

HALLUCINATORY EXPERIENCES IN VISUALLY IMPAIRED INDIVIDUALS: CHARLES BONNET SYNDROME – IMPLICATIONS FOR RESEARCH AND CLINICAL PRACTICE

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SUMMARY

Background: Charles Bonnet syndrome (CBS) refers to visual hallucinations that occur in individuals with preserved cognitive functions associated with visual impairment.

Methods: This article reviews occurrence of visual hallucinations in subjects with CBS by journals published in English in the Pubmed database in the period 1992-2018. Criteria for selection of appropriate papers were sufficient information and perspicuous view on pathogenesis, epidemiology, clinical presentation and treatment possibilities of CBS.

Results: Most commonly, visual hallucinations in patients with CBS are complex, repetitive and stereotyped. Such individuals have preserved insight that those percepts are not real, and there is an absence of secondary explanatory delusions and hallucinations within other modalities. Seeing as the aforementioned percepts do not share all the characteristics of hallucinations, it remains unresolved how they should be referred to. Terms as release hallucinations, one that is reflecting its underlying pathogenesis, or confabulatory hallucinatory experiences have been proposed. Moreover, CBS has also been referred to as phantom vision syndrome and may occur in any ophthalmological disease. It is not particularly connected with loss of function along any level of the visual pathway. Although this syndrome is mostly associated with age-related macular degeneration, glaucoma and cataract, it could be related to almost any other ophthalmological conditions. The incidence of CBS alongside with mostly other ocular pathology is rising as population is ageing.

Conclusions: Nonetheless, CBS remains commonly underreported, under recognized and/or misrecognized. Albeit the treatment recommendations and guidelines are not yet fully established, it is important to raise awareness of this specific and distinct condition, which inevitably implicates many differential diagnostic deliberations.

Key words: visual hallucinations - Charles Bonnet syndrome - low vision - mental health in elderly

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INTRODUCTION

Visual hallucinations may be a feature of many different medical conditions such as psychiatric and neurodegenerative diseases, metabolic disorders and use or abuse of some medications. However, visual hallucinations may be also experienced by mentally healthy individuals with reduced visual function due to ophthalmological conditions, most commonly age-related macular degeneration (ARMD), glaucoma and cataract (Al-Zubidi & Lee 2015). Charles Bonnet syndrome (CBS) is characterized by the occurrence of complex visual hallucinations in individuals with preserved cognitive functions which are associated with visual impairment. Charles Bonnet was first to describe such visual hallucinations experienced by his grandfather in his late eighties that were caused by visual deterioration after bilateral cataract surgery (Menon et al. 2003). He was mentally stable and fully aware that these experiences, which consisted of vivid images of people, animals and buildings with variations in size and shape, were not real (Menon et al. 2003). Interestingly, Charles Bonnet himself experienced visual hallucinations because of visual im-

pairment in his early age. The term Charles Bonnet syndrome (CBS) was latter introduced in literature in the 1936 by De Morsier who recognized the importance of this phenomenon and since then it has been widely accepted. CBS came into focus of many medical specialties, particularly neurology, psychiatry, ophthalmology and geriatrics (gerontology). Visual hallucinations in CBS are also known as “phantom vision” as they may be caused by the lesion along the visual pathway (O'Farrell et al. 2010, Pang 2016). Furthermore, they are also named “release hallucinations” due to the widely accepted theory of their pathogenesis (Pelak 2017). More recently, Charles Bonnet plus syndrome, or atypical CBS has been described. Such a condition is characterized by any kind of visual hallucinatory experiences that could be considered as CBS but accompanied by low awareness of patients (low insight), cognitive decline and other hallucinatory experiences (Engelberg & Vaidya 2016). Thus, we aimed to review the available evidence on CBS and emphasize its importance in order to improve its detection and avoid all possible unnecessary inconveniences that such experiences might cause to already vulnerable patients.

EPIDEMIOLOGICAL CONSIDERATIONS

The nature, frequency of occurrence and duration of hallucinations in mentally healthy elderly individuals is still not fully understood. Advanced age with all its accompanying issues brings certain additional risks that could contribute to occurrence of hallucinatory experiences, such as age-related decline in sensory capacity, psychological and psychosocial risk factors and other age-related specific factors (Badcock et al. 2017). Prolongation of life expectancy and ageing population, issues in today's society towards aging and abnormal experiences in general could all contribute to the inducement of a large range in the prevalence of this disorder (Pang 2016, Badcock et al. 2017). Furthermore, considering the fact that patients with hallucinatory experiences which they are aware of, most commonly avoid to report them to their physicians, friends or family members, because they might think that patients with CBS could have a problem with mental health and may be pronounced as mentally "unstable". The prevalence of CBS varies due to several reasons: inconsistencies of diagnostic criteria, the fact that patients (especially critical ones) are unwilling to report hallucinatory experiences and possibility that the condition is not recognized or it is misrecognized. It was reported recently that CBS occurs in 11 to 15 % of individuals with visual impairment without any significant difference between genders (Boller et al. 2018). Different studies presented significant differences in CBS prevalence. For example, the established prevalence of CBS in China was 1.4 % (Hou & Zang 2012), in Turkey 6.4 % (Nalcaci et al. 2016), in Denmark 8.3% (Singh et al. 2012), in Spain 0.4 to 15% (Santos-Bueso et al. 2014), in Australia 17.5% (Vukicevic & Fitzmaurice 2008) and in Canada 18.8% (Gordon 2016).

Although visual hallucinations may develop in any patient with damage to the visual system, major risk factors for CBS are worse bilateral visual acuity, age above 64 years, lower cognitive function, history of stroke, certain living conditions and social isolation (Holroyd et al. 1992, Schadlu et al. 2009, Russell & Burns 2014). The incidence of CBS is significantly higher in patients with profound visual impairment, while reduction of visual function increases the risk of visual hallucinations (Khan et al. 2008). Another study confirmed that patients with worse visual acuity as well as those who did not live alone had higher risk of developing visual hallucinations. There is no significant difference in the likelihood of experiencing hallucinations between patients with ARMD, glaucoma and diabetic retinopathy, nor was hallucination frequency associated with the patients' age. Based on these findings, the authors concluded that the presence of CBS is due to vision loss rather than due to special features of specific eye disease (Gordon 2016). Vast minority of patients with CBS consulted their physicians for this particular condition, while almost one

third of health professionals were uninformed or unsure about the diagnosis of CBS (Gilmour et al. 2009, Cox & Ffytche 2014). Studies consistently showed that CBS is often under-reported, under recognized and may be misrecognized by clinicians as psychosis or early dementia (Pelak 2017).

DIAGNOSTIC CRITERIA

Diagnostic criteria for CBS are still not clearly defined and diagnosis of CBS remains a real challenge in clinical practice. In psychiatric literature, the most commonly used definition of CBS is that of Gold and Rabins, which describe CBS as formed, complex, repetitive and stereotyped visual hallucinations in patients who have insight that these presences are not real, as well as the absence of delusion and other hallucination modalities (Gold & Rabins 1989). In other words, visual impairment is not specifically emphasized within psychiatric diagnostic criteria (Ffytche 2007, Al-Zubidi & Lee 2015). By contrast, ophthalmologists and neurologists propose that visual hallucinations in CBS are a result of damage in visual pathway and structures considering that the age of the patients and type of hallucinations are not of primary importance (Madill & Ffytche 2005). Therefore, it seems that the definition used by ophthalmologists and neurologists is more closely related to Charles Bonnet's original observations in a sense that a reduction of visual function or ocular disease is a contributing factor for the appearance of visual hallucinations (Pang 2016). Patients with CBS are aware that visual hallucinations are unreal and most of the hallucinations are of pleasant or unthreatening content, but they could also evoke anxiety. Sometimes, patients do not even notice the hallucinatory experiences as they can fit in and be imperceptible from real objects (Vukicevic & Fitzmaurice 2008, Schadlu et al. 2009). It is of crucial importance to explain to the patients that visual hallucinations are associated with visual impairment and that such an experience is not uncommon. Patients need to be relieved of fear and suspicion accompanied with thoughts they could be "losing their minds". To be able to do so, physicians need to make full diagnostic workup in order to exclude other possible causes of hallucinations. Such a workup requires psychiatric and neurologic evaluation in order to exclude disorders such as schizophrenia, psychosis, dementia, delirium, epilepsy, narcolepsy, migraine, drug intoxication or withdrawal syndromes and metabolic encephalopathy (Menon et al. 2003).

PATHOGENESIS

There are three established theories of CBS pathogenesis: irritative theory, release phenomenon and sensory deprivation theory (deafferentiation theory). The most widely accepted is deafferentiation theory, in which a loss of visual input into the brain causes spon-

taneous compensatory excitability of the visual association cortex (Madill & Ffytche 2005). When it is due to the lesion of the visual pathway or ocular disease, visual input into the cortex is completely removed causing spontaneous neuronal discharge, which elevates excitability in visual cortex and results in the release of visual hallucinations (Kazui et al. 2009, Vale et al. 2014). Findings from functional magnetic resonance imaging (fMRI) studies support this theory, since the occurrence of hallucinations have been correlated to spontaneous activity in the ventral occipital lobe. Moreover, the content of visual hallucinations was correlated to the activation of highly specific regions of the visual association cortex (Santhouse et al. 2000, Pelak 2017). The release theory of CBS presumes that divestment within the visual system interferes, in form of the lack of inhibition, with the visual association cortex, which results in inap and exaggerated excitation with subsequent release of visual hallucinations (Merabet et al. 2004, Vale et al. 2014). The disinvested eye makes the images to compensate for its stimulatory needs (Engelberg & Vaidya 2016). Sensory deprivation theory is closely related to the release theory in so much that it presumes release of abnormal electrochemical impulses within the brain. The main difference between the release and the deafferentiation theory is that the deafferentiation theory assumes a reduction in sensory input, which in turn results in spontaneous discharge in the visual cortex. It is assumed that this series of events is proximate consequence of decreased stimulation that is a result of ocular pathology (Vukicevic & Fitzmaurice 2008). Irritative theory suggests that distal provocative injuries send abnormal input to the visual cortex, where abnormal excitatory activity occurs and spreads onto temporal and occipital lobes. Such an activation of these brain regions results in visual hallucinations (Alao & Hanrahan 2003).

CLINICAL PRESENTATION

CBS most usually affects the patients aged from 70 to 85 years with visual field loss and/or moderate to severe visual impairment. Usually, CBS is present in patients with bilateral and central visual loss. Hallucinations in CBS are only visual without involvement of any other sensory modality and appear in patients who are completely conscious, in a qualitative and quantitative sense, and widely awake (Pliskin et al. 1996). The hallucinations may be simple or complex and can also be static or dynamic (moving across the visual field). More so, visual hallucinations can be monocular or binocular and even restricted to one half of the visual field (Pelak 2017). Usually, the location of hallucinations in the visual field corresponds with the underlying vision loss. Simple visual hallucinations consist of simple shapes, photopsias, grid-like patterns and branching patterns. Rarely, hallucinations appear as flashes of

light, repetitive geometric patterns (tesselopsia) or geometric shapes (Al-Zubidi & Lee 2015, Lapid et al. 2012, Coletti Moja et al. 2005). Complex hallucinations include vivid and miniature images of people, animals, figures, forms and plants (Wilkinson 2004). Hallucinatory images can be very colorful and complex and usually represent something that has no personal meaning or symbolic representation to the patient. Furthermore, images characterized as micropsia with distorted faces wearing hats and costumes and having realistic movement have been reported (Vojniković et al. 2010, Hartney et al. 2011). According to their duration and course, literature offers three distinct types of visual hallucinations related to the CBS: 1. episodic – that last from three days to three months; 2. periodic – that are characterized by phases of remission of several months; and 3. continual ones (Coletti Moja et al. 2005). Most patients have chronic hallucinations, which intensity rises and recedes, although there could be hallucinations that last only a few seconds. Recent studies accentuate that CBS may not be a temporary condition as previously thought. In other words, typical duration of CBS seems to be much longer, appearing over a long period of time with negative impact on the quality of life in one third of the patients (Cox & Ffytche 2014). Nonetheless, when reporting, patients usually give an expressive statement of pleasant hallucinations but variable in frequency and complexity (Nguyen et al. 2013). Visual hallucinatory experiences are more likely with open than with closed eyes (or by other means of decreasing visual input). They could also be precipitated by poor lighting and when the patient directs his or her sight on a white background and they disappear when the patient looks away or closes his or her eyes (Pelak 2017).

CBS AND EYE DISEASES

CBS may occur at any age after sudden or progressive visual loss or visual field loss more frequently in patients with a profound and bilateral visual impairment (Wilkinson 2004, Merabet et al. 2004). Although CBS presentation is most common in elderly population, because of the rising incidence of ocular pathology, studies showed that advancing age itself does not increase risk for CBS (Menon et al. 2003, Khan et al. 2008). Release hallucinations were reported even in children after severe visual deterioration with a slight difference in the content of hallucinations when compared to hallucinations in adults. In literature so far there has been no evidence of release hallucinations in cases with congenital blindness (Schwartz & Vahgei 1998). Although the damage of any part of the visual system could cause CBS, the most common ocular disease which may lead to this condition is ARMD. The results of the study performed by Vukicevic and colleagues showed that 54.5% patients with CBS had ARMD, 20% had diabetic retinopathy and 20% exhibited

anterior segment pathology (Vukicevic & Fitzmaurice 2008). It was also published that 75% patients with macular disease had release hallucinations that lasted five years or longer (Cox & Ffytche 2014). Gilmour and colleagues reported that the prevalence of CBS positively correlated with visual impairment (Gilmour et al. 2009) and it is most common in patients with visual acuity 0.3 or worse, more often with binocular disease (Engelberg & Vaidya 2016, Pelak 2017). In contrast, some studies reported that CBS occurred in patients with relatively well preserved visual acuity, or more closely, that acuity loss is not mandatory for the occurrence of hallucinations (Tan et al. 2004, Madill et al. 2005). Visual hallucinations are not rare in glaucoma patients with significant visual reduction (Nesher et al. 2001). Furthermore, CBS has been reported in many other ophthalmological diseases such as cataract, diabetic retinopathy, optic neuritis, retinitis pigmentosa, central retinal artery occlusion, retinal vein occlusion, anterior ischemic optic neuropathy and occipital infarction. Besides, there were reports of CBS cases after cataract surgery, bilateral laser iridotomies and enucleation, as well as after laser photocoagulation for neovascularization and macular translocation (Lapid et al. 2012, Tan et al. 2004).

In conclusion, CBS may occur in any ophthalmological disease and it is not particularly connected with loss of function in the retina, lens or optic nerve (Singh et al. 2012). The results of most studies support ophthalmological definition of CBS emphasizing the ocular disease or lesion at some level of the visual pathway as a cause of visual hallucinations.

PHENOMENOLOGICAL AND PSYCHOPATHOLOGICAL CONSIDERATIONS

From the stance of descriptive psychopathology, CBS remains a very interesting phenomenon. Hallucinations are considered as perceptions without an object (without external stimulus), that have a psychological impact of real perception and are spontaneous, unwilled and outside the control of perceiver (Oyebode 2015). Furthermore, hallucinations are perceived as normal, real experiences, and the person experiencing them usually does not doubt their reality. Visual hallucinations, the ones that appear in CBS, can be simple or complex, and they usually occur in organic states, rather in functional psychoses (Jardi et. al 2013). More generally stated, impairments of sensory organ functions, along with impairments that occur along the sensory processing pathway or their final cortical destinations can give raise to hallucinations. Some neurological ailments when they affect primary or association sensory cortical areas have been associated with different types of hallucinations, such as brain tumors, cerebrovascular incidents, migraines and epilepsy. Many visual hallucinations particularly occur after the damage of thalamus, parietal or occipital cortex

(Jardi et. al 2013). To visual hallucinatory experiences within CBS we have already referred to as “release” hallucinations, the term that is reflecting its proposed pathogenesis. We also referred to CBS as “phantom vision”, the term that is evoking its similarity with phantom limb phenomenon, being more informative on its possible proximal causes. Similarly, the association between auditory hallucinations (most commonly musical) and acquired deafness has been reported (Stefanis et al. 2006). Moreover, when auditory hallucinations occur in such a context, they are most usually neutral, that is in stark contrast with threatening and abusive character of auditory hallucinations in schizophrenia (condition that is most commonly associated with auditory hallucinations). The debate whether such a phenomena should be termed as hallucination in first place is one that is touching the foundations of psychopathology of perception. In some instances, the term pseudohallucinations was used to describe hallucinations with preserved insight, but this definition has not been widely accepted. For example, pseudohallucinations is also used to describe vivid internal images, hallucinations in persons without mental illness, real perceptions perceived as unreal etc (Oyebode 2015). Similarly, term hallucinosis, was used to describe hallucinatory experiences associated with neurological diseases or sensory impairments. Specific type of hallucinosis, peduncular hallucinosis, was used to describe hallucinatory experiences which do not compel the emergence of reflective delusions (Oyebode 2015). Similarly, this specific term did not endure the passage of time. Fundamental distinction between hallucinatory experiences in CBS and prototypical hallucinations is that hallucinatory experiences in CBS are accompanied with awareness (insight) that one is hallucinating, that it does not have quality of objectivity and independence. One should keep in mind that insight, although perceived as complex multifaceted phenomenon within psychiatry (as awareness of illness, signs and symptoms, existence of certain self-legislative will and recognition of the need for treatment), here refers to awareness of the nature of the percept (Cooke et. al 2010). Nonetheless, insight, not even in this sense, should not be treated as a categorical phenomenon, as it usually does spread from the nonexistent, onto delayed, fluctuating, towards a complete one. Moreover, content of hallucinations in CBS is most commonly a pleasant (or neutral) one, with some relevance to the individual. More so, they are perceived as egodystonic and they are in a certain sense integrated into the real environment (the impairments are filled, one could say confabulated). The origin of their content, remains a mystery. Existing explanatory models of sensory processing mechanisms in form of bottom-up and top-down process are fundamentally unsuitable for the explanation of hallucinatory experiences in CBS (Jardi et. al 2013). The sensation that hallucinatory experiences produce in CBS could be some kind of spontaneous, basic or residual activity, or a representation of the inner world. Besides, at least in

cognitive tradition, we became fully aware that cognitive distortions are omnipresent and inevitable companions of human perception. Moreover, it seems that perception aspires towards wholeness and towards closure. It seems, and this becomes evident in the existence of such a phenomena as CBS, that the capacity to humans distinguish between external and internal reality is highly dependent on the existence of adequate external stimulus. More so, when perceptual apparatus is disinvested by external stimulus due to sensory impairments or even more obvious in sensory deprivation, it turns towards the internal stimulus and becomes flooded in it.

THERAPY

When visual hallucinations appear, it is important to exclude all other possible causes such as neurologic, psychiatric, toxic or metabolic disorders. Moreover, we should consider the possibility that visual hallucinations could be a symptom of visual impairment in order to recognize CBS (Jackson & Ferencz 2009). The ophthalmologists' task is to try all achievable therapeutic options in order to improve visual acuity. In some cases after a complete visual loss, the condition might improve spontaneously (Al-Zubidi & Lee 2015). Visual rehabilitation includes corrected spectacles, contact lenses, monocular telescopic or low vision optical aids (Hartney et al. 2011). Results from published studies show a reduction of the CBS symptoms after cataract surgery, laser procedures, intravitreal injections and surgery of retinal pathology (Eperjesi & Akbarali 2004, Meyer et al. 2011). Nonpharmacological treatment include rapid blinking, closure of the eyes, leaving the specific environment or increase the intensity of the light at home. These methods may prevent, reduce or even stop visual hallucinations (Nguyen et al. 2013). The intensity and frequency of visual hallucinations in CBS may be reduced by applying certain changes in individuals' immediate environment, as restricting rapid changes in illumination (as with sunglasses or different neutral filters) (Hartney et al. 2011, Pang 2016). It is considered reasonable to wait with pharmacological therapy due to real possibility of spontaneous remission and periodic CBS occurrence (Hartney et al. 2011). Pharmacological treatment could be indicated in patients who are frightened and to whom hallucinations appearance decreases vision specific and general health quality of life. When treatment is justified, medications such as anticonvulsants, agents for the treatment of dementia and antipsychotics could be used (Al-Zubidi & Lee 2015). Several studies indicate that some of patients with CBS may develop dementia latter on and thus, recommendations are to emphasize frequent neurologic monitoring in order to detect cognitive impairments as early as possible (Pliskin et al. 1996, Lapid et al. 2013, Russell 2017). Use of atypical antipsychotic

medications (olanzapine, quetiapine, risperidone) showed different success, where anticonvulsants (clonazepam, valproate, carbamazepine) were useful only in selected cases (Boller et al. 2018). It is regarded that atypical and even more so typical antipsychotic medications should be avoided as much as possible because of the side effects in elderly patients. Some authors recommended usage of donepezil, because it has been shown that it minimizes visual hallucinations and improves memory and cognitive functions (Nguyen et al. 2013). It has been proposed that CBS has influence on cognitive functions and by so far general recommendations or guidelines in treating CBS are inexistent. It is recommended that physicians should warn and inform low vision patients on the likelihood of onset of hallucinations and to explain the nature of these symptoms in order to reduce patients' adverse psychological reactions (Hartney et al. 2011). The stress that arises as a result of experience of visual hallucinations is more closely associated with patients concern about mental health than with the content of hallucinations (Nesher et al. 2001, Shadlu et al. 2009). In addition, healthcare professionals should encourage patients with CBS to work on the improvement of social functioning and on occupying themselves with another interests.

Finally, when approaching CBS from therapeutic perspective one should bear in mind all the complexity of human beings. Unique and specific characteristics of this condition bring upfront the importance of person-centered care (Jakovljević 2015). In other words, such care should be holistic, integrative, individualized, personalized, and creative including many different treatment modalities that should be provided by different healthcare, and related, professionals (Jakovljević 2015, Jakovljević & Ostojić 2015). The decision of whether or not to initiate certain therapeutic intervention is not straightforward one, and should be left to the fully informed patient with the full respect of his autonomy and wellbeing (Jakovljević 2013).

CONCLUSIONS

CBS, which pathogenesis is not yet fully clarified, is a phenomenon of recurrent visual hallucinatory experiences in patients with acquired gradual or sudden visual loss. It occurs in different ocular diseases and is characterized by the absence of primary or reflective delusion and hallucinations in other sensory modalities. Patients with binocular visual deficits and with sensory deprived environments have preserved intellectual functioning and have maintained insight into hallucinatory quality of their experiences and corresponding reality. Although such hallucinations are most often not accompanied with anxiety, such experiences could influence the quality of life of patients with CBS. This specific issue is important for clinical and research practice because of population aging and rising incidence of ocular pathology.

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