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Migraine and Photophobia: Physiological and Therapeutic Hypotheses, using Visual Evoked Potentials

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Abstract

This article takes a dual look at how the migraine brain works, and more specifically at the problem of photophobia: both from the point of view of brain function, and from the ophthalmological point of view. Our approach is supported by the study of visual evoked potentials and by clinical studies in the literature.

Keywords: Migraine; Photophobia; Visual Evoked Potential; Migraine Brain; Physiopathology

Introduction

Migraine and Photophobia

The brain awakens, the eyes open to the world. Spontaneously, the brain and the eyes adapt to give us clarity of our environment. Health is the silence of the organs, as René Leriche, a surgeon from the early 20th century, would say. But what about our patients whose brains have difficulty "getting used to" visual stimulation and whose light hurts them? If we still had to define "photophobia", we could say: "a fear of light", referring you to your notions of etymology: from the ancient Greek φωτός, *phôtós*, genitive singular of φῶς, *phôs* ("light"). and -*phobia*, itself derived from the ancient Greek φόβος phóbos ("dread, fear").In any case, it's an aversion to light, discomfort and quite often, in the case of migraine sufferers, an exacerbation of the headache secondary to light stimulation.

As for migraine, it is defined in the ICHD -3 (The International Classification of Headache Disorders 3rd edition) define migraine as a *primary disabling headache presenting in two main forms. Headache without aura or with aura. Prodromal and postdromal symptoms include hyperactivity, hypoactivity, depression, food cravings, repetitive yawning, fatigue and neck stiffness and/or pain.*

In his famous text " *On Megrim, Sick Headache, and Some Allied Disorders: A Contribution to the Pathology of Nerve-Storms",* Edward Liveing [2] describes migraine as the result of a "nervous storm, a hereditary tendency to discharge nervous force, a 'neuronal crisis'" [3].

One of the factors contributing to this problem is obviously light. With this trigger, the discourse can be binary: exposure to light can cause a migraine. This obvious fact leads patients to avoid or adapt (tinted glasses, etc.). But most patients are in a multi-trigger configuration where light is not a sufficient factor to trigger the migraine mechanism. This leaves patients with a constant sense of insecurity, potentially anxiety-provoking, as they are convinced that they constantly have a sword of Damocles hanging over their heads. This situation leads to stress, which in turn is known to be a potential migraine generator. We could thus imagine that anxiety contributes to the hyperexcitability of alert systems, notably the visual system. Without playing too much on words, and daring to take a more global, perhaps somato-psychic stance, we could say that "everything happens in the head". In saying this, it's interesting to hear the environmental component as Anita Violon [4] describes it: "*Migraine is a neurological condition largely dependent on lifestyle factors. ... For the system to be triggered, several factors must appear, some of which are predominant, such as stress, lifestyle, the way we react to stimuli from the outside world...".*

Migraine and Photophobia: Physiopathology

Various theories have been put forward to explain the mechanisms underlying migraine, including the trigeminovascular theory, which remains the most widespread [5]. M A Moskowitz*'s* 1984 *article* : "The neurobiology of vascular head pain" is a reference.

Migraine has many specific features:

- The link between perception of the outside world and cerebro-pain symptoms.

- The predominance of ophthalmological symptoms: visual aura, altered visual perception, hemianopsia, photophobia, etc.

- Its tempo: it's both a chronic pathology with a predisposition to trigger headaches, and a pathology that occurs in attacks, taking a characteristic course of prodrome, headache and postdromic phase. However, between attacks, the patient remains asymptomatic.

Is migraine, and more specifically photophobia, of central or peripheral origin? In a 2018 review by Noemi Maylakh [6], the authors discuss either a peripheral or central pre-established change to migraine. These include cerebrovascular changes due to peripheral sensitization of meningeal nociceptors leading to activation of trigeminovascular neurons and cephalalgic throbbing pain (Borsook & Burstein, 2012; Bernstein & Burstein, 2012). While the idea that a peripheral trigger is essential for migraine generation, there is growing evidence that changes in the central nervous system may also play a critical role (Akerman, Holland, & Goadsby, 2011; Goadsby, 2009; Goadsby, Charbit, Andreou, Akerman, & Holland, 2009). It has recently been proposed that migraine results from dysfunction of subcortical sites driving pain perception from "basal levels of primary traffic" (Goadsby & Akerman, 2012). This "central generator" theory is hotly debated.

The majority of migraine sufferers experience a range of pre-

monitory symptoms long before the typical migraine begins; such as: changes in mood and activity, irritability, fatigue, food cravings, repetitive yawning, stiff neck and hyperaccusis. In Shibata's article [7], a hypothalamic hyperactivity component is proposed as an explanation for this predromic phase. In her 2018 study, Noémie Meylakh [6] clearly shows the observation of infra-slow oscillatory activity of the trunk and hypothalamus, indicative of gliotransmitter release measured by fMRI immediately prior to migraine attacks. So, beyond the debate about an external or internal cause, there is evidence of a susceptibility terrain that clearly shows the chronic background aspect underlying migraine.

The problem thus begins in the predromic phase, and migraine is conceptualized as a disorder of the gain and plasticity of the sensory network, starting with the hypothalamus and the cervical trigeminal complex and including the sub-nucleus of the trigeminal caudalis. After this predromic primum movens, composed of hypothalamic activation, follows an aura, often visual, which is not systematic. For this phenomenon, the authors evoke a transient wave of neuronal depolarization of the cortex from posterior (occipital) to anterior (frontal): the cortical propagation depression, to explain the pathophysiological mechanism of the brain underlying the clinical phenomenon of the migraine aura [3].

Hence, migraine involves activation and sensitization of the trigeminovascular pathways and, as mentioned above, the cortex and more particularly the occipital cortex. In summary, from a neurological point of view, the headache phase of migraine depends on the flow of nociceptive signals from meningeal nociceptors to the cortex via central trigeminovascular neurons in the spinal trigeminal nucleus and thalamus.

To take our discussion of photophobia a stage further, we present here a review of the literature on this phenomenon. For example, Rodrigo Noseda's review of the mechanisms underlying photophobia, in which he discusses the various hypotheses common to photophobia phenomena [16]. The author divides his presentation between analysis of the visual pathways for light-induced headache exacerbation and analysis of the role of the thalamo-cortical loop in migraine photophobia. It is reasonable to assume that the intensification of headaches by light involves crosstalk between the brain pathways that process vision and those responsible for the classic pain of migraine [17]. This crosstalk between brain pathways is explained by Harisson Mc Adams on the basis of animal models

- Light enhances the activity of thalamic trigeminovascular neurons in a way that resembles the way light activates melanopsinergic retinal ganglion cells (RGCs);
- A subset of thalamic neurons sensitive to dura receives a monosynaptic supply of melanopsinergic and non-melanopsinergic RGC axons.
- The axons of these dura-sensitive thalamic neurons, whose activity is enhanced by light, project to the primary and secondary somatosensory cortices and to the insula. These structures form the pain matrix.

To this thalamo-cortical study, we must add the involvement of the hypothalamus, as noted in the first paragraph. Indeed, data from preclinical neuroanatomical studies have also shown that axons from retinal ganglion cells converge on hypothalamic neurons [16]. Clinical results had indeed demonstrated that light triggers more changes in hypothalamic autonomic functions and emotions in migraine sufferers. These findings extend the definition of photophobia beyond that of the commonly used criteria of "headache (intensity) aggravated by light" insofar as it explains why migraine patients avoid light even when it does not appear to aggravate their head pain.

Let's talk about the visual pathways and bring in the data concerning retinal ganglion cells.

The question of peripheral effector causation in migraine photophobia stems from the observation of the variety of causes of photophobia. Many neurological conditions have been associated with photophobia, including migraine, traumatic brain injury, concussion, meningitis, intracranial tumors and subarachnoid hemorrhage. But there are also a variety of neuro-ophthalmic disorders such as uveitis, iritis, keratitis, retinitis pigmentosa, cone-stick dystrophy, corneal lesions and blepharitis that also present photophobia.For the study of visual pathways, the literature focuses on a particular group of retinal ganglion cells. This group of cells has been identified on the basis of both animal models and clinical observations. This study is well documented in Harisson Mc Adams's [17] article entitled "Selective amplification of ipRGC signals explains interictal photophobia in migraine", and highlights the

aforementioned observation based on rodent animal models.

The basic idea is as follows. Since light is the cardinal stimulus for photophobia, photoreceptors must be involved. In the review by Yiwen WuetMark Hallett, [18] we review the different candidates responsible for light perception. There are at least five different types of photoreceptor in humans: different kinds of cones and rods and recently identified ganglion cells that are intrinsically photosensitive retinal ganglion cells (ipRGCs), which contain the melanopsin photopigment. The rods and cones of the outer retina are the predominant photoreceptor cells in the mammalian retina. Their high temporal and spatial sensitivity to light forms the basis of image--forming vision. The designated players are cones, rods and ipRGC cells.

Based on animal models, we know that intrinsically photosensitive retinal ganglion cells (ipRGCs) are able to respond to light without synaptic input. They project to the somatosensory thalamus, where they innervate neurons that are also sensitive to dural stimulation carried by trigeminal afferents: the latter relays being involved in headache. It is the argument of direct connection without multiple synapses that points to the importance of ganglion cells (ipRGC) in the genesis of photophobia.

Since then, scientists have been studying models devoid of these cones and rods to investigate this new ipRGC pathway. Observations were made both on animal models and on cohorts of blind patients. In a very similar way to the animal models, the same phenomenon is observed in humans who have become blind due to a total absence of rod and cone function, still suffering from photoallodynia. This is another argument in favor of identifying ipRGCs as being involved in photophobia.

Rami Burstein's very elegant 2019 article on the clinical observation of patients [19]. The author reports another fact concerning 'a "non-image-forming" pathway, which originates from melanopsinergic retinal ganglion cells (RGCs) that may explain a very particular observation made in the blind. Indeed, photophobia and preferential sensitivity to blue light are observed in blind migraine patients, who, despite losing the ability to form images due to cone and rod degeneration, can still detect light. In these results, the color or wavelength of the light could play a role, observing that blue light could be fundamental to migraine-like photophobia and that the exacerbation of headache by light could be minimized by devices (sunglasses, contact lenses) that block blue light [17].

These studies shed light on the importance of studying retinal ganglion cells. The literature mentions a certain type of ganglion cell. Nevertheless, we shall see that there are others of significant interest.

Contribution of Evoked Potentials

Observations of visual evoked potentials provide us with relevant evidence of increased susceptibility in migraine sufferers. Beyond the fundamental and theoretical questioning of the migraine terrain, clinical neurophysiology using visual stimulation provides us with proof of this basic hypersensitivity and an easy and usable approach to everyday testing of this particularity as a diagnostic element of migraine.

To test this contribution of clinical neurophysiology, we report a study using visual evoked potentials on a cohort of 40 migraine patients.

Pattern Visual Evoked Potentials And Migraine's Neurophysiology

Method

In a study carried out in our laboratory, we report on 40 migraine patients who benefited from a study of visual evoked potentials with the checkerboard, in monocular stimulation, over a total of 30 stimulations, at the 4 stimulation angles usually used, namely: 16 - 32 - 64 - 128 squares.

The checkerboard stimulation screen is placed 1 meter in front of the patient, who stares monocularly at a central target while the checkerboard alternates between black and white. An occipital response is systematically recorded, and its amplitude and latency analyzed. The classic set-up is with active electrode in Oz and reference in Cz (ground in Fpz), on Natus and Medatec equipment.

Amplitude was estimated to be increased if above 10 µV, according to classic data reported in reference works by JM Guérit [21] and MJ Aminoff [20].

Similarly, latencies were compared with reference data from the literature and [20,21]. A variation between the first and last stimulation angles of 20 ms is described for the P100 la-

tency. Indeed, recorded P100 latencies fluctuate from 101 - 114 ms (at 1 degree of stimulation angle or 16 checkerboard squares) to 118 - 134 ms (at 7 min 30 of stimulation angle or 128 checkerboard squares) [21].

A visual habituation test was performed on a single stimulation angle, either 32 or 64 squares choosing the largest starting amplitude, by 15 trains of 30 stimulations. The normality criterion used was that of the literature (Schoenen and PYL article), i.e. a 30% drop in response amplitude between the1st and 15th stimulation. The examination of visual habituation was deemed pathological when a recording of stability, an increase or a fall <30% in amplitude between the1st and 15th stimulation concomitantly with the same amplitude progression between stimulation train 1 and 5 over the 3 successive blocks of 30 stimulations.

According to these classic data from the literature, the latency of P100 or major positivity obtained in the occipital region shows a spontaneous tendency to be delayed by around 20 ms between the first and last stimulation angles, Cfr. Guérit JM. Masson 3rd edition: The visual evoked potentials [21].

Table 1

References admises (14-65 ans)	1 degree	30 min	15 min	7 min 30	Diff 16-128	Ampl Max
	16	32	64	128	en ms	en µV
Valeur inferieure	87	87	82	104	17	
Moyenne	101	101	106	118	17	10 µV
Valeur superieure	114	113	122	134	20	

Three criteria were studied: P100 amplitude, change in visual habituation and progression of P100 latency between the 4 stimulation angles.

For each patient, we searched the clinical record for the presence or absence of a visual aura.

Results

Description of the Cohort

-40 migraine patients (IHS criteria): 8 males and 32 females with an age range from 15 to 60 (and 1 patient aged 74);

-7 patients reported visual auras (17% of the cohort);

Table 2: Recorded results

N.	SEX	AGE	AURA	Habituation	monocular	1° (1)	30'	15'	7'30" (2)	diff. (2) - (1)	Ampl Max
			y="yes"	Pathology	stimulation	16 square	32	64	128	en ms	en µV
						latency(ms)	latency(ms)	latency(ms)	latency(ms)		
1	F	39	n	POS.	*right eye*	112	110	111	110	-2	9,6
					left eye	115	107	120	118	3	12,1
2	F	34	y	POS.	*right eye*	106	99	106	102	-4	18,4
					left eye	99	106	107	110	11	18,7
3	F	18	y	POS.	*right eye*	99	110	114	120	21	14
					left eye	101	106	113	119	18	12,5
4	F	17	n	POS	*right eye*	108	104	103	113	5	29,4

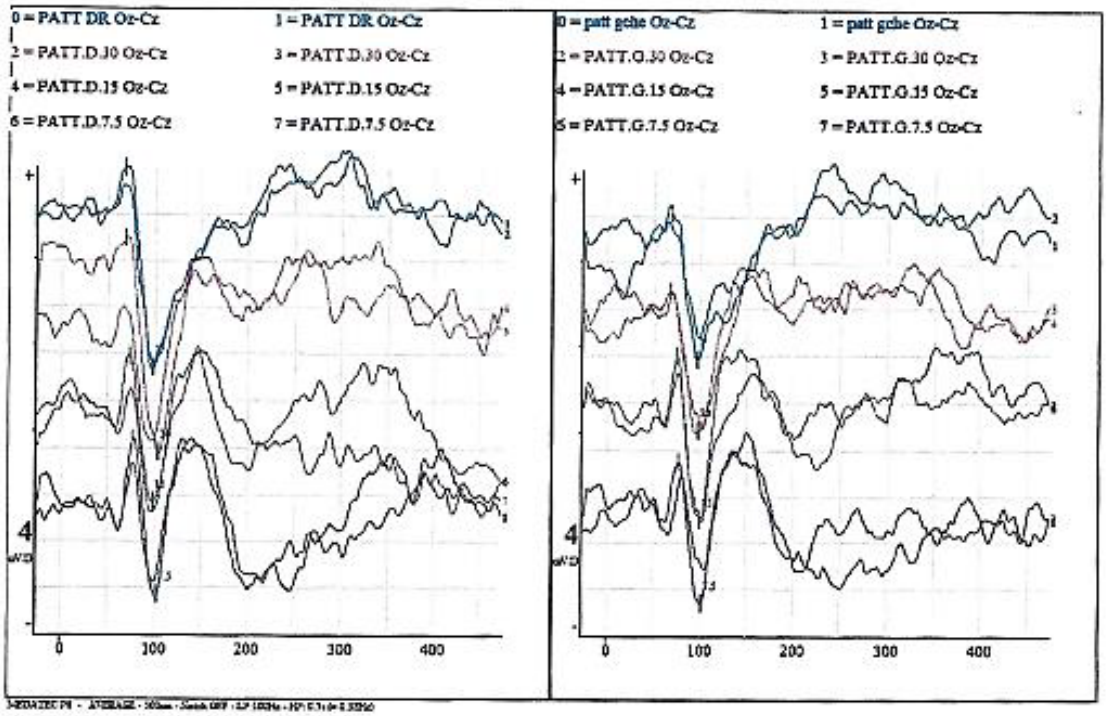
					left eye	100	104	106	109	9	28,4
5	F	34	y	POS.	*right eye*	103	103	102	111	8	16,6
					left eye	102	109	99	107	5	17,2
6	F	51	n	POS.	*right eye*	109	99	108	126	17	13,4
					left eye	113	103	103	119	6	15,6
7	F	35	n	POS.	*right eye*	105	101	105	113	8	15,3
					left eye	109	100	102	111	2	13,2
8	F	60	n	POS	*right eye*	89	95	99	106	17	16,1
					left eye	94	112	107	110	16	22
9	F	58	n	POS	*right eye*	121	111	94	101	-20	18,5
					left eye	132	114	94	109	-23	19,5
10	F	46	n	POS	*right eye*	100	98	98	97	-3	23,1
					left eye	103	110	97	103	0	22,6
11	F	53	Y	POS	*right eye*	106	106	106	108	2	23,3
					left eye	112	107	103	110	-2	22,3
12	M	28	Y	small	*right eye*	113	105	110	114	1	12,8
					left eye	116	110	105	116	0	12,4
13	F	39	n	POS	*right eye*	101	103	99	105	4	18,6
					left eye	105	102	103	105	0	19,1
14	F	39	n	POS	*right eye*	99	102	102	106	7	9,79
					left eye	105	104	109	118	13	10,4
15	F	22	n	POS	*right eye*	99	96	95	103	4	24,7
					left eye	94	94	96	99	5	23,2
16	M	0	n	POS	*right eye*	108	100	104	115	7	8,42
					left eye	112	100	93	105	-7	15,2
17	M	55	n	POS	*right eye*	109	108	107	112	3	14,5
					left eye	105	103	109	114	9	14,3
18	F	16	n	small	*right eye*	110	107	107	100	-10	12,1
					left eye	108	102	102	101	-7	12,2
19	F	56	n	absente	*right eye*	99	98	98	106	7	15,2
					left eye	94	96	99	109	15	15,3
20	F	20	n	absente	*right eye*	98	103	98	101	3	18,3
					left eye	97	98	99	101	4	14,1
21	F	53	n	POS	*right eye*	99	99	97	101	2	15,4
					left eye	102	99	98	103	1	17
22	M	31	n	absente	*right eye*	101	103	106	108	7	19,9

					left eye	99	105	104	110	11	19,5
23	M	39	n	small	*right eye*	99	101	101	106	7	13,9
					left eye	105	104	99	105	0	11,2
24	F	42	Y	POS	*right eye*	105	101	104	112	7	12,9
					left eye	99	102	104	113	14	15,4
25	F	53	n	POS	*right eye*	105	107	108	115	10	9,14
					left eye	108	109	109	112	4	9,21
26	F	28	n	POS	*right eye*	110	101	99	101	-9	18,4
					left eye	107	101	99	100	-7	16,9
27	F	29	n	POS	*right eye*	105	106	104	113	8	10,8
					left eye	105	102	102	113	8	11,7
28	F	20	n	POS	*right eye*	119	108	110	101	-18	19,6
					left eye	119	112	109	103	-16	14,6
29	F	35	n	POS	*right eye*	96	96	99	106	10	13,5
					left eye	91	97	98	104	13	12,5
30	F	18	n	POS	*right eye*	99	102	99	100	1	21
					left eye	99	98	105	104	5	19,9
31	F	28	n	POS	*right eye*	98	98	97	101	3	33,9
					left eye	103	103	100	105	2	22,1
32	F	41	n	POS	*right eye*	106	99	96	104	-2	16
					left eye	103	102	102	107	4	19,6
33	F	47	n	POS	*right eye*	101	106	109	116	15	28,6
					left eye	110	112	112	125	15	26,1
34	M	22	n	small	*right eye*	99	106	104	108	9	18,3
					left eye	105	103	104	110	5	16
35	F	47	y	POS	*right eye*	103	100	96	99	-4	16,3
					left eye	102	99	94	100	-2	14,8
36	M	15	n	small	*right eye*	115	108	101	110	-5	17,9
					left eye	109	101	99	112	3	14,6
37	F	74	n	POS	*right eye*	91	96	101	108	17	17,9
					left eye	93	97	100	108	15	17,4
38	F	54	n	POS	*right eye*	113	113	116	114	1	25,9
					left eye	113	113	107	115	2	21,6
39	F	52	n	absente	*right eye*	108	107	110	113	5	17,7
					left eye	108	108	105	116	8	10,8
40	M	46	n	POS	*right eye*	110	111	98	107	-3	12,3
					left eye	102	104	107	107	5	10,4

Results Presentation

Amplitude

The amplitude of the P100 responses recorded in the occipital region was greater than 10 µV (mean 16.91 µV) in at least 1 eye in 37 cases (93% of the cohort).



LATENCES ŒIL DROIT	LATENCES ŒIL GAUCHE
1' : 98.0	1' : 97.0
30'' : 103	30'' : 98.0
15'' : 98.0	15'' : 99.0
7.5'' : 101	7.5'' : 101

amplitudes ŒIL DROIT	amplitudes ŒIL GAUCHE
1' : -17.1	1' : -12.6
30'' : -18.3	30'' : -12.0
15'' : -12.3	15'' : -14.1
7.5'' : -13.5	7.5'' : -12.2

Figure 1

Habituation

The study of visual habituation was frankly pathological in 31 cases (77% of the cohort); weakly pathological in 5 cases and borderline normal in 4 cases.

Variation in Latency of Major Positivity Between the First and Last Stimulation Angles

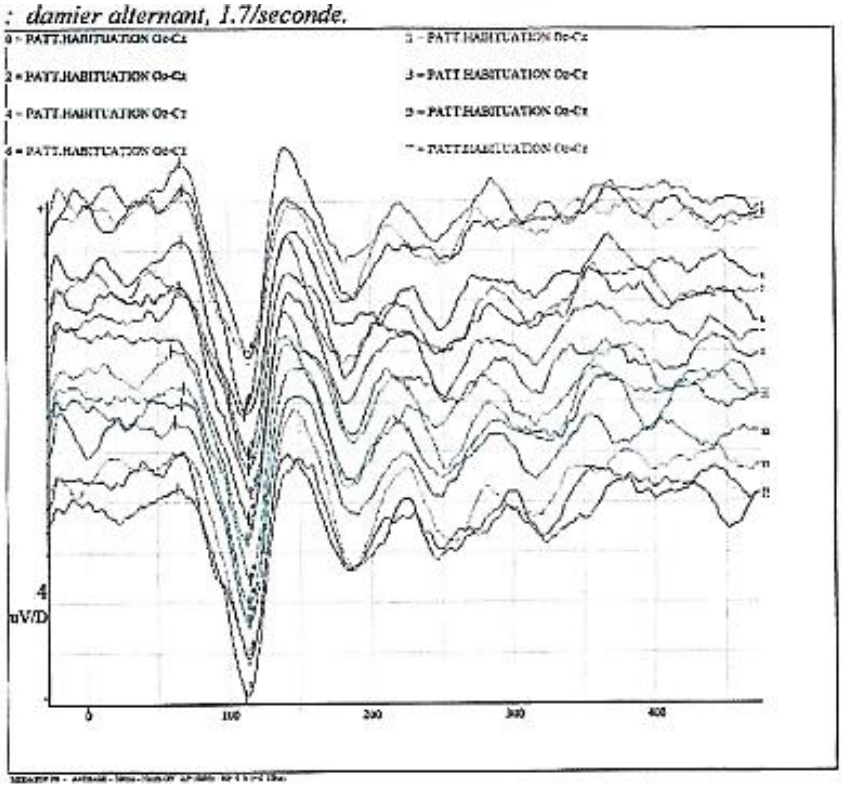
The P100 latency progression study was recorded as less than 10 ms in at least 1 eye in 36 patients (90% of the cohort); and greater than 10 ms, in both eyes in 4 patients;

In order to better highlight the difference between migraine patients and the reference values used in our reference book (Guerit's reference), we extracted 20 files of so-called "normal" visual potentials.

These examinations were carried out either as part of a screening for multiple sclerosis or as part of an assessment of a functional disorder. No migraine was noted in these patients. these patients form the control group

Normal values: from Guerit's references (graph for women 45-65 year).

Stimulation : damier alternant, 1.7/seconde.



Amplitudes en µV

1	-15.6	6	-14.4	11	-15.9
2	-12.9	7	-15.8	12	-15.9
3	-17.4	8	-14.3	13	-16.0
4	-13.7	9	-15.0	14	-16.4
5	-13.2	10	-15.2	15	-16.5

Figure 2

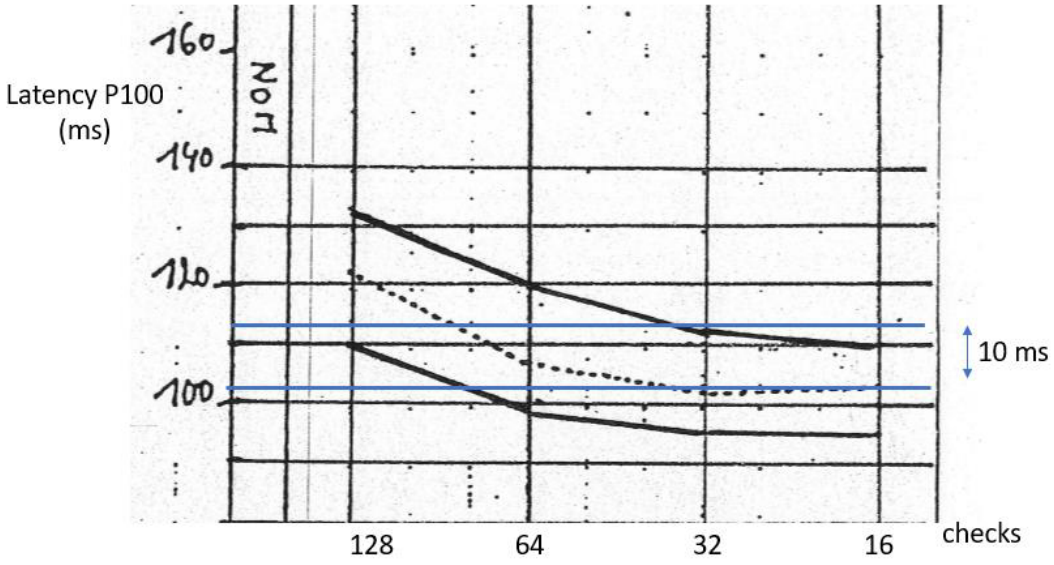


Figure 3

Table 3: Values recorded in control group: difference of latencies (ms)

Patient	Right	Left	Patient	Right	Left
1	9	16	11	15	16
2	17	20	12	11	13
3	13	9	13	15	16
4	14	7	14	17	15
5	4	14	15	10	11
6	5	15	16	10	14
7	11	9	17	18	14
8	9	11	18	8	13
9	17	13	19	11	10
10	10	0	20	10	12

We observed 9 patients with a progression of P100 latency of less than 10ms in at least one eye in the group of 20 controlled patients.

with this analyzes (2X2 contingency table):

- 36 patients with progression minor than 10 ms in the migraine's cohort (40 patients)

- 9 patients with progression minor than 10 ms in th controle's group (20 patients)

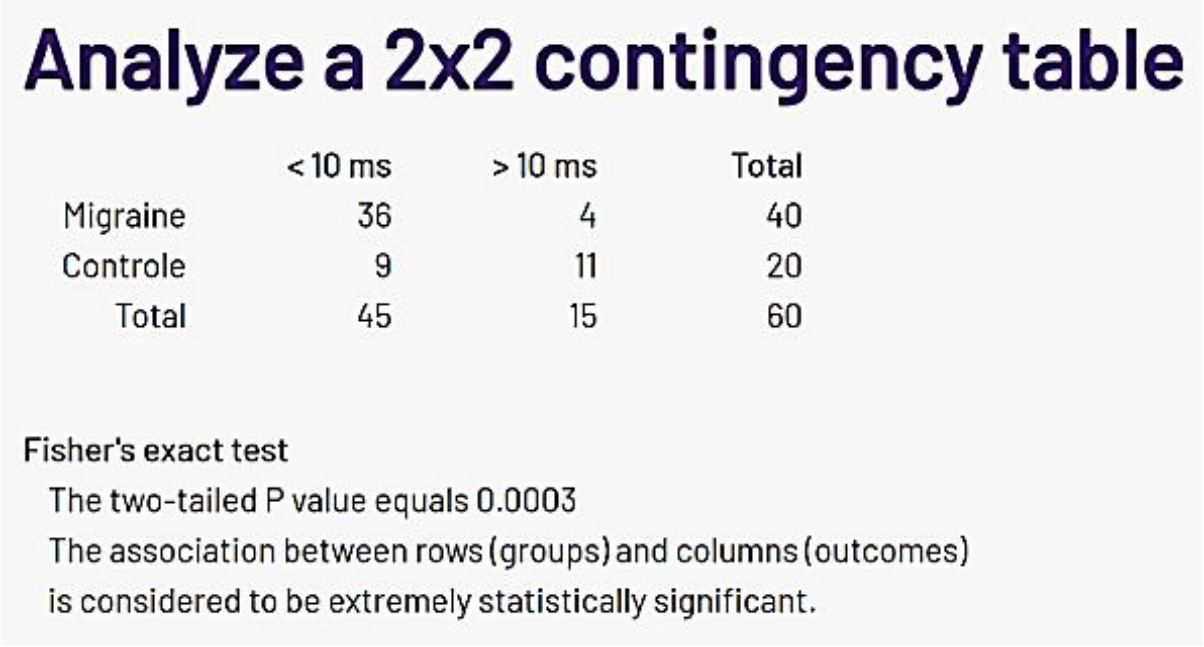


Figure 4

Statistical Analysis

Fisher test was used for 2X2 contingency tables. Statistical hypotheses were tested at the 5% significance level (α = .05) against 2-sided alternatives.

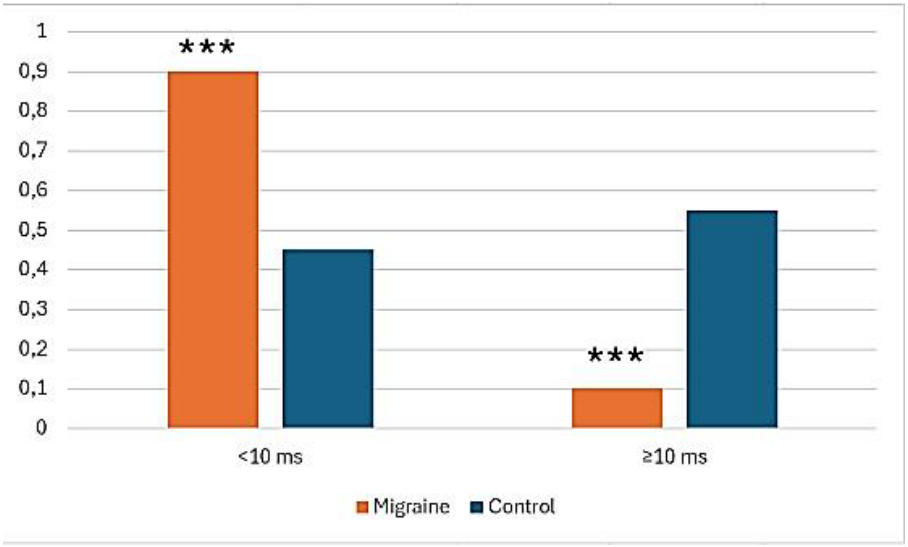


Figure 5

Discussion

Our study shows the singularity of light processing by the migraine sufferer's cortex: high amplitude and disturbed visual habituation. These elements have already been discussed in the literature. We report a new finding: the lack of variation in the latency of major P100 positivity when stimulated at different angles.

Modification of Visual Amplitude and Habituation and Previously Reported Data on Migraine and Photophobia

The study of habituated and wide-amplitude VEPs is edifying in objectifying the "hypersensitivity". There is a fairly broad consensus on the observation of both ample amplitude and habituation disturbance in migraine with and without aura. Msallam Abbas Abdulhussein's 2022 study [9] is quite telling on the subject. It seems that habituation disorder is in fact a feature of genetic predisposition to migraine.

Msallam Abbas Abdulhussein's 2022 study [9] confirms the findings of earlier studies, which stated that migraine patients in the inter-ictal phase suffer during continuous sensory stimulation from increased amplitude and habituation deficit. Note another article by Gianluca Coppola [10] in 2015, studying the subgroup of migraine sufferers with visual aura and the article of Jayantee Kalita [30]. They discusse the lack of habituation and the phenomenon of pervasive cortical depression associated with the aura.

The author describes that groups of migraine patients with aura suffer from more pronounced pathophysiological dysfunction as a result of genetic abnormalities that produce spreading cortical depression. This dysfunction and depression fuels meningeal nociception in migraine with aura, and is particularly affected by the lack of habituation between inter-ictal. Whether the visual aura is clinically present or not, the consensus of visual habituation disorder remains robust.

These two known elements - wide amplitude and lack of habituation - suggest an inability to control or modulate the processing of visual intensity, providing an explanation for its intolerance. This is one explanation for photophobia.

Changes in Visual Potentials: Last-angle Latencies

In the neurophysiology of migraine, we have previously shown the peculiarity of the response of VEPs by their wide amplitude and by the lack of modification of this amplitude during repetitive stimulation, signalling a disturbance in habituation.

Another peculiarity that we have observed in our laboratory leads us to go beyond the cerebral mechanism and to consider the magno and parvo-cellular visual component.

Let's take a look at the latencies of visual evoked potentials obtained by checkerboard stimulation. According to the literature and the data recorded in reference works: Aminoff [20] and Guérit [21], the amplitude of evoked potentials is generally less than 10 µV, with recorded latencies fluctuating from 101 - 114 ms (at 1 degree of stimulation angle or 16 checkerboard squares) to 118 - 134 ms (at 7 min 30 of stimulation an-

gle or 128 checkerboard squares).

In our study carried out in our laboratory, we report on the study of 40 migraine patients who benefited from a checkerboard visual evoked potential study, in monocular stimulation at the 4 stimulation angles usually used, namely: 16 - 32 - 64 - 128 squares. Our observation shows a clear defect in latency progression at all 4 stimulation angles.

In the literature, we found few articles studying P100 latency. We cite Alshamrani's 2023 study, which deals with variations in P100 latency in migraine with aura, without studying modifications according to stimulation angles for the same patient [22]. Furthermore, a rather distant study from 1999 refers to variations in the latency of later visual evoked potentials according to stimulation angles [23], but does not deal with either P100 or N75. Nevertheless, this study suggests the notion of two parallel visual pathways: the luminescence pathway and the contour study pathway. These pathways are now well established, and correspond to the magnocellular and parvocellular pathways.

- The magnocellular pathway (M pathway) is of interest in the context of movement and context management, and responds to low-frequency spatial or wide-field visual stimuli, and response to low contrast.

- The parvocellular pathway (P pathway), of interest for the study of object observation and responding to high spatial frequency stimuli or central visual field and have low sensitivity to light.

Here's our explanatory approach, in the light of our recorded results and Oelkers' first attempts at explanation in 1999 [23]. The first stimulation angles away from the macula tend to correspond to the magnocellular system (fairly fast and phasic), while the last stimulation angles involve a retinal zone fairly close to the macula, corresponding to the parvocellular system (slower and tonic).

This explanation is supported by articles by V.L. Marcar [22] and K. Ahmadi [23]. In her article, V.L. Marcar explains the differentiation of the magnocellular and parvocellular pathways and their relationship through the exploration of visual evoked potentials, in particular the study of P100 and N75. This author shows us the possibility of highlighting the magnocellular pathway by low-frequency checkerboard stimulation with contrast reduced to 10% (to saturate the parvocellular pathway). K. Ahmadi [26] provides us with a protocol of the target to be used to perform evoked potentials to study the magnocellular and parvocellular pathways. Referring to previous studies, and in particular to the work of Munk [13], the parvocellular system is composed of several relays and is therefore slower than the magnocellular system.The difference between the M and P pathways is 20 ms, as already described in the above-mentioned article by V.L. Marcar.[24].

For the literature, it's interesting to note whose work of Coppola and Sand [29,30]. This article presents a study of variations in late potentials, irrespective of the different stimulation angles.

Diagnostic Hypotheses and Therapeutic Suggestions

We put forward the following hypothesis: the lack of progression of P100 could correspond to the identification of both Magnocellular and Parvocellular pathways.

Our study of a cohort of 40 migraine sufferers and the difficulty of varying the latency of major positivity according to stimulation angles provides a new hypothesis. The magnocellular pathway, which is faster than the parvocellular pathway and sensitive to luminescence, could be more active in migraine patients. In this way, the lack of variation in P100 latency could reflect persistent functioning of the magnocellular pathway, even at angles where the parvocellular pathway would have the advantage. Photophobia would therefore reflect an imbalance between these two pathways, with persistent processing by the magnocellular pathway under specific parvocellular stimulation. Our observation would therefore be an easy, practical and rapid way of objectifying a dysfunction of the parvocellular versus magnocellular ratio in the last angles of stimulation.

This hypothesis is reinforced by the patient's observation of progressive blurring of the visual target during the checkerboard test. This could reflect a reduction in parvocellular capacity.

Beyond the diagnostic hypothesis, these findings lead us to imagine new therapeutic avenues. Indeed, other authors have studied the respective contributions of the magnocellular and parvocellular pathways. As an example, we propose the use of the Bauwens stereoscopic panoramic panel (PPS) [27,28], a

device consisting of a large half-cylinder-shaped display, printed with high-contrast, very regular patterns, at the centre of which the patient, seated and concentrating on a motion-sensitive fixation target, is rocked on a low-frequency (0.02 Hz) pendulum swivel chair. Based on the principle of reciprocal inhibition put forward by Thomas Brandt et al [25], it encourages central fixation through vestibular activation while reducing the impact of the peripheral retina.

In theory, the Bauwens PPS is proposed as a rehabilitation method for resolving vestibulo-visual sensory conflicts secondary to vestibular disorders, which are the source of specific symptoms, forming a nosological entity in its own right known as vestibular asthenopia. It brings together symptoms such as visual blur, sensitivity to retinal slippage, photophobia, tiredness and difficulty with eye movements; symptoms which result from the disruption of a series of sensory-motor processes (fixation, fusion, accommodation, vergence) which affect the quality of vision. These symptoms are quite similar to migraines caused by imbalances between the parvocellular and magnocellular pathways [28]. In rehabilitation, the PPS procedure, by favouring the parvocellular pathway and inhibiting the magnocellular, resolves most of the problems caused by the disruption of these low-level visual processes. We could postulate that such a treatment mechanism could also find its place in the treatment of migraines. A study of the EEG at rest [32], under visual and auditory stimulation rather than a single modality, would provide a better understanding of the association of EEG patterns with migraines by finding a more effective criterion for differentiation if the EEGs of different migraine subgroups were studied separately.

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Conclusion

Our review of the literature and our ability to study the functioning of migraine sufferers has shed light on photophobia in this particular case.

Far from focusing solely on brain function, we bring the light of recent data and neurophysiology to bear on both protagonists: the brain and the eye. Our article opens the discussion on the interest and contribution of evoked potentials in clinical practice, as a practical diagnostic tool. Our study shows the value of using data on visual habituation, response amplitude and, in particular, the progression of the latency of major positivity according to stimulation angles. We report, in an innovative way, the observation of a clear lack of progression of P100 latency during different angles of stimulation to the checkerboard. This observation seems to us to be a useful third criterion in the neurophysiology of migraine, in addition to the study of P100 amplitude and its variations during visual habituation tests.

We also discussed the value of studying the magnocellular and parvocellular pathways, suggesting a hypothesis to explain the phenomenon of photophobia in migraine, through persistence of processing by the magnocellular pathway in specific parvocellular stimulation.

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