Eyes on the move: causes and consequences of nystagmus

Chair: Prof. dr. J. (Hans) van der Steen
Co-Chair: Chris Harris

Prof. Hans van der Steen is Full Professor at the department of Neuroscience, Erasmus MC Rotterdam, The Netherlands. He holds the chair on visual information processing endowed by Royal Dutch Visio at Erasmus University. Over the years he has acquired extensive research experience on oculomotor physiology. He started his PhD training in Rotterdam under the supervision of Prof Han Collewijn and had further international training at prestigious institutions such as University College, London (Royal Society Fellowship) and the National Eye Institute, (NIH) in Bethesda, USA. He currently supervises a team of 12 researchers, PhD students and Research Master students. He has published in total 100 research papers and book chapters.
As eye movements are the motor system that sees the world, the precise monitoring of eye movements play an increasingly important role in the diagnosis and monitoring of visual sensory loss by neurological damage or disease. In close collaboration with clinical departments and national visual rehabilitation centers, his team currently focusses both on visual development of young and premature born children using eye tracking technology as well as on the changes that occur in oculomotor control elderly as a result from neurodegenerative diseases. This work has led to several innovative technologies to detect cerebral visual pathologies at an early stage of the disease. In this endeavor his team works together with (inter-) national teams at Royal Dutch Visio, Neonatology, Neurology, ENT, Ophthalmology and Geriatrics at Erasmus MC, with TU Delft, Sankara Nethralaya, Chennai, India, Belgium, Sweden and Norway.

Symposium abstract

Nystagmus is a condition of involuntary eye movement, acquired in infancy or later in life, that may result in reduced or limited vision. There is a broad variety in causes and presentations of nystagmus. It affects people in many ways in their visual performance and the effects vary from person to person.
In this symposium, we will give a short overview of the different causes and forms of nystagmus. Next the effects of nystagmus on visual acuity will be discussed, followed by a

presentation of the personal experiences of how nystagmus affects their daily life and how they have organized themselves to create awareness.
As an example of how nystagmus manifests itself from in early childhood, clinical presentations of nystagmus with a genetic cause will be presented, followed by a presentation on the latest fundamental research findings to find the underlying mechanisms.

Presenters and working titles:

1- **A brief introduction to nystagmus**
Prof. dr J van der Steen, Dept. Neuroscience, Erasmus MC

2- **Do Nystagmus Eye Movements have an Impact on Visual Acuity?**
Prof J T. Erichsen, School of Optometry and Vision Sciences, Cardiff University

3- **Nystagmus and the power of communication**
R. van der Marel, Nystagmus in beweging

4- **Living with Nystagmus: Support in the Internet Age**
J. Ambrico, American Nystagmus Network

5- **Sequence of development of tonic downgaze, high-frequency horizontal nystagmus and low-frequency, upgaze-evoked nystagmus in Nightblindness-Associated Transient Tonic Downgaze (NATTD).**
Prof.dr. H.J. Simonsz, Department of Ophthalmology, Erasmus MC

6- **A retinal origin of congenital nystagmus.**
Prof.dr. M . Kamermans, Netherlands Institute for Neuroscience

1- A brief introduction to nystagmus

Hans van der Steen,
Dept. Neuroscience, Erasmus MC, www.neuro.nl

The theme of this nystagmus symposium is introduced by discussing the different forms of nystagmus as well as underlying facts and theories on different causes of nystagmus.

2- Do Nystagmus Eye Movements have an Impact on Visual Acuity?

Jonathan T. Erichsen
School of Optometry and Vision Sciences
Cardiff University, http://www.cardiff.ac.uk/optometry-vision

Recent studies have challenged a long-standing assumption that it is the oscillations of the eyes that underlie the reduced visual acuity found in those with INS. This presentation will consider the latest findings about the impact of stress, visual demand and gaze angle on nystagmus intensity and the impact of changes in eye movements on visual acuity. The implications for therapeutic interventions will be discussed.

3- Nystagmus and the power of communication

Roelie van der Marel
Nystagmus in beweging, www.nystagmusinbeweging.nl

In her presentation Roelie van de Marel will give a short overview of her background, the family she came from and where she grew up. This in the perspective of having nystagmus, with insufficient attention and communication from parents and teachers. This had consequences for her career opportunities and her self-image. When she lost her job as a secretary, she started with the webpage and Facebook page nystagmusinbeweging.nl. She learnt that communication plays an important role among people with nystagmus and towards others. The main message is that communication is the key to create awareness and helps people with nystagmus getting the best possible chances and opportunities

4- Living with Nystagmus: Support in the Internet Age

Joe Ambrico
American Nystagmus Network, www.nystagmus.org

Nystagmus affects people to varying degrees. For some, the affect on vision is profound, for others it is quite minor. But a common trend has been a sense of isolation and confusion

about the condition. People have often been told by doctors only that they won't see well, glasses won't help, and are given few if any options for treatments. The American Nystagmus Network and Nystagmus grew out of an online community that was searching for better information and shared experiences. It seeks to improve the quality of life for all persons and families affected by nystagmus, through organized community support, education, and public awareness.

5- Sequence of development of tonic downgaze, high-frequency horizontal nystagmus and low-frequency, upgaze-evoked nystagmus in Nightblindness-Associated Transient Tonic Downgaze (NATTD)

Huib Simonsz

Department of Ophthalmology, Erasmus MC, http://www.erasmusmc.nl/oogheelkunde/

In 1994 we described an X-linked disorder in male infants who presented at age 2-4 months with tonic downgaze, chin-up head posture and low-frequency, upgaze-evoked nystagmus that disappeared at age two, accompanied by high-frequency, horizontal nystagmus that persisted after age two. In 1998 we reported abnormal ERGs and CACNA1F, NYX or GPR179 mutations confirming CSNB in most of these children. In 2009 we surmised that this specific combination of horizontal and vertical nystagmus had a retinal cause, as the proteins affected by these mutations reside on either side of the rod-ON-bipolar synapse and this pathway carries a motion signal. In this presentation, the sequence of development of the tonic downgaze, the rapid horizontal and the low-frequency upgaze-evoked nystagmus measured with a Tobii eye tracker in a male infant with a hemizygous CACNA1F mutation will be described. In NATTD, the downgaze with chin-up head posture occurred as the primary event at 2-3 months. The horizontal nystagmus started with a minimal, hardly noticeable, pendular eye movement. Upgaze-evoked nystagmus starts when the infant tries to look ahead 1-2 months thereafter. In all previously observed, approximately 20, cases with NATTD the upgaze-evoked nystagmus disappeared at around 2 years, in one case before 8 months, however. Amazingly, two of our cases were operated at age 10 for chin-down head posture, with the null zone of the rapid horizontal nystagmus being in upgaze. A normal ERG has been found by us previously in a minority of our cases with NATTD, either without any of the known CSNB mutations or, in a girl, with a heterozygote GPR179 mutation. All of these patients had structural eye anomalies, however. Interestingly the opposite, an abnormal ERG in female carriers of CACNA1F, was explained recently by mosaicism (Michalakis, 2014).

6- A retinal origin of congenital nystagmus.

Maarten Kamermans

Netherlands Institute for Neuroscience

http://herseninstituut.nl/onderzoek/onderzoeksgroepen/kamermans-groep/

Retinal motion detection is elemental to image stabilizing eye movement reflexes. In nob mice a mutation in the X-chromosomal gene encoding for nyctalopin causes defective synaptic input of retinal ON-bipolar cells, leading to congenital stationary night blindness (CSNB) and malfunction of the ON-pathway. Loss of ON-bipolar cell function affects ON-direction selective ganglion cells (ON-dsGCs) that underlie the optokinetic reflex. Analysis of the eye movement response to optokinetic stimulation using sine gratings showed substantial impairment of the optokinetic reflex and defective gaze holding. Furthermore, eye movements of nob mice exhibited a prominent horizontal oscillation with an average frequency of 5 Hz. To check whether this pathological eye movement behavior could have an anatomical origin, we crossed nob mice with SPIG1-GFP knock-in mice that show GFP-labeling in a subtype of ON-dsGCs sensitive to downward movement. Analysis of SPIG1-GFP expression combined with anterograde labelling of ganglion cells with CTB-Alexa 555 showed no apparent miswiring of the central projections of ON-dsGCs to the MTN of the accessory optic system.

Electrophysiological recordings in the retina confirmed that ON-dsGCs of nob mice are unresponsive to light stimulation. Moreover, robust sub-threshold oscillations of on average 5 Hz were observed in all ganglion cells. These oscillations could be eliminated or significantly reduced by simultaneously blocking both AMPA and NMDA, using application of DNQX and D-AP5. Intravitreal injection of this cocktail in both eyes of nob mice also abolished the 5 Hz oscillation in spontaneous eye movements, when the animal was awake, which strongly suggests that synchronous oscillation of ON-dsGCs in the retina is the direct cause of the horizontal eye movement oscillation. This mechanism might also explain the small amplitude horizontal nystagmus observed in CSNB patients (Simonsz et al., 2007).