

# Visual snow syndrome: a comparison between an Italian and British population

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**Background and purpose:** Visual snow manifests as a pan-field, dynamic visual disturbance described as continuous television static-like tiny flickering dots. Current diagnostic criteria further require at least two additional symptoms for visual snow syndrome (VSS) from: palinopsia (afterimages and trailing); entoptic phenomena (floaters, blue field entoptic phenomenon, photopsia, self-light of the eye); photophobia and nyctalopia. Our objective was to compare the phenotype of VSS in an Italian and British population.

**Methods:** Patients with VSS were characterized clinically using the current criteria. An online survey was prepared in collaboration with the patient group Eye-on-Vision. Patients were directed to the site if they contacted us by email asking to be involved in research. After data collection, we compared the phenotypic characteristics of a subgroup of British versus Italian patients taking part in the survey. As we expected more responses from the UK, we matched 100 UK patients for gender and age with our Italian cohort.

**Results:** Patients were enrolled from the UK ( $n = 100$ ) and Italy ( $n = 100$ ). The populations had similar demography. After multiple correction testing there were no differences in VSS features between the two groups. The same was true for the prevalence of migraine and previous use of recreational drugs.

**Conclusion:** This is the first study comparing the phenotype of VSS between two distinct populations. Our findings suggest that the visual snow phenotype, as well as migraine comorbidity, is similar across the two groups.

## Introduction

Visual snow manifests as a pan-field, dynamic visual disturbance described as continuous television static-like tiny flickering dots, termed 'static' or snow [1]. Current diagnostic criteria for the complete visual snow syndrome (VSS) require at least two additional visual symptoms from: palinopsia (afterimages and trailing); entoptic phenomena (floaters, blue field entoptic phenomenon, photopsia, self-light of the eye); photophobia and nyctalopia [1]. Migraine and tinnitus

are common comorbidities of visual snow, reported in up to three-quarters of patients [2,3].

So far, systematic collections of the VSS phenotype on wide populations from a specific geographical area have been performed in only two countries: in 78 subjects in the USA [1] and 58 in the Netherlands [4]. A formal comparison of two groups affected by visual snow and belonging to different geographical and cultural backgrounds has not been conducted.

Our objective was to compare the phenotype of VSS, including its common clinical characteristics, in an Italian and UK population of affected subjects. The results were presented in preliminary form at the 4<sup>th</sup> Congress of the European Academy of Neurology (Lisbon, Portugal, 16–19 June 2018) [5].

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## Methods

This study was part of a web-based survey conducted in a larger population with VSS [6].

In the present study, we conducted a cross-sectional analysis on two different subpopulations of subjects taking part in the online survey: one from Italy and the other from the UK. All of the analysed subjects fulfilled the complete diagnosis of VSS, according to the current criteria [1]. Data for the study were collected between April 2016 and May 2018. The study was approved by the KCL Research Ethics Panel. The online survey we used was prepared in English in collaboration with the patient group Eye-on-Vision [6]. For patients who required a translation, authors M.V. and F.P. translated the questionnaire into Italian following the appropriate guidelines [7].

After data collection, we compared the phenotypic characteristics of UK patients versus Italian patients. As we expected more responses from the UK, we matched 100 UK patients for gender and age with our Italian subpopulation. Comparisons between the two groups of patients were performed with the Mann–Whitney *U*-test or chi-squared test for continuous or categorical variables, respectively. Due to multiple testing, adjusted *P* values based on the Bonferroni correction are presented with a significance level set at  $P < 0.0026$ .

## Results

Patients were enrolled from the UK ( $n = 100$ ) and Italy ( $n = 100$ ). Table 1 shows demographic and clinical data from the two groups. After correction for multiple testing, we found that all the VSS features, in particular the history of the disease, the types of static reported and the frequency of additional visual symptoms, were no different between the two groups. The same was true for the prevalence of comorbidities (migraine and tinnitus) and previous use of recreational drugs.

## Discussion

Visual snow syndrome is a poorly recognized neurological condition, characterized by persistent and disabling visual disturbances that are not matched by any underlying structural, drug-related, psychiatric or epileptic cause. The diagnosis can be formulated based on the fulfilment of specific clinical criteria that have been validated in a large population [6].

This is the first study comparing the clinical phenotype of two populations of patients experiencing VSS,

**Table 1** Demographic and clinical data of the two populations of patients with visual snow syndrome

	UK ( $n = 100$ )	Italy ( $n = 100$ )	<i>P</i>	
			<i>U</i> -test	Chi-squared test
Female, <i>n</i>	53	53		0.88
Age, years	30 ± 10	32 ± 10	0.1	
History of disease				
Sudden onset, <i>n</i>	32	51		0.009
VSS age of onset	24 ± 10	22 ± 10	0.44	
Disease years	19 ± 14	15 ± 14	0.09	
VSS: static type, <i>n</i>				
Black and white	65	58		0.30
Coloured	40	23		0.01
Flashing	50	44		0.39
Transparent	41	54		0.06
Number of static types				
Mean ± SD	1.96 ± 1.1	1.79 ± 1.1	0.28	
Median; IQR	2; 2–3	1; 1–2		
VSS: additional symptoms, <i>n</i>				
Afterimages	83	70		0.03
Trailing	66	53		0.06
Blue field entoptic phenomenon	78	76		0.73
Floaters	83	93		0.03
Self-light of the eye	70	65		0.45
Flashes	70	52		0.009
Nyctalopia	79	76		0.61
Photophobia	74	87		0.02
Number of VSS symptoms				
Median; IQR	6; 5–7	6; 5–7	0.63	
Medical history and comorbidities, <i>n</i>				
Migraine	69	70		0.96
Tinnitus	79	63		0.01
Previous use of recreational drugs	26	21		0.40

IQR, interquartile range; VSS, visual snow syndrome. Data are mean ± SD, unless otherwise stated. UK patients were matched for gender and age with our Italian subpopulation. Due to multiple testing across 19 variables, adjusted *P* values based on the Bonferroni correction were considered. The significance level was therefore lowered to  $P < 0.0026$ . *P* values for Mann–Whitney *U*-test or chi-squared test are shown.

who spoke different languages and had different geographical and cultural backgrounds. Our findings show that the clinical criteria available for VSS are generalizable to different populations and that when these criteria are carefully followed and translated they can be used in different languages.

It is important to demonstrate that a syndrome characterized by subjective symptoms and without objective measures to aid the diagnosis presents with similar clinical features in populations with different languages and genetic backgrounds. Whether clinical

similarities also correspond to a similar prevalence of VSS in these different populations remains to be determined.

A methodological limitation of the study could arise from the process of translation of the questionnaire from the English version to the Italian one. In this respect, it should be noted that the authors who performed the translations are of Italian origin and have long experience in working in the English language. Furthermore, *ad hoc* guidelines were followed in order to ensure a high-quality translation (7). It is possible that strict multiple comparison correction could have masked some relevant differences between the two populations. Without correction, the Italian population had a higher prevalence of certain visual symptoms, particularly of photophobia. Given the geographical and environmental differences between the two countries, it is indeed possible that different exposure to sunlight could have affected the Italian subjects with VSS.

In conclusion, this is the first study comparing the phenotype of VSS between two geographically distinct and culturally different populations. Our findings suggest that the VSS phenotype, as well as the comorbidities of migraine and tinnitus, are similar across different populations.

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### Disclosure of conflicts of interest

M.V. and F.P. declare no financial or other conflicts of interest. P.J.G. reports grants and personal fees from Amgen and Eli-Lilly and Company, a grant from Celgene, and personal fees from Alder Biopharmaceuticals, Aeon Biopharma, Allergan, Biohaven Pharmaceuticals Inc., Clexio, Electrocore LLC, eNeura, Epalex, Impel Neuropharma, MundiPharma, Novartis, Pfizer, Santara Therapeutics, Teva Pharmaceuticals, Trigemina Inc. and WL Gore, and personal fees from MedicoLegal work, the Massachusetts Medical Society, Up-to-Date, Oxford University Press, and Wolters Kluwer; and a patent magnetic stimulation for headache assigned to eNeura without fee.

### Data availability statement

Data are available from the corresponding author upon reasonable request.

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