VESTIBULAR-EYE MOVEMENT RESEARCH
AT JOHNS HOPKINS – 2007

This newsletter is the 2007 update on the Eye Movement/Vestibular Research Program at Johns Hopkins. We summarize our research goals, major accomplishments and discoveries, new research directions and educational activities. We thank our donors to our research program whose continued support allows us to pursue new ideas, make important discoveries and train new physician-scientists.

THE GOALS OF OUR RESEARCH

The focus of our research continues to be on disorders that affect balance, vision and eye movements. We continue to emphasize two major health problems but with several exciting new directions to our research:

1) **How does the brain coordinate the movements of the two eyes?** If the eyes don’t work together, we see double. If they are not held still, producing nystagmus or jumping of the eyes, vision is blurred. These are common problems among children (called strabismus) and adults who have diseases that also affect balance.

2) **How can we better diagnose and treat patients with symptoms of dizziness, vertigo, ataxia and loss of balance?** Disease of the balance apparatus occurs with both inner ear (vestibular) problems, and many diseases of the brain including stroke, trauma, cerebellar degeneration, Arnold-Chiari malformation, Parkinson’s disease and related conditions, such as progressive supranuclear palsy (PSP). These disorders can be extremely disabling, physically and psychologically, leading to marked alterations in the quality of life, and sometimes to serious injury from falls. In order to understand how these symptoms can be treated, we are investigating the vestibular reflexes associated with the types of movement of the head that occur with walking and running. Therapeutically, we are developing ways to speed recovery of balance, and so prevent falls, and relief from dizziness and vertigo. Accordingly, a major research emphasis is on how the brain learns to compensate for disease and trauma, and how we can promote this compensation though drug treatment and better programs of physical therapy.

OUR RESEARCH PROGRESS AND LATEST DISCOVERIES

THE RESEARCH TEAM (Dale Roberts (MS, computer scientist) Corena Bridges (chief lab technician), Mark Walker (MD, engineer, neurologist), Xiaoyan Shan, (MD, ophthalmologist), Dave Zee, (MD, neurologist), Adrian Lasker (MS, research engineer), Howard Ying, (MD, PhD, ophthalmologist).

2006 has been extraordinarily productive for us. More than 30 academic papers have been published from our laboratory this year and a fourth edition of our eye movement textbook appeared this spring. We especially thank
the patients and friends who made generous contributions supporting our research. In a climate of drastically reduced government support for medical research this private funding has been critical to our overall success and the recent expansion of our efforts. Some highlights and future directions include:

Diagnosing and Treating Balance Disorders

Our work on the eye movement responses to motion of the head when we walk and turn has been published in several important papers this year. We have especially concentrated on understanding how the brain distinguishes between rotation (spinning around) and translation (side-to-side or front-to-back motion, like as when walking or running) motion. If the brain becomes confused when trying to decipher how the head and body are moving, patients become extremely ‘dizzy’, imbalanced, and often frightened and panicky. This past year we discovered that visual information about objects that are moving in front of us is processed in the same way that the brain processes labyrinthine information about head and body motion coming from our inner ear (vestibular) apparatus when we are actually moving. This result gives us a new way to design new types of visual rehabilitation techniques for dizzy patients. In another but related type of study we have developed a novel learning paradigm to study adaptation of the rapid eye movements we use to scan the visual scene. Our research has suggested important new learning rules for how to increase the rate of learning and decrease the rate of forgetting, related to rehabilitation of eye movement and balance reflexes.

Cerebellar Ataxia, Arnold-Chiari malformation and PSP

We completed our first studies of cerebellar ataxia using a variety of new MRI techniques including diffusion tensor imaging (largely developed here at Hopkins), high resolution MRI, and functional MRI. We have discovered in which parts of the cerebellum are important for adaptation to strabismus (and double vision), and are now finding out how the brains of patients with cerebellar disease cope with disabling double vision.

Patients with a variety of brain disease often have disabling nystagmus (jumping of the eyes) and visual blurring. We have developed a mathematical model to study the effects of drugs on various types of abnormal eye movements including nystagmus that interfere with vision. Specifically, we have proposed a theoretical basis to investigate how the membranes (outer walls) of brain cells can become too excitable, leading to excessive discharge of the cells so they cause the eyes to oscillate (uncontrollably jump around). By investigating how the excitability of brain cell membranes can be controlled (which we are doing in a computer simulation), we can make predictions about which drugs to use to relieve these visual disturbances. We are investigating a similar approach for tremor of the hands and body, which, of course, occurs in many neurological diseases.

Eliminating Double Vision – Keeping the Eyes Aligned

We continue to study the treatment of strabismus or ‘crossed eyes’, which produces double vision. By recording eye movements before and after eye muscle surgery, we are investigating how the brain keeps the images seen by both eyes together so objects do not appear double. We have discovered a possible mechanism that accounts for why patients with double vision due to a variety of causes may get worse over time and not respond well to prisms or surgery. Based on our recent experimental findings, we think that there may be a special brain mechanism that comes into play when only one eye is allowed to focus on what you want to look at (the other is patched). This mechanism is not able to work when both eyes are open but only when one is focusing well. Specifically we have discovered that by carefully controlling the pattern of which eye is viewing (though a specific eye patching protocol) we may be able to actually lessen the strabismus (and the diplopia) and improve the results with surgery or prism therapy. Our eventual goal is to perform a clinical trial of this new method.
Dizziness in the Emergency Room

Dr. David Newman-Toker in our group has performed a landmark study of patients who come to the Emergency Department because of dizziness. Using a legion of research associates (many Hopkins undergraduate students) they interviewed every patient who came to the Johns Hopkins and Bayview Hospital Emergency departments (whether or not they came to the emergency room for dizziness) 24 hours a day for three weeks. They developed a novel questionnaire, easily understood and manipulated by the patient on a touch screen laptop computer, which has shown how the diagnosis of dizziness (including potentially devastating strokes) can be improved and medical errors can be minimized. This was the first study of its kind and will be a model for many future studies of a variety of symptoms in patients who need emergency medical care.

EDUCATION AND TRAINING ACTIVITIES

In keeping with our mission to disseminate new ideas to the community at large, we continue to lecture at the local and national levels. A major focus is to train physicians and scientists in our areas of clinical practice and research so they can establish clinical and research programs throughout the United States, and the world. Thanks to the generosity of one of our patients, we have made a series of videotapes and now a DVD dealing with different conditions, which we are now giving gratis to our patients to take home after their clinic visit. These tapes explain the nature and treatment of a patient's particular condition and have been exceedingly well received, winning a National Health Information Award. Our overall goal is to develop new ways to bring the technology revolution to practical aspects of patient care and education.

OUR LABORATORY STAFF

THE CLINICAL TEAM: Dave Newman-Toker, MD, Dave Solomon, MD PhD, Vennie Matthews, senior office coordinator, Dave Zee, MD, Mark Walker, MD, Sarah Ying, MD

OUR BIOENGINEERING COLLEAGUES: Faisal Karmali (PhD graduate student), Mark Shelhamer, PhD, Wilssan Joiner (PhD graduate student)

David Zee, M.D., director of the vestibular-eye movement center, began his career at Johns Hopkins in 1965 as a medical student. He is a Professor of Neurology, with secondary appointments in the Departments of Otolaryngology, Ophthalmology, and Neuroscience. He devotes his efforts to clinical care, research, education, treatment and the well being of patients diagnosed with vertigo and balance disorders, double vision and nystagmus (jumping of the eyes).
Dr. Zee is a member of numerous organizations and has received recognition both nationally and internationally. He is a former member of the advisory council of the National Eye Institute of the National Institutes of Health. He is received the Ottorino Rossi prize (Pavia, Italy), the Hallpike-Nylén Medal of the Bárány Society (Uppsala, Sweden) for outstanding research. At Johns Hopkins he received the inaugural Frank Ford award and the Johns Hopkins Professor’s award for outstanding teaching of neurology and the clinical sciences. Dr. Zee was the first visiting professor for neurological education at the Mayo Clinic and he gave the inaugural Swwithin Meadows Lecture at the National Hospital, Queen Square, London. In 2003, he was given the inaugural Houston Merrit award for outstanding contributions to research in neurology by the American Academy of Neurology. In the summer of 2004, an international scientific meeting was held in his honor in Siena, Italy and was attended by 170 colleagues world wide. This year he has been invited to speak about both his research and his clinical approaches in Germany, England, Japan, and Switzerland, and was the annual “Visiting Brain Scholar” Enland during which he spent a week in London, teaching and lecturing in three well known neurological and eye hospitals. Since 1976, Dr. Zee has received an individual research grant continuously from the NIH, which included a special ten-year merit award. He has authored or coauthored more than 335 scientific papers. He is coauthor of The Neurology of Eye Movements, the authoritative textbook on eye movements, which appeared in its fourth edition this past spring.

OUR FACULTY

Dave Newman-Toker, MD, trained the University of Pennsylvania and at Harvard is a neuroophthalmologist and neurootologist, with a special interest in emergency room medicine and medical education.
Mark Shellhamer, PhD, MIT graduate is a bioengineer with a special interest in mathematical approaches to motor learning and prediction
Dave Solomon, MD, PhD, trained at Mt Sinai hospital in New York and the University of Pennsylvania is a vestibular neurologist with special expertise in gait and falls
Mark Walker, MD, is an electrical engineer and vestibular neurologist with special expertise in vertigo and ataxia.
Sarah Ying, MD, trained at Johns Hopkins and the University of Washington, St. Louis and UCLA is a vestibular neurologist with special expertise in ataxia and MRI brain imaging

We also have a number of research and clinical collaborations with colleagues in Ophthalmology, Otolaryngology, Radiology, Psychiatry and Physical Therapy, with all of us studying impaired vision, vertigo and imbalance and how to treat the disabling physical symptoms and mental anguish suffered by these patients.

ON THE WEB...You can learn more about our program at http://hopkinsneuro.org/vesitibular/

COME VISIT US... We invite you to visit our laboratories for more in depth information about our current research. Please call Dr. David Zee at 410-955-3319.