Vision Research 81 (2013) 1–5

Contents lists available at SciVerse ScienceDirect

Vision Research

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

Spared cognitive processing of visual oddballs despite delayed visual evoked potentials in patient with partial recovery of vision after 53 years of blindness

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ARTICLE INFO

Article history:
Received 9 July 2012
Received in revised form 29 November 2012
Available online 8 February 2013

Keywords:
Visual deprivation
Recovery from blindness
Motion-onset VEPs
Pattern-reversal VEPs
Oddball ERPs
P3b

ABSTRACT

We examined the visual and cognitive functions of a 72-year-old subject, KP, who recovered his sight after 53 years of visual deprivation. We used visual evoked potentials (VEPs) to pattern-reversal and motion-onset stimuli and cognitive responses (ERPs) during the oddball paradigm to assess the effect of long-term deprivation on a mature visual system. KP lost his sight at the age of 17 years, and light projection onto his right retina was restored at 71 years by a corneal implant. Nine months after sight recovery we recorded reproducible responses to all examined stimuli. The response to pattern reversal contained two P100-like peaks with the later peak being dominant and significantly delayed (260 ms) when compared to the P100s of two control subjects, to whom the stimuli were adjusted in size and contrast to mimic KP's vision. KP's motion-onset VEPs to full-field and peripheral stimuli had a characteristic shape with a well-defined N2 peak; however, both peaks were significantly delayed (262 and 272 ms) compared to control responses. Unlike the P100 and N2 peaks, which represent sensory detection, the P3b/P300 component of the ERP to a target event in the oddball paradigm was not further delayed. In spite of degraded vision and sensory deprivation lasting 53 years, KP displayed reproducible responses to all reported stimuli. Long-term visual deprivation and retinal detachment degraded KP's visual sensory processing, assessed by pattern-reversal and motion-onset VEPs, whereas the cognitive processing of appropriate visual stimuli was not compromised.

1. Introduction

Cortical structures involved in the analysis and interpretation of visual information are plastic, and their long-term deprivation can lead to a change in or limitation of visual functions. From the sparse literature, it is known that the restoration of optical projection to the retina after long-term light deprivation is not associated with full recovery of active vision (Carlson & Hyvarinen, 1983; Carlson, Hyvarinen, & Raninen, 1986; Sacks, 1995; Valvo, 1972).

Here we report electrophysiological examination of a 72-year-old subject, hereafter referred to as KP, whose sight was recovered after 53 years of visual deprivation. Measuring evoked/induced brain activity enabled us to assess his cortical functions and to investigate the changes in a fully-matured visual system due to deprivation of normal visual experience.

Examination of such subjects is interesting from the medical point of view, as the development of implantable visual prosthetics is in progress (Ahuja et al., 2011) and the limitations of cortical plasticity are an important issue. In a literature search, we found only one relevant report of pattern-reversal VEPs following vision restoration. Subject MM lost his vision at 3 years and light projection was restored to his right eye after 40 years by corneal replacement (Fine et al., 2003) (supplementary material of the article).

Our aim was to compare KṔs sensory vs. cognitive processing. On the level of sensory detection we assessed VEPs in response to (i) – reversal of a checkerboard pattern to evaluate P100 peaks originating from primary visual areas (V1)(Barnikol et al., 2006; Di Russo et al., 2005) and (ii) – motion-onset of low-contrast structures activating magnocellular input of the dorsal stream (Heinrich, 2007; Kuba & Kubova, 1992) to evaluate the dominant N2 peak originating in extrastriate areas (V3A, V5) (Schellart et al., 2004). On the level of cognitive processing we measured P3b waves recorded in response to visual target stimuli during the oddball paradigm (Duncan et al., 2009). This paper discusses KP's electrophysiological results in detail and compares his sensory and cognitive responses to reactions of two controls examined with stimuli adjusted to match KP's impaired vision.

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http://dx.doi.org/10.1016/j.visres.2012.12.013

2. Methods

2.1. Subjects

KP lost his sight at the age of 17 years due to burning of his cornea caused by an explosion of molten metal in a factory where he worked. The burn left only a sparse sense of light with no form or shape perception.

Full projection of light onto KP's right retina was restored, after a series of unsuccessful corneal implantations, at the age of 71 years (September 2009) by implantation of a Boston KPRO type I keratoprosthesis. The cornea was attached to his eyelid, meaning saccades were limited in either direction. The cornea was opaque and vascularized.

A few weeks after the surgery, his visual acuity was 0.33. We had the opportunity to examine KP 9 months later (June 2010), when his vision had significantly deteriorated. Eleven months after surgery (August 2010), his eye surgeon diagnosed retinal detachment, and KP's vision rapidly returned to the pre-treatment level. In spite of the short period of regained vision, KP considered this time as "the best gift", allowing him, for example, to see his wife for the first time.

On the day of the examination conducted KP's right eye visual acuity was 0.04 and its contrast sensitivity was 33.8 %; the left eye was without shape/contrast discrimination. Visual acuity and contrast sensitivity were measured before electrophysiological acquisition from the distance used for stimulus presentation (0.6 m) on computer monitor by the Freiburg Visual Acuity Test (4 choices, 24 trials, screen resolution 1600 × 1200 pixels, luminance contrast 96%) (Bach, 2007). Michelson contrast sensitivity was determined using a Landolt's circle of 180 arc min.

KP's responses were compared to the responses of two healthy age-matched controls (C1 and C2) that we recruited by advertisement in a local newspaper. The right eye was examined in all subjects. The visual acuity for C1 was 0.38 and for C2 was 0.74 all examined without correction glasses correspond to natural presbyopia. The contrast sensitivity was 0.9% for C1 and 2.36% for C2. Both controls' latencies of assessed VEPs/ERPs components were shorter than 95 percentile of age related subgroup of healthy subjects ($n = 35$, age 55–85, median 71 years) (Kuba et al., 2012).

We obtained informed consent from KP and both controls after the test procedure was explained. The examination was part of a study approved by the Ethical Committee of the Faculty of Medicine in Hradec Králové, and experiments were conducted in accordance with the Declaration of Helsinki (2004).

2.2. Procedure

Examination was performed in a darkened, sound-attenuated, electromagnetically shielded room with a background luminance of 0.1 cd/m^2. During the experiment, the subjects were sitting in a comfortable dental chair with a neck support to reduce muscle artifacts. Correct fixation was monitored via a near-infrared CCD camera.

All stimuli including visual acuity and contrast sensitivity measurement were presented on a 21″ computer monitor (Vision Master Pro 510, Iiyama, Japan) subtending 37 × 28 deg of the visual field from observing distance of 0.6 m.

VEP/ERP were recorded from 6 unipolar derivations (O_L, O_Z, O_R, P_Z, C_Z, F_Z) with a right earlobe reference. The minimum set of recording derivations was chosen on the basis of a previous topographical study concerning the scalp distribution of motion-onset VEPs (Kremlacek & Kuba, 1999). The ground electrode was connected to the reference. All electrode impedances were kept below 5 kΩ. After amplification in the frequency band of 0.3–100 Hz (PSYLAB, System 5, Contact Precision Instruments, USA), the signal was stored for offline processing on a personal computer. The recording was synchronized with a backward trace of the monitor's electron beam just before the first video frame of an appropriate stimulus change.

Forty time periods were recorded, and those time periods with amplitudes exceeding 70 μV were rejected (suspected artifacts). The rest of the responses were smoothed by a second-order polynomial Savitzky–Golay filter (across 47 samples).

2.3. Pattern-reversal

Over 20 s, forty reversals of a high contrast black and white checkerboard pattern were used to evoke pattern-reversal VEPs. Check size was changed during examination from 40 to 240 arc min, contrast was kept 96%. Controls were examined using parameters evoking a stable response in KP, i.e., a contrast of 96% and a check size 160 arc min. Then, to simulate KP's low vision, check size was decreased to *160 arc min* (KP's VA/controls VA)*, that was 16 arc min for C1 and 9 arc min for C2. The contrast was decreased to two levels: (a) the same absolute amount of contrast above controls' contrast threshold (CS) as KP had *(96% – KP's CS)*, i.e., 60% for both C1 and C2, or (b) a proportion above their contrast threshold *((96%/KP's CS)∗ controls CS)*, i.e., 3% for C1 and 7% for C2.

The pattern-reversal was presented using Visual Stimulus Generator 2/5 (CRS Ltd., UK) at a vertical refresh frequency of 105 Hz. The mean luminance of 17 cd/m^2 was kept constant. 440 ms of post-stimulus EEG sampled at 500 Hz were averaged for VEPs. Subjects were instructed to keep their gaze on the fixation point during recording, which took about 30 s for one VEP.

2.4. Motion-onset

To elicit motion-onset VEPs, we used a radial circular pattern corrected for equal visibility in the whole stimulus field by a magnification factor [CMF = 1/(0.1 × eccentricity [deg] + 1)] used for motion stimuli in our lab (Kremlacek et al., 2004). The local motion velocity increased (5–25 deg/s) while spatial frequency decreased (1–0.2 c/deg) toward the periphery (the temporal frequency of 5.1 c/s was kept constant over the whole stimulus field).

The structure moved for 200 ms and then it was stationary for 1 s. To avoid direction-specific adaptation that would result in a motion after-effect, we changed the motion direction randomly (centrifugal or centripetal).

Two variants of motion stimulation were used: full field and peripheral. During the full field variant, the stimulus occupied the whole monitor area, while for the peripheral variant, the central 20 deg were masked by a grey circle of average luminance with a fixation point in its center.

The Visual Stimulus Generator 2/5 presented motion-onset stimuli at a vertical refresh frequency of 105 Hz and the constant mean luminance of 17 cd/m^2. EEG post-stimulus periods of 440 ms duration was sampled at 500 Hz. Subjects' task was to keep their gaze on the fixation point during recording, which took about 60 s for one VEP. For KP, we had to increase the Michelson contrast to 96%. Controls were examined using a contrast value of 96%, 10% and proportionally above their contrast threshold *((96%/KP's CS)∗ controls CS)*, i.e., 3% for C1 and 7% for C2.

2.5. Oddball

The cognitive processing of visual information was tested in the oddball paradigm. The stimulus consisted of a black outline of a square (the frequent stimulus) and a circle (the rare stimulus) appearing with probability 0.12. ISI was randomized between