

June 2017

cological treatment.⁵ Additionally, higher neck-related disability is associated with migraine chronification.⁶

The influence of musculoskeletal disorders of the cervical spine in migraine is under debate since previous studies investigating the association between musculoskeletal disorders of the neck and migraine had reported conflicting results.⁷ Some authors have found restricted cervical range of motion or altered head posture in individuals with migraine,^{8,9} whereas others did not find such differences.^{10,11} Musculoskeletal disorders in the cervical spine may contribute to migraine pain by sensitization of trigemino-cervical nucleus caudalis, the anatomical area where nociceptive afferent inputs from the upper cervical roots (C1-C3), the first division of the trigeminal nerve, and cranial dura converge.¹² This is clinically manifested by the presence of referral pain head in subjects with headache during manual examination of symptomatic upper cervical joints.¹³⁻¹⁵

An important contribution of the cervical spine is its role in the maintenance of human posture and balance. A greater contribution is attributed to the upper cervical spine since it contains most of mechanoreceptors and muscle spindles connected with visual, vestibular and sympathetic systems to provide proper proprioception.¹⁶ Cervicocephalic kinesthesia is defined as the ability to perceive both movement and position of the head in space related to the trunk, and it is usually measured by the joint position sense error (JPSE) test.¹⁷ It seems consistent that individuals with primary neck disorders exhibit higher JPSE than controls;¹⁸ however, studies investigating JPSE in patients with migraine are scarce. The only two studies investigating this topic did not find significant differences in JPSE between patients with migraine and healthy controls.^{10,11}

It is important to note that none of the previous studies investigating musculoskeletal disorders of the cervical spine in migraine distinguished between episodic and chronic migraine. It is possible that chronification of the condition can lead to worse musculoskeletal impairments. In this context, it would be possible that the presence of musculoskeletal disorders of the cervical spine can be more pronounced in the chronic form of the disease. Therefore, the objective of the current study was to investigate differences in musculoskeletal disorders of the cervical spine including global and upper cervical spine mobility, presence of symptomatic upper cervical spine joints, JPSE, and head/neck posture

among women with episodic migraine, chronic migraine and controls. We hypothesized that women with chronic migraine would exhibit greater reduction on cervical spine mobility, referred pain to the head from symptomatic upper cervical joints, greater JPSE and worse head/neck posture than those with episodic migraine or healthy controls.

Materials and methods

Participants

Consecutive women with migraine attending their routine neurological visits were recruited from a tertiary university-based hospital from November 2014 and September 2015. Migraine was diagnosed according to the International Classification of Headache Disorders criteria, third edition (ICHD3 beta 2013) down to third-digit level (code 1.1, 1.3) by a neurologist expert in headache.¹⁹ Demographic and clinical data including location, quality of pain, onset of migraine (years), migraine frequency (days/month), intensity of migraine attacks (Numerical Pain Rate Scale - NPRS, 0-10), migraine duration (hours/attack), headache-family history, and medication intake were collected. We also collected the presence of self-reported neck pain, including the intensity and years with neck pain.

Participants were excluded if they presented any of the following: 1) any other primary or secondary headache, including medication overuse headache accordingly to the ICHD3 criteria; 2) history of neck or head trauma (*i.e.*, whiplash); 3) pregnancy; 4) history of cervical herniated disk and/or cervical osteoarthritis; 5) any systemic medical disease, *e.g.*, rheumatoid arthritis, lupus erythematosus; 6) comorbid diagnosis of fibromyalgia syndrome; 7) anesthetic block within the past 6 months; 8) dizziness; or, 9) visual disturbance symptoms.

A comparable control group without headache history and no headache during the last year, matched by age as much as possible to the migraine group, was also recruited from the general population by local advertisements. Exclusion criteria for the control group were the same as the migraine group. All subjects signed the informed consent form before their inclusion in the study. The local Ethics Committee of Hospital Rey Juan Carlos (URJC 23/2014-HRJ 07/14) approved the study design.

Cervical range of motion

A cervical range of motion (CROM®) device (Performance Attainment Associate, St. Paul®, MN, USA) was used to assess cervical range of motion. Audette *et al.* reported between-day reliability ranging from 0.89 to 0.98 and a standard error of measurement (SEM) across cervical movements from 1.6° to 2.8°. In fact, a systematic review has concluded that the CROM® device has been shown to be clinimetrically sound.²¹

Cervical range of motion was assessed following previously published guidelines.²² Cervical range of motion was evaluated in a relaxed sitting position. Subjects were asked to sit comfortably in a chair with feet flat on the floor, both hips and knees in 90° of flexion, and buttocks positioned against the back of the chair. The CROM® device was placed on the top of the participant's head with the neck in a neutral position. Participants were asked to move the head as far as they can without pain in a standardized sequence of movement: forward (flexion), backward (extension), right/left rotation, and right/left lateral flexion. Two measurements were recorded for each motion and the mean was used in the statistical analysis. Cervical range of motion was recorded by an assessor blinded to the participants' condition.

For the analysis, sides were considered accordingly to the symptoms. In women with unilateral attacks on the right side, the affected side was placed on the right; whereas in those with pain on the left side, the affected side was placed on the left. In those women with bilateral symptoms, the most painful side was considered as the affected side and the less painful side as the unaffected side.

C1-C2 dysfunction

The presence of segmental dysfunction at C1-C2 was assessed with the cervical flexion-rotation test (CFRT) using the CROM®.²³ Participants laid supine with their occipital protuberance resting on the examiner's abdomen. They were asked to relax while the clinician passively moved their neck to end-range cervical flexion. In this flexed position, the head/neck was passively rotated as far as possible within comfortable limits to the right and to the left. The end of rotation was determined when the therapist perceives resistance or when the volunteer reports the onset of pain.²³⁻²⁶ The CFRT was repeated twice on each direction with a 30-second interval between each trial. The median score was cal-

culated and used for the analysis. The CFRT is considered positive when the range of rotation is less than 32°. This test has shown almost perfect intra- and inter-rater reliability,²⁴ high sensitivity (91%) and specificity (90%) in identifying subjects with cervicogenic headache from asymptomatic controls or subjects with migraine with aura.²⁶

Symptomatic upper cervical joints examination

Manual examination was used to determine the presence of symptomatic upper cervical spine segments. Passive accessory intervertebral motion (PAIVM) was used to evaluate the presence of referred pain to the head elicited by a posterior to anterior (PA) pressure applied to the targeted segment.²⁷ With subjects lying prone, the assessor applied unilateral PA pressure over the articular pillars of C0-C1 and C1-C2 levels in an attempt to provoke a pain response. Pressure was maintained for 20 seconds if participant reports the onset of pain. Since manual examination was conducted in blinded fashion, sides were randomly assigned. An upper cervical joint segment was considered symptomatic based on perceived presence of abnormal displacement, abnormal tissue resistance to displacement and provocation of referred pain to the head mimicking pain features experienced during a migraine attack on the testing procedure. This procedure has been previously used in headache literature^{10, 11} and has shown moderate to substantiate inter-examiner reliability (kappa from 0.40 to 0.70).²⁸

Cervical kinesthetic sense (JPSE)

JPSE was measured following the protocol described by Revel *et al.*²⁹ and used in previous studies on headaches.^{10, 11} Subject ability to relocate the head to a natural head posture, whilst blindfolded, was assessed for active cervical extension, left and right rotations. The difference between the starting (zero) and the position on return (JPSE) was calculated in absolute degrees (°) for each movement tested; therefore positive and negative values (undershoot or overshoot of the target) were not considered. Three trials were performed in each direction and the mean JPSE was used in analysis. The JPSE test has exhibited moderate to substantiate intraexaminer ($0.48 \leq \text{ICC} \leq 0.82$) and interexaminer ($0.51 \leq \text{ICC} \leq 0.75$) reliability.³⁰

Head/neck posture

Head and neck posture was assessed following previous guidelines.^{8, 11, 31} Briefly, adhesive markers were fixed with adhesive tape on the occipital bone and spinous processes of C4 and C7 vertebrae. These marks were considered as anatomical reference points for determining the cranio-vertebral and cervical lordosis angles. A metal plumb line was positioned 33 cm beside the subject for a vertical reference. A digital camera (Samsung Lens WB350F®) was positioned on a tripod 4 meters from the subject with the center set at the mid-point of the individual being used a lens of 23 mm.³¹ All photographs were obtained by the same technician who was blinded to the subject's condition and analyzed using the CorelDraw-X7® software. Participants were photographed in standing and sitting. They were instructed to keep a comfortable position without shoes with their feet apart in a comfortable distance, the arms alongside the body and the head in relaxed natural position looking forward.

The cranio-vertebral angle, the angle created between the horizontal plane and a line from the tip of the C7 spinous process to the tragus of the ear, was calculated for assessing forward head posture. A smaller angle reflects a greater forward head posture. In addition, the lordosis angle, the angle composed by the intersection of a line from occipital bone to C4 and a line from the C7 to C4 was used to determine neck posture. In this case, a higher angle reflects a lesser lordosis curvature. This produce has exhibited almost perfect reliability in individuals with cervicogenic headache.³²

Statistical analysis

Data were analyzed with the SPSS statistical package (20.0 Version). Descriptive analysis was applied for all variables. Student *t*-tests for independent samples were used to determine the differences in clinical characteristics between patients with episodic and chronic migraine. Mixed-model ANCOVAs were used to determine the difference in cervical range of motion, upper cervical spine mobility, JPSE and head/neck posture among 3 groups (episodic migraine, chronic migraine and healthy controls) with the presence/absence of neck pain as covariate. *Post-hoc* comparisons were conducted with the Bonferroni test. To contrast the frequency

of symptomatic upper cervical joints between both migraine groups, the χ^2 test was used. Finally, Pearson correlation coefficients (*r*) were used to determine associations between the variables on each group, separately. Correlations <0.3 were considered small; from 0.3 to 0.7 moderate; and >0.7 strong.³³ In general, the statistical analysis was conducted at a 95% confidence level, so *P* values <0.05 were considered statistically significant. For multiple comparisons, a Bonferroni-corrected alpha level of 0.017 (3 independent-samples *t*-tests) was used as threshold for significance

Results

Clinical features of the sample

From 100 eligible subjects with migraine who accepted to participated, 29 were excluded for the following reasons: other headaches (*N*.=14), receiving anesthetic block (*N*.=6) or botulinum toxin A (*N*.=6) in the past 3 months, and reporting previous head or neck trauma (*N*.=3). Finally, 55 women with episodic migraine, 16 with chronic migraine were included. Similarly, from 30 subjects who answered to the advertisements, 8 were excluded: previous whiplash (*N*.=5), neck surgery (*N*.=2) and diagnosis of fibromyalgia (*N*.=1). Therefore, 22 comparable healthy controls satisfied all criteria and agreed to participate. Episodic and chronic migraine groups were only different on the frequency of migraine attacks (*F*=11.973; *P*<0.001). The presence of self-reported neck pain was significantly higher (χ^2 =26541; *P*<0.001) in both migraine groups as compared to the control group. Neck pain intensity for those women with migraine was also significantly higher (*F*=4.150; *P*=0.015) than in healthy controls. **Demographic and clinical characteristics** of both migraine groups and healthy women are presented in Table I.

Cervical range of motion

The mixed-model ANCOVA did not reveal significant differences for cervical flexion (*F*=0.168; *P*=0.845), extension (*F*=2.097; *P*=0.129), and lateral-flexion (right *F*=1.459, *P*=0.238; left: *F*=2.035, *P*=0.136) between migraine women and healthy controls (Figure 1). Significant differences were observed for rotation (right *F*=5.729, *P*=0.005; left: *F*=4.605,

TABLE I.—Clinical and demographic characteristics of women with episodic migraine, chronic migraine, and healthy controls.

	Episodic migraine (N.=55)	Chronic migraine (N.=16)	Healthy controls (N.=22)
Age (years)	41±12	44±13	44±11
Migraine characteristics			
Side (right/left/bilateral)	11 (20%)/9 (17%)/35 (63%)	1 (6%)/1 (6%)/14 (88%)	
Time of onset (years)	18.3±12.9	24.1±16.7	
Frequency (days/month) #	6.1±3.6	21.9±6.1	
Intensity (NPRS, 0-10)	8.2±2.0	7.9±2.2	
Neck pain features			
Prevalence, N. (%) *	44 (80%)	15 (93%)	5 (23%)
Time of onset (years)	10.0±12.3	13.9±15.8	5.0±4.6
Intensity (NPRS, 0-10)*	5.2±2.9	6.6±2.7	3.8±1.4

NPRS: Numerical Pain Rate Scale (0-10).

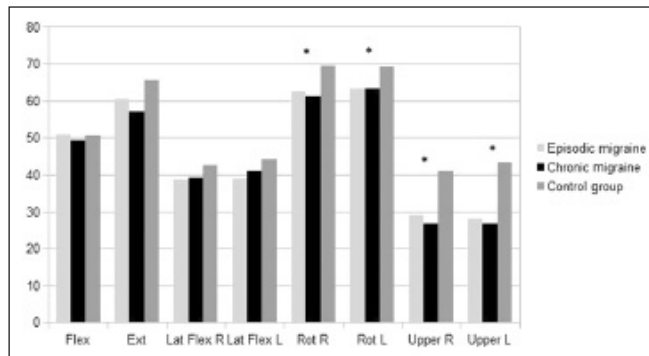
*Significant differences between patients with migraine (both groups) and healthy controls ($P<0.001$); #significant differences between patients with episodic and chronic migraine ($P<0.001$).

Figure 1.—Cervical range of motion and upper cervical spine mobility in woman with episodic and chronic migraine and healthy controls.

*Significant differences between patients with migraine (episodic and chronic) and healthy controls (ANOVA, $P<0.001$).

$P=0.012$): women with migraine, either episodic or chronic, had lesser cervical rotation bilaterally (Bonferroni, $P=0.012$, Figure 1).

The ANCOVA found significant differences for flexion-rotation test bilaterally (right: $F=21.406$, $P<0.001$; left: $F=48.466$, $P<0.001$): both migraine groups exhibited a higher prevalence of C1-C2 dysfunction ($P<0.001$, Figure 1). Accordingly, a greater number of women ($\chi^2=61.723$; $P<0.001$) with episodic (85%) and chronic (100%) migraine exhibited a positive flexion-rotation test (range $<32^\circ$) (Table II).

Symptomatic upper cervical spine

The referred pain elicited during manual examination of the upper cervical spine mimicked similar pain symptoms than during the migraine attack in almost

TABLE II.—Flexion-rotation test, passive accessory inter-vertebral motion, cervicocephalic kinesthesia and head/neck posture in women with episodic migraine, chronic migraine, and healthy controls.

	Episodic migraine (N.=55)	Chronic migraine (N.=16)	Healthy controls (N.=22)
Flexion-Rotation Test (FRT - N., %)*			
FRT positive	47 (85.5%)	16 (100%)	1 (4.5%)
Right side	6 (11%)	2 (12.5%)	1 (4.5%)
Left side	7 (13%)	2 (12.5%)	0 (0%)
Bilateral	34 (61.5%)	12 (75%)	0 (0%)
Negative	8 (14.5%)	0 (0%)	21 (95.5%)
Symptomatic upper cervical joint (N., %)			
C0/C1 right	13 (23.6%)	8 (50%)	
C0/C1 left	13 (23.6%)	5 (22.5%)	
C1/C2 right	13 (23.6%)	5 (22.5%)	
C1/C2 left	12 (21.8%)	4 (25%)	
Joint positioning sense error (degrees)			
Extension	4.5±2.3	4.9±2.3	4.7±2.3
Rotation right	5.7±2.2	5.4±2.4	5.6±2.0
Rotation /left	6.5±2.1	6.0±2.2	5.3±1.7
Posture (degrees)			
Cranio-vertebral angle stand	35.7±7.0	34.5±6.6	37.9±5.3
Cranio-vertebral angle sit	40.4±5.2	38.4±4.8	41.4±4.4
Cervical lordosis angle stand	5.7±2.1	5.6±2.0	6.7±2.9
Cervical lordosis angle sit	7.9±2.5	7.6±1.2	8.6±3.1

*Significant differences between patients with migraine (both groups) and healthy controls ($P<0.001$).

50% of the patients with migraine, at least one segment. The pain elicited during examination lasted no more than 15-20 minutes. No significant differences were observed on the frequency of symptomatic upper cervical joint segment between women with episodic or chron-

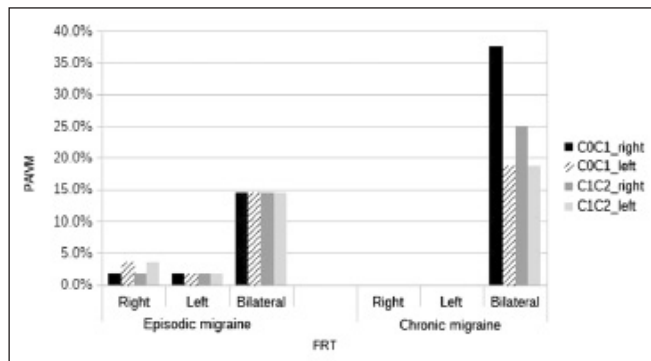


Figure 2.—Frequency of symptomatic upper cervical spine joints in women with episodic and chronic migraine grouped by positive flexion-rotation test (FRT).

ic migraine (C0/C1: right: $\chi^2=3.021$, $P=0.078$; left: $\chi^2=0.154$, $P=0.46$; C1/C2 right: $\chi^2=0.154$, $P=0.458$; left: $\chi^2=0.005$, $P=0.589$, Table II). However, when women with migraine were grouped by the flexion-rotation test, those women with a bilateral positive flexion-rotation test exhibited higher number of symptomatic upper cervical joints (Figure 2).

Cervical kinesthetic sense

No significant differences were observed among the groups for the JPSE measured from cervical rotation (right: $F=0.121$, $P=0.886$; left: $F=1.204$, $P=0.305$) or extension ($F=1.055$, $P=0.352$, Table II).

Head/neck posture

The ANCOVA did not find differences in head (cranio-vertebral angle sit: $F=1.380$, $P=0.257$; stand: $F=1.790$, $P=0.187$) or cervical spine (lordosis angle sit: $F=1.851$, $P=0.163$; stand: $F=0.920$, $P=0.402$) between women with migraine and healthy controls (Table II).

Associations

Within women with episodic migraine, cervical rotation was positively and moderately associated with the cervical lordosis angle ($r=0.381$; $P=0.004$): the lesser the cervical rotation, the lesser the lordosis angle, *i.e.*, the greater lordosis curvature of the cervical spine. Furthermore, JPSE in extension was negatively associated with the CFRT (right: $r=-0.288$, $P=0.033$; left: $r=-0.355$,

$P=0.008$): the decrease the range of motion of the upper cervical spine, the greater the JPSE in extension.

In women with chronic migraine, the cranio-cervical angle was positively and moderately associated with JPSE in rotation ($r=0.546$, $P=0.029$): the greater the craniocervical angle, *i.e.*, the greater the forward head posture, the higher the JPSE in rotation.

Discussion

This study found that women with migraine exhibit musculoskeletal disorders of the upper cervical spine expressed as restricted cervical rotation, C1-C2 dysfunction assessed by the flexion-rotation test and the presence of symptomatic upper cervical spine joints. No differences were found between women with episodic or chronic migraine in the musculoskeletal disorders. No difference in cervicocephalic kinesthesia and head/neck posture was observed between women with migraine and healthy controls.

The presence of musculoskeletal disorders in the cervical spine in migraine is controversial.⁷ Our results agree with some previous studies reporting restricted cervical range of motion in these patients,^{8, 9} but contrary to several others.^{10, 11, 13} In fact, it has been suggested that the presence of restricted cervical range of motion is a feature of cervicogenic, but not migraine, headache.^{10, 11} This hypothesis is related to the fact that migraine is not a primary cervical spine disorder, such as cervicogenic headache. Nevertheless, our result does not completely support this assumption since we observed lesser cervical rotation in our sample of migraine women. Discrepancies maybe related to the fact that previous studies did not distinguish between episodic and chronic migraine.^{10, 11} However, no differences in cervical rotation were observed between episodic and chronic migraine in our study. It is also possible that cervical range of motion is restricted in some directions, but not all, in individuals with migraine.

CFRT has been previously used for identification of dysfunction at the C1/2 segment in patients with cervicogenic headache.²³⁻²⁶ A range of motion less than 32° is considered a positive test.²⁴⁻²⁶ Our study found that women with migraine exhibited lower upper cervical spine mobility during the flexion-rotation test and that at least 80% of patients exhibited a positive flexion-rotation test. These findings are contrary to those previ-

ously reported by Ogince *et al.*;²⁶ however, this study included a small sample of patients with migraine without classifying if they were episodic or chronic. The fact that women with migraine exhibit reduced cervical range of motion in rotation and during the flexion-rotation test supports an impairment of the upper cervical spine, since C1/C2 mostly supports the rotation motion of the cervical spine in this population.

We found that almost 50% of women with migraine exhibited symptomatic upper cervical joints. The presence of referred head pain during manual examination of symptomatic segmental dysfunctions in the upper cervical spine is not new in the headache literature; however, again the results are controversial. Some studies reported the presence of symptomatic upper cervical joints in individuals with migraine,^{13, 14} whereas other did not.^{10, 11} Accordingly to our study, 50% of women with episodic and 36% with chronic migraine exhibited referred pain to the head elicited by C0/C1, whereas 50% of the women with either episode or chronic migraine reported referred pain to the head elicited by C1/C2. Interestingly, migraineurs with a positive flexion-rotation test also exhibited higher prevalence of referred pain from upper cervical joints. The prevalence rate observed in our study was higher than others where no symptomatic upper cervical joints were observed,^{10, 11} but inferior to the rate reported by Watson and Drummond.¹⁴ Variation in application pressure across studies may also account for differing rates of headache reproduction. Our study applied sustained pressure on C0/C1 and C1/C2 joints, similarly to Watson and Drummond.¹⁴ Interestingly, the role of referred pain from muscles, *i.e.*, myofascial pain, in patients with migraine is better described in the literature.³⁴ It is possible that referred pain elicited by upper cervical spine segments, as reported in the current study, can be also associated to referred pain from myofascial trigger points in head and neck muscles innervated by these segments. Therefore, the presence of myofascial trigger points in the cervical muscles in our sample, which were not explored, could also be associated to our findings.

No differences in cervicocephalic kinesthesia (JPSE) were observed between women with migraine and healthy women. Our findings agree with previous studies supporting that JPSE is not significantly different in individuals with headaches.^{10, 11} Current results would further confirm that individuals with migraine do not

exhibit altered cervicocephalic kinesthesia as people with primary neck disorders.¹⁸ Nevertheless, the fact that no differences in cervicocephalic kinesthesia have been observed in subjects with migraine, does not exclude the possibility that migraine sufferers exhibit other sensory-motor disturbances of the neck musculature. The presence of disturbances in cervical sensory-motor control in this population may be related to the fact that a high proportion of patients with migraine also exhibit from neck pain.^{2, 3} In fact, a recent study has demonstrated that women with chronic migraine exhibit altered muscle recruitment strategy to stabilize their head and neck manifested as an increased activity of their superficial neck extensor musculature when acting as antagonists during low-load isometric craniocervical flexion contractions in comparison to non-headache subjects.³⁵

The presence of altered head/neck posture in migraine is also controversial. Our study did not find between group differences in the craniovertebral and cervical lordosis angles suggesting that individuals with migraine do not exhibit an altered posture. Again, these results are similar to some studies¹¹ but opposite to some others.^{8, 32} Discrepancies between studies maybe related to age differences or assessment procedure; nevertheless, a recent study has confirmed that women with migraine do not exhibit forward head posture compared to women with no history of headache in either radiographic or photographic postural analysis.³⁶

Finally, although no differences in the cervicocephalic kinesthesia and head/neck posture were found, we observed an association between head posture and JPSE in the chronic migraine group. This is similar to the results reported by Lee *et al.* where the presence of forward head posture was correlated to greater JPSE in all movements.³⁷ The presence of worse head posture may lead to changes in the lengths of the cervical muscles influencing the activity of the muscle spindles and inducing a greater JPSE.³⁸ In the episodic migraine group, JPSE was negatively associated with the CFRT. A positive flexion-rotation test is associated with C1/C2 dysfunction. It would be expected that individuals with upper cervical spine disorders exhibit worse JPSE since the musculature of the upper cervical spine has high density of muscle spindles.¹⁷ In such a scenario, current and previous evidence suggest that association of musculoskeletal disorders of the cervical spine,

including those assessed in the current study, muscle pain and motor control disturbances, in people with migraine is highly complex and further studies are needed.

Limitations of the study

Although this study expands our knowledge on the presence of musculoskeletal disorders of the cervical spine in migraine; some limitations should be considered. First, patients were recruited from a university-based hospital; therefore, it is possible that they represent a specific group of the general population with migraine. Second, we only included women with migraine; therefore, we do not know if the same results would be observed in men. Third, the sample size was relatively small, particularly for the chronic migraine and healthy control groups. It is possible that the lack of differences in some outcomes was underpowered and with a greater sample size some differences could reach statistical significance. Fourth, the cross-sectional nature of the study does not permit to establish a cause and effect relationship between musculoskeletal disorders of the cervical spine and migraine. Longitudinal clinical studies should be conducted to further determine the role of these musculoskeletal disorders in the evolution of migraine. Finally, we should recognize that we did not assess muscle tenderness, a disorder highly prevalent in individuals with migraine.³⁸ It is possible that tenderness may be associated with some of the musculoskeletal disorders found in our study. Similarly, muscle tenderness is associated with anxiety and depression,³⁹ but we did not also assess the psychological state of our patients. Future studies including muscle impairments and also the psychological state of individuals with migraine will help to determine if possible associations exist between all these musculoskeletal disorders in headache populations.

Conclusions

This study found that women with episodic or chronic migraine exhibited similar restricted cervical range of motion in rotation, C1-C2 dysfunction assessed with the flexion-rotation test, and the presence of symptomatic upper cervical joints suggesting that musculoskeletal disorders of the neck seem to be related to the upper

cervical spine. No differences in cervicocephalic kinesthesia and head/neck posture were observed between patients and controls.

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Authors' contributions.—All authors contributed to the study concept and design. Gabriela N. Ferracini, Lidiane L. Florencio and César Fernández-de-las-Peñas did the statistical analysis. All authors contributed to analysis and interpretation of data. Gabriela N. Ferracini and Lidiane L. Florencio contributed to draft the text. Débora Bevilacqua Grossi and César Fernández-de-las-Peñas obtained funding, provided administrative, technical, and material support and supervised the study. All authors revised the text for intellectual content and have read and approved the final version of the manuscript.

Conflicts of interest.—Financial disclosure statements have been obtained, and no conflicts of interest have been reported by the authors or by any individuals in control of the content of this article.

Funding.—The first author received a grant from Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) (FAPESP) to develop this research (process number 2014 /13159-0).

Article first published online: January 24, 2017. - Manuscript accepted: January 19, 2017. - Manuscript revised: January 13, 2017. - Manuscript received: June 29, 2016.