NEUROPHYSIOLOGICAL EVALUATION OF VISUAL CORTEX EXCITABILITY IN SIGHTED AND BLIND SUBJECTS USING IMAGE-GUIDED TRANSCRANIAL MAGNETIC STIMULATION

#4485

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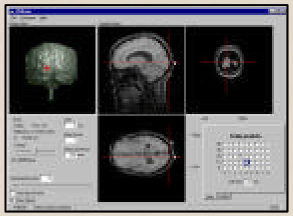
Purpose

The induction of visual perceptions by cortical stimulation, establishes the visual nature of the stimulated cortex and provides the basis for the development of a cortical visual neuroprosthesis (Penfield et al. 1950, 1974; Brindely et al. 1968, 1972; Dobelle et al. 1974, 1976, 2000; Bak et al. 1990; Schmidt et al., 1996; Normann et al. 1999, 2001). However direct cortical stimulation requires occipital craniotomy and anesthesia, is usually restricted to patients with brain pathology requiring neurosurgical interventions, and has therefore limited utility for the investigation of the functional organization of human visual cortex.

Transcranial magnetic stimulation (TMS) is a noninvasive and relatively painfree technique for cortical stimulation that has been applied with success in the study of motor and sensory physiology. TMS applied over the occipital cortex induces either visual suppression or localized phosphenes depending on coil design, current intensity, pulse polarity, duration, and use of single or repetitive pulses. However, a method to reliably induce phosphenes is not available and no sampling standards have been yet described for topographic mapping of the human visual cortex by TMS.

The present study was designed to conduct a systematic mapping of the human visual cortex by focal TMS in sighted and blind subjects.

Methods



The subject's MRI is broughtup on a computer monitor, and the Brainsight program is used to guide theprecise location of TMS coil relative to the head and brain surfaces. The position of the TMS coil and the subject's head are co-registered from small pieces of refractory material (trackers) placed on them. Trackers are monitored, or "seen" by an infrared optical position sensor. This information is send to a computer which, after a calibration procedure, displays the position and orientation of the coil relative to the subject's MRI. This procedure allows analyze the visual induced perceptions related to the cortical site stimulated, which it is not reliable with externals landmarks given the individual variability of this region of the head.

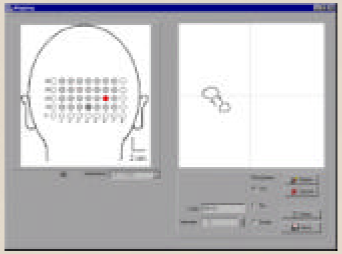
TMS was delivered with a figure-of-eight coil (Cadwell Labs, Kennewick, WA, USA) to 28 positions arranged in a 2x2 cm grid over the occipital area. A frameless image-guided neuronavigational device (Brainsight 1.4?, Rogue Research, Montreal, Canada) was used to describe the position of the actual sites of the stimulation coils relative to the cortical surface. A digitizing tablet connected to a PC computer running customized software, and audio and video recording were used for detailed and accurate data collection and analysis of evoked visual perceptions.

The protocol was applied on a group of 19 sighted and 15 legally blind volunteers. All gave their written informed consent prior to entering the study, which had been approved by the institutional review board.

Features of blind subjects

Cause of blindness	*Age*	*Residual vision*
Retinopathy of prematurity	14	-
Retinopathy of prematurity	15	-
Retinopathy of prematurity	26	-
Optic nerve atrophy	49	+
Chilhood trauma	70	-
Cone cell distrophy	68	+
Retinosis pigmentosa and cataract	70	+
Retinosis pigmentosa and cataract	30	+
Retinosis pigmentosa	50	+
Uveitis and cataract	59	-
Optic nerve atrophy	36	-
Optic nerve atrophy	68	+
Optic nerve atrophy	37	-
Optic nerve atrophy	29	-
Citomegalovirus (CMV) retinitis	36	-

Interface of the program developed to facilitate the recordings of phosphene data



Example of the impressions elicited in blind subject #14 by stimulation of a position in the right hemisphere, 2 cm above the inion and 4 cm lateral. The subject described this as "movement of a small spot in a static field".

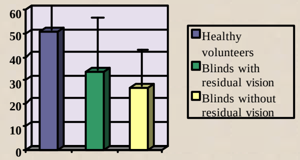
Results

1. **All subjects tolerated the procedure without complications.** Specifically no seizure activity was induced by TMS.

2. **Percentage of subjects perceiving phosphenes**

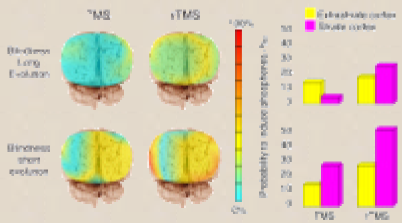
	TMS	rTMS
Healthy volunteers	**96%**	**100%**
Blind subjects	**30,7%**	**54%**
-With some residual vision	37,5%	70%
-Without any residual vision	20%	40%

3. **Percentage of sampled positions able to elicit the perception of phosphenes**

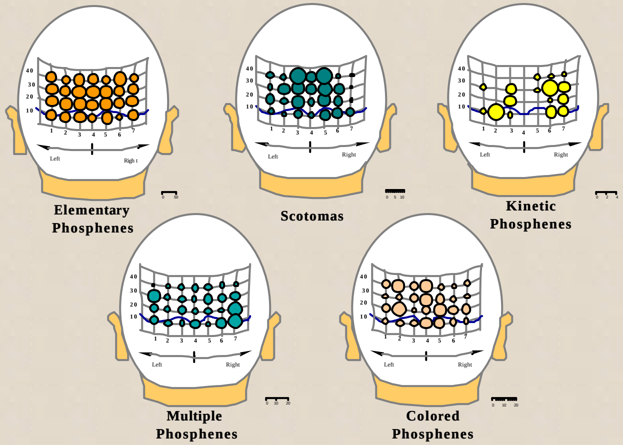


4. **Characteristics of phosphenes in blind subjects**

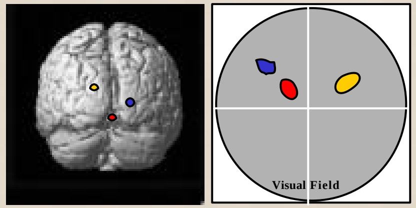
Types of Phosphenes	TMS	rTMS
Elementary phosphenes	60,8%	33,5%
Chromophosphenes	0%	31,8%
Scotomas	0%	1,4%
Kinetic phosphenes	39,1%	33,3%



5. **Preferential location of different types of visual perceptions induced by TMS in sigthed subjects.** Buble size indicates number of phosphenes (see attached scales)



6. **Examples of retinotopic mapping of TMS induced phosphenes in blind subject #8**



Conclusions

- TMS is able to reliably evoke phosphenes in all sighted subjects and in some proportion of blind subjects although not in all sampled positions, hence the relevance of a systematic mapping.
- Evoked perceptions were topographically organized. Despite minor inter-individual variations, the mapping results was reproducible and showed good congruence among different subjects.
- Phosphenes are subjective perceptions, and their descriptions are highly variable. This makes it necessary to build a protocol to analyze together the location of the stimulation, the region of the visual field activated and the evoked perception.
- TMS, in combination with other brain image technologies and methods, could be useful to improve our understanding of the physiologic organization and plastic changes in the brain of blind subjects as a consequence of their adaptation to the loss of sight. Such a non-invasive method could be used for the selection of suitable subjects for a cortical visual prosthesis.