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'Visual snow' – a disorder distinct from persistent migraine aura

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Patients with 'visual snow' report continuous tiny dots in the entire visual field similar to the noise of an analogue television. As they frequently have migraine as a comorbidity with ophthalmological, neurological and radiological studies being normal, they are offered various diagnoses, including persistent migraine aura, post-hallucinogen flashback, or psychogenic disorder. Our aim was to study patients with 'visual snow' to characterize the phenotype. A three-step approach was followed: (i) a chart review of patients referred to us identified 22 patients with 'visual snow'. Fifteen had additional visual symptoms, and 20 patients had comorbid migraine, five with aura; (ii) to identify systematically additional visual symptoms, an internet survey (*n* = 275) of self-assessed 'visual snow' subjects done by Eye On Vision Foundation was analysed. In two random samples from 235 complete data sets, the same eight additional visual symptoms were present in >33% of patients: palinopsia (trailing and afterimages), entoptic phenomena (floaters, blue field entoptic phenomenon, spontaneous photopsia, self-light of the eye), photophobia, and nyctalopia (impaired night vision); and (iii) a prospective semi-structured telephone interview in a further 142 patients identified 78 (41 female) with confirmed 'visual snow' and normal ophthalmological exams. Of these, 72 had at least three of the additional visual symptoms from step (ii). One-quarter of patients had 'visual snow' as long as they could remember, whereas for the others the mean age of onset was 21 ± 9 years. Thirty-two patients had constant visual symptoms, whereas the remainder experienced either progressive or stepwise worsening. Headache was the most frequent symptom associated with the beginning or a worsening of the visual disturbance (36%), whereas migraine aura (seven patients) and consumption of illicit drugs (five, no hallucinogens) were rare. Migraine (59%), migraine with aura (27%), anxiety and depression were common comorbidities over time. Eight patients had first degree relatives with visual snow. Clinical investigations were not contributory. Only a few treatment trials have been successful in individual patients. Our data suggest that 'visual snow' is a unique visual disturbance clinically distinct from migraine aura that can be disabling for patients. Migraine is a common concomitant although standard migraine treatments are often unhelpful. 'Visual snow' should be considered a distinct disorder and systematic studies of its clinical features, biology and treatment responses need to be commenced to begin to understand what has been an almost completely ignored problem.

Introduction

Patients with so-called 'visual snow' describe a persistent disturbance in the entire visual field resembling the 'static' or 'snow' of a badly-tuned analogue television. The symptoms are continuous and can persist over years. Although many primary care providers, ophthalmologists, neuro-ophthalmologists and neurologists have seen patients with such complaints, the problem remains undefined. Persistent visual disturbance is discussed infrequently in the literature (Haas, 1982; Liu *et al.*, 1995; Rothrock, 1997; Chen *et al.*, 2001; Jager *et al.*, 2005; Relja *et al.*, 2005; San-Juan and Zermeno, 2007; Wang *et al.*, 2008; Belvis *et al.*, 2010); some patients described have a disturbance more like migraine aura than visual snow, and others are not so clear. In these reports, patients frequently have comorbid migraine with or without aura leading to the assumption of visual snow being a migraine- or aura-related condition.

The exposure to hallucinogenic drugs, such as lysergic acid diethylamide (LSD), can result in post-hallucinogen perceptual disorder (PHPD) or 'flashbacks', which can last years (Abraham and Aldridge, 1993). As patients with visual snow also have continuous visual disturbances, they have been regarded by some as having post-hallucinogen perceptual disorder. Current explanations for visual snow seem inadequate, and current descriptions have not captured the detail of the clinical picture. Moreover, the presence of this disturbance in children and its remarkably stereotypic phenotype, which seems clearly distinct from migraine aura (Jager *et al.*, 2005), suggest the problem should be defined to allow its proper study.

The aim of our work was to characterize clinically patients with visual snow. We present criteria for the syndrome and discuss possible pathophysiological mechanisms. The description should enable studies leading to a better understanding of the disorder and treatment options for individuals affected by this disabling problem. The data have been presented in preliminary form to the 64th Meeting of the American Academy of Neurology (Schankin *et al.*, 2012*a*) and the 54th Meeting of the American Headache Society (Schankin *et al.*, 2012*b*).

Patients and methods

This is a three-step study starting with patients with visual snow who presented to us for diagnosis and management. In a second step, visual symptoms were retrospectively mapped by using data from an internet-based survey. Finally, prospective personal interviews were used to confirm the diagnosis and prevalence of these additional symptoms, to describe the clinical course and to assess the relevance of migraine, migraine aura, and drug use.

Retrospective chart review

We identified patients with visual snow by searching available outpatient clinic letters at the National Hospital for Neurology and Neurosurgery (NHNN, London, UK) as an audit of practice (P.J.G.) and the UCSF Headache Centre from 2001 to 2011. Keywords were either 'visual snow' or 'primary persistent visual disturbance'

(Jager *et al.*, 2005). All patients had been seen by at least one of the authors (P.J.G.).

A standardized approach was followed. The diagnosis of visual snow was confirmed when the description in the notes corresponded to the most specific currently available literature [Patients 6–9 from Liu *et al.* (1995), Patient 1 from Jager *et al.* (2005), and Patients 1 and 2 from Wang *et al.* (2008)] requiring a visual disturbance of 'tiny dynamic or flickering dots in the entire visual field like an analogue television that has not been tuned properly' or similar. Demographics, age of onset, relation to headache, additional visual symptoms, and past investigations were collected only in cases with a clear diagnosis of visual snow.

Retrospective identification of additional visual symptoms

Study population

We next analysed data sets without personal identifiers provided by the self-help group for visual snow, Eye On Vision Foundation (http://www.eyeonvision.org/). Independently from ourselves, Eye On Vision had performed an internet-based survey between June and October 2010. The survey was announced on their website and patients with self-assessed visual snow could participate. The questions in the survey were defined by the Eye On Vision Foundation and were based on their experience with visual snow. The following items had been interrogated: age (categorized as 13–23, 24–34, 35–45, 46–56, 57–67, older than 68 years), age at onset and duration of visual snow (both in years), and gender. The survey asked for the presence of visual snow, which was not specifically defined. The additional visual symptoms were phrased in lay language and consisted of (i) moving objects leave 'trails'; (ii) prolonged after images; (iii) floaters (physical spots or strands in your vision); (iv) bright flashes occur briefly, then fade; (v) dark spots occur briefly, then fade; (vi) little cells that travel on a wiggly path; (vii) hard time seeing at night; (viii) waves or swirls during daylight hours; (ix) swirls, clouds or waves with eyes closed; (x) photophobia (light sensitivity); (xi) colour vision changes; (xii) vision seems to be 'dim'; and (xiii) astigmatism.

Data analysis

Only complete data sets with the presence of visual snow were analysed. To control for outliers and other inhomogeneities, a random 50% sample (Group A) was drawn to identify additional candidate symptoms. In a second step, these candidate symptoms were confirmed in the remaining 50% (Group B). To obtain a reasonable number of meaningful additional visual symptoms in patients with visual snow, we arbitrarily used a cut-off frequency of 33% in both groups. As the absolute age of the participants was not reflected in the age categories, the mean age of each category was chosen (i.e. 18, 29, 40, 51, 62, and 73 years) for the calculation of demographic parameters.

Prospective clinical characterization

Study population

The study was listed on social media sites for visual snow asking for subjects with self-assessed visual snow to contact us. No additional information was given in these announcements. Patients were included from November 2011 to March 2012. A semi-structured telephone interview was performed after obtaining verbal consent from the patient. After the interview, patients were asked to keep the content of the interview to themselves to avoid influencing potential future study

subjects. The study was approved by the Institutional Review Board of the University of California, San Francisco (# 11-07270).

Telephone interview

In addition to age in years and gender, the interview covered:

(i) Current visual symptoms in the patient's own words. No clues were given by the interviewers to reduce the risk of suggestion.

(ii) Based on that information, a checklist on visual symptoms was completed by the interviewer. If necessary, additional open questions were asked to enable a decision on the presence and absence of the 'additional candidate symptoms' derived from the retrospective survey. These were defined by translation into the most likely underlying medical term as shown in Supplementary Table 1. Some of the visual symptoms (floaters, blue field entoptic phenomenon, self-light of the eye) are noted under specific conditions by normal individuals. These were only counted as an additional symptom if the patient stated that they were either present during everyday conditions or when they started together with visual snow. Photophobia was defined as normal light being either too bright or painful. If present, patients should further state which visual symptom was responsible for nyctalopia (impaired night vision). Typical features of visual migraine aura: unilaterality (homonymous), development over 5 min, duration, reversibility, zigzag lines, and scotoma (Headache Classification Committee of The International Headache Society, 2004; Eriksen et al., 2005), were probed for specifically.

(iii) Non-visual symptoms were noted.

(iv) Patients were asked about the beginning of their visual symptoms: age of onset of visual snow, continuous or episodic visual snow, progressive or stepwise worsening of all visual symptoms, worsening over how many years, duration of symptoms at current level.

(v) Patients who recalled the beginning of the visual snow or who had stepwise worsening were asked to describe further whether they had (a) headache attacks 3 days before or after; or (b) intake of illicit drugs [cannabis, ecstasy, cocaine, lysergic acid diethylamide (LSD), amphetamines, hallucinogenic mushrooms, and others] 7 days before the beginning/worsening of the visual symptoms. Headache was diagnosed according to the International Classification of Headache Disorders – 2nd edition (ICHD-II; Headache Classification Committee of The International Headache Society, 2004).

(vi) Headache history was assessed according to ICHD-II. Family history was noted.

(vii) Past medical history: as anxiety and depression were mentioned voluntarily by a substantial number of patients, all patients were contacted again and asked to complete Patient Health Questionnaire (PHQ)-8 to assess for depression (Kroenke et al., 2009) and Generalized Anxiety Disorder (GAD-7; Lowe et al., 2008) for anxiety. Current and past medication were noted, as well as a family history for visual snow.

(viii) We assessed the results of examination by a neurologist and ophthalmologist (dilated fundus exam, visual acuity, visual fields), electroretinogram, visual evoked potentials, MRI, electroencephalogram, and laboratory tests. No new tests were ordered solely for the study.

(ix) Patients were further asked to provide reports of their ophthalmology exams and to illustrate their visual symptoms. A selection is presented in Fig. 1 (with permission from the patients).

Data analysis

Only data sets of patients who met the following criteria were analysed to achieve a homogeneous study group: (i) spontaneous description (without clues) of visual snow as defined above for the retrospective chart review (Liu et al., 1995; Jager et al., 2005; Wang et al., 2008), regardless of the colour of the dots reported; and (ii) absence of any ophthalmological pathology in fundoscopy and perimetry assessed by an ophthalmologist or neuro-ophthalmologist.

Statistics

SPSS (v20, IBM Corp.) was used for data analysis. Standard descriptive statistics were applied. If appropriate, data are presented as mean ± standard deviation (SD).

Results

Retrospective chart review

The letters of 38 patients were identified. Sixteen were excluded because of incomplete description of visual snow. The remaining 22 (mean age ± SD: 27 ± 9 years, range 13–45 years, 12 female) are reported.

Fifteen patients had visual symptoms in addition to visual snow with continuous photophobia (in eight, 36%; three had chronic migraine in addition) and palinopsia (eight, 36%, with four having trailing of moving objects in addition) being the most common (Table 1). Three patients had continuous tinnitus, and four concentration problems. Nineteen letters mentioned the duration of visual snow: one had visual snow as long as she could remember; in the remaining 18, mean age of onset was 23 ± 9 years. Only seven letters mentioned how visual snow started: three patients had headaches, one of these migraine with aura, and none had illicit drug use. The most common comorbidity was migraine (in 17; three migraine with aura, seven chronic migraine), and 17 patients had a positive family history of migraine. One patient noted some incomplete relief from propranolol (80 mg), another from lamotrigine (150 mg/day). Worsening of symptoms was mentioned by one patient each on topiramate and amitriptyline. All patients had a normal neurological exam. An ophthalmological exam was reported in 11 letters (all normal) and an MRI was done in 12 patients (normal in 11 and unspecific in one, Supplementary Table 2).

Retrospective identification of visual symptoms

Data sets from 275 subjects with self-assessed visual snow were randomly assigned to Group A (n = 140) and Group B (n = 135). In each group, 19 participants did not enter any symptom and one did not provide information on visual snow resulting in 120 patients to be analysed in Group A and 115 in Group B. Demographics are depicted in Supplementary Table 2.

The mean age was 26 years, age of onset was 17 years and mean duration of visual symptoms was 9 years. There were fewer females than males in both groups. In Group A, floaters were the most common additional symptom (73%), followed by
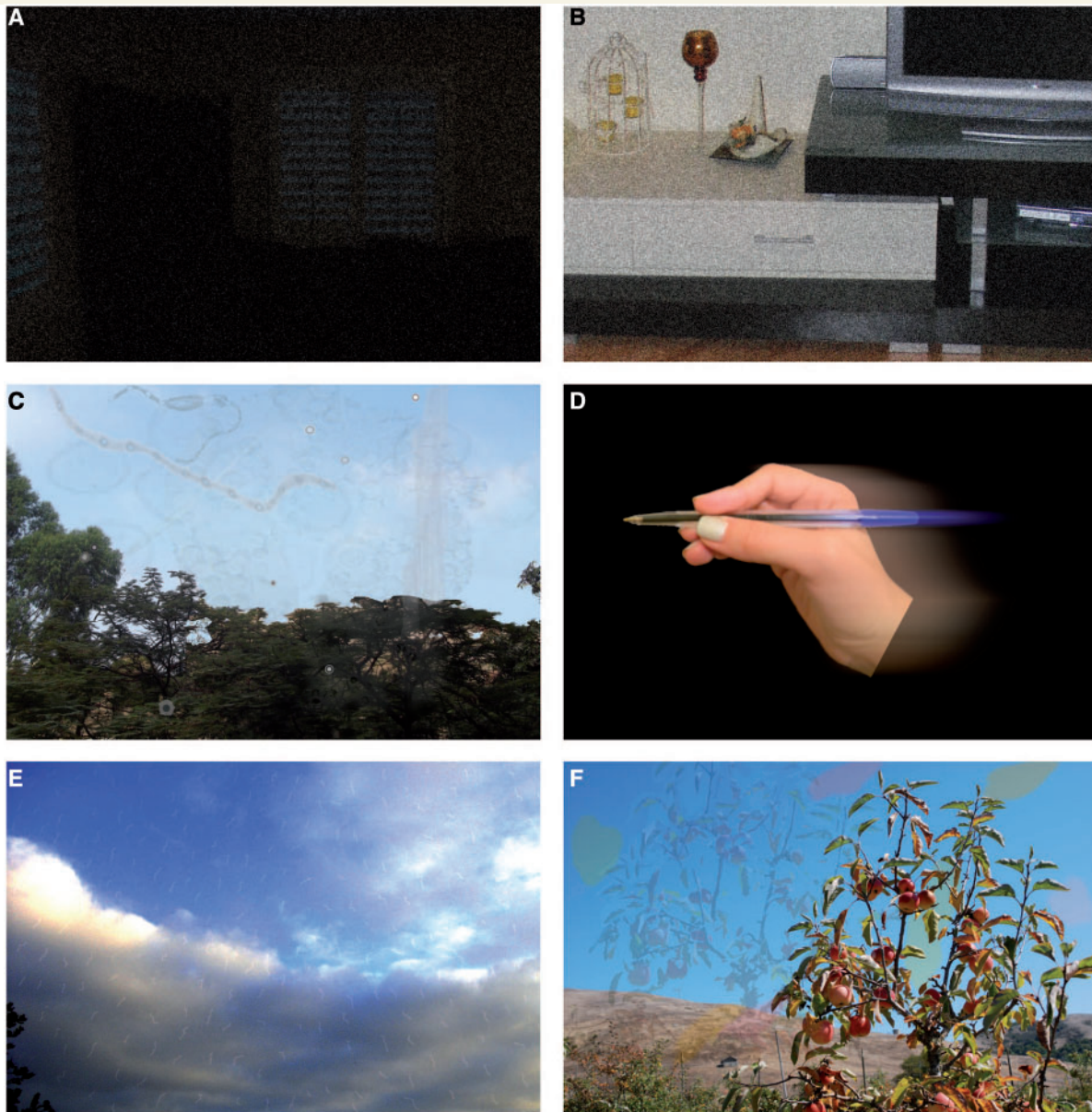
Figure 1 Illustrations done by three patients to demonstrate 'visual snow' (tiny dynamic flickering dots in the entire visual field) in the dark (**A**), during the day (**B**), floaters (**C**), palinopsia ('trailing') in (**D**), blue field entoptic phenomenon (**E**), and palinopsia (positive after images) in (**F**).

prolonged after images (63%), difficulties seeing at night (58%), little cells that travel on a wiggly path (57%), photophobia (54%), moving objects leave 'trails' (48%), bright flashes (44%), and swirls, clouds or waves with eyes closed (41%). In Group B, the same additional symptoms were present in more than one-third of participants.

Prospective clinical characterization

One hundred and forty-two patients contacted the UCSF Headache Centre. Twenty-two (15%) had visual symptoms that did not meet criteria for visual snow. Of the remaining 120 patients with visual snow, 26 had not been seen by a (neuro-)ophthalmologist and 16 had abnormal findings in fundoscopy or perimetry. The

remaining 78 patients will be described here in more detail. Three patients had also taken part in the Eye on Vision survey.

Patient demographics and clinical course

The mean age of patients with visual snow was 30 ± 10 years, range 10–60 years. Interviews were carried out with subjects from the USA, Australia and 11 European countries. The female:male ratio was balanced. One-quarter of patients had visual snow as long as they could remember (Table 2). Age of onset in the remaining patients was in early 20s ('later onset'). Mean duration in these patients was 8 ± 10 years. The large majority of patients

Table 1 Demographics, comorbid migraine, additional visual symptoms and test results of patients seen at the NHNN and UCSF Headache Centre between 2001 and 2011

ID	Age (years)	Gender	Age of onset of visual snow	Comorbid migraine	Comorbid visual aura	Additional visual symptoms	Examinations		
							Neurological	Ophthalmological	MRI
1	21	M		+			a		
2	40	M	13			Bright flashes	+	+	+
3	37	M	33	+			+		
4	34	M	24	+	-		+		
5	31	M	31			Straight lines moving across the visual field, trailing, persistent after images, photophobia	+		
6	21	F	20	+			+	+	
7	20	F				Water running down a window, metamorphopsia, déjà vu	+		
8	31	M	30				+	+	+
9	20	M	18	+		Geometric and coloured images that distort vision	+	+	+
10	24	M	22	+		Excessive floaters	+		+
11	31	F	26	+	+	Persistent afterimages, photophobia	b		
12	21	F	17	+	-	Persistent afterimages, photophobia	+		
13	17	F	13	+	+		+	+	+
14	45	M	45	+	+	Flashing lights, photophobia	+	+	c
15	21	F	19	+	-		+		+
16	26	F	#	+		Trailing, persistent after images, excessive floaters, bright flashes, uncountable fast moving dots when looking at the blue sky, coloured clouds when closing eyes, photophobia	+	+	+
17	19	F	19	+		Photophobia	+		+
18	37	F	35	+		After images, trailing of moving objects	+		
19	20	F	19			Excessive floaters, coloured swirls with eyes closed	+	+	+
20	13	F	12	+	-	Bright flashes, twisting/moving of things, such as walls in the exam room, after images, photophobia	+	+	+
21	40	M	18	+	-	After images	+	+	+
22	25	F		+	-	Trailing, persistent afterimages, halos around light-sources, excessive floaters, fast moving tiny rings when looking at the blue sky, photophobia	+	+	

Symptoms present for as long as the patient can recall.
empty cells = no information available from clinical notes, + : present/normal, - : not present.
[a]Duane's syndrome.
[b]Mild postural and action tremor.
[c]Subcortical T_2 hyperintensities.

with later onset of visual snow had continuous symptoms from the beginning. Five patients had initial episodic visual snow. Continuous visual snow started in these patients 2 weeks to 15 years after the first episode. Less than half of patients had constant visual symptoms from the beginning (Table 2). The remaining patients had either progressive or stepwise worsening.

Additional visual symptoms

Some of the additional visual symptoms are illustrated in Fig. 1. Palinopsia manifesting with afterimages from stationary scenes was present in 86%, and with trailing in 60% (Table 3). Excessive floaters were the most frequent entoptic phenomenon (81%). Second most common was blue field entoptic phenomenon (79%). About two-thirds of patients had spontaneous photopsia, photophobia and nyctalopia. Consistent self-light of

the eye occurred in half of patients. Nearly all patients complained of at least one additional symptom (76 of 78; 97%) and 72 (92%) had at least three additional visual symptoms.

Additional non-visual symptoms

The majority of patients complained about bilateral non-pulsatile tinnitus and concentration problems. Further, some patients felt lethargic and irritated (Table 3).

Events with the beginning or worsening of the visual disturbance

Sixty-four patients recalled the onset of their visual disturbance and/or a stepwise worsening. Twenty-three (36%) of these patients had a headache attack within 3 days before or after the

Table 2 Demographics, past medical history, family history, beginning of 'visual snow', and temporal development of the severity of all visual symptoms

	All patients with visual snow n = 78	
Age	30 ± 10	
Females (female:male)	41	1.1:1
History of headache	68	87%
Worsening with visual snow	29 of 68	37%
Chronic headache	17 of 68	22%
History of migraine	46	59%
History of typical migraine aura	21	27%
Only visual	18 of 21	86%
Visual and others	3 of 21	14%
Family history of headache	44	56%
Family history of headache in patients without history of headache	7 of 10	70%
History of anxiety	12 of 53	23%
History of depression	11 of 53	21%
Visual snow present since childhood[a]	19	24%
Later onset of visual snow[b]	59	76%
Start age (years)	21 ± 9	
Duration (years)	8 ± 10	
Continuous from beginning	54 of 59	92%
Initial episodic	5 of 59	8%
Constant from start	32	41%
Duration of constant symptoms (years)	14 ± 18	
Progressive worsening	33	42%
Duration of progressive worsening (years)	6 ± 8	
Now constant symptoms	16 of 33	48%
Duration of constant symptoms (years)	3 ± 3	
Stepwise worsening	10	13%
Now constant	10 of 10	100%
Duration of constant symptoms (years)	3 ± 2	
Both progressive and stepwise	3	4%

[a]Symptoms present as long as the patient can recall.
[b]Patient recalls period of life without visual snow.
About two-thirds of patients had visual snow starting later in life. A minority of these patients had initial episodes of visual snow before the beginning of the continuous visual snow. Anxiety (defined by a GAD-7 score ≥ 10) and depression (PHQ-8 ≥ 10) could not be assessed in all patients as indicated in the respective field.

worsening of the visual symptoms. Sixteen could be classified as migraine according to the ICHD-II criteria (Headache Classification Committee of The International Headache Society, 2004). Only seven patients in total had a typical visual aura, and five patients recalled consumption of cannabis (one used amphetamines in addition, no LSD or hallucinogenic mushrooms) before such beginning or worsening of the visual symptoms.

Experience with the consumption of illicit drugs

Cannabis has been tried at least once in 31 patients with visual snow (40%). In addition to the patients, who had a start of the visual snow after using cannabis, one experienced a temporary worsening of the visual snow while smoking. Ecstasy has been

Table 3 Additional visual and non-visual symptoms in patients with visual snow

	All patients with visual snow n = 78	
Palinopsia ('after images')	67	86%
Palinopsia ('trailing')	47	60%
Floaters	63	81%
Blue field entoptic phenomenon	62	79%
Spontaneous photopsia	49	63%
Self-light of the eye	41	53%
Photophobia	58	74%
Light is too bright	43	74%
Light is painful	15	26%
Nyctalopia	53	68%
Due to visual snow	25	47%
Due to palinopsia	3	6%
Due to halos	3	6%
Due to a combination	22	41%
Tinnitus	48	62%
Concentration problems	47	60%
Lethargy	43	55%
Irritability	29	37%

tried by eight patients with visual snow (10%). Cocaine produced a temporary worsening of the visual symptoms in one patient. Seven patients (9%) had experience with cocaine. LSD did not induce visual snow or any additional visual symptoms and was tried by three patients (4%). For recreational purposes, amphetamines were taken at least once by four patients (5%). None of our patients has tried hallucinogenic mushrooms.

Past medical history and family history

Headache

Sixty-eight patients had a history of headache with 46 meeting the ICHD-II criteria for migraine (Table 2). Typical migraine aura was present in 21 (27%). A subjective worsening of the headache together with a worsening of the visual disturbance was noted by 29 and chronic headache was present in 17. Patients without personal headache history frequently stated a positive family history for headache.

Anxiety and depression

Moderate to severe anxiety defined as a GAD-7 score of ≥10 was present in 12, and 11 had a PHQ-8 score of ≥10 indicating moderate to severe depression.

Other past medical history

The main comorbidities mentioned by the patients were allergies, gastroesophageal reflux disease, vertigo and attention deficit disorder (all in <12%).

Family history of visual snow

Eight patients (10%) with visual snow had first degree family members with visual snow.

Previous investigations

Only patients with normal ophthalmological exams in terms of fundoscopy and perimetry were included in this study. Thirty-four patients (44% of 78) had normal uncorrected visual acuity, 34 were myopic and 10 were hyperopic. According to the patients, best corrected visual acuity was, in general, normal. The original ophthalmology reports could be obtained from 21 patients: 20 had normal best-corrected visual acuity and one patient had 20/25-1 bilateral. Fourteen patients had an electroretinogram (all normal). Fifty-four patients were seen by a neurologist (all had a normal exam) and 22 had visual evoked potentials (all normal). An electroencephalogram was abnormal in 2 of 29 (one had mild encephalopathy and one with history of epilepsy had epileptiform patterns). An MRI of the brain was done in 57 patients (four had non-specific white matter lesions; one patient had a pituitary microadenoma). Routine blood tests and medical exams (blood pressure, electrocardiogram) were normal or not contributory.

Effect of medication

Most patients have been treated empirically in the past by their primary care physician, a neurologist or an ophthalmologist. The main groups of medications include standard psychopharmaceuticals, pain medication, antiepileptics, and migraine prophylactics. No patient reported complete resolution of symptoms by treatment, and no medication has shown consistently to improve or worsen visual snow or its associated visual symptoms.

Discussion

Here we describe three substantial cohorts of patients with a persistent dynamic whole field visual disturbance that is stereotypic and, by clinical characterization, not at all like migraine aura. The syndrome has undoubtedly been seen in practice, certainly by ophthalmologists or neurologists, yet has not been hitherto formally characterized. The normal findings on routine ophthalmological and neurological tests have led to the condition being either dismissed as psychological, attributed to drug use or wrongly classified as migraine aura. The remarkable clinical congruence between each patient group, the minimal history of drug abuse, presence of symptoms in childhood and adolescence, minimal psychiatric co-morbidity and poor response to conventional treatments suggests the syndrome is real and unique. The disturbance has been called 'visual snow' by patients because of its remarkable similarity to the noise on analogue television, and we suggest naming the syndrome after this 'visual snow', or if one prefers a more classic approach 'chionous dysblepsia' named after the ancient Greek goddess of snow (Chione).

Retrospective chart review

Over one decade, we have personally seen almost 24 patients with the chief complaint visual snow as documented specifically in the clinical notes that we could access for details. Chronologically seen, the letters of the earlier patients only mentioned the main visual symptom. Over time, additional visual complaints were listed reflecting increased experience and the literature available (Liu *et al.*, 1995; Jager *et al.*, 2005; Wang *et al.*, 2008). After having seen a number of patients with identical descriptions from different origins, including children, our interest was aroused and with it, more detailed histories taken. Our main findings from this retrospective chart review were that patients with visual snow have (i) additional visual symptoms; (ii) often comorbid migraine; and (iii) typically normal ophthalmological exams.

Retrospective survey

The question of additional visual symptoms was approached by retrospectively analysing survey data provided by a self-help group on visual snow. A cut-off frequency of one-third was chosen to obtain a reasonable number of symptoms for future studies. More than one-third of patients complained about the same additional symptoms in both random groups (Groups A and B) suggesting a homogenous distribution of these visual symptoms.

Prospective study

All subjects in the prospective study underwent a detailed interview by experienced neurologists and headache specialists. A thorough history was taken to make sure that only patients with visual snow meeting the description of our chart review patients (spontaneous description of 'noise of an analogue television') were included in the final analysis. To avoid including ophthalmological disorders that might mimic visual snow, we excluded subjects who never had an exam by a (neuro-) ophthalmologist or who had pathological findings on fundoscopy or perimetry. Only a minority of patients were finally excluded because of pathological findings (16 of 94), and most of our patients had normal best-corrected visual acuity, consistent with Alissa *et al.* (2012), who have shown among nine patients with visual snow, that all had normal visual acuity, colour and rapid flicker sensitivity. The data indicate that visual snow is not a primary eye disease. However, three patients studied by Alissa *et al.* (2012) had absence of recovery of pupillary response following a coloured stimulus indicating prolonged retinal afferent signals, the first objective finding in visual snow.

Additional visual symptoms

The high prevalence of additional visual symptoms in our patients indicates that patients with visual snow have a unique 'syndrome' of visual disturbances. We propose that the additional visual symptoms can be grouped into: (i) palinopsia; (ii) entoptic phenomena; (iii) photophobia; and (iv) nyctalopia.

Palinopsia

Palinopsia is the persistence of a visual image following the removal of the exciting stimulus (Critchley, 1951). When such removal of the exciting stimulus occurs by movement relative to the retina, patients may experience the after image being behind the original ('trailing'). Palinopsia has to be distinguished from physiological retinal after images (Kinsbourne and Warrington, 1963). Palinopsia is associated with multiple conditions including consumption of illicit drugs (Abraham, 1983; Kawasaki and Purvin,

1996), with neurological diseases, such as focal neurological lesions (Critchley, 1951; Bender *et al.*, 1968), and migraine (Belcastro *et al.*, 2011). Pomeranz and Lessell (2000) described nine patients with palinopsia, of whom six did not have any pathology of the eye or the CNS. Notably, one patient had 'snow—like watching a television channel that isn't broadcasting' and another reported 'particles of snow floating around' suggesting that these patients also had visual snow. Therefore, the visual snow syndrome might represent an important aetiology for palinopsia in patients without cerebral pathology or drug use.

Entoptic phenomena

Entoptic phenomena have been recognized by physiologists and ophthalmologists for more than a century (von Helmholtz, 1896). Tyler (1978) summarizes them as 'phenomena arising from [any] structure of the visual system as a result of specific stimulation'. Entoptic phenomena thus can be perceived by healthy subjects, but according to our data, they occur 'during everyday conditions' in patients with visual snow indicating that such 'specific' stimulation is not necessary. For 'blue field entoptic phenomenon' (or Scheerer's phenomenon), the 'specific stimulation' is thought to be 'staring' at the sky or a bright snowfield through a blue glass (von Helmholtz, 1896) or through an entoptoscope resulting in up to 25 corpuscles seen with sudden acceleration in any direction by healthy individuals (Priestley and Foree, 1956). These corpuscles are thought to be leucocytes flowing within the macular retinal microvasculature (Sinclair *et al.*, 1989). The description of our patients 'little cells that travel on a wiggly path' corresponds well with such blue field entoptic phenomenon suggesting an identical mechanism although this was not formally tested using a blue field entoptoscope. The 'self-light of the eye' has been described as luminous clouds of orange or violet colour moving centrifugally or centripetally (Marshall, 1935), which suits well the phenomenon of 'swirls, clouds or waves with eyes closed' experienced by our patients. The cause of this perception is unknown, but it has been attributed to retinal circulation and intracerebral or intraocular pathologies (Marshall, 1935). Its prevalence and significance in the general population is unknown, but our patients seem to be frequently affected.

Photophobia

There is no completely standard medical definition of photophobia. Usually, patients avoid light as they either perceive it being too bright (abnormal sensitivity to light: photic photophobia or hypersensitivity) or painful (causing or worsening head pain or eye pain: photic allodynia). There is no evidence that photophobia is caused by typical ocular pathology (Garcia-Valenzuela *et al.*, 2003) in our patients. Vanagaite *et al.* (1997) have shown that healthy individuals can tolerate significantly higher luminance than migraineurs even outside a headache attack. Our patients with visual snow frequently had a history of headache and more than half of patients had a history of migraine although there was no influence of headache frequency on visual snow.

Nyctalopia

With lowering light intensity, the rod system is more and more involved in mesopic and scotopic vision (Stockman and Sharpe,

2006). In our patients, electroretinography, as one of the key diagnostic tests to assess cone and rod function (Petzold and Plant, 2006), and fundoscopy has been unremarkable. It is therefore unlikely to be a dysfunction of the photoreceptors that contributes to impaired night vision in visual snow.

Additional non-visual symptoms: tinnitus

The high prevalence of bilateral tinnitus indicates that other sensory systems might also be involved in patients with visual snow supporting that visual snow is a disorder of the brain and not the eyes. One could describe tinnitus as acoustic noise in this context. Whether tinnitus is part of the 'syndrome' of visual snow is currently unclear. The high prevalence in patients with visual snow (62%) in comparison with the general population, 7.9% have frequent tinnitus (Shargorodsky *et al.*, 2010), suggests that both disorders might share some pathophysiological mechanisms. Clinically, visual snow might be for the visual system what tinnitus, i.e. phantom auditory perception, is for the auditory system. Tinnitus is associated with changes in neuronal activity of central auditory structures, such as the primary auditory cortex (Arnold *et al.*, 1996) or with thalamocortical dysrhythmia (Llinas *et al.*, 1999). Similar to patients with visual snow, pharmacological treatment trials are often not able to suppress chronic tinnitus completely. The promising response of tinnitus sufferers to new approaches using neuromodulation (Vanneste and De Ridder, 2012*a*, *b*) thus might support the use of these techniques in patients with visual snow. Similarly, concentration problems, irritability or lethargy could be part of the biology of visual snow. Alternatively, these symptoms could be a consequence of the visual disturbance causing distraction, e.g. for visual tasks, or be migrainous as a coincidence. Whether there is an over-arching disorder of the brain in which sensory dysmodulation is the key, and to which each of migraine, visual snow and primary tinnitus belong, among other syndromes, remains a fascinating question.

The relevance of headache, migraine and migraine aura

In patients with visual snow, the prevalence of migraine and migraine with typical aura (Headache Classification Committee of The International Headache Society, 2004) is high in comparison with the general population (Lipton *et al.*, 2002). The lack of association with acute headache attacks or migraine aura episodes initially in visual snow suggests a link to interictal migraine pathophysiology. This is supported by psychophysical studies showing that migraineurs might experience some of the symptoms that are characteristic for visual snow. As an example, migraineurs have an elevated contrast threshold in the presence of high external luminance noise (Webster *et al.*, 2012), a lower threshold for interictal photophobia (Vanagaite *et al.*, 1997), a higher susceptibility for palinopsia (Belcastro *et al.*, 2011), and reduced visual contrast sensitivity (McKendrick and Sampson, 2009). Altered cortical excitability is discussed in migraine (Afra *et al.*, 1998; Mulleners *et al.*, 2001) and may be relevant in visual snow. None of the patients described the additional visual symptoms as being consistent with typical migraine aura, which is most likely an event analogous to cortical spreading depression (Hadjikhani *et al.*,

Table 4 Proposed criteria 'visual snow' syndrome

A   Visual snow: dynamic, continuous, tiny dots in the entire visual field lasting longer than 3 months.[a]

B   Presence of at least two additional visual symptoms of the four following categories:

   (i)   Palinopsia. At least one of the following: afterimages (different from retinal after images)[b] or trailing of moving objects.

   (ii) Enhanced entoptic phenomena.[c] 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 (impaired night vision)

C   Symptoms are not consistent with typical migraine visual aura.[d]

D   Symptoms are not better explained by another disorder.[e]

[a]Patients compare it to 'TV static' or 'TV snow'. The dots are usually black/grey on white background and grey/white on black background. Alternatives could be transparent dots, white flashing dots, or coloured dots.

[b]Palinopsia includes after images and trailing of moving objects. After images should be different from retinal after images, which occur only when staring at a high contrast image and are in complementary colour.

[c]Phenomena arising from the structure of the visual system itself and include: excessive floaters in both eyes, excessive blue field entoptic phenomenon (uncountable little grey/white/black dots or rings shooting over visual field in both eyes when looking at homogeneous bright surfaces, such as the blue sky), self-light of the eye (coloured waves or clouds when closing the eyes in the dark), or spontaneous photopsia (bright flashes of light).

[d]Typical migraine aura (IHS 1.2) as defined by the International Headache Society in the International Classification of Headache Disorders 2nd edition (Headache Classification Committee of The International Headache Society, 2004). Main features of typical migraine aura are: similarity to previous visual auras, unilaterality, movement, edges, positive and negative visual phenomena, zigzag lines (Eriksen et al., 2005).

[e]Normal ophthalmology tests (best corrected visual acuity, dilated fundus exam, visual field and electroretinogram), no intake of psychotropic drugs.

2001). In the literature of visual snow and persistent migraine aura, some patients were described as having flashing lights, zigzag lines (Rothrock, 1997; Jager et al., 2005), scintillating scotoma (Relja et al., 2005; San-Juan and Zermeno, 2007) occurring in one visual hemifield (Haas, 1982; Rothrock, 1997; Chen et al., 2001; Jager et al., 2005; Relja et al., 2005; Wang et al., 2008) or showing directed movement (Belvis et al., 2010), which have developed with a typical migraine attack. These patients likely have migraine aura and have contributed to confusion over the syndrome.

Limitations

One limitation of this study is that all information was interview-based and thus exposed to the risk of suggestibility to patients by the interviewers. However, all questions were asked as openly as possible without any clues to reduce the likelihood of such errors. Similarly, the recruitment through the internet might result in patients coordinating answers with each other. This, however, seems to be highly unlikely, given the long time period covered by the chart review involving two headache clinics in two different countries and the high variability of our prospective study population (age range 10–60 years) coming from 13 different countries distributed over three continents. Given that the initial clinical patients were seen in the pre-social media era, and the same visual disturbance was reported in children, collusion seems a most unlikely explanation. Certainly, internet-based sampling attracts a younger more pro-active population, however, the clinical picture was so homogenous from all three cohorts, it seems likely that visual snow is a real entity.

Conclusion

From the data presented here, almost all patients with 'visual snow' have a variety of additional visual symptoms (palinopsia,

enhanced entoptic phenomena, photophobia, and nyctalopia), which do not sound like typical migraine aura at all. Visual snow therefore represents a unique clinical syndrome. Our data acknowledge an overlap of migraine and visual snow but do not support the hypothesis that migraine attacks or individual episodes of migraine aura 'cause' visual snow. Our data do not support a view the visual snow syndrome is caused by anxiety, depression or the intake of illicit drugs, such as LSD. Remarkably, most patients with visual snow have normal best corrected visual acuity, perimetry and fundoscopy. Any association with visual loss or acute onset of visual symptoms similar to visual snow, especially floaters and photopsia, would therefore require appropriate assessment by a specialist before calling it 'visual snow'.

We would define the 'visual snow' syndrome by the presence of visual snow as the main criterion, with some additional visual criteria, and exclusion of migraine aura, and overlapping diseases, such as ophthalmological pathology or intake of psychotropic drugs (Table 4).

Supplementary material

Supplementary material is available at *Brain* online.

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