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The role of depression and anxiety in pain perception

[1]Ina Timotin, [1]Andrei Ganenco, *[1]Svetlana Lozovanu, [1]Oleg Arnaut, [1]Ion Grabovschi, [2]Ion Moldovanu, [1]Victor Vovc

[1]Department of Human Physiology and Biophysics, *Nicolae Testemitanu* State University of Medicine and Pharmacy
[2]Cerebrovascular Diseases and Neurorehabilitation Research Unit, *Diomid Gherman* Institute of Neurology and Neurosurgery
Chisinau, the Republic of Moldova

Authors' ORCID iDs, academic degrees and contribution are available at the end of the article

*Corresponding author – Svetlana Lozovanu, e-mail: svetlana.lozovanu@usmf.md
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Abstract

Background: Depression and anxiety are associated with increased perception of pain severity. Because patients with a depressive disorder and anxiety often report pain, their sensitivity to experimental pain is controversial, probably due to differences in sensory testing methods and the lack of normal values.
Material and methods: The study was conducted on 140 selected subjects. The pain test was performed using a technique, called the submaximal effort tourniquet technique. Before the start of the study, a set of psychometric inventories and tests was prepared (visual analog scale, Beck Depression Inventory, Spielberger's State and Trait Anxiety Inventory).
Results: No differences in pain perception have been found in men and women as well as in relation to age, thus gender and age cannot be a predictor in pain perception. The anxiety has no effect on pain perception. The depression can be considered a predictor of pain intensity because a change in depression levels determines a change in pain intensity perception at the 3rd minute. If the depression category was changed from a patient with no depression to one with mild depression, pain intensity at minute 3 increased by approximately one point on the visual analog scale (B=.954, CI95% .200, 1.709, p=.014).
Conclusions: Depression can be considered a predictor in the evolution of pain perception. Not so much the depression score, but the increase in the severity of depression can predict the evolution of pain perception.
Key words: anxiety, depression, pain, visual analog scale, pain test.

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Introduction

The International Association for the Study of Pain defines pain as "an unpleasant subjective feeling and emotional experience associated with actual or potential tissue damage", which is an interaction of psychological, emotional, behavioral, and social factors [1].

Pain is a subjective experience that is influenced by genetic, gender, social, cultural, and personal factors. This is accompanied by increased sympathetic and noradrenergic activity and a reduction in parasympathetic activity. Generally, an anxiety reaction develops due to acute pain. The link between mood disorders and acute pain has been shown to be increasingly significant because the link is bidirectional and, in both cases, they act as risk factors for each other. Depression and anxiety are associated with increased perception of pain severity, while the prolonged duration of acute pain leads to increased mood dysregulation.

Affective processes may interact with nociception and pain at different levels, namely, pain modulation, pain response, and pain behavior [2]. Negative emotional states, including fear and anxiety, are found to alter pain-related responses. A number of studies have shown an increase in pain and hyperalgesia, while others have reported inhibition of pain (analgesia) during stressful situations [2].

Several human experimental studies show that negative affective states, including anxiety, have been consistently associated with increased pain and hyperalgesia. However, there is evidence in the literature demonstrating that high levels of negative affect inhibit nociceptive and pain-like responses [3].

Pain is a common symptom in patients suffering from a depressive disorder. Both depression and chronic pain are common conditions in medical and psychiatric practice. Although depression and chronic pain can occur independently, they are often comorbid. In turn, chronic pain conditions trigger a depressed mood, which may finally meet the diagnostic criteria for a depressive disorder. Pain and depression are hypothesized to share common neuroanatomical pathways and neurobiological substrates, which could explain the increased vulnerability to pain complaints in depression and vice versa.

Pains often co-occur with depression and anxiety and together represent a considerable social and economic burden. However, no systematic review has been conducted to examine the covariation between these conditions [4]. Data on the etiological factors underlying the co-occurrence of common pain in individuals with symptoms of anxiety and depression are very limited [5]. Most studies found that the covariation of pain with depression and/or anxiety was explained by genetic or both genetic and environmental factors [4].

As both depression and anxiety are associated with acute pain, the link between depression and acute pain is being studied more thoroughly. Although fewer data are published on anxiety and pain, the relationship is consistent across studies, as increased anxiety leads to increased perceived pain severity and decreased pain tolerance. Different studies show that anxiety, fear, and stress which have been shown to be mediators in the causal pathway between pain and disability can alter the pain threshold, demonstrating both increased and decreased pain threshold and pain tolerance [6].

Reports on the perception of experimentally induced pain in depressed patients are mixed, showing both increased and decreased pain threshold and pain tolerance in different studies. Because patients with a depressive disorder and anxiety often report pain, their sensitivity to experimental pain is controversial, probably due to differences in sensory testing methods and the lack of normal values [7].

The aim of the study was to analyze the role of depression and anxiety in pain perception in the experimental study.

Material and methods

The study was performed on 140 subjects selected out of 187 persons visiting the Department of Headache and Autonomic Disorders of the Institute of Neurology and Neurosurgery (Chisinau, the Republic of Moldova) from March 2018 to February 2022. They signed an informed agreement to be included in this study, which continued at the Department of Human Physiology and Biophysics of *Nicolae Testemitanu* State University of Medicine and Pharmacy. The subjects with acute or chronic cardiac or respiratory diseases were excluded.

Before beginning the study, a set of inventories and psychometric tests was prepared.

A visual analog scale (VAS) is used to assess the severity of a patient's pain. It is 10 cm long with 0= no pain, written at one end, and 10= most severe pain, written at the other. Patients are asked to mark where along the scale they would place the pain they perceived. The distance is measured in centimeters. The value shows the severity of pain perceived by the patient.

Beck Depression Inventory (BDI) was developed by Beck to measure a variety of symptoms of depression. It is a 21-item checklist that the patients fill in themselves. They select the most appropriate of the four choices.

Spielberger's state and trait anxiety inventory is made up of 40 questions and distinguishes between a person's state anxiety and their trait anxiety. The two forms of anxiety are separated in the inventory, and both are given their own 20 separate questions. When participants rate themselves on these questions, they are given a 4-point frequency scale. The frequency scales differ between the two types of anxiety.

The pain test was performed using a technique, called the submaximal effort tourniquet technique [8]. The pain was produced by a tourniquet which had been inflated around his upper arm to 200 mm Hg. The assessed parameter was pain sensation in 1st, 2nd and 3rd minutes after applying a tourniquet as chosen by the subject on the VAS.

Statistical analysis was performed using the software Statistical Package for Social Sciences version 26 (IBM SPSS 26). Descriptive statistics for numerical variables were presented by minimum, maximum, mean, standard deviation, median, 25th percentile, and 75th percentile. Descriptive statistics for discrete variables were presented by count, relative frequencies, and 95.0% CI for relative frequencies. Correlation analysis was performed using the Spearmen test, completed by bootstrap estimation of 95% CI. The form of relationships of potential predictors on pain perception at the third minute was estimated using regression analysis, with bootstrap being applied for model stability estimation.

Results

As can be seen in table 1, the research group included 140 subjects aged between 17 and 70 years, with an average age of 37 years (standard deviation 18 years), the median being 29 years, and interquartile range of 36 years. Of those included in the study, 55.7% (95% CI 47.4, 63.8) were males and 44.3% (95% CI 36.2, 52.6) were females. According to the methodology described above, the perceived pain intensity at 1, 2, and 3 minutes of painful stimulation was measured. The recorded values for the level of pain measured in the first minute ranged between 0 and 10 points on the VAS. The mean intensity at this time point was 4.9 points with a standard deviation of 2.3 points. The median of the recorded results was 5 points, and the interquartile range was 3.5 points. The pain at 2 minutes had values between 0 and 10 points with an average of 5.6 points, the standard deviation being 2.6. A median of 6 points and an interquartile range of 3 points were observed on VAS. In the research subjects, the pain at 3 minutes was between 0 and 10 points, with a mean intensity of 5.8 (standard deviation 2.7 points), the median being 6 points on the VAS, and the interquartile deviation of 4.5 points. The majority of those included in the research – 42.1% (CI95% 34.2, 50.4) did not have depression according to the Beck score. Another 24.3% (95% CI 17.8, 31.9) of study subjects had mild depression, and approximately one-third, 33.6% (95% CI 26.1, 41.7), had moderate depression according to the Beck scale score. The absolute values of this score

recorded in research participants varied between 0 and 24 points. The average of the recorded values was 6 points with a standard deviation of 6 points. The median value of the Beck test was 4 points, and the interquartile range was 7 points. The state anxiety level had values between 6 and 56 points with a mean of 31 points, the standard deviation being 11. A median of 30 points and an interquartile range of 16 points were observed.

Starting from the variables included in the study, in order to identify those that could show some relationships or interdependencies, the correlation matrix presented in table 2 was created. As can be seen, age had a statistically significant correlation coefficient only with the pain values measured at 1 minute (CC=.309, CI95% .158, .444, p<.001), at 2 minutes (CC=.356, CI95% .206, .496, p<.001) and at 3 minutes (CC=.263, CI95% .093, .419, p=.002). The gender of the people included in the study also correlated statistically significantly with the pain values measured at 1 minute (CC= -.223, CI95% -.379, -.065, .444, p=.008), at 2 minutes (CC=– .241, IC95% -.390, -.082, p=.004), at 3 minutes (CC=-.187, IC95% -.343, -.021, p=.027) at which, there were added the Beck test values grouped according to the degree of depression manifestation (CC=-.191, CI95% -.348, -.021), state anxiety (CC=-.170, CI95% -.331, -.002, p=.045) and trait anxiety (CC= -.188, CI95% -.347, -.024). Pain at 1 minute, in addition to those mentioned, correlated strongly with pain intensity at 3 minutes (CC= .632, CI95% .498, .738, p<.001). To the correlation coefficients described for the pain recorded at the 2nd minute, the one describing its relationship with the pain intensity at the 3rd minute was added (CC= .854, CI95% .774, .915, p<.001). The Beck test score transformed into an ordinal variable obviously correlated with the Beck test scale depression values in the form of a continuous variable (CC= .938, CI95% .921, .945, p<.001). Statistically significant correlations were also observed with state anxiety values (CC= .566, CI95% .440, .669, p<.001) and with those for trait anxiety (CC= .581, CI95% .448, .689, p<.001). The Beck test score included in the statistical analysis as a numerical variable, in addition to the described coefficients, correlated with state anxiety (CC= .569, CI95% .443, .672, p<.001) and with trait anxiety (CC=.587, CI95% .449, .699, p<.001). State anxiety, apart from the coefficients described above, correlated with trait anxiety (CC=.626, 95% CI .501, .726, p<.001).

Considering the correlation coefficients in table 2 and the complex relationships between factors, multivariate analysis was performed. Two models have been developed that aim to predict pain intensity at minute 3 of painful stimulation.

The first model included predictors of the pain variables at minute 1 and the Beck test score as an ordinal variable (tab. 3). Pain at minute 2 was not included in the model due to a strong correlation with pain at minute 1. As can be seen, 42.2% of the variability in pain intensity at minute 3 was explained by this model.

The coefficient of determination (Adjusted R Square) was 0.422, the sum of squares constituted 441,454 out of 1016,234 possible, which means that the proposed model explains almost half of the dispersion of the pain variable at minute 3. The null hypothesis (none of the parameters included in the model cannot predict the pain intensity value at minute 3 better than some arbitrary model) was rejected (F = 34.818, p = 0.000).

Table 1. Descriptive analysis of the research group. IBM SPSS 26 output

		Minimum	Maximum	Mean	Standard Deviation	Median	The 25th percentiles	The 75th percentiles	Count	Column N %	95.0% Lower CL for Column N %	95.0% Upper CL for Column N %
Age		17	70	37	18	29	21	57				
Sex	F								78	55.7%	47.4%	63.8%
	M								62	44.3%	36.2%	52.6%
Pain 1 min		.0	10.0	4.9	2.3	5.0	3.0	6.5				
Pain 2 min		.0	10.0	5.6	2.6	6.0	4.0	7.0				
Pain 3 min		.0	10.0	5.8	2.7	6.0	3.5	8.0				
Beck test score	No depression								59	42.1%	34.2%	50.4%
	Mild depression								34	24.3%	17.8%	31.9%
	Average depression								47	33.6%	26.1%	41.7%
Beck test score		0	24	6	6	4	2	9				
State anxiety		6	56	31	11	30	24	40				
Trait anxiety		25	72	46	11	43	37	54				

Table 2. Analysis of correlations between measured variables. IBM SPSS 26 output

			Age	Sex	Pain 1 min	Pain 2 min	Pain 3 min	Beck test total score	Beck test grade of depr-ession	State anxiety	Trait anxiety
Age	Correlation Coefficient		1,000	-.088	.309	.356	.263	.028	.056	.065	.095
	Sig. (2-tailed)		.	.302	.000	.000	.002	.741	.515	.442	.262
	95% Confidence Interval	Lower	1,000	-.249	.158	.206	.093	-.132	-.108	-.113	-.056
		Upper	1,000	.075	.444	.496	.419	.179	.212	.237	.264
Sex	Correlation Coefficient		-.088	1,000	-.223	-.241	-.187	-.191	-.162	-.170	-.188
	Sig. (2-tailed)		.302	.	.008	.004	.027	.024	.056	.045	.026
	95% Confidence Interval	Lower	-.249	1,000	-.379	-.390	-.343	-.348	-.329	-.331	-.347
		Upper	.075	1,000	-.065	-.082	-.021	-.021	.007	-.002	-.024
Pain 1 min	Correlation Coefficient		.309	-.223	1,000	.848	.632	.062	.062	.047	.082
	Sig. (2-tailed)		.000	.008	.	.000	.000	.467	.467	.578	.338
	95% Confidence Interval	Lower	.158	-.379	1,000	.775	.498	-.115	-.115	-.106	-.086
		Upper	.444	-.065	1,000	.895	.738	.236	.241	.208	.245
Pain 2 min	Correlation Coefficient		.356	-.241	.848	1,000	.854	.080	.053	.077	.135
	Sig. (2-tailed)		.000	.004	.000	.	.000	.346	.533	.368	.111
	95% Confidence Interval	Lower	.206	-.390	.775	1,000	.774	-.091	-.127	-.091	-.036
		Upper	.496	-.082	.895	1,000	.915	.239	.218	.245	.299
Pain 3 min	Correlation Coefficient		.263	-.187	.632	.854	1,000	.105	.051	.077	.142
	Sig. (2-tailed)		.002	.027	.000	.000	.	.217	.551	.366	.095
	95% Confidence Interval	Lower	.093	-.343	.498	.774	1,000	-.069	-.134	-.083	-.034
		Upper	.419	-.021	.738	.915	1,000	.272	.219	.244	.306
Beck test score	Correlation Coefficient		.028	-.191	.062	.080	.105	1,000	.938	.566	.581
	Sig. (2-tailed)		.741	.024	.467	.346	.217	.	.000	.000	.000
	95% Confidence Interval	Lower	-.132	-.348	-.115	-.091	-.069	1,000	.921	.440	.448
		Upper	.179	-.021	.236	.239	.272	1,000	.945	.669	.689
Beck test score	Correlation Coefficient		.056	-.162	.062	.053	.051	.938	1,000	.569	.587
	Sig. (2-tailed)		.515	.056	.467	.533	.551	.000	.	.000	.000
	95% Confidence Interval	Lower	-.108	-.329	-.115	-.127	-.134	.921	1,000	.443	.449
		Upper	.212	.007	.241	.218	.219	.945	1,000	.672	.699
State anxiety	Correlation Coefficient		.065	-.170	.047	.077	.077	.566	.569	1,000	.626
	Sig. (2-tailed)		.442	.045	.578	.368	.366	.000	.000	.	.000
	95% Confidence Interval	Lower	-.113	-.331	-.106	-.091	-.083	.440	.443	1,000	.501
		Upper	.237	-.002	.208	.245	.244	.669	.672	1,000	.726
Trait anxiety	Correlation Coefficient		.095	-.188	.082	.135	.142	.581	.587	.626	1.000
	Sig. (2-tailed)		.262	.026	.338	.111	.095	.000	.000	.000	.
	95% Confidence Interval	Lower	-.056	-.347	-.086	-.036	-.034	.448	.449	.501	1.000
		Upper	.264	-.024	.245	.299	.306	.689	.699	.726	1.000

Table 3. Statistical data of multivariate analysis for model 1. IBM SPSS 26 output

Model Summary [b]									
Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	Change Statistics				
					R Square Change	F Change	df1	df2	Sig. F Change
1	.659 [a]	.434	.422	2.0558	.434	34.818	3	136	.000
a. Predictors: (Constant), Pain 1, Beck test score									
b. Dependent Variable: Pain 3									

Table 4. ANOVA test for model 1. IBM SPSS 26 output

ANOVA [a]						
Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	441.454	3	147.151	34.818	.000 [b]
	Residual	574.780	136	4.226		
	Total	1016.234	139			
a. Dependent Variable: Pain3						
b. Predictors: (Constant), Beck test score, Pain1, Beck test score						

The data in table 5 show that an increase in pain intensity at minute 1 by one point on the VAS causes an increase in pain intensity at minute 3 by 0.742 points on the VAS under conditions where the degree of depression was constant (B=.742, IC95 % .594, .890, p<.001). If the depression category was changed from a patient with no depression to one with mild depression, pain intensity at minute 3 increased by approximately one point on the VAS (B=.954, CI95% .200, 1.709, p=.014).

The elaborated model also respects the conditions for residuals and linear regression. The distribution of the residuals is normal, and the lack of associations between the predictive standardized values and the standardized residuals (fig. 1). All these together allow to consider the model as a functional one.

Model 2 initially included sex, age, first-minute pain intensity, and levels of reactive and trait anxiety as potential predictors. The data from table 6 show that about 40% of the variability of pain intensity at minute 3 was explained by model 2 (tab. 6).

The coefficient of determination (Adjusted R Square) was 0.407, the sum of squares was 435,678 out of 1016,234 possible (tab. 7), and which means that the proposed model explains approximately 0.4 of the dispersion of the pain variable at minute 3. The null hypothesis, according to which no parameter of those included in the model can predict the pain intensity value at minute 3 better than some arbitrary model, was rejected (F = 20.112, p < .001).

Table 5. Predictor coefficients for model 1. IBM SPSS 26 output

Coefficients [a]								
Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95.0% Confidence Interval for B	
		B	Std. Error	Beta			Lower Bound	Upper Bound
1	(Constant)	1.090	.611		1.783	.077	-.119	2.298
	Pain1	.742	.075	.640	9.906	.000	.594	.890
	Beck test score	.954	.381	.307	2.502	.014	. 200	1.709
a. Dependent Variable: Pain3								

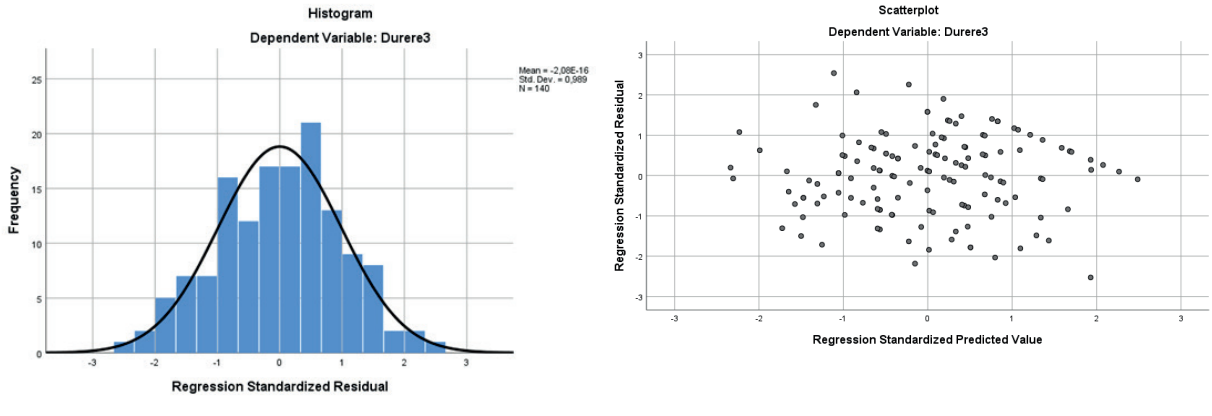

Fig. 1. Distribution of residuals (left); scatterplot of standardized predictive values and standardized residuals (right) for model 1. IBM SPSS 26 output

Table 6. Statistical data of multivariate analysis for model 2. IBM SPSS 26 output

Model Summary [b]									
Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	Change Statistics				
					R Square Change	F Change	df1	df2	Sig. F Change
2	.655 [a]	.429	.407	2.0815	.429	20.112	5	134	.000
a. Predictors: (Constant), Trait anxiety, Age, Sex, Pain1, State anxiety									
b. Dependent Variable: Pain3									

Table 7. ANOVA test for model 2. IBM SPSS 26 output

ANOVA [a]						
Model		Sum of Squares	df	Mean Square	F	Sig.
2	Regression	435.678	5	87.136	20.112	.000 [b]
	Residual	580.556	134	4.333		
	Total	1016.234	139			
a. Dependent Variable: Pain3						
b. Predictors: (Constant), Trait anxiety, Age, Sex, Pain1, State anxiety						

Table 8. Predictor coefficients for model 2. IBM SPSS 26 output

Coefficients [a]								
Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95.0% Confidence Interval for B	
		B	Std. Error	Beta			Lower Bound	Upper Bound
2	(Constant)	1.268	1.587		.798	.426	-1.872	4.407
	Pain1	.686	.081	.592	8.439	.000	.525	.847
	Sex	-.001	.002	-.022	-.326	.745	-.004	.003
	Age	.018	.010	.123	1.791	.076	-.002	.039
	1. State anxiety	.007	.023	.028	.309	.758	-.038	.052
	2. Trait anxiety	.012	.022	.049	.541	.589	-.032	.056
a. Dependent Variable: Pain3								

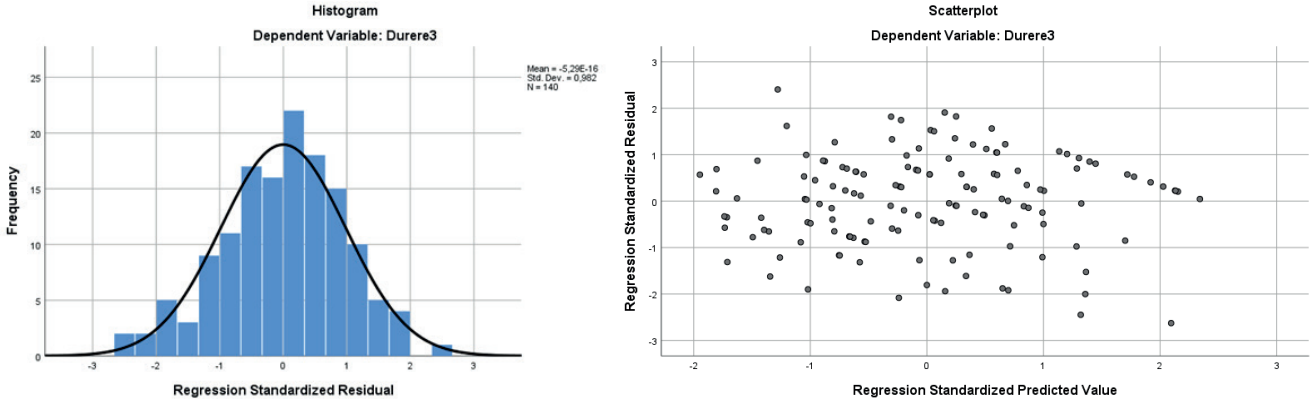

Fig. 2. Distribution of residuals (left); scatterplot of standardized predictive values and standardized residuals (right) for model 2. IBM SPSS 26 output

As can be seen in table 8, only pain intensity at minute 1 showed statistical significance and caused an increase in perceived pain at minute 3 by .686 points when it increased in intensity by one point on the VAS (B=. 686, CI95% .525, .847, p<.001). Therefore, the other parameters measured in the research subjects cannot be considered predictors of the level of pain at the 3rd minute at the time of the research.

It was also noted that the developed model fulfilled the two conditions of the linear regression for the residuals. Their analysis showed a nearly normal distribution and lack of associations between standardized predictive values and standardized residuals (fig. 2). All these together allow to consider the model as a suitable one.

It was proposed to examine in this study the role of depression and anxiety on pain perception. There were found no differences in pain perception between males and females as well as in relation to age, thus gender and age cannot be a predictor in pain perception. These results are consistent with recent data. Detailed analysis of the literature reports that gender-related differences in pain perception still exist, and they are explained by the diversity of methods used in pain modeling. Several papers which characterize pain perception caused by low temperature or high temperature show that the pain threshold is not different in women, while the pain threshold caused by ischemia is lower in women [9].

Several studies about pain show that anxiety rises

sensibility to experimental pain. Moreover, anxiolytic medication can reduce pain perception. However, gender does not influence pain perception. The conducted research shows that anxiety has no effect in the pain perception. Just like in the control group, the pain numeric score rises at the 1st and 2nd minutes and stays the same at the 3rd minute.

There was not found any correlation between depression and pain perception. Just like in the control group, the pain numeric score rises at the 1st and 2nd minutes and stays the same at the 3rd minute. The literature data about depression and pain perception are very controversial. Some data suggest that depression increases the pain threshold, while others show that there is no correlation between depression and pain perception. Analyzing all variables included in the study, it results that depression can be considered a predictor of pain intensity because the change in depression levels determines the change in pain intensity perception at the 3rd minute. If the depression category was changed from a patient with no depression to one with mild depression, pain intensity at minute 3 increased by approximately one point on the VAS (B=.954, CI95% .200, 1.709, p=.014).

Conclusions

Depression can be considered a predictor in the evolution of pain perception. Not so much the depression score, but the increase in the severity of depression can predict the evolution of pain perception.

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Authors' ORCID iDs and academic degrees

Ina Timotin, MD, Assistant Professor – https://orcid.org/0000-0001-9750-5504
Andrei Ganenco, MD, Assistant Professor – https://orcid.org/0000-0002-9835-5461
Svetlana Lozovanu, MD, PhD, Associate Professor – https://orcid.org/0000-0002-5777-1805
Oleg Arnaut, MD, PhD, Associate Professor – https://orcid.org/0000-0002-5483-8672
Ion Grabovschi, MD, Assistant Professor – https://orcid.org/0000-0002-7716-9926
Ion Moldovanu, MD, PhD, Professor – https://orcid.org/0000-0002-1709-0319
Victor Vovc, MD, PhD, Professor – https://orcid.org/0000-0001-7624-9644

Authors' contributions

IT, AG, SL designed the research; OA, IG interpreted the data, did statistics; IM, VV drafted the manuscript and revised the manuscript critically. All the authors revised and approved the final version of the manuscript.

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Ethics approval and consent to participate

The research protocol No 1 of 27.02.2020 was approved by the Research Ethics Committee of *Diomid Gherman* Institute of Neurology and Neurosurgery and the tests have been done according to the contemporary principles in biological standardization of experiences and Declaration of Helsinki with further amendments (Somerset West Amendment, 1996).

Conflict of interests

No competing interests were disclosed.