Comparison of the effect of psychological stress on the temporomandibular joint and the knee joint (Experimental Study)

Original Article

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ABSTRACT

Background: The persistent stresses of modern life have a serious negative impact on the psychological wellbeing of a considerable number of the current population. Nowadays, many researchers reported a positive correlation between psychological stress (PS) and TMD. However, a proven causative relationship is difficult to be justified on clinical basis. Thus, we designed an experimental model that compares the effect of psychological stress on two discrete joints, in order to prove the substantial influence of PS on TMJ when compared to the knee joint.

Study Design.: The study was conducted on 32 albino rats randomly divided into 3 groups control group (Ctrl), foot shock group (SH) and psychological stress (PS) group. PS was induced to PS group by communicating with the suffering of the SH group during their electric shock periods. After 1-month Synovial fluids from both joints were compared regarding inflammatory mediators (IM).

Results: Synovial levels of TNF- α and IL-6 were significantly higher in TMJ of the PS group versus Ctrl group ($P<0.05$). Whereas, knee joints levels were comparable in their corresponding groups.

Conclusion: PS exclusively affects the TMJ by elevating its synovial inflammatory mediators. Moreover, PS can solely induce TMJ synovitis

Key Words: Temporomandibular joint, knee joint, Psychology, Stress, rats.

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INTRODUCTION:

Psychological Stress (PS) can influence health throughout the lifespan,[1- 3] yet there is a little agreement about the type and extent of its negative impact on human health as well as the area that is mostly influenced by it.[4- 8]More researchers have paid attention to the role of PS in the occurrence of temporomandibular disorders (TMD).[9- 13]

First, Moulton et al.[14] observed that stress affects masticatory muscle but they were not able to empirically verify their theory, until, this relation experimentally using a rat model was successfully proven by other researchers [15- 17] that have revealed that stress and anxiety induce muscle hyperactivity and fatigue which in turn would cause muscle spasms.[18- 21] It is worth noting that these disorders in the musculature, which are often aggravated by PS, are the basis for the majority of TMD.[22, 23]

Recently, TMD have been included in a spectrum of stress-associated syndromes characterized by frequent somatic and psychological complaints, including fatigue; sleep disturbances, anxiety, and depression.[24- 26] Stress-affected TMD are occasionally associated with physical symptoms of comorbid disorders.[27] however, this comorbidity has not been extensively studied to assess stress-affected disorders in discrete joints,[4] specifically in the knees versus TMJ.[28, 29] This influence can be evaluated by analysis of expression levels of synovial fluid for TNF- α and IL-6 that Increase in synovitis and degenerated cartilaginous tissue and bone of joints.[30- 34]

Thus, we designed an experimental model in order to prove the substantial influence of PS on TMJ when compared to the knee joint regarding these inflammatory mediators (IM).

MATERIALS AND METHODS:

The current prospective randomized controlled experimental study was conducted on thirty-two young adult Albino specified pathogen-free rats to assess the effect of PS on TMJ and knee joint. All experimental and animal care procedures were approved by the ethical approval committee, faculty of dentistry, Minia University, performed in accordance with standard laboratory operating procedures and according to the guidelines of the International Association for the Study of Pain (IASP) in conscious animals. Rats aged from 1: 2 months, and the weight range from 250: 300 g. were obtained from laboratory animal center, faculty of medicine, Minia University.

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All rats were acclimated to laboratory conditions one week before the experiment with a regular diet and drinking tap water: temperature 20–24 °C, relative humidity 30–60%, and 12-hour light cycle. A total of 32 animals randomly were divided into three groups: Ctrl group (n=8) animals were not exposed to any physical or psychological stimulation; FS group (n=16) animals were subjected to a regular morning electric shock at 48 V for 60 min, and were considered to an inducer for PS. Eight rats were randomly selected from this group daily to receive a shock in order to minimize anticipation and to prevent adaptation to the stress; and PS group (n=8) animals experienced PS by sensing the hair erection and scream of the animals in the FS group.

Communication box: 16 chambers, each 35 _ 35 _ 25 cm, separated by transparent porous plastic plates, which prevented physical contact between animals but allowed them to receive visual, auditory, and olfactory cues from neighboring animals. The chamber bottoms were comprised a grid floor of 5-mm-diameter stainless steel rods placed at 0.3-cm intervals, through which a foot shock could be given if the wire was electrified. A 48-V electric generator connected to the grid floor generated a foot shock every 3 s for SH group in only 8 chambers. PS group were placed in the remaining chamber with wood plates-covered bottom to insulate them from electric shocks.

One week prior to experiment, SH and PS groups were individually confined and placed into each compartment of the communication box for 1 h daily without any stressors to acclimatize them to the new surroundings. During the stress stimulation period, the electric shock was introduced to SH group for 60 min/d at a fixed time (10:00-11:00 AM).

PS group in isolated chambers who do not receive foot shock are likely to experience PS by proximity and witnessing to SH group during their screaming and jumping resulting from the electric shock, via visual, auditory, and gustatory routes through transparent and porous walls of the chambers. All the parameters were set as, reported to make animals reach the state of shock but without visible physical injury.

Biochemical Analysis: After 4 weeks, PS and Ctrl groups were anesthetized with Ketamine (70mg/kg) and Xylazine (10mg/kg). Then Synovial fluid samples collected from TMJ and knee joint of each group. The samples were immediately centrifuged for biochemical analysis findings with Enzyme-linked immunosorbent assay (ELISA).

STATISTICS

Statistical analysis was performed with IBM® SPSS® (ver. 26. SPSS Inc., IBM Corporation, Armonk, NY, USA). Data explored for normality using Shapiro-Wilk test. TNF- α and IL-6 showed non-normal distribution, so quantitative data were presented by median and interquartile range (Q1-Q3). Mann Whitney test used to compare between two independent groups. Box plot was used for graphical presentation of data. A statistically significant level was considered when p value < 0.05.

RESULTS:

The primary objective of the present study was to compare between the effects of a psychological stress on TMJ and knee joint. So, we first analyzed the synovial fluid levels of TNF- α and IL-6 in TMJ and knee joint for Ctrl and PS groups. The concentrations of TNF- α and IL-6 in TMJs of the PS group after 4 wks. of psychological stimulation were significantly higher than the concentrations measured in Ctrl group (table I). In addition, the same mediator's values in knee joints of PS group were not significantly different from those of Ctrl group (P > 0.05) (table II). % differences of TNF- α in TMJs were significantly higher than in knee joints (P < 0.05) (table III). However, that differences of other mediator between TMJs and Knee joints were not significant differences. (table IV) Presence of clear difference in Synovial levels of TNF- α expression level between two joints in ctrl group and this is not shown with IL-6. (P=0.001) (table V) represent high significant differences for two mediators in PS group between two joints.

Table I: Comparison of IM in TMJs between Ctrl and PS groups

P value		Ctrl group	PS group	Mean difference	% difference	P value
TNF-α	IQR	0.90	4.1		55.8%	0.001*
	Mean ±SD	31.3±0.6	70.9±2.2	39.6		
IL-6	IQR	0.26	0.84		43.7%	0.001*
	Mean ±SD	8.5±0.2	15.1±0.5	6.6		

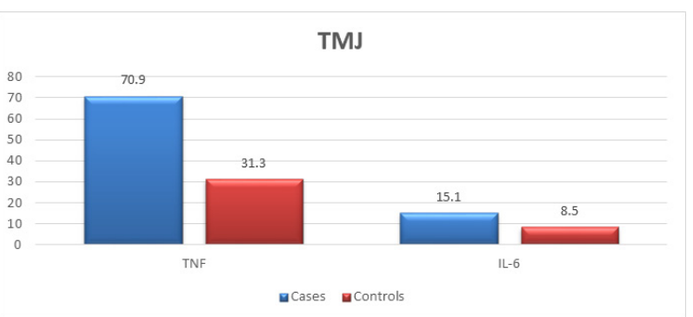


Table II: Comparison of IM in Knee joints between Ctrl and PS groups

Knee joint		Ctrl group	PS group	Mean difference	% difference	P value
TNF- α	IQR Mean ±SD	0.88 36.06±0.6	1.02 37.4±0.6	1.4	3.7 %	0.09*
IL-6	IQR Mean ±SD	1.16 8.4±0.5	1.22	2.6	23.5 %	0.06*

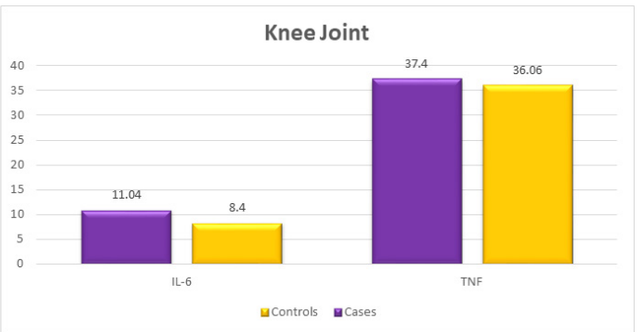


Table III: Comparison of Percentage of differences between IM in (PS group and Ctrl group) of knee joint and TMJ

	% difference TMJ	% difference Knee	P value
TNF- α	55.8%	3.7%	0.8
IL-6	43.7%	23.5%	0.09

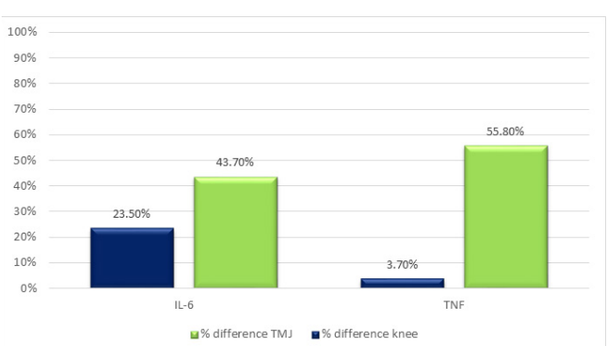


Table IV: Comparison of IM between Knee and TMJ joint among Ctrl group

		Knee joint in Ctrl group	TMJ in Ctrl group	P value
TNF- α	IQR Mean ±SD	0.88 36.06±0.6	0.90 31.3±0.6	0.4
IL-6	IQR Mean ±SD	1.16 8.4±0.5	0.26 8.5±0.2	0.7

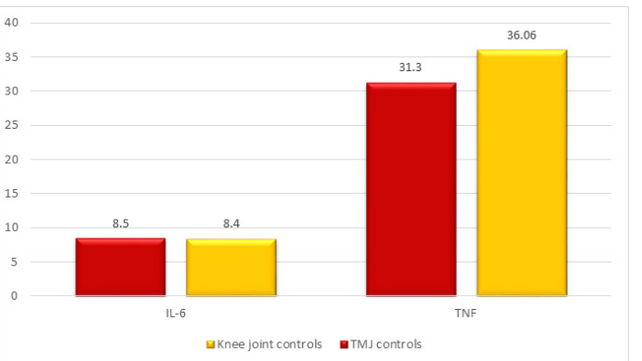
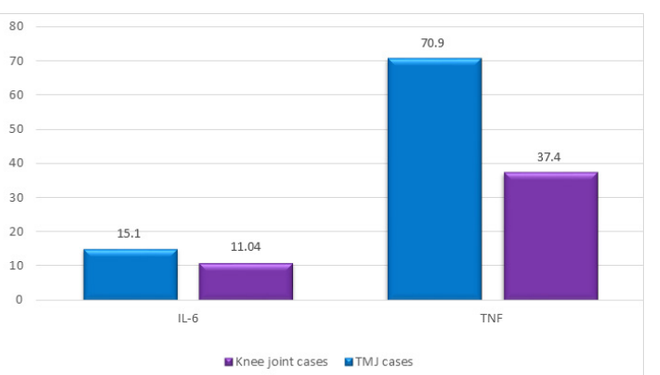


Table V: Comparison of IM between Knee and TMJ among PS group

		Knee joint in Ctrl group	TMJ in Ctrl group	P value
TNF- α	IQR Mean ±SD	1.02 37.4±0.6	4.1 70.9±2.2	0.001*
IL-6	IQR Mean ±SD	1.22 11.04±0.6	0.84 15.1±0.5	0.01



DISCUSSION:

The purpose of this study was to compare the effect of PS on two discrete joints by the biochemical analysis of valuable degradation markers. We hypothesized that the contribution of TNF- α and IL-6 would be comparable in the two joints by exposure of rats for PS 1h/d/4wks which was considered an appropriate time to cause anxious effect on rats according to previous studies.[16]

We noticed behavioral changes of PS group throughout the experiment; PS rats were trying to avoid visual contact with adjacent SH rats, turning their faces to the opposite corner and continuous screaming through experiment time that cause hyperactivity of masticatory muscles. This confirms what has been proven by previous studies on the relationship between PS and masticatory muscles disorders (MMD), followed by the occurrence of pathological changes in TMJ [23]. On the contrary, we did not observe any hyperactivity in movement of rats that cause strain in the muscles of knees.

Long-term exposure to such stress caused changes in the ultrastructural morphology of the TMJ in rats and degenerative changes, which are coordinated by the action of inflammatory mediators. Various studies proposed that tumor necrosis factor- α and interleukins are among the main IM of TMJ disorders and knee osteoarthritis. The majority of inflammatory mediators can be detected in the SF of both healthy (Ctrl group) and diseased joints (PS group). Nevertheless, significant differences in concentrations levels were observed. Here, we present the results of an extensive analysis correlating inflammatory mediators with TMD; Synovial levels of TNF- α and IL-6 were significantly higher in TMJs of PS group versus Ctrl group, Whereas, knee joints levels were comparable in their corresponding groups, suggesting that there are differences in pathophysiology and that the inflammatory component might be more distinct in the TMJ. These results indicate that PS has a direct effect on TMJ and this should be taken into consideration in diagnosis and management of TMD patients.

CONCLUSIONS:

PS exclusively affects the TMJ by compared to knee joints. Although TMJ and Knee pathologies have several similarities, there are some biomechanical and biochemical differences between the two joints. So, Future studies should be carried out with larger sample size for more dependable statistical evidence.

CONFLICT OF INTEREST

This clinical study was self-funded by the authors, with no conflict of interest.

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