



Investigating the Effect of Pain Neurophysiology Education in the Treatment of Cervicogenic Headache: A Randomized Clinical Trial

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Abstract

Background: Cervicogenic headaches that stem from musculoskeletal disorders of the upper cervical spine are among the most common types of chronic headaches. In recent years, physiotherapy has emerged as a potential treatment for this type of headache.

Objectives: Given the emphasis on educational methods such as pain neurophysiology education (PNE) for musculoskeletal pain, the aim of this study is to investigate the effect of PNE in treating cervicogenic headaches.

Methods: This study was a single-blind clinical trial. A sample of 30 participants with cervicogenic headache was divided into two groups using the block method: An experimental group of 15 participants and a control group of 15 participants. Experienced physiotherapists provided conventional physiotherapy for 10 sessions, and the experimental group also received pain neurophysiology education for four additional sessions. Pain severity, disability, and pain catastrophizing information were collected using the visual analog scale, headache disability index, and pain catastrophizing scale, respectively, at the beginning of the study, after the study, and at the one-month follow-up. Statistical analysis was conducted using SPSS software version 22, and the significance level was set at 0.05.

Results: A significant difference was observed in pain intensity assessment at different times ($P < 0.001$), headache disability index ($P = 0.003$), and pain catastrophizing ($P < 0.001$). The time-by-group interaction was significant for pain intensity ($F = 49.051$; $P < 0.001$; $\eta_p^2 = 0.637$) and pain catastrophizing ($F = 25.528$; $P < 0.001$; $\eta_p^2 = 0.477$); however, there was no significant difference in disability ($F = 1.781$; $P = 0.178$; $\eta_p^2 = 0.060$).

Conclusions: Pain neurophysiology education can have a positive effect on pain reduction, as well as the attitude and knowledge of individuals who experience pain in the short term.

Keywords: Cervicogenic Headache, Conventional Physiotherapy, Pain Neurophysiology Education

1. Background

Headache is a common and debilitating condition that affects individuals of all ages, resulting in decreased performance, disruption of quality of life, and a heavy economic burden on society (1). Cervicogenic headaches (CH) were first mentioned in medical literature in 1860 by Hilton; however, the term was coined by Sjaastad in 1983 to describe this type of chronic headache (2). The prevalence of CH in the general population is estimated to be between 0.4% and 2.5%, while in pain management clinics, it can reach up to 20% of patients with chronic headaches (3). The average age of individuals with this disorder is 42.9 years, and it is four times more common

in females than in males (3). Cervicogenic headaches originate from musculoskeletal disorders of the upper cervical spine, and factors such as age, gender, and occupation can influence their prevalence (4). In recent years, physiotherapy has been identified as an effective treatment for this type of headache (4), and the use of educational methods such as pain neurophysiology education (PNE) has been suggested for managing pain associated with musculoskeletal disorders (5).

Pain neurophysiology education, or pain neurophysiology education, involves educating patients about the neurobiology and neurophysiology of pain processing in the nervous system (6, 7). This method has

been used by physiotherapists since 2002 in various countries (8). The complex process of the nervous and brain system is explained in a way that is easily understood by everyone, using methods such as simple images, examples, pamphlets, and books (7, 9). Chronic pain affects sensory processing in the cerebral cortex, and beliefs play a role in modifying the pain experience, which is why psychological therapy is important (9). Pain neurophysiology education can help change inaccurate pain beliefs, which can lead to improved movement ability and reduced fear of movement (10). A 2011 review by Louw et al. found that educating patients about the neurophysiology and neurobiology of pain can have a positive impact on pain, disability, catastrophizing, and physical functioning in chronic musculoskeletal pain (7). Other studies have measured the effect of PNE on fatigue (10), fibromyalgia (11), chronic low back pain (12-15), and chronic neck pain (5, 16-18). Systematic review studies have shown strong evidence for the effectiveness of PNE in reducing pain ratings, disability, anxiety, and stress, as well as improving physical performance and reducing pain catastrophizing in patients with musculoskeletal pain (7, 19, 20).

The discussion about CHs is not solely academic. New analyses show that neck and back pain impose significant economic costs on society and are among the most important factors of disability.

2. Objectives

Considering the lack of studies on the effect of PNE in CHs and based on our findings, the purpose of this study is to investigate the effectiveness of PNE in treating cervicogenic headaches through a clinical trial.

3. Methods

3.1. Study Design

This study was a single-blind, randomized, controlled clinical trial conducted at the Physiotherapy Department of Kashani Hospital in Isfahan city, with data collected between July 2021 and December 2021. The research plan was approved by the Physiotherapy Department of Isfahan Faculty of Rehabilitation Sciences and subsequently submitted to the Ethics Committee of Isfahan University of Medical Sciences to obtain the code of ethics (IR.MUI.RESEARCH.REC.1399.301). The desired protocol was then registered in the Iranian Clinical Trial System (IRCT20200101045970N2).

3.2. Participants

A non-probability simple sampling method was used to select a sample of 30 people among the patients with CHs referred from neurology and physiotherapy clinics affiliated with Isfahan University of Medical Sciences. The sample size was determined based on the confidence level of 95%, the power of the test of 80%, and information ($d = 1.7$, $\sigma = 1.54$) obtained from a previous study (12) using the following formula. The sample size was calculated to be 26 people, with 13 people in each group. Considering the possibility of 4 people attrition, the final sample size was set at 30 people.

$$n = \frac{2 \left(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta} \right)^2 \sigma^2}{d^2} \quad (1)$$

Subjects were selected for the study based on inclusion and exclusion criteria assessed by a neurologist. The inclusion criteria consisted of having neck headaches according to the Sjasstad criteria (2) that caused unilateral head pain without changing direction and radiated to the frontotemporal area, as well as pain intensification with movement or unsuitable neck positions. Other criteria included moderate to severe non-throbbing pain based on the pain intensity scale chart, age between 18 and 60 years, a history of headaches at least once a week for more than 3 months, and being literate and able to write. The exclusion criteria consisted of neck radiculopathy pain, a history of neck trauma, any other cause of neck pain, including osteoarthritis, having received manual therapy or dry needling for neck trigger points within the last 6 months, cognitive disorders, a previous diagnosis of primary headaches such as migraine and tension headache, history of neck or shoulder surgery, and non-cooperation of the patient.

3.3. Randomization and Blinding

After the completion of the questionnaires, the participants were randomly allocated into two groups, an experimental group ($n = 15$) and a control group ($n = 15$), using the block randomization method by a third-party individual who was blinded to the study details. The participant enrollment process is illustrated in Figure 1.

3.4. Procedure

Two trained physiotherapists performed conventional physiotherapy on all patients, both in the experimental and control groups. However, the experimental group also received PNE from one of the researchers (physiotherapists), in addition to conventional physiotherapy.

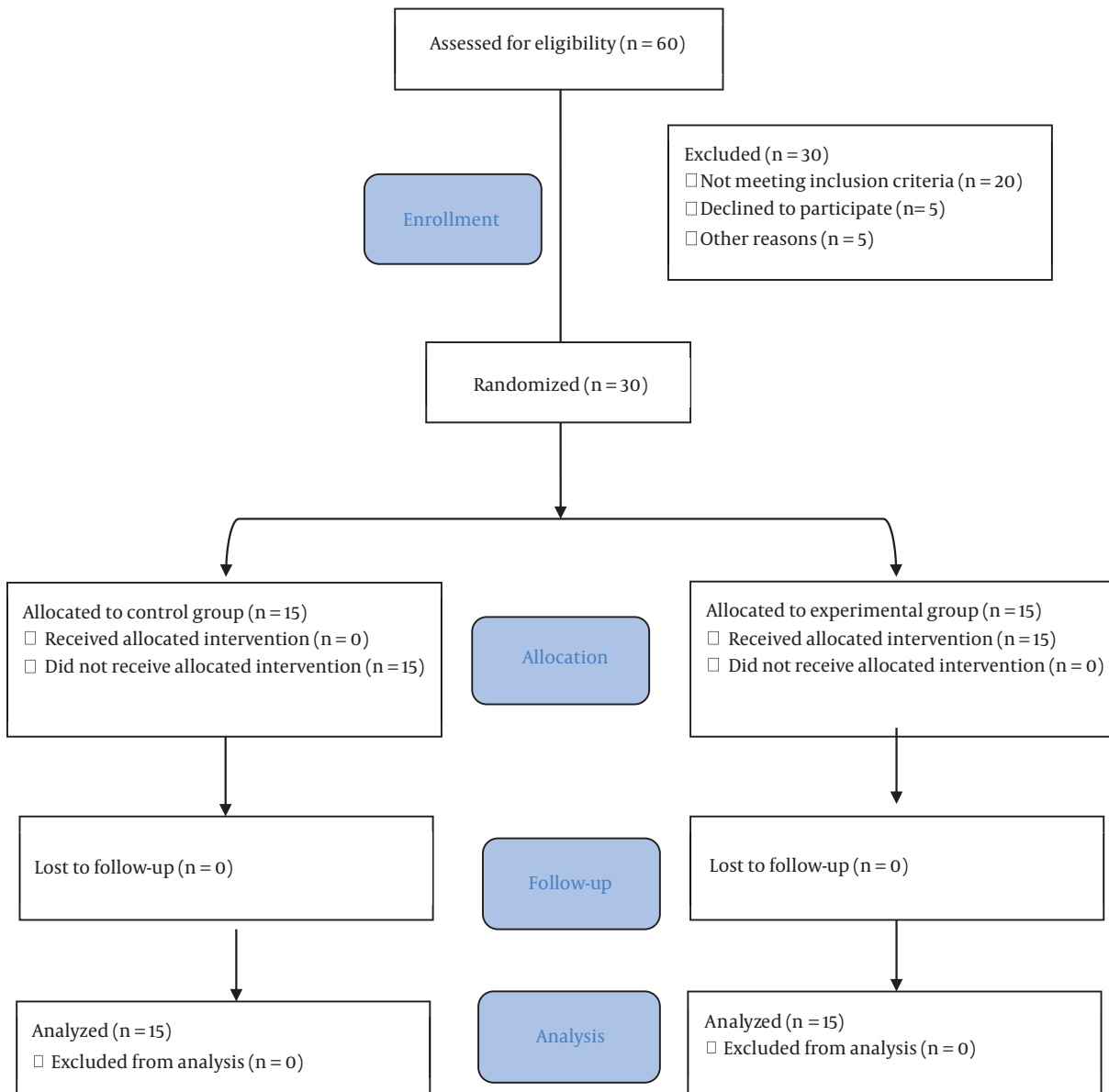


Figure 1. The CONSORT 2010 diagram for attrition of participants

3.4.1. Treatment Method in the PNE Group

In the PNE group, pain transfer methods were taught in simple ways using face-to-face training and pictures. The group sessions consisted of 3 to 5 people and were conducted once a week for four sessions, each lasting 45 - 60 minutes. Pain neurophysiology education was taught using the book "explain pain supercharged" by Butler and Moseley (21). The training focused on providing pain information to reduce fear beliefs and behaviors and

to promote self-efficacy using verbal instructions, charts, and freehand drawings. The training covered topics such as the source of acute pain in the nervous system, the transformation of acute pain into chronic pain, the role of the brain in understanding pain, psychosocial factors that affect pain, and cognitive and behavioral responses related to pain and pain management. The training did not include the anatomy and biomechanics of the cervix. Patients were encouraged to participate interactively in

the educational topics during the sessions.

3.4.2. Treatment Method in Conventional Physiotherapy Group

In this study, a conventional physiotherapy treatment method was used for 10 sessions over 4 weeks. The method involved using conventional transcutaneous electrical nerve stimulation (TENS) for 20 minutes with a frequency of 100 Hz and a duration of 100 microseconds (22). In addition, continuous ultrasound waves with a frequency of 1 MHz and an intensity of 1 w/cm² were applied for 5 minutes on the suboccipital area of the posterior muscles of the upper cervical vertebrae (23). Patients were also taught therapeutic exercises, including active exercises such as chin tucks (24).

3.5. Data Collection Tools and Methods

Measurements related to headaches were taken before and after the treatment sessions and one month after completing the treatment sessions. The data was collected by a person who was completely unaware of the two groups.

In this study, pain intensity data was collected using the visual analog scale (VAS), and information regarding the disability of the patients was gathered using the headache disability index (HDI). The pain catastrophizing scale (PCS) was used to measure the degree of catastrophizing.

3.5.1. Pain Intensity

The intensity of pain was measured using the VAS. This scale consisted of a 10-cm straight line with two endpoints, "no pain" and "most severe pain". The distance between the "no pain" point and the point marked by the patient indicated the intensity of their pain. In the reliability study, the P-values varied from 0.60 to 0.77, and in the validity study, the P-values for VAS pain scores ranged from 0.76 to 0.84 (25).

3.5.2. Headache Disability Index

To evaluate the impact of headaches on daily life, the Persian version of HDI was used. The questionnaire comprised 25 items, and each item was answered with "yes" (score 4), "sometimes" (score 2), or "no" (score 0) based on the patient's experience. The questionnaire also included emotional and functional subscales. The total score ranged from zero to 100, with a higher score indicating greater disability. The validity and reliability of the HDI were assessed by Jabbari et al. (26). The content validity indices were 0.85, 0.99, and 0.97 for simplicity, relevance, and clarity, respectively. The internal consistency reliability was evaluated using Cronbach's alpha, which was found to be 0.91.

3.5.3. Pain Catastrophizing Scale

This scale, created by Sullivan and colleagues, aims to measure various dimensions of pain catastrophizing and its mechanisms. The scale comprises 13 questions with three subscales: Rumination, magnification, and helplessness, all of which evaluate negative thoughts related to pain. Participants rated each question on a scale from zero (never) to 4 (always) to describe 13 different feelings and thoughts related to their pain experience. Lower scores indicate lower levels of catastrophizing (27). In Rahmati et al.'s research, they measured the validity and reliability of the PCS and its subscales (28). Results indicated good internal consistency (alphas ranged from 0.80 to 0.89). Correlation analyses between the PCS and its subscales with measures of pain, interference, disability, depression, anxiety, catastrophizing, positive and negative effects, and pain self-efficacy beliefs support both convergent and divergent validity for the PCS and the two subscales of magnification and rumination/helplessness.

3.6. Data Analysis Method

In this study, the normal distribution of the data was checked using the Shapiro-Wilk test, and the homogeneity of dependent variables was checked using Levene's test. After confirming both, a 2 × 3 mixed model of repeated measures, ANOVA (group × time) with Bonferroni correction post hoc, was conducted. Frequency distribution in the two intervention and control groups was compared using a *t*-test. A P-value < 0.05 was considered statistically significant, and effect size (ES) was calculated using partial eta squared (η_p^2) values. All of the mentioned tests were performed using SPSS software version 22 (SPSS, version 22, SPSS Inc. Chicago, IL, USA).

4. Results

Before testing the research hypotheses, the normality of the variables was confirmed. Each group comprised 12 females and 3 males, and there was no significant difference between the two groups in terms of age ($P = 0.22$) and duration of the disease ($P = 0.86$), as shown in Table 1.

4.1. Pain Intensity

Table 2 shows the pain intensity variables of the study participants. A significant difference was observed in the various stages of pain intensity assessment ($F = 49.051$; $P < 0.001$; $\eta_p^2 = 0.637$). The interaction between time and group ($F = 7.060$; $P = 0.002$; $\eta_p^2 = 0.201$) was significant, but the difference between the groups was not

Table 1. Demographic Characteristics of the Participants

	Experimental (N=15)	Control (N=15)
Age (y)		
26 - 60	46.33 ± 11.13	
28 - 60		41.40 ± 10.37
Duration of disease (mo)		
3 - 60	31.20 ± 25.35	32.80 ± 23.20
Gender		
Male	4	4
Female	11	11
Educational level		
Diploma	6	7
Undergraduate	7	6
Master degree	2	2

statistically significant ($F = 0.305$; $P = 0.585$; $\eta_p^2 = 0.011$). Post hoc analysis in the experimental group revealed a significant difference between pre-treatment and post-treatment ($P < 0.001$), pre-treatment and follow-up ($P < 0.001$), and post-treatment and follow-up ($P < 0.001$). In the control group, there was a significant difference between pre-treatment and follow-up ($P = 0.002$) and post-treatment and follow-up ($P = 0.002$), but no significant difference was observed between pre-treatment and post-treatment ($P = 0.060$).

4.2. Disability

The details of the disability variables of the study participants are given in [Table 2](#).

There was a significant difference in the levels of disability among participants at different assessment stages ($F = 6.653$; $P = 0.003$; $\eta_p^2 = 0.192$). However, the interaction between time and group was not significant ($F = 1.781$; $P = 0.178$; $\eta_p^2 = 0.060$). Additionally, the difference between the experimental and control groups was not statistically significant ($F = 0.517$; $P = 0.478$; $\eta_p^2 = 0.018$). Post-hoc tests in the experimental group revealed a significant difference between before treatment and after follow-up ($P = 0.007$) and between after treatment and after follow-up ($P = 0.007$), but no significant difference between before treatment and after treatment ($P = 0.095$). In the control group, there was no significant difference observed at different measurement times according to post-hoc tests. The details of the disability variables of the study participants are provided in [Table 2](#).

4.3. Pain Catastrophizing

The pain catastrophizing variables for the study participants are presented in [Table 2](#). The analysis revealed a significant difference in pain catastrophizing evaluation across different stages ($F = 25.528$; $P < 0.001$; $\eta_p^2 = 0.477$). The interaction between time and group was also significant ($F = 9.043$; $P < 0.001$; $\eta_p^2 = 0.244$), whereas the difference between the groups was not statistically significant ($F = 0.027$; $P = 0.871$; $\eta_p^2 = 0.001$). Post hoc analysis in the experimental group showed a significant difference between before treatment and after treatment ($P < 0.001$), before treatment and after follow-up ($P < 0.001$), and after treatment and after follow-up ($P < 0.001$). However, post hoc analysis in the control group did not reveal any significant difference between the different measurement times.

5. Discussion

The results of this study indicate that the combination of pain neurophysiology training and conventional physiotherapy leads to a significant improvement in pain intensity, disability, and psychosocial factors compared to conventional physiotherapy alone among patients with CHs. These effects were sustained during a short-term follow-up period of one month.

5.1. Pain Intensity

However, while pain intensity declined in both groups, the combination of pain neurophysiology training and physical therapy produced a more significant improvement at all stages. These results are consistent with previous studies that used PNE alone (29), in combination with other treatments (6, 12, 16, 30), or with exercise therapy (14, 15, 17, 31, 32). Pain is a complex phenomenon, and the authors emphasize that pain perception is often a better indicator of potential harm than actual tissue damage. For topics related to chronic pain rehabilitation, factors such as pain, beliefs, attitudes toward pain, and strategies for managing chronic pain are crucial (33). Pain neurophysiology education is effective in changing a person's understanding and beliefs about pain, a concept often referred to as "reconceptualization" (9). Since neurophysiology training does not specifically focus on tissue damage (such as disc or joint damage) but instead targets pain processing, it may be considered a possible mechanism for reducing the perceived threat and subsequently reducing the patient's perception of pain (34).

Table 2. Variables of the Study Population ^a

Variables	Baseline		P	Post Treatment		P	Follow Up		P
	Experimental (n = 15)	Control (n = 15)		Experimental (n = 15)	Control (n = 15)		Experimental (n = 15)	Control (n = 15)	
VAS	6.80 ± 1.47	5.93 ± 2.02	0.190	3.07 ± 1.39	4.27 ± 1.62	0.038	4.07 ± 2.09	4.67 ± 1.99	0.427
HDI	39.87 ± 13.38	38.13 ± 26.77	0.824	22.93 ± 12.55	32.67 ± 23.86	0.173	29.07 ± 16.78	35.07 ± 23.84	0.432
PCS	29.87 ± 8.21	22.47 ± 12.58	0.067	16.00 ± 7.86	18.13 ± 12.76	0.586	16.27 ± 8.89	19.80 ± 12.14	0.371

Abbreviations: VAS, visual analog scale; HDI, headache disability index; PCS, pain catastrophizing scale.

^a Values are expressed as mean ± SD.

5.2. Disability

Our study findings demonstrate that although the difference between the groups was not significant, the combination of PNE and conventional physical therapy resulted in improved performance, which is consistent with several studies (14, 16, 17, 31). In contrast, Pires et al. reported that PNE combined with aquatic exercises did not offer any advantage over pain neurophysiology training alone in improving patient performance (32). A change in pain perception can alter the perception of received pain, which in turn can affect pain generation and the ability to perform tasks (35). Patients who receive pain neurophysiology education are more likely to develop coping strategies and behaviors that lead to a reduced fear of movement and improved functioning (5). Pain neuroscience education is believed to be a useful strategy to provide people with chronic pain with the knowledge to manage their fear of movement and dependence on disability (9). The cognitive restructuring obtained through pain neuroscience education can lead to changes in the quantity and quality of movement (36).

5.3. Pain Catastrophizing

This study demonstrates that pain neurophysiology training, in combination with conventional physical therapy, resulted in a reduction in pain catastrophizing in patients with CH. These findings are consistent with previous studies on patients with chronic back pain (7, 8, 14, 29), chronic fatigue (10), fibromyalgia (11), lumbar radiculopathy (15), and chronic neck pain (17). However, some studies have failed to identify significant differences between PNE and other treatments in different patient populations (18, 37). The present study also found that PNE increased patients' awareness of the physiopathology of headaches with cervical origin, leading to a change in attitude and a reduction in pain catastrophizing when headaches occur. These results align with the findings of Javdaneh et al.'s study, which reported a significant reduction in pain catastrophizing following pain neuroscience education (17).

The use of PNE is increasing today. Pain neurophysiology education provides a detailed

explanation of the biology and physiology of the nervous system and the brain's processing of pain and pain input. This concept is in direct contrast to common biomedical models that focus solely on tissues and tissue damage. Orthopedic-based professionals such as orthopedic surgeons and physical therapists commonly use models based on anatomy and anatomic pathology to describe pain to their patients. However, these models have not only shown limited effects in reducing pain and disability, but may also increase fear in patients, which in turn can amplify their pain (29, 31).

The primary limitation of this study was the lack of registration of social and demographic factors, such as occupation, social status, and economic status, which could potentially affect the results. As all evaluation criteria were assessed using self-report tools, different social statuses could be among the confounding factors in the results. Therefore, future studies aiming to evaluate outcome measures with objective measurements, such as accelerometers, are needed. Furthermore, due to the COVID-19 pandemic, it was not possible to implement the ideal grouping of participants into different groups.

Future studies should aim to evaluate outcome measures using objective measures, such as an ergometer. Additionally, the effect of the intervention was only evaluated at the 1-month follow-up, making it necessary to investigate the long-term effects of this combined intervention in future studies.

5.4. Conclusions

The use of PNE can have a positive impact on the attitude and knowledge of individuals experiencing pain in the short term. It has been shown to decrease pain and improve the ability of patients with CH. The findings of this study indicate that PNE leads to greater improvements in reducing pain and pain catastrophizing, and to some extent in reducing disability and improving physical performance.

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Footnotes

Authors' Contribution: Conception and design: Ehsan Ghasemi, Seyed Shayan Naji, and Abdolkarim Karimi; obtaining of funding, data collection, data analysis and interpretation, statistical expertise, and final approval of the article: Ehsan Ghasemi; administrative, technical, or logistic support: Ehsan Ghasemi and Seyed Shayan Nnaji; provision of study materials or patients: Mohammad Reza Najafi and Majid Ghasemi; critical revising of the article for important intellectual content: Ehsan Gasemi, Mohammad Reza Najafi, Majid Ghasemi, and Abdolkarim Karimi.

Clinical Trial Registration Code: [IRCT20200101045970N2](https://www.clinicaltrials.gov/ct2/show/study?term=IRCT20200101045970N2).

Conflict of Interests: The authors have no conflicts of interest. Besides, Dr. Ehsan Ghasemi and Dr. Majid Ghasemi are not related.

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References

1. Rezayat A, Yavari M. [Introducing a new category of headache derived from Iranian traditional medicine]. *Journal of Islamic and Iranian Traditional Medicine*. 2014;**4**(4):322-32. Persian.
2. Sjaastad O, Bakketeig LS. Prevalence of cervicogenic headache. Vaga study of headache epidemiology. *Acta Neurol Scand*. 2008;**117**(3):173-80. [PubMed ID: 18031563]. <https://doi.org/10.1111/j.1600-0404.2007.00962.x>.
3. Biondi DM. Cervicogenic headache: a review of diagnostic and treatment strategies. *J Am Osteopath Assoc*. 2005;**105**(4 Suppl 2):16S-22. [PubMed ID: 15928349].
4. Sizer Jr PS, Phelps V, Azevedo E, Haye A, Vaught M. Diagnosis and Management of Cervicogenic Headache. *Pain Pract*. 2005;**5**(3):255-74. <https://doi.org/10.1111/j.1533-2500.2005.05312.x>.
5. Khosrokiani Z, Letafatkar A, Hadadnezhad M, Sokhanguie Y. Comparison the Effect of Pain Neuroscience and Pain Biomechanics Education on Neck Pain and Fear of Movement in Patients with Chronic Nonspecific Neck Pain During the COVID-19 Pandemic. *Pain Ther*. 2022;**11**(2):601-11. [PubMed ID: 35312949]. [PubMed Central ID: PMC8935612]. <https://doi.org/10.1007/s40122-022-00371-3>.
6. Tellez-Garcia M, de-la-Llave-Rincon AI, Salom-Moreno J, Palacios-Cena M, Ortega-Santiago R, Fernandez-de-Las-Penas C. Neuroscience education in addition to trigger point dry needling for the management of patients with mechanical chronic low back pain: A preliminary clinical trial. *J Bodyw Mov Ther*. 2015;**19**(3):464-72. [PubMed ID: 26118519]. <https://doi.org/10.1016/j.jbmt.2014.11.012>.
7. Louw A, Diener I, Butler DS, Puentedura EJ. The effect of neuroscience education on pain, disability, anxiety, and stress in chronic musculoskeletal pain. *Arch Phys Med Rehabil*. 2011;**92**(12):2041-56. [PubMed ID: 22133255]. <https://doi.org/10.1016/j.apmr.2011.07.198>.
8. Clarke CL, Ryan CG, Martin DJ. Pain neurophysiology education for the management of individuals with chronic low back pain: systematic review and meta-analysis. *Man Ther*. 2011;**16**(6):544-9. [PubMed ID: 21705261]. <https://doi.org/10.1016/j.math.2011.05.003>.
9. Fletcher C, Bradnam L, Barr C. The relationship between knowledge of pain neurophysiology and fear avoidance in people with chronic pain: A point in time, observational study. *Physiother Theory Pract*. 2016;**32**(4):271-6. [PubMed ID: 27049810]. <https://doi.org/10.3109/09593985.2015.1138010>.
10. Meeus M, Nijs J, Van Oosterwijck J, Van Alsenoy V, Truijien S. Pain physiology education improves pain beliefs in patients with chronic fatigue syndrome compared with pacing and self-management education: a double-blind randomized controlled trial. *Arch Phys Med Rehabil*. 2010;**91**(8):1153-9. [PubMed ID: 20684894]. <https://doi.org/10.1016/j.apmr.2010.04.020>.
11. Van Oosterwijck J, Meeus M, Paul L, De Schryver M, Pascal A, Lambrecht L, et al. Pain physiology education improves health status and endogenous pain inhibition in fibromyalgia: a double-blind randomized controlled trial. *Clin J Pain*. 2013;**29**(10):873-82. [PubMed ID: 23370076]. <https://doi.org/10.1097/AJP.0b013e31827c7a7d>.
12. Moseley L. Combined physiotherapy and education is efficacious for chronic low back pain. *Aust J Physiother*. 2002;**48**(4):297-302. [PubMed ID: 12443524]. [https://doi.org/10.1016/s0004-9514\(14\)60169-0](https://doi.org/10.1016/s0004-9514(14)60169-0).
13. Dolphens M, Nijs J, Cagnie B, Meeus M, Roussel N, Kregel J, et al. Efficacy of a modern neuroscience approach versus usual care evidence-based physiotherapy on pain, disability and brain characteristics in chronic spinal pain patients: protocol of a randomized clinical trial. *BMC Musculoskelet Disord*. 2014;**15**:149. [PubMed ID: 24885889]. [PubMed Central ID: PMC4028010]. <https://doi.org/10.1186/1471-2474-15-149>.
14. Bodes Pardo G, Lluch Girbes E, Roussel NA, Gallego Izquierdo T, Jimenez Penick V, Pecos Martin D. Pain Neurophysiology Education and Therapeutic Exercise for Patients With Chronic Low Back Pain: A Single-Blind Randomized Controlled Trial. *Arch Phys Med Rehabil*. 2018;**99**(2):338-47. [PubMed ID: 29138049]. <https://doi.org/10.1016/j.apmr.2017.10.016>.
15. Modares Gorji S, Mohammadi Nia Samakosh H, Watt P, Henrique Marchetti P, Oliveira R. Pain Neuroscience Education and Motor Control Exercises versus Core Stability Exercises on Pain, Disability, and Balance in Women with Chronic Low Back Pain. *Int J Environ Res Public Health*. 2022;**19**(5):2694. [PubMed ID: 35270384]. [PubMed Central ID: PMC8910692]. <https://doi.org/10.3390/ijerph19052694>.
16. Valiente-Castrillo P, Martin-Pintado-Zugasti A, Calvo-Lobo C, Beltran-Alacreu H, Fernandez-Carnero J. Effects of pain neuroscience education and dry needling for the management of patients with chronic myofascial neck pain: a randomized clinical trial. *Acupunct Med*. 2021;**39**(2):91-105. [PubMed ID: 32370545]. <https://doi.org/10.1177/0964528420920300>.
17. Javdaneh N, Saeterbakken AH, Shams A, Barati AH. Pain Neuroscience Education Combined with Therapeutic Exercises Provides Added Benefit in the Treatment of Chronic Neck Pain. *Int J Environ Res Public Health*. 2021;**18**(16):8848. [PubMed ID: 3444594]. [PubMed Central ID: PMC8394804]. <https://doi.org/10.3390/ijerph18168848>.
18. Andias R, Neto M, Silva AG. The effects of pain neuroscience education and exercise on pain, muscle endurance, catastrophizing and anxiety in adolescents with chronic idiopathic neck pain: a school-based pilot, randomized and controlled study. *Physiother Theory Pract*. 2018;**34**(9):682-91. [PubMed ID: 29319386]. <https://doi.org/10.1080/09593985.2018.1423590>.

19. Louw A, Zimney K, Puentedura EJ, Diener I. The efficacy of pain neuroscience education on musculoskeletal pain: A systematic review of the literature. *Physiother Theory Pract.* 2016;**32**(5):332-55. [PubMed ID: 27351541]. <https://doi.org/10.1080/09593985.2016.1194646>.
20. Puentedura EJ, Flynn T. Combining manual therapy with pain neuroscience education in the treatment of chronic low back pain: A narrative review of the literature. *Physiother Theory Pract.* 2016;**32**(5):408-14. [PubMed ID: 27362980]. <https://doi.org/10.1080/09593985.2016.1194663>.
21. Butler DS, Moseley GL. *Explain Pain*. 2nd ed. Adelaide City West: Noigroup Publications; 2013.
22. Martimbianco ALC, Porfirio GJ, Pacheco RL, Torloni MR, Riera R. Transcutaneous electrical nerve stimulation (TENS) for chronic neck pain. *Cochrane Database Syst Rev.* 2019;**12**(12):CD011927. [PubMed ID: 31830313]. [PubMed Central ID: PMC6953309]. <https://doi.org/10.1002/14651858.CD011927.pub2>.
23. Yildirim MA, Ones K, Goksenoglu G. Effectiveness of Ultrasound Therapy on Myofascial Pain Syndrome of the Upper Trapezius: Randomized, Single-Blind, Placebo-Controlled Study. *Arch Rheumatol.* 2018;**33**(4):418-23. [PubMed ID: 30874250]. [PubMed Central ID: PMC6409164]. <https://doi.org/10.5606/ArchRheumatol.2018.6538>.
24. Chaibi A, Russell MB. Manual therapies for cervicogenic headache: a systematic review. *J Headache Pain.* 2012;**13**(5):351-9. [PubMed ID: 22460941]. [PubMed Central ID: PMC3381059]. <https://doi.org/10.1007/s10194-012-0436-7>.
25. Boonstra AM, Schiphorst Preuper HR, Reneman MF, Posthumus JB, Stewart RE. Reliability and validity of the visual analogue scale for disability in patients with chronic musculoskeletal pain. *Int J Rehabil Res.* 2008;**31**(2):165-9. [PubMed ID: 18467932]. <https://doi.org/10.1097/MRR.0b013e3282fc0f93>.
26. Jabbari S, Salahzadeh Z, Sarbakhsh P, Rezaei M, Farhoudi M, Ghodrati M. Validity and Reliability of Persian Version of Henry Ford Hospital Headache Disability Inventory Questionnaire. *Arch Iran Med.* 2021;**24**(10):752-8. [PubMed ID: 34816697]. <https://doi.org/10.34172/aim.2021.111>.
27. Sullivan MJ, Bishop SR, Pivik J. The Pain Catastrophizing Scale: Development and validation. *Psychological Assessment.* 1995;**7**(4):524-532. <https://doi.org/10.1037/1040-3590.7.4.524>.
28. Rahmati N, Asghari Moghadam MA, Shairi M, Paknejad M, Rahmati Z, Ghassami M, et al. [A Study of the Psychometric Properties of the Pain Catastrophizing Scale Amongst Iranian Patients with Chronic Persistent Pain]. *J Ilam Univ Med Sci.* 2017;**25**(1):63-79. Persian. <https://doi.org/10.29252/sjimu.25.1.63>.
29. Moseley GL, Nicholas MK, Hodges PW. A randomized controlled trial of intensive neurophysiology education in chronic low back pain. *Clin J Pain.* 2004;**20**(5):324-30. [PubMed ID: 15322439]. <https://doi.org/10.1097/00002508-200409000-00007>.
30. Rondon-Ramos A, Martinez-Calderon J, Diaz-Cerrillo JL, Rivas-Ruiz F, Ariza-Hurtado GR, Clavero-Cano S, et al. Pain Neuroscience Education Plus Usual Care Is More Effective Than Usual Care Alone to Improve Self-Efficacy Beliefs in People with Chronic Musculoskeletal Pain: A Non-Randomized Controlled Trial. *J Clin Med.* 2020;**9**(7):2195. [PubMed ID: 32664552]. [PubMed Central ID: PMC7408875]. <https://doi.org/10.3390/jcm9072195>.
31. Moseley GL. Joining Forces - Combining Cognition-Targeted Motor Control Training with Group or Individual Pain Physiology Education: A Successful Treatment For Chronic Low Back Pain. *J Man Manip Ther.* 2003;**11**(2):88-94. <https://doi.org/10.1179/106698103790826383>.
32. Pires D, Cruz EB, Caeiro C. Aquatic exercise and pain neurophysiology education versus aquatic exercise alone for patients with chronic low back pain: a randomized controlled trial. *Clin Rehabil.* 2015;**29**(6):538-47. [PubMed ID: 25200879]. <https://doi.org/10.1177/0269215514549033>.
33. McCracken LM. Social context and acceptance of chronic pain: the role of solicitous and punishing responses. *Pain.* 2005;**113**(1-2):155-9. [PubMed ID: 15621376]. <https://doi.org/10.1016/j.pain.2004.10.004>.
34. Coudeyre E, Demaille-Wlodyka S, Poizat S, Burton K, Hamonet MA, Revel M, et al. Could a simple educational intervention modify beliefs about whiplash? A preliminary study among professionals working in a rehabilitation ward. *Ann Readapt Med Phys.* 2007;**50**(7):552-7. 545-51. [PubMed ID: 17597246]. <https://doi.org/10.1016/j.annrmp.2007.05.005>.
35. Moseley GL. Evidence for a direct relationship between cognitive and physical change during an education intervention in people with chronic low back pain. *Eur J Pain.* 2004;**8**(1):39-45. [PubMed ID: 14690673]. [https://doi.org/10.1016/S1090-3801\(03\)00063-6](https://doi.org/10.1016/S1090-3801(03)00063-6).
36. Maeda Y, Kan S, Fujino Y, Shibata M. Verbal Instruction Can Induce Extinction of Fear of Movement-Related Pain. *J Pain.* 2018;**19**(9):1063-73. [PubMed ID: 29702257]. <https://doi.org/10.1016/j.jpain.2018.03.014>.
37. Van Oosterwijck J, Nijs J, Meeus M, Truijzen S, Craps J, Van den Keybus N, et al. Pain neurophysiology education improves cognitions, pain thresholds, and movement performance in people with chronic whiplash: a pilot study. *J Rehabil Res Dev.* 2011;**48**(1):43-58. [PubMed ID: 21328162]. <https://doi.org/10.1682/jrrd.2009.12.0206>.