BRAIN ACTIVITY DURING REMOTE INFORMATION ACCESS

Scientific report of the grant 54/08 submitted to Fundacao Bial by

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1. INTRODUCTION AND OBJECTIVES

Out of body experiences (OBEs) are curious, usually brief sensations in which a person's consciousness seems to become detached from the body and take up a remote viewing position (disembodiment). Disembodiment refers to an altered sense of spatial unity between self and body, because the self is not experienced as residing within the limits of the body.

OBEs have attracted the most interest when reported by patients suffering from cardiac arrest and other life-threatening experiences referred to as near-death experiences (e.g., Parnia and Fenwick, 2002). To verify the reality of an OBE several researchers used a 5-digits target number placed out of sight near the ceiling of the hospital room and the patients were asked to recall the presented numbers. However, the output of this clinical research was an accumulation of cases somewhat deficient with regard to their recording and investigation methods (Cook et al., 1998). Problematic with this approach is already the fact that it is in general not possible to adequately instruct the patients to be aware of the presented digits *before* having near-death experiences and entering an OBE state. Most intriguingly, Blanke et al. (2002; 2005) reported that electrical stimulation of the right temporoparietal junction (TPJ) can consistently induce OBEs in an epileptic patient undergoing a neurosurgical intervention.

The aim of this study was therefore to investigate in a larger sample, if transcranial magnetic stimulation (TMS) of the right TPJ can induce OBEs. In case a subject reported an OBE, he/she was asked to recall a five digits target number displayed on a computer screen near the ceiling of the room. Moreover, the EEG was continuously recorded receiving trigger signals from the TMS device and the computer displaying the target digits. The continuous EEG recording allowed us to investigate neurophysiological correlates of OBEs and disembodiment illusions. In order to control for nonspecific effects of brain stimulation and possible suggestibility effects of the subjects, a control site (5 cm posterior to the TPJ) was stimulated with same parameters as the TPJ. Also in order to test the specificity of the stimulation effect subjects received in randomized order high-frequency 15 Hz repetitive TMS (rTMS) or low-frequency 1 Hz rTMS of the TPJ and the control site, respectively. From a neurophysiological point of view it is crucial to understand whether OBE and disembodiment illusions are due to cortical facilitation or disinhibition processes.

2. CONDUCTED EXPERIMENTS AND RESULTS

In accordance with our time schedule we first implemented the experimental setup with 15 subjects combining EEG and TMS. The stimuli and the coordination of the TMS and the EEG device were programmed with Presentation (Neurobehavioral Systems, NINDS).

A Medtronic-Dantec Magnetic Stimulator (Skovlunde, Denmark) connected to a focal eight-shaped coil (MC-B70) was used for the application of TMS. At the beginning of each experimental session, the subject's resting motor thresholds (MT) were measured at the left abductor pollicis brevis muscle (APB) using single pulse TMS. MT was defined as the lowest intensity capable of evoking five out of ten motor evoked potentials (MEPs) with peak-to-peak amplitudes of at least 50 µV. The stimulation intensity for high-frequency 15 Hz rTMS was set at 90% of each individual's MT, which is in accordance to the common safety guidelines.

According to our pre selection screening we applied in 15 subjects high-frequency 15 Hz rTMS over CP6 (according to the 10-20 EEG system) with a duration of 2 seconds and an intertrain interval of 10 seconds. Despite applying rTMS trains for 40 min over CP6 and testing the locations 1 to 2 cm surrounding CP6, none of the subjects reported an OBE in this experiment. Therefore, as mentioned in the interim report, in order to validate the stimulation location we conducted in cooperation with the Max-Planck Institute of Biological Cybernetics in Tübingen, Germany a very extensive second experiment in which we applied an MRI-based neuronavigation system. Fig. 2.1 and 2.2 illustrate the neuronavigation procedure. 20 subjects were tested on four days. On the first day we conducted MRI measurements of each subjects' brain. MRI data were then processed using Brain Voyager 2000 (Brain Innovation, Maastricht). On the second day we used an MRI-based neuronavigation system to exactly localize the TPJ in each subjects' brain. Although several studies have used the 10-20 EEG system to localize the TMS coil, an MRI-based neuronavigation system can provide a much more precise method for TMS localizing (Karim et al., 2006; 2007). This improvement of the experimental setup was necessary to debunk if a potentially negative result is due to the miss of the TPJ or because transcranial stimulation of the TPJ can not induce OBEs. In randomized order the 20 subjects received on the one day low-frequency 1 Hz rTMS of the TPJ or the control area (5 cm posterior to the

TPJ) and on the second day high-frequency 15 Hz rTMS of the TPJ or the control area.

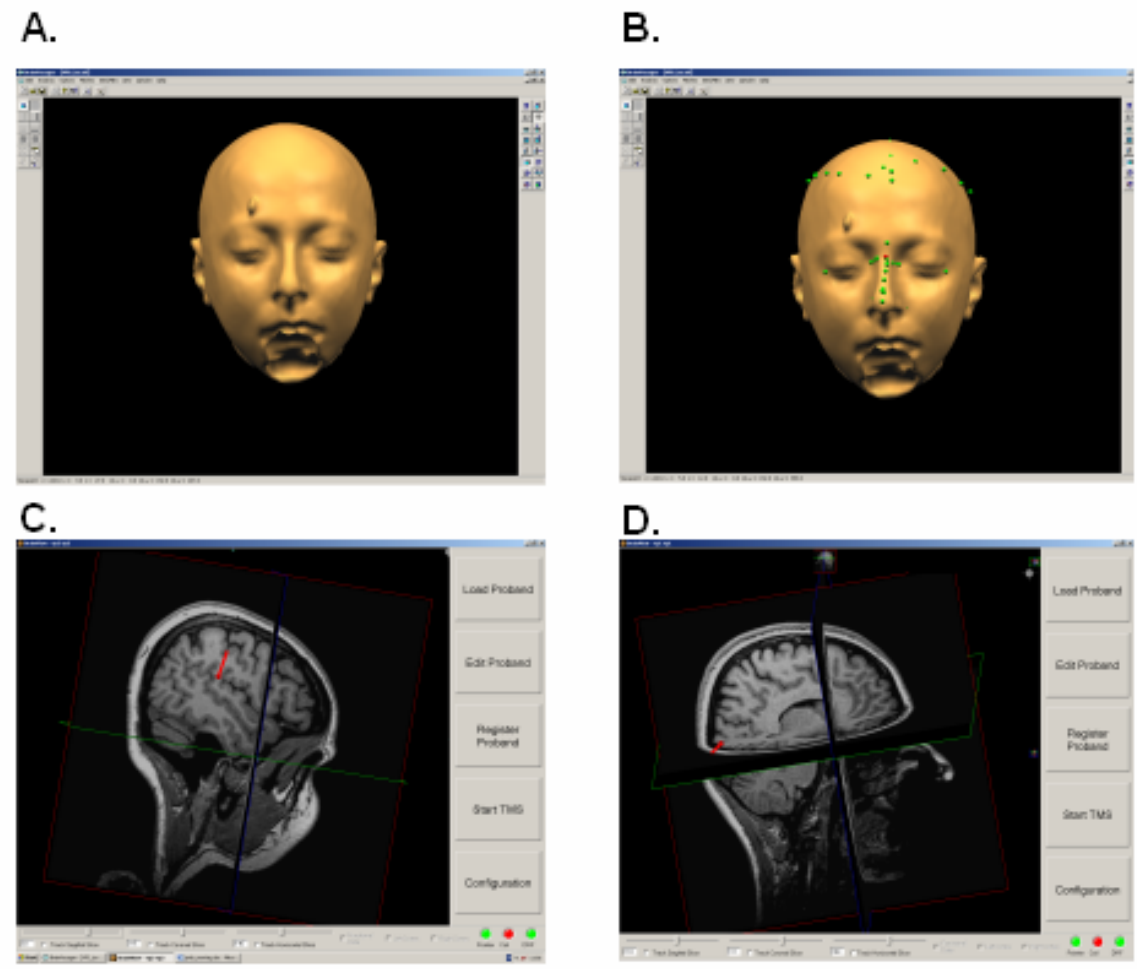

Fig.2.1. Neuronavigation process for each subject. An anatomical MRI was obtained from each participant with a vitamin E capsule over the right eye brow marking the right prefrontal cortex. Surface reconstruction of the skull was obtained with Brain Voyager 2000 (a). Specific landmarks on the participant's head were localized in 3-D space via a digitizing pen with transmitting senders (b). By superimposing the defined landmarks on the anatomical reconstruction of the brain, the TMS coil, which hosted transmitting senders as well, was neuronavigated to the right TPJ (c) and to the control site (d) in each participant.

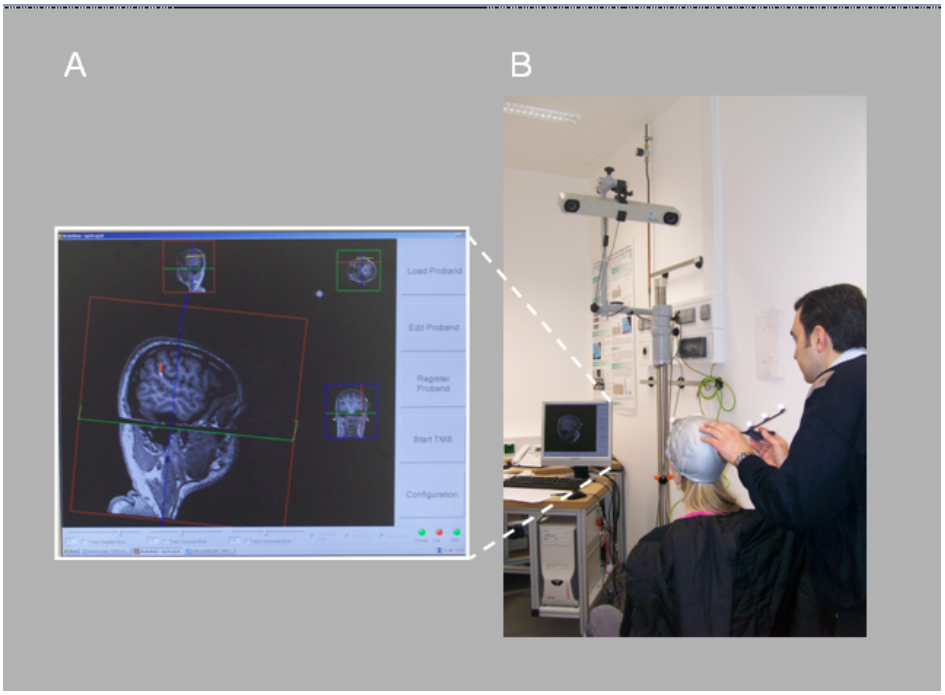

Fig. 2.2. Setup of the MRI-based neuronavigation system (Brain View, Frauenhofer IPA) for exact localization of the right temporoparietal junction (TPJ) and the control site (CS) in each subject.

According to our experience in publishing TMS studies in international high impact factor journals (see e.g. Karim et al., 2010, *Cerebral Cortex*; Karim et al., 2006; *Journal of Cognitive Neuroscience*; Sauseng et al., 2009, *Current Biology*) we included also a control task, since many reviewers do not only ask for a control area to be stimulated but also for a control task. To investigate the differential effect of high- and low-frequency rTMS over the TPJ on body perception we used the own-body transformation task (OBT task) as a control task (s. Blanke et al., 2005; Zacks et al., 1999). Fig. 2.3. illustrates this task.

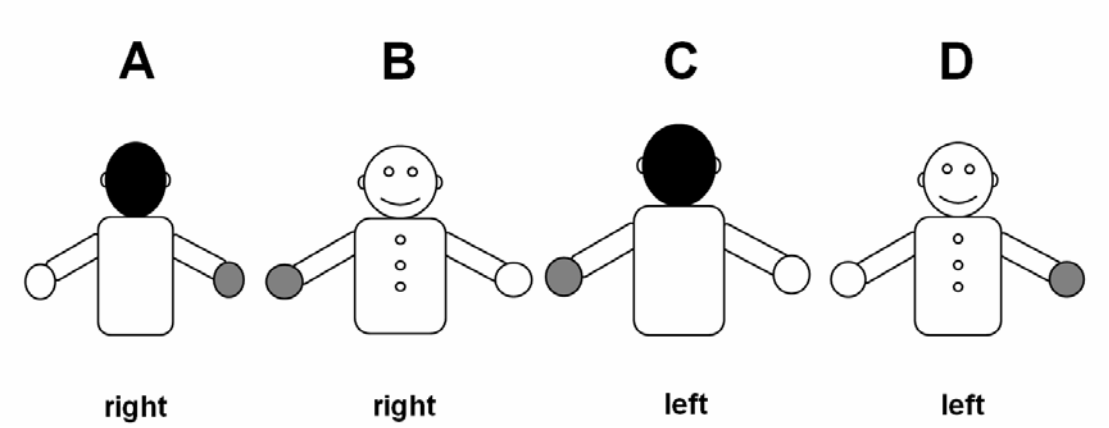

Fig.2.3. The own body transformation task (OBT task) as a control task.

In the OBT task the subjects are instructed to indicate as fast as possible with a button press whether the marked hand (with the grey glove) was the right or left hand. Front- and back facing figures had the same outline and differed only in the rendering of the clothing and the presence of a face. Thus, the OBT task requires the subjects to make right-left judgments about a human figure *after having imagined themselves to be in the body position of the figure*. We hypothesized that increasing the excitability of the TPJ by high-frequency rTMS would enhance the performance of the subjects in this task (higher correct rates and faster reaction times), whereas decreasing the excitability of the TPJ by low frequency rTMS would result in opposite effects and impair the subjects' performance. Moreover, we hypothesized that stimulation of the control area (5 cm posterior to the TPJ) would have no effect on this task.

2.1. Effects of rTMS of the TPJ on own body perception

Remarkably, as depicted in figure 2.4. facilitating the excitability of the rTPJ by high-frequency 15 Hz rTMS had no effect on inducing own body perceptions. However, *inhibiting* the excitability of the rTPJ by low frequency 1 Hz rTMS induced a significant increase in own body perceptions ($Z = 2.043$; $P < .05$; Wilcoxon matched pairs test).
In our sample 14 subjects (70%) reported own body perceptions during 1 Hz rTMS of the rTPJ. Among the 14 subjects who had own body perceptions, no subject reported an OBE. However, 2 subjects had somatosensory tingling sensations in their arms or legs, 9 subjects reported twitching sensations in their body parts (arms and/or legs) and, most remarkably, three subjects reported complete *illusory movements of body parts*. These subjects did not *see* their body parts move, but they *felt* illusory

movements of body parts like arm deflections and stretching legs. Most importantly, these observations were confined to TPJ stimulation and were not observed during the stimulation of the control area. Moreover, these effects were frequency specific, i.e., they occurred only during inhibition of the TPJ by low-frequency 1 Hz rTMS and did not occur during facilitation of the TPJ by high-frequency 15 Hz rTMS.

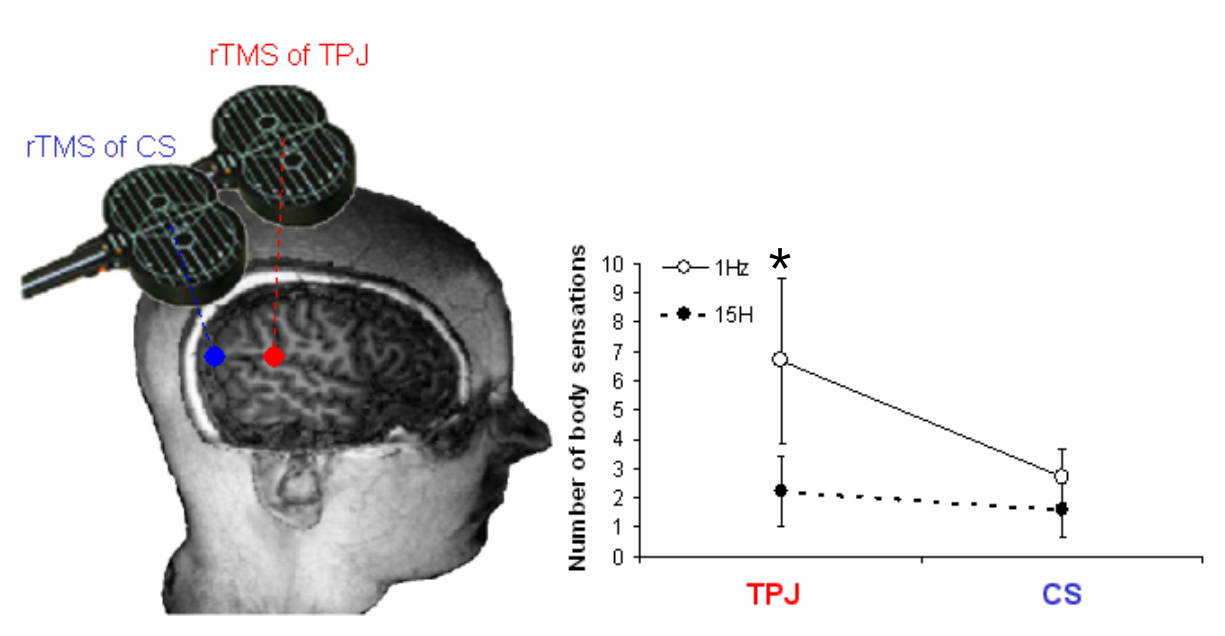

Figure 2.4. Panel A illustrates the technique used for repetitive transcranial magnetic stimulation (rTMS) of the right TPJ and the control site (CS). Panel B depicts the effect of rTMS on the number of perceived body sensations. Error bars denote standard error of the mean (SEM). *$P < 0.05$.

2.2. Effect on reaction time in the own body transformation task

The Wilcoxon test revealed that low frequency 1 Hz rTMS over the TPJ significantly reduced reaction time in the own body transformation task compared to high-frequency 15 Hz rTMS ($Z = 2.651$; $P < .01$), whereas no significant difference could be found between 1 Hz rTMS and 15 Hz rTMS over the control area ($Z = 1.157$; $P = .247$).

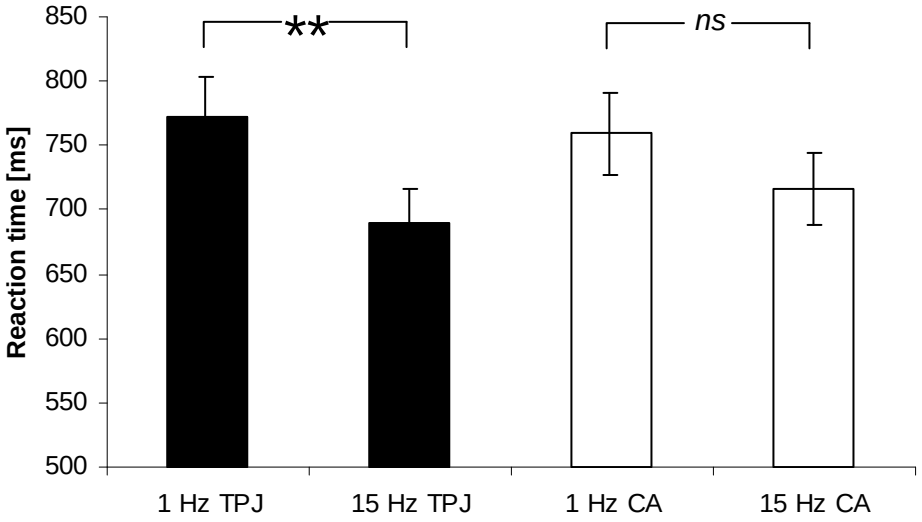

Figure 2.5. Effects of rTMS over the right TPJ and the control area (CA) on reaction time in the own body transformation task. Error bars denote SEM. ***P* < 0.01.

2.3. Neurophysiological effects

Frequency domain EEG data was transformed by means of a Fast Fourier Transformation (FFT; Brain Vision Analyzer, Brain Products GmbH, Gilchen) applied on 3 seconds segments before participants pressed a button indicating if they have or have not perceived body sensations. As shown in figure 2.6., in the first row low-frequency 1 Hz rTMS induced cortical deactivation in the stimulated site as indicated by increased delta activity. However, intriguingly illusory own body perceptions occurred only if the *right TPJ* and *the frontopolar cortex* were both deactivated as indicated by significantly increased delta activity in these regions (s. panel A in fig. 2.6). Neither low frequency rTMS of the control site, nor low frequency rTMS of the TPJ were sufficient to induce illusory own body perceptions, if deactivation of the TPJ was not associated with deactivation of the frontopolar cortex. This selective effect of low-frequency rTMS on the TPJ and the frontopolar cortex was observed only in the delta spectral power and were absent in other spectral ranges (such as theta and beta activity; s. panels D-I in figure 2.6).

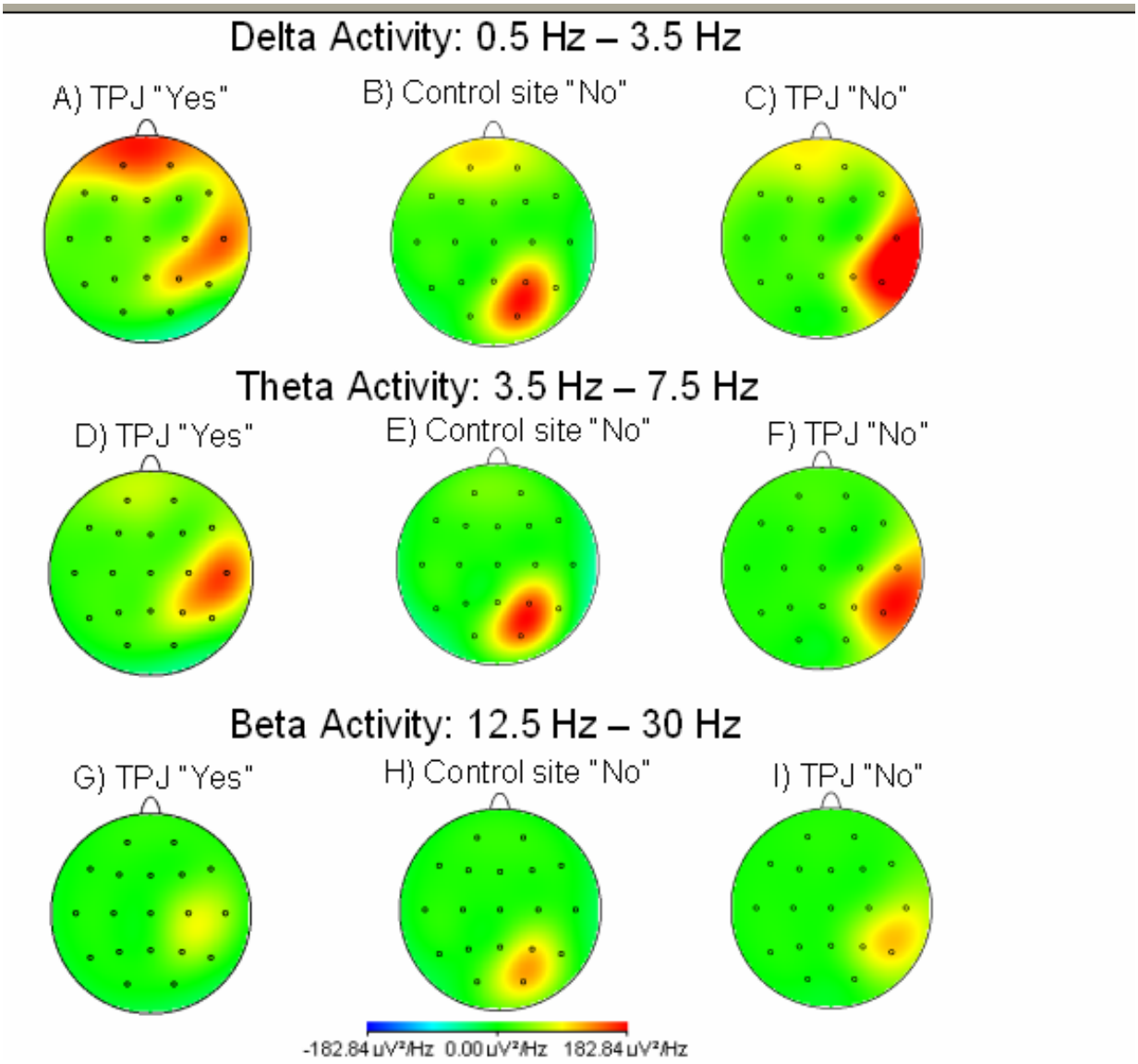

Figure 2.6. Spectral power maps (μV^2) for delta, theta and beta activity during three experimental conditions: The left panel illustrates spectral power while subjects reported having illusory own-body perceptions during low-frequency rTMS of the right TPJ. The middle panel illustrates spectral power while subjects reported having no own-body perception during rTMS of the control site. And the right panel illustrates spectral power in subjects having no own-body perceptions during rTMS of the right TPJ.

Low Resolution Brain Electromagnetic Tomography (LORETA) was applied to estimate the sources of significant differences found by the spectral analyses. LORETA has been validated by studies comparing the electromagnetic dipole analyses results with results from fMRI (e.g. Mulert et al., 2005) and positron emission tomography (Zumsteg et al., 2005). It computes electrical activity by assuming similar activation among neighbouring neuronal clusters. As shown in figure 2.7. dipole analyses with LORETA revealed the TPJ (BA 42), the Cingulum and the Medial Frontal Gyrus (BA 10) as main dipole sources during illusory own body perceptions.

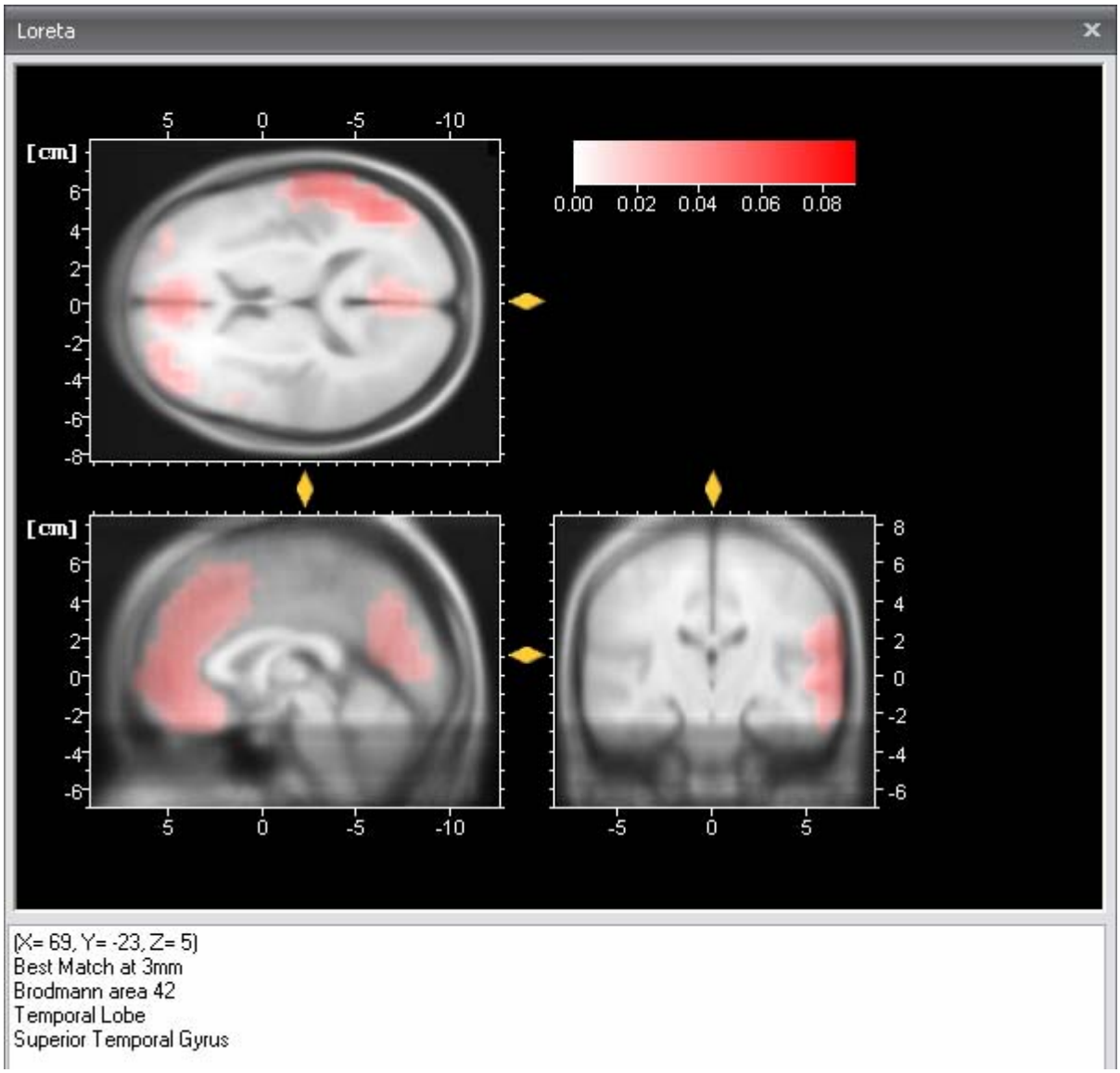

Figure 2.7. Dipole sources during illusory own body perception according to LORETA analyses.

3. DISCUSSION AND CONCLUSIONS

In this study we investigated for the first time the effects of non invasive repetitive transcranial magnetic stimulation of the right TPJ on illusory own body perceptions.

Illusory own body perceptions such as Out-of-body experiences (OBE) have attracted the most interest when reported by people who have had near-death experiences, but they have also been reported to occur spontaneously in patients with epilepsy (Blanke et al., 2002; Ridder et al. 2007). However, the neurophysiological mechanisms involved in such illusory body perceptions remain elusive. Until now there have been world wide only three patients, in which direct electrical stimulation of the cortex induced OBE (for a review s. Ridder et al. 2007). It remains unclear to what extent the particular experiences of these patients were determined by the stimulation or by some (unknown) details of their brain damage. In this extensive study we combined in a larger sample of healthy participants MRI-based neuronavigated TMS for exact localisation of the TPJ in each subject. Moreover, we investigated for the first time the assumed differential effect of inhibitory low-frequency and excitatory high-frequency rTMS of the TPJ. Form a neurophysiological point of view it is crucial to understand, if OBEs are due to cortical facilitation or deactivation processes. Most remarkably, we found that only inhibition of the TPJ by low-frequency rTMS induced illusory own body perceptions. Neither high-frequency rTMS of the TPJ nor low-frequency rTMS of the control site induced such effects. Thus, our effects were area and frequency specific. Although none of our subjects reported OBEs, low-frequency rTMS of the right TPJ could induced in several subjects illusory own body perceptions such as twitching sensations and illusory movements of body parts. Further, spectral EEG analyses revealed that illusory own body perceptions could only be induced, if the deactivation of the right TPJ was associated with the deactivation of the frontopolar cortex, which implies that the impairment of a temporoparietal and frontal network is responsible for illusory own-body perceptions. It is conceivable that direct invasive electric stimulation of the TPJ could induce stronger illusory own-body perceptions like an OBE as reported by Blanke et al. (2002). Therefore, in future studies the neurophysiological effects of direct cortical electric stimulation of the TPJ should be tested in a larger sample. Currently we are conducting such a pilot study in collaboration with the department of Neurosurgery at the University of Tuebingen. In our publication list and in the attachment you can find our first publication on the neurophysiological and psychophysiological effects of intracortical stimulation (s. Bauer et al., submitted).

4. PUBLICATIONS

We have already published two review articles on modulation of body perception and disembodiment in the awake and the sleeping mind with transcranial cortex stimulation techniques. (Karim, 2010; Noreika et al., 2010). A third paper on the neurobiology of "theory of mind" and the ability to take the perspective of other persons (Krippl & Karim, in press) as well as a book chapter on invasive and non invasive neuroprostheses are in press (Karim & Birbaumer, in press). The main data of this research project are currently being prepared to be submitted to *Cerebral Cortex*, in which Dr. Karim has published an influential paper on the neurobiology of deception last year (s. Karim et al., 2010; *Cerebral Cortex*). A further paper on the neurophysiological effects of intracortical electric stimulation, which was done in cooperation with the Department of Neurosurgery at the University of Tuebingen, has been submitted to *Biological Psychiatry*. At an international symposium at the Institute of Neuroscience in Turku, Finland and at the Max Planck Institute of Psychiatry in Munich Dr. Karim was invited to give key-note lectures on the clinical and neuroethical implications of transcranial cortex stimulation and own body perception. In all publications and conference contributions during the funding period the *Fundacao Bial Foundations was gratefully mentioned in the Acknowledgements (see Publications in the attachments).*

Karim AA (2010). Transcranial cortex stimulation as a novel approach for probing the neurobiology of dreams: Clinical and neuroethical implications. **International Journal of dream research**. 3(1): 17-20.

Noreika, V., Windt, J., Lenggenhager, B. & Karim, A. A. (2010). New Perspectives for the study of lucid dreaming: From brain stimulation to philosophical theories of self-consciousness. **International Journal of Dream Research**. 3(1), 27-36.

Karim AA (2010). Transcranial Cortex Stimulation: Clinical and Neuroethical implications. **Invited talk at the international Symposium on the Neurobiology of Consciousness**, University of Turku, Finland.

Karim AA (2010). Transcranial Cortex Stimulation. **Invited talk at the Max Planck Institute of Psychiatry**. Munich, Germany.

Krippl M & Karim AA, (in press). Theory of Mind und ihre neuronalen Korrelate bei forensisch relevanten Störungen. **Nervenarzt**.

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Karim AA (invited review) Probing the brain with transcranial magnetic stimulation. **Experimental brain research**.

Bauer R, Schwippel T, Karim AA, Gharabaghi A. (submitted). Effect of Deep Brain Stimulation of the Nucleus Accumbens on Affective Picture Processing. **Biological Psychiatry**.

Karim AA, Daltrozzo J, Thielscher A, Kotchoubey B. Debunking the role of the temporoparietal junction in out of body experience. To be submitted to **Cerebral Cortex.**

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