Clinical Neurophysiology Practice 4 (2019) 224–229

Contents lists available at ScienceDirect

Clinical Neurophysiology Practice

journal homepage: www.elsevier.com/locate/cnp

Case report

Latency-shift of intra-operative visual evoked potential predicts reversible homonymous hemianopia after intra-ventricular meningioma surgery

Erisela Qerama [a,c,*], Anders R. Korshoej [b,c], Mikkel V. Petersen [d], Richard Brandmeier [e], Gorm von Oettingen [b,c]

[a] Aarhus University Hospital, Department of Neurophysiology, Aarhus, Denmark
[b] Aarhus University Hospital, Department of Neurosurgery, Aarhus, Denmark
[c] Aarhus University, Department of Clinical Medicine, Aarhus, Denmark
[d] Aarhus University, Center for Functional and Integrative Neuroscience, Aarhus, Denmark
[e] Richards Brandmeier, Electroneurophysiology Consultant, Biomedical Engineer, Lausanne, Switzerland

ARTICLE INFO

Article history:
Received 17 April 2019
Received in revised form 18 October 2019
Accepted 31 October 2019
Available online 14 November 2019

Keywords:
Visual evoked potentials
Intra-ventricular meningioma
Hemianopia
Optic radiation
Latency

ABSTRACT

Objectives: Intraoperative visual evoked potentials (VEPs) are used to monitor the function of optic radiation during neurosurgery with the P100 amplitude decrement as a predictor of post-operative visual deficit. However, there is currently no evidence of early VEP changes indicating reversible visual field affection.

Methods: In this case report, we used VEPs during surgery for a benign meningioma located in the atrium of the right lateral ventricle. The tumor was accessed through a transcortical approach via a two-centimeter corticotomy in the lateral aspect of the superior parietal lobule. We performed flash VEPs and simultaneous recordings of electroretinography alongside with multimodal intraoperative monitoring.

Results: We observed a significant and sustained unilateral latency shift of the P100 component of VEPs, while amplitudes temporarily dropped to 80% of baseline but recovered entirely at the end of surgery. After the operation, the patient had a left-sided lower-quadrant anopia, which recovered completely during the following three months. Diagnostic VEP with pattern reversal monocular full field stimulation at one month postoperatively showed normal latencies bilaterally.

Conclusion: Our case indicates that the VEP (P100) latency may be a new and valuable indicator (in addition to VEP amplitude) of the visual pathways.

Significance: Monitoring VEPs may be useful to detect an imminent injury and a potentially *reversible* functional deficit.

1. Introduction

The optic radiation covers the lateral aspect of the temporal horn and atrium as it extends to the occipital horn (Kawashima et al., 2006). Consequently, surgery for lesions in this area is associated with risk of visual field impairment. In this case study, we aimed to monitor the function of the optic radiation during surgery for a benign meningioma located in the atrium of the right lateral ventricle by using intraoperative visual evoked potentials (VEPs). VEPs are evoked electrophysiological signals measured over the visual cortex and assess the functional integrity of all levels of the visual pathway, including the eye, retina, the optic nerve, optic radiations and the occipital cortex. Pattern reversal VEPs are widely used in awake patients, as they are able to maintain attention and focus on the presented visual stimulus, while flash VEPs are a useful tool in children and anaesthetized patients. Waves recorded from the occipital region include N75, P100 and N145, of which the P100 (positive waveform at 100 ms) is the most consistent and least variable peak. The signal conduction time is slowed by low temperatures, nerve compression/stretch, vascular changes, etc. Increases in the VEP latency, can be indicative of evolving nerve/pathway injury (Galetta and Balcer, 2013).

Monitoring intraoperative flash VEPs has been controversial since the first report of Wright et al. (1973), mainly due to

* Corresponding author at: Department of Neurophysiology, Aarhus University Hospital, Palle Juul-Jensens Boulevard 165, Plan 2, J209, 8200 Aarhus N, Denmark.
E-mail address: erimon@rm.dk (E. Qerama).

https://doi.org/10.1016/j.cnp.2019.10.004
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technical insufficiencies. However, recent advances in the technology have made it possible to record reproducible flash VEPs in 73% to 97.2% of cases (Luo et al., 2015; Ota et al., 2010; Sasaki et al., 2010; Kodama et al., 2010). In most studies on intraoperative VEPs, the surgical decision-making was based on amplitude reduction, i.e. an amplitude reduction of 50% was used as a warning of an imminent visual field deficit.

In this study, we describe a previously unreported significant latency shift of the P100 component of the VEP that warned the surgeon of impending visual tract injury and predicted a *reversible* post-operative lower-quadrant anopia. Our findings indicate that VEP latency shifts may represent a valuable predictive parameter for visual outcome in patients undergoing asleep surgery for tumors close to the optic radiation.

2. Methods

2.1. History

The patient was a 48 year-old male surgeon, with a history of increasing concentration difficulties, neck pain and unspecific sensory disturbances in the tongue and all four extremities over a period of a few months. Previous MRI of the cerebrum, ten years before the current admission, had revealed a small tumor in the atrium of the right lateral ventricle. The tumor was suspected to be a benign plexus papilloma or meningioma and follow-up was terminated due to benign and stable radiographic appearance. MRI was repeated following the development of recent symptoms and the examination showed considerable progression of the tumor to 40 $\times$ 31 mm, now extending from the atrium of the right lateral ventricle into the posterior horn but without intra-parenchymal invasion (Fig. 1A-C). There was slight peritumoral edema and dilation of the right temporal lobe. The patient was referred to elective surgery at the Department of Neurosurgery, Aarhus University Hospital, Denmark. Prior to surgery, the patient had no subjective visual disturbances and pre-operative ophthalmological examination including computer perimetry revealed a normal vision. There was obtained informed consent from the patient, prior to using the collected data for this case report.

2.2. Preoperative MR and DTI

All pre-operative MRI data were acquired on a 3T MRI scanner (Siemens Skyra) using a 32-channel head coil. A gadolinium enhanced T1-weighted scan (MP2RAGE; TR 5000 ms; TE 2.98 ms; Resolution 1 mm isotropic) was acquired for anatomical reference and for tumor outline. Multi-shell diffusion weighted imaging (DWI) was acquired using a Multi-Band accelerated Echo Planar Imaging (EPI) sequence (180 diffusion encoding directions; B-values 700, 1200, 2800 s/mm^2; 11 nondiffusion-weighted (B = 0) volumes; TR 4000 ms; TE 110 ms; Resolution 2.0 mm isotropic). DWI data was preprocessed using FSL tools to correct for motion, eddy currents and EPI distortions. The visual pathways were delineated from the lateral geniculate body (seed region) to the occipital cortex (inclusion region) using a multi-fiber diffusion model (CSD) and probabilistic tractography (iFOD2) as implemented in the MRtrix3 software (Fig. 1). The tractography streamlines were resampled to a voxel-based track-density map, fused with the T1 image and exported as standard DICOM data to the StealthStation system (Medtronic, Inc.). Subsequently, this T1-tractography dataset was merged with the anatomical reference and a transcortical trajectory towards the tumor was chosen to avoid damage to the visual pathways (Fig. 1).

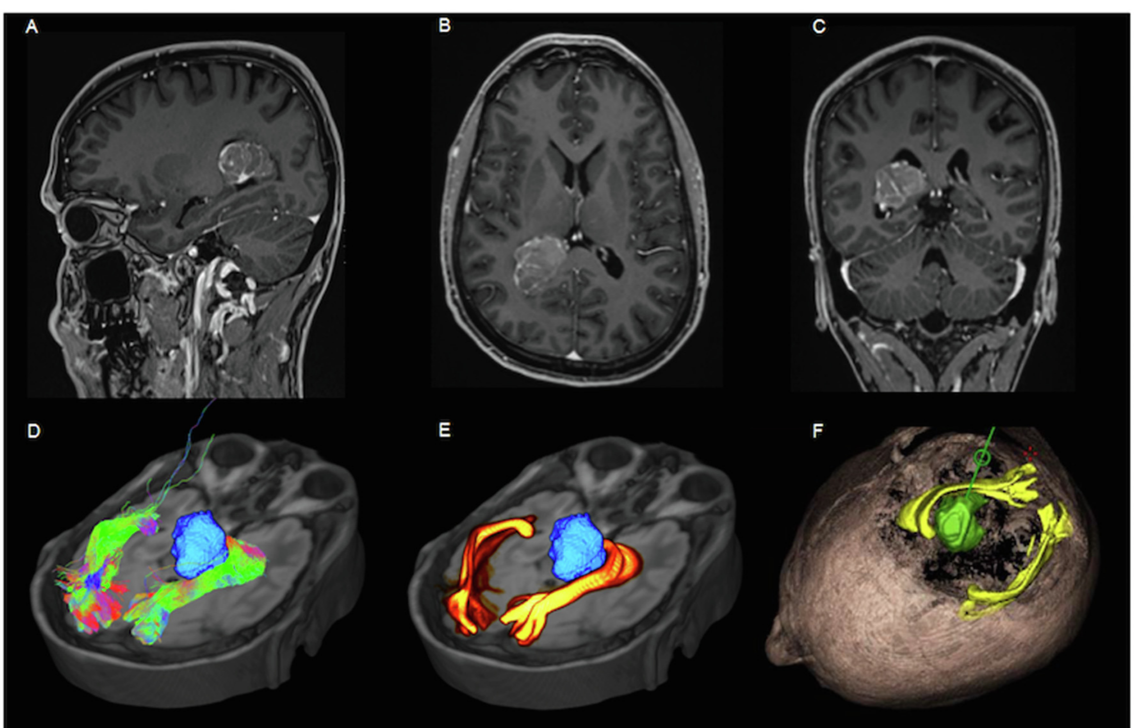

Fig. 1. A-C. Sagittal, axial and coronal sections of a gadolinium enhanced T1 MRI showing the tumor situated in the atrium of the right lateral ventricle. D. Probabilistic tractography streamlines of the optic radiation superimposed on anatomical T1 image. E. Resampled track-density map of the optic radiation for fusion with T1. F. Surgical navigation plan showing a 3D reconstruction of the patient's head, tumor (green volume) and optic radiations (yellow). A parietal entry point was chosen as described in the main text and the green line shows the trajectory line towards the tumor.

2.3. Surgical approach

The patient was anesthetized with Propofol and Remifentanil for induction and maintenance anesthesia and subsequently placed in a Sugita head holder (Mizuho America, Inc.), in a left-sided three-quarter (park bench) position with 30 degree left rotation of the head. Neuronavigation was performed using the StealthStation S7™ surgical navigation system (Medtronic, Inc.). A linear incision was performed followed by a five-centimeter circular craniotomy. The tumor was accessed through a transcortical approach via a two-centimeter corticotomy in the lateral aspect of the superior parietal lobule.

2.4. Intraoperative neuromonitoring

The following intra-operative neuromonitoring was performed: Transcranial electric motor evoked potentials (tceMEPs) from the bilateral hand muscles, i.e. abductor pollicis brevis (APB) and abductor digiti minimi (ADM), the bilateral rectus femoris, vastus medialis, tibialis anterior, and abductor hallucis muscles; somatosensory evoked potentials (SSEPs) from the bilateral median nerves (MN) with C3' and C4' as recording electrodes; train of four (TOF) from the left MN to the left APB/ADM; running (R) and electrically-triggered (T) electromyography (EMG) from all above mentioned muscles; 2-channel electroencephalography (EEG); bilateral flash VEPs and electroretinography (ERG).

2.4.1. Visual evoked potentials

Visual stimuli were induced using Medtronic VG202 goggles. The goggles were used without rubber bands but instead fixed with tape as shown in Fig. 2A. The stimulus duration was 10 ms and the stimulation frequency 0.9 Hz. Luminescence was 500 Lx to 20 kLx and the intensity was 15% or 2200 mCd. To minimize retinal stimulation by ambient light, both eyes were covered with aluminum foil (Fig. 2A). The visual evoked potential was recorded with subdermal screw electrodes Oz, O1, O2, with a ref A1A2 or Fz. The band pass filter was set to 2–800 Hz, averaging filter was set to 30–200 Hz.

2.4.2. Electroretinography

We performed bilateral ERG using needle electrodes in the cantus area to record retinal activity following visual flash stimulation (Fig. 2B). The purpose of the ERG was to verify the proper visual stimulation and activation of the optic nerve. Corneal eye electrodes were also tried but not used due to high impedance (Fig. 2B). We were unable to record left sided ERG due to high impedance. Right-sided ERGs were robust and showed acceptable signal-to-noise ratios (Fig. 3).

Separate left- and right-sided VEPs were recorded from O1 and O2, respectively, with Oz as the reference electrode (Fig. 3) and repeated runs with 500–600 averaged stimuli were stored. The time sweep was 20 ms/div and the latency at baseline was approximately 80–85 ms.

VEPs and ERGs were obtained at specific times during the surgery, at which the optic tract was expectedly at risk. Surgery was paused during the VEP/ERG acquisition.

2.5. Peri- and postoperative course

Gross total resection of the tumor was performed and pathology revealed a diagnosis of benign meningioma. During the operation, right-sided ERGs remained stable at the baseline level. VEPs on the right side showed a significant P100 latency shift of more than 10 ms (Fig. 4), which occurred in connection with the placement of minimally invasive selfretaining tube-retractors. The surgeons paused the procedure shortly once alerted about the change. As the right-sided VEP amplitudes also dropped to 80% of the baseline value later on during the procedure, the surgeons performed the excision by pausing once in while. The amplitude reduction recovered completely at the end of surgery (Fig. 4), while the latency shift persisted throughout the operation. On the first postoperative day the patient had left-sided visual disturbances and computer perimetry confirmed a left inferior congruent homonymous quadrant anopia. The deficit improved following induction of prednisolone therapy. An MRI scan conducted two days postoperatively confirmed gross total resection and showed expected post-operative radiographic sequelae but no signs of ischemia (Fig. 5). Similar findings were confirmed on repeated MRI three months post-operatively. Ophtamological examination was repeated three months post-operatively and showed total recovery of the visual deficit. Diagnostic VEP with pattern reversal monocular full field stimulation was conducted one month postoperatively and showed a normal latency of P100 bilaterally (104 ms for the right side and 108 ms for the left side). However, the half field stimulation showed markedly reduced amplitudes of the VEP responses from the left field compared to the right field responses (Fig. 6).

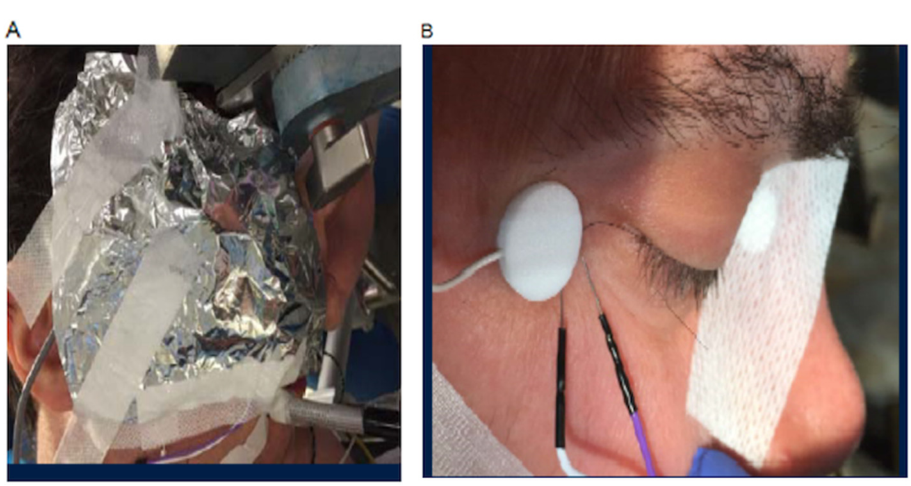

Fig. 2. Panel A shows the mounted VEP googles fixed to the patient's face with tape and covered with aluminium foil to reduce noise. Panel B shows ERG needle electrodes placed in the lateral canthus area. In addition, corneal electrodes where placed but not used due to high impedance.

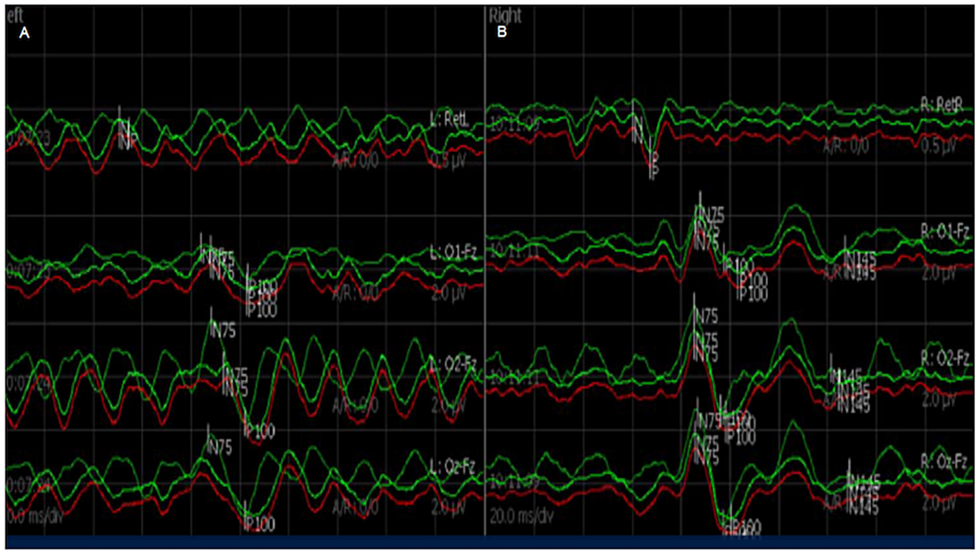

Fig. 3. ERG and VEP recordings from the left (A) and right (B) eye, respectively. ERG is shown in the upper trace and VEPs recorded from O1, O2, and Oz are shown in the three lower traces in that order.

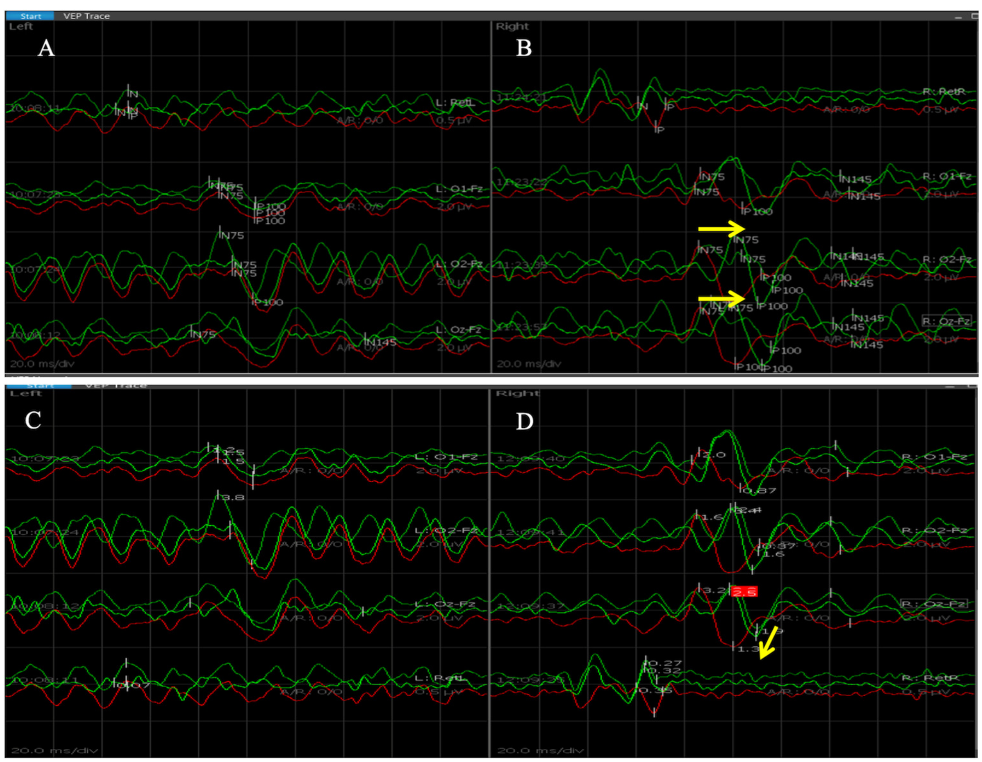

Fig. 4. This figure shows the latency shift of the P100 on the right side (B), and the amplitude reduction on the right side (D) while the waveform on the left side (A) (C) remain unchanged. The upper trace depicts the ERG recording which remained unchanged. The red average shows the recordings done at baseline and the green ones show averages of the latest recordings. The arrow shows the latency shift and the amplitude reduction between the baseline and the latest recording.

3. Discussion

This case report is the first to demonstrate the potential clinical prognostic value of intra-operative VEP latency shift during brain surgery under general anesthesia. We present a surgical case of an intraventricular benign tumor in the right atrium with close relation to the posterior bundle of the optic radiation. Intra-operative VEP showed transient amplitude reduction, which recovered during the operation. Meanwhile, a persistent VEP latency shift was observed. The patient experienced immediate post-operative left lower quadrant anopia, however, the deficit recovered nearly completely after the first post-operative month. Interestingly, half field VEPs recordings showed markedly reduced (nearly absent) responses from the left half field for both eyes.

Changes in VEP can be related to several mechanisms. Both in human and animal studies (Halliday et al., 1973; You et al.,

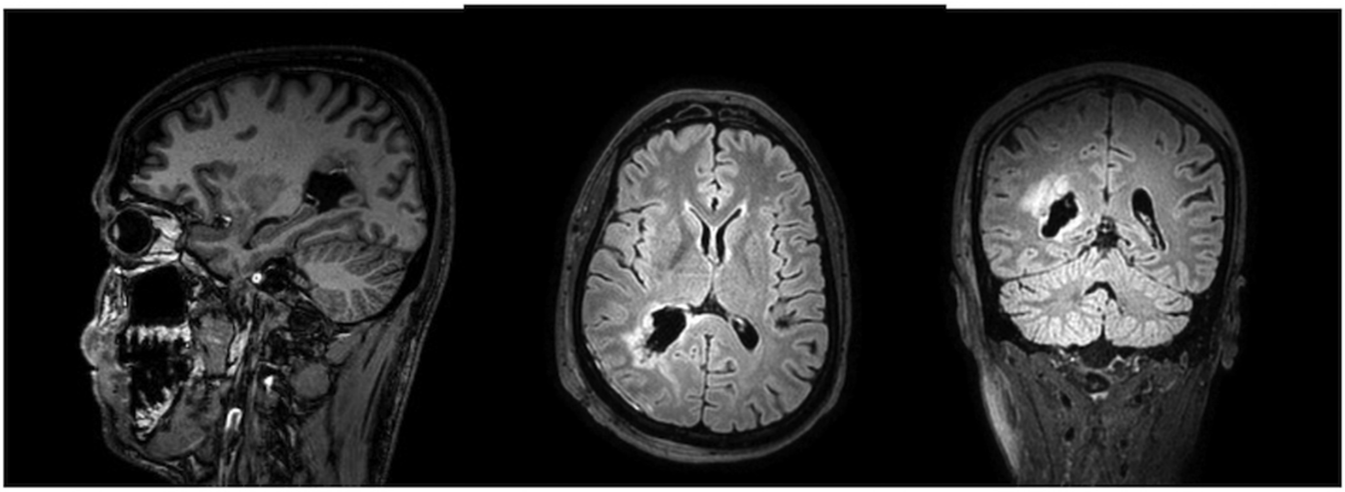

Fig. 5. A-C. Sagittal (T1), axial (FLAIR) and coronal (FLAIR) sections of MRI two days postoperatively showing no rest tumour.

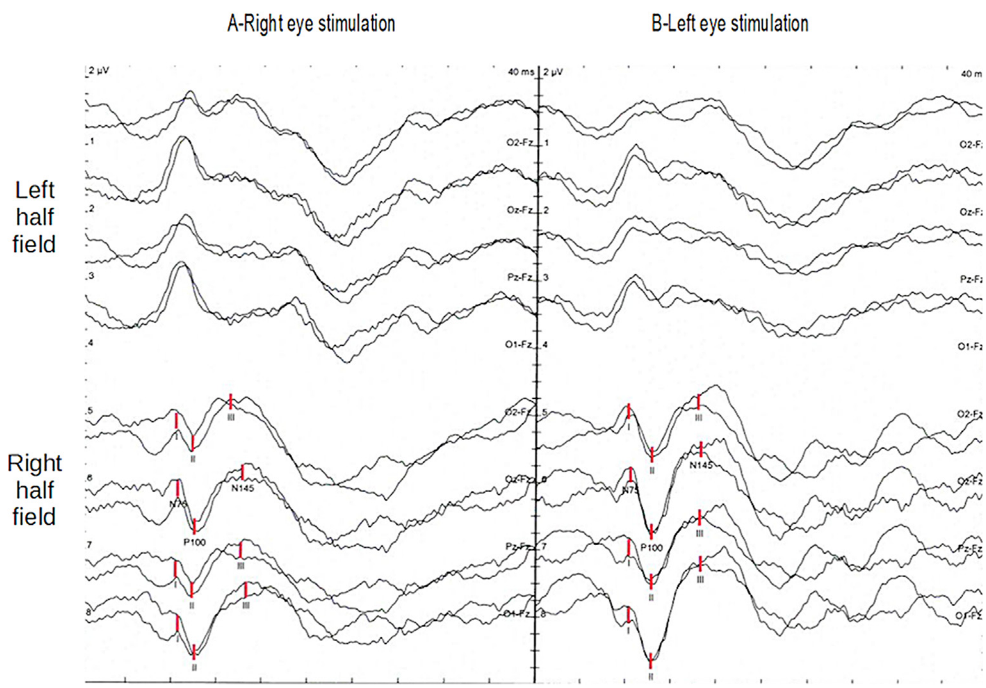

Fig. 6. This figure shows half field stimulation for A-right eye and B-left eye. The upper four curves in both A and B depict the VEP curves after left half field stimulation for the right (A) and for the left eye (B). Those curves are not well defined and thus the cursors were not placed. The responses were considered not present. The lower four curves in both A and B depict the VEP curves after right half field stimulation for the right (A) and for the left eye (B). The responses were well defined with normal latencies and amplitudes.

2011), the axonal loss was found to correlate with the reduction in VEP amplitudes, while the VEP latency was prolonged and reflected the amount of demyelination. In the operating room, the mechanisms may be quite different. Surgical maneuvers such as direct manipulation of the optic nerve, resection through or in vicinity of optic tract and ischemia may cause direct lesion of the neural pathways and thus be reflected as a reduction/loss in VEP amplitudes (Luo et al., 2015) or only disturb the neural transmission and thus be reflected as prolonged latencies. On the other side, as the nerve conduction velocity is determined by the fastest nerve fibers, direct lesion of those fibers could cause the latency prolongation. Other reasons that could influence the VEP signals include anesthesia with volatile agents (Wang et al., 1985). We did not use anesthesia with volatile agents and as the changes were observed only in one side, we do not believe that the generalized anesthesia caused the changes in the observed potentials.

We speculate that the reason for the amplitudes of the potential to recover and prolonged latency to persist is that the surgical procedure only caused disturbance of the fibers neuronal transmission but did not actually damage the fibers and did not cause axonal loss.

One of the limitations of this case report is that the presence of the noise in the operating room as shown in Fig. 4, may have obscured more clear visualization of changes. We do believe though that the latency shift og almost 10 ms shown the Fig. 4 can be appreciated despite the presence of the noise.

A clear correlation between the VEP changes and postoperative outcome has not been firmly established and conflicting results have been reported. Based on the 50% threshold, one study (Lou et al., 2015), showed that intraoperative monitoring of VEPs had a high negative predictive value (90%), and specificity (87–99%), while the sensitivity was very low (0–45%). It was not possible to report a positive predictive value because of lack of true positive cases.

Another study (Gutzwiller et al., 2018) reported that a decrease in amplitude of the VEP P100 wave of 20% correctly identified only 66.7% of cases with any postoperative change.

Consequently, it is difficult to base intra-operative surgical decision-making on the VEP amplitude alone, because signal impairment is not always associated with a post-operative visual deficit. On the other hand, a permanent visual deficit may have already been inflicted once a VEP amplitude reduction is detected. Furthermore, other studies have failed to confirm the association between VEP amplitude reduction and visual field impairment (Wiedemayer et al., 2003; Chung et al., 2012). Thus, alternative parameters are warranted to provide reliable intraoperative warning indications to the surgeon and help identify gradual and potentially reversible visual lesions.

As a conclusion, our case indicates that the VEP (P100) latency may hold additional valuable information, indicative of an imminent visual pathway injury and a potentially reversible functional deficit. Future studies are required to confirm the validity of the presented findings and establish an appropriate safety range of latency shifts.

Declaration of Competing Interest

None of the authors have any conflict of interest to disclose.

Acknowledgement

The work was not funded by a specific fund. All the authors, apart of Richard Brandmeir, work at the Aarhus University hospital, thus the work was funded by Aarhus University Hospital.

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