Charles Bonnet syndrome and periodic alternating nystagmus
Moving visual hallucinations

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Abstract

Objective
To describe and discuss potential mechanisms for modulation of visual hallucinations by nystagmus.

Methods
We present 2 patients with coexistent Charles Bonnet syndrome and periodic alternating nystagmus in the context of acquired visual loss.

Results
The combination has given rise to a rare phenomenon: visual hallucinations that move in a manner governed by the nystagmus, specifically by the direction and velocity of the slow phase. The perceived modulation of movement is selective for a surface in one case and a landscape in the other but not present for hallucinated individual objects and people separate from the hallucinated background visual scene.

Conclusions
The collision of Charles Bonnet syndrome and periodic alternating nystagmus in these 2 patients has demonstrated that some visual hallucinations can be modulated by, or collaterally with, ocular movements. We propose 2 potential mechanisms based on ocular proprioceptive input from extraocular muscles projecting to either extrastriate processing of visual scene, or to higher-order visual cortical areas involved in analysis of motion signals across the whole visual field.
In Charles Bonnet syndrome (CBS), visual hallucinations occur following visual impairment. Spontaneous activity in extrastriate visual cortex may be the mechanism.1,2 Periodic alternating nystagmus (PAN) is a central vestibular nystagmus characterized by continuous cycles of horizontal left-beating nystagmus followed by a transition phase, then right-beating nystagmus. PAN can be congenital, acquired (cerebellar), or develop following visual loss.3 Both CBS and PAN may resolve with visual restoration.4

We present 2 patients with CBS and PAN whose visual hallucinations were in constant motion synchronous with the nystagmus.

Case 1

Case 1 was a 62-year-old woman, blind from bilateral retinal detachment. Her medical history included nephrotic syndrome, hypertension, left mastoidectomy (without vertigo), and migraine with visual aura.

Several months after losing sight, she developed visual hallucinations. Constantly present was the hallucination of a surface, textured like a brown brick wall, in horizontal rotational motion around her. In addition, she experienced intermittent formed hallucinations of people and objects (e.g., “toby jugs”), lasting seconds to minutes, which remained stationary, between her and the moving “wall.” She continued to experience migraine aura (teichopsia), which did not exhibit rotational motion.

On examination, visual acuity was no perception of light bilaterally. A horizontal jerk nystagmus was observed that periodically changed direction, each cycle lasting approximately 80 seconds (range 30–90 seconds measured by infrared corneal reflection oculography). A vertical component was present as the direction changed (windmill nystagmus). The nystagmus increased in amplitude and frequency when, on verbal instruction, she directed her eyes toward the fast component (Alexander’s law) and was suppressed by attempted fixation on her own stationary hand. She generated pursuit eye movements by following her hand.

She described the hallucinatory wall as moving, first in one direction, gathering speed, slowing down, and stopping before reversing direction in repeating cycles. Her description correlated with the velocity and direction of the slow phase of the nystagmus (figures 1 and 2). Other hallucinatory objects and people did not move. She had no residual vision and plunging her into total darkness affected neither the nystagmus nor hallucinations. The remainder of the neurologic examination was normal apart from conductive deafness (mastoidectomy). Blood investigations including thiamine levels, EEG, and brain CT were normal.

She found the constant motion of the surface disturbing. Baclofen had no effect. Botulinum toxin injections in all 4 horizontal recti extraocular muscles exacerbated the nystagmus’ vertical component, correspondingly causing the perceived wall to move vertically. Retrobulbar bupivicaine 0.5% injection partially reduced both the nystagmus amplitude and corresponding movement of the wall. Immobilizing the eyes temporarily by grasping both lateral rectus tendons with forceps (under local anaesthesia) halted the motion of the hallucination.

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**Glossary**

CBS = Charles Bonnet syndrome; PAN = periodic alternating nystagmus.
Case 2

Case 2 was an 85-year-old man with bilateral, slowly progressive, visual impairment secondary to anterior segment and retinal pathology with no significant medical history. He experienced intermittent visual hallucinations of rows of "London-style" town houses and red buses in the distance. The scene was in constant horizontal motion and periodically changed direction. He experienced no oscillopsia of real objects seen with his residual vision.

On examination, visual acuity was perception of hand movements bilaterally with extensive visual field loss. He had jerk nystagmus in the horizontal plane that periodically changed direction, each cycle lasting approximately 40 seconds. He described houses as moving in one direction, slowing to a stop (at which point he was able to "see" down the alleys between houses), then moving in the opposite direction. The buses drove forward, slowed to a stop, then drove backward. His description of the hallucinatory movements in real time correlated with the clinical intensity and direction of the slow phase of the nystagmus, recorded on video tape. Neurologic examination was normal. The patient declined further investigations or treatment.

Data availability statement
Any further anonymized data will be shared by request from qualified investigators.

Discussion

We describe a unique phenomenon: visual hallucinations in cyclical motion modulated in synchrony with PAN.

Both our patients developed CBS and PAN following visual loss. Neither patient was troubled by the hallucinatory images, only by their constant motion. Neither patient had cerebellar dysfunction, the usual cause of acquired PAN. In acquired PAN, smooth pursuit and visual suppression of nystagmus are absent, and baclofen, a γ-aminobutyric acid type B receptor agonist, can be effective at reducing nystagmus. None of these were true for case 1. Possible etiology in our cases is latent congenital PAN or, more likely, destabilization of the visual cortex, including areas controlling motor function and eye movements. These cases lead us to propose that hallucinatory visual percepts can be modified by nonvisual information. The hallucinations themselves were typical for CBS: objects and people (case 1), surfaces or textures (case 1), and landscapes (case 2). The perceived motion is selective for hallucinations occupying the entire visual field—a surface (case 1) and an urban landscape (case 2), with no modulation of isolated objects or people (case 1). Furthermore, there was neither modulation of migraine aura (case 1) nor real objects (case 2).

We suggest that the nystagmus influenced the visual hallucinations by ocular proprioceptive signals modulating neural activity in higher cortical visual centers. This is supported by case 1, in whom mechanical fixation of extraocular muscles was the only intervention stopping motion of the hallucinations.

The extraocular muscles have stretch receptors and proprioceptive organs, from which afferent input is carried in the trigeminal nerve to Purkinje cells of the cerebellum. Although a role for ocular proprioceptors in eye movement control has long been debated, experimental data suggest ocular proprioceptors have a role in signaling eye-in-orbit position during visuo-postural control, specifically reorienting visuo-postural responses according to gaze direction. There are strong interactions between visual, vestibular, and ocular-proprioceptive inputs in multiple CNS areas, including cerebellum and visual cortex, where ocular proprioceptive signals could add a sense of motion to spontaneously generated images.

Functional MRI studies of CBS have demonstrated a correlation between location of activity and semiology of hallucination. Hallucinations of surfaces are associated with activity in the collateral sulcus, an area that responds normally to visual textures. Hallucinations of unfamiliar faces correlate with the left middle fusiform gyrus and objects with the right middle fusiform gyrus, again as in normal visual processing. One explanation for the phenomenon reported here is that extraretinal ocular proprioceptive signals input to extrastriate visual areas involved in perception of visual scene, including the collateral sulcus, but not to visual areas involved in object or face analysis, or striate cortex where tachyopsia is generated.

An alternative explanation is that perceived motion of visual hallucinations is processed by cortical areas V5 and V6, as for normal vision. V5 analyzes motion signals in the central visual field, like that of individual objects relative to the background. V6 analyzes self-motion relative to the whole visual field, utilizing extraretinal input to real-motion cells. Modulation of ocular proprioceptive input by nystagmus may selectively influence the perceived motion of full-field hallucinations such as the wall (case 1) and urban landscape (case 2), processed by V6, but not hallucinations occupying the central visual field like the toby jugs and people seen in front of the wall (case 1), processed by V5.

Other examples of afferent modulation of hallucinations include precipitation of hallucinations at low-light levels and elimination by improvement in vision, e.g., after cataract surgery. An unusual case of monocular hallucinations has been reported whereby occlusion of the affected eye (not totally blind) eliminated the hallucinations.

Author contributions
N. Minakaran: conceptualization of the study, interpretation of the data, drafted the manuscript for intellectual content.
T. Soorma: drafted the manuscript for intellectual content. A.M. Bronstein: conceptualization of the study, major role in acquisition of data, revised the manuscript for intellectual content. G.T. Plant: conceptualization of the study, major role in acquisition of data, revised the manuscript for intellectual content.

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