Neck Pain and Other Location Patterns in Episodic and Chronic Migraine: A Cross-Sectional Study

Marco Antonio Takashi Utiumi
Universidade Federal do Parana Hospital de Clinicas
João Guilherme Bochnia Küster
Universidade Federal do Parana Hospital de Clinicas
Keryn Sporh Godk
Universidade Federal do Parana Hospital de Clinicas
Nikolai José Eustátios Kotsifas
Universidade Federal do Parana Hospital de Clinicas
Pedro André Kowacs
Universidade Federal do Parana Hospital de Clinicas
Elcio Juliato Piovesan (piovesan1@hotmail.com)
Universidade Federal do Paraná: Universidade Federal do Parana https://orcid.org/0000-0002-0915-0430

Research article

Keywords: Migraine, Pain location, Pain extent, Neck pain, Allodynia, Medication overuse

Posted Date: October 15th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-90824/v1

Abstract

Background: The pain location of migraine has limited diagnostic value and has usually been assessed using non-standard verbal descriptors.

Methods: This study uses non-verbal descriptors of pain location in episodic and chronic migraineurs seen at 3 centers of different complexities (tertiary-level hospital and outpatient clinics) and from different sectors (public and private). The explicit pain location was recorded by asking patients to indicate in an electronic form 3 points on the anterolateral side and 3 points on the posterolateral side of the head and neck. A multivariate logistic regression model was fitted to assess the association of different pain location patterns with demographic and clinical variables.

Results: Ninety-seven episodic migraine and 113 chronic migraine patients were included, with the most commonly affected sites being the frontal (73% and 65%, respectively), temporal (67% and 73%, respectively) and parietal (27% and 34%, respectively) regions. The posterior cervical site was most often involved in the chronic migraine group (21% vs. 33%, p=0.034). No other locations showed a significant difference. The adjusted model showed that diffuse pain (OR=13.74, CI=4.89-49.85) and the presence of medication overuse associated with tactile allodynia (OR=2.65, CI=1.05-6.87) were associated with increased odds of neck pain. Disease duration was marginally relevant (p=0.078).

Conclusions: The migraine attacks most commonly involve the fronto-temporal regions, although neck pain can be more often found in chronic migraine. Some features commonly found in this group such as more diffuse pain, tactile allodynia, and medication overuse are associated with this extratrigeminal site of pain.

Background

Unilateral throbbing headache is one of the core diagnostic criteria for migraine, as defined by the International Classification of Headache Disorders 3rd edition (ICHD-3) (1). Comments about migraine clinical expression in the ICHD-3 recognize the frontotemporal region as the usual migraine pain site; however, other spatial information has no formal diagnostic value.

In 1978, Olesen described 750 migraine attacks in 750 patients (2). The most common locations were right hemicrania (n = 168), whole head (n = 147), left hemicrania (n = 134), and bifrontal (n = 98). Among those with unilateral pain (56%), there were more patients with right-sided headaches ($p < 0.01$).

In the largest study (n = 1283) dedicated to the migraine pain location topic, Kelman found that the orbital, frontal, and temporal sites were the most prevalent regions affected by migraine (3). Interestingly, this study highlighted the diagnostic value of pain topography by demonstrating that episodic migraine (EM) affects the eyes more frequently than chronic migraine (CM) which, in turn, is characterized by neck, occipital, and more diffuse pain.

In 2008, Chakravarty et al. compared the pain location of episodic migraine between a pediatric and an adult sample (4). The adult group showed bilateral/holocranial (26.62%), temporal/bitemporal (20%), hemicranial (19.75%), ocular/binocular (13.25%), and occipitocervical (9.38%) as the most frequent locations of established headaches. Each patient's headache was classified in a mutually exclusive way to record pain location in the majority of migraine attacks within the last six months.

These studies used verbal descriptors to categorize migraineurs' pain location. However, terms like “diffuse”, “holocranial,” and even “hemicranial” describe composite sites that might hinder future comparisons.

Fernándes-de-las-Peñas et al. demonstrated the use of drawings to explore pain extent in migraineurs (5). More recently, Uthaikhup et al. used the drawings of 114 participants to compare pain location in EM, CM, and cervicogenic headache (6). They found that the frontal and temporal regions were the most commonly affected sites in migraineurs, with a trend towards more posterior pain in the CM group.

In this study, we evaluated episodic and chronic migraine patients to determine the distribution pattern of trigeminal and extratrigeminal pain by correlating this pattern with different clinical aspects of migraine.

Methods

Study objective and design

This analytical cross-sectional study aims to use non-verbal descriptors of migraine pain location to explore potential differences between the EM and CM groups. If differences are found, we will explore the factors associated with them.

Study headache centers

Three centers participated in this research. A tertiary-level healthcare center that exclusively serves the public health system (Headache Unit, Federal University of Paraná General Hospital) and two headache outpatient clinics that exclusively serves health insurance companies and private patients. The public unit and one of the private clinics (Marcelino Champagnat Hospital) are located in Curitiba, the capital city of the State of Parana, Brazil. The other private clinic is in the metropolitan region of Curitiba (São José Headache Clinic).

Participant characteristics

All subjects were invited to participate in the study if: (1) They had a definitive diagnosis of EM or CM (either associated with analgesic abuse or not) according to the ICHD-3 (1); (2) had been suffering from migraine symptoms for at least six months before the visit; (3) had no limitations to provide information (e.g., severe aphasia, severe hearing loss with limitations in understanding written questions, etc.); (4) had no associated condition that could make migraine diagnosis uncertain (e.g., HIV infection, active cancer, use of immunosuppressive drugs); (5) were 18 years or older; (6) had complete medical records; and (7) agreed to participate in the study. All subjects underwent a diagnostic interview with one of the authors (MATU or EJP) experienced in the management of headache cases to make decisions on the inclusion in the study.

We excluded subjects who: (1) withdrew the consent form and (2) developed a new headache in the interval between the invitation and the study interview.

Data collection tools and methods

Interviews were performed by using a semi-structured questionnaire and took place between August 2018 and January 2020.

The body mass index (BMI) was calculated using the self-reported weight and height.

Cardiovascular risk factors were recorded as a binary variable that indicated the presence of at least one of the following: Hypertension, diabetes, dyslipidemia, cardiovascular or cerebrovascular disease.

The regular amount of cigarette and illicit drug consumption were recorded as three-level categorical variables: Never, Past, and Current. The presence of alcohol consumption on a weekly basis was recorded in a binary variable (i.e., Present or Absent).

The adequacy of aerobic physical activity followed the World Health Organization recommendations: ≥150 min (moderate intensity) or ≥ 75 min (vigorous intensity) per week (7).

The monthly household income per resident was calculated to evaluate possible effects of the socioeconomic class. The monthly income of all working residents was added up and divided by the total number of residents (either active workers or not).

Migraine years were considered as the period between the onset of typical migraine symptoms and the interview date. As aforementioned, only those whose migraine was present for at least six months were included.

Pain description as pulsatile and/or pressing was recorded as four-level variables: Never, Occasionally, Most Times, and Always.

Pain intensity was classified as Mild (no limitation), Moderate, or Severe (disabling) pain.

Associated symptoms during migraine attacks were recorded as a binary variable and included nausea, vomiting, photophobia, phonophobia, and movement and tactile allodynia. Movement allodynia was considered to exist if the C4 criterion (1) for migraine without aura was present. Tactile allodynia was considered to be present if touch-evoked pain was common in the head/neck regions.

Headache frequency (days/month) was based on the average of the last six months. Because some headache diaries recorded this variable in intervals, we classified each case as: (1) 0–9 headache days/month; (2) 10–14 headache days/month; and (3) 15 days or more headaches/month.

The presence of medication overuse and prodromic nuchal rigidity (within the 72 hours prior to the headache) were recorded as binary variables.

The use of preventive pharmacological treatment for migraine was classified into Never, Past or Current.

The headache impact was assessed using the Migraine Disability Assessment (MIDAS) (8, 9). Symptoms of depression and anxiety were quantified using the Patient Health Questionnaire-9 (PHQ-9) and the Generalized Anxiety Disorder-7 (GAD-7) scales, respectively (10, 11). Sleepiness symptoms were analyzed using the Epworth scale (12, 13). All patients were assessed for suicide risk using the Columbia-Suicide Severity Rating Scale (C-SSRS) tool (14).

Pain location data

Each subject was asked if the attacks were: (1) predominantly on the right side; (2) predominantly on the left side; (3) predominantly unilateral, but with eventual side shifts during attacks; or (4) predominantly bilateral.

Then, patients were instructed to select the locations that represented the most prevalent areas involved in the usual attacks with mouse clicks on an electronic form. We limited the number of points each subject could indicate in each image (anterolateral and posterolateral views of a two-dimensional head model) to three. Each point's coordinates and the region involved were recorded. The software classified each point according to the head/neck region. We distinguished and mapped 20 different regions as shown in Fig. 1.

The three-dimensional head model was created using the free software MakeHuman 1.1.1 (15). Our goal was to create a female model with clear surface anatomical reference points to facilitate pain location by patients.

Statistical analysis

All statistical analysis were conducted using R version 4.0.2 (16). The Shapiro-Wilk test and quantile-quantile plots were used to check for normality. Accordingly, the sample data were summarized as mean ± standard deviation, median (interquartile range), and count (percent proportion).

A kernel estimation was used to analyze the density of points in the two-dimensional plane through a color code (green-to-red spectrum, where red represented higher densities).

To analyze variables associated with the CM group in contrast with the EM group, unadjusted models and likelihood ratio tests were used. The same approach was applied to explore the association of each variable with the presence of neck pain (NP).

A multivariate logistic regression model was fitted with the presence of NP as the dependent variable to calculate odds ratios (OR) and profile likelihood ratio intervals. The least absolute shrinkage and selection operator (LASSO) algorithm was used as the variable selection procedure (17). The model selection process used an exhaustive exploration algorithm (18) in such a way that all possible combinations of the main effects and their pairwise interactions were considered. The final model was chosen based on the corrected Akaike information criterion. To assess the model fit, we used residual analysis, the ratio of residual deviance to residual degrees of freedom, the Hosmer and Lemeshow test, the Osius-Rojek test, the Stukel test, and influence analysis (19).

The Fisher's exact test was used to compare differences in the affected regions between the EM and CM groups because some expected counts were small ($n < 5$) for some anatomical sites.

Listwise deletion method was used to handle with missing data.

Results

We invited a total of 254 subjects of whom 212 agreed to participate in the study (83%). After the study interview, we decided to exclude two patients. One of them experienced a new headache that resembled an episodic paroxysmal hemicrania. The other patient experienced NP not associated with the migraine attacks. The specific examination showed an abnormal Spurling test and we excluded her after a positive response to a cervical facet joint blockade. Both patients suffered from CM and the decision to exclude them was based on the potentially confusing effect from other pain syndromes. A total of 97 patients (46%) were diagnosed with EM and 113 (54%) with CM. The former group consisted of 76 cases of migraine without aura (78%) and 21 cases of migraine with aura (22%). For the CM group, 78 patients (69%) overused medications to alleviate their condition. The mean age was 39.45 ± 12.63 years and 189 (90%) were female. The general sample characteristics are shown in Table 1.

Table 1
General characteristics of the sample

Variables	Episodic migraine (n = 97)	Chronic migraine (n = 113)	p value
Age (years)	38.21 ± 12.54	40.54 ± 12.67	0.187
Female	88 (91%)	101 (89%)	0.746
Married	56 (58%)	71 (63%)	0.451
Caucasian	79 (81%)	83 (73%)	0.167
MIDAS score	20 (39)	57 (73)	< 0.001***
Duration (years)	10 (14.75)	13 (18)	0.093
Medication overuse	24 (25%)	78 (69%)	< 0.001***
Adequate aerobic physical activity§	20 (21%)	19 (17%)	0.480
Body mass index	25.32 (6.73)	25.49 (7.43)	0.446
Household income (R$/resident/month)	2500 (2500)	1500 (1500)	0.131

Pain location according to the groups: CM vs. EM

The pain location mapping showed a similar point concentration in the frontotemporal regions in both groups. However, the point density was higher in the posterior cervical region for the CM group (Fig. 2).

Proportionally, the frontal (CM, 65%; EM, 73%), temporal (CM, 73%; EM, 67%), and parietal (CM, 34%; EM, 27%) areas were the most prevalently affected regions (Fig. 3). However, the posterior cervical area (CM, 33%; EM, 21%) was the only region that showed a significant difference between the two groups (OR = 1.87, $p = 0.034$, two-way Fisher's test), which corroborates the previous visual analysis. The suboccipital region (CM, 22%; EM, 15%) is adjacent to the posterior cervical area and presented the second major difference, although it was not significant at an alpha level of 0.05 ($p = 0.147$).

Factors associated with neck pain probability in migraineurs

To explore the factors associated with migraineurs' pain in the posterior neck region, we decided to consider the presence of pain in the posterior cervical region as "neck pain" (NP).

In our sample, a total of 57 patients reported pain in the neck (37%). An unadjusted analysis of some candidate variables potentially associated with the presence of NP is summarized in Table 2.

Table 2
Unadjusted analysis: variables associated with the probability of neck pain

Variables	No neck pain (n = 153)	Neck pain (n = 57)	p value
Diagnosis: chronic migraine[$]	76 (50%)	37 (65%)	0.047*
Age (years)	38.6 ± 12.67	41.79 ± 12.35	0.111
Female	138 (90%)	51 (89%)	0.877
Generalized Anxiety Disorder-7 score	9 (8)	10 (9)	0.191
Patient Health Questionnaire-9 score	8 (8)	10 (8)	0.230
Body mass index	24.79 (7.03)	26.95 (7.3)	0.261
MIDAS score	30 (61)	40 (74)	0.104
MIDAS class: 1	25 (16%)	8 (14%)	0.767
MIDAS class: 2	14 (9%)	5 (9%)	-
MIDAS class: 3	23 (15%)	6 (11%)	-
MIDAS class: 4	91 (59%)	38 (67%)	-
Cardiovascular risk: present	57 (37%)	30 (53%)	0.045*
Smoking: never	121 (79%)	40 (70%)	0.347
Smoking: past	25 (16%)	12 (21%)	-
Smoking: current	7 (5%)	5 (9%)	-
Weekly alcohol consumption: present	30 (20%)	8 (14%)	0.341
Use of illicit drugs: never	145 (95%)	55 (96%)	0.134
Use of illicit drugs: past	8 (5%)	1 (2%)	-
Use of illicit drugs: current	0 (0%)	1 (2%)	-
Adequate aerobic physical activity[§]	29 (19%)	10 (18%)	0.814
Married	90 (59%)	37 (65%)	0.420
Caucasian	119 (78%)	43 (75%)	0.721
Household income (R$/resident/month)	1750 (1987.5)	1812.5 (2280)	0.744
Duration (years)	10 (16)	15 (22)	0.005**
Side: most attacks in one side	43 (28%)	20 (35%)	0.338
Side: most unilateral attacks but the side varies	50 (33%)	13 (23%)	-
Side: most attacks are bilateral	60 (39%)	24 (42%)	-
Anatomical regions with pain: 1	22 (14%)	0 (0%)	< 0.001***
Anatomical regions with pain: 2	58 (38%)	4 (7%)	-
Anatomical regions with pain: 3	41 (27%)	19 (33%)	-
Anatomical regions with pain: 4	21 (14%)	21 (37%)	-
Anatomical regions with pain: 5	5 (3%)	10 (18%)	-
Anatomical regions with pain: 6	2 (1%)	3 (5%)	-
Pulsatile pain: never	8 (5%)	6 (11%)	0.196
Pulsatile pain: occasionally	32 (21%)	6 (11%)	-
Pulsatile pain: most	61 (40%)	26 (46%)	-
Pulsatile pain: always	52 (34%)	19 (33%)	-

Variables	No neck pain (n = 153)	Neck pain (n = 57)	p value
Pressing pain: never	26 (17%)	6 (11%)	0.607
Pressing pain: occasionally	37 (24%)	13 (23%)	-
Pressing pain: most	51 (33%)	23 (40%)	-
Pressing pain: always	39 (25%)	15 (26%)	-
Usual pain intensity: mild	6 (4%)	0 (0%)	0.033*
Usual pain intensity: moderate	71 (46%)	20 (35%)	-
Usual pain intensity: severe	76 (50%)	37 (65%)	-
Movement allodynia during attacks	111 (73%)	49 (86%)	0.035*
Nausea during attacks	118 (77%)	46 (81%)	0.574
Vomiting during attacks	64 (42%)	28 (49%)	0.345
Photophobia during attacks	129 (84%)	52 (91%)	0.179
Phonophobia during attacks	128 (84%)	47 (82%)	0.836
Tactile allodynia during attacks	88 (58%)	46 (81%)	0.001**
Prodromic nuchal rigidity	25 (16%)	18 (32%)	0.018*
< 10 headache days/month	57 (37%)	11 (19%)	0.029*
10–14 headache days/month	31 (20%)	12 (21%)	-
≥ 15 headache days/month	65 (42%)	34 (60%)	-
Preventive treatment: never	67 (44%)	16 (28%)	0.093
Preventive treatment: past	27 (18%)	15 (26%)	-
Preventive treatment: current	59 (39%)	26 (46%)	-
Medication overuse	67 (43%)	35 (57%)	0.023*
C-SSRS class: 0	114 (75%)	34 (60%)	0.309
C-SSRS class: 1	18 (12%)	13 (23%)	-
C-SSRS class: 2	0 (0%)	0 (0%)	-
C-SSRS class: 3	1 (1%)	0 (0%)	-
C-SSRS class: 4	0 (0%)	0 (0%)	-
C-SSRS class: 5	0 (0%)	1 (2%)	-
C-SSRS class: 6	1 (1%)	0 (0%)	-
C-SSRS class: 7	2 (1%)	0 (0%)	-
C-SSRS class: 8	3 (2%)	1 (2%)	-
C-SSRS class: 9	14 (9%)	8 (14%)	-
Epworth sleepiness scale score	6 (7)	6 (7)	0.681

The variable selection process for the multivariate model indicated that the number of pain-affected anatomical regions was the most important covariate to be included. Tactile allodynia, medication overuse, and migraine duration were also selected.

Because the sample size is relatively small, we turned two of these explanatory variables into binary ones in such a way that the events per variable would be suitable for a logistic regression model. We classified subjects' pain as: (1) Slightly diffuse (1–2 anatomical areas affected) or (2) Diffuse (3–6 areas). A median migraine duration of 12 years was used as the cut-off to classify this variable.

The exhaustive algorithm included a pairwise interaction between medication overuse and tactile allodynia in the final model. The anatomical location and the pairwise interaction were considered relevant ($p < 0.001$ and $p = 0.018$, respectively), while migraine duration was marginally relevant (p = 0.078) to the model. The OR and its lower and upper limits considering a 95% confidence interval are shown in Table 3. The estimated odds of NP were 5.86 times as large for migraineurs with tactile allodynia than for those without it when the other variables remained constant and – due to the interaction in the model – the subject overuses analgesics. With a 95% confidence, the odds are between 1.59 and 28.64 times as large. Similar interpretations can be made with the other comparisons. Figure 4 shows the estimated NP probability according to the adjusted model.

Table 3
Odds ratios: point estimate and 95% confidence intervals

Comparison	Estimate	95% CI
Presence vs. absence of tactile allodynia (no overuse)	0.68	0.21–2.29
Presence vs. absence of tactile allodynia (with overuse)	5.86	1.59–28.64
Presence vs. absence of drug overuse (no tactile allodynia)	0.31	0.05–1.41
Presence vs. absence of drug overuse (with tactile allodynia)	2.65	1.05–6.87
≥ 3 vs. ≤2 pain-affected anatomical regions	13.74	4.89–49.85
Migraine duration > 12 years vs. ≤12 years	2.05	0.92–4.63

Discussion

Most commonly affected anatomical areas

This study showed that the broadest anatomic areas of the head are the most commonly affected sites during migraine attacks in both EM and CM groups – i.e., the frontal, temporal, and parietal regions.

The temporal and frontal involvement in migraine pain have already been reported by Kelman as the second (58.3%) and third (55.9%) most prevalently affected regions one-to-two thirds of the time (3). Kelman's paper was the first to focus on migraine pain location in a sizable sample – 1,283 subjects (350 CM cases). However, this report showed the orbital region (67.1%) as the most prevalent area.

In a study of 200 EM subjects conducted in a headache center, the most prevalent areas were the frontal (43.8%) and temporal (42.4%) sites (20) as well. The orbital and occipital sites gain more importance in a population study in Hungary, where the most common sites were temporal (45%), orbital (45%), occipital (40%), frontal (28%), vertex (22%), and generalized (18%) (21). Therefore, it is possible that the study design has a role in these different pain location patterns.

Pain drawings were used to explore differences between EM (n = 48), CM (n = 30) and cervicogenic headache (n = 36) (6). The most commonly affected sites in the EM group were right frontal, right temporal, and left orbital (81.25% for each location). For the CM group, the sites were left frontal and left temporal (83.33%) followed by right frontal and right temporal (80%). These results are quite similar to our findings, probably due to the use of direct recording of pain location. However, we notably found smaller proportions for these areas (frontal – CM, 65% and EM, 73%; temporal – CM, 73% and EM, 67%). The differences in the recording method might have contributed to this discrepancy. The limitation to no more than 3 points per image could have been responsible for some underestimation in our findings in relation to the use of pain drawings. We decided on this limit with the purpose of better characterizing the most important areas that are affected in migraine attacks. Therefore, it is possible that subjects have selected the most affected sites and/or the ones presenting the most severe pain.

Finally, recording pain location during a migraine attack might possibly lead to different results. Olesen studied 750 patients during a migraine attack in order to extract more precise data. The most common pain locations were right hemicrania (n = 168), whole head (n = 147), left hemicrania (n = 134), and bifrontal (n = 98) (2).

Neck pain, migraine and chronification

In our sample, only the posterior cervical region showed a different prevalence between the two groups, with more patients being affected in the CM group (CM 33%, EM 21%).

The intriguing involvement of the neck – a structure outside the area supplied by the trigeminal nerve – in migraine pain has been long recognized (22). When compared to our findings, most studies report a higher NP prevalence in migraine. A study conducted in a headache clinic showed a 70.5% NP prevalence (20). In a population study, NP prevalence was 76.2% for those with pure migraine, 89.3% for those with coexisting tension-type headache (TTH), and 83.3% for those with episodic migraine with or without episodic TTH (23). As discussed earlier, our recording method and the 3-point limitation per image might have been responsible for this discrepancy.

Interestingly, the aforementioned population study (23) showed that the frequency of migraine attacks is correlated with the number of days with NP ($r = 0.33$, $p < 0.001$). The largest study dedicated to the topic reported a higher frequency of NP with migraine chronification (3) as well as a higher frequency of occipital and diffuse pain (3, 24). In a prospective study of a sample selected in a headache clinic and the general community, NP prevalence varied according to headache pain intensity: mild (42.8%), moderate (61.1%), and severe (72.6%) (24). Again, NP prevalence directly correlated with headache frequency ($r = 0.32$). Lastly, the recent use of pain drawings (6) showed a marginal evidence for higher pain extent in the posterior region of the head in the CM group when compared with the EM group ($p = 0.07$). Therefore, the association of frequent migraine attacks and/or CM with the presence of NP has been a recurrent finding in different studies.

Other neck pain-associated factors in migraineurs

In addition to group classification, NP was also associated with the presence of at least one cardiovascular risk factor; longer-term migraine; more diffuse, frequent, and intense attacks; the presence of mechanical and tactile allodynia; and the presence of medication overuse and prodromal nuchal rigidity. The multivariate analysis adjusted for migraine duration, number of affected anatomical regions, tactile allodynia, and medication overuse. An increase in the odds of NP would be expected with the presence of the two latter factors and/or more diffuse pain. The absence of factors considered to be associated with NP using unadjusted analysis in the final model does not mean that they exert no effect on the odds of NP. It simply means that only these four terms were included in the simplest model that was best fitted to our sample. This is particularly important in the case of high correlated covariates during the model selection process.

The presence of more diffuse pain was the most important NP-associated factor. NP could simply represent a preferred location in the pain spreading process seen in those with higher chronification risk. Data from the Chronic Migraine Epidemiology and Outcomes Study (CaMEO) were used to investigate the association of the presence of non-cephalic pain in eight body regions with the EM-to-CM progression and CM persistence over a 3-month period (25). At baseline, the CM group showed 1.09–1.29 more non-cephalic pain locations than the EM group. At 3 months, each additional location exerted some effect on CM odds independently of other covariates (demographics, depression/anxiety, allodynia, BMI, and baseline acute headache treatment).

A latent class analysis of CaMEO data provided interesting results (26). Firstly, the conditional probability of self-reported NP was more common in the latent class characterized by having the most comorbidities (82%) and in the two classes in which pain was a distinguishing feature – respiratory/pain (79%) and pain (76%). This is consistent with our findings of an association of cardiovascular comorbidity with NP (in the unadjusted analysis only). Secondly, these 3 classes had a higher CM prevalence, higher MIDAS scores, and more allodynia and medication overuse. The association of NP and CM has been previously discussed. We did not find an association of headache intensity/severity with NP, probably because our definition of NP was based on patients indicating the sites affected by pain rather than self-report. An association of allodynia in EM with attacks of higher intensity ($p = 0.016$) has been reported (27).

Our final model explicitly showed that the interaction between allodynia and medication overuse was more important than each individual factor. The large Migraine in America Symptoms and Treatment (MAST) study investigated allodynia predictors and included 15,133 subjects (28). The fully adjusted model showed that medication overuse was independently (other variables included sociodemographic characteristics, headache frequency, migraine severity, pain intensity, depression and anxiety) and significantly associated with increased odds of having allodynia (OR 1.23, CI 1.09–1.38).

Although we did not explore the sensitivity to pressure, several studies demonstrated lower pressure-pain thresholds (PPT) in migraineurs when compared with controls including the cervical and distant extra-trigeminal areas (29–31). There is an anterior-to-posterior crescent gradient of PPT in the scalp (29) of migraineurs (and healthy controls) mimicking the sites discussed above as the most frequently affected by migraine pain.

Finally, migraine years showed marginal evidence ($p = 0.078$) of association with NP. The largest migraine pain location study showed that a trend towards pain in the neck and the eyes might exist for longer-term migraine (3). The same author found that 50 year-and-older patients might have attacks without the typical migraine characteristics (photophobia, phonophobia, nausea, vomiting, throbbing pain) (32). The presence of NP was also more common ($p = 0.004$) in the 30–49 (42.5%) and > 50 (41.1%) age groups than in the 16–29 age group (30.7%).

Possible mechanisms of neck pain in migraine

The involvement of extratrigeminal areas – such as the neck – in migraine could be explained by the convergence of trigeminal and cervical inputs (33) and/or may represent the clinical manifestation of the peripheral sensitization mechanisms found in chronic pain conditions (34). Calhoun et al. have explored the role of NP in migraineurs through a series of studies, and they found that: (1) NP is prevalent in migraine; (2) its presence on the day preceding migraine is associated with treatment resistance; and (3) it is a predictor of disability independent of migraine frequency and severity (35). They raised the possibility that NP in migraineurs represents hyperalgesia or allodynia.

A mechanical process may be present. Women with CM have greater neck extensors (splenius capitis and upper trapezius) activity compared to healthy controls, which suggests that motor adaptations may play a role in the chronification process (36).

Migraine pain location has been reported to potentially change to the region of an injury ("migraine remapping"), and the authors state that this could impact the evaluation of facial and neck pain (37).

Migraine and the neck in clinical practice

A neck pain complaint presented by a patient could represent some disorder other than migraine, with a special concern for the cervicogenic headache (CH) in clinical practice. A detailed clinical history and a careful physical examination are generally enough to differentiate between these two types of headache. A side-locked pain and a posterior-to-anterior radiation pattern favor the diagnosis of CH (1). Some provocative maneuvers can be used to assess the neck of patients without pain during evaluation, and the distraction test could be used otherwise (38, 39). However, care must be taken not to base the diagnosis solely on these maneuvers. The eliciting of local pain and referred pain to the head upon upper cervical spine palpation are more common in migraineurs (88.8% and 46.6%) than in healthy controls (49.3% and 15.5%) (40). It seems reasonable to assume that NP in migraineurs is mostly a manifestation of their migraine. Up to 77% of patients who believe they suffer from a "cervical pain syndrome" receive a final diagnosis of migraine after an evaluation in a tertiary headache center (41).

For some migraineurs, it may be harder to understand that their pain is due to migraine. Less than 8 years of formal education (OR = 1.72-20; $p = 0.004$), absence of migraine aura (OR = 1.37-20; $p = 0.015$), and pain in the back of the head at attack onset (OR = 14.2–167; $p < 0.0001$) are predictors of migraine that is self-diagnosed as a different NP syndrome (41). The latter is also associated with the initiation of a late acute treatment ($p < 0.01$) in face of greater pain intensity ($p < 0.001$) (35). The authors speculate that migraineurs may fail to relate NP to their migraine attack, which potentially leads to suboptimal treatments. This could, in turn, increase the chances of chronification. NP has been considered as an important predictor of disability (42), and higher Neck Disability Index scores may be found in CM than EM ($p < 0.001$), indicating a role of NP in the overall burden of chronification (43).

Other studies focused on the prevalence of cervical musculoskeletal dysfunction in the migraine group (44). This is a debated topic with divergent results from different studies (45), and it is beyond the scope of this text.

Strengths and limitations

To the best of our knowledge, this is the largest study that used an explicit non-verbal recording method to locate migraine pain. The diagnosis and evaluation by a headache specialist further support our findings, as well as balanced groups of individuals with EM and CM.

Some limitations must be considered, namely: (1) The cross-sectional design allows us to establish associations of some explanatory variables with NP not as a causal relationship; (2) we did not stipulate a migraine-free period before the interview, and memory bias may have interfered with our results; (3) we did not use a standardized instrument to measure allodynia; (4) as discussed earlier, the 6-point limitation may cause an underestimation of the sites affected by migraine pain; (5) our results are mainly based on patient reports and medical records. Future studies should consider a prospective record of pain location. Also, recording whether the neck and other subregions respond differently to established migraine treatments would be interesting.

Conclusions

While migraine attacks most commonly involve the frontotemporal regions, NP is more common in chronic migraineurs, with some commonly observed features such as more diffuse pain, tactile allodynia, medication overuse and long-term disease being associated with increased odds of NP.

Abbreviations

CM, chronic migraine; C-SSRS, Columbia-Suicide Severity Rating Scale; EM, episodic migraine; GAD-7, Generalized Anxiety Disorder-7; ICHD-3, International Classification of Headache Disorders 3rd edition; MIDAS, Migraine Disability Assessment; NP, neck pain; PHQ-9, Patient Health Questionnaire-9

Declarations

Ethics approval and consent to participate

This study was originally designed to explore the role of certain genetic polymorphisms in the clinical expression of migraine in the Southern region of Brazil. The present study is a clinical data analysis regarding the pain location pattern in our sample.

The study was approved by the ethics committee of the Federal University of Paraná General Hospital (registration: 2.732.610) and registered in the Brazilian Registry of Clinical Trials (RBR-9wgwnj).

Consent for publication

Not applicable.

Availability of data and materials

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests in this work.

Funding

This work was sponsored by Allergan [grant number PG-2020-10985]. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Authors' contributions

MATU, JGBK, KSG and NJEK carried out the interviews. MATU and EJP evaluated and confirmed the clinical diagnosis of all subjects. MATU derived the models and analyzed the data. MATU, PAK and EJP wrote the manuscript. EJP was involved in work planning and supervision. All authors reviewed and approved the final manuscript.

Acknowledgements

Not applicable.

Prior publication

This research was first presented in a poster format at the XXXIII Brazilian Headache Congress (46).

References

1. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. Cephalalgia. 2018 Jan;38(1):1–211
2. Olesen J (1978 Nov) Some clinical features of the acute migraine attack. An analysis of 750 patients. Headache 18(5):268–271
3. Kelman L (2005 Sep) Migraine pain location: a tertiary care study of 1283 migraineurs. Headache 45(8):1038–1047
4. Chakravarty A, Mukherjee A, Roy D. Migraine pain location: how do children differ from adults? J Headache Pain. 2008 Dec;9(6):375–9
5. Fernández-de-Las-Peñas C, Falla D, Palacios-Ceña M, Fuensalida-Novo S, Arias-Buría JL, Schneebeli A et al (2018 Mar) Perceived Pain Extent is Not Associated With Widespread Pressure Pain Sensitivity, Clinical Features, Related Disability, Anxiety, or Depression in Women With Episodic Migraine. Clin J Pain 34(3):217–221
6. Uthaikhup S, Barbero M, Falla D, Sremakaew M, Tanrprawate S, Nudsasarn A. Profiling the Extent and Location of Pain in Migraine and Cervicogenic Headache: A Cross-sectional Single-Site Observational Study. Pain Med. 2020 Sep
7. World Health Organization. Global recommendations on physical activity for health [Internet]. 1st ed. WHO Press (2010) 60 p. Available from: https://apps.who.int/iris/bitstream/handle/10665/44399/9789241599979_eng.pdf;jsessionid=AED3EB47F7B8B392D984B002CF84BF10?sequence=1
8. Stewart WF, Lipton RB, Dowson AJ, Sawyer J (2001) Development and testing of the Migraine Disability Assessment (MIDAS) Questionnaire to assess headache-related disability. Neurology 56(6 Suppl 1):S20–S28
9. Fragoso YD (2002 Jul) MIDAS (Migraine Disability Assessment): a valuable tool for work-site identification of migraine in workers in Brazil. Sao Paulo Med J 120(4):118–121

10. Spitzer RL, Kroenke K, Williams JBW, Löwe B (2006 May) A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med 166(10):1092–1097
11. Kroenke K, Spitzer RL, Williams JB (2001 Sep) The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med 16(9):606–613
12. Johns MW (1991 Dec) A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep 14(6):540–545
13. Bertolazi AN, Fagondes SC, Hoff LS, Pedro VD, Menna Barreto SS, Johns MW (2009 Sep) Portuguese-language version of the Epworth sleepiness scale: validation for use in Brazil. J Bras Pneumol publicacao Of da Soc Bras Pneumol e Tisilogia 35(9):877–883
14. Posner K, Brown GK, Stanley B, Brent DA, Yershova KV, Oquendo MA et al (2011 Dec) The Columbia-Suicide Severity Rating Scale: initial validity and internal consistency findings from three multisite studies with adolescents and adults. Am J Psychiatry 168(12):1266–1277
15. Briceno L, Paul G. MakeHuman: A Review of the Modelling Framework. In: Bagnara S, Tartaglia R, Albolino S, Alexander T, Fujita Y, editors. Proceedings of the 20th Congress of the International Ergonomics Association (IEA 2018). Cham: Springer International Publishing (2019) p. 224–32
16. R Core Team. R: A Language and Environment for Statistical Computing [Internet]. Vienna, Austria: R Foundation for Statistical Computing (2020) Available from: https://www.r-project.org/
17. Tibshirani R (1996) Regression Shrinkage and Selection via the Lasso. J R Stat Soc Ser B [Internet]. Aug 25;58(1):267–88. Available from: http://www.jstor.org/stable/2346178
18. Calcagno V: Model Selection and Multimodel Inference Made Easy [Internet] (2020) Available from: https://cran.r-project.org/package=glmulti
19. Hosmer DW, Hosmer T, Le Cessie S, Lemeshow S (1997 May) A comparison of goodness-of-fit tests for the logistic regression model. Stat Med 16(9):965–980
20. de Queiroz LP, Rapoport AM, Sheftell FD (1998 Mar) [Clinical characteristics of migraine without aura]. Arq Neuropsiquiatr 56(1):78–82
21. Bánk J, Márton S (2000 Feb) Hungarian migraine epidemiology. Headache 40(2):164–169
22. Blau JN, MacGregor EA (1994 Feb;34(2):88–90) Migraine and the Neck. Headache [Internet]. Available from: http://doi.wiley.com/10.1111/j.1526-4610.1994.hed3402088.x
23. Ashina S, Bendtsen L, Lyngberg AC, Lipton RB, Hajiyeva N, Jensen R (2015) Prevalence of neck pain in migraine and tension-type headache: A population study. Cephalalgia [Internet]. Mar 22;35(3):211–9. Available from: http://journals.sagepub.com/doi/10.1177/0333102414535110
24. Calhoun AH, Ford S, Millen C, Finkel AG, Truong Y, Nie Y (2010 Sep;50(8):1273–7) The Prevalence of Neck Pain in Migraine. Headache [Internet]. Available from: http://doi.wiley.com/10.1111/j.1526-4610.2009.01608.x
25. Scher AI, Buse DC, Fanning KM, Kelly AM, Franznick DA, Adams AM et al (2017) Comorbid pain and migraine chronicity. Neurology [Internet]. Aug 1;89(5):461–8. Available from: http://www.neurology.org/lookup/doi/10.1212/WNL.0000000000004177
26. Lipton RB, Fanning KM, Buse DC, Martin VT, Reed ML, Manack Adams A et al (2018 Jul;58(7):933–47) Identifying Natural Subgroups of Migraine Based on Comorbidity and Concomitant Condition Profiles: Results of the Chronic Migraine Epidemiology and Outcomes (CaMEO) Study. Headache [Internet]. Available from: http://doi.wiley.com/10.1111/head.13342
27. Guy N, Marques AR, Orliaguet T, Lanteri-Minet M, Dallel R, Clavelou P. Are there differences between cephalic and extracephalic cutaneous allodynia in migraine patients? Cephalalgia. 2010 Jul;30(7):881–6
28. Dodick DW, Reed ML, Fanning KM, Munjal S, Alam A, Buse DC et al (2019 Jun) Predictors of allodynia in persons with migraine: Results from the Migraine in America Symptoms and Treatment (MAST) study. Cephalalgia 39(7):873–882
29. Barón J, Ruiz M, Palacios-Ceña M, Madeleine P, Guerrero ÁL, Arendt-Nielsen L et al (2017 Feb;57(2):226–35) Differences in Topographical Pressure Pain Sensitivity Maps of the Scalp Between Patients With Migraine and Healthy Controls. Headache [Internet]. Available from: http://doi.wiley.com/10.1111/head.12984
30. Palacios-Ceña M, Lima Florencio L, Natália Ferracini G, Barón J, Guerrero ÁL, Ordás-Bandera C et al (2016 Nov;17(11):2127–33) Women with Chronic and Episodic Migraine Exhibit Similar Widespread Pressure Pain Sensitivity. Pain Med [Internet]. Available from: https://academic.oup.com/painmedicine/article-lookup/doi/10.1093/pm/pnw056
31. Florencio LL, Giantomassi MCM, Carvalho GF, Gonçalves MC, Dach F, Fernández-de-las-Peñas C et al (2015) Generalized Pressure Pain Hypersensitivity in the Cervical Muscles in Women with Migraine. Pain Med [Internet]. Aug 1;16(8):1629–34. Available from: https://academic.oup.com/painmedicine/article-lookup/doi/10.1111/pme.12767
32. Kelman L (2006) Migraine changes with age: IMPACT on migraine classification. Headache 46(7):1161–1171
33. Piovesan EJ, Kowacs PA, Oshinsky ML (2003 Oct) Convergence of cervical and trigeminal sensory afferents. Curr Pain Headache Rep 7(5):377–383
34. Goadsby PJ, Holland PR, Martins-Oliveira M, Hoffmann J, Schankin C, Akerman S (2017 Apr;97(2):553–622) Pathophysiology of Migraine: A Disorder of Sensory Processing. Physiol Rev [Internet]. Available from: https://www.physiology.org/doi/10.1152/physrev.00034.2015

35. Calhoun AH, Ford S, Pruitt AP (2011 Mar) Presence of neck pain may delay migraine treatment. Postgrad Med 123(2):163–168
36. Florencio LL, Oliveira AS, Lemos TW, Carvalho GF, Dach F, Bigal ME et al. Patients with chronic, but not episodic, migraine display altered activity of their neck extensor muscles. J Electromyogr Kinesiol [Internet]. 2016 Oct;30:66–72. Available from: http://dx.doi.org/10.1016/j.jelekin.2016.06.003
37. Hussain A, Stiles MA, Oshinsky ML. Pain remapping in migraine: a novel characteristic following trigeminal nerve injury. Headache. 2010 Apr;50(4):669–71
38. Magee DJ. Cervical spine. In: Magee DJ, editor. Orthopedic Physical Assesment. 6th ed. Elsevier; 2014. p. 148–223
39. Luedtke K, Boissonnault W, Caspersen N, Castien R, Chaibi A, Falla D et al (2016 Jun) International consensus on the most useful physical examination tests used by physiotherapists for patients with headache: A Delphi study. Man Ther 23:17–24
40. Luedtke K, May A. Stratifying migraine patients based on dynamic pain provocation over the upper cervical spine. J Headache Pain. 2017;18(1)
41. Viana M, Sances G, Terrazzino S, Sprenger T, Nappi G, Tassorelli C. When cervical pain is actually migraine: An observational study in 207 patients. Cephalalgia [Internet]. 2018 Feb 7;38(2):383–8. Available from: http://journals.sagepub.com/doi/10.1177/0333102416683917
42. Ford S, Calhoun A, Kahn K, Mann J, Finkel A. Predictors of Disability in Migraineurs Referred to a Tertiary Clinic: Neck Pain, Headache Characteristics, and Coping Behaviors. Headache [Internet]. 2008 Apr;48(4):523–8. Available from: http://doi.wiley.com/10.1111/j.1526-4610.2008.00859.x
43. Florencio LL, Chaves TC, Carvalho GF, Gonçalves MC, Casimiro ECB, Dach F et al (2014) Neck pain disability is related to the frequency of migraine attacks: a cross-sectional study. Headache 54(7):1203–1210
44. Ferracini GN, Florencio LL, Dach F, Grossi DB, Palacios-Ceña M, Ordás-Bandera C et al (2017) Musculoskeletal disorders of the upper cervical spine in women with episodic or chronic migraine. Eur J Phys Rehabil Med 53(3):342–350
45. Robertson BA, Morris ME. The role of cervical dysfunction in migraine: a systematic review. Cephalalgia. 2008 May;28(5):474–83
46. Küster JGB, Utiumi MATU, Gonçalves LB, Godk KS, Souza PS, de A, Boldt ABW, et al (2019) Migranosos crônicos apresentam dor cervical posterior com maior frequência que migranosos episódicos: progressão espacial como parte do processo de cronificação? In: XXXIII Congresso Brasileiro de Cefaleia [Internet]. p. 155–6. Available from: https://headachemedicine.com.br/materias/HM_10_3_Posteres.pdf

Figures

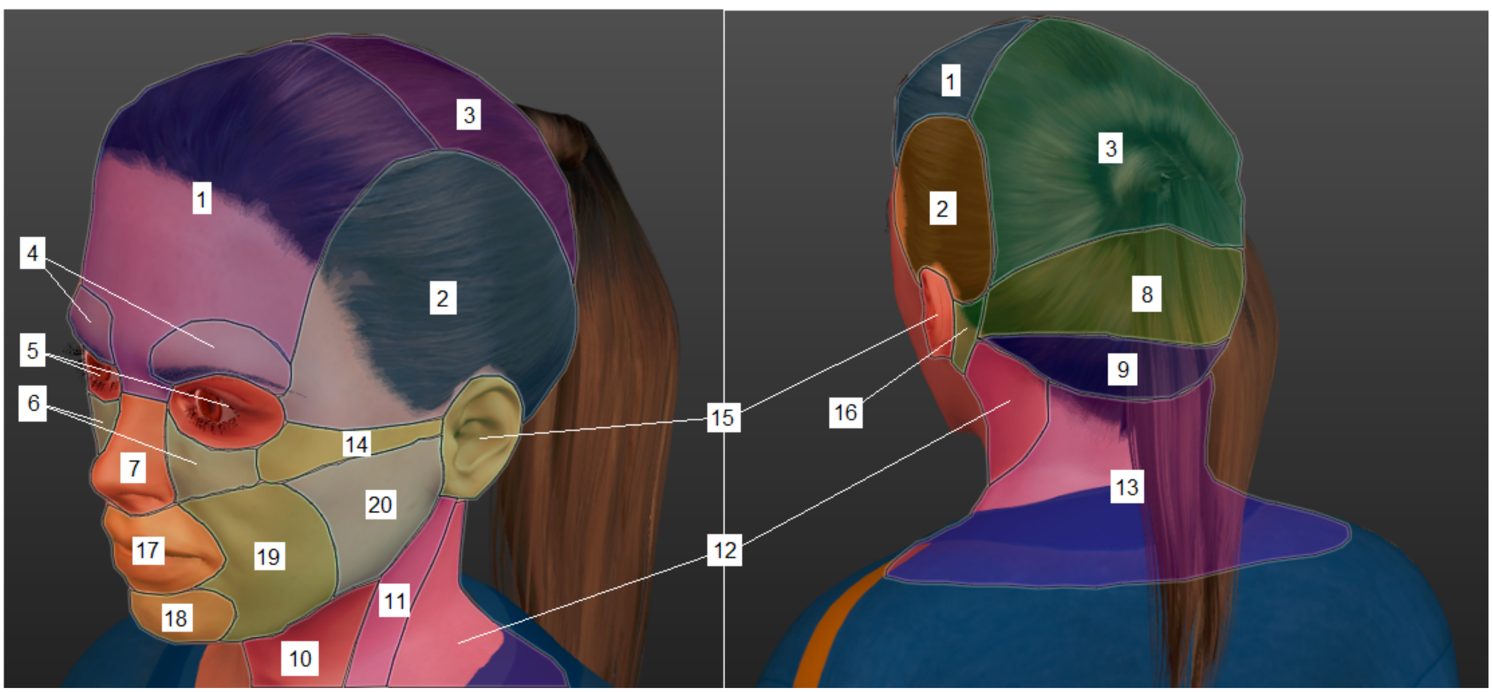

Figure 1

The head and neck model used to explore the location of migraine attacks. Patients were asked to select up to 3 locations in the image depicting the anterolateral view (left) and up to 3 locations in the posterolateral (right) view of the model. The image shows the 20 head regions used to classify each selected point: (1) frontal, (2) temporal, (3) parietal, (4) supraorbital, (5) orbital, (6) infraorbital, (7) nasal, (8) occipital, (9) suboccipital, (10) anterior cervical, (11) sternocleidomastoid, (12) lateral cervical, (13) posterior cervical, (14) zygomatic, (15) auricular, (16) mastoid, (17) oral, (18) mental, (19) buccal, (20) parotid. Note that the images without subdivisions were shown to patients at the time of the location recording.

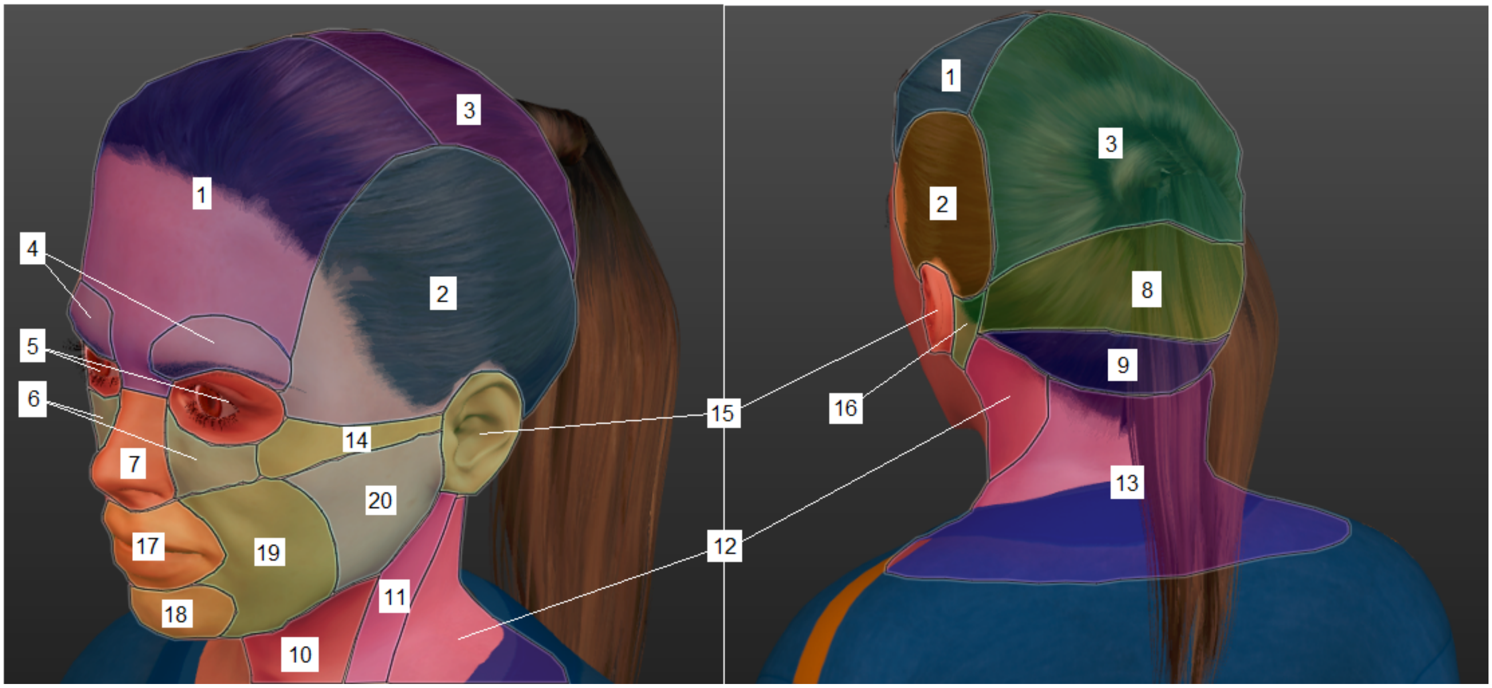

Figure 1

The head and neck model used to explore the location of migraine attacks. Patients were asked to select up to 3 locations in the image depicting the anterolateral view (left) and up to 3 locations in the posterolateral (right) view of the model. The image shows the 20 head regions used to classify each selected point: (1) frontal, (2) temporal, (3) parietal, (4) supraorbital, (5) orbital, (6) infraorbital, (7) nasal, (8) occipital, (9) suboccipital, (10) anterior cervical, (11) sternocleidomastoid, (12) lateral cervical, (13) posterior cervical, (14) zygomatic, (15) auricular, (16) mastoid, (17) oral, (18) mental, (19) buccal, (20) parotid. Note that the images without subdivisions were shown to patients at the time of the location recording.

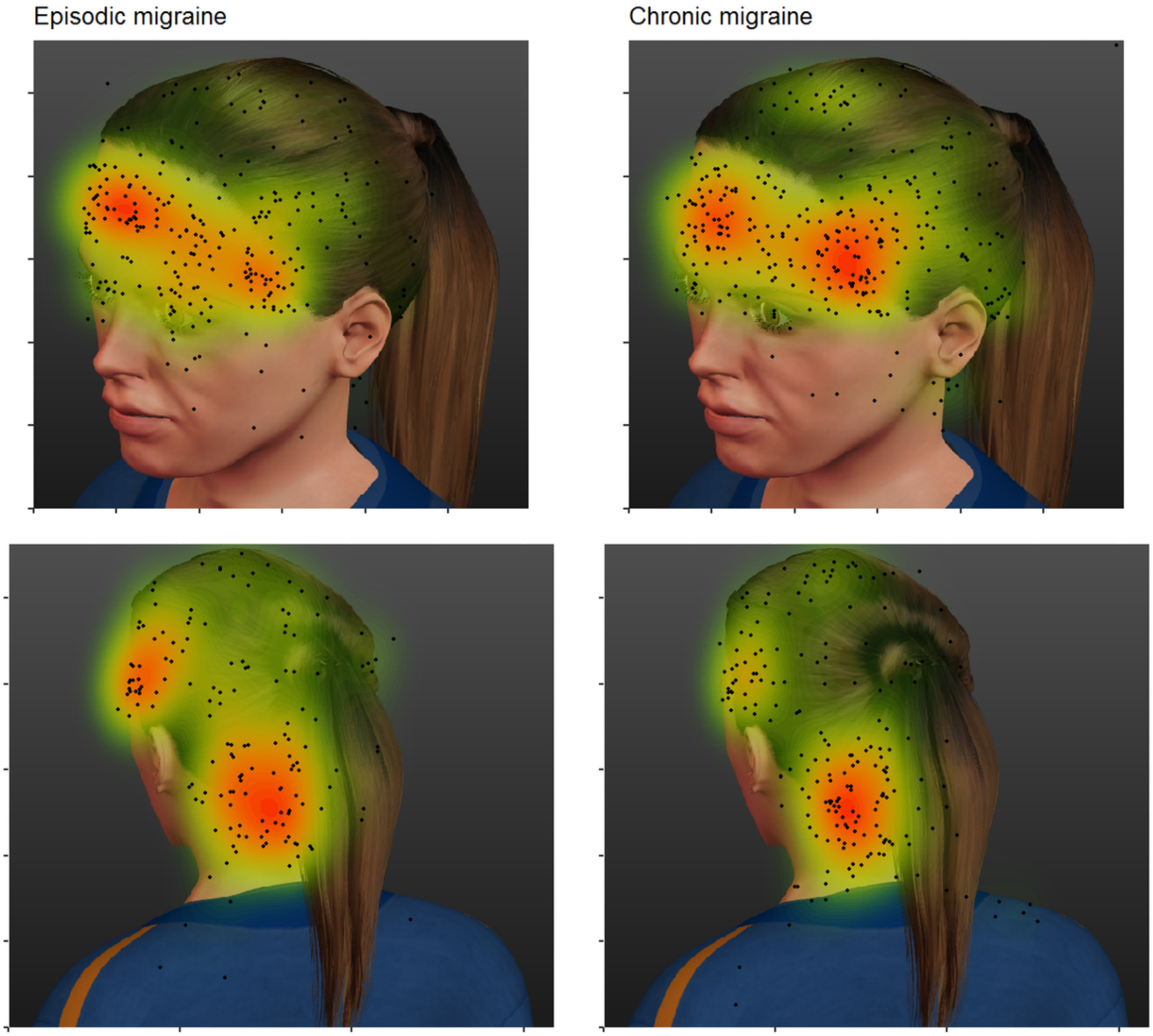

Figure 2

Pain location in episodic and chronic migraine. Each dark point represents a pain location selected by a patient. This heat map scale employs a Kernel density estimate that translates the proportion of points in an area into a color scale. Therefore, the scales are not the same for all images. However, all color scales vary from green to red, with the latter indicating a higher point density. Top left: episodic migraine anterolateral view; lower left: episodic migraine posterolateral view; top right: chronic migraine anterolateral view; lower right: chronic migraine posterolateral view.

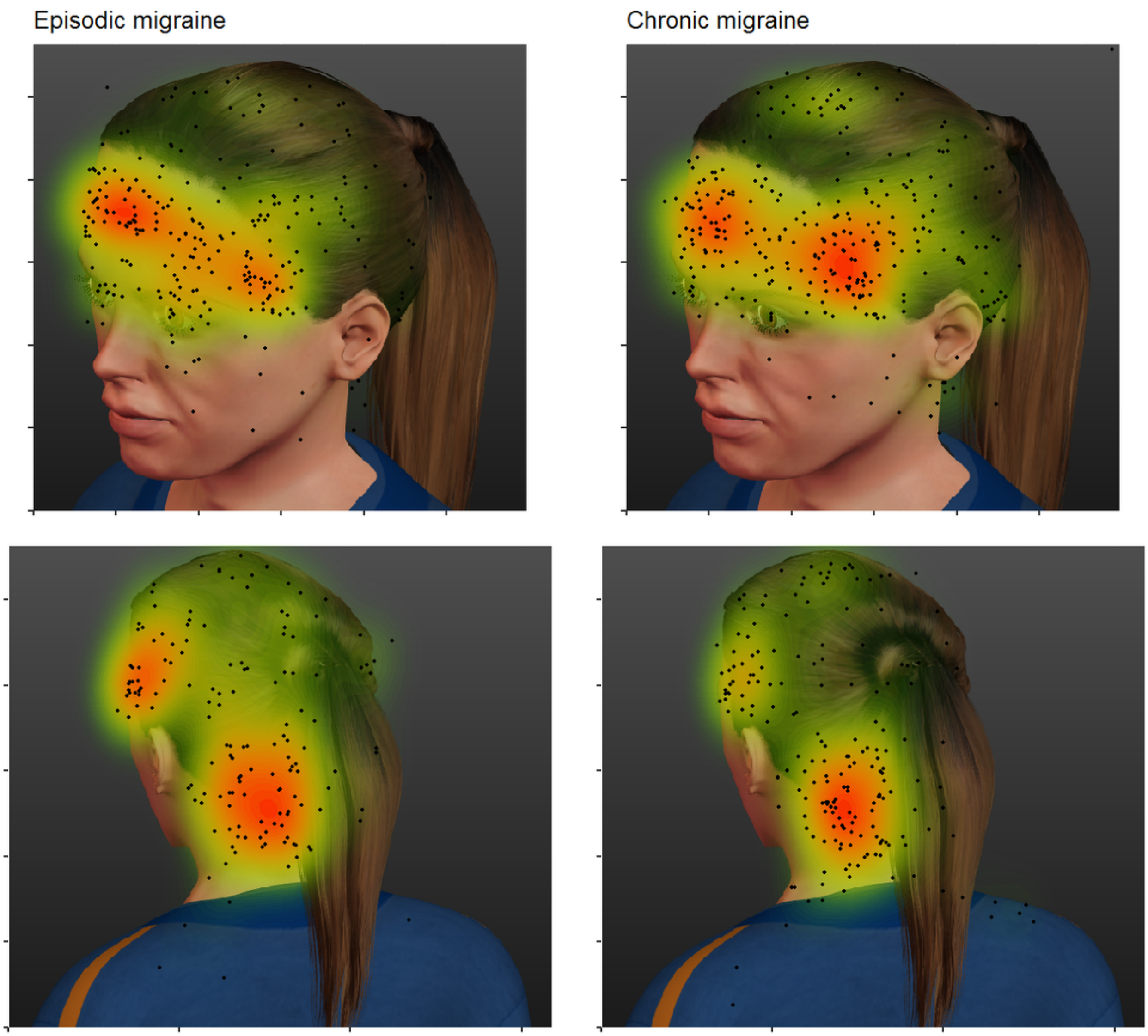

Figure 2

Pain location in episodic and chronic migraine. Each dark point represents a pain location selected by a patient. This heat map scale employs a Kernel density estimate that translates the proportion of points in an area into a color scale. Therefore, the scales are not the same for all images. However, all color scales vary from green to red, with the latter indicating a higher point density. Top left: episodic migraine anterolateral view; lower left: episodic migraine posterolateral view; top right: chronic migraine anterolateral view; lower right: chronic migraine posterolateral view.

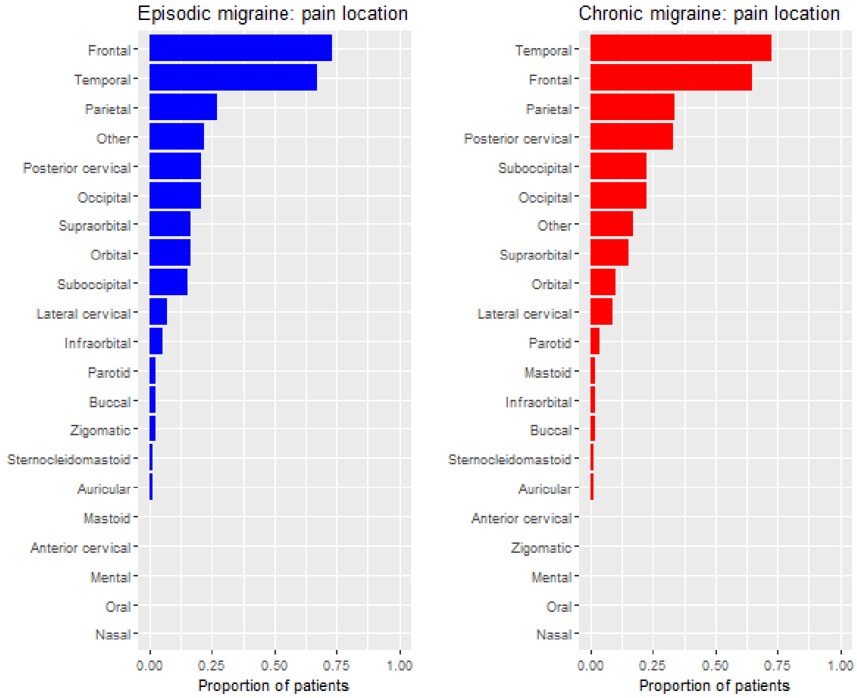

Figure 3

Distribution of migraine pain by head and neck subregions.

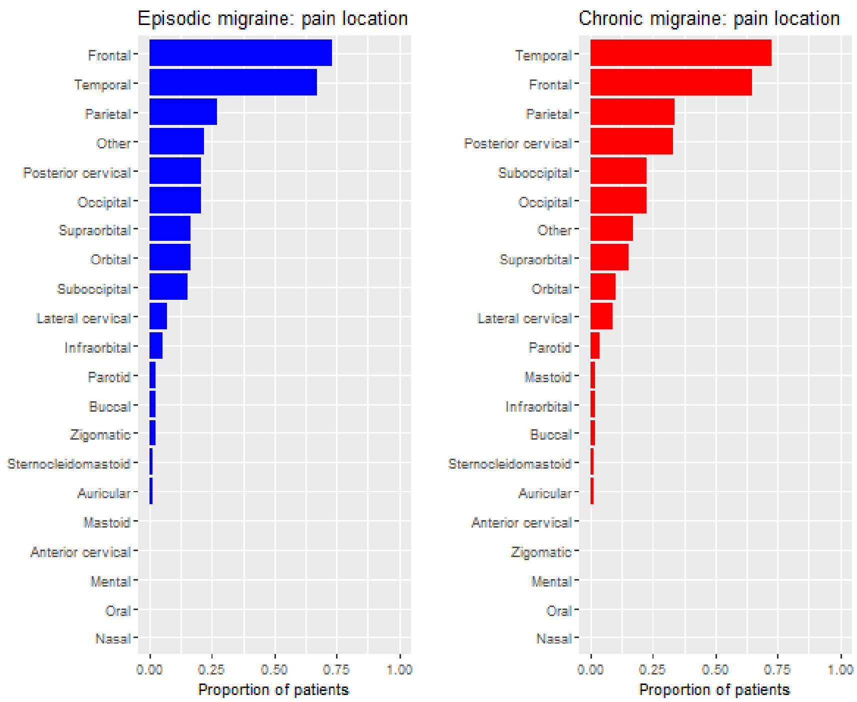

Figure 3

Distribution of migraine pain by head and neck subregions.

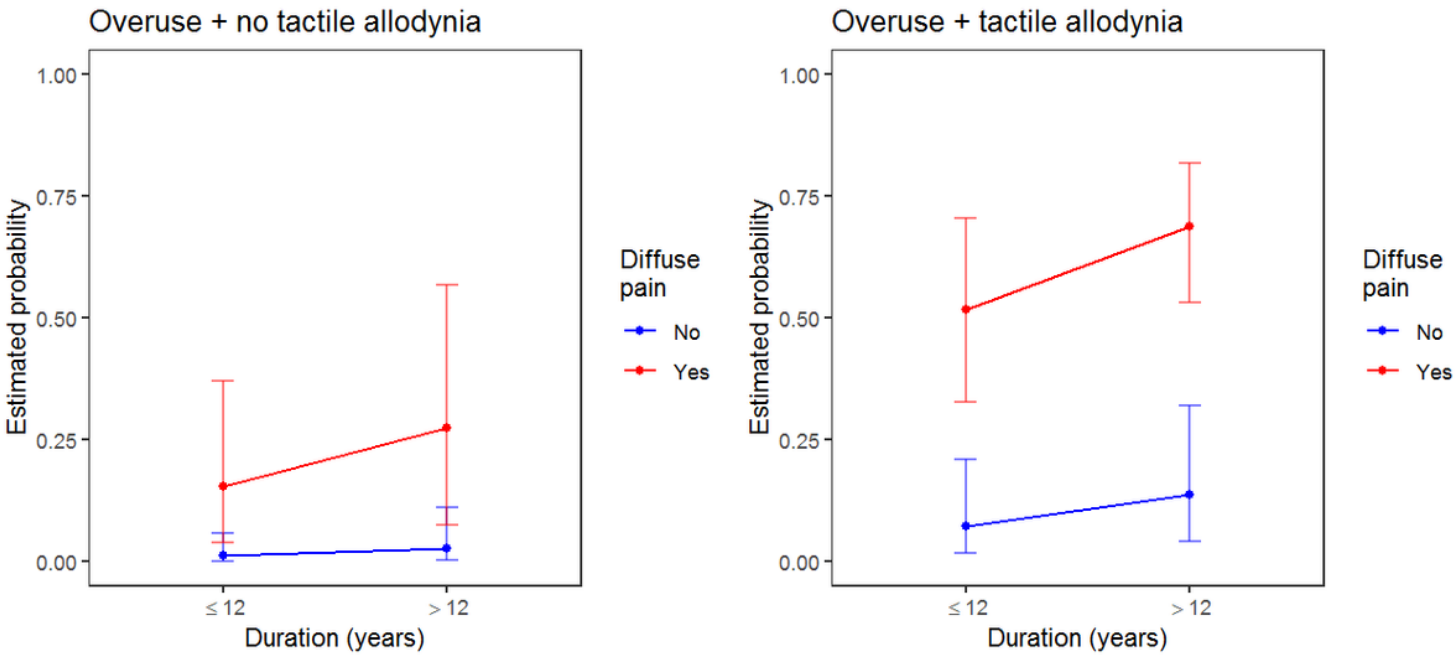

Figure 4

Estimated probabilities of neck pain. Estimated probabilities of neck pain plotted against migraine duration. The red symbols indicate diffuse pain (≥3 anatomical regions affected during attacks) and the blue symbols refer to slightly-to-moderately diffuse pain (≤2 regions). The vertical lines show the interval for the estimated probability. According to this model, drug overuse and tactile allodynia do not show significant association with the estimated probability of neck pain individually; however, their interaction increases this probability.

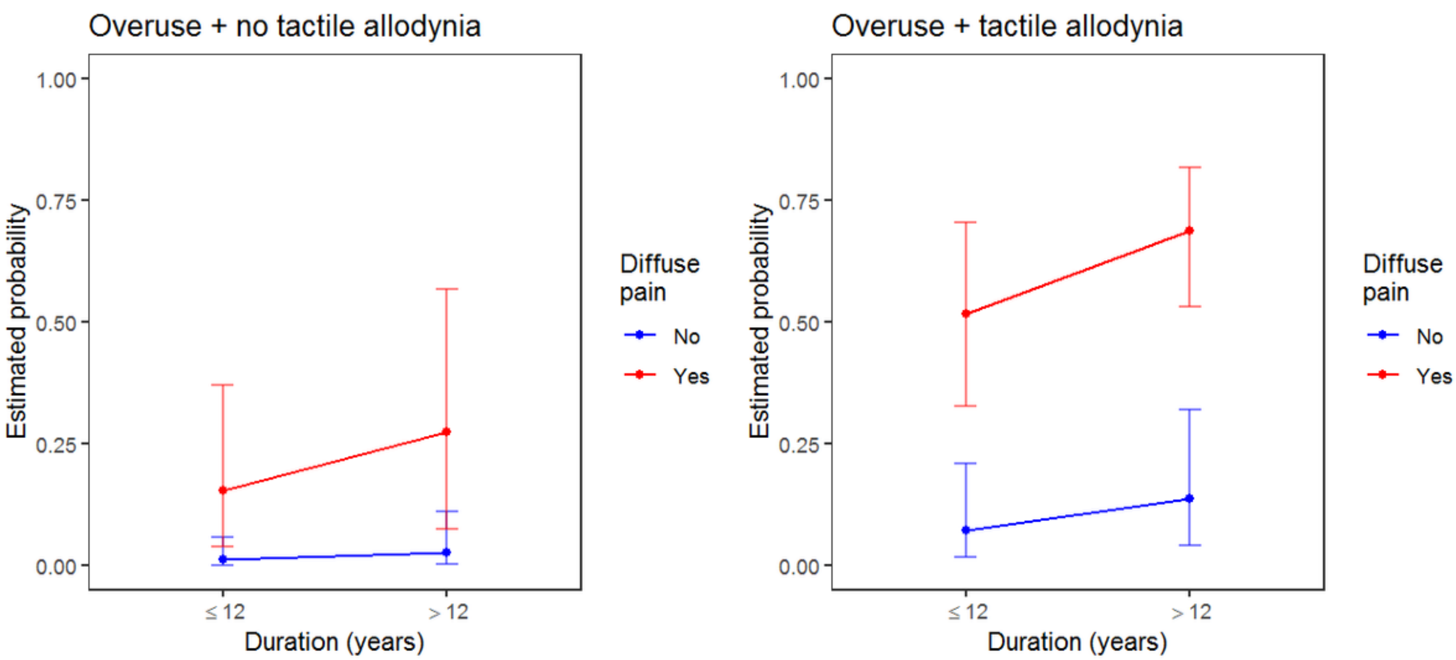

Figure 4

Estimated probabilities of neck pain. Estimated probabilities of neck pain plotted against migraine duration. The red symbols indicate diffuse pain (≥3 anatomical regions affected during attacks) and the blue symbols refer to slightly-to-moderately diffuse pain (≤2 regions). The vertical lines show the interval for the estimated probability. According to this model, drug overuse and tactile allodynia do not show significant association with the estimated probability of neck pain individually; however, their interaction increases this probability.