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Involvement of cervical disability in migraine: a literature review

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Abstract

Background: The trigeminal nerve theory has been proposed as a pathophysiological mechanism of migraine; however, its association with the triggers of migraine remains unclear. Cervical disability such as neck pain and restricted cervical rotation, have been associated with not only cervicogenic headaches but also migraine. The presence of cervical disability could worsen of the migraine, and also the response to pharmacologic treatment may be reduced. The aim in this review is to highlight the involvement of cervical disability in migraine, considering contributing factors.

Findings: In recent years, evidence of neck pain complaints in migraine has been increasing. In addition, there is some recent evidence of cervical musculoskeletal impairments in migraine, as detected by physical assessment. However, the main question of whether neck pain or an associated cervical disability can act as an initial factor leading to migraine attacks still remains. Daily life imposes heavy loads on cervical structures (i.e. muscles, joints and ligaments), for instance, in the forward head position. The repetitive nociceptive stimulation initiating those cervical skeletal muscle positions may amplify the susceptibility to central migraine and contribute to chronicity via the trigeminal cervical complex.

Conclusion: Further studies are needed to explain the association between cervical disability as a source of pain and the development of migraine. However, evidence suggests that cervical disability needs to be considered in the prevention and treatment of migraine.

Keywords

migraine, neck pain, cervical disability, trigeminal cervical complex

Introduction

Migraine is characterized by a severe unilateral head pain that is often accompanied by other symptoms, including nausea, vomiting and light and sound hypersensitivities. Cervicogenic headaches caused by cervical disabilities can lead to similar symptoms, and both syndromes are difficult to distinguish during clinical diagnoses. Accompanying symptoms, such as neck pain or restricted neck rotation, were described first by Sjastastad et al.[1] in 1983 as features of 'cervicogenic headaches', and neck region involvement was originally thought to be absent in migraines.[2] However, neck pain has become more commonly recognized in migraine,[3–7] and it may be a predictor of migraine disability.[5,8] Calhoun et al.[9] reported that the intensity of neck pain is associated with great headache intensity and treatment delays. In addition, in their study evaluating the association between neck disability and migraine in patients with single migraine attacks and chronic migraine (CM), Carvalho et al.[10] indicated a 7.6-fold higher risk of developing CM in patients with strong posterior neck pain than in others. This review will focus on the possible involvement of neck pain, cervical

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disability, cervical impairment and trigger points (TrPs) in migraine, and also discuss pathophysiological implications associated with migraine.

Method

Search strategy

A literature search was done in PubMed for studies published between January 1980 and September 2019 using the following search terms: 'migraine', 'neck pain', 'cervical musculoskeletal impairment', 'forward head posture (FHP)', 'myofascial TrPs' and 'trigeminal cervical complex (TCC)'. Each of these search terms was cross-referenced with 'migraine'. Abstracts and studies were chosen according to their relevance to the topic of interest and the quality of their data and papers were analysed to assess the association between cervical musculoskeletal impairment factors and migraine. The literature on relevant migraine and cervical region pathophysiology was also reviewed (Figure 1).

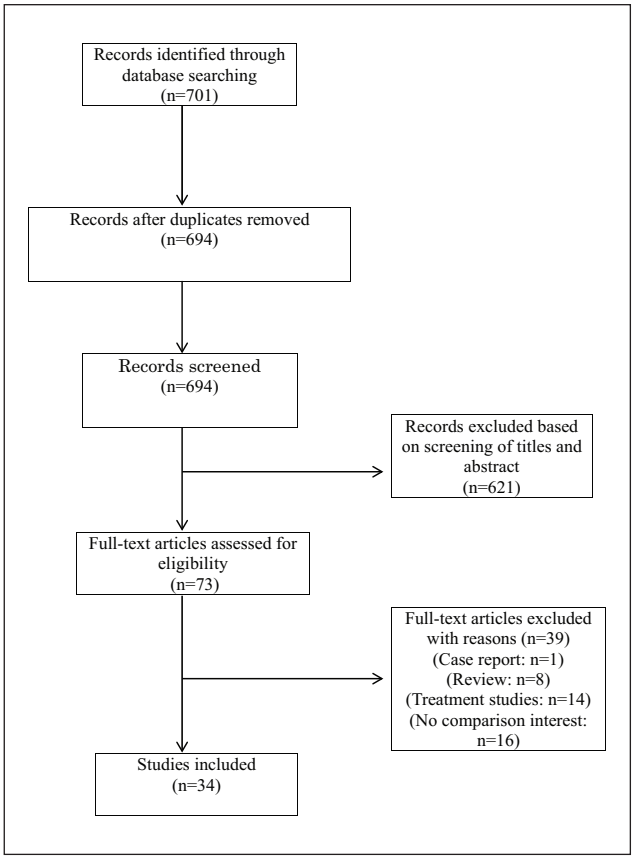


Figure 1. Flow chart for the identification of studies.

Findings

Self-reported neck pain

Regarding relation with neck pain in migraine, self-report or questionnaire have been used in some studies. Viana et al.[11] simply reported that the majority of patients, 91% of cases, with neck pain suffered from typical migraine in 207 migraine patients. A study on 797 patients suffering from tension-type headache (TTH) or migraine showed headache accompanied with neck pain in 85.7% of the patients during a 1-year follow-up; the association between neck pain and headache was 89.3% in patients with combined migraine and TTH, 88.4% in those with TTH alone and 76.2% in those with migraine alone.[12] In a study on adolescents, Blaschek et al.[13] observed the presence of neck/shoulder muscle pain and headache, not only in patients with chronic TTH, but also in those with migraine and those with mixed migraine and TTH. However, in their subsequent study on younger patients, they found a higher prevalence of pain in the neck/shoulder region in patients with either migraine or migraine plus TTH than in those with TTH alone.[14] Krøll et al.[15] reported that migraine attacks coexisted with TTH and neck pain in 100 (67%) of 148 patients with migraine. Thus, the prevalence of neck pain and migraine seems to be high, especially in patients with mixed migraine and TTH.

Blau and MacGregor[5] studied the occurrence of neck symptoms during different headache attack phases. Around 32 of 50 patients complained of neck pain, 30 had pain during the headache phase, and 10 had pain before and 10 had pain after the headaches. Pradhan et al. reported that 166 of a total of 391 patients with migraine had neck pain at some point during the migraine phase. In the same study, 89.2% of the patients reported having neck pain at the onset of the headaches, and 32% of the headache attacks initiated with neck pain.[16] In addition, Özer and Benlier[17] reported that 89.1% of patients with migraine had attack onsets accompanied with neck pain and that 10.9% of the patients had neck pain starting at different times than the migraine. In the study by Lampl et al.[18] on accompanying symptoms before and after the onset of headache in 487 patients with migraine, approximately 70% were aware of neck pain before and after the onset of the headache.

Some studies have covered the involvement of neck pain in the frequency of migraine attacks. Calhoun et al.[19] found that neck pain is more frequently accompanied by migraine than by nausea and that it is associated with the chronicity of the headache as attacks move from episodic to daily chronic headaches. Landgraf et al.[20] also reported a strong link between neck/shoulder pain and migraine, leading to an increase in the frequency of migraine attacks in secondary-school students (Table 1).

Table 1. Assessment of neck pain in migraine (self-report and interview).

	Type of headache	Mean age (range)	Number	Assessment	Finding results
Blau et al.[5]	M	38	50	Interview about prevalence of neck pain in headache during different phase	In total, 32 of all patients reported neck pain or stiffness. In total, 30 of them note during headache phase, 10 during pre-attack phase, and 10 post-attack phase
Viana et al.[11]	M	18–75	207	Questionnaire regarding detail of neck pain in migraine	Of 207 patients, 132 (64%) reported suffering from cervical pain. These patients suffered from migraine or probable migraine in 91% of cases.
Ashina et al.[12]	M, TTH and M + TTH	25–76	797	Self-report and interview regarding neck pain	The prevalence of neck pain was 89.3% in M + TTH, 88.4% in pure TTH and 76.2% in pure migraine.
Blaschek et al.[13]	No headache, M, TTH, M + TTH and MH	15–18	1260 No headache: 213 M: 129 TTH: 614 M + TTH: 249 MH: 55	Questionnaire on headache and associated lifestyle factors Assessment of neck pain via denoting affected areas in schematic drawings	Pain-sensitive spots in the shoulder/neck region were around 17% in non-headache adolescents, up to 33% in TTH and around 50% in migrainers or mixed migraine + TTH. Muscular pain is particularly important factor not only for adolescents in chronic TTH but also for individuals in migraine.
Blaschek et al.[14]	No headache, M, TTH and M + TTH	12–19	1445 No headache: 244 M: 136 TTH: 596 M + TTH: 469	Questionnaire on headache and associated lifestyle factors Assessment of neck pain via denoting affected areas in schematic drawings	83.1% of all had experienced headache. Higher prevalence of pain in the neck/shoulder region on migraine and migraine + TTH, but not in TTH, was reported.
Krøll et al.[15]	M and CTRLs	18–65	M: 148 CTRLs: 100	Modified semi-structured headache interview Questionnaire consists of 79 items covering pain, triggers, psychosocial, socioeconomic and work related aspects	67% of total in migraine group suffered from co-existing tension-type headache and neck pain. They had lower level of physical activity, higher level of perceived stress and poorer self-rated health compared to healthy controls.
Pradhan and Chodhury[16]	M	14–65	391	Questions regarding detail of headache and neck pain. Analysis of headache and neck pain characteristics, the associated conditions, and other clinical features	89.2% of all patients reported neck pain at the onset of headache, while 34.3% felt neck pain before the onset of headache and 27.7% experienced neck pain after the resolution of headache.
Özer and Benlier[17]	M	12–61	50	Interview about the occurrence of neck symptoms during different phases of their attacks	89.1% of all patients were onset migraine attack and neck pain at started and ended simultaneously, and 10.9% of them had neck pain starting at different times.
Lampl et al.[18]	EM	18–65	487	Self-fulfilled questionnaire on neck pain and premonitory symptoms in a migraine cohort	24.2% of patients reported neck pain within 2 hours before the headache phase. In this group, a high proportion of typical migraine associated symptoms and neck pain progressed into the headache phase in 82.2%
Calhoun et al.[19]	M	37.4	113	Recording the intensity of headache and neck pain, and presence or absence of nausea	Neck pain was more frequent associated with migraine than nausea, and was correlated with chronicity of attack
Landgraf et al.[20]	M	12–19	601	Questionnaire about headache appearance, type and frequency, neck/shoulder pain and lifestyle factors	The association between neck/shoulder pain and migraine was most pronounced in migraine with high frequency of attack.

M: migraine; TTH: tension-type headache; MH: miscellaneous headache; CTRLs: controls; EM: episodic migraine.

Also, Yu et al.[21] identified that the presence of neck pain was found to be associated with increased neck and scalp sensitivity in episodic migrainers.

Neck disability in migraine

The evaluation of cervical disability can extract not only the impairments caused by neck pain, but also potentially reveal subclinical restrictions to activity. Ferracini et al.[22] found that a longer history of neck pain, higher pain intensity and neck pain–related disability are all features associated with a higher risk of migraine attacks in patients with migraine than in healthy controls. According to Florencio et al., the Neck Disability Index (NDI), the most commonly used self-administered questionnaire for neck pain, revealed disabilities in 69% of patients with episodic migraine (EM) and in 92% of patients with CM. Particularly in patients with CM, the correlation between the degree of cervical disability and headache was significant.[23] Moreover, Gonçalves et al. assessed the NDI and pressure pain thresholds (PPTs) to investigate the association between cervical disability due to neck pain and migraine in affected patients. Although they found no linear association, the NDI moderately correlated with the PPTs over the sternocleidomastoid, upper trapezius and suboccipital muscles.[24]

Cervical musculoskeletal impairment in migraine

Regarding physical examination of cervical musculoskeletal impairment in headache patients, 11 tests are considered to be useful.[25] Among them, Luedtke et al.[26] showed that set of six tests, which are number of TrPs, flexion-rotation test (FRT), thoracic screening, manual joint testing of the upper cervical spine, cranio-cervical flexion test (CCFT) and reproduction and resolution, have high prevalence of cervical musculoskeletal impairment in patients with migraine.

Ferracini et al.[27] investigated the differences in the range of cervical rotation between women with EM, women with CM and healthy women. During FRT, both migraine groups (EM and CM) showed a significant cervical rotation reduction (restricted upper cervical mobility) compared to healthy women. Carvalho et al.[10] also showed moderate negative correlation between the cervical range of motion (CROM) and disability in both patients with CM and in those with EM, but no significant differences in CROM alone were identified between the groups. Oliveira-Souza et al.[28] reported similar result that FRT mobility was lower in both CM and EM than control.

In addition, studies investigating the relative level of cervical alignment also were performed. Vernon et al.[29] compared muscle contraction headache (MCH) to migraine and found at least two major fixations from C0 to C2 on motion palpation in 84% of patients with CM, and they also found that 92% of patients with CM had at least one tender point in the midcervical (C2–C3), lateral and suboccipital regions, for results similar to those in MCH. Cervical facet joint stiffness (in occiput–C1 and C1–C2) in patients with EM was found to be more prevalent than in controls.[30] Ferracini et al.[31] found that patients with migraine lacked FHP, but they found a weak association between the frequency of migraine attacks and a high cervical angle variation. Horwitz and Stewart reported the involvement of cervical dysfunction in patients with perimenstrual migraines. The factors associated with neck stiffness and pain included reduced muscle length (especially in the trapezius, sternocleidomastoid and suboccipital muscles) and increased pain response to muscle stretches of the levator scapulae, the trapezius, the sternocleidomastoid and the suboccipital muscles. In addition, reduced neural mobility and stiffness of C5 and C7 were likely to be present as well.[32]

Furthermore, it has been observed that individuals with migraine show lower strength and increased activity of the neck flexors and extensors. Florencio et al.[33] identified that cervical extension peak force was moderately associated with the migraine frequency, neck pain frequency and neck pain intensity compared to normal control. Tolentino et al.[34] also reported that neck extensor strength was negatively correlated with all clinical variables and also lateral flexor strength was negatively correlated with headache frequency, neck pain intensity and neck-related disability in migraine patients. In CM, FHP was moderately correlated with an increased in electrical activity of the upper trapezius and splenius muscle during the performance of the CCFT (Table 2).[35]

TrPs in migraine

Myofascial TrPs are identified as hypersensitive tender spots located in the muscles or soft tissue, giving rise to characteristic referred pain. In migraine condition, there is controversy over whether TrPs reflects peripheral or central phenomenon. Surface activation changes in neck and extensor muscles during craniocervical movements depend on the existence of active TrPs in patients with migraine.[36] Luedtke et al.[37] evaluated referred pain over the upper cervical spine by activating it using a palpation technique in 179 patients with migraine and in 73 age- and gender-matched healthy controls. They found that 89% of all patients with migraine had some sort of pain (local pain in 42% and head referred pain in 47%) during a sustained pressure test compared to healthy controls.[38] In other studies, patients with migraine have

Table 2. Assessment of related cervical disability in migraine.

	Type of headache	Mean age (range)	Number	Assessment	Finding results
Carvalho et al.[10]	EM and CM	EM: 37 ± 10 CM: 39 ± 9	EM: 91 CM: 34	Cervical range of motion (CROM) Neck Disability Index (NDI)	Disability was positively and moderately correlated to pain evoked during CROM in both groups. Severe disability causing by neck pain was related with 7.6-fold risk of developing CM.
Yu et al.[21]	EM with neck pain EM without neck pain	EM with neck pain: 34.76 ± 8.04 EM without neck pain: 34.26 ± 9.39	EM with neck pain: 50 EM without neck pain: 50	NDI Von Frey hairs (mechanical pain threshold) on the forehead (V1) and the posterior neck (C2 and C3) Pericranial muscle tenderness score	There were no significant differences in pain intensity, migraine disability, duration or frequency of headache between EM with and without neck pain. In compared with EM without neck pain, those with neck pain had higher neck tenderness and higher cephalic tenderness scores.
Ferracini et al.[22]	M and CTRLs	M: 34 ± 11 CTRLs: 34 ± 12	M: 50 CTRLs: 50	Four angles (high cervical angle (HCA), low cervical angle, atlas plane angle and cervical lordosis Cobb angle), and four distances (anterior translation distance, C0–C1 distance, C2–C7 posterior translation and hyoid triangle) by digitalised radiographs	Patients with migraine exhibited a smaller anterior translation distance and hyoid triangle than healthy controls. That means the exhibition of straightening on cervical lordosis curvature in migraine patients.
Florencio et al.[23]	EM and CM	EM: 36.8 ± 10.7 CM: 38.7 ± 10.2	EM: 104 CM: 65	NDI	Any cervical disability was found in 69% of episodic migraine and 92% in chronic migraine. Time since episodic or chronic migraine onset significantly influenced the model, but not age and headache intensity.
Gonçalves et al.[24]	M	18–55	32	NDI Pressure pain thresholds (PPTs) over the sternocleidomastoid, upper trapezius and suboccipital muscles	Moderate negative correlations between NDI and PPTs were shown for all cervical muscles (the sternocleidomastoid, upper trapezius and suboccipital muscles).
Ferracini et al.[27]	EM, CM and CTRLs	EM: 41 ± 12 CM: 44 ± 13 CTRLs: 44 ± 11	EM: 55 CM: 16 CTRLs: 22	CROM Cervical flexion-rotation test (CFRT) Passive accessory intervertebral motion (PAIVM) JPSE test Cranio-vertebral (CV) and cervical lordosis angles	In both migraine groups, the flexion-rotation test showed significant differences, suggesting that upper cervical spine mobility was limited compared to control. There was no difference between episodic migraine and chronic migraine.
Oliveira-Souza et al.[28]	EM CM CTRLs	EM: 35.4 (30.7–39.4) CM: 35.1 (31.8–38.9) CTRLs: 32 (27.8–36.2)	EM: 30 CM: 25 CTRLs:30	CROM Flexion rotation test ND)	In both migraine group, upper cervical range of motion was lower than control group. Reduction in mobility was influenced by migraine frequency and disability-related neck pain.

(Continued)

Table 2. (Continued)

	Type of headache	Mean age (range)	Number	Assessment	Finding results
Vernon et al.[29]	MCH and CM	18–55	MCH: 19 CM: 28	Standardized headache history morphological assessment (plain film and dynamic spinal X-rays) Motion palpation and pressure algometry	84% of CM and MCH subjects exhibited at least two major fixations from C0 to C2 on motion palpation. 92% of CM and 85% of MCH subjects had at least one tender point in the upper cervical region, which were mid-cervical (C2–C3), lateral and suboccipital region.
Tali et al.[30]	EM and CTRLs	EM: 24.95 ± 1.79 CTRLs: 25.65 ± 1.42	EM: 20 CTRLs: 20	Active neck ROM Presence of MTrPs Cervical facet joint mobility Forward head posture (FHP)	In EM, significant prevalence of cervical facet joints stiffness in Occiput–C1 and C1–C2, but not in other segments, were found.
Ferracini et al.[31]	M and CTRLs	M: 32 ± 11.3 CTRLs: 33 ± 12.6	M: 33 CTRLs: 33	HCA Vertical distance (C0–C1) CV angle	Migraine patients did not exhibit FHP compared to controls. Rather, weak association between the frequency of migraine attacks and variation in the HCA was found.
Horwitz and Stewart[32]	PMM and CTRLs	21–45	PMM: 40 CM: 46	CROM Flexion and rotation tests Muscle-length test Trigger points (in bilateral trapezius, sternocleidomastoid muscle) Neural mobility Segmental cervical joint movement assessment	In the migraine group, neck stiffness and neck pain were reported, compared to the control group. In addition to reduced muscle length, especially in trapezius, sternocleidomastoid and suboccipital muscles, increased pain response on muscle stretch of levator scapulae, trapezius, sternocleidomastoid and suboccipital muscles were found. There was greater C4–C6 pain reported on the VAS in the migraine group than in the control group. Also increased cervical stiffness in C5 and C7 was shown.
Florencio et al.[33]	EM, CM and CTRLs	EM: 33 CM: 34 CTRLs: 31	EM: 31 CM: 21 CTRLs: 31	Cervical flexion, extension and bilateral lateral flexion strength Measurement of surface electromyography (EMG) from sternocleidomastoid, anterior scalene and splenius capitis muscles during maximal isometric voluntary contraction (MIVC)	Patients with chronic migraine showed lower cervical extensibility and spent significantly longer time to generate peak force between cervical flexion and left lateral flexion. Antagonist muscle coactivity of the splenius capitis muscle during cervical flexion in both migraine groups were significantly higher than health controls. Cervical extension peak force was moderately associated with the migraine frequency, neck pain frequency and pain intensity.

(Continued)

Table 2. (Continued)

	Type of headache	Mean age (range)	Number	Assessment	Finding results
Tolentino et al.[34]	M	18–55	70	NDI Maximum voluntary contraction (MVC) during flexion, extension and lateral flexion	Neck extensor strength was negatively correlated with all clinical variables, while lateral flexor strength was negatively correlated with headache frequency, neck pain intensity and neck-related disability. In addition, flexor strength also correlated negatively with neck pain intensity and related disability. Neck extensor and lateral flexor strength variability could be a predictor for headache.
Florencio et al.[35]	EM CM CTRLs	EM: 42 (38–46) CM: 44 (37–51) CTRLs: 44 (39–49)	EM: 52 CM: 16 CTRLs: 23	CV angle Cervical lordosis angle Surface electromyography signals record from sternocleidomastoid, anterior scalene, splenius capitis and upper trapezius muscles during performance of the cranio-cervical flexion test (CCFT)	In both migraine groups, splenius capitis muscle activity significantly increased at the last stage of CCFT compared with controls. In chronic migraine, FHP was moderately correlated with an increased in electrical activity of the upper trapezius and splenius muscle during the performance of the CCFT.
Fernández-De-Las-Peñas et al.[38]	UM and CTRLs	UM: 33 ± 10 (17–57) CTRLs: 30 ± 8 (19–55)	UM: 20 CTRLs: 20	CV angle CROM Trigger points (in the upper trapezius, sternocleidomastoid, temporalis and suboccipital muscles)	Neck mobility in migraine subjects was less than in controls only for extension and the total range of motion in flexion/extension. Active TrPs were mostly located ipsilateral to migraine headaches.

MTrPs: myofascial trigger points; EM: episodic migraine; CM: chronic migraine; M: migraine; CTRLs: controls; UM: unilateral migraine; MCH: muscle contraction headache (tension-type); PMM: perimenstrual migraine.

been shown to present a significantly higher number of active myofascial TrPs in the cervical muscles (especially in the upper trapezius,[38,39] sternocleidomastoid,[38] temporalis[38,40] and suboccipital[38,40] muscles) compared to their healthy (non-migraine) counterparts. In a study investigating the clinical interdependency between active myofascial TrPs and migraine in children below 18 years of age, manual pressure on the TrPs in the trapezius muscle led to continuing headache after the test in children with migraine (especially in those above 12 years of age), but not in healthy controls.[41] Active TrPs may contribute to cervical disabilities and may facilitate the onset of migraine.[42] On occurrence of unilateral migraines, Fernández-De-Las-Peñas et al.[38] reported a large number of active TrPs and low PPTs[43] for the upper trapezius muscle on the dominant side. Moreover, Boquet et al.[44] found ipsilateral TrPs in the upper neck in patients with unilateral headaches even during pain-free periods (Table 3).

Meta-analysis regarding assessment of cervical impairment in migraine

Two major meta-analyses performed with assessment of cervical impairment in migraine were reviewed. Liang et al.[45] researched the evidence for cervical musculoskeletal impairments in both migraine and tension type headache as compared with non-headache or cervicogenic headache group. In this study, a significant reduction of CROM in flexion, extension and lateral flexion were shown in migraine patients compared to controls in meta-analyses. However, there were no significant differences of cervical muscle strength in flexion and extension, sternocleidomastoid activity during final stage of CCFT, joint position error (JPE) and FHP in between groups. Although the evaluation was limited due to the few studies, greater FHP and reduced CROM were only shown in the subgroup analyses of EM. Meanwhile, Szikszay et al.[46] reported that all of these factors showed significant differences in migraine compared to controls: CROM in extension and rotation, FRT, strength testing of cervical extensors, PPTs at the temporalis, sternocleidomastoid and upper trapezius muscles, and cervicovertebral angle and cervical lordosis in standing position as a measure of FHP.

Discussion

Comprehensive assessment regarding the involvement of cervical disabilities in patients with migraine

Studies investigating self-reports and cervical disability assessments have found a high correlation between subjective neck pain and migraine attacks. Laimi et al.[47] reported that the frequency of neck pain was associated with the presence of intractable headache (ineffective response to analgesics). Chronic neck pain is not only associated with more frequent migraine attacks, but is also associated with increased headache intensity.

Cervical disability could be triggered by not only neck pain but also by stiff muscle. Since patients often have an accurate description of the pain in their neck, a rough location of neck pain can be detected through self-report assessment. However, some patients are unaware of the exact whereabouts of the stiff muscle that is causing the stiffness in the neck. Therefore, self-report is not an adequate assessment to identify cervical disability associated with migraine.

The main question is whether neck pain or an associated cervical disability can act as an initial factor leading to migraine attacks, that is, whether those can be considered nociceptive stimuli or whether they are concomitant referred pains. If cervical impairments cause attacks, then this will be regarded as essential information for effective treatments, and studies should clarify the timing of the pathophysiological events of migraine attacks.

First, few studies have addressed the timing of neck pain in patients with migraine, but between 54% and 93.8% of the patients presented neck pain simultaneously with headaches.[5,16–18] In addition, 27.1–70% of the patients developed continuous or emerging neck pain after the migraine attack.[16,18] Importantly, 31.3–70% of the patients developed neck pain before the onset of migraine, suggesting that neck pain may act as a trigger of migraine.[5,16,18] In a study focusing on EM, 70% of the patients presented neck pain before the onset of the migraine attack.[18] However, neck pain can be one of migraine symptoms. A causal relationship to migraine cannot be determined solely from neck pain information.

Second, ipsilateral pain or muscle tenderness in the cervical region in patients with migraine supports the hypothesis that focal nociception stimuli from the neck can trigger attacks. In fact, more TrPs have been detected on the ipsilateral upper cervical muscles than on the other side in patients with unilateral migraines.[38,44] This suggests that active TrPs are a peripheral source of nociceptive stimuli contributing to propagation and widespread pain.[48,49] TrPs are localized tender or painful spots initiated and activated by peripheral sensitization, which depends on nociceptive input from primary muscle pain induced by repetitive muscle overuse (acute muscle overload).[50,51] In addition, prolonged or repetitive peripheral nociceptive input from myofascial tissues may induce more active stimuli into supraspinal neurons, resulting in central sensitization.

Moreover, biochemical substances such as bradykinin, serotonin, prostaglandins and substance P, released from damaged muscles or from active TrPs, activate nociceptors.[52] It was found in some research

Table 3. Assessment of trigger points in migraine.

	Type of headache	Mean age (range)	Number	Assessment	Finding results
Ferracini et al.[31]	M	34.1	50	MTrP in masseter, suboccipital, temporalis, masseter, suboccipital, sternocleidomastoid, upper trapezius and splenius capitis muscles. Craniocervical posture	Migraine subjects showed significantly active and latent TrP in all the muscles, especially in the suboccipital, upper trapezius, sternocleidomastoid and temporal muscle. The higher number of active TrPs was positively associated with a reduction in cervical lordosis.
Florencio et al.[36]	M	42 ± 12	70: F	Active MTrPs in the sternocleidomastoid, upper trapezius and splenius capitis muscle. Recording surface EMG on superficial flexor and extensor muscles bilaterally as subjects performed a graded task of cranio-cervical flexion (CCF)	Active TrPs in the cervical muscles altered activation of superficial neck and extensor muscles during low-load, isometric CCF contractions in migraine patients.
Luedtke et al.[37]	M and CTRLs	M: 40 ± 15 CTRLS: 40 ± 13	M: 179 CTRLs: 73	Simple palpation, combination of oscillating movements and sustained pressure over the upper cervical spine.	The combination of both assessments (palpation and continuous pressure) provides high sensitivity and specificity for migraine. In migraine patients, response to palpation of the upper cervical spine could show a migraine subtype
Fernández-De-Las-Peñas et al.[38]	UM and CTRLs	UM: 33 ± 10 (17–57) CTRLs: 30 ± 8 (19–55)	UM: 20 CTRLs: 20	MTrPs in upper trapezius, sternocleidomastoid, temporalis and suboccipital muscles. Cranio-vertebral angle CROM	Active TrPs were mostly located ipsilateral to migraine headaches. Migraine subjects showed a smaller cranio-vertebral angle than controls, indicating presence of a greater FHP
Palacios-Ceña et al.[39]	EM	40 (37–43)	95	Active and latent TrPs in the temporalis, masseter, suboccipital, sternocleidomastoid, upper trapezius and splenius capitis muscles. Pressure pain thresholds (PPTs) over the trigeminal area (i.e. temporalis muscle), extratrigeminal (i.e. C5/C6 zygapophyseal joint) and a distant pain-free point (i.e. tibialis anterior muscle).	Active TrPs in the temporalis and upper trapezius muscles were the most prevalent. The number of active, but not latent, TrPs was significantly and negatively associated with PPTs. Active TrPs could contribute to sensitization processes in migraines
Calandre et al.[40]	M and CTRLs	M: 38.5 ± 13.5 (15–75) CTRLS: 41.4 ± 16.8 (21–83)	M: 98 CTRLs: 32	Manual palpitation of the scalp, in the frontal, temporal, occipital, suboccipital area and superior trapezius in the neck.	Trigger points were found in 93.9% of migraine patients, while 29% of controls. The number of individual trigger points was identified to be related with both the frequency of migraine attacks and the duration of pain.
Landgraf et al.[41]	M	14.5 (6.3–17.8)	26	Trigger point PPTs in the trapezius muscle and recording the occurrence and duration of induced headache.	Manual pressure to trigger points in the trapezius muscle resulted in persistent headache even after termination. This study supports the association of a trigemino-cervical-complex in the pathophysiology of migraine.
Ferracini et al.[42]	EM and CM	37 ± 12 (18–60)	EM: 98 CM: 45	MTrP in temporalis, masseter, suboccipital, sternocleidomastoid, upper trapezius and splenius capitis muscles. Migraine Disability Assessment Scale (MIDAS) questionnaire.	No significant difference was in the total number of MTrPs between two groups. Active MTrPs in the temporalis and masseter muscle were most prevalent in both groups. The number of MTrPs did not correlate with migraine related disability nor migraine features.

M: migraine; CTRLs: controls; UM: unilateral migraine; EM: episodic migraine; CM: chronic migraine.

investigating brain activity by TrP stimulation that some brain areas, including the somatosensory cortex, the inferior parietal cortex and the mid and anterior insula, were activated, suggesting induced central sensitization by TrPs stimulation.[53,54] Therefore, multiple or prolonged TrPs propagate pain associated with central sensitization. Active TrPs in the upper cervical muscle seem to be linked to both peripheral and central sensitization, and active or continuous peripheral nociceptive stimuli initiate trigeminal nerve nucleus caudalis activation, inducing central sensitization.[55] In fact, TrPs anaesthetic injections into neck muscles rapidly reduce scalp palpation and facial tenderness that are associated with the symptoms of migraine. This can be considered evidence of reduced central sensitization through relieving of peripheral nociceptive stimuli.[56]

However, TrPs or pericranial muscle tenderness could be reflecting central hypersensitivity. Increased pericranial muscle tenderness has been detected during attacks and even during pain-free periods in patients with migraine.[57–59] In studies of cervicogenic headaches, higher pericranial muscle tenderness scores were found on the pain side, suggesting the presence of focal cervical nociceptive factors.[60,61] In similar reports on patients with unilateral migraines, Fernández-De-Las-Peñas et al.[62] reported that the PPTs levels and muscle tenderness scores were negatively correlated with clinical pain in the sternocleidomastoid, suboccipital, temporalis and upper trapezius[43] muscles, on the pain side. Similarly, the increased muscle tenderness may represent localized central sensitization in the activated unilateral signalling pathway in migraines.[63,64] Thus, TrPs and pericranial muscle tenderness could reflect both peripheral and central sensitization activated in patients with migraine.

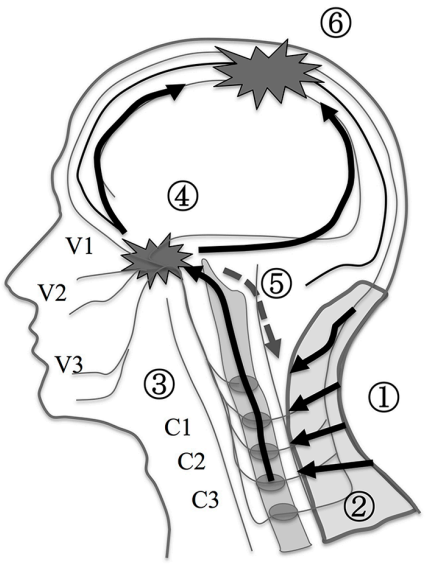
In meta-analyses reported by Liang et al.,[45] there were no differences reported between migraine and controls in terms of FHP, strength of cervical muscles, craniocervical flexion test and joint position, except for a slight difference in CROM. Regarding this results, Liang et al. speculated that the failure to exclude coexisting idiopathic cervical disorders like cervicogenic headache could reflect the methodological difficulties to detect such disorders on symptomatic bias. On the contrary, the CROM, flexion rotation test, PPTs and FHP were shown to be useful in identifying the difference between migraine and controls in another meta-analysis.[46] Therefore, based on understanding so far, several combinations of physical assessment could be useful for cervical disorder contributing to migraine instead of a single evaluation.

In terms of data collection, the selection of the study patients is important because the pathophysiology is dependent on the type of migraine. Both research works in meta-analyses could not evaluate in between migraine types due to the limited number of studies. In patients with CM, peripheral and central sensitization factors may play a role. Therefore, in comprehensive assessment, selecting patients with a simple condition like EM can eliminate confounding factors as much as possible. In addition, a combination of physical assessments could provide further supporting or negative evidence to thoroughly evaluate cervical disability in patients with migraine.

Anatomical association of migraine with the TCC

The association between neck pain or impairment and migraine can be inferred from anatomical features. The convergence of afferent neurons from the upper cervical nerves (C1–C3) and from the trigeminal nerve to the TCC can account for the interaction between cervical and trigeminal pains. In human studies, stimulation of the supraorbital trigeminal nerve branch has proven the presence of a trigeminal cervical reflex response, which activates the posterior cervical muscle in healthy subjects.[65] In addition, direct stimulation of the great occipital nerve, a C2 afferent nerve, and of the dura mater leads to the activation of the secondary trigeminal afferent nerves.[66,67] The TCC is thought to facilitate central sensitization by nociceptive stimuli from the peripheral myofascial tissues. From studies on myofascial TrPs and cervical disability in patients with migraine, restricted movement or stiffness of C1–C3 joint segments and tenderness of the sternocleidomastoid, upper trapezius, suboccipital and splenius muscles, which are innervated by upper cervical nerves (C1–C3), may be explained by TCC activation (peripheral stimulation), which results in central stimulation (Figure 2).

Active myofascial TrPs promote nociceptive peripheral sensitization, thereby exciting the central nervous system. Therefore, repeated abnormal sensory afferent stimuli from cervical structures (including the dura, fascia and muscles) seem to reach the trigeminocervical nucleus, leading to central hypersensitivity. In patients with migraine, trigeminal pathways exhibit hyperexcitability via the TCC during pain-free periods.[68] Moreover, the activation or sensitization of peripheral sensory afferents may play a role in the initiation or aggravation of migraine attacks.[69] Thus, the involvement of persistent peripheral stimuli via TCC may lead to central sensitization and the onset of migraine. Elliot and Egilius[70] also concluded that cervical musculoskeletal structures contribute to the activation of the trigeminovascular system through nociceptive stimuli triggered by muscle stiffness or tenderness in patients with migraine. Moreover, Akerman and Romero-Reyes[71] suggested in their review that the TCC may be an anatomical target for future treatments to replace the current cranial vascular targets.



① Cervical musculoskeletal impairment induced by forward head position, work-related and psychological stresses and vision overuse.
② Nociceptive stimuli caused by cervical musculoskeletal impairments (peripheral sensitization).
③ Activation of the trigeminocervical complex (TCC).
④ Hyperactivation of trigeminal nerves (central sensitization).
⑤ Impairment of diffuse nociceptive inhibitory control (DNIC).
⑥ Migraine attack

Figure 2. Schema of a possible migraine mechanism.

Cervical impairment and inhibition of diffuse noxious inhibitory control

Diffuse noxious inhibitory control (DNIC) produces analgesic effects by suppressing dorsal horn nociceptive neurons through descending antinociceptive regulation.[72] The DNIC system is activated in response to nociceptive stimuli, and it further corresponds to persistent pain. Inadequate inhibition has been detected in patients with chronic pain. The efficiency of DNIC has been shown to be lower in patients with chronic pain (e.g. temporomandibular disorder (TMD), fibromyalgia (FM), migraine and TTH) than in normal controls.[73–76] This low DNIC response is related to an extended history of pain.[77] Moreover, a gender difference has been shown regarding DNIC pain regulation: Granot et al.[78] indicated a greater endogenous analgesia response in men than in women after performing a contact heat pain test. Similarly, Ge et al.[79] asserted gender differences in terms of DNIC characteristics, in which men tolerate more pain than women, after repeated bilateral injections of hypertonic versus isotonic saline into both trapezius muscles. This evidence as well as the differences in neck muscle strength may explain why women suffer headache attacks more frequently than men. Shahidi et al.[80] reported that the descending pain modulation impairment is more pronounced in patients with chronic musculoskeletal pain than in those without pain, suggesting that patients with chronic musculoskeletal pain have a higher risk of developing chronic neck pain.[81] In fact, in patients with migraine, induced central sensitization and decreased DNIC sensitivity by continuous nociceptive inputs from the peripheral fascias cause chronicity.[82] As described above, DNIC impairment due to chronic cervical musculoskeletal disorders could be a trigger cascade of neurophysiological events implicating in migraine attack.

Conclusion

Studies focusing on the association between migraine and cervical disability have been increased. However, these data have not yet provided sufficient evidence that the presence of cervical disability is a direct source of migraine. Morphological and anatomical factors suggest that repeated abnormal afferent sensory stimuli from cervical structures may initiate headaches. In migraine, cervical impairments should not be ignored, and further research is needed to explore the link between migraine symptoms and cervical disability.

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References

1. Sjaastad O, Saunte C, Hovdahl H, et al. 'Cervicogenic' headache. An hypothesis. *Cephalalgia* 1983; 3: 249–256.

2. Sjaastad O. Cervicogenic headache: the controversial headache. *Clin Neurol Neurosurg* 1992; 94(Suppl.): S147–S149.
3. Amiri M, Jull G, Bullock-Saxton J, et al. Cervical musculoskeletal impairment in frequent intermittent headache. Part 2: subjects with concurrent headache types. *Cephalalgia* 2007; 27(8): 891–898.
4. Bakal DA and Kaganov JA. Muscle contraction and migraine headache: psychophysiologic comparison. *Headache* 1997; 17: 208–215.
5. Blau JN and MacGregor EA. Migraine and the neck. *Headache* 1994; 34: 88–90.
6. Kaniecki RG. Migraine and tension-type headache: an assessment of challenges in diagnosis. *Neurology* 2002; 58(9 Suppl. 6): S15–S20.
7. Tfelt-Hansen P, Lous I and Olesen J. Prevalence and significance of muscle tenderness during common migraine attacks. *Headache* 1981; 21(2): 49–54.
8. Ford S, Calhoun A, Kahn K, et al. Predictors of disability in migraineurs referred to a tertiary clinic: neck pain, headache characteristics, and coping behaviors. *Headache* 2008; 48(4): 523–528.
9. Calhoun AH, Ford S and Pruitt AP. Presence of neck pain may delay migraine treatment. *Postgrad Med* 2011; 123(2): 163–168.
10. Carvalho GF, Chaves TC, Gonçalves MC, et al. Comparison between neck pain disability and cervical range of motion in patients with episodic and chronic migraine: a cross-sectional study. *J Manipulative Physiol Ther* 2014; 37(9): 641–646.
11. Viana M, Sances G, Terrazzino S, et al. When cervical pain is actually migraine: an observational study in 207 patients. *Cephalalgia* 2018; 38(2): 383–388.
12. Ashina S, Bendtsen L, Lyngberg AC, et al. Prevalence of neck pain in migraine and tension-type headache: a population study. *Cephalalgia* 2015; 35(3): 211–219.
13. Blaschek A, Milde-Busch A, Straube A, et al. Self-reported muscle pain in adolescents with migraine and tension-type headache. *Cephalalgia* 2012; 32: 241–249.
14. Blaschek A, Decke S, Albers L, et al. Self-reported neck pain is associated with migraine but not with tension-type headache in adolescents. *Cephalalgia* 2014; 34: 895–903.
15. Krøll LS, Hammarlund CS, Westergaard ML, et al. Level of physical activity, well-being, stress and self-rated health in persons with migraine and co-existing tension-type headache and neck pain. *J Headache Pain* 2017; 18(1): 46.
16. Pradhan S and Choudhury SS. Clinical characterization of neck pain in migraine. *Neurol India* 2018; 66(2): 377–384.
17. Özer G and Benlier N. Neck pain: is it part of a migraine attack or a trigger before a migraine attack? *Acta Neurol Belg* 2018; 120: 289–293.
18. Lampl C, Rudoloh M, Deligianni CI, et al. Neck pain in episodic migraine: premonitory symptom or part of the attack? *J Headache Pain* 2015; 16: 556.
19. Calhoun AH, Ford S, Millen C, et al. The prevalence of neck pain in migraine. *Headache* 2010; 50: 1273–1277.
20. Landgraf MN, Von Kries R, Heinen F, et al. Self-reported neck and shoulder pain in adolescents is associated with episodic and chronic migraine. *Cephalalgia* 2016; 36(8): 807–811.
21. Yu Z, Wang R, Ao R, et al. Neck pain in episodic migraine: a cross-sectional study. *J Pain Res* 2019; 12: 1605–1613.
22. Ferracini GN, Chaves TC, Dach F, et al. Analysis of the cranio-cervical curvatures in subjects with migraine with and without neck pain. *Physiotherapy* 2017; 103(4): 392–399.
23. Florencio LL, Chaves TC, Carvalho GF, et al. Neck pain disability is related to the frequency of migraine attacks: a cross-sectional study. *Headache* 2014; 54(7): 1203–1210.
24. Gonçalves MC, Chaves TC, Florencio LL, et al. Is pressure pain sensitivity over the cervical musculature associated with neck disability in individuals with migraine. *J Bodyw Mov Ther* 2015; 19(1): 67–71.
25. Luedtke K, Boissonnault W, Caspersen N, et al. International consensus on the most useful physical examination tests used by physiotherapists for patients with headache: a Delphi study. *Man Ther* 2016; 23: 17–24.
26. Luedtke K, Starke W and May A. Musculoskeletal dysfunction in migraine patients. *Cephalalgia* 2018; 38(5): 865–875.
27. Ferracini GN, Florencio LL, Dach F, et al. Musculoskeletal disorders of the upper cervical spine in women with episodic or chronic migraine. *Eur J Phys Rehabil Med* 2017; 53(3): 342–350.
28. Oliveira-Souza AIS, Florencio LL, Carvalho GF, et al. Reduced flexion rotation test in women with chronic and episodic migraine. *Braz J Phys Ther* 2019; 23(5): 387–394.
29. Vernon H, Steiman I and Hagino C. Cervicogenic dysfunction in muscle contraction headache and migraine: a descriptive study. *J Manipulative Physiol Ther* 1992; 15: 418–429.
30. Tali D, Menahem I, Vered E, et al. Upper cervical mobility, posture and myofascial trigger points in subjects with episodic migraine: case-control study. *J Bodyw Mov Ther* 2014; 18(4): 569–575.
31. Ferracini GN, Chaves TC, Dach F, et al. Relationship between active trigger points and head/neck posture in patients with migraine. *Am J Phys Med Rehabil* 2016; 95(11): 831–839.
32. Horwitz S and Stewart A. An exploratory study to determine the relationship between cervical dysfunction and perimenstrual migraines. *Physiother Can* 2015; 67(1): 30–38.
33. Florencio LL, De Oliveira AS, Carvalho GF, et al. Cervical muscle strength and muscle coactivation during isometric contractions in patients with migraine: a cross-sectional study. *Headache* 2015; 55(10): 1312–1322.
34. Tolentino GA, Bevilaqua-Grossi D, Carvalho GF, et al. Relationship between headaches and neck pain characteristics with neck muscle strength. *J Manipulative Physiol Ther* 2018; 41(8): 650–657.
35. Florencio LL, Ferracni GN, Chaves TC, et al. Analysis of head posture and activation of the cervical neck extensors during a low-load task in women with chronic migraine and healthy participants. *J Manipulative Physiol Ther* 2018; 41(9): 762–770.

36. Florencio LL, Ferracini GN, Chaves TC, et al. Active trigger points in the cervical musculature determine the altered activation of superficial neck and extensor muscles in women with migraine. *Clin J Pain* 2017; 33(3): 238–245.
37. Luedtke K and May A. Stratifying migraine patients based on dynamic pain provocation over the upper cervical spine. *J Headache Pain* 2017; 18: 97.
38. Fernández-De-Las-Peñas C, Cuadrado ML and Pareja JA. Myofascial trigger points, neck mobility and forward head posture in unilateral migraine. *Cephalalgia* 2006; 26(9): 1061–1070.
39. Palacios-Ceña M, Ferracini GN, Florencino LL, et al. The number of active but not latent trigger points associated with widespread pressure pain hypersensitivity in women with episodic migraines. *Pain Med* 2017; 18: 2485–2491.
40. Calandre EP, Hidalgo J, García-Leiva JM, et al. Trigger point evaluation in migraine patients: an indication of peripheral sensitization linked to migraine predisposition. *Eur J Neurol* 2006; 13(3): 244–249.
41. Landgraf MN, Biebl JT, Langhagen T, et al. Children with migraine: provocation of headache via pressure to myofascial trigger points in the trapezius muscle? A prospective controlled observational study. *Eur J Pain* 2018; 22(2): 385–392.
42. Ferracini GN, Florencio LL, Dach F, et al. Myofascial trigger points and migraine-related disability in women with episodic and chronic migraine. *Clin J Pain* 2017; 33(2): 109–115.
43. Fernández-De-Las-Peñas C, Madeleine P, Caminero AB, et al. Generalized neck-shoulder hyperalgesia in chronic tension-type headache and unilateral migraine assessed by pressure pain sensitivity topographical maps of the trapezius muscle. *Cephalalgia* 2010; 30(1): 77–86.
44. Boquet J, Boismare F, Payenneville G, et al. Lateralization of headache: possible role of an upper cervical trigger point. *Cephalalgia* 1989; 9(1): 15–24.
45. Liang Z, Galea O, Thomas L, et al. Cervical musculoskeletal impairments in migraine and tension type headache: a systematic review and meta-analysis. *Musculoskelet Sci Pract* 2019; 42: 67–83.
46. Szikszay TM, Hoenick S, von Korn K, et al. Which examination tests detect differences in cervical musculoskeletal impairments in people with migraine? a systematic review and meta-analysis. *Phys Ther* 2019; 99(5): 549–569.
47. Laimi K, Salminen JJ, Metsähonkala L, et al. Characteristics of neck pain associated with adolescent headache. *Cephalalgia* 2007; 27(11): 1244–1254.
48. Fernández-De-Las-Peñas C and Dommerholt J. Myofascial trigger points: peripheral or central phenomenon? *Curr Rheumatol Rep* 2014; 16: 395.
49. Wang C, Ge HY, Ibarra JM, et al. Spatial pain propagation over time following painful glutamate activation of latent myofascial trigger points in humans. *J Pain* 2012; 13(6): 537–545.
50. Arendt-Nielsen L and Svensson P. Referred muscle pain: basic and clinical findings. *Clin J Pain* 2001; 17(1): 11–19.
51. Rubin TK, Gandevia SC, Henderson LA, et al. Effects of intramuscular anesthesia on the expression of primary and referred pain induced by intramuscular injection of hypertonic saline. *J Pain* 2009; 10(8): 829–835.
52. Gerwin RD, Dommerholt J and Shah JP. An expansion of Simons' integrated hypothesis of trigger point formation. *Curr Pain Headache Rep* 2004; 8(6): 468–475.
53. Niddam DM. Brain manifestation and modulation of pain from myofascial trigger points. *Curr Pain Headache Rep* 2009; 13(5): 370–375.
54. Niddam DM, Chan RC, Lee SH, et al. Central representation of hyperalgesia from myofascial trigger point. *NeuroImage* 2008; 39(3): 1299–1306.
55. Fernández-De-Las-Peñas C, Cuadrado ML, Arendt-Nielsen L, et al. Myofascial trigger points and sensitization: an updated pain model for tension-type headache. *Cephalalgia* 2007; 27(5): 383–393.
56. Mellick GA and Mellick LB. Regional head and face pain relief following lower cervical intramuscular anesthetic injection. *Headache* 2003; 43(10): 1109–1111.
57. Göbel H, Weigle L, Kropp P, et al. Pain sensitivity and pain reactivity of pericranial muscles in migraine and tension-type headache. *Cephalalgia* 1992; 12(3): 142–151.
58. Jensen R, Rasmussen BK, Pedersen B, et al. Muscle tenderness and pressure pain thresholds in headache. *Pain* 1993; 52(2): 193–199.
59. Jensen R, Tuxen C and Olesen J. Pericranial muscle tenderness and pressure-pain threshold in the temporal region during common migraine. *Pain* 1988; 35(1): 65–70.
60. Knackstedt H, Bansevicius D, Aaseth K, et al. Cervicogenic headache in the general population: the Akershus study of chronic headache. *Cephalalgia* 2010; 30(12): 1468–1476.
61. Sjaastad O. Cervicogenic headache: comparison with migraine without aura: the Vaga study. *Cephalalgia* 2008; 28: 18–20.
62. Fernández-De-Las-Peñas C, Cuadrado ML, Arendt-Nielsen L, et al. Side-to-side differences in pressure pain thresholds and pericranial muscle tenderness in strictly unilateral migraine. *Eur J Neurol* 2008; 15(2): 162–168.
63. Burstein R. Deconstructing migraine headache into peripheral and central sensitization. *Pain* 2001; 89(2–3): 107–110.
64. Burstein R, Jakubowski M, Garcia-Nicas E, et al. Thalamic sensitization transforms localized pain into widespread allodynia. *Ann Neurol* 2010; 68(1): 81–91.
65. Serrao M, Coppola G, Di Lorenzo C, et al. Nociceptive trigeminocervical reflexes in healthy subjects. *Clin Neurophysiol* 2010; 121(9): 1563–1568.
66. Bartsch T and Goadsby PJ. Stimulation of the greater occipital nerve induces increased central excitability of dural afferent input. *Brain* 2002; 125(Pt. 7): 1496–1509.
67. Bartsch T and Goadsby PJ. Increased responses in trigeminocervical nociceptive neurons to cervical input after stimulation of the dura mater. *Brain* 2003; 126(Pt. 8): 1801–1813.
68. Serrao M, Perrotta A, Bartolo M, et al. Enhanced trigemino-cervical-spinal reflex recovery cycle in pain-free migraineurs. *Headache* 2005; 45(8): 1061–1068.
69. Bendtsen L. Sensitization: its role in primary headache. *Curr Opin Investig Drugs* 2002; 3(3): 449–453.

70. Elliot S and Spierings EH. Cervical muscles in the pathogenesis of migraine headache. *J Headache Pain* 2004; 5: 12–14.
71. Akerman S and Romero-Reyes M. Insights into the pharmacological targeting of the trigeminocervical complex in the context of treatments of migraine. *Expert Rev Neurother* 2013; 13(9): 1041–1059.
72. Le Bars D. The whole body receptive field of dorsal horn multireceptive neurons. *Brain Res Brain Res Rev* 2002; 40(1–3): 29–44.
73. Maixner W, Fillingim R, Booker D, et al. Sensitivity of patients with painful temporomandibular disorders to experimentally evoked pain. *Pain* 1995; 63: 341–351.
74. Kosek E and Hansson P. Modulatory influence on somatosensory perception from vibration and heterotopic noxious conditioning stimulation (HNCS) in fibromyalgia patients and healthy subjects. *Pain* 1997; 70(1): 41–51.
75. Pielsticker A, Haag G, Zaudig M, et al. Impairment of pain inhibition in chronic tension-type headache. *Pain* 2005; 118(1–2): 215–223.
76. Sandrini G, Rossi P, Milanov I, et al. Abnormal modulatory influence of diffuse noxious inhibitory controls in migraine and chronic tension-type headache patients. *Cephalalgia* 2006; 26(7): 782–789.
77. Edwards RR, Ness TJ, Weigent DA, et al. Individual differences in diffuse noxious inhibitory controls (DNIC): association with clinical variables. *Pain* 2003; 106(3): 427–437.
78. Granot M, Weissman-Fogel I, Crispel Y, et al. Determinants of endogenous analgesia magnitude in a diffuse noxious inhibitory control (DNIC) paradigm: do conditioning stimulus painfulness, gender and personality variables matter? *Pain* 2008; 136(1–2): 142–149.
79. Ge HY, Madeleine P and Arendt-Nielsen L. Sex differences in temporal characteristics of descending inhibitory control: an evaluation using repeated bilateral experimental induction of muscle pain. *Pain* 2004; 110(1–2): 72–78.
80. Shahidi B, Curran-Everett D and Maluf KS. Psychosocial, physical, and neurophysiological risk factors for chronic neck pain: a prospective inception cohort study. *J Pain* 2015; 16(12): 1288–1299.
81. Shahidi B and Maluf KS. Adaptations in evoked pain sensitivity and conditioned pain modulation after development of chronic neck pain. *Biomed Res Int* 2017; 2017: 8985398.
82. Boyer N, Dallel R, Artola A, et al. General trigeminospinal central sensitization and impaired descending pain inhibitory controls contribute to migraine progression. *Pain* 2014; 155(7): 1196–1205.