Malfunctioning cones and remedial tinted filters

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Objective: To compare photophobic migraine patients (CM) with photophobic patients without headache in regard to the incidence of dysfunctional cones due to Irlen Syndrome. Design: Prospective, observational case-control study. Patients: Three study-groups (20 subjects each) were recruited as follows: (1) photophobic patients suffering from chronic migraine (CM); (2) photophobic patients without headaches; (3) healthy subjects. Methods: The photophobia was evaluated as total error score (TES) at Farnsworth-Munsell 100 hue test and by electroretinography. Results: About 85% of the photophobic tested patients were suffering from Irlen Syndrome (IS). Tinted filters, shifting daylight towards blue or towards green/red, markedly reduced the photophobic discomfort. The benefit was more evident in CM patients ($p<0.05$ ANOVA). Conclusions: IS appears to be a hereditary disease related to a sectorial reduction in cones photopigment. There was a high incidence of IS in the CM patients, and these mainly responded well to tinted filters prompting further research. Key words : photophobia, chronic migraine, Irlen Syndrome, tinted filters, electroretinogram.

Introduction

Olive Meares, a teacher in New Zealand, was the first to provide a detailed written account (1980) of the spatial distortion affecting the reading of some individuals, and to report that the troubles could be reduced or eliminated by the use of colored paper or by using colored plastic overlays over the text to be read [1]. Helen Irlen, educational psychologist, as Director of the Adult Learning Disabilities University Program, obtained in 1980 a government grant to investigate the mismatch of potential and performance in adult students at California State University. Her work [2,3] established a link between visual disturbance on the page and reading achievement, since, by using color, she could eliminate the perceptual difficulties that were preventing students from accessing print and causing physical discomfort during reading. Irlen has been recognized as the first person to research, categorize, and develop a testing method for a specific type of perceptual difficulty, usually referred to as Irlen Syndrome (IS) and occasionally as Meares-Irlen Syndrome [4]. As the research proceeded, different groups of photophobic patients were tested and the following definition of IS was proposed by Barbolini et al. [5]:

- inability to process full spectral daylight for a supposed cones malfunction related to macular photopigment content,
- evidence of a hereditary trait;
- pure or associated with other pathological conditions;
- liable to benefit from remedial technology (tinted filters).

Photophobia is a common complaint, but in headache sufferers this symptom is widely referred to. Among headache sufferers, over 90% of migraine patients refer to photophobia [6] and this symptom is well reported and common in migraine patients and could predict diagnostic categories [7]. The effect of different wavelengths of light causing photophobia in migraine patients has been shown [8], and the use of colored filters individually prescribed in migraine patients is likely to be related to pattern glare and seems to be an effective treatment to reduce symptoms from such stimuli [9]. Recently it has been shown that the after-image phenomenon in patients with migraine with aura probably reflects the heightened sensitivity to visual stimuli of patients with migraine [10]. Also patients with a benign essential blepharospasm were more sensitive to light than control group and as sensitive to light as patients with migraine, and tinted lenses seem to be able to ameliorate symptoms [11]. Moreover, there are suggestions of a probable genetic influence on headache disorders, and in chronic headache patients [12, 13].

So we decided to study two series of subjects concerning photophobia: chronic migraine sufferers, and subjects with photophobia but without headaches, to confirm the hypothesis of malfunctioning cones due to IS in different diseases.

Patients and methods

Three study groups of 20 subjects each were recruited after screening performed by an Irlen diagnostician as follows:

1) photophobic-patients suffering from chronic migraine (CM), mostly classified as 1.5.1 and 8.2 according to the criteria of the International Headache Classification of Headache disorders [14];
2) photophobic patients suffering from photophobia without headaches;
3) healthy subjects (control group).

The photophobic patients suffering from chronic migraine were 11 females and 9 males, aged 35–65 with an average age of 48,51 years, and were enrolled as a consecutive series of patients attending the Headache Study Center of Modena University in the period Jan-Nov 2006.

The second group of patients suffering from IS without headaches were 8 females and 12 males, aged 35–60, with an average age of 46,52 years, reporting photophobia without a history of migraine, and attended consecutively in the same period the Ophthalmology Clinic of the same University.

Photophobic negative healthy subjects (10 females and 10 males, aged 25–65, with an average of 45,71 years), belonging to the staff of this University were recruited as control group.

The grading (slight, moderate, severe) of IS, which is impacted by light brightness, glare, black and white contrast, depth perception, equilibrium, and gross motor activities was diagnosed as follows:

IS-slight. The patients reveal a certain effort in carrying out the perception tasks required. The selected tinted overlay facilitates the reading and the selected tinted filter(s) offer physical comfort.

IS-moderate. The patients need a great effort in carrying out the tasks. Many of the tasks are not possible. They are disturbed by the white and black contrast. Glare disturbs them. Strain and fatigue influence their daily and professional life. The difference with and without tinted filters is obvious.

IS-severe. The patients are affected with most of the aforesaid symptoms. Photo-

phobia may be so severe that they do not go outside because of the light. At home, illumination is reduced and they often wear sunglasses inside. The difference with and without tinted filters is equally obvious. Tinted filters (in the form of mono- or polylayers) of known absorbance and transmittance curves (fig.1) were put near the orbit or superimposed on the glasses during screening.

Measurements

The Total Error Score (TES) at Farnsworth-Munsell 100 hue test was processed according to the scoring software version 2.1 [15,16]. Ocular coherence tomography (OCT) inclusive of foveal thickness and total macular volume was carried out using OCT3 Zeiss. Electroretinogram (ERG) inclusive of photopic amplitude and peak time was performed using the EREV-2000 Lace System. The digitalized foveomacular images obtained by fluoroangiograph TOP CON were processed by a dedicated software for RGB (red, green, blue) and HIS (hue, saturation, intensity) measuring procedures. The use of non-tinted filters made from the same plastic (CR39) employed for the tinted filters was tried and subsequently left out since it only induced minor variation.
Statistical analysis data were expressed as mean ± SD and the t-paired test was used. ANOVA followed by Bonferroni test was used when appropriate. Values ≤ 0.05 were considered significant (SPSS 13.00, statistical package for social sciences).

Results

About 85% of the photophobic tested patients were suffering from IS, resulting in severe or moderate IS prevalently in the CM group, and slightly prevalent in photophobic subjects without headaches. In all IS-patients both retinal (macular) thickness and macular volume did not differ significantly from the corresponding values of the control group. The use of tinted filters individually and hierarchically selected for hue, saturation and luminance was able to reduce total error score (TES) in the Farnsworth-Munsell 100 hue test. The benefit of using selected tinted filters was confirmed by ERG results showing a significant balanced decrease in photopic amplitude (μV) after wearing filters (fig. 2). Moreover, more than 70% of IS-patients showed a significant balanced reduction in the difference in ms (peak time) between the left and right eye after wearing filters (figs. 3 and 4). This behavior was observed in all IS-patients when the difference between the eyes exceeded 1.3 ms. The morphochromatic analysis of the foveomacular region revealed that IS patients had – in comparison with the control group – a reduction in red, green, and blue, more pronounced for red and blue (fig. 5). Conversely, IS patients presented higher values of saturation and lower values of intensity (luminance). Finally the reduc-

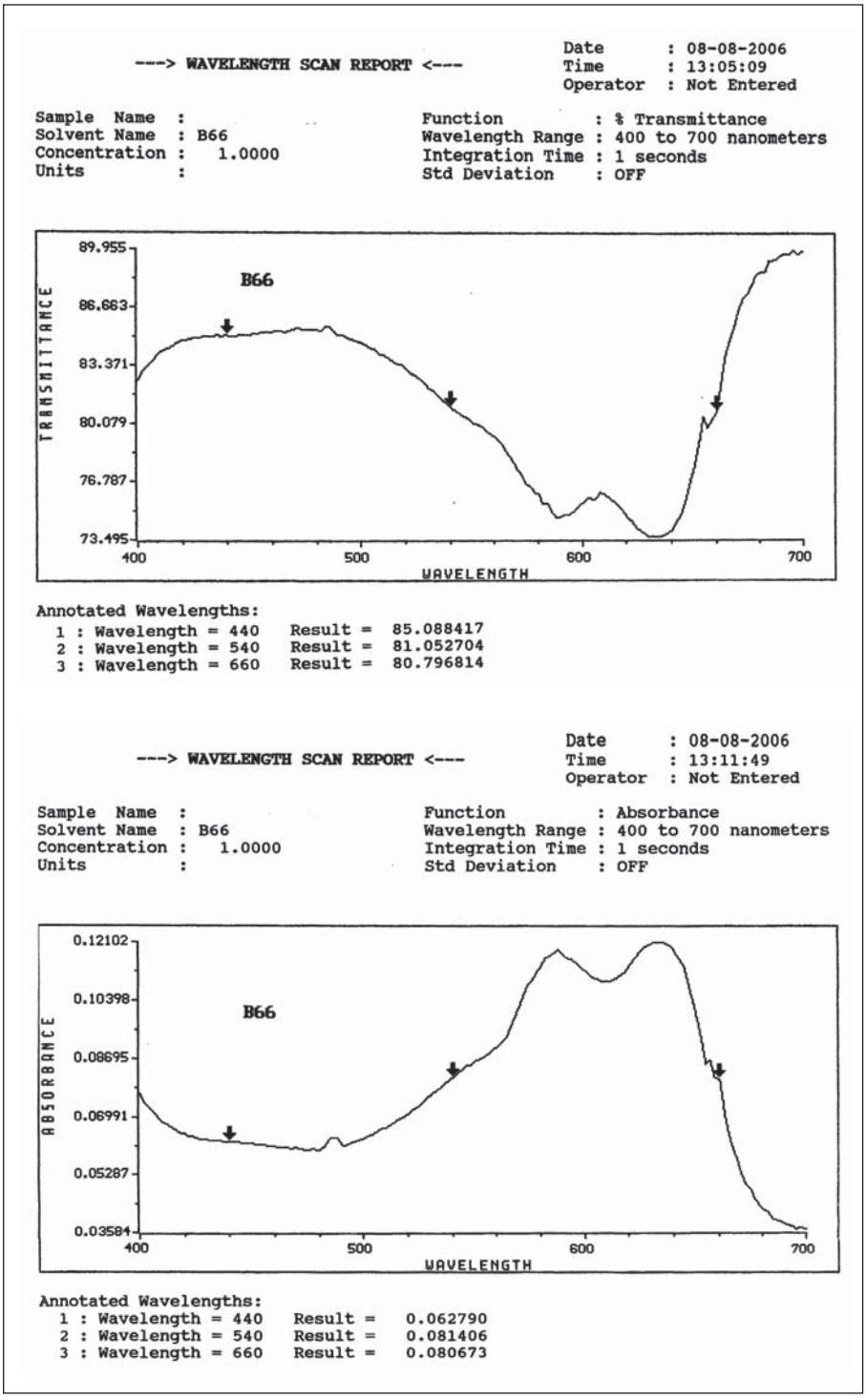

Fig. 1 Wavelength scan report of a tinted filter (color B66). The resulting shifting of the daylight towards blue (short wavelength cones) enabled an exemplifying IS-moderate patient to reduce TES changing from low to average discrimination of the colors.

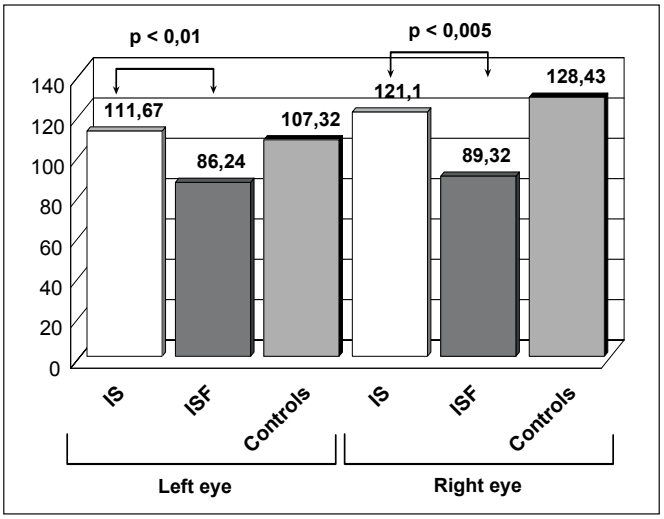

Fig. 2 Electroretinogram (ERG) photopic amplitude (μ v) of IS patients without filter (IS), with tinted filters (ISF), and controls p= T-paired test.

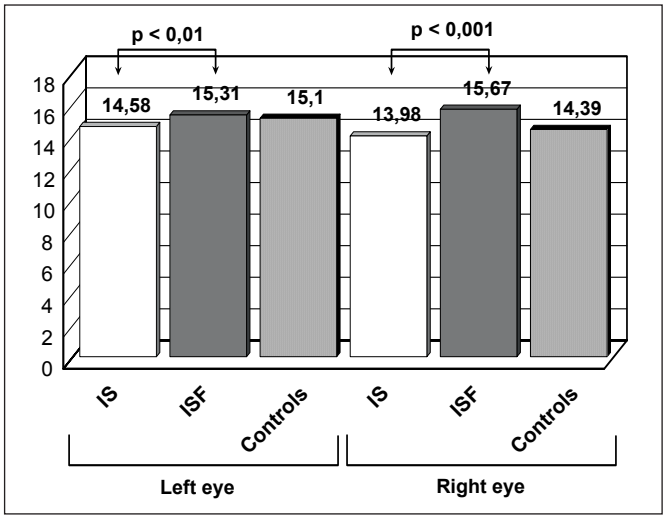

Fig. 3 Electroretinogram (ERG) peak time (ms) of IS patients without filter (IS) and with tinted filter (ISF), and controls p = T-paired test.

tion of TES in photophobic patients was 29 ± 4.3%, whereas the improvement of CM patients it was 41 ± 5.9% These parameters were significantly different from control group (differences from coloured lenses and white < 2%) by using ANOVA followed by Bonferroni post hoc test.

Discussion

Irlen Syndrome is not related to an anatomical (macular) defect but to a hereditary deficiency in the amount of cones–photopigments. As is known [17], there are two kinds of cones photopigments: one for blue (short wavelength-cones) coded by chromosome 7 and one for green-red (middle and long wavelength cones) coded by chromosome X. The use of tinted filters leads to a shifting of daylight towards blue or green-red, shown by transmittance curves (fig.1) and occurring in 63% and 37% respectively of our series of patients. This shifting, inducing a benefit in color discrimination and reducing visual stress, is related to a recruitment of well functioning cones (for the shifted light) and induces the rest of the cones unable to process the fraction of the light which must have been shifted.

This statement is also proven by the paper of Adams, and by two anecdotal cases: a protanopic young patient (i.e. congenitally defective for blue and yellow) who reduced TES, from 164 to 116, by using selected tinted filters. The second case was a healthy post office worker who, during a very cold winter, was exposed to the emanation of an enamel painted over the walls and the warm radiators for several days in a small room with closed windows. After a few weeks he noticed confluent bleaching spots in his black hair and sudden inability to process full spectral daylight. Subsequently he was diagnosed IS-moderate and obliged to wear selected tinted lenses for his job.

It is well known that it is possible to correct refractive defects with corrected (not tinted) lenses without surgical intervention. Analogously, the use of selected tinted filters may artificially facilitate

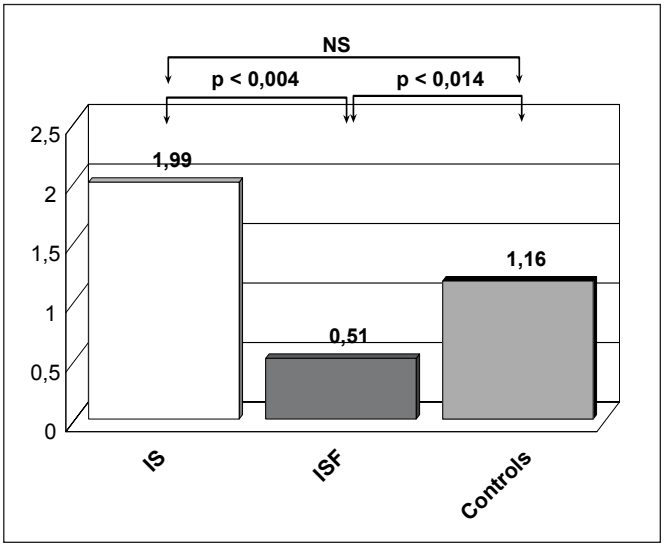

Fig. 4 Peak time (ms) difference between left and right eye of IS patients without filters (IS) and with tinted filter (ISF) and controls p=T-paired test.

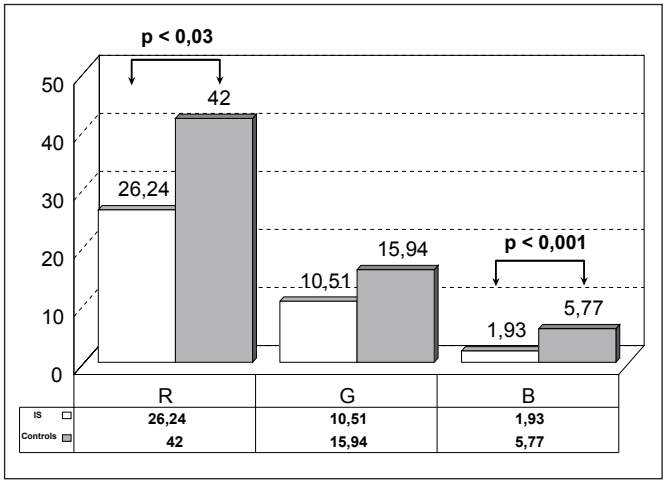

Fig. 5 RGB procedure. Compared with the controls, the macular region of IS patients reveals a decrease in red, green. and blue, greater for red and blue, which correlates with the lowering of the cones photopigment linked to color discrimination.

the color recognition and discrimination in the case of cones with a low content of photopigments. This consideration is in contrast with the prejudice that the use of colored glasses may impair the recognition of colors. In fact, when an IS-patient wears proper lenses, the white background (books, papers, walls, etc.) remains white without taking the color of the lenses. The evidence of a hereditary trait for IS was ascertained in families with children suffering from pervasive developmental disorders [5]. Analogously a possible hereditary trait has been suggested for CM patients [9, 13, 18].

In fact, these patients were able to improve their TES, (meaning a reduction of their photophobia) significantly. IS appears therefore to be considered a hereditary condition related to a sectorial reduction of cones photopigment for blue or for green/red, coded by two different genes in chromosome 7 and X, respectively. The high incidence of IS in the CM patients, who mainly responded well to the tinted filters, suggests continuing with further research.

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Abstracts

But : comparer des patients photophobes, souffrant de migraine chronique (CM), et des patients photophobes sans céphalées pour déterminer l'incidence de cônes photorécepteurs défaillants du fait d'un syndrome d'Irlen dans ces groupes.

Etude : Observation prospective cas-témoins

Patients : trois groupes ont été recrutés :
1) patients photophobes, migraineux chroniques, 2) patients photophobes sans céphalées, 3) témoins exempts de symptômes.

Méthodes : évaluation de la photophobie par le score total d'erreurs au test Farnsworth Munsell 100 Hue et par électrorétinographie.

Résultat : environ 85 % des personnes photophobes souffraient des symptômes du syndrome d'Irlen (IS). Les filtres colorés utilisés qui modifient la lumière du jour vers le bleu ou le vert/rouge réduisaient nettement la gêne à la lumière. Le bénéfice des verres filtrants était significativement supérieur chez les patients photophobes migraineux ($p<0.05$, ANOVA).

Conclusion : le syndrome d'Irlen semble être une maladie héréditaire due à une réduction sectorielle du pigment photosensible des cônes. L'étude a démontré une grande incidence du syndrome d'Irlen chez les patients migraineux chroniques qui répondaient particulièrement bien aux filtres colorés. Il conviendrait de mener d'autres études pour approfondir cet aspect.

Mots clés : photophobie, migraine chronique, syndrome d'Irlen, filtres colorés, électrorétinogramme

Abstracts

Ziel: Vergleich lichtempfindlicher Patienten mit chronischer Migräne (CM) und lichtempfindlichen Patienten ohne Kopfschmerzen zur Frage der Inzidenz fehlfunktionierender Zapfen aufgrund eines Irlen-Syndroms in diesen Gruppen.

Design: Prospektive Fall-Kontroll-Beobachtungsstudie.

Patienten: Rekrutiert wurden drei Studiengruppen:
1. Photophobe Patienten mit chronischer Migräne, 2. Photophobe Patienten ohne Kopfschmerzen, 3. Symptomfreie Kontrollpersonen.

Methoden: Evaluierung der Lichtempfindlichkeit als Total Error Score (TES) mit dem Farnsworth-Munsell 100 Hue Test und mittels Elektroretinographie.

Ergebnis: Etwa 85% der lichtempfindlichen Personen litten an den Symptomen des Irlen Syndrom (IS). Die verwendeten Farbfilter, welche Tageslicht in Richtung Blau oder Grün/Rot verschieben, reduzierten deutlich die photophobischen Beschwerden. Der Nutzen der Filtergläser war bei den lichtempfindlichen Migränepatienten signifikant stärker ($p<0.05$ ANOVA).

Schlussfolgerung: Das Irlen Syndrom scheint eine vererbbare Krankheit zu sein, zurückzuführen auf eine sektorielle Reduktion des Photopigments der Zapfen. Eine hohe Inzidenz des Irlen Syndroms konnte bei den Patienten mit chronischer Migräne nachgewiesen werden, die besonders gut auf die Farbfilter ansprachen. Weitere Studien sollten dies genauer untersuchen.

Key words: Lichtempfindlichkeit, chronische Migräne, Irlen Syndrom, Farbfilter, Elektroretinogramm

Obiettivo: confrontare pazienti affetti da emicrania cronica (CM) con pazienti fotofobici esenti da cefalea rispetto all'incidenza della disfunzione dei coni da sindrome di Irlen nei due gruppi.

Pazienti: Sono stati indagati 3 gruppi di 20 pazienti ciascuno suddiviso nel modo seguente: (1) pazienti fotofobici affetti da emicrania cronica (CM); (2) pazienti fotofobici esenti da cefalea; (3) soggetti sani e non fotofobici (controlli). Metodi: La fotofobia è stata valutata come punteggio totale di errori (TES) al test Farnsworth-Munsell 100 e mediante elettroretinografia.
Risultati: L'85% circa dei pazienti fotofobici è risultato affetto da Sindrome di Irlen (IS). L'impiego di filtri colorati, in grado di spostare la luce diurna verso il blu o verso il verde/rosso ha ridotto fortemente il disagio fotofobico in modo più evidente nei pazienti con CM ($p<0.05$ ANOVA).

Conclusioni: L'IS sembra da considerare un difetto ereditario dovuto ad una perdita settoriale del fotopigmento dei coni. L'alta frequenza dell'IS nei pazienti con CM, che spesso traggono giovamento dall'impiego di filtri colorati, incoraggia a proseguire le ricerche al riguardo.