring an appropriate reaction. Cognition allows us to convert that excess information into a smart, useful action."

Fall-related incidents can lead to broken bones, hospitalization or longer-term admission to a care facility. There are plenty of statistics to support this claim: in the Netherlands alone, there are over one million fall-related incidents each year in people over 65. But, in addition to societal and financial aspects, falls can have a major personal or emotional effect. Anyone who has once fallen down the stairs will recognize that. Falling is an alienating sensation, partly because of the loss of control, and it can lead to lasting fear. Its effects can linger in your arms and legs, but above all in your head, making you less confident as you move through life.

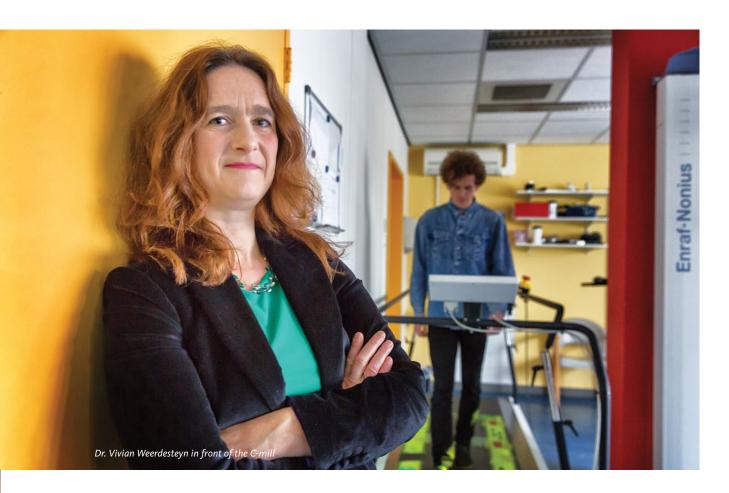
FROM HIGH-LEVEL JUDOKA TO HIGH-IMPACT SCIENTIST

Vivian Weerdesteyn realized early in her career that mobility plays a major part in an enjoyable life. "When I was younger, I practiced judo at a high level, in national competitions. I became fascinated by the art of falling through engaging in that sport. And, during my training as a physiotherapist, I investigated the value of judo in the rehabilitation of children with cerebral palsy." She continued studying to become a movement scientist and started working at the rehabilitation department of the Radboudumc. "During my PhD, I developed the fall prevention plan 'Vallen Verleden Tijd' (Falls become a thing of the past)". Right now, more than 2,000 physiotherapists throughout the Netherlands have been trained to implement that plan. What's more, it's still the only plan in its kind that is recognized as 'proven to be effective' by the Centre for

REALISTIC TRAINING SITUATIONS

To translate this research to daily practice, Vivian Weerdesteyn and her colleagues investigate and train people with gait and balance problems in situations that are as life-like as possible. They use a balance platform as a fall simulator and train people's walking skills on a special treadmill called the C-mill, which challenges users with unexpected objects that need to be either stepped on or avoided. "We train the gait adaptability of our patients by introducing distractions, interaction with the environment or natural tasks such as looking around while walking." These clues are unexpectedly projected on the treadmill with light and always appear in different locations, just like in real life.





Healthy Living, the Dutch centre for health promotion and prevention, which is part of the National Institute for Public Health and the Environment (RIVM). It also played a major role in applying for the Veni grant which I received in 2010."

Currently, Vivian Weerdesteyn is an associate professor at the rehabilitation department at Radboudumc and a junior Principal Investigator in the Neurorehabilitation research group at the Donders Institute. In her research, she aims to unravel the mechanisms underlying balance and gait problems caused by neurological disease. From investigating the interaction between perception, cognition and motor control to the details of neuroplasticity and novel treatment options: her group does it all.

"Wow, why haven't I been doing these exercises for the past three years?" Vivian Weerdesteyn remembers one of the enthusiastic reactions from a patient after training on the C-mill [see box *Realistic training situations*] for the first time. "It's a typical example of how much our patients appreciate the life-like situations that the C-mill presents them with. It's more fun, but also much more effective to train in this way, compared to the isolated, repetitive and often boring exercises used in physiotherapy."

COMPENSATION VERSUS REPAIR

"What I ultimately want to discover is where precisely the cortex's control originates and what the options are for controlling movement from a lower level. For instance, we do research involving patients with a rare and very specific lesion in their spinal cord; a degraded connection between the motor cortex and the motor neurons that control the leg muscles. Because of that, direct muscle control from the cortex is no longer possible, and yet they can still walk. Alright, it's maybe not the most elegant kind of movement, but it's functional. I want to find out which compensation mechanisms take place in cases like this. And how that works on a neuronal level."

"Of course, repair is also a very interesting mechanism, but we know from experience that it's very limited and only happens within a specific timeframe. Some scientists are looking for a specific recipe for this, which they see as the Holy Grail. But I think it's much more interesting to focus on the working mechanisms of compensation, which are clearly much more flexible."

This requires a shift from a traditional to a more practical approach. Movement scientists should not only investigate movement in isolation, but rather develop an abstraction of reality by investigating movement in reallife situations. "Just like we do using our C-mill."

"This is a dynamic research field. We're still trying to find out about all the different repair mechanisms available and technology is moving ahead fast; we can now use neuroimaging and implantable stimulators in movement research. And I'm calling for a shift to a more practical, real life-like approach." She smiles: "We have a lot to do."

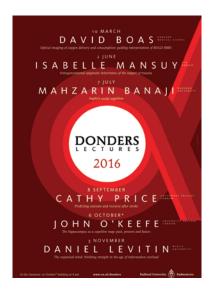
Iris Kruijen

Epigenetic inheritance of the impact of trauma

One of the big treats of next year's Donders Lecture programme is the planned visit of Isabelle Mansuy to Nijmegen on June 2 2016. This professor in neuro-epigenetics at the Zürich Brain Research Institute and the renowned ETHZ will give a lecture on the question how experiences in the lives of the parents are passed on to their children. Neuro-epigenetics is a rapidly expanding field, which provide an explanation of how early-life experiences, such as traumatic events as well as learning and memory, affect the expression of the genetic code.

"We find that the effects of experiences in the cellular memory are long lasting. Early-life experiences can have an important influence on the expression of subclinical psychiatric disorders in the genome," Hans van Bokhoven explains. Van Bokhoven is Professor in Molecular Neurogenetics at the Donders Institute and Radboudumc.

He explains that Isabelle Mansuy takes epigenetics one step further: to the next generation. "The big question is, of course, how epigenetic changes pass on to the germline," he says. "Her research suggests relevant molecular mechanisms that could explain the transgenerational effects." She recently demonstrated that early stress in mice causes depression and impulsivity, while impairing social skills and cognitive functions. Interestingly she has found that these behavioural symptoms are transmitted across several generations. Her work shows that epigenetic mechanisms involving DNA methylation and microRNAs are associated with the inheritance of



The Donders Lectures take place on the University campus at the Linnaeus Building, Heyendaalseweg 137, Nijmegen and they start at 4.00 p.m. More about the 2016 series at www.ru.nl/donders

David Boas will speak in March, Mahzarin Banaji in July, Cathy Price in September, John O'Keefe in October and Daniel Levitin in November. behavioural characteristics. Her work is highly multidisciplinary, combining genetically and environmentally modified animal models, epigenetic methods as well as molecular, behavioural, electrophysiological, proteomic and imaging techniques.

"I know Isabelle Mansuy from conference lectures. She is a fascinating speaker - she combines excellent research with an eloquent speaking style. Her research addresses some of the burning issues in neuroscience and her results are published in top journals such as Science, Nature and Cell. That reflects her ambition," Van Bokhoven says. Isabelle Mansuy's research has several important links to research lines within the Donders Institute, including his own research on disrupted epigenetic pathways in neurodevelopmental disorders. "It would be great to work on a project together."

Iris Roggema

PHD DEFENCES

- 2 September 2015. Nonnekes, J., Balance and gait in neurodegenerative disease: what startle tells us about motor control (Donders Series 188)
- 4 September 2015. Stapel, J., Action prediction and the development thereof (Donders Series 189)
- 18 September 2015. Vogel, S., The runner-up: on the role of the mineralocorticoid receptor in human cognition (Donders Series 186)
- 21 September 2015. Clemens, I., Multisensory integration in orientation and self-motion perception (Donder Series 187) 5 October 2015. Atucha Treviño, E., Emotional Modulation of Memory: Mechanisms underlying strength and accuracy of memory (Donders Series)
- 28 October 2015. **Grauwe de, S.**, The Processing of Derivations in Native and Non-Native Speakers of Dutch (Donders Series 190)
- 17 November 2015. Janssen, C., Nourishing the brain from cradle to grave: The role of nutrients in neural development and neurodegeneration (Donders Series 198)
- 23 November 2015. Richards, J., Plasticity genes, the social environment, and their interplay in adolescents with and without ADHD from behaviour to brain (Donders Series 197) 26 November 2015. Bosch, P., Needles on the Couch; acupuncture in the Treatment of Depression, Schizophrenia and Sleep Disorders (Donders Series 192)
- Schizophrenia and Sleep Disorders (Donders Series 192)

 1 December 2015. Van der Eijk, M., Patient-centred care in Parkinson's disease

 3 December 2015. Bakker, I., Magic moments: On the neural
- mechanisms of novel word consolidation and integration 8 December 2015. Rijken, N., Balance and gait in facioscapulohumeral muscular dystrophy. Relations with individual muscle involvement (Donders Series 194) 15 December 2015. Lozano Soldevilla, D., GABAergic modulations of gamma and alpha oscillations: consequensus for working memory performance (Donders Series 201)
- 22 December 2015. Blokland, Y., Moving towards awareness detection-from brain-computer interfacing to anaesthesia monitoring (Donders Series 200)

- 21 December 2015. Rhein von, D., Neural mechanisms of reward processing in attention deficit hyperactivity disorder (Donders Series 203)
- 8 January 2015. Bertjens, D., Doin' it right: Assessment and errorless learning of executive skills after brain injury (Donders Series 199)
- 13 January 2016. Jiang, H., Characterizing brain oscillations in cognition and disease (Donders Series 204)
- 14 January 2016. Francken, J., Viewing the world through language-tinted glasses. Elucidating the neural mechanisms of language-perception interactions (Donders Series 205)
- 22 January 2016. **Schlooz, W.**, Drawing out the visuomotor abilities of children with mild autism spectrum disorders (Donders Series nn)
- 3 February 2016. Marshall T., On the Control and Manipulation of Alpha and Gamma Oscillations in Visual Cortex 19 February 2016. Ly V., Affective biasing of instrumental behavior: how emotion shapes behavior (Donders Series)

Meanwhile at www.ru.nl/donders

Go to our website to check out the latest news and events.

ALZHEIMER DISPOSITION COMPROMISES THE BRAIN'S 'GPS' IN YOUNG ADULTS

An international research team led by Christian Doeller shows that a genetically increased risk for Alzheimer's disease affects a brain region known as the brain's GPS. (*Science*)

DIFFERENT MEMORY RESOLUTIONS MAP ONTO DIFFERENT BRAIN LOCATIONS

Neuroscientists from the Donders Institute have shown that memories of the same events co-exist at different resolutions in the brain. (*Nature Neuroscience*).

CLINICAL RESEARCH COLLABORATION WITH CHINA: SIZE MATTERS

Radboud UMC has initiated a clinical research collaboration with Jilin University, Changchun, China. The collaboration is expected to boost clinical research at both institutions.

BRAIN CONSOLIDATES MEMORY WITH THREE-STEP BRAINWAVE

A team of neuroscientists, among who Mathilde Bonnefond and Til Ole Bergmann from the Donders Institute, have shown how a three-step brain oscillation plays an important part in our memory consolidation. (*Nature Neuroscience*)

TESTOSTERONE SEEMS TO HELP PEOPLE WITH SOCIAL ANXIETY

Testosterone makes anxious people less likely to avoid the gaze of other people. This is one of the conclusions of a study by behavioural scientists at Donders. The study is the first to demonstrate that testosterone can help people with social anxiety. (*Psychoneuroendocrinology*)

HOMOLOGUE REGIONS FOR SPACE AND MEMORY IDENTIFIED ACROSS SPECIES

The 2014 Nobel prize in Medicine was awarded for the discovery of the brain's GPS in the rodent entorhinal cortex. This brain region supposedly creates a neural map of the world. For the first time, researchers of the Donders Institute were able to find evidence for this homoloque in humans. (*Translational Neuroscience*)

ICT FOR BRAIN, BODY & BEHAVIOUR

The Donders Institute is now part of ICT for Brain, Body & Behaviour (i3B), a European network of ICT companies and knowledge institutes in the field of brain, cognition, physiology and behaviour. The i3B mission

is to connect science and business, innovate through joint R&D projects, accelerate business of innovative ICT solutions for Brain, Body and Behaviour and train and foster career opportunities within the network.

PRIZES AND AWARDS

- Researchers of the Max Planck Institute for Psycholinguistics have won the Ig Nobel prize for showing that the expression 'Huh?' may, in fact, be universal. Ig Nobel prizes are awarded for studies that are first make you laugh and then make you think.
- Donders scientists succeeded in scoring four VENI grants from NWO to fund their research. These grants will advance our understandings of topics as diverse as long term effects of neglect (Piray Atsak), treatment of antisociality (Inti Brazil), post-traumatic stress disorder (Marloes Henckens), and the interplay between action and perception (Fleur Zeldenrust).
- NWO grant for Janneke Jehee by NWO. She will
 use the additional funding to study neural decisions
 under uncertainty.
- Barbara Franke, professor of Molecular Psychiatry, is elected as member of the Academia Europeae. This academy is a European, non-governmental association whose members are scientists and scholars who collectively aim to promote learning, education and research.
- Marijn Kroes has obtained a highly prestigious Society in Science - The Branco Weiss Fellowship, which will grant him up to five years of complete academic freedom.
- Peter Kok has won a **Rubicon grant**. He will use the funding to reveal how prior knowledge of past events biases our perception of current events.
- Naomi de Haas has obtained one of NWO's 'Research Talent' grant to fund a PhD project. She will use the funds to study spatial and episodic memory in humans.
- Murielle Ferraye has obtained a Fellowship grant from the Netherlands Brain Foundation to study freezing gait in Parkinson's disease.
- Karin Roelofs is selected as new member of The Young Academy of Europe (YAE). Professor Karin Roelofs leads the Experimental Psychopathology and Affective Neuroscience research lab. She has also won a Radboud Science Award.
- The International Foundation for Alzheimer Research has given 200.000 euro to Jurgen Claassen and his group for research on the relation between sleep and Alzheimer's disease.

DIARY

17 December 2015. Donders Poster sessions, 10:00, Radboudumc, Tuinzaal.

21 January 2016. Donders sessions, 'Prediction and predictive coding' (Floris de Lange) at 10:30, and 'What drives social behaviour' (Harold Bekkering) at 13:00.
20-22 January 2016. Nijmegen Lecture by David Poeppel, New York University, about '(Un)conventional wisdom: three neurobiological provocations about brain and language'. Information: www.mpi.nl/events/nijmegen-lectures-2016
22 January 2016. Inaugural lecture Richard van Wezel, professor in Visual Neuroscience at the Science Faculty. 'Over zien, over denken'. Academiezaal Aula, 15:45.
18 February 2016. Donders sessions 'Sensation and action' (Pieter Medendorp) at 10:30, and 'Virtual reality in cognitive neuroscience' (Christian Döller) at 13:00.

10 March 2016. Donders Lecture by David Boas, Harvard Medical School, about 'Optical imaging of oxygen delivery and consumption: guiding interpretation of BOLD fMR!'. Linnaeus Building, 16:00-17:15.
17 March 2016. Donders sessions, 10:30. Special session: 'computational modeling'.
18-21 April 2016. 4-day toolkit course 'Advanced analysis

and source modeling of EEG and MEG data'. Information: www.ru.nl/donders or tildie.stijns@donders.ru.nl 21 April 2016. Donders sessions, 'Language and memory' (Kristin Lemhoefer & Guillen Fernandez) at 10.30, and 'Neuronal oscillations: causal determinants or epiphenomenon?' (Ole Jensen) at 13:00.

9-11 May 2016. 3-day toolkit course 'Computational approaches to neuroimaging'. Information: www.ru.nl/donders or tildie.stijns@donders.ru.nl.

19 May 2016. Donders sessions, 10:30: 'Neural development' (Judith Homberg), second lecture at 13:00: Mechanisms of Interpersonal Communication (Ivan Toni)

2 June 2016. Donders Lecture by Isabelle Mansuy, ETH Zurich about 'Transgenerational Epigenetic Inheritance of the Impact of Trauma'. Linnaeus Building, 16:00-17:15. 16 June 2016. Donders sessions, 10:30. Special session on: 'societal impact'.

7 July 2016. Donders Lecture by Mahzarin Banaji, Harvard University, about 'Implicit Social Cognition'. Linnaeus Building, 16:00-17:15.

22-26 August 2016. 5-day toolkit course 'Essentials of major neuroimaging techniques (EEG, MEG, fMRI, PET, TMS)'. Information: www.ru.nl/donders or tildie.stijns@donders.ru.nl.

New not-so-merry-go-round for science

The new vestibular chair of the biophysics group at Donders Institute is a tailor-made instrument. It can tilt, turn and spin a person in every direction in space. Meanwhile it measures eye movements that reveal the subject's reaction to these complex rotations. It's not a theme park attraction, but serious science: a way to find out how we deal with moving around in a moving world. It fools the equilibrium system controlled by the vestibular organ that is close to our ears. This organ consists of six vulnerable fluid-filled loops – three on each side – that can measure rotations of the head.

Apart from scientific research, the vestibular chair will also be used on patients by ENT and neurology physicians. It will help to detect disturbances in the vestibular system in other dimensions than just the horizontal one. In current clinical set-ups 70% of vestibular damage cannot be monitored. What's more, the device will become available for third-party research (think virtual reality builders and aircraft industry) via the Radboud Research Facilities. The vestibular chair was designed and built by Radboud University's techno centre.

Iris Roggema

Besides the vestibular system, the new chair can fool all the other variables that come into play: the visual, auditory and tactile senses and our motor system. Together, these systems provide the physical information we use to stand and move in the world.

What's new is that this chair has two motors – for even more degrees of freedom of movement; tests with free head movement are also possible; auditory stimuli are available (with 24 speakers); the subject has clear views on a movie screen for more realistic visual input. According to Prof. John van Opstal, this combination of features is unique in the world.

In addition, a combined NIRS-EEG neuro-imaging device will soon be available, enabling researchers to measure the brain activity of the spinning test subject in real time.

DONDERS INSTITUTE Newsletter

The Donders Newsletter is published twice a year by the Donders Institute for Brain,
Cognition and Behaviour, which brings together research groups at Radboud University and the Radboudumc as well as the Max Planck Institute for Psycholinguistics. Its purpose is to keep you informed of developments within the Donders Institute and the field of neuroscience.

Editors: Iris Roggema, Nathalie Bovy-van der Lugt, and Mike Gould Associates
Editorial Board: Nathalie Bovy-van der Lugt,
Marcel van Gerven, Iris Kruijen, Robert Oostenveld,
Iris Roggema, Indira Tendolkar
Text: Iris Kruijen, Iris Roggema
Photography: Dick van Aalst
Graphic design: Hartebeest

Do you want a subscription to the Donders Newsletter or send us a change of address? Please send an e-mail to Marie-Louise Beenen: ml.beenen@donders.ru.nl

Printing: Drukkerij Efficiënt

