Acta Neurologica Belgica

ANALYSIS AND CLINICAL CORRELATES OF 20 Hz PHOTIC DRIVING ON ROUTINE EEG IN MIGRAINE

--Manuscript Draft--

Manuscript Number:	ANEB-D-13-00423
Full Title:	ANALYSIS AND CLINICAL CORRELATES OF 20 Hz PHOTIC DRIVING ON ROUTINE EEG IN MIGRAINE
Article Type:	Original article
Corresponding Author:	Yannick FOGANG Fann teaching Hospital Dakar, SENEGAL
Corresponding Author Secondary Information:	
Corresponding Author's Institution:	Fann teaching Hospital
Corresponding Author's Secondary Institution:	
First Author:	Yannick FOGANG
First Author Secondary Information:	
Order of Authors:	Yannick FOGANG
	Pascale GERARD
	Victor DE PASQUA
	Jean Louis PEPIN
	Moustapha NDIAYE
	Delphine MAGIS
	Jean SCHOENEN
Order of Authors Secondary Information:	
Abstract:	Enhanced photic driving (PD) during high frequency flicker stimulation, the so-called H response, is a classical feature of migraine patients between attacks, but is thought to be of poor clinical utility. Visual inspection of the EEG for its detection may not be reliable, however, and data on its possible correlations with clinical features and migraine pathophysiology are scarce. We have compared visual inspection and EEG spectral analysis to detect abnormal PD in 280 consecutive migraine patients of our headache clinic (episodic migraine without aura, n=171; chronic migraine, n=48; migraine with aura, n=61) and in a group of 24 non-migrainous neurological controls. Spectral frequency analyses were performed blindly by one of us (YF). On visual inspection, 50.4% of migraineurs were thought to have increased 20Hz PD. After spectral analysis, only 62.4% of them had PD power superior to the mean+95%CI of the control group. Sensitivity of visually identified PD was 82.24%, specificity 69.36%. Increased PD on spectral analysis was more prevalent in episodic migraine than in chronic migraine, in patients with low attack frequency, in those with ictal autonomic symptoms in addition to nausea and in those with a strong family history of migraine. We confirm therefore that 20Hz photic driving is of little diagnostic utility and its prevalence in migraine overestimated on visual inspection. Its presence on spectral analysis of the EEG, however, might be of pathophysiological interest, as it identifies subgroups of migraineurs of whom the common denominator could be lack of habituation of cortical responses during repetitive stimulation.
Suggested Reviewers:	Peter J Goadsby peter.goadsby@kcl.ac.uk

	Paemeleire Koen Koen.Paemeleire@uzgent.be
	Christoph H DIENER h.diener@uni-essen.de

ANALYSIS AND CLINICAL CORRELATES OF 20 Hz PHOTIC DRIVING ON ROUTINE EEG IN MIGRAINE

Fogang Y[1,2], Gérard P[1], De Pasqua V[1], Pepin JL[1], Ndiaye M[2], Magis D[1], Schoenen J[1]

[1]Headache Research Unit, University of Liège, CHR Citadelle. Liège. Belgium,

[2]Fann Teaching Hospital, Cheikh Anta Diop University, Dakar.Senegal

Corresponding author:

Fogang Yannick M.D., M.Sc.

[2]Fann Teaching Hospital,

Cheikh Anta Diop University,

Dakar.Senegal

yanfogang@yahoo.fr

Tel: +221771135018

Key words: migraine with aura, migraine without aura, photic driving, EEG, clinical correlates

ABSTRACT

Enhanced photic driving (PD) during high frequency flicker stimulation, the so-called H response, is a classical feature of migraine patients between attacks, but is thought to be of poor clinical utility. Visual inspection of the EEG for its detection may not be reliable, however, and data on its possible correlations with clinical features and migraine pathophysiology are scarce.

We have compared visual inspection and EEG spectral analysis to detect abnormal PD in 280 consecutive migraine patients of our headache clinic (episodic migraine without aura, n=171; chronic migraine, n=48; migraine with aura, n=61) and in a group of 24 non-migrainous neurological controls. Spectral frequency analyses were performed blindly by one of us (YF).

On visual inspection, 50.4% of migraineurs were thought to have increased 20Hz PD. After spectral analysis, only 62.4% of them had PD power superior to the mean+95%CI of the control group. Sensitivity of visually identified PD was 82.24%, specificity 69.36%.

Increased PD on spectral analysis was more prevalent in episodic migraine than in chronic migraine, in patients with low attack frequency, in those with ictal autonomic symptoms in addition to nausea and in those with a strong family history of migraine.

We confirm therefore that 20Hz photic driving is of little diagnostic utility and its prevalence in migraine overestimated on visual inspection. Its presence on spectral analysis of the EEG, however, might be of pathophysiological interest, as it identifies subgroups of migraineurs of whom the common denominator could be lack of habituation of cortical responses during repetitive stimulation.

INTRODUCTION

Migraine is a complex and heterogeneous disorder, in which genetics and environment interact to generate dysfunctions at several levels of the central nervous system. These intricate phenomena are responsible for the multifaceted clinical features of the disorder and especially repetition of attacks as part of a cycling ictal-interictal temporal profile [1]. Electrophysiological methods are particularly suited to study the functional and cycling brain changes associated with migraine pathophysiology [2]. Given the increased sensitivity to light between, and even more so during migraine attacks, many studies have focused on the EEG responses induced by repetitive light stimuli: photic driving (PD), steady-state visual evoked responses (SSVEPs), visual evoked potentials, or more recently visual-induced changes in connectivity for various EEG frequency bands [4,5]. SSVEPs are not generated by amplitude modulation but primarily due to phase alignment of the ongoing background EEG, with changes in frequency components according to the characteristics of repetitive stimulus [5]. The frequency components of SSVEPs are generated by magnocellular (MC), parvocellular (PC) and koniocellular (KC) visual pathways, differentially activated depending on the different stimulus features: the MC pathway is achromatic and activated by low spatial contrast stimuli, the PC pathway by both high spatial contrast and spectral stimuli (shape and color), the KC pathway by spectral stimuli carrying the blue/yellow color information. The tendency of EEG rhythms to synchronize to external repetitive stimuli varies with stimulation frequency in the low (approximately 10 Hz), medium (approximately 20 Hz) or high frequency range (approximately 40 Hz) [6]. An increased photic driving was described in the medium range in migraine patients, and called the H response [7]. That PD is abnormal in migraine irrespective of age and migraine subtype has been confirmed in other studies [8,9], although the same authors also reported greater abnormalities of SSVEPs in migraine with aura, and in patients with autonomic symptoms or a family history of migraine [10]. Unlike visual evoked potentials [3], PD responses are not well studied over the migraine cycle, but in women they are known to vary over the ovarian cycle with blood levels of hormones [11]. In a recent study using brief trains of intermittent visual stimulation, there was no change in SSVEP amplitude throughout the migraine cycle in the medium frequency range [12].

PD, if prominent, can be recognized by visual inspection of the EEG. Although it is in general subtle in non-migrainous subjects, the limit between normal and abnormal EEG patterns may be difficult to determine on visual inspection. Spectral frequency analysis, now available routinely on most paper-less EEG devices, allows quantifying the PD response. It is not known, however, whether it has greater sensitivity and/or specificity than

visual inspection in migraine patients. We undertook therefore this study to determine the prevalence of PD at 20 Hz by visual inspection and by spectral analysis, to evaluate the diagnostic yield by comparing migraine patients and non-migraineurs, and to search for correlations between PD power on qEEG analysis and clinical features of migraine.

METHODS

Subjects

We included from March 2012 to February 2013, 280 consecutive migraine patients aged between 18 and 65 years consulting the Headache Clinic at Liège University. All patients fulfilled ICHD-II criteria for episodic migraine (EM) without (MO: ICHD-II code 1.1; n=171) or with aura (MA; 1.2.1; n=61), chronic migraine (CM: A 1.5.1; n=48) or medication overuse headache (MOH: A 8.2; n=37) [**Table 1**]. As controls we studied 24 patients consulting the Neurology Department for symptoms other than pain and without any personal history of headache or a history of migraine in 1st and 2nd degree relatives. We excluded participants with structural brain lesions, epilepsy or dementia, patients who received preventive migraine medications in the last 6 months before the study or high doses of psychotropic drugs, and those with another primary headache.

We collected demographic and clinical data from all included subjects by face to face interview. Migraineurs were questioned about several clinical features of their headaches; i.e. attack triggers, disease duration, attack duration, attack frequency during the last month, ictal sensoriphobia, nausea or vomiting, number of other autonomic symptoms (diarrhea, syncope, conjonctival injection), acute medication use. We subdivided migraine with aura (MA) patients in 3 groups according to the aura characteristics: strictly visual aura (MAV), visual and sensory aura symptoms (MAS), visual, sensory and aphasic aura symptoms (MAP). We searched for a history of migraine in 4 groups of patients' relatives (children, siblings, parents, grandparents) and gave for each group a score of 1 or 0 depending on presence or not of migraine. We computed a "family history score" by summing the 4 scores.

Study protocol

EEG recording and light stimulation

Participants underwent a routine EEG recording with a 10-20 system montage supplemented by a channel recording the ECG. EEG was recorded digitally using the NicVue 2.9 software with eyes closed for

approximately 20 mn. The sampling rate was 256 per second. The band pass filter setting was 0.5–70 Hz. The subjects were lying down in a dimly lit room. Light stimulation was delivered with the standard photostimulation program of NicVue 2.9 at maximum intensity. Flash power was 1.0 J. The stroboscope was positioned 30 cm in front of the eyes for the two trains. Intermittent photic stimulation was presented as 15 s trains for each of 5, 10, 15 and 20 Hz frequencies with a 15 s inter-train interval. The 15 s train was delivered two times and divided in 3 epochs: 5 s with eyes closed, 5 s with eyes open and again 5 s with eyes closed.

EEG analysis

We manually selected the EEG segments during photic stimulation at 20 Hz. We restricted the analysis to the occipital derivations (O1-P3 and O2-P4) because the dominant sources of the SSVEP signals are located in the occipital cortex [4, 13]. If not contaminated by artifacts, the entire stimulus period (15 s) was sampled. In the case of occasional movement artifacts, we used the longest artifact-free part of the segment. The Fast Fourier transformation application included in the Nic Vue 2.9 software yielded power per Hertz (μV^2/Hz) spectra. We estimated the narrow-band driving power for each of the stimulus frequencies in question (X) ± 0.25 Hz. According to Nyrke et al, the contribution to the evoked signal from outside the X ± 0.25 Hz band is negligible [14,15].

JS and DM inspected visually the EEGs while YF performed blindly the spectral frequency analysis with Fast Fourier Transformation on occipital derivations O1-P3 and O2-P4, taking into account for further analyses the derivation with the greatest PD power.

Statistical analyses

We used STATISTICA v8.0 for statistical computations. Data are expressed as means ± SEM or 95%CI. We used ANOVA to compare variables. Means were compared using the Chi-square test. Spearman's test was used for correlation between variables, and the statistical significance was set at $p<0.05$.

RESULTS

Sensitivity and specificity of visual inspection for photic driving (PD) on EEG

On visual inspection, 141 migraineurs (50.4%) were considered to have PD (VPD group), and 139 (49.6%) to have not (nVPD group). On spectral analysis, mean PD power at 20 Hz was 6.84 ± 2.38 μV^2 in controls, 5.42 ± 1.09 μV^2 in nVPD and 15.01 ± 2.71 μV^2 in VPD migraineurs. The difference in PD power between the latter and the nVPD group or controls was significant (**Table 2)**.

When the mean PD power of controls + 95% CI, i.e. 9.22 μV^2, was taken as the upper threshold of normal PD power, 107 (38.21%) migraine patients had increased photic driving (PD+) while 173 (61.79%) had not (PD-). Eighty-eight out of the 141 VPD migraineurs (62.41%) were PD+, while 120 out of 139 nVPD patients (85.61%) were PD- (**Fig. 1**). Based on this criterion, sensitivity of visually identified PD was 82.24% and specificity 69.36%.

Clinical correlates of visually identified 20Hz photic driving

Patients in the VPD group had lower attack frequency, lower incidence of ictal photophobia, but higher attack duration (**Table 3**).

Clinical correlates of increased photic driving power on spectral analysis

In the global patient population, presence of an aura was associated with increased PD power (p= 0.004), but on closer inspection this was mainly due to 2 outliers with values at 260.41 μV^2 and 284.09 μV^2. When these 2 outliers were excluded, there was no significant difference between migraine with or without aura.

The mean PD power for episodic migraine without aura (EM), chronic migraine (CM), migraine with aura (MA) and controls was respectively 10.56 ± 1.79 μV^2, 6.88 ± 2.33 μV^2, 11.92 ± 4.91 μV^2 and 6.84 ± 2.38 μV^2. It was higher in EM patients than in CM sufferers (p=0.046) [**Fig. 2**].

Mean PD power was numerically higher in CM patients with medication overuse (n=37; 7.48±2.65 μV^2) compared to CM without such overuse (n=11; 5.34 ± 3.92μV^2, p= 0.40).

Mean photic driving power was greater in women (11.31 ± 1.88 μV^2) than in men (5.55 ± 1.47 μV^2) (p= 0.004). There were almost two times more men in the PD- group compared to the PD+ group (p= 0.017).

Patients in the PD+ group had significantly lower migraine attack frequency than those belonging to the PD- group (p=0.04). However, they had longer attack duration (p= 0.045) and more frequently ictal autonomic symptoms other than nausea (p= 0.02). Vomiting was also numerically more frequent in the PD+ (35.51%) than in the PD- group (30.06%), but this difference did not reach the level of significance (p=0.34). **[Table 4]**

The migraine family history score was not statistically different between the PD+ and PD- groups taken separately. However, when both groups were pooled, there was a significant positive correlation between PD power and the migraine family history score (r= 0.14, p< 0.05). There was no significant linear correlation between PD power and age, disease duration, frequency or duration of attacks.

Acute medication overuse frequency was 14.95% in the PD- group versus 14.45% in the PD+ group (p= 0.39).

DISCUSSION

The aims of our study were to determine sensitivity and specificity of visual EEG inspection for photic driving at 20 Hz ('H' response) in migraine patients and to search for clinical correlates of abnormal photic driving power.

We found a good sensitivity (82.24%) but moderate specificity (69.36%) of the visually identified photic driving H response in migraineurs. In a similar study Chorlton & Kane (2000) found a comparable high sensitivity (86.4%) but a clearly better specificity (97.5%) [16]. This difference could be due to the low number of patients (n=33) in Chorlton & Kane's study contrasting with 280 patients in ours. In our study visual inspection of the EEG 20Hz tends to overestimate presence of abnormal PD in migraineurs, which is likely due to the fact that PD is not an abnormal feature of the visual cortex and not restricted to migraine. PD is often present in non-migrainous subjects and, as shown by spectral frequency analysis, it is merely its degree that characterizes a subgroup of migraine patients. Whether this subgroup with enhanced PD has particular clinical features is obviously a question of diagnostic, and even more so, of pathophysiological interest.

PD power on spectral EEG analysis was on average not different between migraineurs and controls in our study. This is in line with the majority of studies that evaluated the utility of the H response on EEG to distinguish migraine from normal subjects, or migraine from other headache types [17]. In a few studies, nonetheless, PD was found useful to discriminate primary headaches sufferers (migraine and tension type headache) from controls [18], while failing to differentiate primary headaches [19].

We included patients without taking into account the period in their migraine cycle. Reactivity of the cerebral cortex, as explored by evoked potentials, was shown to vary with the migraine cycle [20]. However, there seems to be no significant variation of steady state visual EEG evoked-responses (SSVEPs) in the medium frequencies range (15-30 Hz) over the migraine cycle [7, 12, 21].

We found that attack frequency was significantly lower in the group of patients with an abnormal PD power. PD power was also significantly superior in episodic migraine as compared to chronic migraine. This could be related to the changes in visual cortex responsiveness over the migraine cycle [20, 22] and between episodic and chronic migraine [23]. For instance, during stimulus repetition, EEG and magnetoencephalographic visual evoked responses lack habituation in episodic migraine between attacks, but habituate normally during attacks and in chronic migraine [24, 25, 26]. Since the response pattern in chronic migraine is indistinguishable from that found during attacks in episodic migraine, it was suggested that chronic migraine patients are locked in an "ictal-like state" [23, 27]. Patients with a high attack frequency are at greater risk of being recorded close to an attack than those with a low number of monthly attacks. Thalamo-cortical dysrhythmia could be responsible for the changes in habituation [28, 29]. Whatever the underlying mechanisms might be, however, the differences in habituation pattern could explain why amplitude of the responses induced during repetitive flicker stimulation at 20Hz would not decrease interictally in episodic migraine producing an increased PD power on spectral analysis, while in chronic migraine PD power would be lower because of a normal habituation of the evoked activities.
Acute medication overuse was present in most of our chronic migraine patients, but we found no significant difference in 20Hz PD power between patients with and without overuse.

The higher mean 20 Hz PD power in migraine with aura patients was due to two outliers with exceptionally high power. When these patients were excluded, there was no significant difference anymore compared to migraine without aura. Some authors found an increased SSVEP in migraine with aura compared to migraine without aura [10], but others found no such difference [12]. From a pathophysiological point of view, it is of interest that migraine with aura, a condition where the visual cortex is susceptible to cortical spreading depression and thought to be hyperexcitable, is not associated with a PD power superior to migraine without aura, except in rare patients.

Ictal autonomic symptoms were more frequent in migraineurs with abnormal PD power on spectral analysis. Puca et al. also found a positive correlation between PD and autonomic symptoms [10]. There is no

straightforward explanation for this relationship. The hypothalamus could be a common denominator as long as one accepts that it may mediate some of the autonomic features of migraine attacks. The hypothalamus may indeed influence cortical responsiveness via GABA-ergic connections with the reticular nucleus of the thalamus (TRN) [30]. The TRN is an important component of the circuitry that is malfunctioning in thalamo-cortical dysrhythmia [31], a proposed mechanism for the abnormal interictal cortical responsiveness in migraine [27].

In our subjects, PD power was significantly greater in women than in men. A sexual dimorphism of PD was not studied or reported in previous studies. Such dimorphism is present in migraine and sex hormones are well known to modulate cortical excitability in humans and in animals [32]. Unfortunately, in our study we have no information about the stage of the menstrual cycle during which recordings were performed.

A strong family history of migraine was significantly correlated to PD power at 20 Hz in our patients. This is in accordance with a study of SSEVP at mean frequencies (21, 23 and 27 Hz) where a positive family history of migraine was linked with a significant increase in visual reactivity over the temporo-parieto-occipital regions [10]. By contrast, another study found a negative correlation between family history of migraine and photic driving power at 12 Hz [12]. Genetic factors are likely to influence the response of visual cortical areas to flicker stimulation, and this influence may depend on the frequency range of stimulation. Evidence for such a genetic relationship also comes from the study of visual evoked potentials [33] and contingent negative variation [34].

To conclude, photic driving of the EEG at 20Hz flicker stimulaion *per se* is by no means specific to migraine patients, but present in the majority of individuals. What characterizes a subgroup of migraineurs is the increased power developed in the 20Hz frequency band during this stimulation. Searching for 20Hz photic driving by visual inspection of EEG traces overestimates the prevalence of an H response in migraine patients. With spectral frequency power analysis, almost 38% of patients have interictally a significant increase in power during 20Hz photic stimulation compared to non-migrainous controls. These patients are more likely to suffer from episodic migraine, to have a low attack frequency, to have ictal autonomic symptoms in addition to nausea and vomiting, to have a family history of migraine and to be females.

Although enhanced PD is of little utility for diagnosing migraine or its subtypes, this study suggests nonetheless that it may identify subgroups of migraine patients in whom lack of habituation of cortical responses during repetitive stimulation could be the common denominator. This hypothesis can be tested in a study combining spectral analysis of the EEG during 20Hz flicker stimulation and evoked potentials.

Acknowledgments: Y. Fogang was supported by a Fellowship of the Headache Education Program of the International Headache Society

References

1. Sprenger T, Borsook D (2012) Migraine changes the brain: neuroimaging makes its mark. Curr Opin Neurol 25:252–262
2. Magis D, Ambrosini A, Bendtsen L, Ertas M, Kaube H, Schoenen J (2007) Evaluation and proposal for optimalization of neurophysiological tests in migraine: part 1 electrophysiological tests. Cephalalgia 27(12): 1323–1338
3. Ambrosini A, De Noordhout AM, Sandor PS, Schoenen J (2003) Electrophysiological studies in migraine: a comprehensive review of their interest and limitations. Cephalalgia 23:13-31
4. Vialatte FB, Maurice M, Dauwels J, Cichocki A (2010) Steady-state visually evoked potentials: focus on essential paradigms and future perspectives. Prog Neurobiol. 90(4): 418-438
5. Moratti S, Clementz BA, Gao Y, Ortiz T, Keil A (2007) Neural mechanisms of evoked oscillations: stability and interaction with transient events. Hum. Brain Mapp. 28(12):1318–1333
6. Regan D (1966) Some characteristics of average steady-state and transient responses evoked by modulated light. Electroenceph. Clin. Neurophysiol. 20:238–248
7. Golla FL, Winter AL (1959) Analysis of cerebral responses to flicker in patients complaining of episodic headache. Electroencephalogr Clin Neurophysiol 11:539–549
8. Puca FM, de Tommaso M, Savarese MA, Genco S, Prudenzano A (1992) Topographic analysis of steady-state visual evoked potentials (SVEPs) in the medium frequency range in migraine with and without aura. Cephalalgia 12:245-249
9. Genco S, de Tommaso M, Prudenzano A, Savarese M, Puca FM (1994) EEG features in juvenile migraine: topographic analysis of spontaneous and visual evoked brain electrical activity: a comparison with adult migraine. Cephalalgia 14:42-46
10. Puca FM, de Tommaso M, Tota P, Sciruicchio V (1996) Photic driving in migraine: correlations with clinical features. Cephalalgia 16:246–250
11. Vogel W, Broverman DM, Klaiber EL (1971) EEG responses in regularly menstruating women and in amenorrheic women treated with ovarian hormones. Science 172(3981):388-391
12. Bjørk M, Hagen K, Stovner LJ, Sand T (2011) Photic EEG-driving responses related to ictal phases and trigger sensitivity in migraine: A longitudinal, controlled study. Cephalalgia 31(4):444–455
13. Pastor MA, Valencia M, Artieda J, Alegre M, Masdeu JC (2007) Topography of cortical activation differs for fundamental and harmonic frequencies of the steady-state visual-evoked responses. An EEG and PET H215O study. Cereb Cortex 17:1899–1905
14. Nyrke T, Lang AH (1982) Spectral analysis of visual potentials evoked by sine wave modulated light in migraine. Electroencephalogr Clin Neurophysiol 53:436–442

15. Nyrke T, Kangasniemi P, Lang AH (1989) Difference of steady-state visual evoked potentials in classic and common migraine. Electroencephalogr Clin Neurophysiol 73:285–294
16. Chorlton P, Kane N (2000) Investigation of the cerebral response to flicker stimulation in patients with headache. Clin Electroencephalogr. 31(2):83-87
17. Gronseth GS, Greenberg MK (1995) The utility of the electroencephalogram in the evaluation of patients presenting with headache: a review of the literature. Neurology 45(7):1263-1267
18. Simon RH, Zimmerman AW, Tasman A, Hale MS (1982) Spectral analysis of photic stimulation in migraine. Electroencephalogr Clin Neurophysiol 53(3):270-276
19. De Tommaso M, Sciruicchio V, Bellotti R, Guido M, Sasanelli G, Specchio LM, Puca F (1999) Photic driving response in primary headache: diagnostic value tested by discriminant analysis and artificial neural network classifiers. Ital J Neurol Sci. 20(1):23-28
20. Schoenen J, Ambrosini A, Sándor PS, Maertens de Noordhout A (2003) Evoked potentials and transcranial magnetic stimulation in migraine: published data and viewpoint on their pathophysiologic significance. Clin Neurophysiol. 114(6):955-972
21. Smyth VO, Winter AL (1964) The EEG in migraine. Electroencephalogr Clin Neurophysiol 16:194–202
22. De Tommaso M, Sciruicchio V, Guido M, Sasanelli G, Specchio LM and Puca FM (1998) EEG spectral analysis in migraine without aura attacks. Cephalalgia 18:324–328
23. Coppola G, Schoenen J (2012) Cortical excitability in chronic migraine. Curr Pain Headache Rep 16(1): 93-100
24. Schoenen J (1996) Deficient habituation of evoked cortical potentials in migraine: a link between brain biology, behavior and trigeminovascular activation? Biomed Pharmacother 50:71–78
25. Chen W, Wang S, Fuh J, Lin C, Ko Y, Lin Y (2009). Peri-ictal normalization of visual cortex excitability in migraine: an MEG study. Cephalalgia 29(11):1202-1211
26. Chen W, Wang S, Fuh J, Lin C, Ko Y, Lin Y (2011) Persistent ictal-like visual cortical excitability in chronic migraine. Pain 152 (2):254-258
27. Schoenen J (2011) Is chronic migraine a never-ending migraine attack? Pain 152:239–240
28. Steriade M, Gloor P, Llinas RR, Lopes de Silva FH, Mesulam MM (1990) Report of IFCN Committee on Basic Mechanisms. Basic mechanisms of cerebral rhythmic activities. Electroencephalogr Clin Neurophysiol 76:481–508
29. Coppola G, Pierelli F, Schoenen J (2007) Is the cerebral cortex hyperexcitable or hyperresponsive in migraine? Cephalalgia 27:1427–1439
30. Shepherd GM (2004) The synaptic organization of the brain. Oxford university press, New York
31. Llinas RR, Ribary U, Jeanmonod D, Kronberg E, Mitra PP (1999) Thalamocortical dysrhythmia: A neurological and neuropsychiatric syndrome characterized by magnetoencephalography. Proc Natl Acad Sci USA 96:15222–15227
32. Chauvel V, Vamos E, Pardutz A, Vecsei L, Schoenen J, Multon S (2012) Effects of systemic kynurenine on cortical spreading depression and its modulation by sex hormones in rat. Exp Neurol 236:207-214

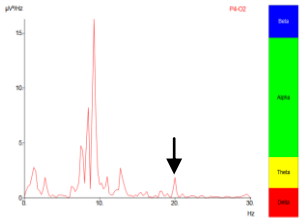
33. Sándor PS, Afra J, Proietti-Cecchini A, Albert A, Schoenen J (1999) Familial influences on cortical evoked potentials in migraine. Neuroreport. 10(6):1235-1238
34. Siniatchkin M, Kirsch E, Kropp P, Stephani LU, Gerber WD (2000). Slow cortical potentials in migraine families. Cephalalgia 20:881-892

Fig. 1 The upper part shows illustrative examples of the frequency power spectra during 20 Hz intermittent flash stimulation of a migraine patient with low photic driving power (nVPD; 3.2 µV, left) and of another patient with high photic driving power (VPD; 45.26 μV^2, right). The lower part shows the distribution of individual values of photic driving power (μV^2) at 20 Hz in 139 patients without (nVPD) and 141 patients with visually identified photic driving (VPD). The horizontal bars in both groups indicate means, the dashed horizontal lines ± 95% CI of PD power in the control group

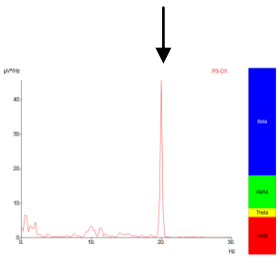
Fig. 2 Photic driving power (mean ± 95%CI) in migraine subtypes and controls.

* significant difference between episodic migraine (EM) and chronic migraine (CM)

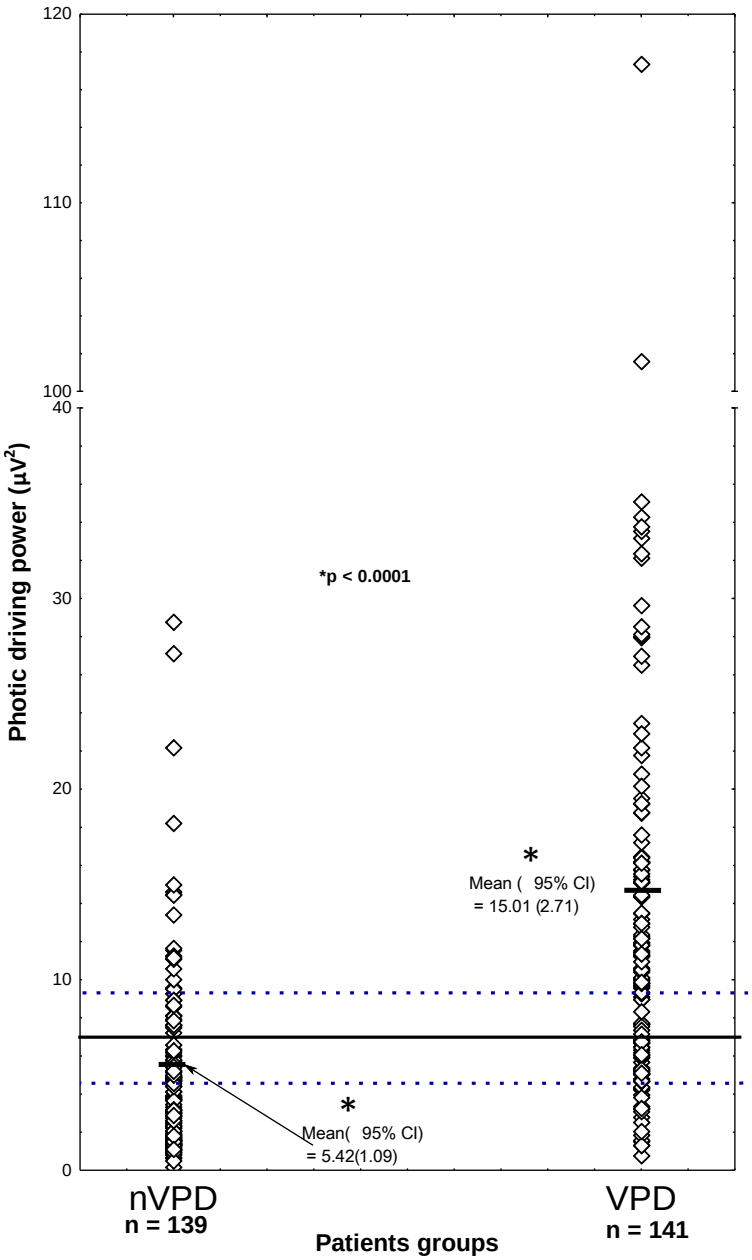
Figure



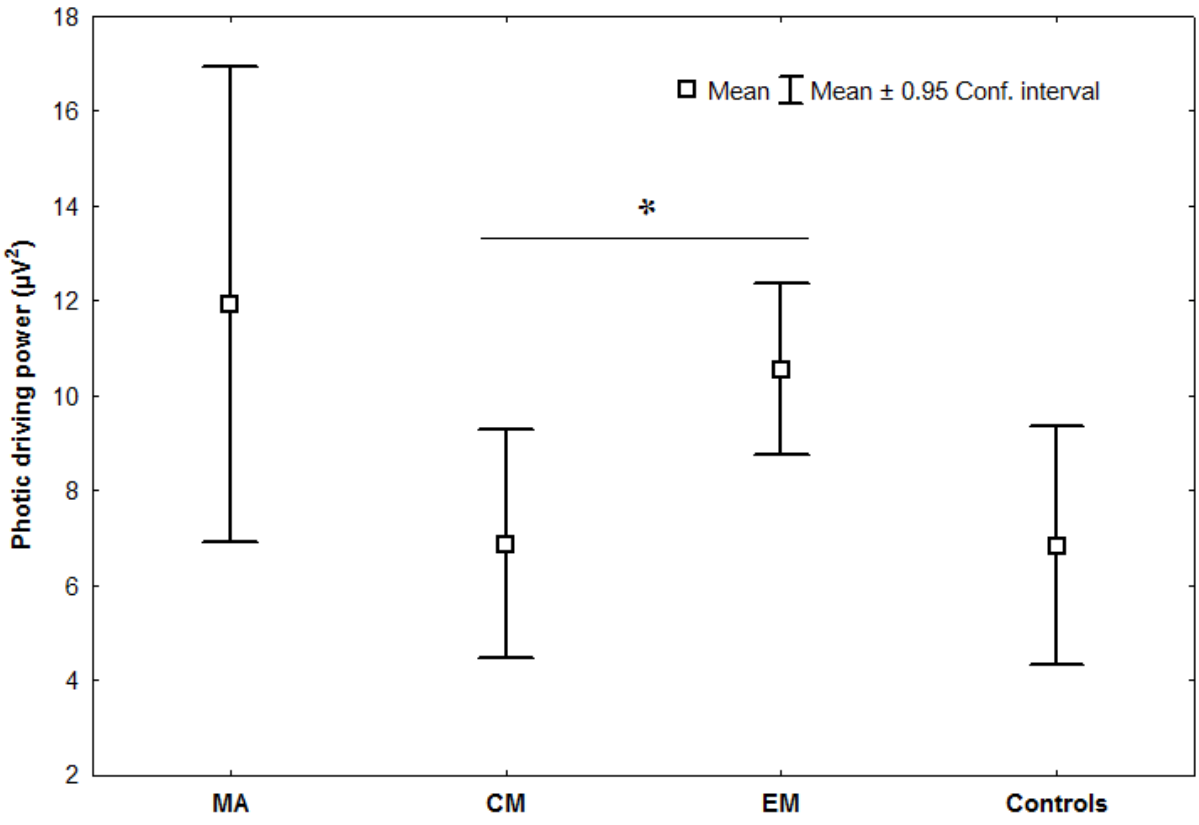
Migraineur with low PD power



Migraineur with high PD power



Figure


Mean
Mean ± 0.95 Conf. interval
Photic driving power (μV²)
18
16
14
12
10
8
6
4
2
*
MA
CM
EM
Controls

Table

Table 1 Distribution of subjects according to their diagnoses

Diagnoses	Migraine without aura (MO) (n= 219)		[$]Migraine with aura (MA) (n= 61)			Controls (n= 24)
Subtypes	Episodic Migraine (EM) (n= 171)	Chronic Migraine (CM) (n= 48) (n= 37 with medication overuse)	MAV (n= 59)	MAS (n= 18)	MAP (n= 6)	Anxiety & memory complaints (n= 9) Vaso-vagal syncope (n= 5) Routine neurological work-up (n= 4) Malingering (n= 3) Bell's palsy (n= 2) Myopathy (n= 1)

[$]MAV, MAS, MAP: migraine with visual, sensory, aphasic aura respectively.

Table

Table 2 Statistical comparison of photic driving power between the 3 groups of patients, with migraine patients subdivided into those with (VPD) or without (nVPD) 20Hz photic driving identified on visual inspection of the EEG

	t-value	p-value
VPD vs nVPD	6.395	**< 0.00001**
nVPD vs [$]Ctr	-0.992	0.32
VPD vs Ctr	2.405	**0.017**
Migraineurs vs Ctr	1.225	0.22

[$]Ctr: Controls

Table

Table 3 Demographic and clinical features of the study population with migraine patients subdivided into those with (VPD) or without (nVPD) 20Hz photic driving identified on visual inspection of the EEG

	Migraine patients			Controls
	Patients	**VPD group**	**nVPD group**	
Age	37.21 ± 12.10	38.88 ± 12.17	35.26 ± 12.07	38.84±14.32
Male (%)	19.3	12.86	25.90	24.0
Disease duration (Months)	173.88 ± 124.78	181.77 ± 129.13	165.86 ± 120.13	
Migraine with aura(%)	21.79	20.57	22.30	
Migraine days/month	8.46 ± 9.17	6.25 ± 7.08***	10.71 ± 10.44	
Attack duration (h)	31.93 ± 24.65	35.82 ± 25.65**	27.99 ± 23.03	
Ictal Photophobia (%)	82.14	76.6*	87.77	
Nb of Attack triggers	0.66 ± 1.02	0.77 ± 0.42	0.57 ± 1.0	
Family history score (0-4)	1.22 ± 0.92	1.29 ± 0.98	1.15 ± 0.86	
Photic driving power at 20 Hz (μV^2)	9.46 ± 1.37	15.01 ± 2.71 ***	5.42 ± 1.09	6.84 ± 2.38

(*p<0.05, **p<0.001, ***p<0.0001 VPD vs nVPD group) VPD: visually-identified 20Hz photic driving; nVPD: no photic driving identified visually

Table

Table 4 Demographic and clinical features of subjects according to their photic driving power on spectral analysis

	Migraine patients			Controls
	All Patients	**PD+ group (+ 95% CI)**	**PD- group (-95%CI)**	
N (%)	280	107 (38.21)	173 (61.79)	24
Age	37.21 ± 1.42	38.32 ± 2.40	36.52 ± 1.75	38.84 ± 14.32
Male (%)	19.3	12.15*	23.70	24
Disease duration (Months)	173.88 ± 14.62	180.91 ± 24.74	169.53 ± 18.07	
Migraine with aura (%)	21.79	22.43	20.81	
Episodic migraine (%)	61.07	64.49	58.96	
Chronic migraine (%)	17.14	12.15	20.23	
Migraine days/month	8.46 ± 1.07	7.10 ± 1.47*	9.30 ± 1.47	
Attack duration (h)	31.93 ± 2.89	35.68 ± 5.06*	29.62 ± 3.44	
Ictal photophobia (%)	82.14	81.31	82.66	
Vomiting (%)	32.14	35.51	30.06	
Autonomic symptoms other than nausea (Nb)	0.18 ± 0.06	0.26 ± 0.11*	0.13 ± 0.06	
Attack triggers (Nb)	0.66 ± 0.12	0.69 ± 0.19	0.65 ± 0.15	
Family history score (0-4)	1.22 ± 0.11	1.33 ± 0.17	1.16 ± 0.13	
Acute Medication Overuse (%)	14.64	14.95	14.45	
Photic driving power at 20 Hz (μV^2)	9.46 ± 1.10	20.37±3.28***	4.05 ± 0.34	6.84 ± 2.38

*p< 0.05, *** p< 0.0001 PD+ vs PD- group. PD+ : photic driving power > mean of controls + 95%CI ; PD- : PD power < mean of controls + 95% CI .