Visual Loss and Visual Hallucinations in Patients with Age-Related Macular Degeneration (Charles Bonnet Syndrome)

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Purpose. The condition in which visual hallucinations (VHs) are solely associated with a visual impairment is termed Charles Bonnet Syndrome (CBS). The study was undertaken to investigate whether the extent of visual acuity (VA) loss and central visual field loss predisposes a patient with age-related macular degeneration (AMD) to develop a CBS VH and, in addition, whether the progression in loss is mirrored in the complexity of the VHs reported. VH phenomenology and CBS prevalence were also examined.

Methods. Sixty-six patients (age range, 63–96 years, mean ± SD 81.2 ± 7.1 years) with bilateral AMD were questioned as to whether they had experienced any hallucinatory episodes exclusive to vision. The four-point primary inclusion criterion ensured that all patients had bilateral AMD, a bilateral central scotoma, best monocular VA poorer than or equal to 0.6 logMAR (logarithm of the minimum angle of resolution) and intact cognition (using the Mini Mental State Examination for the Blind and the Telephone Interview for Cognitive Status). The patients who did not report VH were classified into the non-VH group, with the remainder in the VH group. An extended Institute of Psychiatry Structural Interview characterized the phenomenology of the VH. A secondary inclusion criterion subdivided the VH group into the apparent CBS group, in which personal medical history may have contributed to VH generation, and the manifest CBS group, where VHs were solely as a result of the visual loss.

Results. Fifty-three patients met the primary inclusion criterion: 32 were classified into the non-VH group and 21 into the VH group. The VH group were slightly younger (median difference, 4 years, $P = 0.03$) and appeared to have a lower VA (median difference, 0.20 logMAR, $P = 0.08$) and a more extensive visual field loss ($P = 0.06$) than did the non-VH group. However, when these variables were evaluated simultaneously by logistic regression, only age emerged as a statistically significant predictor of VH (odds ratio 0.88, 95% confidence interval [CI] 0.8–0.99, $P = 0.03$). The prevalence of apparent CBS and manifest CBS in the AMD population was found to be 25% and 15%, respectively. With no clinical and phenomenological differences between the two CBS groups, the secondary inclusion criterion was withdrawn, the VH group was renamed the CBS group, and a prevalence of 40% was recalculated. Of the 82 visual phenomena experienced by the CBS group, 21 were classified as simple VHs and 39 as complex VHs, with the remainder classified as either entopic phenomena or visual inference. Patients who experienced both simple and complex VHs appeared to have a greater visual field loss ($P = 0.06$) compared with those patients who reported either solely simple or solely complex VHs.

Conclusions. The extent of visual loss did not appear to be a predictor for the likelihood of a patient with AMD experiencing a CBS VH, nor was the progression of loss reflected in the complexity of the VHs reported. (*Invest Ophthalmol Vis Sci.* 2007;48:1416–1423) DOI:10.1167/iovs.06-0942

Hallucinations are perceptions in the absence of an external stimulus,[1,2] can occur in any sensory modality, and are most often generated through neurologic disease, psychopathology, and the use of drugs.[2–6] When visual hallucinations (VHs) follow marked visual acuity (VA) loss, in the absence of cognitive impairment, the condition is termed Charles Bonnet Syndrome (CBS),[7–9] with an estimated prevalence of 0.5% to 17%.[10–16] The content of the VH range from colored shapes and/or patterns (simple VH),[7,8,10–12,17–27] to well-defined recognizable forms such as faces, animals, objects, and scenes (complex VH).[7–12,17,19–26,28–31] The phenomenology of the VH does not appear to correlate with the underlying ocular disease, although significant bilateral loss in VA appears to be a primary trigger.[8–12,17,20,21,32,33]

Our study was designed to investigate both VA loss and central visual field loss in a group of patients with CBS and low vision attributable to age-related macular degeneration (AMD) and to compare these measures with a control AMD group. In addition, we wanted to investigate the complexity and the phenomenology of the VH reported and to determine CBS prevalence.

To ensure that there was little likelihood that factors such as cognitive impairment would contribute to the perception of the VH we applied a four-point primary inclusion criterion to the group of patients with AMD. A secondary two-point criterion subdivided the VH group into two groups: an apparent CBS group, in which concurrent medication and/or a diagnosed medical condition could have contributed to the generation of the VHs, and a manifest CBS group, in which there were no obvious causes for the VHs other than the marked visual impairment. Our findings suggest that the VH experienced by the apparent CBS group could not be differentiated from those described by the manifest CBS group. Furthermore, the extent of visual loss did not predict which patients would visually hallucinate, nor did it determine the complexity of the VHs reported.

Materials and Methods

Study Inclusion Criteria

An initial group of 66 consecutive fluent-English-speaking patients with AMD were recruited from the Manchester Royal Eye Hospital and

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underwent a full ophthalmic examination. The protocol adhered to the tenets of the Declaration of Helsinki. Informed consent was obtained from all subjects after the nature and the possible consequences of the study had been explained.

For this study, the primary inclusion criterion was (1) a diagnosis of bilateral AMD and bilateral central scotoma as measured using a 4/1000W circular target (14 minutes of arc) on a 30° Bjerrum screen. Monocular visual fields were plotted and overlapped to provide a binocular representation of everyday viewing. Areas of loss within this binocular field were computed; (2) best monocular VA poorer than or equal to 0.6 logMAR (6/24 Snellen); (3) a score of ≥18 on the Mini Mental State Examination for the Blind (MMblind; score range, 0–22)[34–36]; (4) for the patients who reported VH a score of ≥30 on the Telephone Interview for Cognitive Status (TICS) was also necessary (score range, 0–41).[23,37–39] A history of drug abuse was also a potential excluding factor, although no one was excluded on this basis.

After an informal discussion about visual status, patients were asked if they had ever experienced any hallucinatory episodes exclusive to vision. An extended Institute of Psychiatry Visual Hallucination Interview[23,37–39] was conducted on patients who reported VHs. Critically, all CBS VHs should be exclusively visual, should not be confused with entopic phenomena or visual inference, should coexist with veridical perception, and, after subsequent reflection, should not reflect reality. Insight into the authenticity of these VHs varied with the duration and repeatability, such that it was gained over time.

Classification of Patients

Patients who did not report VHs were classified into the non-VH group. A secondary two-point criterion was applied to subdivide the VH patients into two groups:

Apparent CBS Group. Included were patients with concurrent medication and/or a diagnosed medical condition that, however tenuous, could have contributed to the generation of VHs.[40]

Manifest CBS Group. This group included patients with no obvious cause for the VHs other than marked visual impairment. The secondary two-point criterion ensured the patient had (1) no concurrent medication with known visual hallucinatory or psychotic side effects and (2) no diagnosed condition associated with hallucinatory symptoms (e.g., migraine, Parkinson's disease, Alzheimer's disease, Lewy body dementia, schizophrenia, narcolepsy, psychotic depression and mania, epilepsy, stroke, or delirium tremens).

Categorization of Visual Phenomena

To ensure that other visual phenomena (e.g., entoptic phenomena and visual inference) were not incorrectly categorized as VHs, distinctions were made based on patient's descriptions and were further clarified by direct questioning.

Sensations that arise from within the eyes are called entoptic phenomena and include photopsias, such as phosphenes, and the appearance of moving blobs or lines.[41] These phenomena are frequently reported in patients with AMD and are often secondary to tractional forces acting on the retina or the physical movement of the vitreous. Visual inferences are based on mistakenly ascribing meaning to ill-defined perceptions of external stimuli using prior knowledge. Such descriptions are invariably prefaced with the phrase, "it looked like," and lack the vivid and precise features that are so characteristic of a VH description.

For a visual phenomenon to be categorized as a VH, it must not be entoptic in origin or visually inferred. We categorized VH as either simple or complex. Herein, we defined a simple VH as the perception of a colored shape or pattern that did not have a recognizable form. We defined a complex VH as the perception of a shape that had a recognizable form (e.g., an object, face, or scene).

Statistical Analysis

Groups of patients were compared using Mann-Whitney and Fisher's exact tests. Spearman's rank correlation determined the relationship between VA loss and visual field loss. Logistic regression analyses were performed to determine any association between the visual and nonvisual variables and the presence, or absence, of a VH. A Kruskal-Wallis ANOVA by ranks was used to test the relationships between the complexity of the VH (simple only, complex only and a combination of simple and complex) with age, VA, and visual field loss.

Results

Comparison of Patients with AMD Who Did and Did Not Report VH

Of the original 66 patients, 13 were excluded for failing to meet all points of the primary criterion. Six non-VH patients were excluded: Five did not exhibit bilateral central scotoma, and one patient did not meet the VA threshold. Seven VH patients were excluded: one did not exhibit bilateral central scotomata, five did not meet the VA threshold, and one did not pass the TICS. Of the 53 remaining patients, 21 (40%) reported VHs. The distributions of age, best monocular VA, and binocular visual field loss showed a large degree of overlap between those patients who did and did not report VH (Fig. 1). Those patients who experienced VH were slightly younger (median difference, 4 years; $P = 0.03$) and appeared to have a lower VA (median difference, 0.20 logMAR, $P = 0.08$) and a more extensive visual field loss ($P = 0.06$) than those patients who did not report VHs (Table 1). However, when these variables were evaluated simultaneously by logistic regression, only age emerged as a significant predictor of VH (odds ratio, 0.88; 95% CI, 0.8–0.99; $P = 0.03$).

The MMblind median (range) values were found to be 21 (18–22) and 22 (20–22) for the non-VH and VH groups, respectively.

Figure 2 illustrates the relationship between binocular field loss and best monocular VA for the non-VH (+) and the VH groups. The VH group was further subdivided on the basis of VH complexity—that is, simple (□), complex (△), and a combination of the two (○). No differences between the non-VH and the VH groups (the three subgroups) were evident.

Nineteen (90%) patients of the former group were registered blind or partially sighted compared with only 18 (56%) of the latter group. The proportion of patients who lived alone appeared to be similar in both groups ($P = 0.18$).

Classification of the VH Patients

Of the 21 patients who reported VH, 13 (62%) were classified into the apparent CBS group and 8 (38%) into the manifest CBS group (Table 2). The MMblind and TICS median (range) values were found to be 22 (21–22) and 35 (31–36) for the apparent CBS group and 22 (20–22) and 36 (33–39) for the manifest CBS group.

Table 3 details the VA and visual field loss for the 13 patients classified into the apparent CBS group and the 8 patients classified into the manifest CBS group. The complexity of the VHs and the possible confounding factors for the VH generation in the apparent CBS group (e.g., medication and/or medical condition) are also given. Note that although the principal confounding factor was concurrent medication, the listed side-effects were both uncommon and rare.

Category and Phenomenology of VHs

A breakdown of the content of the 60 VHs reported by the apparent and manifest CBS groups is given in Figure 3. The prevalence of VHs in the AMD population ($n = 53$) was 15% when only patients classified into the manifest CBS group were included. Because no significant differences were found between the data relating to the apparent CBS and manifest CBS

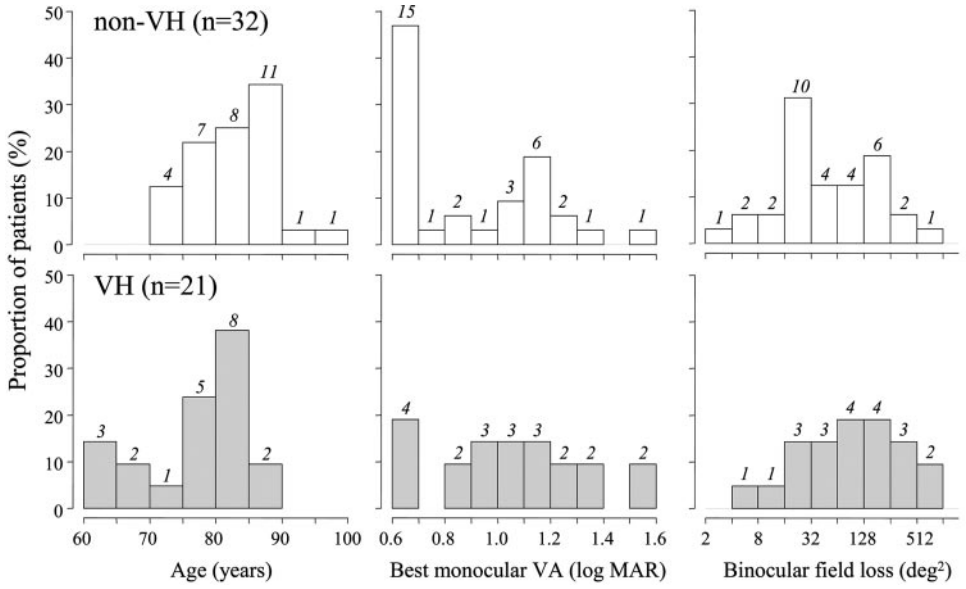


FIGURE 1. Distributions of age, best monocular VA and binocular visual field loss in the non-VH and the VH patients.

groups, except in the case of their living conditions, the secondary criterion was withdrawn, and the prevalence was recalculated by combining the two groups. This adjustment gave a prevalence of 40%, and henceforth this merged group was termed the CBS group.

The category and phenomenology of the VHs reported by the apparent CBS, manifest CBS, and CBS groups are described in Table 4. In summary, the VHs appeared suddenly, and patients were unable to control what subsequently happened to the image. Common triggers included relaxation, solitary conditions, and evening periods. No common stoppers were evident. The VHs generally lasted no more than a few seconds and were rarely restricted to the area corresponding to the visual field loss.

Eighty-two visual phenomena were reported: 21 (26%) were categorized as simple VHs, 39 (48%) as complex VHs, 21 (26%) as entoptic phenomena, and 1 (1%) as a visual inference. Historically, previous CBS studies had considered entoptic phenomena as simple VHs and visual inferences as complex VHs. Accordingly, our study uncovered different ratios of simple to complex VHs (1:1.9) to those previously reported. If we were to recategorize the entoptic phenomena as simple VHs and visual inferences as complex VHs the ratio would become 1:1.

The majority of patients (57%, $n = 12$) reported both simple and complex VHs. Five (24%) patients reported solely simple VHs and four (19%) reported solely complex VHs. Those patients who experienced both simple and complex VHs appeared to have the greater visual field loss ($P = 0.06$, Kruskal-Wallis ANOVA by ranks), but similar VA ($P = 0.23$) and age ($P = 0.19$) compared with those patients who reported only simple or only complex VHs. Accordingly, there was no strong evidence for the hypothesis that increasing visual loss is linked to a progression in the complexity of VH experienced.

The content of the VHs showed a broad variation, with the majority being faces ($n = 19$, 32%) and patterns ($n = 16$, 27%). Figures were often reported ($n = 10$, 17%) whereas colored shapes, objects, scenes, and words were less common.

Fifteen (71%) patients had no prior knowledge of CBS and did not know that VHs could be a feature of their low vision.

DISCUSSION

The purpose of this study was to explore CBS by investigating whether the extent of visual loss, in terms of VA and central visual field, predisposes a patient to develop a VH, and furthermore if the progression of visual loss is mirrored in the complexity of the VH experienced. In addition, we wanted to investigate phenomenology, prevalence, and whether, when stringent inclusion criteria were used, a homogeneous group of patients with CBS AMD could be identified and, moreover, differentiated from other visually hallucinating patients.

Despite the differences in VA and central field losses between the non-VH and the VH groups we were still unable to predict which of our 53 patients were likely to report a CBS VH. This would suggest that cognitive factors, such as state of arousal, play a central role in the appearance of the VH once the visual loss has reached a critical threshold level.

TABLE 1. Summary Details of the AMD Patients

	Non-VH ($n = 32$) (14 Men, 18 Women)	VH ($n = 21$) (3 Men, 18 Women)	*P*
Age (y)	84 (72–96)	80 (63–89)	0.027*
Best monocular VA (logMAR)	0.82 (0.60–1.56)	1.02 (0.60–1.60)	0.081*
Binocular field loss (deg²)	36 (3–586)	128 (6–711)	0.061*
Registered blind or partially sighted	$n = 18$ (56%)	$n = 19$ (90%)	0.39†
Living alone	$n = 15$ (47%)	$n = 11$ (52%)	0.18†

For calculation purposes, all VA levels >2.00 logMAR were rounded down to 2.00 log MAR. Values reported for age, VA and field loss are medians and ranges.

* Mann-Whitney test.

† Fisher's exact test ($n = 53$).

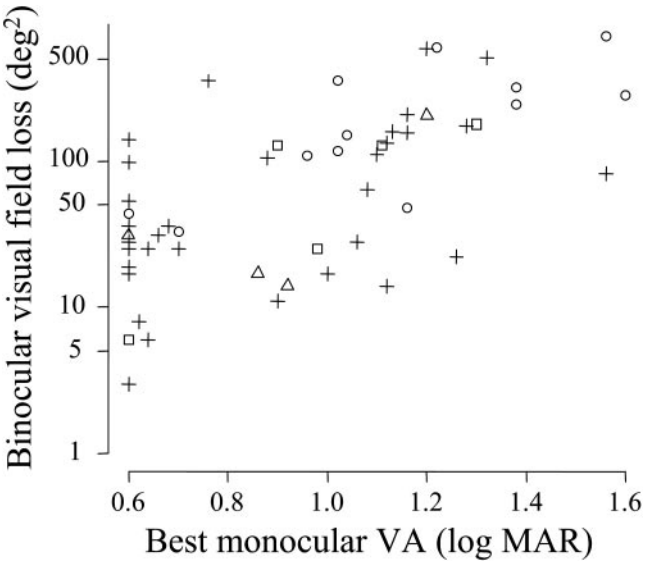


FIGURE 2. The relationship between binocular visual field loss and best monocular VA in the non-VH (+) and the VH groups, identified by the complexity of their VHs (□, simple only; △, complex only; ○, both simple and complex). Spearman's rho = 0.63; $P < 0.001$.

The question arises as to the nature of the visual loss and the cognitive, environmental, or medical factors required to initiate the hallucinatory process. Although we have exclusively studied patients with AMD who had both VA loss and central visual field loss, many other CBS studies have included patients with low vision attributable to a broad set of etiologies.[11,15,16] Recently, Tan et al.[15] and Madill and ffytche[42] emphasized that reduced VA (and presumably central visual field loss) may not be a prerequisite for patients to report CBS VHs. If indeed extensive peripheral field loss can trigger VHs, then quantification of this reduced sensory stimulation could indicate whether the likelihood of patients experiencing a VH is due to the percentage of visual field loss per se or the percentage loss in cortical processing.

That age was found to be a predictor of VH does not exclude the possibility that the older patients were less capable of recollecting their VHs. Although the MMblind and the TICS cognitive tests included memory assessments, these evaluations were superficial and limited in number.

In common with previous studies, we found a strong preponderance of CBS among women[11,19,33,43,44]; reflecting the female bias of an elderly population.

We found that most patients reporting VHs had no prior knowledge of CBS despite 90% of them being registered blind or partially sighted. This finding suggests that a greater awareness of CBS is critical, not only for the provision of emotional relief[30] but ultimately to avoid inappropriate psychosis labeling and therapy.

Living alone did not appear to predispose a patient to VHs. However, we appreciate that living alone per se does not demonstrate the extent of social interaction a patient encounters since visits and excursions to and from the home are not considered.

Classification of Patients

No obvious differences, in terms of both clinical and phenomenological issues, were found between the apparent CBS and manifest CBS groups. This suggests that either our inclusion criterion may have been unnecessarily rigid and/or medical history was not a contributing factor in the generation of the VH. Other possibilities include that the prevailing medical condition or the side effects of the medications could trigger a VH indistinguishable from those produced solely by the visual loss.

Visual Phenomena

Despite the historical precedence of categorizing entoptic phenomena and visual inference as simple and complex VHs, respectively, we regarded these visual phenomena as disparate from VH. Clearly generated differently, we felt that to consider them as a unity could obscure any possible explanations as to the underlying mechanisms responsible for the VH occurrence.

Visual Hallucinations

There appeared to be no relationship between the occurrence of solely simple and solely complex VHs with the extent of visual loss, thus suggesting that there is not a progression in the complexity of the VH reported as the extent of the visual loss increases. However, those patients who experienced both simple and complex VHs exhibited greater visual field loss, which could suggest a failure in serial processing rather than a breakdown in hierarchical processing for a VH appearance.

Of the 21 patients in the CBS group just 4 experienced 44% of the complex VHs. This finding may be explained by either a predilection for certain personality types to have a complex VH (possibly reflecting a greater creative disposition), our small sample size, or recall bias in our patients.

Phenomenology alone provides no information to differentiate apparent CBS from manifest CBS, or furthermore AMD CBS from CBS caused by other visual disorders.[9,23–26] In agreement with other studies, the content of the VHs showed a broad variation, with the majority being faces and patterns.

Similar triggers and stoppers were found to be consistent with previous findings, including states of relaxation, solitary conditions, and evening periods.[9,21,45,46] The aforementioned situations universally describe conditions of reduced sensory stimulation; the patient could be considered to be on "stand-by

TABLE 2. Summary Details of the Apparent CBS and the Manifest CBS Groups

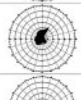
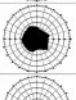
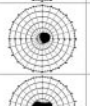
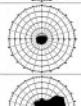
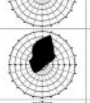
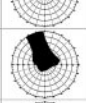
	Apparent CBS Group (n = 13)	Manifest CBS Group (n = 8)	P
Age (y)	83 (63–89)	80 (63–83)	0.3*
Best monocular VA (logMAR)	1.02 (0.6–1.6)	1.07 (0.6–1.38)	0.97*
Binocular field loss (deg²)	128 (6–711)	88 (25–317)	0.75*
Registered blind or partially sighted	n = 12 (92%)	n = 7 (88%)	1.0†
Living alone	n = 10 (77%)	n = 1 (13%)	0.007†

Computations are as for previous table 1.

* Mann-Whitney test.

† Fisher's exact test.

TABLE 3. Details of the Apparent and Manifest CBS Groups

	R VA L VA BVF loss	Bjerrum Plot (30°) ($^4/_{1000}$ W, 14' arc) R	 L	No. of SVH No. of CVH PCF
Apparent CBS	**1.56** ≥2.00 711			1 1 M
	≥2.00 **1.60** 280			1 2 M
	1.10 **0.86** 17			0 1 M
	0.96 1.60 108			1 4 M
	0.70 1.26 33			3 1 M
	1.02 1.50 117			1 1 M
	1.60 **0.92** 14			0 4 M
	1.06 **1.04** 150			1 1 M, MC
	1.11 1.30 128			1 0 M, MC
	1.02 1.42 353			2 3 M
	1.30 **1.22** 597			1 3 M
	≥2.00 **1.20** 203			0 2 M
	0.60 0.72 6			1 0 M
Manifest CBS	**0.98** 1.06 25			1 0 -
	1.30 1.56 178			1 0 -
	1.52 **0.90** 128			1 0 -
	1.04 **0.60** 31			0 2 -
	0.60 1.40 44			2 5 -
	1.38 1.38 317			1 3 -
	1.38 1.56 244			1 2 -
	1.16 1.22 48			1 4 -

The left column states right and left VA (logMAR, best monocular VA in bold) and binocular visual field (BVF) loss (deg^2 in the central 30°). The right column gives the number of different simple (SVH) and complex (CVH) hallucinations experienced, and possible confounding factors (PCF) such as medication (M) or medical conditions (MC) that may have contributed to the VHs.

mode" and would probably employ cognitive constructs to interpret the visual scene. Although typically associated with organic diseases and psychoactive substances, VHs among the normal population are not unusual, with frequent reports of VHs during the transitional states between waking and sleeping (hypnagogic) and sleeping and waking (hypnopompic).[31] This further emphasizes the importance of the patient's state of arousal.

Quantifying the triggers and stoppers for the VH would be fruitful yet challenging, since thorough experimentation requires repeated measures and sustained attention. Of interest, the process of measuring the spatial and temporal characteristics of a VH may in itself act as a stopper; thus, alternative investigative methodologies must be sought. One such technique, used by ffytche et al.,[24] is functional magnetic resonance imaging. Activity in the ventral extrastriate visual cortex was found to correlate with VHs of colors, faces, texture, and objects, with the increased activity persisting between the interhallucinatory periods. Simple VHs were found to originate early in the visual pathway (V1 and/or V2),[24,27,47,48] whereas more complex VHs were generated in the higher visual areas.[24]

Surprisingly, only 8% of the reported VHs were restricted to the area of binocular field loss, indicating that both bottom-up and top-down processing are operating concurrently, further emphasizing the complexity of the underlying mechanisms.

Prevalence of CBS in Low-Vision Patients

When both our primary and secondary inclusion criteria were applied, the prevalence of CBS was found to be 15%, in line with previously reported data.[11,13] However, when only the primary criterion was applied, the prevalence increased to 40%. Clearly, prevalence is highly dependent on the inclusion criteria used to define the population—thus making comparisons with other cross-sectional studies difficult. In two recent publications[14,15] a low CBS prevalence of ~0.5% was reported in two separate samples of 1000 elderly low-vision patients. This finding (30–80 times lower than that found in our study) may be attributed to the use and content of the initial screening questionnaire and/or the cultural differences between Asian and non-Asian patients. Of note, the Singapore group[15] reported that none of their patients felt the need to hide their symptoms for fear of being labeled psychiatrically unstable, whereas here in England, we have encountered this fear as a common concern.

Although nearly all CBS studies have described elderly patients (probably due to the greater likelihood of acquiring a visual impairment), occasional reports of CBS in the young have been published.[41,45] Reasons for this apparent rarity in the visually impaired infant or child could include a greater

FIGURE 3. The distribution of the 60 VHs in the apparent CBS (n = 13) and the manifest CBS (n = 8) groups.

TABLE 4. Phenomenology of the VH for the Apparent CBS, the Manifest CBS, and the CBS Groups

	Apparent CBS (n = 13)	Manifest CBS (n = 8)	CBS (n = 21)
Entoptic phenomena (n)	15	6	21
Inferences (n)	1	0	1
VHs (n)	36	24	60
Simple VH:complex VH	13:23 (36:64)	8:16 (33:66)	21:39 (35:65)
VH triggers			
Relaxation	11 (85)	8 (100)	19 (90)
Solitary conditions	10 (77)	5 (63)	15 (71)
With people	1 (8)	0 (0)	1 (5)
Evening periods	10 (77)	4 (50)	14 (67)
Daytime periods	0 (0)	1 (13)	1 (5)
Watching TV	1 (8)	1 (13)	2 (10)
Negative emotional state	1 (8)	1 (13)	2 (10)
Looking through window	1 (8)	1 (13)	2 (10)
VH stoppers			
Walking through image	2 (15)	0 (0)	2 (10)
Change of gaze	1 (8)	1 (13)	2 (10)
Blinking	3 (23)	2 (25)	5 (24)
Intervals between VHs			
Days	7 (54)	3 (38)	10 (48)
Weeks	4 (31)	2 (25)	6 (29)
Months	2 (15)	3 (38)	5 (24)
Duration of VHs			
Seconds	11 (85)	6 (75)	17 (81)
Minutes	2 (15)	2 (25)	4 (19)
VH restricted to scotoma	2 (15)	0 (0)	2 (10)
Hyper-realistic VH	6 (46)	5 (63)	11 (52)
Able to hallucinate with eyes closed	3 (23)	1 (13)	4 (19)

Data in parentheses are percentages.

plasticity of the immature afferent pathway and an inability of the patient to understand or describe the visual experiences; although the small patient numbers clearly hamper scientific validation.

Prevalence of CBS in AMD

AMD is the most commonly reported ocular disease associated with CBS.[9] This fact is not surprising, as AMD is by far the most prevalent sustained cause of central vision loss in the Western world. Moreover, the likely bilateral nature of the condition is clearly a significant feature.

To date, we are aware of only one paper[20] and two separate case study reports[49,50] specifically dedicated to investigating the relationship between VH and AMD. In the only serial study, Holroyd et al.[20] found the prevalence of VHs within a group of 100 patients with AMD to be 13%. This prevalence is comparable with our CBS group (40%), as patients with diagnosed medical conditions and/or concurrent medication with known visual hallucinatory and/or psychotic side effects were not excluded from the cohort. Despite this threefold difference, both studies found similar triggers, stoppers, and temporal characteristics for the VHs. The Holroyd study did not report on size, shape, or position of the visual field loss or quantify the VH's complexity; therefore, further comparison is impossible.

Mechanisms Responsible for the VHs Experienced in CBS

The neural basis underlying the generation of VHs in CBS remains controversial, with many hypotheses proposed.[27,46,48,51,52] Although it is important to understand how the brain contends with both limited and absent sensory input, there is a need to realize that adaptive and compensatory mechanisms are likely to be recruited.

VHs are an order of magnitude more complex than the comparatively low-order perceptual completion of the physiological blind spot or small acquired areas of visual field loss.[47,53] In the past, CBS has been considered a visual analogue to the phantom limb phenomenon in amputees, in which a sensation is generated by brain activity in the absence of a sensory input.[19] Such cognitive constructs represent strong top-down processing (hypothesis driven) and are actively influenced by the extent of sensory loss in bottom-up processing (data driven).

Over the years, several models have been proposed to account for VH in CBS. The most supported model involves deafferentation, whereby the reduced afferent input creates, or releases, waves of discharges in the visual areas of the brain. Recently, a neural network model approach has been used to understand VH formation.[48,54–56] The recurrent nature of the VH has been suggested to be due to the adaptive resonance of neural networks,[57] possibly explaining why the VHs loose their sustainability. However, it is clear that, whatever the primary mechanism for hallucinating, all models will need to incorporate feedback loops and pathways that include the commonly found triggers that underpin relaxation.

Concluding Remarks

This is the first AMD study that has adopted rigid inclusion criteria to investigate the relationship between VA loss and central visual field loss with reports of VHs. We also examined the complexity and phenomenology of the VHs. In summary, CBS is a common finding in low-vision patients with intact cognition. The extent of visual loss did not appear to be a predictor for the likelihood of a patient with AMD experiencing a CBS VH, nor was it reflected in the complexity of the VH. The only statistically significant predictor was age, with the younger patients more likely to report a VH. In the present study we found a CBS prevalence of 40%. The phenomenology and prevalence of the VHs are not ocular disease specific and reflect the consequences of the profound loss of bottom-up

visual processing. Factors such as states of arousal have been shown to trigger the onset of the VHs. Early reassurance is important in patient care, with sympathetic understanding and explanations providing emotional relief. Greater awareness of CBS is necessary, to avoid inappropriate labeling and treatment for nonexistent psychosis.

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