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The long-term results of subthalamic nucleus stimulation for Parkinson's disease

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Objectives: STN-DBS has been performed for Parkinson's disease (PD) patients whose medication is wearing off and/or causing adverse effects. We retrospectively investigated the effects of STN-DBS in all PD patients treated at our institute.
Methods: Between 1999 and 2012, we performed STN-DBS in 224 PD patients (98 males; mean age at surgery: 64.1 years). The mean Yahr stage was 2.89/4.18 (on-medication/off-medication) and the Schwab and England scores (S&E scale) were 87.0/52.9. Postoperatively, we investigated the following parameters: Yahr stage, S&E scale, UPDRS, complications and mortality.
Results: STN-DBS has been continued in 160 patients and discontinued in four. Twenty-seven patients died and 33 were lost during follow-up. One year after surgery, the mean Yahr stage had improved to 3.08 and the mean S&E score had improved to 77.8 in the off-medication state. After 10 years, STN-DBS had improved Yahr stage and S&E scores as well as UPDRS II and UPDRS III in the off-medication state compared with preoperative data. The complication rate was 7.14% (16 cases/224 surgeries: six cases were infection, two were intracranial hemorrhage and eight were device-related problems). Median age at death during follow-up was 74 years and major cause of death was aspiration pneumonia (seven cases/33 patients).
Conclusions: The effects of STN-DBS continued in long-term follow-up. In particular, rigidity and tremor were remarkably improved over several years. Aspiration pneumonia is a major cause of death in PD patients who have undergone STN-DBS.

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The value of navigated transcranial magnetic stimulation in clinical neurosurgical practice

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Objective: Avoiding postoperative motor or sensory speech disorder by performing preoperative speech mapping via nTMS, making awake- craniotomy unnecessary.
Material and methods: All patients with gliomas near anatomic speech areas and a planned operative resection were included in our study prospectively. The medical ethics committee permitted the study.

In most cases nTMS was performed the day prior to surgery. After acquiring the nTMS data, they were transferred to our Brainlab® workstation for surgical navigation. Each surgeon studied the data and planned the operative approach as well as a possible complete versus incomplete tumor resection.
Results: We included 14 patients in our study. Speech disorder was the leading symptom in 6 patients. One reported of seizure- like symptoms, during which he wasn't able to talk. Surgery was performed in general anesthesia in all patients.

Speech disorder was unchanged in five of seven patients, improved in one and one was symptom-free postoperatively. A new speech deficit occurred in 1 patient resected from a left fronto-parasagittal anaplastic oligoastrocytoma (WHO III) with a postoperative left temporal bleeding. The symptoms improved by neurolinguistic therapy and were hardly detectable on discharge. Ten tumors [3 glioblastomas(WHO IV), 3 anaplastic astrocytomas (WHO III), 3 anaplastic oligoastrocytomas (WHO III) and 1 oligoastrocytoma (WHO II)] could be resected completely. Four patients had residual tumor. Two of those were glioblastomas (WHO IV) with tumor growth into eloquent brain areas temporomesial and near the basal ganglia. Histologic evaluation revealed seven glioblastomas (WHO IV), three anaplastic astrocytomas (WHO III), three anaplastic oligoastrocytomas (WHO III) and one oligoastrocytoma (WHO II).
Conclusions: For surgical resection of brain lesions near speech-areas, preoperative cortical mapping via nTMS is a noninvasive, safe and reliable alternative to awake- craniotomy. Results of our study are comparable to the update literature [Wilden JA, Neurosurg focus 34 (2):E5, 2013].

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Human magnetophosphene perception and EEG response to 50 and 60 Hz magnetic stimuli up to 50 mT

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Introduction: Uncertainties persist regarding magnetophosphenes perception threshold (flickering lights perceived as a consequence of a time-varying magnetic field - MF) in humans. This threshold is reported to be the lowest at 20 Hz (5 to 10 mT) and to increase with higher frequencies, but it is only extrapolated at 60 Hz. This project aims establishing magnetophosphene perception threshold in humans exposed to 50/60 Hz MF and associated electroencephalographic response (EEG).
Methods: Two groups of healthy volunteers (30 at 60 Hz, 30 at 50 Hz) are tested in 2 localized exposure conditions (eyeball, occipital cortex) and 1 global head exposure condition. Each frequency condition (2 groups) undergoes 11 MF conditions (0 to 50 mT, 5 mT increments, 5 s each). MF conditions are repeated 5 times (random order). Volunteers are sitting eyes closed in a dark room. They report magnetophosphenes by button-press, while occipital EEG is recorded with a MRI-compatible EEG system. Magnetophosphene perception is expected to be associated with a decrease in EEG alpha (8-12 Hz) spectral power in the visual cortex.
Results: Preliminary results confirm magnetophosphene perception for retinal and global exposures at 50 and 60 Hz, but not for occipital exposure. The detection threshold is between 10 and 15 mT at 50 Hz, and between 25 and 30 mT at 60 Hz. Interestingly, the threshold is lower at 50 Hz than at 60 Hz. Detailed results will be reported at the conference.
Discussion: Magnetophosphenes are a direct biophysical effect of human MF exposure, and EEG provides an objective neurophysiological outcome. The detection threshold is between 10 and 30 mT depending on local/global – 50/60 Hz exposure conditions. The lower threshold at 50 than at 60 Hz indicates a differential frequency-response. These results obtained in humans will provide solid data for exposure guidelines, also offering opportunities for translational research.

Human magnetophosphene perception and EEG response to 50 and 60 Hz magnetic stimuli up to 50 mT

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INTRODUCTION

In the Extremely Low Frequency (**ELF**) range, international guidelines on magnetic field (**MF**) exposure are based on acute 'well-established effects' on the **human central nervous system**, characterized by the best estimate of threshold for retinal **magnetophosphene** perception [1,2]. Magnetophosphenes are described as 'flickering-lights' perceived in a dark environment when exposed to a time-varying MF. Although magnetophosphenes are the most robustly exposure-related established effect, the perception threshold at power frequencies (50 and 60 Hz) remains uncertain, since it is based on extrapolated estimates from non-replicated experimental data acquired at lower frequencies. The threshold for magnetophoshene perception is estimated to be lowest at 20 Hz (between 5 and 10 mT - 50 to 100 mV/m of induced E-field – 10 to 14 mA/m^2 of induced current density) and then to increase with frequency [1-6]. **The main aim of this project is to experimentally test the magnetophosphene detection threshold in humans exposed to MF flux densities between 0 and 50 mT at 50 and 60 Hz**. The electroencephalographic (**EEG**) responses will also be investigated.

METHODS

Experiment (ethics: HSREB 18882):

- **Protocol: 0-50 mT** incremental protocol (5 mT steps x 5 repetitions each - 5s rest in between), given at **50 Hz** (n=25) and **60 Hz** (n=26), 2 local (eyeball and occipital) and 1 global head exposure conditions. Subject sitting in an armchair at rest, eyes closed in the dark.
- **Endpoints: Magnetophospene perception** (button press) and simultaneous **EEG** recordings (classical frequency analysis - O1, O2, OZ).

MATERIAL

Our local (Figure 1) and global (Figure 2) exposure systems are controlled using a LabView™ program driving one of three MTS™ Magnetic Resonance Imaging gradient amplifier capable of delivering up to 200 A (rms) at ± 345 V (MTS Automation 433 Caredean Dr. Horsham PA).

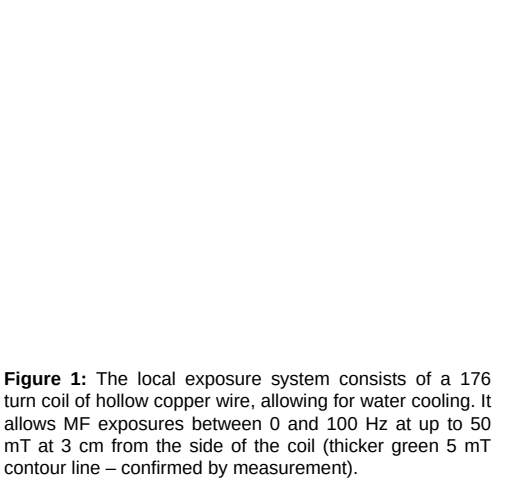

Figure 1: The local exposure system consists of a 176 turn coil of hollow copper wire, allowing for water cooling. It allows MF exposures between 0 and 100 Hz at up to 50 mT at 3 cm from the side of the coil (thicker green 5 mT contour line – confirmed by measurement).

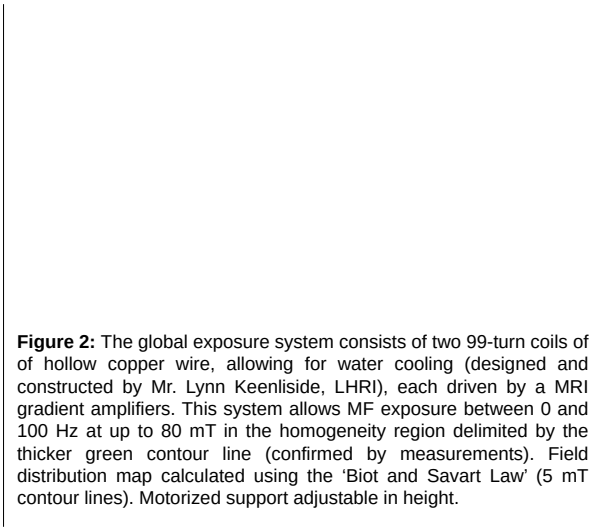

Figure 2: The global exposure system consists of two 99-turn coils of of hollow copper wire, allowing for water cooling (designed and constructed by Mr. Lynn Keenliside, LHRI), each driven by a MRI gradient amplifiers. This system allows MF exposure between 0 and 100 Hz at up to 80 mT in the homogeneity region delimited by the thicker green contour line (confirmed by measurements). Field distribution map calculated using the 'Biot and Savart Law' (5 mT contour lines). Motorized support adjustable in height.

RESULTS

Occipital cortex, right eyeball and entire head sequentially exposed between 0 and 50 mT, 50 and 60 Hz (5s each x 5 repetitions): **magnetophosphene perception systematically reported** by button press (Figure 3).

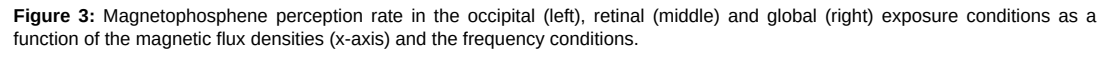

Figure 3: Magnetophosphene perception rate in the occipital (left), retinal (middle) and global (right) exposure conditions as a function of the magnetic flux densities (x-axis) and the frequency conditions.

A main flux density effect is observed for **magnetophosphene perception** both in the retinal ($F=94.21$, $p<.001$, Partial $Eta^2=.66$, Power=1) and global ($F=133.91$, $p<.001$, Partial $Eta^2=.70$, Power=1) exposure conditions.

EEG was collected using a MRI-compatible EEG system (Neuroscan-Compumedics Inc.) and power in the alpha frequency band was calculated for O1, OZ, O2 in each experimental condition (8-12 Hz – using Matlab). EEG results in O2 are presented in Figure 4 and show a significant flux density main effect ($F=9.1$, $p<.001$, Partial $Eta^2=.149$, Power=1)

Figure 4: EEG alpha power in the global exposure condition.

DISCUSSION - CONCLUSION

- **Occipital exposure: No direct magnetophosphene perception –** indication of possible perception at 50 mT but likely due to the residual field at the retina
- Magnetophosphene perception results from **retinal exposure**
- Hypothesis: effect on the **graded potential of rods** " need to test different frequencies, field orientations
- Lowest threshold for **magnetophosphene perception: 15 mT at power frequency**
- **Description**: stroboscopic/flickering **white** light, **periphery of the visual field** (bottom left in retinal, all the periphery and brighter in global). Sometimes described as **vibrations** and reports of **line patterns** [7]
- **Differential responses at 50 and 60 Hz**
- **Objective neurophysiological marker**: **EEG Alpha** waves **decreasing** with higher flux densities (predicted in [8])

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