

## ORIGINAL ARTICLE

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## PAIN THRESHOLD MEASUREMENTS IN HIGH AND LOW ALTITUDE AMONG HEALTHY VOLUNTEER ADULTS: A COMPARATIVE STUDY

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## ABSTRACT

**Background:** Majority of high altitude residents have certain clinical, physiological, anatomical and biochemical changes. Pain threshold is one of the numerable changes that may occur due to chronic hypoxia. The aim of this research was to study the long term effects of high altitude exposure on pain perception among healthy volunteer subjects.

**Methods:** This is an observational case-control study. Two groups of healthy volunteer subjects, highland group (n=242) and lowland group (n=242) in two different cities. Assessment methods used were: Pressure algometer, was measured bilaterally three times on ten body points and Situational pain scale, which is 18 items self-report questionnaire measuring the mental representation of pain intensity in imaginary painful situations.

**Results:** pain sensitivity was lower in highlanders compared to lowlanders ( $p < 0.0005$ ). While the participants' attitudes towards imaginary painful situations through SPS showed lesser pain sensitivity in highlanders compared to lowlanders in 72% from the total scale items.

**Conclusion:** According to the results of the current study, pressure pain threshold is higher (pain sensitivity is lower) in highlanders compared to lowlanders. And attitudes towards imaginary painful situations are lower in highland population compared to lowland population as a long-term effect of chronic hypoxia.

**Keywords:** Pain threshold, algometer, high altitude, healthy adults.

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## INTRODUCTION

An elevation of more than 1500 meter above the sea level is considered high-altitude. Mild tissue hypoxia may result from low arterial blood oxygen pressure due to oxygen insufficiency in the ambient air [1]. Majority of high altitude residents have certain clinical, physiological, anatomical and biochemical changes. This change occurs due to the low oxygen pressure in the circulating blood which decreases the ability of the active tissue cells to receive and utilize oxygen effectively [2]. Acclimatization refers to the adaptive changes that occur in order to improve the human beings tolerance to high altitude. These adaptive changes reduce the classical oxygen cascade which is the gradual saturation of oxygen partial pressure from ambient air to tissues. Acclimatization is different from the pathological changes that lead to high altitude sickness. The first stages in altitude acclimatization deal with sensory perception [3]. Although there are several studies discussing human adaptation to high altitude [4-6], there are very limited researches discussing the effect of high altitude on pain threshold. The effect of high altitude on respiratory sensations within lowland or highland populations has been discussed in many previous studies [2,7-8]. Authors of the previous studies concluded that respiratory sensation appears to participate in the first stages of hypoxia acclimatization: the subject has to perceive at altitude the decrease in oxygen pressure in the inspired air in order to trigger his physiological adaptive processes. Human response to high-altitude is divided into the study of short-term changes that occur with exposure to hypobaric hypoxia (the acute response to hypoxia) and study of long-term acclimatization and adaptation. One study conducted in 1996 by Noel-Jorand et al [9] investigated pain perception on European lowlanders, during an expedition on the Bhrikuti peak, Himalaya. The results of this study showed more indifferent attitude toward pain and decreased pain threshold in the expedition group compared to the control group (sea level). This study investigated only the effect of short-term changes on pain perception due to high altitude exposure.

According to our knowledge, there was only one study comparing the short-term differences of pain threshold in highlander and low lander healthy subjects which was conducted by (Noel-Jorand et al, 1996). Accordingly, the aim of the present study was to compare between pressure pain threshold in high altitude and low altitude residents, thus, studying the long-term effect of high altitude exposure on pressure pain threshold on healthy subjects.

### Materials and methods:

#### Study design:

This is an observational case-control study. Two groups of healthy volunteer subjects were involved in the study; highland group and lowland group in two different cities. The lowland city is at the sea level "Jeddah" and the high land city is "Taif" and it is almost 1900 meter above sea level. The study was conducted between January 2016 till May 2016. The study proposal was approved by the ethical

committee of the Faculty of Applied Medical Sciences, Taif University.

#### Power test:

Calculation of the sample size was performed before starting the study using G power software version 3.0.10 (<http://www.psych.uni-duesseldorf.de/abteilungen/aap/gpower3/>, 2016). For t-testing of the mean differences in both groups, the suggested sample size was 242 for each group (total 484), with an estimate power of  $(1-\beta \text{ err}) = 0.95$ , effect size ( $d=0.3$ ) and  $\alpha (=0.05)$

#### Participants:

A total of 484 healthy volunteer subjects (197 males and 287 females) were encouraged to participate in the present study, through advertisement in local shopping centers, health care facilities and universities, in both highland and lowland cities, with 242 participants in each city. A full explanation of the study purpose and the procedures, that would be applied, was provided to all participants prior involvement in the study. An informed consent form was signed by all participants, before involvement in the study procedure according to Helsinki declaration protocol [10].

The inclusion criteria were: healthy volunteer subjects, age range between 18 to 53 and residency for more than 10 years in high or low altitude cities.

Exclusion was applied to: pain from the musculoskeletal system, previous injuries or burns in the points of algometer pressure areas, analgesic or anti-depressive medications, and any neurological condition that interferes with sensory perception such as diabetic neuropathy, multiple sclerosis.

#### Assessment:

##### Pressure Algometer:

Pressure pain threshold (PPT) is defined as the minimal amount of pressure that produces pain [11]. The pressure pain threshold device used in the assessment is "Baseline Push-pull force gauge" "model number 12-1443". It is commercially available through Fabrication Enterprises, PO Box 1500, White Plains, New York 10602 USA. Pressure algometry was proved to be a valid and reliable method for measuring pressure pain threshold, and in detecting tender points [12-14]. It consists of 1 cm<sup>2</sup> rubber disc connected to a force gauge by a metal rod which is calibrated in Newton's or in Kg/cm<sup>2</sup> (30 Kg maximum). For measuring the pressure pain threshold a force (pressure) is applied on certain body points through the rubber disk. The pressure exerted is transmitted to the force gauge and moves the indicator needle in clockwise direction. The indicator needle remains at the measured force value until the zeroing knob is pressed. After each measurement the zeroing knob must be pressed in order to return the indicator needle to zero again.

Assessments were performed by the same five well trained physiotherapists in both cities. The pressure pain threshold was measured three times respectively by the same assessor and calculated the mean value for each point.

**Points of measurements:**

Pressure pain threshold was measured bilaterally three times on ten body points in a fixed order without breaks (Table:1). On each body point, the three measurements were taken successively before moving to the next point. Time intervals between measurements were 30–40 seconds. During pressure-pain threshold (PPth) measurement, the participant was lying on a massage table head facing down in a prone lying position in a face rest. Pressure was applied perpendicularly over the points using the algometer and gradually increased until the participant indicated that the pressure became unpleasant by saying “stop”, after which the algometer was immediately removed from the skin and maximum pressure was copied from the algometer screen. The pressure is continuously increased at an even rate of approximately 1 Kg/ second. A metronome was used to apply the pressure rate constantly. However the participants did not know the reason of its presence. Pressure pain points were suggested in many previous studies [12, 15-17].

**Table 1:** Points of pressure pain threshold measurements (sample copy).

	Points	Rt (Kg)				Lt (Kg)			
		1 <sup>st</sup> trial	2 <sup>nd</sup> trial	3 <sup>rd</sup> trial	mean	1 <sup>st</sup> trial	2 <sup>nd</sup> trial	3 <sup>rd</sup> trial	mean
1	left and right calf (one third of total calf muscle length below the popliteal space)								
2	the lower back, (5cm left and right from the L4 spinous process) horizontal line crossing high points of iliac crest								
3	left and right forearm (thickest part of brachioradialis muscle)								
4	Trapezius muscle (mid-point along a straight line from the spinous process of the 7th cervical vertebra to the lateral edge of the acromion)								
5	Mid-point of deltoid muscle (mid-point between acromion process and deltoid tuberosity, on muscle belly)								

**Situational pain scale:**

The Situational Pain Scale (SPS) is 18 items self-report questionnaire measuring the mental representation of pain intensity in imaginary painful situations. The origin of the SPS was first originated in French [18], later on it was translated into English. The English version is available at (<http://www.arsalis.com/rehab-scales/situational-pain-scale-downloads.html>). The SPS has been evaluated on healthy subjects and on chronic pain patients as well. The SPS describes some painful situations that a person might be subjected to, as: I disinfect a sore, I have a splinter under the skin of one finger and I burn my tongue tasting scorching hot food. Each subject has to score every painful situation from not painful (0), slightly painful (1), moderately painful (2) and extremely painful (3). The score ranges from 0 to a maximum of 54 which indicates the worst attitude towards pain. Missing values were treat-

ed as 0 [18-19]. Participants completed the SPS questionnaire with assistance of the examiner while sitting in a quiet room with a fixed ambient temperature “23-25°C”. Personal data were gathered at the beginning of the evaluation session. Test-retest reliability of the SPS has been measured in a previous study [20].

**Statistical analysis:**

Summaries and descriptive statistics were generated, and the data were statistically analyzed according to the objectives of the study. All data of the Situational Pain Scale questionnaire were coded and transformed into numerical form to be suitable for computer entry process. SPSS (statistical Package for Social Science) program version 16 for Windows was used for data entry and analysis. Appropriate statistical test was used, parametric t-test for PPth testing and age, weight, height, BMI while non-parametric test for SPS questionnaire, dominance and sex differences. P values less than 0.05 will be considered significant with confidence interval 95%.

**RESULTS**

Descriptive statistics of all measured data “means and standard deviations” are presented in table (2). Demographic data of both groups were compared with no statistical significant difference suggesting homogeneity between both groups (P>0.05). Data are presented in table (3).

**Table 2:** Descriptive statistics “means and standard deviations” of all measured data

Group HN= (242) LN=(242)		Mean	Std. Deviation	Std. Error Mean
Age (Years)	H	28.42	10.352	.665
	L	26.90	8.131	.523
Sex (males-females)	H	1.61	.488	.031
	L	1.57	.495	.032
Weight (Kg)	H	68.89	18.748	1.205
	L	65.44	20.219	1.300
Height (m)	H	1.6252	.09094	.0585
	L	1.6285	.10009	.0643
BMI Kg/m2	H	25.868	6.2699	.4030
	L	24.337	6.3241	.4065
Dominance (Rt-Lt)	H	1.06	.242	.016
	L	1.15	.361	.023
P1Rt	H	8.988	3.2093	.2063
	L	5.848	3.5570	.2287
P1Lt	H	8.840	3.2429	.2085
	L	5.906	3.7391	.2404
P2Rt	H	8.362	3.1496	.2025
	L	5.273	3.3787	.2172
P2Lt	H	8.726	3.3081	.2127
	L	5.295	3.3165	.2132
P3Rt	H	6.514	2.9410	.1891
	L	5.037	3.3657	.2164

P3Lt	H	6.353	2.6717	.1717
	L	4.922	3.3159	.2132
P4Rt	H	6.590	2.5403	.1633
	L	4.199	2.5259	.1624
P4Lt	H	6.469	2.4301	.1562
	L	4.260	2.9191	.1876
P5Rt	H	6.651	2.7448	.1764
	L	4.996	3.4912	.2244
P5Lt	H	7.064	2.9688	.1908
	L	5.072	3.6943	.2375
S1	H	2.57	.749	.048
	L	3.03	.924	.059
S2	H	2.32	.730	.047
	L	2.72	1.106	.071
S3	H	2.94	.820	.053
	L	3.23	.884	.057
S4	H	3.27	.686	.044
	L	3.30	.811	.052
S5	H	2.48	.893	.057
	L	2.86	1.076	.069
S6	H	3.35	.732	.047
	L	3.12	.761	.049
S7	H	3.06	.864	.056
	L	2.91	.864	.056
S8	H	3.12	.803	.052
	L	3.36	.799	.051
S9	H	3.31	.798	.051
	L	3.20	.828	.053
S10	H	3.07	.880	.057
	L	3.17	.768	.049
S11	H	2.72	.806	.052
	L	2.91	.879	.056
S12	H	2.93	.842	.054
	L	2.90	1.005	.065
S13	H	2.35	.945	.061
	L	2.78	1.001	.064
S14	H	2.67	.928	.060
	L	2.85	.914	.059
S15	H	2.81	.659	.042
	L	2.98	.830	.053
S16	H	3.73	.515	.033
	L	3.38	.720	.046
S17	H	2.00	.786	.051
	L	2.64	.897	.058
S18	H	2.50	.865	.056
	L	3.00	.890	.057

### Pressure algometer:

Pressure pain threshold (PPT) points are labeled from P1 to P5 right and left in table (2&3). Pressure pain thresholds were higher in highlanders compared to lowlanders which means decrease the highlanders sensitivity to pain compared to lowlanders with very highly statistically significant difference in all measured points right and left ( $p < 0.000$ ) (table, 3).

### Situational pain scale:

The 18 items of the questionnaire were labeled from S1 to S18 in both table 2&3. There are statistical significant differences between highlanders and lowlanders considering imaginary pain situations (SPS) in the high and low altitude long-term exposure in items number (S1, S2, S3, S5, S6, S8, S11, S13, S14, S15, S16, S17, and S18) ( $P < 0.05$ ). However, there was no statistical significant differences in items number (S4, S7, S9, S10, and S12) with 28% from total SPS items ( $p > 0.05$ ). Data are presented in table (3).

**Table (3):** Comparisons between highlanders and lowlanders in all measured data

	t-test for Equality of Means						
	t	df	Significance (2tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
						Lower	Upper
Age (Years)	1.792	482	.074	1.517	.846	-.146	3.179
Sex(-males-females)	.832	482	.406	.037	.045	-.051	.125
Weight (Kg)	1.944	482	.052	3.446	1.773	-.037	6.929
Height (m)	-.371	482	.711	-.322	.869	-2.030	1.386
BMI (Kg/m <sup>2</sup> )	2.674	482	.018	1.5308	.5725	.4060	2.6556
Dominance (Rt-Lt)	-1.521	482	.129	-0.41	0.27	-0.95	0.012
P1Rt	10.196	482	.000	3.1399	.3080	2.5348	3.7450
P1Lt	9.221	482	.000	2.9338	.3182	2.3086	3.5590
P2Rt	10.402	482	.000	3.0886	.2969	2.5052	3.6720
P2Lt	11.394	482	.000	3.4309	.3011	2.8392	4.0225
P3Rt	5.143	482	.000	1.4777	.2873	.9132	2.0423
P3Lt	5.225	482	.000	1.4303	.2737	.8925	1.9682
P4Rt	10.382	482	.000	2.3908	.2303	1.9383	2.8433
P4Lt	9.047	482	.000	2.2090	.2442	1.7293	2.6888
P5Rt	5.795	482	.000	1.6544	.2855	1.0934	2.2153
P5Lt	6.538	482	.000	1.9918	.3047	1.3932	2.5904
S1	-5.999	482	.000	-.459	.076	-.609	-.308
S2	-4.704	482	.000	-.401	.085	-.568	-.233
S3	-3.731	482	.000	-.289	.078	-.442	-.137
S4	-.423	482	.672	-.029	.068	-.163	.105
S5	-4.274	482	.000	-.384	.090	-.561	-.208
S6	3.409	482	.001	.231	.068	.098	.365
S7	1.946	482	.052	.153	.079	-.001	.307
S8	-3.291	482	.001	-.240	.073	-.383	-.097
S9	1.398	482	.163	.103	.074	-.042	.248
S10	-1.266	482	.206	-.095	.075	-.243	.052
S11	-2.427	482	.016	-.186	.077	-.337	-.035
S12	.392	482	.695	.033	.084	-.133	.199
S13	-4.857	482	.000	-.430	.088	-.604	-.256

S14	-2.122	482	.034	-.178	.084	-.342	-.013
S15	-2.487	482	.013	-.169	.068	-.303	-.036
S16	6.174	482	.000	.351	.057	.239	.463
S17	-8.301	482	.000	-.636	.077	-.787	-.486
S18	-6.317	482	.000	-.504	.080	-.661	-.347

## DISCUSSION

According to our knowledge, this is a novel research in studying the long term effects of high altitude exposure on pain perception in healthy volunteer subjects. The results of the current research showed that pain sensitivity was lower in highlanders compared to lowlanders. While, the participants' attitudes towards imaginary painful situations through SPS showed lesser pain sensitivity in highlanders compared to lowlanders in 72% from the total scale items.

Hypoxia is the main cause of high altitude manifestations. Oxygen is critical to normal cellular function, because it is an essential part of the electron transport chain for energy production in cells. One of the possible causes of reduced oxygen maximal consumption at high altitude is the reduction of partial oxygen pressure in mitochondria, which interferes with the function of the electron transport chain responsible for providing cellular energy [3], although it was believed that the reduction of maximal oxygen consumption is produced by central inhibition from the brain [21]. Long-term exposure to high altitude leads to chronic hypoxia. Genetic signature has been identified in some populations through the hypoxia inducible factor (HIF) pathway which manage the transcriptional response to hypoxia. The cellular responses to oxygen deprivation have been clarified by the discovery of the hypoxia-inducible complex, which regulates gene transcription. This complex is responsible for specific hypoxic-responsive sequences present in various genes encoding for glycolytic enzymes, growth factors, and vasoactive peptide [22].

According to the results of the current research, pain sensitivity was lower in highlanders compared to lowlanders. These results could be postulated to the effect of chronic hypoxia on the central nerves system (CNS). There are two types of effects of hypoxia on CNS: short-term and long-term. As regards short-term effects, many neuropsychometric tests showed a decline in their results after sudden exposure moderate hypoxia "2000 to 4500 m" above sea level. The main response to acute hypoxia is a slowed performance, particularly on more complex tests of cognitive and motor function. Also, a decline in a visual-positioning test conducted during easy work has been observed at an altitude as low as 1500 m. Hence, it is clearly evident that even with moderate hypoxia, brain function is merely impaired [23]. As with acute hypoxia, the long-term effects of hypoxia on CNS manifest itself by a decline of the brain function performance as slowing reaction time without affecting the error rates [24]. These decrements of brain functions are more noticeable with more complex tests demanding higher levels of cognitive function. Also, changes in mood, behavior and neurological function were reported [25].

Grandjean(1948) [26] evaluated the sudden exposure to hypoxia and found an instant decrease of many sensations as taste, smell, touch and light perception upon arriving on high altitude. However, with oxygen administration, all these changes returned to normal. These results could be strongly biased by attention and motivational factors as there were lack of precise laboratory conditions, and well-trained examiners [27].

A recent study conducted by Noel et al in 1996 [9] studied short term effects of hypoxia in European lowlanders during an expedition on the Bhrikuti peak, Himalaya. The expedition group showed a decrease in pain threshold and stoic attitude more than the sea level group. However, the small number of participants (only seven) and lack of precise laboratory conditions, such as ambient temperature control could add a difficulty in generalizing the research results. Moreover, this research studied only short term effects of hypoxia. The expedition had only 24 hours stay in the highest point of the mountain.

Grandjean research and Noel's et al researches were considered old researches and short-termed in case of hypoxia about pain perception in high altitude. Thus, the need for a new study is indispensable for studying long-term effects of hypoxia, which was achieved through our current study.

Pain perception includes both a subjective domain with affective-motivational features, and an objective domain of the somatic sensory processes as a result of actual or potential tissue damage (nociception) [28]. In the current study we tried to use both domains of pain perception evaluations; the objective measure of PPTh for the objective "somatic" domain and SPS for the subjective "affective" domain.

Situational pain scale results of the current study showed lesser pain sensitivity in highlanders in comparison with lowlanders but not in all the scale items 28% of the items showed no significant difference. As we discussed before, the inherited physiological responses to high altitude are the result of acclimatization and developmental adaptation. As a result new characteristics are acquired and become fixed during the period of growth and development which is known as genetic adaptation or modulation [29]. From the previous study we could conclude that, exposure to chronic hypoxia in highlanders generates new genetic traits that affect both somatic and affective domains of pain. As SPS is an imaginary pain scale, personal variations could affect the results which in turn produced 28% of non-significant difference between highlanders and lowlanders.

### Study limitation:

Successive repetition of the PPth test (3 times) in the same area sometimes is considered painful to some participants that is why the examiner had to wait for 10-20 seconds before taking the next measure. However, this was only in 20% of all participants.

## CONCLUSION

According to the results of the current study, pressure pain threshold is higher (i.e. pain sensitivity is lower) in highlanders compared to lowlanders. And attitudes towards imaginary painful situations are lower in highland population compared to lowland population as a long-term effect of chronic hypoxia

## Disclosure

In this study the author reports no conflict of interest.

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