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Visual Snow: a Potential Cortical Hyperexcitability Syndrome

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Opinion statement

The purpose of this review is to provide an overview of visual snow (VS) and provide information regarding current treatment options for VS. Visual snow (VS) is a rare disorder manifesting with a persistent visual phenomenon of seeing numerous tiny snow-like dots throughout the visual field, and it can cause debilitating visual and psychological consequences. It is emerging as a disorder separate from, but associated with, migraine visual aura, and neuronal cortical hyperexcitability is being considered as a theoretical mechanism for the persistent-positive visual symptoms. There are few studies that have investigated the treatment of VS, but as our understanding of this entity begins to change, we expect that new treatment approaches and treatment trials will emerge in the next decade. Currently, our approach is to consider pharmacologic treatment for all patients with VS who report decreased quality of life as a result of VS. Resolution of the disorder is difficult to accomplish with treatment, but in our experience, even when symptom intensity is simply reduced, many patients find that there is an improvement in their quality of life that is beneficial. Our preferred treatment options include: (1) oral lamotrigine with a slow increase from 25 mg daily to a maintenance dose of 200–300 mg daily in divided doses as tolerated, and this is typically achieved by advancing the dose in increments of 25–50 mg weekly following the first 2 weeks of therapy; (2) oral acetazolamide with an initial dose of 250 mg daily followed by a slow increase over 1–2 weeks to a total of 1000 mg daily in divided doses, and higher doses can be tolerated by some without increasing the risk-benefit ratio; or (3) oral verapamil long-acting at 120–240 mg daily, and if side effects limit the dose the can be initiated, then lower doses with short-acting verapamil two or three times daily

can be substituted until higher doses with the long-acting formula can be tolerated. By initiating drug treatments with low doses and slowly increasing over 1 to 4 weeks, tolerability and compliance improves and allows patients to realize the full benefits of treatment. The proposed mechanisms of microstructural cortical abnormalities and hyperexcitability as a cause of VS may lead to new treatment approaches in the future. Until such a time, medications reported to relieve persistent visual phenomena of migraine and visual aura of migraine are treatment options worth considering and these are reviewed for that purpose. Although clinical trials for the treatment of visual snow are lacking due to the rarity of the disorder, medications reviewed here should be considered for use in patients with VS who experience an impact on their quality of life. Theoretical mechanisms that lead to cortical hyperexcitability are being investigated and could lead to new treatment options. In the meantime, medications may provide benefits in this disabling condition.

Introduction

Visual disturbances are common complaints that ophthalmologists and neurologists encounter in their clinics. Although "negative" visual disturbances are readily recognized and consist of blindness, decrease in visual acuity, visual field defects, and scotoma, other disturbances that can be described as "positive," can be more difficult to identify and consist of the perception of false visual images. These positive visual images can be classified as a distortion of a real visual sensory stimulus, known as an illusion, or as the perception of a visual image without the existence of a visual stimulus, which is referred to as a visual hallucination. Illusions comprise palinopsias, afterimages, diplopia, metamorphopsias, and dysmetropsias. Examples of hallucinations include formed images, such as people and objects, and unformed images, such as geometric designs, scintillating scotomas, and visual snow (VS).

Visual snow is an infrequently discussed persistent visual disturbance that is not common but is very disturbing when experienced. Patients with VS complain of numerous flickering tiny dots that fill the entire visual field in both eyes in a manner similar to a badly tuned television [1]. It was first examined closely in three patients by Liu and colleagues in 1995, and the authors referred to the phenomenon as "persistent positive visual phenomena in migraine" [1]. The phenomenon of persistent positive visual disturbances, including descriptions consistent with VS, has been noted by other authors in association with migraine for the past 30 years [2–10]. Criteria for VS that was proposed by Schankin and colleagues [11••] consist of the following:

A. Dynamic, continuous, tiny dots in the entire visual field lasting longer than 3 months.

B. Presence of at least two additional symptoms of the four following categories:
   i. Palinopsia. At least one of the following: after images (different from retinal afterimages) or trailing of moving objects.
   ii. Enhanced entoptic phenomena with at least one of the following: excessive floaters in both eyes, excessive blue field entoptic phenomenon, self-light of the eye, or spontaneous photopsia.
   iii. Photophobia.
   iv. Nyctalopia.

C. Symptoms not consistent with typical migraine visual aura per ICHD-IIIb.

D. Symptoms are not better explained by another disorder (especially normal eye exams, no previous intake of illicit drugs).

Demographics

VS is a disorder of young adulthood with mean age of onset reported to be in the third decade [12•, 13••, 14–16, 17•, 18•, 19, 20]. The range of onset can vary widely, however. Many patients presenting as an adult have described symptoms starting in early childhood, with the youngest reported age of 10 years [10, 12•]. The oldest patient was part of Schankin and colleagues prospective study and was diagnosed at 60 years of age [19]. Bassero et al. found a 2:1 female predominance, while

all other studies reveal only slightly more females than males encountering this phenomenon [12•, 18•, 19, 20]. In distinction, Laushkae et al. found a male predominance (2.2:1) [13••]. Family history of VS has been reported in 10% of patients by Schankin and colleagues and 3% by Lauschke et al., while reports of family history of migraine range from 10 to 77% of patients [13••, 14–16, 17•, 18•, 19].

Presentation

Symptoms are usually long standing and typically affect the quality of life due to reduced ability to perform visual activities without interference by the VS phenomena. Patients describe that the VS persists with eyes closed and involves both eyes. The dots seen are usually black and white but there are reports of chromatic dots (multicolored or red-purple) [13••]. Many patients describe that symptoms of VS are more prominent when looking into a chromatically homogenous, non-structured background such as a white piece of paper or blue sky [20]. In one report by Schankin and colleagues, approximately 84% of patients with VS report periods without symptoms, with the remainder reporting symptoms that are persistent [14]. In several other reports by the same group, 24% of patients had VS initially presenting in childhood with 41% having constant symptoms, 42% noting progressive worsening, and 13% with stepwise worsening [14–16, 17•, 18•, 19].

Factors that are reported to worsen VS symptoms include high-contrast text, high luminance conditions such as a computer screen, darkness, fatigue, and stress. Alleviating factors are less commonly reported and include alteration of the ambient light. Laushke et al. noted that 65% of their patients were able to identify aggravating factors, while only 43% had an alleviating factor [13••].

Associations

VS is often accompanied by other visual disturbances such as photophobia, nyctalopia, palinopsias, photopsias, and scotomas [13••, 14–16, 17•, 18•, 19, 21], and the discussed proposed criteria acknowledge this disturbance as a means to help define visual snow. Headache is a common condition associated with VS, and most patients with VS have headaches that meet the International Classification of Headache Disorders criteria for migraine. Schankin and colleagues noted that 86% of patients with VS have a history of headaches, and 37% have headaches that are worsened with VS [14]. Specifically, migraine headaches were present in 59% of patients and 27% had typical migraine aura [14–16, 17•, 18•, 19]. This represents a relatively high incidence of migraine aura, which has been found to occur in approximately 15% of all patients with migraine headaches [22]. A few studies reveal a lower prevalence of migraine in VS, ranging from 30 to 48% of individuals suffering from VS [13••, 23].

The close association between migraine and VS has led to the historical assumption that VS is a part of the spectrum of visual aura of migraine, particularly because in some instances, patients describe the onset of VS occurred with a typical migraine with aura. However, VS is more commonly described by patients as clearly distinct from their classic visual aura of migraine at its presentation and certainly in its persistent course [1, 14–16, 17•, 18•, 19]. Furthermore, VS can occur in patients with no history of migraine headache. Thus, it is believed that that migraine headache is associated with VS and potentially increases the risk of developing VS but is not a necessary condition from which VS evolves. Tinnitus has been also been noted in patients with VS and its report varies from 15- 64% [13••, 14, 17•, 20]. Tremors and balance problems have been reported to occur in approximately 20% in one study, and we have also noted this association in our patients [13••]. Interestingly, in one study, the comorbidity of migraine in patients with VS increased the likelihood of associated palinopsia, spontaneous photopsia, photophobia, nyctalopia, and tinnitus [18•].

VS-like phenomenon has been associated with the use of illicit drugs, especially drugs considered to be hallucinogenic. When persistent positive visual phenomena occur concomitant with hallucinogenic drug use, the disorder is more accurately referred to as "hallucinogen persisting perception disorder." In this instance, hallucinations that occurred during the drug, or a variation on such, persist after discontinuation of the hallucinogenic drug for months to years or indefinitely [20]. There is one reported case where VS phenomena coexisted with marijuana use [13••]. The similarities in the conditions cannot be overlooked and drug use as a potential factor in the development of VS should always be considered. In our experience, hallucinogen-persisting perception disorder is more refractory to pharmacologic treatment than VS.

Pathophysiology: the theory of cortical hyperexcitability

VS is typically associated with normal neuroimaging and normal neurologic and ophthalmic examinations. For

this reason, it is not uncommon for patients with symptoms of VS to be diagnosed with psychogenic disorders, including malingering. The stereotypical presentation and evidence to date indicates that there is a biological basis to VS phenomena. The retinotopic distribution of the dots suggest that VS arises in the central nervous system neurons that are beyond, or downstream, to the lateral geniculate body, in contrast to entoptic phenomena [13••, 17•, 19, 23]. The pathophysiology of VS is not known. However, the theory gaining acceptance is that neuronal hyperexcitability leads to detection of subthreshold stimuli that a healthy individual would typically fail to detect or hyperexcitability directly results in the perception of visual stimuli in absence of such due to decreased inhibition of neuronal discharge after subclinical injury [21]. In accordance with the theory of cortical hyperexcitability, Unal-Cevik et al. reported findings from repetitive pattern reversal visual evoked potentials in a patient with VS and demonstrated that, similar to patients with migraine, this patient's response to repetitive stimuli was *potentiation* rather than habituation. Interestingly, after the use of lamotrigine, the patient's VS syndrome improved and the cortical hyperexcitability did as well [24].

A prospective study of 17 patients with VS using [^{18}F]-2-fluoro-2-deoxy-D-glucose positron emission tomography [^{18}F]-FDG PET revealed that the bilateral lingual gyri showed hypermetabolism in affected subjects compared to gender-matched controls [18•]. Interestingly, the primary visual cortex did not reveal differences between controls and VS subjects. The lingual gyrus is considered an area of higher order visual processing and is known to be involved in visual memory, visual imagery, visual word and letter processing, and coding of complex visual stimuli [18•, 25, 26]. The authors, therefore, suggest that VS reflects potential microstructural changes at the level of higher-order visual processing regions [18•]. Of note, if this theory is true, we currently do not have the tools to assess for the type of changes that occur. Using neuroimaging methods that assesses microvasculature and microcellular water movement, diffusion- and perfusion-weighted MRI imaging employed to study four patients with persistent migrainous visual disturbances did not reveal abnormalities or asymmetries on imaging [5].

In people with migraine, hypothalamic and brainstem neurons can lower the threshold for transmitting nociceptive signals to the cortex, making a migraineur sensitive to light and noise [27], and it has been shown that there is an increase in the glutamatergic and serotonergic system excitability with a higher occupation of N-methyl-D-aspartate (NMDA) receptors that can further reinforce pain transmission through cortical spread depression (CSD), and extracellular potassium accumulation has been proposed as the initiating event for CSD found in migraine [28–30]. Although correlations have yet to be proven, this mechanism may be closely related to the proposed pathophysiology related to hyperexcitability in the visual system observed in patients with VS.

Alternatively, or additionally, VS might be considered to result from an imbalance in the koniocellular, magnocellular, and parvocellular pathways in a manner analogous to the described "imbalance between low- and high-frequency oscillations" noted in tinnitus, tremor, and neurogenic pain [12•, 30]. In fact, disordered magnocellular pathways have shown to be correlated with visual shimmering seen in migraine and, for this reason, could also be implicated in VS symptoms [31].

Treatment and prognosis

VS can be refractory to treatment, although knowledge of treatment effectiveness is limited owing to the rarity of the disorder and the historical focus on treating VS as a form of migraine aura. There is a lack of systematic, prospective, or randomized-controlled treatment trials, and future classification and definitions of VS may lead to better recognition of the disorder and, eventually, to treatment trials. Particularly important is the movement toward considering VS as having separate but overlapping origins from migraine aura. Most of the information that we present is based on case reports and clinical expertise with relatively few controlled trials. Several modalities known to abort migraine aura have been used to treat VS and persistent visual phenomena, and results or reports are noted here. Despite the overlapping conditions of migraine and VS, treatments for VS are less effective than treatments for typical visual aura of migraine. An important note is that in describing treatment effectiveness in trials, case reports, or case series, different authors use different definitions for visual phenomena and some are consistent with VS and/or meet the proposed criteria noted above. To avoid confusion, we sought to use the same language used by the authors whose reports we cite, and we refer the readers to the original manuscripts for full descriptions of the visual phenomena. Table 1 provides a summary of the current literature and treatment options. We also include a level of evidence using the American Academy of Neurology Guidelines [32]. Final dosing should be based on

Table 1. Evidence of efficacy of pharmaceutical agents in treating persistent visual phenomena (PVP) and/or visual snow (VS) as indicated in the literature

Medication	Dose	Study	Type of study	Effectiveness (for subjects/ total subjects)	visual symptoms	Level of evidence [32]
Diuretics						
Acetazolamide	500–750 mg for 5 weeks	Haan et al. [34]	Case series	Effective (3/3)	Persistent visual phenomena (PVP)	ClassIV
		De Simone et al.[35]	Longitudinal	Effective (15/22)	PVP	Class IV
		Simpson et al. [12•]	Case report	Ineffective	VS	Class IV
Furosemide	IV 20 mg/day	Rozen [28]	Case series	Effective (2/2)	PVP	Class IV
	Oral 20 mg/day	De Almeida [37]	Case report	Effective	PVP	Class IV
Topiramate	Oral 25–100 mg	Lampl et al. [40]	Longitudinal	Ineffective	PVP	Class IV
Anticonvulsants						
Lamotrigine	50-100 mg orally for 2 weeks	Chen et al. [4]	Case series	Effective (2/2)	PVP	Class IV
		Lampl et al. [46]	Longitudinal	Effective (21/25)	PVP	Class IV
		Pascual et al. [47]	Longitudinal	Effective (>75%)	PVP	Class IV
		Lampl et al. [48]	Longitudinal	Effective	PVP	Class III
		Unal-Cevik et al. [24]	Case report	Effective	VS	Class IV
		Wang et al. [8]	Case series	Mixed results (1/3)	VS	Class IV
		Jager et al. [5]	Case series	Ineffective	VS	Class IV
Divalproex sodium	500 mg twice a day	Rothrock [3]	Case series	Ineffective (2/2)	VS	Class IV
Calcium channel blockers						
Verapamil		Shankin et al. [18•]	One Case	Ineffective	VS	Class IV
Nifedipine	20 mg daily	Goldner, et al. [55]	Case report	Effective	PVP	Class IV
		Hoffert et al. [54]	Randomized control Trial (RCT)	Ineffective	PVP	Class III
Nimodipine	40 mg daily	Jensen et al. [53]	RCT	Ineffective	PVP	Class II
Flunarizine	10 mg daily	Simpson et al. [12•]	Case Report	Ineffective	VS	Class IV
		Jager et al. [5]	Case series	Ineffective	VS	Class IV
Beta blockers						
Metoprolol		Hedman e al. [56]	RCT	Ineffective	PVP	Class II
Propranolol	40 mg daily	Wang et al. [8]	Case series	Partially effective	PVP + VS	Class IV
		Jager et al. [5]	Case series	Ineffective	VS	Class IV
Naproxen		Shankin et al. [18•]	One case	Effective	VS	Class IV
Ketamine	25 mg intranasal	Kaube et al. [57]	Longitudinal	Effective (5/11)	PVP	Class IV
		Afridi et al. [58]	RCT	Effective	PVP	Class II

Table 1. (Continued)

Medication	Dose	Study	Type of study	Effectiveness (for subjects/ total subjects)	visual symptoms	Level of evidence [32]
		Jager et al. [5]	Case series	Ineffective	VS	Class IV
Aspirin		Haas et al. [2]	Case report	Effective	PVP	Class IV
Picotamide	300 mg daily then twice a day for 6 months	Allais et al.[59]	Longitudinal	Effective	PVP	Class IV
Nortriptyline		Liu et al. [1]	Case series	Ineffective	VS	Class IV
Sumatriptan	6 mg subcutaneous	Bates et al.[69]	RCT	Ineffective	PVP	Class I

Level of evidence is based on the criteria indicated by the American Academy of Neurology Guidelines [32]. Class 1 is the highest level of evidence and Class IV is the lowest level of evidence
RCT randomized controlled trial

considerations for each patient, and full prescribing information should be reviewed for side effects and contraindications before starting treatment. In Table 2, we provide our recommendations for first lines of treatment.

A. Pharmacological treatment

a. Diuretics

i. Acetazolamide

Acetazolamide is a carbonic anhydrase inhibitor that has been previously used as a prophylactic treatment for migraine, migraine aura, and persistent visual symptoms related to migraine. Experiments in animals reveal that acetazolamide decreases the susceptibility of neurons to cortical spreading depression—a critical step in pathogenesis of migraine [33], and historically, acetazolamide was used as antiepileptic. Haan et al. described three patients with positive persistent visual aura, despite controlled migraine, who were treated with acetazolamide (500–750 mg daily) that resulted in resolution of the visual symptoms within few days and recurrence of symptoms after discontinuation [34]. Similar results were reported by De Simone et al. with low dose (62.5 mg with titration to 250 mg daily) in 22 patients with persistent migraine aura. Fifteen of 22 patients reported more than 50% reduction in symptoms in 2 months [35]. Simpson et al., however, reported that acetazolamide was unsuccessful in treating a 12-year-old with VS, although it is possible that not enough time was given for follow-up [12•].

We suggest acetazolamide as one of the first lines of treatment for VS, particularly if the patient has failed lamotrigine and verapamil or has a contraindication to use of either of those medications. We recommend divided dosing of a total of 500–1000 mg daily in adults and 125–500 mg in children with caution, with titration according to response and side effects. Initial doses of 250 mg daily will help prevent side effects, which are very common with initial dosing and with doses beyond 1000 mg daily. Treatment should be continued for at least 5 weeks before deciding on effectiveness [12•, 34].

Common side effects include extremity paresthesias, lightheadedness, dry mouth, metallic taste, gastrointestinal disturbances, and polyuria. Other side effects can occur due to hypokalemia. Metabolic acidosis is expected and can lead to renal dysfunction [36].

ii. Furosemide

Furosemide is a potent diuretic that inhibits the cellular membrane Na+/K+-ATPase pump. Animal models demonstrate that furosemide inhibits CSD activity by

Table 2. Authors' recommendations for first line treatment

	Adult starting dose	Adult maintenance dose	Prescribing notations	Other
Lamotrigine	25 mg daily	200–300 mg in divided dose	- Long-acting formula also available - Increase slowly in increments of 25–50 mg weekly and see prescribing information	- Has some effectiveness in migraine headache prevention
Acetazolamide	250 mg daily	1000 mg in divided doses	- Consider long-acting acetazolamide formula to decrease side effects and not that it is available only in 500 mg - Contraindications in those with a history of renal stones, renal insufficiency	- Not recommended for use in conjunction with topiramate
Verapamil extended release formula	120 mg daily	240 mg	- If orthostatic at low dose, can start with 40 mg short acting daily and increase as tolerated to 40 mg three times a day and then switch to 120 mg daily extended release	- Has some effectiveness in migraine headache prevention - Useful in patients meeting criteria for retinal migraine

Additional notations are provided to help with decision-making when choosing which drug to use. See prescribing information for all side effects, contraindications, and dosing before initiating treatment

disrupting extracellular potassium accumulation [28], and it might provide relief from persistent visual phenomena associated with migraine based on limited data. In 2000, Rozen reported two patients, both young women, with persistent positive visual phenomena whose symptoms were recalcitrant to IV prochlorperazine, IV methylprednisolone, IV divalproex sodium in case 1, and to IV droperidol, IV magnesium, and methylprednisolone in case 2. Both patients responded to one dose of IV furosemide (20 mg/dose/day). The effect lasted through discharge 5 days later in one case and up to 2 weeks in the other [28]. Another report from Brazil showed that an 11-year-old girl with persistent "shadow" in her eyes in the setting of treated migraine responded to oral furosemide at a dose of 25 mg daily [37].

Side effects include hypotension, polyuria, dizziness, gout, hyperglycemia, hyperuricemia, hypocalcemia, hypokalemia, hypomagnesemia, hyponatremia, and metabolic alkalosis. It should be avoided in patients with hypotension or renal failure [38].

iii. Other: Topiramate

Topiramate is an inhibitor of carbonic anhydrase, and other mechanisms of action include blockade of voltage-dependent sodium channels, potentiation of GABA-ergic transmission, and inhibition of excitatory pathways. Topiramate is an effective migraine prophylactic, but with minimal data to support its use in persistent visual phenomena in migraine. Some studies have revealed no decrease in *typical* aura of migraine [39, 40].

Thus, we do not recommend topiramate as a first line agent for VS.

b. Anticonvulsants

i. Lamotrigine

The mechanism of action of lamotrigine includes downregulation of the effect of glutamate, which is thought to be involved in propagating CSD in migraine via NMDA receptors [4]. Lamotrigine is one of the most successful drugs in treating positive visual symptoms in patients with migraine [4, 11••, 41–45]. For visual snow, Unal-Cevik reported a good response to 50 mg of lamotrigine twice daily [24], while Wang et al. had mixed results [8]. Our experience in adults with VS has been similar, with success being more likely with total doses of 150–200 mg daily. We typically choose it as our first choice for the treatment of VS. Lamotrigine has been noted to be effective in preventing aura in three longitudinal studies [46–48], although other investigations have shown less promising results [49].

Serious side effects include Stevens-Johnson Syndrome, which is life threatening and can occur up 0.8% in pediatric populations [50]. Other side effects include nausea, drowsiness, fatigue, insomnia, and nystagmus.

ii. Divalproex sodium

Divalproex sodium is effective in preventing episodic migraine and migraine aura. Its main mechanisms of action are to enhance GABA-ergic effect on serotonergic neurons and inhibition of the release of glutamate [51, 52]. Rothrock reported two patients whose persistent migraine aura subsided with divalproex sodium of 500 mg twice daily [3].

Serious side effects include hepatotoxicity, pancreatitis, teratogenicity, and Stevens-Johnson syndrome. It has a narrow therapeutic index and laboratory monitoring is necessary. Other side effects include weight gain, headaches, drowsiness, alopecia, nausea, vomiting, thrombocytopenia, and tremors [3].

iii. Carbamazepine

Carbamazepine is an anticonvulsant that stabilizes the inactivated state of voltage-gated sodium channels, and it also stimulates GABA receptors and potentiates GABA's inhibitory effect. Limited data exists on the use of this medication for the treatment of persistent visual symptoms, although there is a consensus opinion that this medication is relatively ineffective in the treatment of positive visual phenomena similar to VS [1, 12•]. We agree with this opinion.

c. Calcium channel blockers/calcium antagonists

Medications in this class include verapamil, nifedipine, nimodipine, amlodipine, flunarizine, and diltiazem. Calcium channel blockers have proven effective in both prevention and abortive treatment of migraine headaches, but there is limited data on migraine visual aura, persistent visual phenomena in migraine, and VS [5, 12•, 18•, 53–55]. We have found verapamil to be useful in patients with visual snow who continue to suffer from migraine headaches that are poorly controlled in frequency and/or intensity, and we consider verapamil to be our second choice for treatment after lamotrigine.

Side effects of calcium channel blockers include hypotension, headache, dizziness or lightheadedness, flushing, peripheral edema, constipation, and heart block.

d. Beta-blockers

Beta-blockers, particularly propranolol, have been shown to be effective in the prevention of migraine, with mixed results in patients with visual aura of migraine and in those with VS [5, 8, 56].

Side effects of beta-blockers include exacerbation of heart failure, increased airway resistance, hypotension, bradycardia, depression, fatigue, sexual dysfunction, and hypoglycemia.

e. Non-steroidal anti-inflammatory (NSAID) medications

Schankin et al. reported nine patients with VS who had no benefit from sertraline, fluoxetine, propranolol, verapamil, lamotrigine, and amitriptyline, although one patient reported improvement of symptoms on naproxen without mention of dose or duration [18•].

Side effects include gastrointestinal discomfort, ulceration, and bleeding. Serious side effects include increased risk of hemorrhage and renal injury.

f. Ketamine

Ketamine is an NMDA antagonist. Mixed results exist for its use in prolonged visual aura of migraine [5, 57, 58].

Side effects include hypertension, altered mental status, addiction, respiratory depression, and thyroid disorders [57].

g. Antiplatelet agents

i. Aspirin

Aspirin is an anti-inflammatory, antiplatelet agent that has an effect in aborting acute migraine. An individual case report series from 1982 showed that it was effective in treating migraine aura status [2].

Side effects include gastric irritation, ulceration, and bleeding. There is a risk of hemorrhage with its use.

ii. Picotamide

Picotamide is an antiplatelet drug that acts by inhibition of thromboxane A2 synthase and antagonism thromboxane A2 receptors. In 2004, a case series of 22 female patients with intermittent aura of migraine were treated with a maximum dose of 300 mg twice daily for 6 months, and approximately 25% had complete resolution of aura while only 15% reported no effect [59]. These patients did not, however, have VS. Given its effectiveness in typical aura, it can be considered in the appropriate clinical scenario in patients with VS. We do not have experience with its use in VS.

Side effects of menorrhagia, and other bleeding events may limit is usefulness in some patients, however.

h. Antidepressants

i. Tricyclic antidepressants

Tricyclic antidepressants block muscarinic M1, histaminic H1, and alpha-adrenergic receptors. The

commonly used drugs in this class include nortriptyline and amitriptyline, which are effective in the prevention of migraine headaches. Their efficacy in preventing migraine aura and VS does not seem promising, however. In the case series by Liu et al., nortriptyline was effective in treating palinopsias but did not help with the VS [1]. Other reports have shown ineffective results in treating positive visual phenomena [8, 17•].

Tricyclic antidepressants tend to have a narrow therapeutic range and dose-related toxicities. Side effects include cardiac conduction changes, anticholinergic effects, antihistaminic effects, decreased seizure threshold, sexual dysfunction, diaphoresis, and tremor [60].

i. Triptans

Sumatriptan is effective against acute migraine headache [61] and belongs to a class of drugs that have selective serotonin receptor agonist properties.

There is no direct evidence that triptans are effective in treating persistent visual disturbances including VS, but studies have revealed improvement in typical migraine aura.

Side effects include dizziness, tingling, dry mouth, flushing, and chest pain. Triptans should not be used in conjunction with monoamine oxidase inhibitors or in the setting of uncontrolled hypertension or patients with significant risk for cerebrovascular or cardiovascular disease.

j. Antipsychotics

Prochlorperazine is a dopamine receptor antagonist belonging to the class of drugs known as antipsychotics. It is most commonly used to treat nausea and vomiting, and it can be particularly useful in migraine-associated nausea and vomiting. Some reports reveal successful treatment of aura of migraine [62], and it has been proposed that the reason for its success may be due to the finding that people with aura of migraine have an increased frequency of the D2-dopamine receptor gene [63]. This treatment, however, lacks evidence for or against its use in VS.

Side effects include cardiac conduction changes, extrapyramidal symptoms, blood dyscrasias, and hypotension [64].

B. Non-pharmacological treatment:

a. Greater occipital nerve (GON) block:

In 2016, Cudrado et al. published a case series of 22 patients with persistent auras that were treated with 2 ml injection of 0.5% bupivacaine targeting the GON. Symptoms improved in 86.4% of the patients in 24 h, and 50% had complete resolution of symptoms [65]. Rozen also suggested that persistent aura can be alleviated by a GON block as evident by one case report [66]. The mechanism through which GON improves aura is not understood and the efficacy of this technique needs to be studied further, but it is worthwhile considering given these recent results.

Contraindications to nerve blocks include infection, open skull defect, allergic reaction to anesthetic, and open skull wound [67]. Complications of injection include nerve damage with paresthesias [68]. Systemic side effects if the intravascular injection inadvertently occurs and result in seizure or altered consciousness [67]. Other complications include infection and hematoma.

b. Colorimetric lenses

The team at the National Hospital of Neurology in Sydney reported results in treating VS from the effect of colorimetry, which involves the use of colored filters. Improvements in symptoms were noted with blue and yellow filters. Interestingly, blue activates the koniocellular pathway, and as noted previously, the koniocellular pathway may play a role in cancelling low-frequency brain rhythms that can contribute to VS [13••].

Conclusion

Visual snow is a rare and potentially poorly recognized phenomenon that is often resistant to treatment. Although the relationship of VS to migraine cannot be overlooked, in many cases, it occurs independent of migraine headache and patients report that it is distinct from typical visual aura of migraine. Unlike typical visual aura of migraine, VS persists for longer periods of time, responds

less well to treatment, and can persist beyond the symptoms of migraine headache. It is typically associated with other visual phenomena, including entoptic phenomena, palinopsia, and photophobia. VS can be a debilitating disorder that affects quality of life and disrupts common, everyday tasks that involve vision. At the moment, we lack full insight into the pathophysiology of this phenomenon and further research is needed to define our knowledge. However, cortical hyperexcitability is a mechanism that is supported by prior and recent data. Until such a time that we have specific treatments aimed at a specific mechanism, we recommend lamotrigine and acetazolamide as first-line agents for treatment, followed by verapamil. Multiple other treatment options exist with varying degrees of evidence. Even when symptoms are reduced by a fraction, it has been our experience that patients can benefit to a degree that makes a difference in their quality of life.

Compliance with Ethical Standards

Conflict of Interest
The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent
This article does not contain any studies with human or animal subjects performed by any of the authors.

References and Recommended Reading

Papers of particular interest, published recently, have been highlighted as:
- • Of importance
- •• Of major importance

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