Quantitative sensory testing in migraine patients on treatment in comparison to controls

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Abstract

Background: Patients with migraine experience increased sensitivity to external stimuli. Quantitative sensory testing (QST) measures thermal perception and thermal pain thresholds in migraine patients.

Aims: The purpose of our study is to measure thermal and pain perception and thresholds using QST in patients with migraine, and to evaluate the effect of abortive versus prophylactic treatment.

Material and Methods: We performed a case-control study comparing thermal perception and thermal pain thresholds using QST in 25 migraine subjects compared to controls. We compared patients on abortive therapy (16 patients) to those on prophylactic therapy (9 patients).

Results: We found that migraine patients in the Lebanese population are less sensitive to all thermal modalities on QST interictally, which is different than reported studies. Migraine patients had significantly higher heat perception threshold and lower cold perception threshold over the hand and higher heat pain threshold and lower cold perception threshold over the face. Migraine patients on prophylactic therapy were more sensitive than those on abortive therapy.

Conclusion: Migraine patients were less sensitive to thermal and pain sensation compared to published reports. Patients on prophylactic therapy showed lower QST thresholds compared to those on abortive therapy suggesting that the abortive treatment suppressed their hypersensitivity

Keywords: Migraine • QST • Thermal perception • Thermal pain

Background

Migraine is a common headache disorder with prevalence worldwide reaching 14.7% [1]. Migraine patients experience visual, sensory and auditory aura which are related to their increased sensitivity to external stimuli [2]. These patients also suffer chronic pain [1]. This stresses the fact of diffuse up regulation of their nociceptive system [3].

Quantitative sensory testing (QST) measures thermal perception and thermal pain thresholds in migraine patients during headaches and interictally. The purpose of our study is to measure interictal thermal perception and pain thresholds using QST in patients with migraine. Our second aim is to evaluate the effect of abortive therapy versus prophylactic treatment on these variables.

Material and Methods

We performed a case-control study comparing thermal perception and pain thresholds using QST in migraines compared to age and sex matched controls. We studied 25 patients (17 women and 8 men), aged between 20 and 40 years old, diagnosed with migraine according to the International Headache Society at the neurology outpatient clinics at the American University of Beirut Medical Center (AUBMC). The control group were 25 age and sex matched subjects with no history of headaches, recruited from the staff of the medical center. None of the participants in both groups suffered from any other neurologic or medical condition. Approval of the study was obtained from the institutional Review Board at AUBMC. All subjects signed an informed consent before enrollment.

In order to reach our second aim, we further stratified the migraine group into two subgroups: migraine patients on abortive therapy (16 patients) and those on prophylactic therapy (9 patients) and compared their thermal and pain thresholds.

Standardized instructions were delivered to all subjects prior to QST testing. Thermal testing was performed using the Medoc Pathway platform with a 30mm x 30mm thermode. The thermode was applied to the skin of the forehead and the palm. 'Thermal perception threshold' was defined as the first instant that the stimulus is felt by the subject as cold or hot. 'Pain tolerance threshold' was defined as the first instant that the subject feels that the cold/heat sensation is painful. The thermode adjusts to a baseline temperature of 32°. Depending upon the modality being tested (heat or cold), thermode temperature increases or decreases by 1°/s reaching a maximum of 50° and a minimum of 10°. The subject presses a button when the threshold being tested (heat, heat pain, cold, cold pain) is reached. The heating or cooling process stops immediately and the thermode returns to the baseline temperature. This test is performed four times for each modality in each location. The mean of the four trials in each body location is the threshold being studied for each modality.

Statistical Analysis

Pair-wise group comparisons were used to test whether significant differences exist in QST thresholds between the migraine group and control group. For all tests, $P<0.05$ was considered to be statistically significant.

Results

There was no difference in age or gender between migraine group and control group. There was a female predominance at 67% in both groups (17 women out of 25 subjects in each group).

For each group, we studied heat perception, cold perception, heat pain and cold pain over the forehead and the palm area of all participants.

In the migraine group, heat perception threshold was 36.372° at the palm and 35.244° at the forehead area, heat pain threshold was 43.95° over the palm area and 40.168° over the forehead, cold perception threshold was 29.436° over the palm and 30.332° over the forehead, and cold pain thresholds was 19.228° over the palm and 22.72° over the forehead (Table 1, Figure 1 and Figure 2).

In the control group, heat perception threshold was 35.131° at the palm and 34.625° at the forehead, heat pain threshold was 42.969° over the palm and 39.512° over the forehead, cold perception threshold was 30.331° over the palm and 30.919° over the forehead, and cold pain thresholds was 20.906° over the palm and 24.331° over the forehead (Table 1).

In the subgroup analysis, we studied the effect of prophylactic vs abortive treatment on QST values. In the abortive therapy group heat perception threshold was 37.047° over the palm and 35.512° over the forehead, while that in the prophylactic group was lower at 34.938° and 34.675° respectively. Heat pain threshold in the abortive group was 44.529° over the palm and 40.40° over the forehead, while that for the prophylactic therapy group were also lower at 42.725° and 39.675° respectively. Regarding the cold perception threshold; in the abortive therapy group it was 29.059° over the palm and 30.335° over the forehead, while in the prophylactic therapy group it was 30.237° and 30.325° respectively. The cold pain threshold in the abortive therapy group was 18.659° over the palm and 22.965° over the forehead, while that in the prophylactic therapy group was 20.438° and 22.20° respectively (Table 2, Figure 3 and Figure 4).

Table 1: Mean threshold for heat and cold perception and pain in migraines and controls.

	Heat				Cold			
	Perception°		Pain°		Perception°		Pain°	
Area	Palm	Forehead	Palm	Forehead	Palm	Forehead	Palm	Forehead
Migraine	36.372	35.244	43.95	40.168	29.436	30.332	19.228	22.72
Control	35.131	34.625	42.969	39.512	30.331	30.919	20.906	24.331

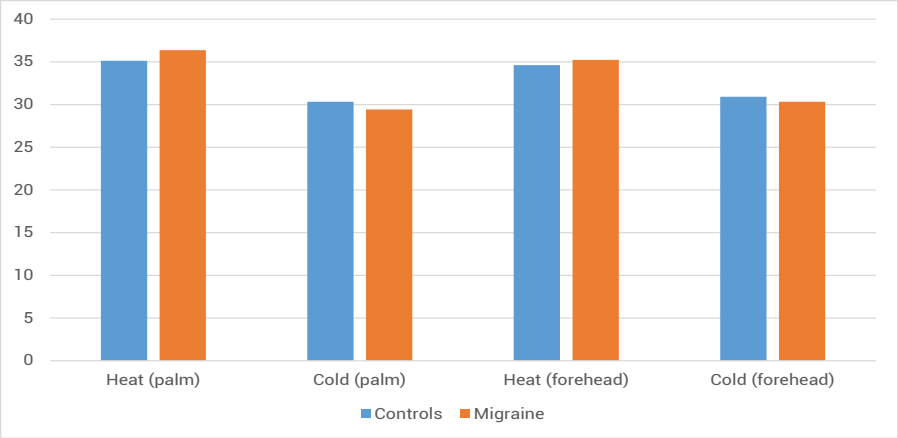

Figure 1. Bar Graph - Heat and Cold perception thresholds over palm and forehead in controls versus migraine patients.

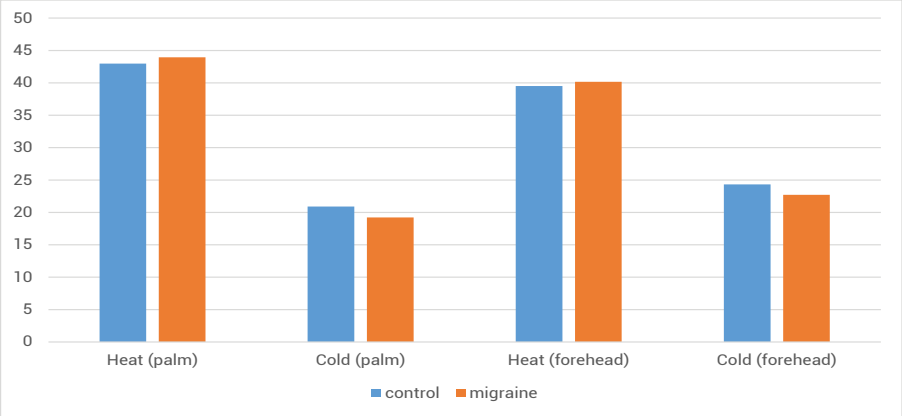

Figure 2. Bar Graph - Heat and Cold pain thresholds over palm and forehead in controls versus migraine patients.

Table 2: Mean threshold for heat and cold perception and pain in migraine patients on abortive versus prophylactic therapy.

	Heat				Cold			
	Perception°		Pain°		Perception°		Pain°	
Area	Palm	Forehead	Palm	Forehead	Palm	Forehead	Palm	Forehead
Abortive	37.047	35.512	44.529	40.4	29.059	30.335	18.659	22.965
Prophylactic	34.938	34.675	42.725	39.675	30.237	30.325	20.438	22.2

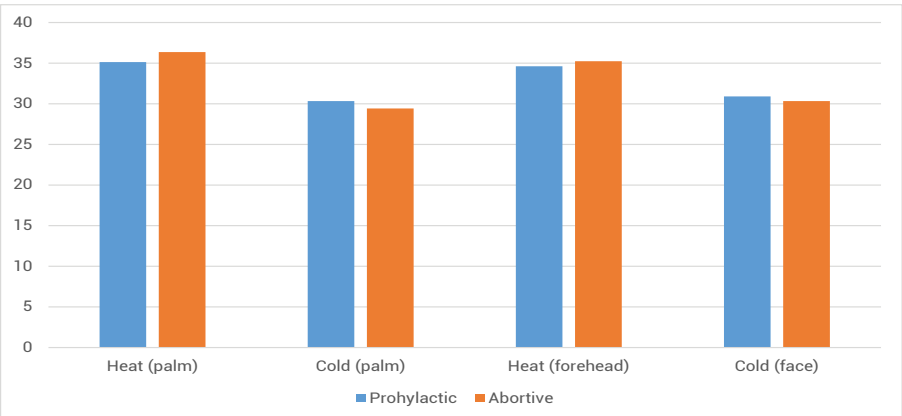

Figure 3. Bar Graph - Heat and Cold perception thresholds over palm and forehead in migraine patients on prophylactic versus abortive therapy.

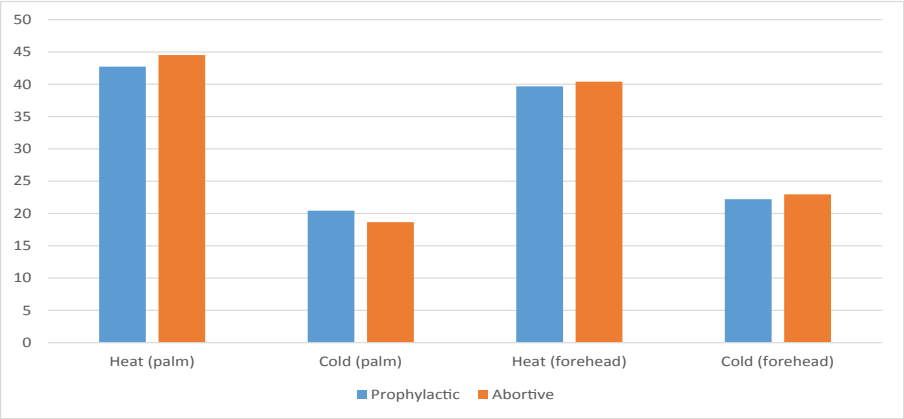

Figure 4. Bar Graph - Heat and Cold pain thresholds over palm and forehead in migraine patients on prophylactic versus abortive therapy.

Discussion

Migraine patients are known to be hypersensitive to light, sound and odor during their headache attack and interictally. They also process sensory stimuli in an abnormal way because they are considered to have both peripheral and central sensitization [4]. Peripheral sensitization results from increased sensitization to an external stimulus due to inflammation peripherally while central sensitization results from stimulation of sensitized neurons in the dorsal horn of the spinal cord [3]. This clinically manifests as allodynia decreased pain perception threshold and increased response to pain [3-6]. QST measures thermal perception and pain thresholds and is a very useful tool in research of pain and headache syndromes [7].

Studies that compared QST values in migraine patients found lower pain thresholds during the attack compared to the pain free interval [8-10]. Sand et al. found decreased cutaneous pain thresholds at 24 hours before the next headache attack when compared to the interictal thresholds. Both findings of increased pain sensitivity during the headache and 24 hours before confirm that the sensitization of central and peripheral nociceptors is behind the pathophysiology of migraine [11]. Todd et al found that migraine subjects are more sensitive interictally when compared to controls with significant lower thermal pain and tolerance thresholds. These lower thresholds were also correlated with the cutaneous allodynia [12]. This study suggests an interictal sensitization of migraine patients which in turn predisposes them to the next migraine attack [12]. This means that migraneurs who are asymptomatic interictally have sub-allodynia or asymptomatic sensitization which is not evident clinically but present when measuring thermal thresholds by QST [12]. A recent meta-analysis of 65 studies done by H. Nahman-Averbuch et al in 2018, showed that migraine patients have greater pain sensitivity to pressure pain thresholds and heat pain thresholds [13].

Our results show that migraine patients had higher perception and pain thresholds to heat. Furthermore, they had lower perception and pain thresholds to cold, when compared to controls. This means that in our cohort, migraine patients showed less sensitivity to all thermal modalities on QST interictally, which is different than previous studies. Out of these results, heat perception threshold over the hand and heat pain threshold over the face was significantly higher in migraine patients compared to controls (p: 0.05 and p: 0.036 respectively). Also, cold perception threshold over the hand and cold pain threshold over the face was significantly lower in the migraine group compared to controls (p: 0.006 and p: 0.014 respectively). These results were contradictory to those published previously where all studies show increased sensitivity in migraine subjects to both heat and cold stimuli. In order to find an explanation to these discrepancies, we did a subgroup analysis by dividing our migraine group into two subgroups. One subgroup was for patients on abortive therapy (16 patients) and another subgroup for patients on prophylactic therapy (9 patients). The prophylactic group had lower thresholds for all heat modalities and higher thresholds for all cold modalities on both hand and face areas. Significant difference was found in heat perception threshold and cold perception threshold over the hand (p: 0.012 and 0.025 respectively). So, we found that migraine patients on prophylactic therapy were more sensitive than migraine patients on abortive therapy.

Conclusion

Previously published data about QST in migraine patients point to the fact that migraineurs are more sensitive to heat and cold stimulation interictally. Our study, however, we found that this hypersensitivity is absent. This was confirmed by significantly higher heat perception and pain thresholds as well as lower cold perception and pain thresholds in these migraine patients interictally when compared to age matched healthy controls. The fact that migraine patients showed lower QST thresholds when they are on prophylactic therapy compared to those on abortive therapy makes us think that the abortive treatment used has probably suppressed the previously described hypersensitivity. Thus, the use of abortive therapy and analgesics like NSAIDs, opiates and triptans produced higher than expected thresholds in these patients. As abortive therapy suppresses the headache pain, this might explain the changes seen in QST values. Our hypothesis is that migraine patients in the Lebanese population are overusing analgesics for their migraine headaches. This might be explained by the lack of public health awareness about the use of analgesics as well as the availability of these pain medications. Thus, these patients choose to use analgesics which are over the counter medication and can be purchased easily without any restrictions.

References

1. Ann, I. Scher., et al. "Comorbid pain and migraine chronicity The Chronic Migraine Epidemiology and Outcomes Study Neurology." *Neurology* 89 (2017): 461-468.
2. Peter, J., et al. "Pathophysiology of migraine: A Disorder of Sensory Processing." *Physiol Rev* 97 (2017): 553-622.
3. Bevilaqua-Grossi1, D., et al. "Temporomandibular disorders and cutaneous allodynia are associated in individuals with migraine Cephalalgia." *Int headache soci* 30 (2009) 425-432.
4. Rami Bursteina, B., et al. "The science of migraine." *J Vestib Res* 21 (2011): 305-314.
5. Alexandre, F., et al. "Dopamine D2/D3 imbalance during migraine attack and allodynia in vivo Neurology." *Neurology* 88 (2017):1634-1641.
6. Nadine Attal, c,d., et al. "A Value of quantitative sensory testing in neurological and pain disorders:NeuPSIG consensus." *Pain* 154 (2013):1807-1819.
7. Chong, PS., & Cros, D.P. "Technology literature review: quantitative sensory testing". *Muscle Nerve* 29 (2004): 734-747.
8. Burstein, R., et al. "An association between migraine and cutaneous allodynia". *Ann Neurol* 47 (2000): 614-624.
9. Bigal, ME., et al. "Prevalence and characteristics of allodynia in headache sufferers: a population study". *Neurology* 70 (2008): 1525-1533.
10. Burstein, R., et al. "The development of cutaneous allodynia during a migraine attack clinical evidence for the sequential recruitment of spinal and supraspinal nociceptive neurons in migraine". *Brain* 123 (2000): 1703-1709.
11. Sand, T., et al. "Thermal pain thresholds are decreased in the migraine preattack phase European Journal of Neurology." *Eur J Neurol* 15 (2008): 1199-1205.
12. Todd Schwedt, J., et al. "Episodic and chronic migraineurs are hypersensitive to thermal stimuli between migraine attacks." *Cephalalgia* 31 (2013) 6-12.
13. Hadas, N.-A., et al. "Quantitative sensory testing in patients with migraine: a systematic review and meta-analysis". *Pain* 159 (2018): 1202-1223.

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