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Research article

Interaction of ^{12}C ions with the mouse retinal response to light☆

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HIGHLIGHTS

- Astronauts report phosphenes possibly caused by heavy radiation.
- The mouse retina was stimulated by light or light + ^{12}C ions in particle accelerator.
- ^{12}C accelerated ions appear to compete with light at photoreceptor level.
- ^{12}C ions enhance the retinal oscillatory and the cortical responses to light.
- A manifold effect of heavy ions on the retina may result in malfunctioning in space.

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ABSTRACT

Astronauts in orbit reported phosphenes varying in shape and orientation across the visual field; incidence was correlated with the radiation flux. Patients with skull tumors treated by ^{12}C ions and volunteers whose posterior portion of the eye was exposed to highly ionizing particles in early studies reported comparable percepts. An origin in radiation activating the visual system is suggested. Bursts (~4 ms) of ^{12}C ions evoked electrophysiological mass responses comparable to those to light in the retina of anesthetized wild-type mice at threshold flux intensities consistent with the incidence observed in humans. The retinal response amplitude increased in mice with ion intensity to a maximum at ~2000 ions/burst, to decline at higher intensities; the inverted-U relationship suggests complex effects on retinal structures. Here, we show that bursts of ^{12}C ions presented simultaneously to white light stimuli reduced the presynaptic mass response to light in the mouse retina, while increasing the postsynaptic retinal and cortical responses amplitude and the phase-locking to stimulus of cortical low frequency and gamma (~25–45 Hz) responses. These findings suggest ^{12}C ions to interfere with, rather than mimicking the light action on photoreceptors; a parallel action on other retinal structures/mechanisms resulting in cortical activation is conceivable. Electrophysiological visual testing appears applicable to monitor the radiation effects and in designing countermeasures to prevent functional visual impairment during operations in space.

1. Introduction

Astronauts on Apollo, Skylab, MIR or International Space Station missions reported positive visual phenomena (phosphenes) in the form of white *flashes of light* varying in shape and orientation across the visual field; colors were occasional [17,41,29]. Incidence depended on orbital height and latitude; a temporal relationship with heavy ion flux was observed [7,35,36,4,3,8]. Comparable percepts were described in early experiments by volunteers whose posterior, but not anterior portion of the eye was exposed to highly ionizing particles at energies below the Cerenkov threshold for visible light [6,22]. Phosphenes were also reported by patients with skull base tumors (chordomas, chondrosarcomas) treated with ^{12}C

Abbreviations: ERG, electroretinogram; VEP, visual (cortical) evoked potentials; OPs, retinal oscillatory potentials.

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ions (80–400 MeV/n energy range); incidence was highest with the energy directly deposited on or near the retina [45]. An origin of phosphenes in radiation activating the visual system is suggested [6,35,22,23,8,41,30] and could add to the manifold health hazard related to orbital flights [11,10].

Irradiation of the anesthetized wild-type C57BL/6J mouse retina by bursts of accelerated ^{12}C ions evoked electrophysiological mass responses in the retina and resulted in activation of the visual cortex [42]. The threshold flux intensity (~1000 particles/response) was consistent with the response incidence in human studies [6,29]. The retinal response was comparable to that evoked by light, although with smaller amplitudes and increased latencies; an early negative *a*-wave preceded the *b*-wave. These findings are consistent with the activation by ^{12}C ions of photoreceptors *in vitro* [32]. However, the retinal response amplitude increased with ion intensity from the ~1000 ions/burst (0.36 mGy/burst) threshold to a maximum at ~2000 ions/burst (0.72 mGy/burst), to decline sharply at higher intensities; the inverted-U relationship suggests the involvement of retinal structure(s) other than photoreceptors and events possibly occurring downstream of photoreceptor activation [42]. The interaction between light stimuli and bursts of ^{12}C ions have been used in this study as a test stimulus condition to obtain additional information on the processes started at retinal level following irradiation.

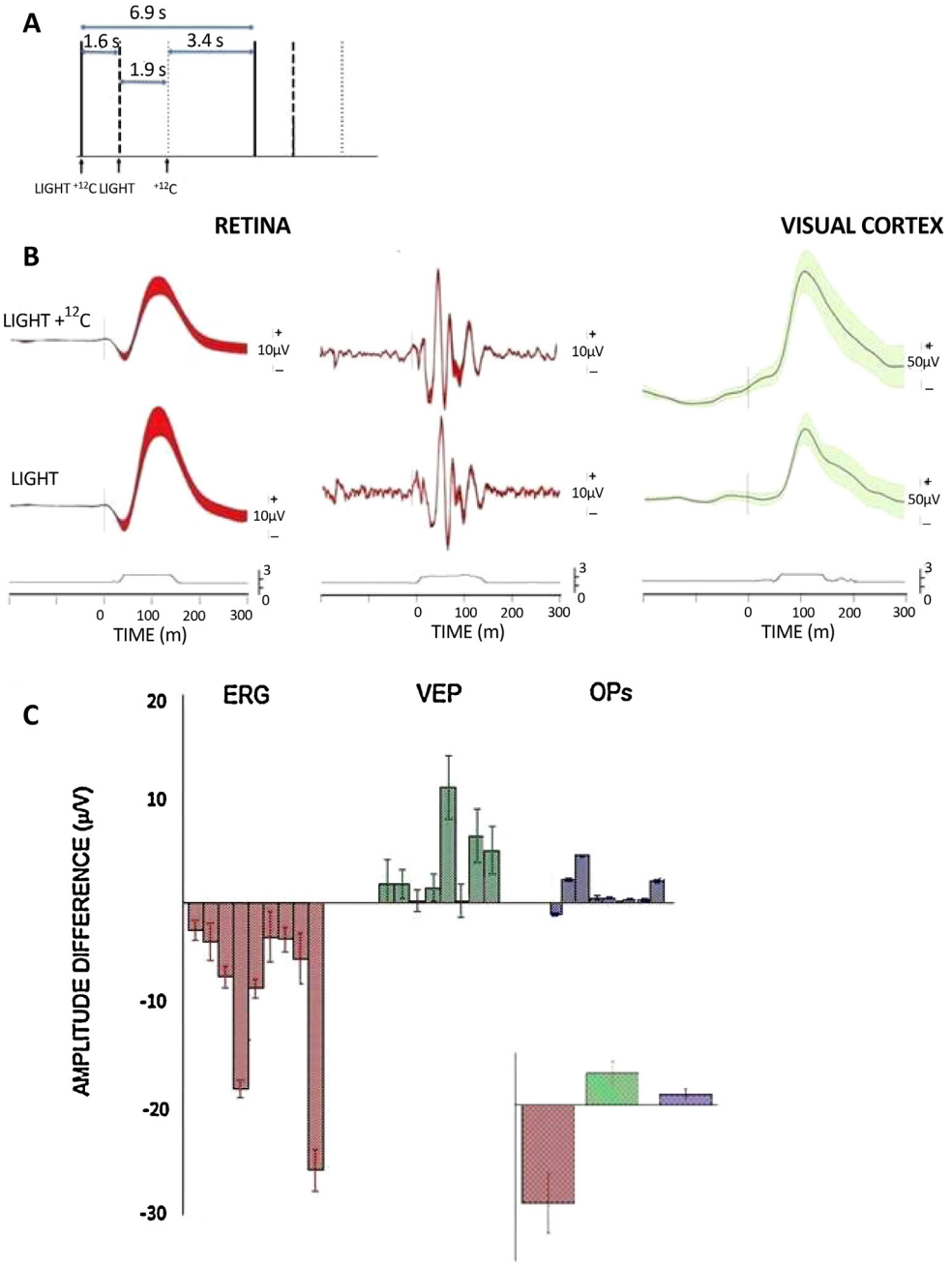

Fig. 1. (A) Schematic outlook of the stimulation paradigm and intervals between stimuli. Each sequence (LIGHT + ^{12}C, LIGHT alone, beam alone) was repeated over 200 times. (B) Grand averages and SE of the retinal low frequency [left], oscillatory and cortical responses to the LIGHT + ^{12}C association (top) or to LIGHT alone (middle). Vertical bars: Light stimuli and beginning of ^{12}C ion bursts. Bottom: significance at the paired *t*-test between the responses to LIGHT or LIGHT + ^{12}C, indicating the time windows for comparing amplitudes of responses in the two stimulus conditions ($p < 0.02$). ERG and VEP signals averages of 9 mice; OPS average of 8 mice. (C) Differences in amplitude between each mouse responses to LIGHT and to LIGHT + ^{12}C; average response (200 stimuli) and SE for each tested animal. Averages and SE across animals of the ERG ($p < 0.002$), retinal OPS ($p < 0.05$) and VEP ($p < 0.003$) are reported in inset at lower right. Statistics in the text.