Visual hallucinations in Parkinson's disease
Meppelink, Anne Marthe

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Chapter 8

Lasting visual hallucinations in visual deprivation; fMRI correlates and the influence of rTMS

A. M. Meppelink\textsuperscript{1,2}, J. Koerts\textsuperscript{1,2}, M. A. Borg\textsuperscript{1}, K. L. Leenders\textsuperscript{1,2}, T. van Laar\textsuperscript{1,2}

(1) Department of Neurology, University Medical Center Groningen, The Netherlands
(2) School of Behavioral and Cognitive Neurosciences, University of Groningen, the Netherlands

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8.1 Abstract

Charles Bonnet’s Syndrome (CBS) is characterized by complex visual hallucinations (VH) following visual impairment in psychologically normal people (Teunisse et al., 1996). We report a blind patient with a CBS-like syndrome, experiencing simple VH of colour and visual motion patterns for more than 20 years after bilateral eye disease. Functional MRI (fMRI) revealed activations of visual colour- and motion areas. Repetitive transcranial magnetic stimulation (rTMS) at these activation areas resulted in transient changes of the perceived visual pattern.

8.2 Case Report

8.2.1 Clinical symptomatology

A blind, otherwise healthy female (50y old) was referred to our hospital with visual complaints concerning ongoing sensations of colour and movement. She had suffered from bilateral eye disease (retinopathy), resulting in irreversible blindness 22 years ago. Ever since, she perceived visual sensations in the entire visual field, consisting of changing colors and a semi-transparent flow. The movement sensations showed a regular cyclic pattern; changing direction every 2 days, being slow when directed to the right and fast when directed to the left. Especially the first day with flow to the left was very disturbing. One year after the start of the visual sensations, both eyes were removed and replaced by prostheses, which of course had no effect on the visual sensations. Anti-epileptic and anti-psychotic drugs had no effect either.

8.2.2 FDG-PET and fMRI

F18-fluorodeoxyglucose Positron Emission Tomography (FDG-PET) and fMRI were performed to get further insight in mechanisms underlying these visual sensations and to define a possible focus for therapeutic rTMS. Cerebral FDG-PET showed a bilaterally reduced occipital and thalamic metabolism (Figure 8.1A). Using fMRI, we localized brain regions specifically involved in either visual motion or color perception, by instructing the patient to focus attention to either color or movement. In a control condition, she counted internally. The
three conditions and a resting condition were balanced, pseudo-randomized and presented in a block design, during 3 Tesla fMRI in two separate runs, lasting 15 minutes together. T1-weighted anatomical images were also made. Image processing and statistical analysis were conducted with Statistical Parametric Mapping (SPM) (Friston et al., 1995) version 5. Each condition was contrasted with the two others, resulting in 6 contrasts. Increased activations related to the visual motion- and color conditions were found in respectively extrastriate visual area V5/MT and the fusiform gyrus (Fig. 8.1B). The observed extrastriate activations were accompanied by increased activation along the anterior calcarine sulcus, containing the peripheral visual field representation of V1 (Fig. 8.1B) during the two conditions with attention to her visual sensations.

8.2.3 rTMS

Our patient was stimulated at 1 Hz at V5/MT in order to reduce the simple VH by rTMS. Suppression of complex VH was previously shown by stimulating the occipital pole (Merabet et al., 2003). The fMRI contrast motion\_counting was loaded into Brainlab. The nearest skull point to the left V5/MT was determined using neuronavigation. Firstly a 10 min sham rTMS session on V5 was performed, single-blinded. After two weeks, a second rTMS session was performed at 1 Hz during 10 minutes at 80 percent of the maximal output. After this second session the patient reported an almost complete disappearance of her slow phase, while a shaking visual motion sensation emerged. After extra rTMS sessions at three consecutive days she reported mild fast phase reduction and a slight shortening of the cycle duration.

8.3 Discussion

Baseline occipital activation was low, as demonstrated by reduced FDG uptake, probably reflecting deprivation of external visual input. fMRI showed activations of both the visual motion area V5/MT and the fusiform gyrus by attending to either motion or color features of the visual sensations. Therefore it can be concluded that these two areas dedicated to visual motion and color processing (Zeki, 2001) were activated in a top-down fashion. Moreover, activation of the peripheral field representation in V1 was similarly enhanced,
Figure 8.1: (A) FDG-PET showing bilateral hypometabolism in the occipital cortex and the thalamus. (B) Cerebral fMRI activation patterns projected on slices of the patient’s own anatomy T1 scans. Attention to motion (upper panel) activated V5/MT (1) when compared to counting and, to a lesser extent, compared to attention to color. Attention to color (lower panel) activated the fusiform gyrus (2), compared to counting and, to a lesser extent, to attention to motion. Activation of the anterior calcarine sulcus (3) was seen in both motion versus counting and color versus counting, with stronger activation in the motion condition.
emphasizing the interactions along the segregated magno- and parvocellular pathways within striate- and extrastriate cortex. One should however remark that only the peripheral- and not central representation in V1 showed modulation of activity. Top-down evoked increases of visual cortex activation is consistent with the concept that central generators are the primary source of hallucinations, while interaction with specific sensory cortical regions defines the content of such hallucinations (Silbersweig et al., 1995; Ffytche et al., 1998). A possible generator of VH might include the left superior frontal gyrus, which was activated in both motion $>$ counting and color $>$ counting (not shown). However, an alternative explanation for this frontal activation might be the attentional effort, needed to perform the task.

Although rTMS at V5/MT slightly suppressed perceived visual motion, no lasting effect was induced. No effect was obtained either by rTMS at V1. Maybe rTMS has to be repeated more frequently, because such long-lasting VH may require a big change in neuronal function Future rTMS strategies perhaps should also combine V5/MT with the left superior frontal gyrus. Our data nevertheless demonstrated logical patterns of increased regional activations associated with the nature of the hallucinations. This procedure may help targeting for rTMS.

8.4 Acknowledgements

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