Navigated brain stimulation shows significant effect in stroke rehabilitation

"The technology is showing that we are actually able to modulate brain healing. This is the wave of the future." – Richard L. Harvey, M.D., Rehabilitation Institute of Chicago

The results of the Nexstim-sponsored CONTRASTIM stroke study presented at the American Heart Association (AHA) and the American Stroke Association’s (ASA) International Stroke Conference in San Diego, February 20, 2014, demonstrated that a combination of navigated repetitive transcranial stimulation (nrTMS) using the NBS System along with occupational therapy (OT) produced significantly greater gains in patient’s motor function than OT alone.

A team at the Rehabilitation Institute of Chicago (RIC) led by Dr. Richard L. Harvey studied 30 patients 3 – 9 months post-stroke with moderate to severe impairment of hand function based on the Upper Extremity Fugl Meyer score (UEFM). For the active NBS therapy group of 20 patients, treatment consisted of 15 minutes of nrTMS, followed by 60 minutes of upper limb task-oriented OT. Patients received treatment during 3 visits per week for 6 weeks, the standard of care in the USA. Patients then returned for follow-up at 1 week, 1 month, and 6 months. Ten of the 30 patients were randomly assigned to a control group – receiving sham stimulation and the same OT as the active group.

The CONTRASTIM study found that adjunct nrTMS using the NBS System promoted lasting improvements in motor function. Patients in the active NBS group improved function by 13+ points on the UEFM score. The study also showed that more than 80% of the patients in the active NBS group gained a clinically meaningful response, compared to 50% of the patients in the control arm. The protocol used by Dr. Harvey’s team used low frequency, 1 Hz nrTMS to downregulate the activity of the unaffected healthy hemisphere of the stroke patient’s brain. Dr. Harvey believes that the effect of the low frequency stimulation is to upregulate the excitability of the injured side of the brain and prime the lesioned motor area to better benefit from the subsequent task-specific intensive training.

The researchers concluded that since notable improvements from the stimulation therapy can still be seen six months after the therapy, nrTMS could offer stroke patients long-lasting functional benefit when added to standard occupational therapy. They added that they are now proceeding to a multi-center clinical trial.

The award for best poster went to Theresa Hauck and a joint team from the Technical University Munich and the University of Oxford for “Task type and frequency determine the distribution of language positive cortical regions during rTMS.” The poster compared the effectiveness of different language tasks in revealing language sub-function and examine the impact of various rTMS frequencies on error rate and location. The poster’s general conclusion was that the object-naming task is the most discriminative test for the detection of language-positive regions. Congratulations!

5th NBS Symposium celebrates two large studies proving NBS mapping improves outcomes

Marking the tenth year since the introduction of the first generation of NBS, the 5th International Symposium on Navigated Brain Stimulation in Neurosurgery heard that two large-scale studies showing the outcome benefits of NBS mapping are soon to be published.

Dr. Sandro Krieg and Prof. Meyer’s team at Munich had their study published in the prestigious Oxford Journals’ Neuro-Oncology (see Clinical Spotlight). The study showed that NBS led to a significantly higher rate of gross total resection, significantly fewer patients experiencing deterioration in postoperative motor function, and smaller craniotomies.

It is expected that the other large study by Prof. Vajkoczy’s team at Berlin will be published soon. Neurosurgeons at Munich and Berlin now strongly advocate the use of NBS. Hundreds of patients with brain disease have now benefitted from NBS mapping for accurate presurgical localization of eloquent cortices and the Symposium heard of the increasing use of NBS in pediatrics, both prior to tumor surgery as well as in diagnostic work-up of epilepsy surgery.

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NBS played leading role at the 2014 DGNC Neurophysiology Section meeting

This was the first time an entire session of the bi-annual meeting of the Neurophysiology Section of the German Society for Neurosurgery (Sektionstagung Neurophysiologie der DGNC) was reserved for discussing recent advances in NBS mapping. The meeting was hosted by the University of Würzburg, Germany in January and featured a total of 8 presentations on NBS. NBS is significantly adding to the understanding of functional localization and networks in the human brain. A presentation by a joint team from the Universities of Munich, Germany and Oxford, England showed the potential feasibility of NBS to locate distinctive neuropsychological functions such as face recognition, categorization and calculation in the cortex. The next step is evaluating the clinical usefulness of these findings for preoperative mapping by NBS in brain tumor patients.

A presentation from a team at Munich University showed that NBS is able to cause language and understanding impairment even in the non-dominant hemisphere. These findings suggest that the right side of the brain is perhaps more strongly involved in sensory language function than previously understood.


New reimbursement code for language mapping by nTMS in Germany

In Germany, a new, separate reimbursement code, OPS code 1-20c.0, for language mapping is now available for use from January 1, 2014. An OPS code is important because it allows tracking of the use and costs associated with new technologies such as NextSpeech. When the data collected via the codes supports granting of a diagnosis related group DRG-code, it will lead to reimbursement being available for speech mapping by NBS. Note that the OPS code for motor mapping is now 1-20c.1. Note also that cortical mapping of both motor and speech areas in a patient allows for the use of both OPS codes.


Clinical Spotlight

Same day, tri-modality functional brain mapping prior to resection of a lesion involving eloquent cortex: technical feasibility

Preoperative motor mapping by navigated transcranial magnetic brain stimulation improves outcome for motor eloquent lesions

In this landmark study, 100 patients with lesions located in motor eloquent areas who had been preoperatively mapped by the Nexstim NBS System were matched with a control group of 100 patients who had been operated on before the availability of NBS mapping. The group of patients preoperatively mapped by NBS showed a significantly lower rate of residual tumor, as determined by postoperative MRI, than the patients operated on before NBS was available. On long-term follow-up, 12% of the patients in the NBS group had improved motor function after surgery, compared to only 1% of the patients in the control group. Additionally, using NBS mapping enabled neurosurgeons to use smaller craniotomies. In their conclusions, the authors strongly advocate navigated TMS to become increasingly used for presurgical mapping of eloquent lesions in the brain, as this large study increases the already existing level of evidence for preoperative motor mapping by navigated TMS. Further, the authors also write in their article that, “Navigated TMS, with comparably easy and cheap availability, represents a remarkable option for non-invasive mapping because it is also based on motor evoked potentials via neuron stimulation – and therefore has a close relationship to direct cortical stimulation, which is widely used by neurosurgeons. Navigated TMS can be performed in an awake patient and allows surgical planning already at the state of indication.”


Inducing transient language disruptions by mapping of Broca’s area with modified patterned repetitive transcranial magnetic stimulation protocol

The purpose of this study was to map Broca’s area where used by event-related navigated transcranial magnetic stimulation (nTMS) to generate an modified patterned nTMS protocol. Initially, the primary motor cortices (M1) for hand and laryngeal muscles were mapped for 15 right-handed subjects. The subjects underwent nTMS to Broca’s area while engaged in a visual object-naming task, with nTMS triggered 100 msec after picture presentation. The modified patterned nTMS protocol consisted of 4 stimuli with an inter-stimulus interval of 6 msec; 8 or 16 of those bursts were repeated with a burst repetition rate of 12 Hz. On M1, the Euclidian distance was measured between the cortical points eliciting transient language disruptions and the M1 for the laryngeal muscle. On stimulating Broca’s area, transient language disruptions were induced in all subjects. The mean Euclidian distance between the cortical points inducing transient language disruptions and M1 for the laryngeal muscle was 17.23 ± 4.73 mm. Currently, there is no reliable stimulation protocol for mapping Broca’s area. This stimulation paradigm with a modified patterned nTMS protocol was shown to be promising and might gain more widespread use for speech localization.


Repeating mapped cortical language sites by preoperative navigated transcranial magnetic stimulation compared to repeated intraoperative DCS mapping in awake craniotomy

Navigated Brain Stimulation (NBS) has been successfully used by clinicians to demonstrate the re-location of motor function following brain surgery in slow-growing brain tumors. This study, however, is the first to show that language function is also plastic. In the study, NBS language mapping was used for the follow-up of three patients undergoing repeated awake surgeries for treatment of language eloquent gliomas. The awake surgeries and language mappings by both NBS and DCS were repeated 7, 10, and 15 months subsequent to the initial resection. A good correlation between the pre-surgical NBS language mapping and intraoperative DCS results was observed in all three patients for the initial surgery. However, the initial NBS and DCS findings only corresponded with the results obtained from the second NBS mapping and awake surgery at 7 months - in one out of the three patients. In their conclusion, the clinicians state that these NBS and DCS data suggest changes of language organization as a consequence of brain plasticity in the other two patients in the study.


Upcoming events

- Deutsche Gesellschaft für Neurochirurgie, 11th–14th May, 2014, Dresden, Germany
- 6th International Symposium on Navigated Brain Stimulation in Neurosurgery, 10th–11th October, 2014, Berlin, Germany
Kuopio University Hospital was one of the first commercial customers for the NBS System and the source of many of the first clinical research papers on NBS. Recently, Kuopio upgraded to NBS System version 4.3. NexTalk interviewed the Kuopio team: Professor Esa Mervaala, MD, PhD, Adjunct Professor Sara Määttä, MD, PhD, Adjunct Professor Petro Julkunen, PhD and Mervi Könönen, MSc on their experiences with the new NBS version.

Q: What kinds of conditions do your presurgical mapping patients have?
A: Some are epilepsy surgery candidates but the majority have brain tumors – in total we map around 20 patients per year. Each year we also perform several therapy response tests prior to pain stimulator implantation.

Q: How has NBS impacted the neurosurgeon’s work?
A: The NBS results impact surgical planning and in some cases also assist during the operation via projection of the mapped locations in the surgical microscope field.

Q: You use your NBS System for rTMS therapy, which brain disorders do you treat?
A: We treat depression, tinnitus and secondary negative symptoms of schizophrenia. We have also performed trials for chronic pain and obsessive compulsive disorder.

Q: Can you reveal what rTMS protocols you use for therapy?
A: In depression, the protocol used depends on the patient’s individual clinical characteristics. We target the left DLPFC with 10Hz – or patient-specific alpha frequency – in 5s trains with a 25s inter-train-interval. When we target the right DLPFC target we employ 1Hz rTMS in 140s trains with a 30s inter-train-interval. Intensity is typically 110% of right hand resting motor threshold (rMT). For tinnitus we perform 1Hz rTMS on the left auditory cortex with 2000 - 4000 stimuli. The protocols for the other therapies are based on literature sources and are still in the trial phase.

Q: Who are responsible for performing the NBS therapy sessions?
A: The planning and therapy takes place at the department of Clinical Neurophysiology where a clinical neurophysiologist plans the protocol. During the first visit a team comprising a clinical neurophysiologist, a medical physicist and a technician determine the coil location, intensity and number of stimuli. A technician or medical physicist then administers the therapy in subsequent sessions.

Q: How have patients reacted to the prospect of NBS therapy and what have the results of rTMS therapy been like?
A: We treat 4 to 5 patients daily. The majority of patients have been motivated and welcomed NBS therapy well. Responses naturally vary, but some patients get a great effect. No negative effects have been reported to us.

Q: What is the latest research you are working on with NBS?
A: We are doing sham-controlled therapy trials in schizophrenia as well as numerous methodological studies and studies of basic neuroscience. These include epilepsy, NBS and TMS-EEG in children and TMS-EEG studies in adolescent binge drinkers.

Q: How has the installation of the new NBS System 4.3 changed your workflow?
A: Use of the System is much smoother. rMT-finding is now determined by the integrated software algorithm. In therapy sessions we now use the cooled coil and the coil holder arm instead of hand-holding the coil. The new chair is also more patient-friendly, and the system is more compact. Overall, our experiences of the upgrade are very positive!