

## **Sensory sensitivity is associated to attention difficulties in migraine**

Authors: Yohana Lévêque\*<sup>1</sup>, Rémy Masson<sup>1</sup>, Lesly Fornoni<sup>1</sup>, Annie Moulin<sup>1</sup>, Aurélie Bidet-Caulet<sup>1</sup>, Anne Caclin<sup>1</sup>, Geneviève Demarquay<sup>1,2</sup>

\*E-mail address: yohana.leveque@inserm.fr, mailing address: CRNL CAP team, 95 Boulevard Pinel 69500 Bron, France

<sup>1</sup> Lyon Neuroscience Research Center (CRNL), INSERM UMRS 1028, CNRS UMR 5292, Université Claude Bernard Lyon 1, Université de Lyon, Lyon, France

<sup>2</sup> Neurological Hospital Pierre Wertheimer, Functional Neurology and Epilepsy Department, Hospices Civils de Lyon and Université Claude Bernard Lyon 1, Université de Lyon, Lyon, France

### **Abstract**

**Objectives:** The aim of the study was to investigate potential interactions between sensory hypersensitivity and attentional difficulties in migraineurs.

**Methods:** Forty-six episodic migraineurs without aura and 46 healthy controls filled out questionnaires on self-perceived attention difficulties and self-reported sensitivity to visual, auditory and olfactory stimulations.

**Results:** Compared to controls, migraineurs reported significantly higher levels of attention difficulty and sensory sensitivity. Sensory hypersensitivity correlated significantly with attentional difficulties in migraineurs ( $p=0.002$ ), but not with migraine disability or levels of anxiety or depression. Ictal and interictal sensory sensitivity were significantly correlated in migraineurs within visual ( $p<.001$ ), auditory ( $p<.001$ ) and olfactory ( $p=.001$ ) modalities.

**Conclusion:** Self-reported attentional difficulties, multimodal sensory hypersensitivity and the association between both may reflect the fact that external stimuli engage attention in an exacerbated manner in migraineurs, yielding distraction.

Keywords : Photophobia – Phonophobia – Osmophobia – Attention – Questionnaire

## **Introduction**

Migraine is characterized by an abnormal sensory processing (1,2). Enhanced sensitivity to uni- or multimodal stimuli such as an exacerbation of headache or discomfort is a striking feature of migraine which varies over the migraine cycle (3-5). Neurophysiological and neuroimaging studies also suggest that the migraine brain is hyperresponsive to sensory stimuli as evidenced by impaired habituation to stimuli and increased BOLD fMRI responses to photic stimuli (6).

In parallel, recent research has pinpointed attentional alterations in interictal migraineurs. Attention is the process which enables to preferentially select salient or relevant stimuli and to attenuate the response to irrelevant incoming stimuli. Neurophysiological and neuroimaging studies suggest an altered top-down attentional control of visual cortex (7) and an enhanced orienting response towards acoustic stimuli (8-9) in migraineurs. Behavioral and neuropsychological studies also report attentional impairments in migraineur children and adults (see for instance (10), for a review) but distinction between executive functions and attention, or hyperactivity symptoms and attention is not always possible given the tests employed (11,12).

To our knowledge, no study has investigated the potential link between these two characteristics of migraine: enhanced sensory sensitivity on one hand and attentional alterations on the second hand. Both point to abnormal sensory processing. As a first approach to this question, the aim of our study was to investigate possible interactions between sensitivity

to light, sound, odor and attentional difficulties by means of questionnaires, in episodic migraineurs without aura and control participants.

## **Methods**

### ***Participants***

Forty-six migraine patients (without aura) and forty-six healthy control participants matched for sex, age, education and music training participated in this study (Table 1). All migraine patients fulfilled the criteria of episodic migraine according to the International Headache Society (13), were aged 18 to 75 years and had at least 1 attack per month. Exclusion criteria were migraine with aura, chronic migraine (>15 days of headache per month), other neurological or psychiatric disease, and use of preventive medication. Attack frequency was  $3.8 \pm 1.9$  per month on average. Twenty-three migraineurs and eleven control subjects were concomitantly participants to a magnetoencephalography (MEG) study investigating auditory attention (14). Participants gave their written informed consent, according to the Declaration of Helsinki.

**Table 1: Demographic characteristics of the participants**

		<b>Patients</b>	<b>Controls</b>	<b>Group comparison</b>	
		(n=46)	(n=46)	Statistics	p-value
<b>Sex (n)</b>	Male	10	13	$\chi^2(1) = 0.52$	0.471
	Female	36	33		
<b>Age (years)</b>	Mean (SD)	29.4 (9.4)	27.4 (11.2)	$t(90) = 0.93$	0.355
<b>Education (years)</b>	Mean (SD)	15.5 (2.4)	15 (1.7)	$t(90) = 1.18$	0.240
<b>Music training (years)</b>	Mean (SD)	3.4 (4.9)	3.4 (4.2)	$t(90) = 0.50$	0.964

### **Material**

We created one questionnaire assessing attentional difficulties in daily life. This questionnaire was inspired from the Attention self-assessment questionnaire (15) and the Wender Utah Rating Scale (16). For each item, the participants rated on a 4-point scale the frequency with which they encounter difficulties in a particular situation.

We also created three questionnaires to assess visual, auditory, and olfactory hypersensitivity. Each item presented a behavioral or emotional response to a sensory stimulation and a 4-point scale from 1 “Rarely” to 4 “Very often”. These questionnaires were divided into two sections: “between attacks” and “during an attack” (see Appendix for the full version, with an English

translation). The “between attacks” auditory questions were selected from the auditory sensitivity questionnaire of Khalfa (1999, French clinical test, published in English under the name HQ – Hyperacusis Questionnaire- (17)). The visual questions were adapted from Choi et al. (18). The olfactory questions were inspired from the Glasgow Sensory Questionnaire (19,20). Finally, migraineurs were requested to fill the HIT (Headache Impact Test, (21)) and the MIDAS scale (Migraine Disability Assessment, (22)) as a measure of migraine general severity, functional impact of migraines and migraine frequency. The 34 participants who underwent an additional MEG experiment also completed the HAD (Hospital Anxiety and Depression Scale (23)) to assess anxiety and depression levels.

### ***Procedure***

Participants (n=92) completed the attention and hypersensitivity questionnaires at home, either on paper, or online. For the hypersensitivity questionnaires, controls were asked to answer only the “between attacks” sections. The migraine patients also completed the HIT and the MIDAS (n=46) at home. The HAD was completed at the lab for the subjects participating to the MEG study (n=23 migraineurs).

### ***Statistical analysis***

Responses “rarely” were recoded as “1”, “sometimes” as “2”, “often” as “3” and “very often” as 4. Missing data in questionnaires were replaced by the group average score to the item. By averaging item scores, we got a total score for each questionnaire. Separate scores were computed for the sections “between attacks” and “during an attack” for the hypersensitivity questionnaires. Internal coherence of each questionnaire was assessed using Cronbach’s alpha.

Group differences in the scores to the attentional difficulties and the visual, auditory and olfactory interictal hypersensitivity questionnaires were assessed using independent t-tests. Pearson correlations between ictal and interictal scores and between modalities were then conducted on migraine patient data. Finally, a multiple linear regression assessed the relationship between interictal sensory hyperactivity with attention difficulties, including age, sex, education level, MIDAS and HIT scores as covariates to control for confounding effects. Modeling assumptions were verified using the gvlma R-package (24)): data fulfilled the statistical assumptions of independence, normality and homogeneity of variances ( $p > .05$ ). The multicollinearity was not excessive with a Variance Inflation Factor (VIF) always inferior to 0.69, under the commonly accepted cutoff value of 5 or 10 (25).

Causality questions (“Is your headache worsened by...?” and “Is your headache triggered by...?”) were analyzed separately, with the aim to examine the link between the perception of a stimulation as a trigger and interictal hypersensitivity in migraineurs.

All the computed p-values were two-tailed and the cut-off for statistical significance was of 0.5.

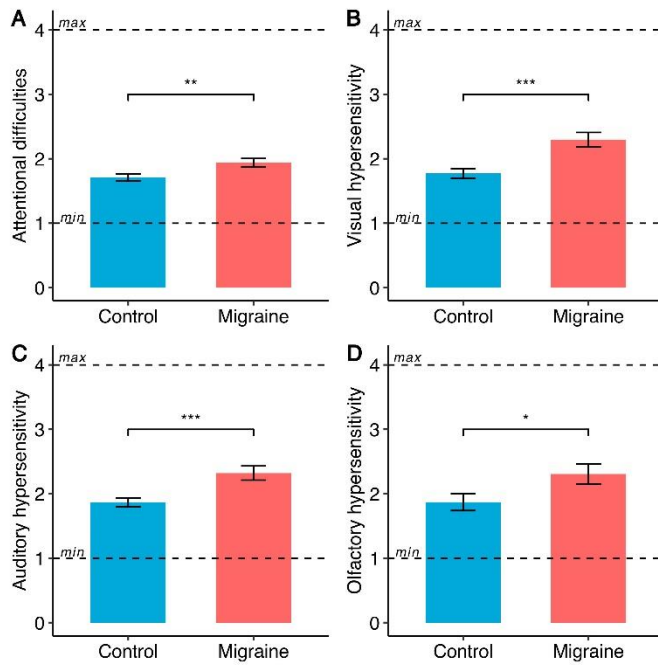
## Results

There was no missing data across the questionnaires for the control group. In the migraine group, the rate of unanswered items was <2% for all questionnaires. Internal coherence was high within each questionnaire (interictal part), as measured by the Cronbach's Alpha computed on the 92 participants: 0.73 for the attention questionnaire, 0.85 for the visual questionnaire, 0.84 for the auditory questionnaire. Olfactory questionnaire comprised only one question in the interictal part. Three migraineurs out of 23 tested showed an anxiety score superior to the pathological cut-off according to the HAD norms, but the depression score was not pathological and their data were retained for the main analyses.

### *Group comparisons*

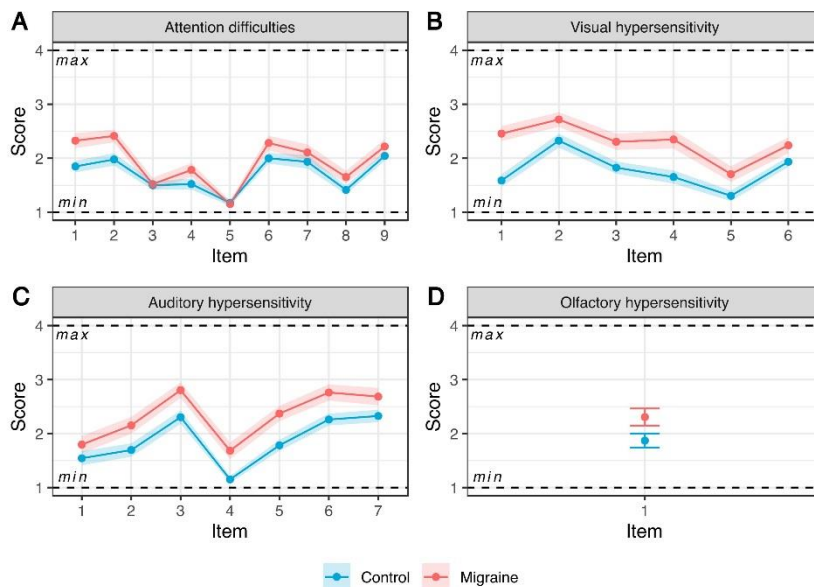
Migraineurs showed significantly higher scores of attention difficulties than control participants ( $t(90)=2.64$ ,  $p=.010$ ,  $d=.53$ ), as illustrated on Figure 1A.





**Figure 1:** Average score to the attention questionnaire (panel A) and the sensory hypersensitivity questionnaires ("between attacks" questions) in control and migraine participants (panels B, C, D). \* $p < .05$ , \*\* $p < .01$ , \*\*\* $p < .001$

**Figure 2:** Profile of average rating (shaded area represents the standard-error) by item and group for the attention questionnaire (panel A) and the sensory hypersensitivity questionnaires ("between attacks" questions) in control and migraine participants (panels B, C, D).



Between attacks, migraineurs showed significantly higher scores of sensory hypersensitivity than controls in the visual ( $t(90)=3.84$ ,  $p<.001$ ,  $d=.75$ ), auditory ( $t(90)=3.22$ ,  $p=.002$ ,  $d=.64$ ), and olfactory modalities ( $t(90)=2.18$ ,  $p=.032$ ,  $d=.45$ ), as illustrated on Figure 1 (panels B, C, and D).

Ratings by items are illustrated on Figure 2.

#### *Correlations in migraineurs*

Visual and auditory hypersensitivity were correlated in migraineurs, slightly in interictal periods ( $r(44)=.30$ ,  $p=.043$ )<sup>1</sup>, more strongly in ictal period ( $r(44)=.432$ ,  $p=.003$ ). Olfactory hypersensitivity did not correlate with the other modalities in interictal period ( $r(44)<.22$ ,  $p>.141$ ). In ictal period, the correlation of olfactory hypersensitivity with auditory hypersensitivity was significant ( $r(44)=.315$ ,  $p=.033$ ), but the correlation with visual hypersensitivity failed to show significance ( $r(44)=.24$ ,  $p=.102$ ). Note however that the olfactory questionnaire was shorter and hence likely to be less robust than the auditory and visual questionnaires.

In the analyses that follow, we used a composite score of interictal sensory hypersensitivity across visual and auditory modalities by averaging visual and auditory scores for each migraineur participant.

<sup>1</sup> While visual and auditory sensitivity did not correlate in control participants:  $r(44)=.08$ ;  $p=.61$

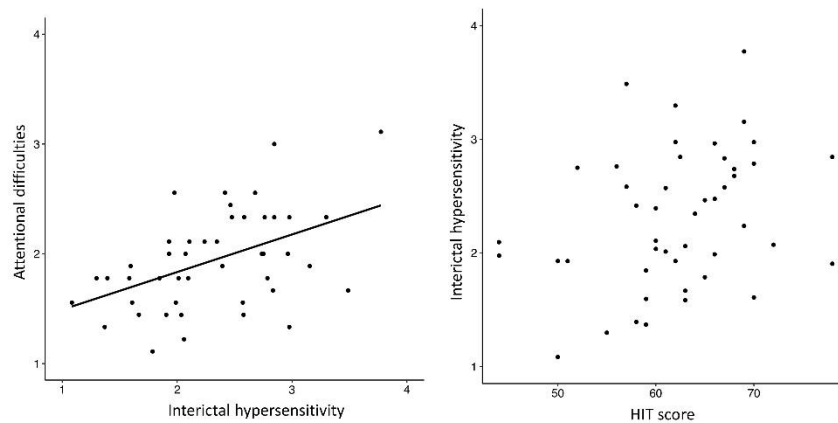
The multiple linear regression revealed a significant correlation between interictal sensory hypersensitivity and attention difficulties ( $t=3.47$ ,  $p=.001$ ) with no significant contribution of the covariates (see Table 2). The model had a multiple  $R^2$  of .38 and an adjusted  $R^2$  of .28 ( $F(6,39)=3.95$ ,  $p=.003$ ). The relationship between sensory hypersensitivity and attention is illustrated in Figure 3.

Tested in a separate analysis because of a sample of lower size ( $n=23$ ), the correlation between the anxiety and depression score (HAD total score) and attentional difficulties revealed a significant association between both variables ( $r(21)=-.45$ ,  $p=.033$ ). However, the anxiety and depression score was not significantly correlated to interictal sensory hypersensitivity ( $r(21)=.09$ ,  $p=.674$ ).

**Table 2: Results of the multiple linear regression in migraineurs data (n=46) with the interictal audiovisual hypersensitivity as the dependent variable.** Attention difficulties are significantly linked to hypersensitivity, while the demographic and migraine variables are not.

	Estimate	Standard error	t-value	<i>p</i>
(Intercept)	0.854875	1.070402	0.799	0.42933
<b>Attention</b>	<b>0.610242</b>	<b>0.175795</b>	<b>3.471</b>	<b>0.00128</b>
Age	-0.003425	0.008243	-0.415	0.68006
Sex	-0.196746	0.175242	-1.123	0.26842
Education	-0.041456	0.032653	-1.270	0.21175
HIT	0.016227	0.011846	1.370	0.17858
MIDAS	0.005301	0.007090	0.748	0.45915

**Figure 3:** Interictal sensory hypersensitivity correlates significantly with attentional difficulties in migraineurs (left) but not with migraine disability (HIT score, right)



### *Attack-related questions in migraineurs*

Sensory hypersensitivity was strongly enhanced during ictal periods compared to interictal periods (During attack composite score:  $2.8 \pm 0.6$ ; Between-attack composite score:  $2.30 \pm 0.6$ ;  $t(45) = -7.8$ ,  $p < .001$ ). Ictal and interictal scores were also significantly correlated within each modality (visual:  $r(44) = .57$ ,  $p < .001$ ; auditory:  $r(44) = .72$ ,  $p < .001$ ; olfactory:  $r(44) = .47$ ,  $p = .001$ ).

To the question “Is your headache worsened by...?” (see Appendix), 70% of migraineur participants answered “often” or “very often” for lights, 65% for sounds, 43% for odors. To the question “Is your headache triggered by...?”, 15% of migraineur participants answered “often” or “very often” for lights, 11% for sounds, 22% for odors. Scores to the question “Is your headache triggered by...?” were significantly correlated to interictal sensory hypersensitivity for visual and auditory modalities (visual:  $r(44) = .43$ ;  $p = .003$ ; auditory:  $r(44) = .38$ ;  $p < .010$ ), and marginally for olfactory modality ( $r(44) = .26$ ;  $p = .077$ ).

### **Discussion**

Compared with controls, migraine patients reported significantly higher levels of sensory sensitivity and attention difficulties. Both variables were positively correlated among migraineurs, after controlling for background variables (age, sex, education, HIT and MIDAS scores). Ictal and interictal sensory sensitivity were significantly correlated in migraineurs within visual, auditory and olfactory modalities. The correlation between visual and auditory hypersensitivity was slight in interictal period in migraineurs, and reinforced in ictal periods.

### *Multimodality of sensory hypersensitivity*

Enhanced sensitivity to light, sound and/or odor stimuli is a common symptom of migraine patients that varies over the migraine cycle. Here we observed a higher self-reported sensitivity to these three types of external stimuli in migraineurs compared to controls, as well as an aggravation of this hypersensitivity during migraine attacks. A recent study showed that patients with ictal photophobia were more likely to complain from interictal photosensitivity as well as visual stimuli as triggers than headache patients without ictal photophobia or controls (26). Our results corroborate this finding in the visual modality and show that these correlations between ictal and interictal states are also observed within auditory and olfactory modalities. A limit of the current study is that ictal and interictal allodynia was not evaluated.

Migraineurs reporting high interictal sensitivity to stimulations in a given modality were also reporting these stimulations as triggers for migraine attacks. The causal link between interictal hypersensitivity and attack triggering is however difficult to draw up. Answers to the hypersensitivity questionnaires may reflect preventive behaviors set up by patients toward a supposed trigger (e.g. *“Do you ever use earplugs?”*). Moreover, attribution of a causal role to certain sensory stimulations may be misinterpretation by patients of a simple co-occurrence of hypersensitivity and migraine attacks (27). Indeed, patients pay an exacerbated attention to certain stimuli in the premonitory phase of the attack.

Correlation between self-reported visual and auditory sensitivity in migraineurs are in line with a set of data linking sensitivities across modalities. For instance, lower sound aversion thresholds

were observed in patients with allodynia compared with non-allodynic patients (28) and patients with olfactory hypersensitivity were more likely to complain of photophobia (29). This multimodal sensitivity would reflect the hypothesis that migraine is “*a paroxysmal disorder of pan-sensory gain*” (2).

#### *Self-reported attentional difficulties in migraine*

The present findings of self-reported attentional difficulties in migraineurs complement a set of studies objectivating complex attentional alterations between attacks (7,14)) for electrophysiology; and more contrasting results for behavioral performances (30,31). Our results suggest that attentional difficulties are not only detected by fine electrophysiology measures in experimental sets-up, but are consciously experienced by migraineurs in daily life, even in patients with episodic migraine. This result is also congruent with a comorbidity reported between Attention Deficit and Hyperactivity Disorder (ADHD) and migraine (see (32) for a review and meta-analysis), in particular migraine with aura (33). Recently, a cross-sectional study among university students showed an association between self-perceived attention difficulties and hyperactivity symptoms levels in students suffering from migraine (12). Attention deficit is also reported in both children and adult patients with migraine (see (10), for a review). Migraine is common in children with ADHD but also in mothers of children with ADHD (34). The underlying mechanism of such comorbidity is unknown but could be related to a genetic predisposition.

#### *Correlations between self-reported attentional difficulties and sensory sensitivity in migraine*

The pathophysiological mechanism of ictal and interictal non-painful symptoms in migraine is still poorly understood. Three hypotheses may be proposed as possible explanations for the association we found between attentional difficulties and sensory hypersensitivity.

First, attentional difficulties may be caused by an increased sensitivity to environmental stimuli. Migraine is characterized by a sensory amplification that occurs both during and between attacks and that implies multimodal sensory systems (see above). External stimuli may engage attention in an exacerbated manner in migraineurs (7-9), yielding distraction, and thus attentional difficulties in daily life. According to this hypothesis, migraine would generate sensory hypersensitivity, which, as a consequence, would disturb attentional processes.

Second, hypersensitivity could be caused by attentional difficulties linked to migraine. An altered bottom-up (involuntary capture of attention by an unexpected salient stimulus) and/or top-down (voluntary attention to sensory stimuli) processes could lead to an abnormal sensory modulation management. For instance, an association between attentional deficit and abnormal sensitivity to sensory stimuli has been reported in patients with ADHD (35-37). According to this hypothesis, migraine generates attentional imbalances, which expose the patients to a sensory hypersensitivity. However, migraine disease is not primarily an attention deficit disorder.

Third, both self-reported attentional difficulties and enhanced sensory responsiveness could originate from individual predisposition to develop migraine. Neurochemical imbalances (noradrenaline, dopamine) could underly the attentional difficulties as well as the ictal and



interictal pathophysiology of the migraineur brain (e.g (38)). This hypothesis could explain that both sensory and attentional anomalies have been reported in adults but also in children with migraine (see above): they would not be consequences of several years of migraine damaging the cognitive functions, but reflects of a source dysfunction. Longitudinal studies are required to enlighten causal relationships and disentangle anomalies which are at the core of migraine disease, and anomalies which are secondary to the source dysfunctions. One could for instance investigate engagement of attention in external stimuli processing in children, and how predictive it is for later migraine disease. .

Importantly, the association we found here between attentional difficulties and sensory hypersensitivity cannot be explained by anxiety and depression nor by the severity of migraine, as both variables were not correlated to sensory hypersensitivity. A personality factor as neuroticism (39) could underlie a higher level of complaint in migraineurs than controls and association between both complaints (hypersensitivity and attention difficulties). However, in that case, we would probably have observed a level of complaint across all scales (including HAD score) proportional to the migraine severity (HIT score), which is not the case. In line with these observations, interictal photosensitivity has been found to be unrelated to duration of migraine, frequency of attacks and mood disorder (40-41).

### *Conclusion*

Overall, this study reveals that migraineurs suffer from attentional difficulties in their daily life, confirms the presence of visual, auditory and olfactory hypersensitivity during the interictal

period, and associates both factors. This suggests that explorations combining behavioral and physiological measures of sensory processing and attention processes in the different modalities are necessary to further understand the between-attack particularities of the migraine brain.

#### KEY FINDINGS

- Migraineurs report higher level of multimodal sensory hypersensitivity and higher level of attentional difficulties than control participants.
- Sensory hypersensitivity significantly correlates with attentional difficulties in migraineurs, but not with migraine disability or levels of anxiety and depression.
- Ictal and interictal sensory sensitivity significantly correlate in migraineurs within visual, auditory and olfactory modalities.

**Acknowledgments:** We thank Cécile Graven for help in recruitment and data collection.

**Funding:** This work was supported by a grant from “Agence Nationale de la Recherche” (ANR) of the French Ministry of Research: ANR-14-CE30-0001-01. This work was conducted in the framework of the LabEx CeLyA ("Centre Lyonnais d'Acoustique", ANR-10-LABX-0060) and of the LabEx Cortex ("Construction, Function and Cognitive Function and Rehabilitation of the Cortex", ANR-11-LABX-0042) of Université de Lyon, within the program "Investissements d'avenir" (ANR-11-IDEX-0007) operated by the French National Research Agency (ANR).

**Conflict of Interest:** The Authors declare that there is no conflict of interest.

## References

1. Goadsby PJ, Holland PR, Martins-Oliveira M, Hoffmann J, Schankin C, Akerman S. Pathophysiology of Migraine: A Disorder of Sensory Processing. *Physiol Rev* 2017;97:553–622.
2. Brennan KC, Pietrobon D. A Systems Neuroscience Approach to Migraine. *Neuron* 2018;97:1004–21.
3. Borini CA, Gatti FR, Grezos, RM.L, Frago YD. Odors as triggering and worsening factors in migraine. *Anxiety* 2008;76:53.
4. Friedman DI, De ver Dye T. Migraine and the environment. *Headache* 2009;49:941–52.
5. Vanagaite J, Pareja JA, Støren O, White LR, Sand T, Stovner LJ. Light-induced discomfort and pain in migraine. *Cephalalgia* 1997;17:733–41.
6. Demarquay G, Mauguière F. Central Nervous System Underpinnings of Sensory Hypersensitivity in Migraine: Insights from Neuroimaging and Electrophysiological Studies. *Headache* 2016;56:1418–38.
7. Mickleborough MJS, Truong G, Handy TC. Top-down control of visual cortex in migraine populations. *Neuropsychologia* 2011;49:1006–15.
8. Demarquay G, Caclin A, Brudon F, Fischer C, Morlet D. Exacerbated attention orienting to auditory stimulation in migraine patients. *Clin Neurophysiol* 2011;122:1755–63.
9. Morlet D, Demarquay G, Brudon F, Fischer C, Caclin A. Attention orienting dysfunction with preserved automatic auditory change detection in migraine. *Clin Neurophysiol* 2014;125:500–11.
10. Vuralli D, Ayata C, Bolay H. Cognitive dysfunction and migraine. *J Headache Pain* 2018;19:109.
11. Strine TW, Okoro CA, McGuire LC, Balluz LS. The associations among childhood headaches, emotional and behavioral difficulties, and health care use. *Pediatrics* 2006;117:1728–35.
12. Carpenet C, Guichard E, Tzourio C, Kurth T. Self-perceived attention deficit and hyperactivity symptom levels and risk of non-migraine and migraine headaches among university students: A cross-sectional study. *Cephalalgia* 2019;39:711–21.
13. Headache Classification Committee of the International Headache Society (IHS) The

International Classification of Headache Disorders, 3rd edition. *Cephalalgia* 2018;38:1–211.

14. Masson R, Leveque Y, Demarquay G, ElShafei H, Fornori L, Lecaigard F, Morlet D, Bidet-Caulet A, Caclin A. Attentional alterations in migraine: a behavioral and M/EEG study. 2009 bioRxiv, 661413.
15. Coyette, F., Arno, P., Leclercq, M., Seron, X., Van der Linden, M., & Grégoire, J. Questionnaire d'Auto-évaluation de l'Attention (QAA). 1999. Unpublished document, Centre deRevalidationNeuropsychologique desCliniquesUniversitaires Saint-Luc,Brussels,Belgium.
16. Ward MF, Wender PH, Reimherr FW. The Wender Utah Rating Scale: an aid in the retrospective diagnosis of childhood attention deficit hyperactivity disorder. *Am J Psychiatry* 1993;150:885–90.
17. Khalfa S, Dubal S, Veuillet E, Perez-Diaz F, Jouvent R, Collet L. Psychometric normalization of a hyperacusis questionnaire. *ORL J Oto-Rhino-Laryngol Its Relat Spec.* 2002;64:436–42.
18. Choi J-Y, Oh K, Kim B-J, Chung C-S, Koh S-B, Park K-W. Usefulness of a photophobia questionnaire in patients with migraine. *Cephalalgia* 2009;29:953–9.
19. Robertson AE, Simmons DR. The relationship between sensory sensitivity and autistic traits in the general population. *J Autism Dev Disord* 2013;43:775–84.
20. Sapey-Triomphe L-A, Moulin A, Sonié S, Schmitz C. The Glasgow Sensory Questionnaire: Validation of a French Language Version and Refinement of Sensory Profiles of People with High Autism-Spectrum Quotient. *J Autism Dev Disord* 2018;48:1549–65.
21. Kosinski M, Bayliss MS, Bjorner JB, Ware JE, Garber WH, Batenhorst A, et al. A six-item short-form survey for measuring headache impact: the HIT-6. *Qual Life Res* 2003;12:963–74.
22. Stewart WF, Lipton RB, Dowson AJ, Sawyer J. Development and testing of the Migraine Disability Assessment (MIDAS) Questionnaire to assess headache-related disability. *Neurology* 2001;56(6 Suppl 1):S20-28.
23. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;67:361–70.
24. Peña EA, Slate EH. Global Validation of Linear Model Assumptions. *J Am Stat Assoc* 2006;101:341.
25. O'brien RM. A caution regarding rules of thumb for variance inflation factors. *Quality & quantity* 2007;41:673-690.

26. Hayne DP, Martin PR. Relating Photophobia, Visual Aura, and Visual Triggers of Headache and Migraine. *Headache* 2019;59:430–42.
27. Schulte LH, Jürgens TP, May A. Photo-, osmo- and phonophobia in the premonitory phase of migraine: mistaking symptoms for triggers? *J Headache Pain* 2015;16:14.
28. Ashkenazi A, Yang I, Mushtaq A, Oshinsky ML. Is phonophobia associated with cutaneous allodynia in migraine? *J Neurol Neurosurg Psychiatry* 2010;81:1256–60.
29. Demarquay G, Royet JP, Giraud P, Chazot G, Valade D, Ryvlin P. Rating of olfactory judgements in migraine patients. *Cephalalgia* 2006;26:1123–30.
30. Wang W, Schoenen J, Timsit-Berthier M. Cognitive functions in migraine without aura between attacks: a psychophysiological approach using the “oddball” paradigm. *Neurophysiol Clin* 1995;25:3–11.
31. Han M, Hou X, Xu S, Hong Y, Chen J, Ma Y, et al. Selective attention network impairment during the interictal period of migraine without aura. *J Clin Neurosci* 2019;60:73–8.
32. Salem H, Vivas D, Cao F, Kazimi IF, Teixeira AL, Zeni CP. ADHD is associated with migraine: a systematic review and meta-analysis. *Eur Child Adolesc Psychiatry* 2018;27:267–77.
33. Hansen TF, Hoeffding LK, Kogelman L, Haspang TM, Ullum H, Sørensen E, et al. Comorbidity of migraine with ADHD in adults. *BMC Neurol* 2018;18:147.
34. Kutuk MO, Tufan AE, Guler G, Yalin OO, Altintas E, Bag HG, et al. Migraine and associated comorbidities are three times more frequent in children with ADHD and their mothers. *Brain Dev* 2018;40:857–64.
35. Kooij JJS, Bijlenga D. High prevalence of self-reported photophobia in adult ADHD. *Front Neurol* 2014;5:256.
36. Bijlenga D, Tjon-Ka-Jie JYM, Schuijers F, Kooij JJS. Atypical sensory profiles as core features of adult ADHD, irrespective of autistic symptoms. *Eur Psychiatry* 2017;43:51–7.
37. Panagiotidi M, Overton PG, Stafford T. The relationship between ADHD traits and sensory sensitivity in the general population. *Compr Psychiatry* 2018;80:179–85.
38. Villa TR, Correa Moutran AR, Sobirai Diaz LA, Pereira Pinto MM, Carvalho FA, Gabbai AA, et al. Visual attention in children with migraine: a controlled comparative study. *Cephalalgia* 2009;29:631–4.
39. Ashina S, Bendtsen L, Buse DC, Lyngberg AC, Lipton RB, Jensen R. Neuroticism, depression and pain perception in migraine and tension-type headache. *Acta Neurol Scand*

2017;136:470–6.

40. Vingen JV, Pareja JA, Støren O, White LR, Stovner LJ. Phonophobia in migraine. *Cephalalgia* 1998;18:243–9.

41. Chong CD, Starling AJ, Schwedt TJ. Interictal photosensitivity associates with altered brain structure in patients with episodic migraine. *Cephalalgia* 2016;36:526–33.

## Annexes

### QUESTIONNAIRES

The French version was used in the present study. The English translation is provided between brackets for the readership of this article. The scale is the same across the questionnaires: “rarely”, “sometimes”, “often” or “very often”.

#### Echelle d’attention

[Attention scale]

1. Au cours de mes activités (lecture, télévision, conversation,...), je perds le fil parce que je suis distrait(e) par les bruits extérieurs et/ou le va-et-vient autour de moi.

[During/throughout my activities (reading, television, conversation,...), I lose the thread because I am distracted by external noises and/or coming and going around me.]

Très rarement  
Parfois  
Souvent  
Très souvent

☐ ☐ ☐ ☐

2. Au cours de mes activités (lecture, télévision, conversation,...), je perds le fil parce que mon esprit vagabonde et que je ne peux pas m’empêcher de penser à autre chose.

[During/throughout my activities (reading, television, conversation,...), I lose the thread because my mind wanders and I cannot keep from thinking to something else.]

☐ ☐ ☐ ☐

3. Quand je mène une activité simple, répétitive et monotone de longue durée, je commets beaucoup d’erreurs.

[When I am carrying on a simple, repetitive, monotonous activity on a long time, I commit a lot of mistakes.]

☐ ☐ ☐ ☐

4. Quand je mène une activité et que je suis interrompu(e) par quelque chose d’imprévu, j’oublie d’y revenir pour la terminer.

[When I am carrying on an activity and I am interrupted by something unexpected, I forget to come back and finish it.]

☐ ☐ ☐ ☐

5. Quand je mène une activité qui comporte plusieurs étapes (comme faire du café), j’en omets une.

[When I am carrying on an activity that include several steps (like making coffee), I omit one.]

☐ ☐ ☐ ☐

6. Je me fatigue lors d'un effort soutenu d'attention.  
[I get tired when making a sustained attention effort.] ☐ ☐ ☐ ☐
7. A l'école j'avais tendance à rêvasser plutôt qu'à suivre les cours  
[At school, I had the tendency to daydream rather than attend the courses.] ☐ ☐ ☐ ☐
8. Je ne prête pas attention aux détails.  
[I don't pay attention to details.] ☐ ☐ ☐ ☐
9. Quand je mène une activité, je commets des erreurs si on me parle en même temps.  
[When I am carrying on an activity, I make mistakes if one talks to me at the same time.] ☐ ☐ ☐ ☐

### Questionnaire de gêne au bruit

[Phonophobia questionnaire]

Si vous présentez des migraines, répondez aux questions suivantes en vous basant sur votre vécu en dehors des crises :  
[If you have migraines, answer the following questions based on your experience between attacks:]

- |   | Très rarement         | Parfois               | Souvent               | Très souvent          |
|---|-----------------------|-----------------------|-----------------------|-----------------------|
| 1. Vous arrive-t-il d'utiliser des bouchons (boules Quiès) pour limiter votre perception du bruit ?<br>[Do you ever use earplugs to reduce your noise perception?]  | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| 2. Avez-vous des difficultés à ne plus faire attention aux sons qui vous entourent dans les situations de la vie quotidienne ?<br>[Do you find it hard to not pay attention anymore to sounds around you in everyday situations?] | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| 3. Etes-vous gêné(e) pour vous concentrer dans un environnement bruyant ?<br>[Do you have trouble concentrating in noisy surroundings?]   | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| 4. Si l'on vous propose une activité (sortie, cinéma, concert), pensez-vous tout de suite au bruit que vous aurez à supporter ?   | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |



*[When someone suggests doing something (going out, to the cinema, to a concert), do you immediately think about the noise you are going to have to put up with?]*

5. Est-ce que le bruit vous fatigue ?

*[Does noise make you tired?]*

☐ ☐ ☐ ☐

6. Trouvez-vous certains bruits ou sons agaçants, irritants ?

*[Do you find certain sounds or noises irritating?]*

☐ ☐ ☐ ☐

7. Est-ce que les bruits forts vous dérangent ?

*[Do loud noises bother you?]*

☐ ☐ ☐ ☐

*Ne répondez aux questions suivantes que si vous présentez des migraines :*

*[Answer the following questions only if you have migraines:]*

8. Lorsque vous avez la migraine, vous arrive-t-il d'utiliser des bouchons (boules Quiès) pour limiter votre perception du bruit ?

*[During your headache, do you ever use earplugs to reduce your noise perception?]*

☐ ☐ ☐ ☐

9. Lorsque vous avez la migraine, avez-vous des difficultés à ne plus faire attention aux sons qui vous entourent dans les situations de la vie quotidienne ?

*[During your headache, do you find it hard to not pay attention anymore to sounds around you in everyday situations?]*

☐ ☐ ☐ ☐

10. Lorsque vous avez la migraine, est-ce que les bruits forts vous dérangent ?

*[During your headache, do loud noises bother you?]*

☐ ☐ ☐ ☐

11. Lorsque vous avez la migraine, trouvez-vous certains bruits ou sons agaçants, irritants ?

☐ ☐ ☐ ☐

*[During your headache, do you find certain sounds or noises irritating?]*

12. Votre migraine empire-t-elle quand il y a du bruit ou certains sons ?

*[Is your headache worsened by noise or certain sounds?]*

☐ ☐ ☐ ☐

13. Votre migraine est-elle déclenchée par le bruit ou certains sons ?

*[Is your headache triggered by noise or certain sounds?]*

☐ ☐ ☐ ☐

### Questionnaire de gêne à la lumière

*[Photophobia questionnaire]*

*Si vous présentez des migraines, répondez aux questions suivantes en vous basant sur votre vécu en dehors des crises :*

*[If you use to have migraines, answer the following questions based on your experience between attacks:]*

1. Est-ce que la lumière vous fatigue ?

*[Does light make you tired?]*

Très rarement  
Parfois  
Souvent  
Très souvent

☐ ☐ ☐ ☐

2. Quand la lumière est vive, vous sentez-vous ébloui(e) ou aveuglé(e) ?

*[Do you have a sense of glare or dazzle in your eyes by bright light?]*

☐ ☐ ☐ ☐

3. Etes-vous dérangé(e) par des lumières vacillantes ou éblouissantes, certaines couleurs, ou des rayures très contrastées ?

*[Do flickering lights, glare, specific colours or high contrast striped patterns bother you?]*

☐ ☐ ☐ ☐

4. Vous arrive-t-il d'éteindre des lumières ou de tirer des rideaux pour éviter une trop grande luminosité ?

*[Do you ever turn off the lights or draw a curtain to avoid bright conditions?]*

☐ ☐ ☐ ☐

5. Portez-vous des lunettes de soleil même lorsque les conditions lumineuses sont normales ?

*[Do you wear sunglasses even in normal daylight?]*

☐ ☐ ☐ ☐

6. Avez-vous mal aux yeux lorsque la lumière est vive ?

*[Do bright lights hurt your eyes?]*

☐ ☐ ☐ ☐

*Ne répondez aux questions suivantes que si vous présentez des migraines :*

*[Answer the following questions only if you have migraines:]*

7. Lorsque vous avez la migraine, vous sentez-vous plus ébloui(e) ou aveuglé(e) que d'habitude par les lumières vives ?

*[During your headache, do you feel a greater sense of glare or dazzle in your eyes than usual by bright light?]*

☐ ☐ ☐ ☐

8. Lorsque vous avez la migraine, êtes-vous dérangé(e) par des lumières vacillantes ou éblouissantes, certaines couleurs, ou des rayures très contrastées ?

*[During your headache, do flickering lights, glare, specific colours or high contrast striped patterns bother you?]*

☐ ☐ ☐ ☐

9. Lorsque vous avez la migraine, vous arrive-t-il d'éteindre des lumières ou de tirer des rideaux pour éviter une trop grande luminosité ?

*[During your headache, do you ever turn off the lights or draw a curtain to avoid bright conditions?]*

☐ ☐ ☐ ☐

10. Lorsque vous avez la migraine, portez-vous des lunettes de soleil même lorsque les conditions lumineuses sont normales ?

*[During your headache, do you wear sunglasses even in normal daylight?]*

☐ ☐ ☐ ☐

11. Lorsque vous avez la migraine, avez-vous mal aux yeux lorsque la lumière est vive ?

*[During your headache, do bright lights hurt your eyes?]*

☐ ☐ ☐ ☐

12. Votre migraine empire-t-elle quand la lumière est vive ?

*[Is your headache worsened by bright lights?]*

☐ ☐ ☐ ☐

13. Votre migraine est-elle déclenchée par une lumière vive ?

*[Is your headache triggered by bright lights?]*

☐ ☐ ☐ ☐

### **Questionnaire de gêne aux odeurs**

*[Osmophobia questionnaire]*

*Si vous présentez des migraines, répondez à la question suivante en vous basant sur votre vécu en dehors des crises :*

*[If you use to have migraines, answer the following questions based on your experience between attacks:]*

1. Cherchez-vous à éviter les lieux avec des odeurs fortes ? (odeurs de cuisine, de friture, de parfum, d'essence).

*[Do you seek to avoid places with strong odors? (kitchen, frying, perfume, petrol smells)]*

Très rarement	Parfois	Souvent	Très souvent
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

*Ne répondez aux questions suivantes que si vous présentez des migraines :*

*[Answer the following questions only if you have migraines:]*

2. Pendant votre migraine, les odeurs fortes (odeurs de cuisine, de friture, de parfum, d'essence) vous dérangent-elles ?

<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
-----------------------	-----------------------	-----------------------	-----------------------

3. Votre migraine empire-t-elle en présence d'odeurs fortes ?

*[Is your headache worsened by strong odors?]*

<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
-----------------------	-----------------------	-----------------------	-----------------------

4. Votre migraine est-elle déclenchée par une odeur forte ?

*[Is your headache triggered by strong odors?]*

<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
-----------------------	-----------------------	-----------------------	-----------------------