



Charles Bonnet Syndrome: Complete Remission of Visual Hallucinations with Trazodone

Ricardo Krause Martinez de Souza^{1,3,4,†}, Rodrigo Tomazini Martins², Pedro André Kowacs^{3,4}

ABSTRACT

Charles Bonnet syndrome (CBS) is a neuro-ophthalmic condition that affects elderly people with visual impairment related to ophthalmological pathologies. It is characterized by complex visual hallucinations with insight into the unreality of the perceptions and preserved cognitive status. Its mechanism involves spontaneous neuronal discharges of the visual cortex secondary to deafferentation of visual input. Treatment should address to its ophthalmologic etiology but pharmacological management of visual hallucinations may be done as well. We report a case of an 86-year-old woman with a characteristic clinical picture of CBS that had complete remission of her visual hallucinations with trazodone treatment. Perhaps trazodone effect on blocking neuronal plasticity through its action at 5-HT_{2C} receptors may control visual hallucinations. Its prescription should be considered as one of the first steps in the management of Charles Bonnet syndrome.

Keywords

Charles Bonnet Syndrome, Trazodone, Visual hallucinations, Antidepressant, Treatment, Neuro-ophthalmology

Introduction

Charles Bonnet Syndrome (CBS) consists of the presence of complex visual hallucinations, in which patients have insight that the visual perceptions are not real. In addition, mental disorders should not coexist and cognitive status should be preserved. Visual loss should be present, mainly that due to age-related macular degeneration (AMD) and other ocular pathologies [1]. The etiology of CBS involves deafferentation of the visual system that leads to spontaneous neuronal discharges and consequently abnormal sensory perceptions [2-4].

The case of a CBS patient in who complete remission of visual hallucinations was attained after trazodone was added-on. The putative mechanism

through which trazodone exerted its effect on CBS visual hallucinations is discussed, and its role on the treatment of CBS is emphasized.

Case Report

An 86-year-old woman sought specialized care because of visual hallucinations and insomnia. Her visual hallucinations had started two years before. The hallucinations were intermittent and characterized by visions of colored animals, people, and faces. Although these symptoms were distressing, she had insight that they were not real. Her major concern was with the possibilities of dementia or a psychiatric illness. Despite regular CPAP use, the patient had several episodes of awakening during the night

¹Memory Center of Curitiba, (CMC), Curitiba, PR, Brazil

²Box Hill Hospital, Neurosciences Department, Melbourne, Australia

³Instituto de Neurologia de Curitiba (INC), Curitiba, PR, Brazil

⁴Clinics Hospital and Federal University of Parana, Curitiba, Brazil

[†]Author for correspondences: Ricardo Krause Martinez de Souza, Rua Marechal Deodoro 2152 – ZIP 80045-235, Curitiba, PR, Brazil, Tel: + 55 (41) 32641020; Fax: + 55 (41) 32641020; email: ricardo.neurologia@gmail.com

and reported her sleep not to be restorative. Her previous medical history included several comorbidities, including hypertension, chronic insomnia, and severe sleep apnea with the use of a CPAP machine, fibromyalgia, tinnitus, bilateral mild sensorineural hearing loss, and sporadic presentation of migraine with aura since a young age. Additionally, bilateral age-related macular degeneration had been diagnosed 20 years ago. At the time, her visual acuity was approximately 20%. The neurological examination was normal. She scored 27 points on the Mini-Mental State Examination (MMSE) [5] and her neuropsychological assessment was normal for her age. Complementary investigation consisted of laboratory tests for dementia [6] and magnetic resonance imaging of the brain (MRI), all unremarkable. She used several medications regularly, such as nortriptyline, pregabalin, losartan, metoprolol, pantoprazole, ginkgo biloba, alprazolam, and PRN naratriptan. She had already been taking donepezil (10 mg) and quetiapine (25 mg) q. d. for two months before starting her follow-up at our center. Trazodone was started with the goal of improving the sleep disturbance. A week after trazodone was added-on her visual hallucinations faded away. Currently, the patient is 90-year-old and has been regularly taking trazodone at a dose of 50 mg, q.d., for four years. At an attempt to wean her off trazodone, visual hallucinations returned, but were controlled again after reinstatement of the drug.

Discussion

In elderly patients with visual hallucinations, it is imperative to differentiate psychiatric diseases (bipolar disorder), neurological diseases (intracranial tumor, epilepsy), delirium, and neurodegenerative diseases, such as Alzheimer's disease, Lewy body dementia, and Parkinson's disease [7]. Regarding the aforementioned case, the presence of ophthalmological impairment associated with awareness of the hallucinatory nature of the visual phenomena and with normality of clinical and neurological investigations characterized the patient as having CBS.

In CBS, spontaneous and/or stimulus-driven hyperexcitability of unimodal associative visual cortex underlies hallucinatory phenomena [3,4]. This mechanism seems to be alike that seen in other sensorial deafferentation conditions, such as tinnitus and musical hallucinations (for hearing) and phantom limb pain (for nociception) [8]. The reason why only some

individuals develop such hallucinations might be related to specific wiring conformation and/or presynaptic neurotransmitters concentrations and/or pre/post synaptic receptor avidities and densities. Since cognitive and behavioral circuitry is not involved, subjects keep aware of the hallucinatory nature of their visual perceptions.

The first step in the management of CBS is to treat the underlying ophthalmologic condition to enhance visual input thus inhibiting hallucinations. If this approach fails, pharmacological therapy may be considered. There is no specific drug treatment for CBS. Several medications were reported to be tried, based on hypothetical mechanisms of the condition at the time of their prescription, such as membrane-stabilizing drugs (carbamazepine, valproic acid, gabapentin, phenytoin), antipsychotics (risperidone, olanzapine, haloperidol, sulpiride, quetiapine) and other medications, such as mirtazapine, trazodone, cisapride, donepezil, pregabalin, clonazepam, and ondansetron [9-11]. Evidence of the efficacy of these drugs is limited and based on uncontrolled studies and case reports. One of these studies reported improvement in visual hallucinations with pregabalin [10]; however, our patient had used pregabalin for 2 years for the treatment of fibromyalgia without control of her visual hallucinations. In this same study, the authors reported lack of response of CBS hallucinations to neuroleptics and anti-dementia drugs. Likewise, in the case herein described, hallucinations did not improve with donepezil and antipsychotics. Quetiapine, prescribed at another medical center, failed to control our patient's visual symptoms. Alamri [11] had noted no improvement in a patient's hallucinations with quetiapine; however, in his report, the changeover to risperidone was effective.

A single study has reported three cases of CBS patients whose hallucinations improved with trazodone [12]. Trazodone has dose-dependent hypnotic and antidepressant effects due to weak serotonin (5-HT) reuptake inhibition and through 5-HT_{2A}, 5-HT_{2C}, α_1 -adrenergic, and histamine H₁ receptor antagonism [13].

It is known that hallucinatory phenomena are based not only on spontaneous or stimulus-driven increased neuronal firing but also on neuroplasticity [14]. Trazodone is reported to block neuroplasticity through its 5-HT_{2C} receptor antagonism [15], and perhaps the same "monoaminergic" effect could explain its efficacy in treating visual hallucinations.

Our report adds to that of Hsu et al. [12] and points trazodone to be considered as a first-line treatment for CBS, due to its good tolerability and few interactions with other drugs. Trazodone is also considered to be a safe medication for the elderly, with fewer side-effects as compared to neuroleptics, anticonvulsants, and acetylcholinesterase inhibitors. Unfortunately, a controlled trial of trazodone for CBS seems unlikely since its patent has already expired. Because of trazodone aforementioned efficacy in CBS, perhaps its use should be more heavily tried in subjects bearing CBS or other hallucinatory phenomena such as tinnitus, musical hallucinations and phantom limb pain.

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