Clinical Study

Visual snow: A thalamocortical dysrhythmia of the visual pathway?

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\textbf{A B S T R A C T}

In this paper we review the visual snow (VS) characteristics of a case cohort of 32 patients. History of symptoms and associated co-morbidities, ophthalmic examination, previous investigations and the results of intuitive colourimetry were collected and reviewed. VS symptoms follow a stereotypical description and are strongly associated with palinopsia, migraine and tinnitus, but also tremor. The condition is a chronic one and often results in misdiagnosis with psychiatric disorders or malingering. Colour filters, particularly in the yellow-blue colour spectrum, subjectively reduced symptoms of VS. There is neurobiological evidence for the syndrome of VS that links it with other disorders of visual and sensory processing such as migraine and tinnitus. Colour filters in the blue-yellow spectrum may alter the koniocellular pathway processing, which has a regulatory effect on background electroencephalographic rhythms, and may add weight to the hypothesis that VS is a thalamocortical dysrhythmia of the visual pathway.

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1. Introduction

Visual snow (VS) refers to the persistent visual experience of flickering fine achromatic dots or static in the whole visual field of both eyes likened to “static analogue television noise” \cite{1}. A recent series of publications highlight the very similar subjective stereotypical descriptions between patients of this frequently distressing phenomenon \cite{2,3}. The symptom frequently occurs with other visual symptoms such as photopsia, nyctalopia, palinopsia (the persistence of previously viewed stimuli) and entoptic phenomena, as well as other disorders of sensory perception such as migraine with or without aura, tinnitus and tremor \cite{1,4}.

VS can be associated with stress, depression and previous illicit drug use, though no clear causative agent has been identified \cite{3}. This results in patients with these symptoms often being misdiagnosed as having migraine with aura, hallucinogen persisting perception disorder (HPPD) or malingering. As a consequence treatments are often inappropriate, ineffective or absent.

Recently Schankin et al. suggested that VS is a unique clinical syndrome, distinct from migraine with aura, and recommended set diagnostic criteria to help identify VS patients \cite{3}. The overlapping symptomatology and therefore potentially pathophysiology between migraineurs and VS patients cannot be dismissed. Indeed, migraine, tinnitus, photopsia and palinopsia all appear to relate to an increase in sensitivity of sensory perception \cite{1–3}. However as distinct from the presumed cortical spreading depression theory in migraine, VS patients are thought to have differences in regional metabolism resulting in modulation of neuronal sensitivity and excitability \cite{3}.

VS patients frequently report persistence of symptoms at all times including when the eyes are closed and with few patients reporting relief of intensity of snow symptoms in bright light \cite{1–3}.

We noticed however that some patients report relief of symptoms from tinted lenses. Intuitive colourimetry, the assessment of optimum tint, has been used in the past to alleviate symptoms of perceptual disorders and visual stress reported by patients with dyslexia, migraine or photosensitive epilepsy \cite{5,6}. When offered to VS patients we identified a pattern of symptom relief from these coloured filters, particularly those in the yellow-blue spectrum.

In this paper we present a review of our patients with VS symptoms to whom we offered the option of undergoing intuitive colourimetry, review the previous hypotheses of VS and propose a new hypothesis – that VS is an imbalance of koniocellular and magnocellular pathway function creating a thalamocortical dysrhythmia that results in a disorder of visual processing.

2. Subjects and methods

Data was collected from 32 VS patients presenting to tertiary referral neuro-ophthalmology services in Sydney, NSW between 2012 and 2014. Patients underwent a standardised series of
questions about their visual symptoms and associated non-visual symptoms. The associated medical and psychiatric co-morbidities were noted from past medical records. Ophthalmic and neurological examination was performed by a consultant neuro-opthalmologist. Previous ancillary investigations were collected and reviewed. Patients were also asked to list any past treatments given for their VS, and the outcomes. All patients were offered the opportunity to undergo intuitive colourimetry testing with the protocol previously employed for dyslexia. In that technique the three parameters of colour, namely hue, saturation and brightness, were independently changed while the eyes were colour adapted to find the final colour tone that suited the individual best and minimised symptoms.

3. Results

The cohort consisted of 22 males and 10 females with ages ranging from 16 to 55 years old (mean age of 29 ± standard deviation of 10 years). Average symptom duration was 3 years with three patients reporting symptoms since early childhood. A summary of the findings can be seen in Table 1. The classic stereotypical description of the VS as fine, predominantly black and white static was reported in 91% of patients. The others reported fine chromatic static. Most patients experienced associated forms of palinopsia such as persistent after-images and trails behind moving objects. Other symptoms included disturbances of peripheral vision, shimmering of static objects, stars bursts and coloured blobs. The majority of patients experienced more than one of these visual phenomena in addition to the classic VS. Altering the ambient light was the most common way patients alleviated the symptoms (35%), however, 52% of patients were unable to identify any alleviating factors. An aggravating factor could be identified in the majority of patients (65%), included high contrast text on a computer screen, darkness, exhaustion and stress.

Associated non-visual symptoms included high-pitched tinnitus (63%), migraine with or without aura (44%), as well as tremor (22%) and balance problems (19%).

Most patients had a previous diagnosis of mental illness including anxiety (44%) and depression (19%) as well as other psychiatric diagnoses (16%) such as post-traumatic stress disorder, obsessive compulsive disorder, attention deficit hyperactivity disorder and personality disorder. None of the patients had any diagnosed neurological disease.

Only one patient reported illicit marijuana use, none admitted to lysergic acid diethylamide or other hallucinogen use, and 9% admitted to social smoking.

One patient reported a family member with VS. A family history of genetic eye diseases and migraine were present in two and three patients, respectively.

Ophthalmic examination was normal in all patients with vision 6/6 or better, normal colour, normal automated visual fields, and normal slit-lamp examination. Minor refractive error was found in 19%. A large proportion of patients had undergone previous ancillary testing including MRI of the brain (88%), blood tests (81%) and electrophysiology (electroretinography and visually-evoked potentials, 50%), all of which were within normal limits. Previous treatment with psychiatric medications as well as cognitive behavioural therapy had been tried in 39% of patients, but either made no difference or in some cases actually worsened the symptoms. Many patients also found side effects of medication troublesome.

Of all patients, 12 participated in an intuitive colourimetry test. Ninety-two percent of patients felt that symptoms improved during the testing with a particular coloured filter. No improvement was noted in a patient with chromatic (purple) static rather than the classic VS. The test was repeated to ensure that the colour preference was reproducible. The chosen colour spectrum that provided relief of symptoms was in the yellow-blue colour spectrum for the majority of patients (83%).

4. Discussion

Our results suggest that VS may be classified as a disorder of central colour-dependant processing and that it does occur as a syndrome associated with other disorders of sensory processing such as tinnitus, tremor and migraine [1,4].

VS has previously been classified as a syndrome [7] and a set of diagnostic criteria were recently proposed in an effort to capture the syndromic nature of this condition [3]. According to these criteria VS syndrome can be diagnosed when a patient presents with black-and-white static with at least one associated symptom of palinopsia, photopsia, nyctalopia or entoptic phenomena, excluding those who have a history consistent with migraine with aura or that occur as a result of drug abuse.

According to this classification 29 of our 32 patients fulfilled the proposed diagnostic criteria (91%). The remaining three reported...
chromatic static (multicoloured or red-purple tones) with at least one other feature of photopsia or palinopsia.

As previously described, the cohort reports a chronic phenomenon lasting years, or in four patients, since childhood, with symptoms occurring mainly in the second to fourth decade of life [2,3]. Our cohort was predominantly male (69%) which is different to the previously reported female predominance [2] or sex neutrality [3,8] and may thus support the notion that this condition is not affected by sex.

Most of the patients report that VS is aggravated by high contrast visual stimuli (such as computer screens) and relieved by brightness, as previously described [3]. Palinopsia are a frequent associated symptom [2,3,8], and occurred in 69% of patients in this case series and were predominantly persistent after-images, light streaks, trails as well as a “shimmer”, all of which are categorised as illusory palinopsia. Gersztenkorn et al. previously reported both illusory and hallucinatory palinopsia to be a feature of VS, which is not supported by this study [3]. This distinction may well help distinguish VS from HPPD, a frequent misdiagnosis.

When reviewing associated non-visual symptoms we also noted a very high prevalence of migraine (with and without aura; 47%) which was reported with a prevalence of 60% and 30% in previous reports [3,8]. One additional patient reported a headache that did not fit the International Classification of Headache Disorders revision II criteria for migraine. It has previously been argued that the high prevalence of migraine (versus non-migrainous headaches) in VS patients suggests an overlapping pathophysiology between the two conditions [2,3,8].

Additionally we also found a very high percentage of associated tinnitus (63%). This is consistent with previous reports [2,3] and makes tinnitus and migraine the most prevalent associated non-visual symptoms. Tinnitus has previously been strongly linked to migraines and both are thought to represent symptoms of a hypersensitivity/sensory allodynia spectrum of cortical dysfunction [9,10]. We also noted fine tremor (22%) and balance problems (19%). These have not been reported in association with VS to our knowledge, though a higher incidence of essential tremor has previously been reported in patients with migraine [11,12].

Neuro-ophthalmic examinations of all participants including visual acuity, pupils, colour vision, visual fields, anterior and posterior segment examination were entirely normal. Nineteen percent of patients had a myopic refractive error (between –1 and –4D). Although this and most of the previous case series report a normal ophthalmic examination [2,3,8] one previous report noted lack of the rapid recovery phase following pupil constriction in three patients [13].

Most VS snow patients undergo electrophysiology, mainly electroretinograms and visually evoked potentials to exclude retinal pathology. This study and all previous reports do not suggest abnormal electrophysiology, to our knowledge [2,3,8]. Interestingly, changes in electrooculogram recordings, in particular reduced fast oscillation ratio, diminished standing potentials of slow oscillations and higher Arden ratios, as well as electrically evoked phosphene thresholds, in particular reduction of thresholds for long pulse durations, were recently reported for HPPD patients [14]. It is unclear whether this is a distinguishing feature to VS or whether this has merely not previously been evaluated in this cohort. Furthermore a large proportion of these patients undergo multiple, and at times unnecessary, investigations including blood tests and brain imaging (CT scan and MRI), all of which have been reported as normal [2,3].

The stereotypical description of the symptoms of VS and their persistence even at times with eyes closed suggests a true biological phenomenon [3]. In fact even spacing of dots throughout the visual field, as compared to a retinotopic organisation, indicates an origin in higher order neurons beyond fusion of visual information from left and right retina, that is, beyond the lateral geniculate nucleus. This is in contrast to entoptic phenomena, though interestingly the incidence of entoptic phenomena is much higher in VS patients with a reported prevalence of up to 79% in previous cohorts [3,8]. In a recent review which attempted to classify palinopsia, it was identified that illusory palinopsia, the preservation of previous visual information, is strongly associated with VS as compared to hallucinogenic palinopsia [1]. The types of palinopsias are indicative of dysfunction of visual perception, as compared to visual memory. A perceptual disturbance may also explain why VS symptoms are affected by background illumination, contrast and level of retinal and cortical adaptation.

The most likely underlying neurobiological mechanism suggested is that of an increase of neuronal excitability [15] resulting in visual pathway hypersensitivity leading to perception of normally sub-threshold stimuli [1]. Visual cortex hypersensitivity was previously noted in patients with migraines and aura [16]. Hypersensitivity has also been theorised to play a role in pathophysiology of palinopsia, one of the main associated symptoms of the VS syndrome [1] and in associated diseases such as migraine and tinnitus [9].

It is thought that in migrainous brains the hypothalamic and brainstem neurons that are responsible for regulation of responses that deviate from physiological and emotional homeostasis can lower the threshold for transmission of nociceptive trigeminal vascular signals from the thalamus to the cortex [12]. This may also explain other associated features such as autonomic symptoms (nausea), affective symptoms (irritability and depression) and cognitive symptoms (attention deficit), some of which have previously been described in associated with VS [3]. In the context of migrainous increase in sensitivity to noise and light it has been previously shown that local application of noradrenaline to the locus coeruleus, a centre involved in sensory processing, facilitates cortical neuronal responsiveness by increasing the signal-to-noise ratio of cortical input and therefore preventing adaptation to trains of action potentials. It furthermore alters the thalamic noradrenergic discharge thus decreasing the likelihood of accurate transfer of spike trains to the cerebral cortex [10]. This explains both the lowered auditory sensitivity and the increased discomfort to loud noises as well as the process of photophobia. This may also explain why additionally to photophobia and phonophobia other sensory hypersensitivities such as cutaneous allodynia are associated with migraine attacks [17].

In the context of migraine, increased activity of the glutamatergic system can lead to excessive occupation of the NMDA receptor which in turn may amplify and reinforce pain transmission, the development of allodynia and central sensitisation [12]. Additionally increased excitation of the serotonergic receptors has previously been documented in HPPD and migraine [3,18], both of which are possibly related diseases to VS. Although environmental triggers clearly play a role there is strong evidence for genetic predisposition to generalised neuronal hyperexcitability [19]. Interestingly the genes involved are regulators of synaptic transmission through the NMDA receptors, glutamatergic excitation and plasticity for development of cortical layers [12,18]. These findings provide plausible mechanisms for the related disorders of VS, namely migraine, HDPD and tinnitus.

Recently hypermetabolism on [18F]-FDG positron emission tomography (PET) in the lingual gyrus and anterior lobe of left cerebellum was found in VS patients [4]. The lingual gyrus is involved in visual memory, facial recognition, attention and colour perception [20,21] and more generally speaking visual postprocessing. An overlap was noted with migraineurs without VS symptoms however, which may mean that the area might instead be the neuroanatomical correlate of photopsia, a shared symptom with migraine [4]. It was suggested by the authors that this may...
represent a biological correlate to VS symptoms, however it is important to note that functional MRI hypermetabolism has previously been reported to occur in both organic and functional disease [22].

When hyperexcitability affects widespread neuronal networks it may drive thalamocortical dysrhythmia, a presumed cause for tinnitus, migraines and tremors, and therefore perhaps VS [12,23]. The presence of increase in low-frequency theta rhythmicity, in conjunction with an increase in coherence among high-low frequency oscillations indicates the presence of thalamocortical dysrhythmias [23]. Research into the edge effect that is created at a cortical area of dysrhythmia, a high-frequency gamma-band activity, is likely the origin for the clinical symptoms. The idea was initially derived from evaluation of auras in migraineurs [24]. The common mechanism may produce a range of symptoms depending on the localisation of the dysfunction in the thalamocortical network [23]. As such illusionary hallucinations can be traced to the V1 to V3 visual cortex, palinopsia can be traced to the parietal lobe coordination system and trilling, as well as after-images, can be located in the parietal association cortex [15]. It may well be that VS reflects high frequency abnormal activity in visual system. This would be in agreement with evidence of hypermetabolism on PET scan in the lingual gyrus [4].

Recently an anatomical area was identified in the posterior thalamus where photic retinal information and nociceptive input converge, revealing an area that likely contributed to perception of photophobia, a shared feature of VS and migraine [25,26]. Additional nuclei in the medial thalamus have furthermore been shown to be responsive to light [27] and make direct connections to the posterior thalamic nuclei [28]. The connections are thought to play a significant role in neuronal substrate of homeostatic balances and my well effect disinhibition of the posterior thalamus, thus affecting negative regulation of light sensitivity [29].

In fact, imbalances between konio- and parvo/magnocellular pathway processing have previously been reported to underlie thalamocortical dysrhythmia in tinnitus, parkinson tremor and neurogenic pain [23]. The koniocellular pathway, also considered the “primitive” visual system, differs significantly from the magno- and parvo-cellular pathways that are involved in conscious vision. The koniocellular pathway contains many different cell types that project diffusely to the superficial cortex and control slow cortical frequencies. In contrast the P and M pathways project topographically to the primary visual cortex (V1) and are linked to fast cortical frequencies [30,31]. It was recently shown that the slow koniocellular rhythms modulate the high frequency oscillations that underlie cognitive perception and influence sensory excitability [32,33], which thus invokes that K activity may gate cortical circuits derived from M and P pathway input [30]. Disordered magnocellular pathway function in particular has been associated with the “shimmering effect” known to occur in migraine sufferers and patients with visual stress [34] and is a symptom reported by many VS patients.

In recent years tinted lenses have been employed to aid children and adults with reading difficulties that appear to relate to dysfunction of magnocellular pathways processing. [34–36]. Furthermore colourimetry has shown benefits in patients suffering from migraine, Meares–Irlen syndrome/visual stress and photosensitive epilepsy [5,34,37]. During colourimetry assessment the colour (hue) and depth of colour (saturation) is adjusted with or without any change in associated brightness (luminance). This appears to ameliorate perceptual distortions and visual stress [38]. Interestingly distinct differences in preferred colour spectra are observed between patients with dyslexia and those with epilepsy or migraine [37].

The team at the National Hospital for Neurology has been investigating the use of intuitive colourimetry in VS patients and we continued this further. The functional description of VS symptoms, its associated palinopsia including shimmer, amelioration with increased luminance and aggravation with high contrast, all support the notion that VS may in fact be a related disorder of colour processing, in particular magnocellular pathway function.

Our patient population responded very positively to colour filters and reported significant improvements in VS symptoms. This occurred particularly with filters in the yellow-blue colour spectrum. Blue and yellow colour signals are carried by a subset of koniocellular pathway cells [32]. Amelioration of symptoms with colour filters in conditions such as VS or as previously reported migraine, epilepsy and visual stress [5,6,38,39], suggests that low-frequency brain rhythms might be entrained or cancelled by visual stimuli that selectively activate the koniocellular pathway [32]. It is unclear whether the blue-yellow spectrum infers a direct benefit or whether the result is from blocking the red-long wave-length component of light thus preferentially activating P pathways processing.

The results from our study suggest that the pathophysiology in VS is an imbalance between the konio- and parvo/magnocellular pathway interaction which underlies thalamocortical dysrhythmia. This explains its associated features of tinnitus, migraine and tremor, all of which have been hypothesised to represent thalamocortical dysrhythmias. The latter symptom of tremor is one that has not been frequently reported in the VS literature, but was noted in 22% of our patient population.

5. Conclusion

VS is a debilitating syndrome that likely results from an underlying neurological deficit in visual perceptual processing. Associated symptoms of palinopsia, photosopia, nyctalopia, entoptic phenomena and associated disorders such as migraine, tinnitus and tremor suggest a common underlying pathophysiology. The most likely pathophysiologival mechanism is that of thalamocortical dysrhythmia secondary to dysfunctional neuronal excitability and impaired habituation response. Improvement of symptoms of VS with yellow-blue colour filters adds evidence that the dysfunction is neurological and likely related to colour, in particular magnocellular pathway processing. Further research is needed to substantiate this hypothesis and further distinguish the different but related disorders of VS, migraine and tinnitus.

Conflicts of Interest/Disclosures

The authors declare that they have no financial or other conflicts of interest in relation to this research and its publication.

References


