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Neural Correlates of Hysterical Blindness

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The neural mechanisms underlying conversion disorders such as hysterical blindness are at present unknown. Typically, patients are diagnosed through exclusion of neurological disease and the absence of pathologic neurophysiological diagnostic findings. Here, we investigate the neural basis of this disorder by combining electrophysiological (event-related potentials) and hemodynamic measures (functional magnet resonance tomography) in a patient with hysterical blindness before and after successful treatment. Importantly, the blindness was limited to the left upper and right lower visual quadrant offering the possibility to use the other 2 sighted quadrants as controls. While the functional magnetic resonance imaging activations were normal for visual stimulation electrophysiological indices of visual processing were modulated in a specific manner. Before treatment, the amplitude of the N1 event–related potentials component had smaller amplitudes for stimuli presented in the blind quadrants of the visual field. Following successful treatment the N1 component elicited by stimuli presented in formerly blind quadrants had a normal distribution without any amplitude differences between the 4 quadrants. The current findings point out that dissociative disorders such as hysterical blindness may have neurophysiological correlates. Furthermore, the observed neurophysiological pattern suggests an involvement of attentional mechanisms in the neural basis hysterical blindness.

Keywords: conversion disorder, ERP, fMRI, hysterical blindness, visual attention

Introduction

Conversion disorder is a clinical condition, where patients present with neurological symptoms such as numbness, paralysis, or blindness, but where no neurological explanation is at hand. The typical approach for diagnosis is to carefully exclude neurological diseases through examination and appropriate investigation (Stone et al. 2005a, 2005b; Stone, Smyth, et al. 2005) with the general assumption that the concerned investigations will not yield any pathological results. However, it is far from being clear whether the examinations do not yield pathological results because of an inexistent pathology or because they are not sensitive enough to detect it.

It also has to be noted that the neural basis of conversion disorders is currently not known. Recent investigations using transcranial magnetic stimulation (TMS) have shown that patients with motor conversion disorder have a decreased corticospinal excitability for the affected extremity during movement imagination but not at rest (Liepert et al. 2008, 2009). In this case, an electrophysiological correlate that can be measured is now at hand. Nevertheless, the question asking for the underlying mechanisms remained still unresolved.

Here, we employed functional magnetic resonance imaging (MRI) and event-related potentials (ERP) to investigate the neural correlates of hysterical blindness in a patient before and after successful psychotherapy treatment. Uniquely, the blindness of the patient was restricted to only 2 of 4 quadrants of the visual field. This permitted to investigate which neurophysiological changes might be characteristic for this type of disease by comparing responses with stimuli in the sighted versus blind quadrants and how they might be related to treatment success by comparing responses with the blind quadrants before and after psychotherapy. In particular, we expected to gain insights about the underlying mechanisms from the excellent temporal information provided by ERP.

Materials and Methods

Patient

The 62-year-old female patient reported a progressive degradation of visual perception during the last 4 years primarily in the upper left visual field (LVF) and to a lesser extent in the lower right visual field (RVF). The subjectively measured visus was 0.4 for the left and 0.3 for the right eye with a Moiré visus of 1.0 and 1.2, respectively (the normal value for the visus is 1.0). All performed ophthalmological and neurophysiological examinations relying on objective measures including MRI, electroretinography, Pattern visual evoked potentials, positron emission tomography, and electroencephalogram (EEG) did not reveal any pathological result. She underwent right eye surgery for cataract, which did not improve the clinical condition. She reported to see black patches in the upper LVF and lower RVF. Beside the visual symptoms, the patient is suffering of a diabetes type I that is satisfactory treated with an insulin pump.

Patient Perspective

A 62-year-old female housewife was referred to psychotherapy because of a progressive degradation of visual perception during the last 4 years. She reported to see black patches in the upper LVF and lower RVF. These patches were reported with either single eye open. Repeated series of previous ophthalmological and neurological examinations in different hospitals and outpatient clinics have failed to reveal a pathological result. She was diagnosed with a loss of vision related to conversion disorder.

During the treatment sessions, she gained an understanding of the psychosomatic aspects of her sight disturbance. Her persistent inability to understand the own feelings became connected to her biography and she started to identify her severe emotional traumas and to see her dysfunctional coping behavior. During the therapy, the black patches in the visual field first changed to swirls and later she started to experience periods of clear sight with increasing duration.

Treatment

Between the first and the second behavioral and neurophysiological measurement, the patient underwent psychodynamic psychotherapy for about 1.5 years—combined with guided affective imagery,

a therapeutic technique in which a facilitator uses descriptive language intended to psychologically benefit mental imagery, often involving several or all senses, in the mind of the listener. This treatment was intermixed with art therapy. During the sessions, the patient was lead progressively toward an understanding of the psychosomatic aspects of her sight loss. A considerable amount of work was dedicated to the reduction of alexithymia in which her inability to understand her feelings was put in a biographical framework. This enabled the patient to identify her emotional traumas, as well as her dysfunctional coping behavior and her alexithymia. After 1.5 years, the patient experienced long duration periods of "clear viewing" in which she could perfectly see.

Functional Magnetic Resonance Imaging

The imaging data were acquired using a 1.5 T Philips Gyroscan NT (Philips Medical Systems). Blood oxygen level–dependent contrast was measured with a T_2^*-sensitive gradient-echo echo-planar imaging (32 axial slices of 3.1-mm thickness with 1-mm gap, field of view of 230 × 230 mm, 80 × 80 matrix, time repetition 2392 ms, time echo 40 ms, flip angle 90°). A total of 245 volumes were acquired per session. The experiment was carried out in 4 sessions, and the data analysis was performed using SPM5 software package. The volumes were realigned to the first image, normalized to the Montreal Neurological Institute reference brain and smoothed using a Gaussian kernel of 8-mm full-width at half-maximum. The time series in each voxel were high pass filtered at 1/128 Hz to remove low frequency confounds.

Event-Related Potentials

The EEG (TMS international, Type Porti S/64) was recorded continuously and digitized with 512 Hz. We used an elastic cap (EASY cap) with 32 scalp electrodes at international 10–20 system locations (average reference) and 2 additional electrodes for controlling eye movements below both eyes. The EEG data were band-filtered from 0.1 to 100 Hz. All impedances were kept below 5 kΩ. The continuous EEG was segmented in epochs from 100 ms prior to 700-ms poststimulus onset. The data were inspected for eye artifacts, and epochs were rejected if they exceeded a maximum of 60 μV in amplitude or a gradient of >75 μV/s. Four averages corresponding to the 4 locations in the visual field, where stimuli were presented were formed.

Experimental Paradigm

The stimulus consisted in a 1.2° × 1.2° checkerboard patch with a local spatial frequency of 4 cycles per degree that was presented at 8° laterally from a central fixation cross and 6° in the upper or lower visual field. The stimulus was presented with a duration of 200 ms and a randomly jittered interstimulus interval of 800–3000 ms. The stimuli were equidistributed in all 4 visual quadrants in that 100 stimuli were presented in each quadrant for each ERP session. For the fMRI measurement, the location of the stimuli was blocked in that during one block of 30 s, all stimuli were presented into the same quadrant.

For the behavioral tests and for the measurements, the fixation cross located in the center of the screen was increased in size until the patient reported to see it well. Several training sessions were performed until the patient did not move the eyes away from the fixation cross during stimulation.

Results

During the first behavioral testing, the patient reported that she could not perceive any of the presented stimuli in the upper LVF and only seldom in the right lower RVF. In the fMRI, all presented stimuli elicited robust activations in the striate and extrastriate visual cortex. First, we analyzed the responses to stimulation in the primary visual cortex. Upper LVF stimulation lead to activation of the right lower calcarine bank, while the lower LVF stimuli elicited activity in the right upper calcarine bank. In the same way, upper RVF stimuli elicited activity in the lower left calcarine bank and lower RVF stimulation lead to activity in the upper left calcarine bank (see also Fig 1*A*). In the extrastriate cortex, the 4 types of stimuli elicited hemodynamic activity of comparable size and distribution. Neither any difference in distribution nor in magnitude was observed for the subjectively not perceived stimuli in the upper LVF or for the qualitatively impaired perception in the lower RVF (see also Fig 1*B*). In summary, the fMRI results parallel the large body of previous clinical investigations, where no neural correlates could be found for subjective perceptual deficits of patients.

ERPs were recorded 1 day after the fMRI. The subjective evaluation of the visual perception was unchanged relative to the previous day. Contrary to the fMRI, the ERP elicited by the 4 types of stimuli had different configurations depending on whether the stimuli were presented in the upper or lower LVF or RVF. Importantly, we observed differences in the amplitude of the N1 component elicited by upper and lower VF stimuli. For stimuli presented in the LVF, the N1 component showed a contralateral distribution (with the maximal amplitude over electrode site P8) with higher amplitude for lower than for upper VF stimuli (see Fig 2*A*, left panel). This finding is consistent with the subjective report of the patient who was not seeing upper but lower LVF stimuli. RVF stimuli elicited a contralateral N1 component (with the maximal amplitude over electrode site P7) that exhibited a higher amplitude when the stimuli were presented in the upper as compared with the lower VF (see Fig 2*A*, left panel). Notably, this was also consistent with the subjective report of the patient. In

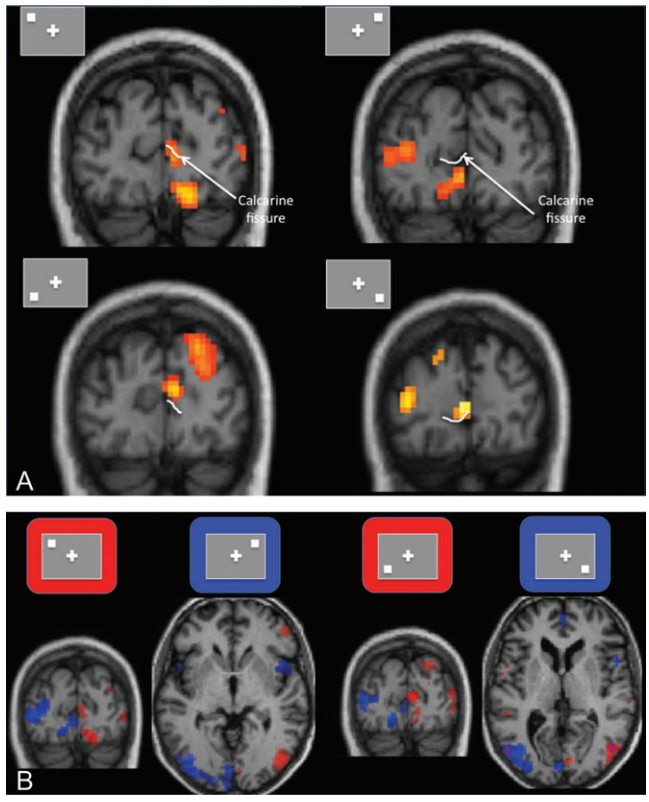

Figure 1. (*A*) fMRI activations elicited by stimuli presented in each of the 4 visual quadrants in relation to the calcarine fissure (in white). Note that upper field stimuli elicited responses in the lower and lower field stimuli in the upper contralateral calcarine bank. (*B*) Extrastriate activations elicited by each of the 4 stimulus types. LVF stimuli are shown in red, RVF stimuli in blue.

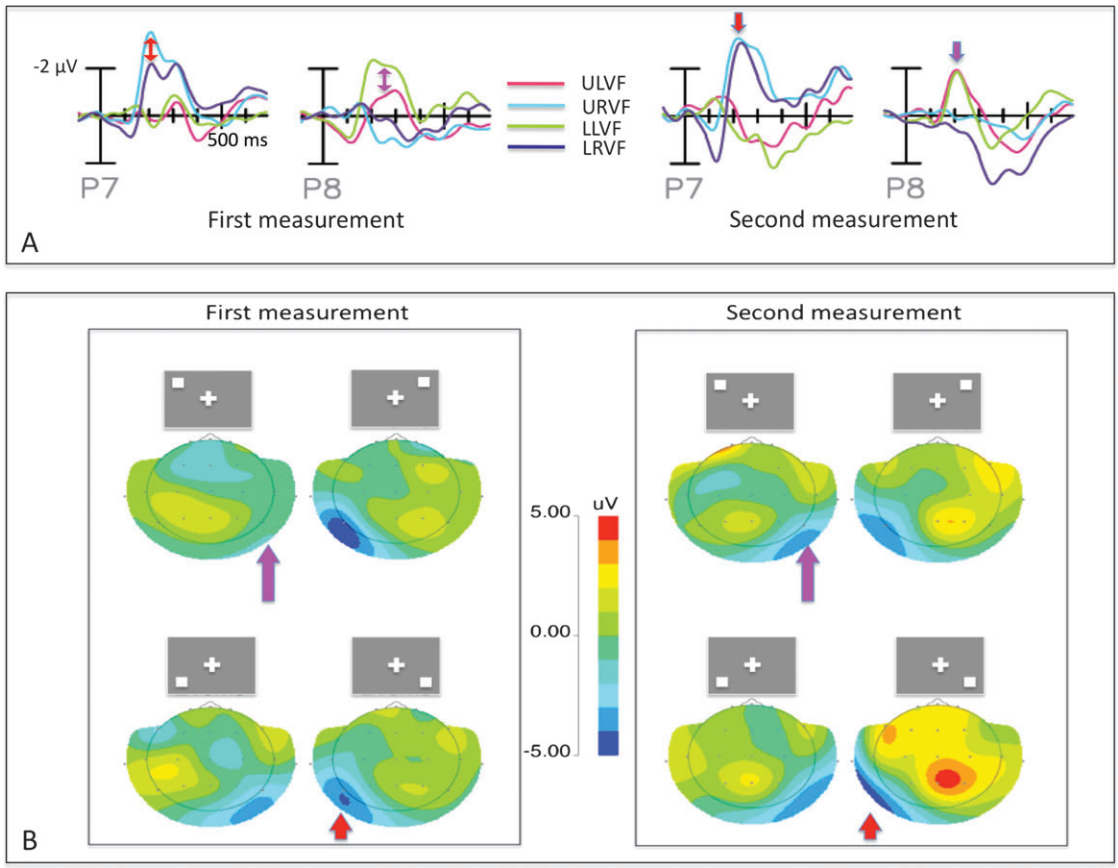

Figure 2. (*A*) Evoked-potential responses to the stimulation of the 4 visual quadrants. The left panel shows ERP responses before treatment (first measurement). Note the reduction of the amplitude of the N1 component (red arrow) to upper (subjectively sighted) and lower (subjectively blind) RVF stimulation. A similar difference is evident for the N1 component amplitudes (violet arrow) between upper (subjectively blind) and lower (subjectively sighted) LVF stimulation. The right panel shows the ERP responses after successful treatment (second measurement). No amplitude differences between the amplitude of the N1 component could be observed anymore (red and violet arrows). Abbreviations: ULVF = upper LVF, URVF = upper RVF, LLVF = lower LVF, LRVF = lower RVF. (*B*) The figure shows the topographical distribution of the N1 component elicited by stimuli presented in the 4 visual quadrants. During the first measurement (left panel), the patients' upper left and lower right visual quadrant were subjectively blind. This is well reflected in the absent contralateral negativity (violet arrow) in response to left upper visual field stimulation and the reduction in amplitude during right lower field stimulation (red arrow). In the second measurement (after successful treatment), all stimulation sites produce a clear contralateral negativity in the N1 component time range (right panel). This also applies for the stimulation of previously blind left upper and right lower quadrants (violet and red arrows).

summary, the earliest components of the visually evoked potential that index processing in the primary visual cortex and that exhibit different polarities for upper versus lower visual field stimulations were not changed in the patient. However, for the N1 component, an amplitude pattern could be observed that perfectly matched the subjective report of the patient (see Fig 2*B*).

Following 1.5 years of psychotherapy, the clinical picture has considerably improved. Now, the patient reported to have "large periods of clear viewing" in which the previously reported perceptual deficits completely disappear. Hence, event-related potentials were recorded again in one of these "periods of clear viewing." During the behavioral testing, the patient reported to have clearly seen all stimuli that were presented in the left and right upper and lower VF. At subjective and behavioral level, the performance of the patient was dramatically improved. The ERPs were recorded using the same experimental setup as 1.5 years before. In contrast to the first recorded ERPs, no major differences could be observed between the N1 component amplitude elicited by upper versus lower VF stimuli (see Fig 2*A*, right panel). The topographical distribution of the electrical field of the N1 component now clearly exhibited a contralateral distribution for all presented stimuli. In direct comparison to the first measurement especially for the stimuli located in the upper LVF, the contralateral N1 is clearly visible now (see Fig 2*B*). In summary, the amplitude pattern of the N1 component again closely paralleled the behavioral measures and the subjective reports of the patient, who reported to have no perceptual deficit this time.

Discussion

The current findings point out that dissociative disorders such as hysterical blindness do have neurophysiological correlates. These correlates can be measured and, hence, used to objectively track the progress/resolution of the disorder. Unlike the fMRI, electrophysiological indices of visual processing exhibited amplitude modulations. More importantly, these modulations occurred in a specific manner, in that stimuli presented in the subjectively unseen parts of the patient's visual field elicited smaller amplitudes of the N1 component during the first measurement. After the therapy, the subjective improvement of the patient as reflected by the large periods of clear viewing was associated with higher N1 amplitudes, in that

no differences in N1 amplitude between upper and lower visual field stimulation could be observed anymore. Thus, ERPs cannot only be used to track the progress of the pathological condition but also to track the success of the treatment objectively. Traditionally, hysterical blindness is not associated with pathologically changed visual evoked potentials (Halliday 1982; Altenmüller et al. 1989). This view is challenged by the current results. In clinical context, the visual ERPs are mainly analyzed in terms of latency and amplitude of the P1 component elicited by a checkerboard pattern reversal. The changes observed in the present work argue for a more detailed stimulation setup and analysis of visually evoked ERPs also in clinical context for patients with dissociative disorders.

A previous study (Waldvogel et al. 2007) also employed ERPs to investigate the neurophysiological changes in a patient with dissociative identity disorder. This patient had personality states in which she was blind or sighted. The sighted personality states were associated with present visual ERPs, whereas ERPs were completely absent during blind personality states. It should be noted that the study by Waldvogel and colleagues only recorded responses from one midline EEG channel (Oz) during pattern reversal stimulation (average of 32 trials) in a relatively small central part (6.7° × 9.3° of visual angle) of the visual field. It can therefore not be excluded that a response might have been observable if the authors would have recorded more channels, have stimulated more peripheral parts of the visual field or acquired more than 32 trials. Due to these methodological limitations, the results by Waldvogel et al. (2007) are rather difficult to interpret.

In the current study, we observed amplitude modulations of the N1 component when stimuli were presented at subjectively unseen locations of the visual field. Importantly, there is a striking analogy to the large body of studies that employed VEPs to study the neural underpinnings of attention in which the P1 and N1 components are enlarged when attention is directed toward the location of the evoking stimulus (reviewed in Mangun et al. 2001; Martinez et al. 2001). The N1 component in these studies has been shown to arise from a multitude of sources around the intraparietal sulcus (Di Russo et al. 2002), a region being part of a top-down control network for spatial attention (Nobre et al. 1997; Corbetta 1998) reportedly involved in tasks that require sustained covert attention to locations in the peripheral visual fields (Kastner et al. 1999; Corbetta et al. 2000; Hopfinger et al. 2000; Sereno et al. 2001). In this framework, the amplitude of the N1 component is modulated as a function of whether the location of the stimulus is attended or ignored. The similarity between the data recorded from the patient under conditions of seeing versus not seeing stimuli in the left upper and right lower visual field with data from tasks, where the stimulus location is attended versus unattended (Di Russo et al. 2002) suggests that the underlying mechanisms are very similar if not the same. Under normal circumstances, attentional mechanisms are used to filter out unwanted information in order to avoid an overflow of the sensory system. In dissociative disorders, the same mechanism might be used in a rather unfavorable way leading to perceptual deficits as observed in our patient.

In contrast to the ERPs, we did not observe any activity modulations in the fMRI data. This does not mean that fMRI is insensitive at all to modulations of neural activity as observed in the ERPs. In the current work, we used a blocked design for the fMRI. This might have lead to adaptation effects thereby obscuring activity modulations as observed with the trial-by-trial elicited ERPs. A previous study was able to show attenuation effects in the visual cortex in a group of patients with medical unexplained blindness using fMRI (Werring et al. 2004). At first glance, this result appears contradictory to ours. However, important methodological differences between the studies need to be taken into account. First, Werring et al. (2004) employed monocular full field stimulation while we binocularily stimulated small parts of the 4 visual quadrants outside the fovea. Furthermore, in our patient, the visual loss was bilateral and restricted to 2 of 4 quadrants while in the patients of Werring et al. (2004), one eye was more affected than the other. Furthermore, medically unexplained visual loss might not necessarily have a psychogenic etiology. The methodological differences make it difficult to directly compare the results of Werring et al. (2004) with the present ones. Nevertheless, the different results of the 2 studies could be well explained by the differences in visual stimulation as well as by the different nature of the 2 studies (single subject vs. group analysis).

The present work shows that clinical symptoms related to conversion disorder may have neural correlates that can be objectively measured. Hence, the severity of the symptoms, as well as the progress or success of the treatment could possibly be assessed with neurophysiological measures, if these are sensitive enough and tailored for the symptom in question. Nevertheless, it should also be kept in mind that the current conclusions are limited by the single-subject nature of the study. The existence of 2 unaffected visual quadrants in our patient provides a good control but does not eliminate the problem entirely. Definitely more patients will need to be investigated in order to completely decipher the mechanisms of this type of psychiatric disorder. Future research could also use an attention design in order to further investigate possible similarities between attention and blindness effects.

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Notes

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