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BIOCHEMICAL MODIFICATIONS IN AFFECTIVE DISORDER OF DEPRESSIVE TYPE

SUMMARY

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AIMS AND PURPOSES OF THE GIVEN RESEARCH

Depression is a very frequent affective illness that affects all social environments and age categories, its incidence rate being continually increasing; this fact makes it to be considered as a disorder of this era.

The affective depressive disorder, in all forms of manifestation, represents a permanent challenge for the scientific research in general and for the clinical one, in particular, due to the fact that the depressive symptoms clinically significant are present in 12-36% from the patients with non-psychiatric affections.

Statistics indicate that depression affects 1 from 5 persons over the course of life and around 10% from the population during one year. It is already known that depression is one of the most frequent illnesses in population; the risk of developing a depressive disorder in a life time is around 15%.

The World Health Organization (WHO) claims that now more than 5% from the world population is suffering from depression which is the fourth cause of disability and estimates that in 2020 it will attend the second place, after the cardiovascular diseases (SADOCK şi SADOCK, 2002).

The studies performed with multiple and various assets sustain the existence of differences according sex, population and age – this disorder presenting particularities in children, adolescents, adults and patients of third age. Practically, as the information about the neurological and biochemical bases of this illness with complex symptoms and debilitating for the individuals accumulates, there would be discovered and applied new treatments more complex and more scientifically sustained.

The known data in genetics, pharmacology, brain imaging indicate that depression is the result of the expression of multiple genes that act together with life events and environmental factors.

Studies of neurochemistry and physiology of the nervous system carried out until now have revealed that depression affects the nervous system in different grades and at different levels being known that:

- ✓ Limbic system is connected to sensibility
- ✓ Prefrontal cortex explains cognitive symptoms;
- ✓ The basal ganglia are involved in the appearance of abnormal movements;
- ✓ The hypothalamus is responsible of somatic symptoms such as sleep, appetite and circadian rhythms disorders, modifications of endocrine system.

Research projects extended in many countries of the world are trying to overcome this disorder whose origins and forms are still in the process of clarification and the means by which iti is approached this affection are multiple and varied.

The main purpose of this thesis is the determination of certain biochemical parameters that that lead to the establishment of correlations between the neurochemical substrate and symptoms of depression, correlations that support and contribute to the achievement of the main objectives of therapeutic strategy in depression represented by:

- ✓ the relieving of symptoms;
- ✓ restoring the patient from the standpoint of social workers, vocational and interpersonal;
- ✓ prevention of suicide.

The proposed objectives will be subordinated to this goal and will contribute to the expansion of the current database of neurobiochemical causes of depression:

1. Determination of the biochemical parameters of lipid metabolism: total lipids, total cholesterol, HDL-cholesterol, LDL-cholesterol, Triglycerides (TAG).
2. Determination of the concentrations of blood electrolytes such as sodium, potassium, calcium, magnesium, iron, inorganic phosphate, knew that their deficit explains a number of signs and symptoms of depression and that some antidepressants contain these elements.
3. Determination of anti-oxidants enzymatic agents (SOD, GR) and non-enzymatic (total bilirubin and uric acid) and other blood biochemical parameters (blood glucose, total protein) starting from the idea that stress leads to increased oxidative free radicals that cause cell death or brain atrophy with the emergence of cognitive impairment and mnezic changes.
4. Conducting statistical correlations between the studied parameters with a view to broadening the base of neurochemical depression -on the one hand – and investigating its causes such as neurophysiological – on the other hand.

DEPRESSION – PREVALENCE AND SPREADING

The problem of ethiology and pathogeny of affective disorders is a permanent challenge for the current research. The contribution of biological psychological and social factors to the emergence of depression is already known, but there are not fully elucidated the percentages of the importance of these factors.

The depression has a complex fundamental cause of genetic vulnerability accompanied by a number of biochemical changes and a sensitivity towards certain life events, known as events that induce a high degree of stress on individuals. Much of the mood disorders are not caused, in particular, by organic lesions or chemical modifications, but of a hyper-reactivity of psychosomatic functions in the struggle to adjust to the realities of life.

Fear, uncertainty and insecurity of tomorrow, as well as the wishes and intrapsihic conflicts produce organo-endo-vegetative disorders of autonomic dysfunctions. Current researches of causality in the mood disorders are focused on the ratio of their endo- and psychogenesis. The current interpretation of the suffering that characterizes the depressive syndrome has been accepted pthe ideea of its plurifactorial determination.

Depressive syndrome has as defining components:

- ✓ depressed mood;
- ✓ slowing the processes of thought;
- ✓ psychomotor slowness;
- ✓ a number of auxiliary symptoms of somatic expression.

Somatic disorders are linked to sympathetic hyperactivity matched by parasympathetic inhibition, epigastric pain, flatulence, constipation or diarrhea, difficulty in breathing, tightness of heart discomfort, heart rhythm disturbances, extrasystoles, dizziness, headache, diffuse pain in the uro-genital tract.

People suffering from depression would represent 4.5% of Europe's population, and every year people resort to 58,000 suicides, 90% of them having mental health problems often related to depression.

The spread of the disease on the european continent affect differently the existing populations. In 2002, according to the WHO study, countries with the highest rate of suicide related to the 10,000 inhabitants were the Baltic States (Lithuania - 88, Estonia -57). In May 2004, Finland was the north country where registered the highest rate of suicide due to depression-between 40-70% of cases. With six hours of daylight per day – starting from November – the principal cause of mental health problems is represented by seasonal affective disorder or seazonal depression that is related to the rhythm of the seasons and which differentiates from the depression through the effects upon sleep and appetite.

The WHO research delegation from Lille has shown that depression in France is associated with anxiety. In this country, one person out of three would be affected by a mental disorder, and 12% of French people would suffer from depression; the French consume a whopping many antidepressants compared to the English, the Germans and Italians.

In the USA, approximately 7.5 million adolescents - 9% of this population - have experienced a depressed mood in 2004, according to the report services for Associations of psychotropic substance abuse and mental health (SAMHSA).

A study in the Journal of the American Medical Association in association with WHO and Harvard University shows that, in Italy, the proportion of people affected by mental disorders is 11% and that only 26% of people who suffer from depression is addressed to a specialist. The studies mentioned data reveals that, in terms of genetic, populations of Latin origin are less prone to depression than the northern populations.

The incidence of depression in Romania has increased between 1994 and 2004 from 113 to 259 people at one hundred thousand inhabitants, mainly due to socio-economic conditions and to the daily stress that influences interpersonal relationshipes.It was found that women get sick more often than men (in three patients – two are women) and before the age of 35 years. Difficult period for men lies to the age group between fifty-five and seventy years.

The prevalence of major depressive disorder (4.7% for men and 6% for women) presents an increasing tendency, especially among the young population aged up to 45 years. Added to this is a very high rate of completed suicide in 15% of depressed patient and 75% of them occurring periods of recurrence. In developed countries, depressive disorder is the second cause of disability (MURRAY and LOPEZ, 1997).

Depressive episodes are often precipitated by stressful life events and they can be compounded with the loss of family and social role, of the skills in personal care (going as far as to disability); these are complications that can lead to suicidal acts. The average number of depressive episodes in the life of a patient is five. In general, the prognosis is good: 50% of the patients are fully repaid, partly by 30% and 20% become chronically (SADOCK and SADOCK, 2002).

Epidemiological studies carried out in recent years in Romania, led to the conclusion that 20% of the population suffers from mental disorders, of which 10% are suffering from depression. In 2005, in Helsinki, WHO have warned that it is important to change the social mentality of people with psychiatric conditions, unfairly stigmatized, and have highlighted the need to carry out treatments both in diagnostic centres as well as at home. Following a study carried out by the League for Mental Health and published in 2011, there was detected a significant increase in major depressive episode with age, from 2.1% to 2.6% (18-49 years old), from 4.4% to 5.2% (over 50 years) with a growth rate of 1.2 percentage points for each age group (55-64 years, 65 years and over). It was also found that depression is twice as common among women than in that of men. One in four women will get treatment for depression at one point compared to one out of ten men.

The particuliarities of the diagnosis and treatment of patients with depression in Romania include:

- ✓ the difficulty of patients to discuss their emotional problems and a tendency to seek medical help only for physical problems;
- ✓ patients ' reluctance to address directly the physician specialist psychiatrist (fear of stigma);
- ✓ ignoring the disease for a long period of time;
- ✓ lack of responsiveness of family, friends, co-workers and, often, all those around him.

PERSONAL CONTRIBUTIONS

The analyzed biochemical parameters were chosen based on the following considerations:

- ✓ all types of depression can be accompanied by quantitative changes – minor or major – of a very large number of biochemical parameters studied separately or concurrently. In addition, in the case of depressions of somatic origin, their evolution depends on improvement or cure of somatic cause, processes that are characterised by the return of the parameters to the values considered normal physiologically.
- ✓ It is recognised that the deficiency of neurotransmitters is not the only cause of depression and it is trying to find some new biochemical parameters or correlations that could explain its endogenous and causes and could help to relieve the symptoms.

The used methods were the enzymatic and colourimetric measurements and were made to two groups of subjects – depressed and non-depressed; the analysis of the results was made quantitative and statistically.

Biochemical determinations were performed on Beckman Coulter Synchron CX7 analyzers in clinical laboratory of the Emergency Military Hospital of Constantza and were observed working protocols provided by the company producing apparatus and reagents. Some of blood electrolytes such as total calcium in serum and inorganic phosphate in serum were determined in the laboratory of Biochemistry at the Faculty of Medicine on a Sherwood-Chroma apapratus and with reagents and protocols of Biosystems**.**

Research has been carried out in the period 2009-2012 on a number of 90 patients diagnosed with moderate depressive affective disorder who were selected in collaboration with the medical staff in Psychiatric Clinic Palazu Mare from the Emergency County Hospital.

Study 1 Determination of some parameters of lipid metabolism in patients with depressive affective disorder

Study hypothes:

1. Cholesterol is one of the components of cell membranes and myelin sheath and it is assumed that changes in serum total cholesterol level can directly influence the brain lipids and cell membrane fluidity with the side effects of serotoninergic transmission and with the possibility to change the emotional states that can lead to depression.
2. Permanent stress to which is subjected the body may result in modification of mood, as well as in the activation of the hypothalamic-pituitaro-adrenal axis. Turn on this axis may result in simultaneous changes of biochemical parameters of lipid metabolism, changes that can induce depression or may enhance its symptoms, mainly through their influence on the balance of neurotransmitters.
3. The appearance of, respectively, the enhance of symptoms of depression may be associated with the existence of statistically significant differences between the values of the parameters analysed according to sex inside the two lots of study.
4. Taking into account that the diagnosis of major depression was based both on the diagnostic criteria of DSM-IV-TR and on the scores obtained at the Hamilton Depression scale, it is assumed that quantitative changes in the analysed biochemical parameters correlate with the scores obtained by the subjects taken in the study as a result of this scale.

Materials and methods

The study group was made up of 30 subjects with moderate depression (27) and severe (3).These were diagnosed according to the diagnostic criteria from DSM-IV-TR and according to the scores obtained from the Hamilton scale for depression. There were excluded individuals with endogenous depression or bipolar disorder.

The control group was composed of 30 non-depressed subjects and with affective disorders without forebears.

The Hamilton Scale for assessing depression (HDRS) has 23 items to evaluate cardinal signs of depression as DSMIV-TR and the answers are listed with 0-4 points each. In practice it is generally estimated that between 7-17 p- is mild depression, between 18-24 p is moderate depression and more than 25 points means severe depression.

Results and discussions

Statistical analysis of the results obtained sepate in both groups and between them had to establish differences and correlations between the values of the analyzed parameters.

In table 1 it is shown the two lots, the composition of study and control, depending on the gender of the patients, while table 2 shows the distribution of patients in both groups on age ranges.

Table 1. Patients distribution in both groups according to gender

Sex

Lot			Frequency	Percent	Valid Percent	Cumulative Percent
Control	Valid	Male	15	50,0	50,0	50,0
		Female	15	50,0	50,0	100,0
		Total	30	100,0	100,0	
Studiu	Valid	Male	10	33,3	33,3	33,3
		Female	20	66,7	66,7	100,0
		Total	30	100,0	100,0	

Table2. Patients distribution in both groups on age ranges

Sex * Intervale varsta Crosstabulation

Count

Lot			Intervale varsta			Total
			(25-35]	(35-45]	(45-…]	
Control	Sex	Masculin	0	1	14	15
		Feminin	4	4	7	15
	Total		4	5	21	30
Studiu	Sex	Masculin	1	4	5	10
		Feminin	4	5	11	20
	Total		5	9	16	30

Distribution of results obtained on each lot has been manufactured on the basis of the test One-Sample Kolmogorov-Smirnov and is shown in table 3.

Table3. Distribution of the obtained results in both groups according to One-Sample Kolmogorov-Smirnov Test

One-Sample Kolmogorov-Smirnov Test

Lot			Colesterol Total (mg/dl ser)	LDL-Colesterol (mg/dl ser)	HDL-Colesterol (mg/dl ser)	TAG (mg/dl ser)	LST (mg/dl ser)
Control	N		30	30	30	30	30
	Normal Parameters[a,,b]	Mean	210,8000	105,0667	82,8333	193,3333	906,4000
		Std. Deviation	25,35867	25,89359	25,69595	32,49226	147,01386
	Most Extreme Differences	Absolute	,122	,079	,220	,130	,182
		Positive	,122	,058	,220	,076	,182
		Negative	-,079	-,079	-,132	-,130	-,132
	Kolmogorov-Smirnov Z		,666	,431	1,207	,713	,996
	Asymp. Sig. (2-tailed)		,767	,992	,109	,689	,274
Studiu	N		30	30	30	30	30
	Normal Parameters[a,,b]	Mean	216,5667	103,2333	84,8667	192,3000	910,7000
		Std. Deviation	32,77792	26,62729	28,81778	31,98723	152,08916
	Most Extreme Differences	Absolute	,149	,068	,243	,139	,205
		Positive	,149	,068	,243	,096	,205
		Negative	-,102	-,059	-,146	-,139	-,138
	Kolmogorov-Smirnov Z		,817	,372	1,331	,759	1,124
	Asymp. Sig. (2-tailed)		,516	,999	,058	,613	,160

a. Test distribution is Normal.

b. Calculated from data.

Sig. (2-tailed) sau p > 0.05 – All the variables under study are normally distributed..

The results obtained for the comparisons between the mean values of parameters to analyze each batch separately according to sex are presented in table 4

Table4. Comparison of mean values (male, female) of the studied variables separately for each study group

Independent Samples Test

Lot	Levene's Test for Equality of Variances	t-test for Equality of Means	
			95% Confidence Interval of the Difference

			F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Control	Colesterol Total (mg/dl ser)	Equal variances assumed	2,473	,127	-1,516	28	,141	-13,73333	9,05914	-32,29013	4,82346
		Equal variances not assumed			-1,516	20,905	,145	-13,73333	9,05914	-32,57806	5,11139
	LDL-Colesterol (mg/dl ser)	Equal variances assumed	1,132	,296	-2,068	28	,058	-18,53333	8,96228	-36,89174	-,17493
		Equal variances not assumed			-2,068	26,410	,059	-18,53333	8,96228	-36,94167	-,12500
	HDL-Colesterol (mg/dl ser)	Equal variances assumed	1,628	,212	-,870	28	,392	-8,20000	9,42233	-27,50077	11,10077
		Equal variances not assumed			-,870	25,793	,392	-8,20000	9,42233	-27,57546	11,17546
	TAG (mg/dl ser)	Equal variances assumed	1,061	,312	-,410	28	,685	-4,93333	12,03846	-29,59299	19,72633
		Equal variances not assumed			-,410	26,997	,685	-4,93333	12,03846	-29,63434	19,76768
	LST (mg/dl ser)	Equal variances assumed	8,847	,006	-1,640	28	,112	-85,60000	52,18210	-192,49018	21,29018
		Equal variances not assumed			-1,640	19,559	,117	-85,60000	52,18210	-194,60742	23,40742
Studiu	Colesterol Total (mg/dl ser)	Equal variances assumed	1,513	,229	,972	28	,339	12,35000	12,70698	-13,67906	38,37906
		Equal variances not assumed			,828	12,463	,423	12,35000	14,91072	-20,00428	44,70428
	LDL-Colesterol (mg/dl ser)	Equal variances assumed	,948	,338	,238	28	,813	2,50000	10,48461	-18,97674	23,97674
		Equal variances not assumed			,228	16,109	,823	2,50000	10,97277	-20,74838	25,74838

HDL-Colesterol (mg/dl ser)	Equal variances assumed	,194	,663	,362	28	,720	4,10000	11,33218	-19,11291	27,31291
	Equal variances not assumed			,385	21,332	,704	4,10000	10,65707	-18,04159	26,24159
TAG (mg/dl ser)	Equal variances assumed	2,790	,106	-,611	28	,546	-7,65000	12,52472	-33,30573	18,00573
	Equal variances not assumed			-,540	13,445	,598	-7,65000	14,16818	-38,15573	22,85573
LST (mg/dl ser)	Equal variances assumed	,012	,913	,833	28	,412	49,35000	59,21659	-71,94968	170,64968
	Equal variances not assumed			,802	16,394	,434	49,35000	61,54142	-80,85762	179,55762

Conclusion:

In all cases, between the average values of the variables under study for male and female groups, separately for each plot (control and study), there are no significant differences $p > 0.05$.

This finding allows the study of the Control and Study Groups, and without split them each side into groups according to gender.

The results of statistical correlation between values of the lipid parameters and the scores obtained by patients in Hamilton depression scale are given in tables 5, 6, 7, 8 and 9 and this data reflects the fact that there is a correlation, because $p > \alpha = 0.05$ in all cases.

Table 5. Correlation of serum total cholesterol values – score HAMD

Correlations

		Colesterol Total (mg/dl ser)	Scor HAMD
Colesterol Total (mg/dl ser)	Pearson Correlation	1	-,142
	Sig. (2-tailed)		,453
	N	30	30
Scor HAMD	Pearson Correlation	-,142	1
	Sig. (2-tailed)	,453	
	N	30	30

Table 6. Correlation HDL-cholesterol values – score HAMD

Correlations

		HDL-Colesterol (mg/dl ser)	Scor HAMD
HDL-Colesterol (mg/dl ser)	Pearson Correlation	1	,021
	Sig. (2-tailed)		,911
	N	30	30
Scor HAMD	Pearson Correlation	,021	1
	Sig. (2-tailed)	,911	
	N	30	30

Table 7. Correlation LDL-cholesterol values – score HAMD

Correlations

		LDL-Colesterol (mg/dl ser)	Scor HAMD
LDL-Colesterol (mg/dl ser)	Pearson Correlation	1	-,158
	Sig. (2-tailed)		,405
	N	30	30
Scor HAMD	Pearson Correlation	-,158	1
	Sig. (2-tailed)	,405	
	N	30	30

Table 8. Correlation serum total lipids values – score HAMD

Correlations

		LST (mg/dl ser)	Scor HAMD
LST (mg/dl ser)	Pearson Correlation	1	-,144
	Sig. (2-tailed)		,449
	N	30	30
Scor HAMD	Pearson Correlation	-,144	1
	Sig. (2-tailed)	,449	
	N	30	30

Table 9. Correlation serum tryglucerides values – score HAMD

Correlations

		TAG (mg/dl ser)	Scor HAMD
TAG (mg/dl ser)	Pearson Correlation	1	-,079
	Sig. (2-tailed)		,679
	N	30	30
Scor HAMD	Pearson Correlation	-,079	1
	Sig. (2-tailed)	,679	
	N	30	30

Conclusions

Determination of biochemical parameters of lipid metabolism – the total lipid serum total cholesterol, LDL-cholesterol, HDL-cholesterol and triacilgliceroli (TAG) – was carried out in order to establish correlations between quantitative changes of these parameters and the severity of symptoms of depression, marked by severity scores obtained from applying the scale for depression Hamilton. The obtained results allow us to formulate the following feedback, comments and conclusions:

- ✓ Processing and statistical analysis of data obtained resulted in establishment of inverse correlations between parameter values such as lipid and the severity of symptoms of depression, which means that these parameters does not affect or enlarge the persistence of these symptoms.
- ✓ In the studied group, the percentages in men with high and normal values for LDL-cholesterol and for HDL-cholesterol were equal – 20% and 80%, and that for serum triacylglycerols were reversed – 80% of them having normal values and only 20% high levels.
- ✓ Taking into account that the percentages in subjects with high values of serum total cholesterol are great in both groups – 30% in the group of patients with depression and 23,33% in the control group – it can be said that the risk of appearance of atherosclerosis increases with age, but it doesn't have statistically significant effects upon the affective mood.
- ✓ High values of serum triacylglycerols can reflect the presence of chronic stress in patients with moderate depression. It is already known that stress determines the increasing of serum cortisol level that mobilizes the lipids from the adipose tissue for preparing the organism in order to prevent stress.
- ✓ One of the causes that can lead to the appearance of high values of lipids parameters in female patients between 45-60 years of age can be represented by the existence of periods of hormonal modifications that can influence their affective moods.
- ✓ Statistical analysis resulted in getting some negative correlations between the values lipid metabolism parameters and scores of patients from the study at Hamilton Depression scale and these correlations rule out the fourth hypothesis of the study and did not support the idea that the rise in depression symptoms can be explained or caused by quantitative changes of these parameters.
- ✓ Starting from the idea that the change of lipid parameters do not correlate with the risk or the enhance of symptoms of depression, it becomes necessary that acute symptoms, remission, nutritional factors to be included in the development of a real, significant statistical correlations between depression and lipid profile.
- ✓ The results of this study fit the kinds of results of other studies in this area and support the hypothesis that there is no uniform idea of statistical values and correlations that can be obtained. At the same time, they suggest that serum levels of total cholesterol, LDL-cholesterol, HDL-cholesterol can be used as biological markers that may distinguish between different forms of depressive disorder, between the different ways of treating them, but they can also have an important role in the prevention of suicidal acts.
- ✓ The results suggest that both serum total cholesterol concentration determinations, LDL-cholesterol and HDL-cholesterol and the calculatation of the total cholesterol\/HDL – cholesterol, total cholesterol/LDL-cholesterol and LDL-cholesterol\/HDL-cholesterol ratios levels may be raised on lots of subjects and can represent biological markers by which to make the differential diagnosis of the clinical subtypes of depression; this issue could have psychofarmacological approach effects specific to each patient and could lead to a reduction in the rate of suicidal behaviors especially in the case of severe depression.

- ✓ The present study was performed on a small number of patients diagnosed with moderate depression according to diagnostic criteria in the DSMIV-TR and did not take into account differences related to their eating habits, smoking, or – if necessary – the tendencies to consume alcohol. It is shown that future research to expand the studies related to the predictive value of serum total cholesterol/HDL-cholesterol and LDL-cholesterol\/HDL-cholesterol ratio in coronary diseases occurrence in patients with depressive disorders according to their clinical subtypes.

Study 2 Determination of serum concentration of electrolytes in patients with affective disorder depressive type

Determination of electrolytes concentrations in patients with depression is necessary from two points of view:

1. their modifications can determine two types of changes at cerebral level:
a) can directly affect the neuronal excitability;
b) can modify the neurotransmitter's equilibrium – especially the monoamine synthesis (5-hydroxy-triptamine) , their role in synaptic transmission being already known.
2. knowing these modifications, therapeutic interventions can allow the reestablishing the electrolyte's equilibrium in the body and can prevent the appearance of depression's complications.

Today the neurochemical base of depression is much more complex and installing it is not the result of a single type of deficiency. Thus, there are studies that reveal a defined and proportional relationship between Mg^{2+} and installing depression or a direct relationship between the serum levels of Ca^{2+} and Mg^{2+} and the emergence of specific symptoms of depression, with their emphasis on the extent of changes in serum concentrations of these cations (TORRES et al., 2008). The role of electrolyte imbalances in blood has been linked to the etiopathogenesis of uni- or bipolar depression (KUMEI et al, 1998; PATHAK and GAUR, 2000) and schizophrenia (ROŞOIU et al., 2013).

Study hypothesis:

Investigation of electrolytes in correlation with the emergence or intensification of depressive symptoms was based on several assumptions:

1. Evaluation of Mg^{2+} in serum in patients with depression is of great interest to both scientifically and clinically, because Mg^{2+} is the natural channel blocker of Ca^{2+}. It is considered that the mechanism of neuronal Mg^{2+} is based on the regulation of Ca^{2+} ions flow through neural channels of Ca^{2+} by Mg^{2+} ions. When the Mg^{2+} requirement is not satisfied, the neural problems occur, respectively, a cerebral impairment characterized by a drop in serotonin levels, neurotransmitter responsible for emotional balance, and one of the consequences of this damage can be lead to the appearance of depression. Taking into account the fact that Mg^{2+} is a natural calcium antagonist, it is assumed that the values of the two electrolytes correlate with each other and may lead to the emergence or maintenance of depressive syndrome.
2. An important cause that can cause changes in the body's electrolytes quantitative is the stress that can be physically (exhaustion, cold, heat, trauma, Burns) or emotional (pain, fear-induced, special events). In the event of prolonged stress, a vicious circle occurs, because a decrease in Mg causes a greater discharge of hormones which in turn leads to a greater excretion of Mg. As a result, the body becomes increasingly more vulnerable to stress, and this can result either in appearance or emphasizing the symptoms of depression and may be supported by a positive correlation between serum magnesium and the values of inorganic phosphorus in serum.

3. Taking into account the involvement of sodium and potassium in the activity of Na\/K-ATP-ase and their roles in maintaining the body's electrolyte balance, their serum values can be determined at the same time in patients diagnosed with depression, and they correlate statistically.
4. Quantitative changes of inorganic phosphate in serum in patients with moderate depression can explain the emergence of imbalances of energy metabolism or clinical signs classics such as chronic fatigue, atonia, states of apathy and disorientation.
5. Considering that iron is a cofactor tyrosine hydroxilase that limitates the catecholamine synthesis is supposed the determination of its values at the same time with those of other electrolytes can give information on the balance of neurotransmitters and can support the emergence of some of the symptoms of depression, if their exists an imbalance.

6. Changes of electrolytes quantitative research can lead to the emergence of statistically significant differences according to sex between the values of the analyzed parameters.
7. Some of the hidden signs of affective disorders in somatic disorders represented by hyperactivity sympathetic matched by parasympathetic inhibition, hiposalivație, epigastric, flatulence, difficulty in breathing, tightness of heart discomfort, heart rhythm disturbances, dizziness, headache, confusion and disorientation coincide with symptoms that appear to increase or decrease the levels of serum electrolytes study.

Material and method

The study group was made up of 30 subjects with moderate and severe depression. They were diagnosed according to the diagnostic criteria from DSM-IV – above – and according to the scores obtained from the Hamilton scale for depression. Of this batch were excluded people with bipolar disorder and to none of these patients have been administered calcium or other minerals.

The group was formed of 13,33% patients with ages between 25-35 years, 13,33% aged between 36 and 45 years old and 74,66% with ages between 46 and 60.

The control group was composed of 30 patients without hidroelectrolitice imbalances and affective disorders in antecedents-free or in their families of origin.

The distribution of the subjects of the study group by age is shown in figure 1, and their distribution according to sex in in Figure 2.

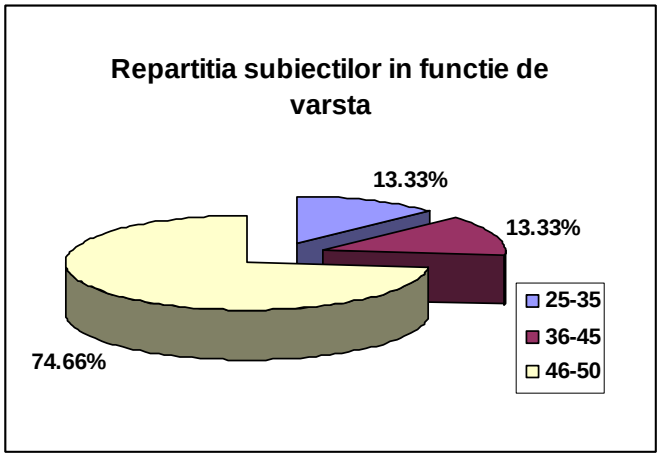

Fig.1. Distribution of patients in study group according to age

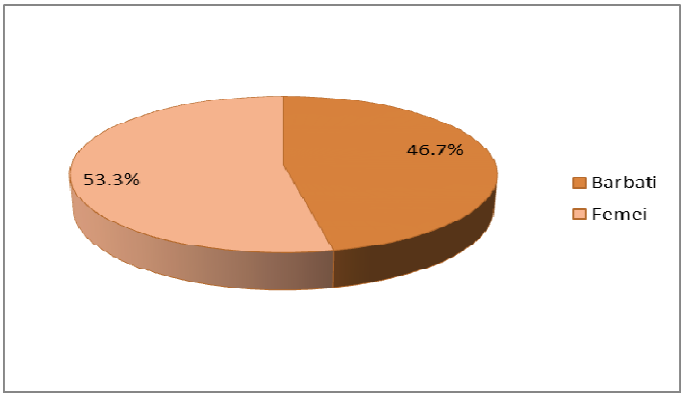

Fig.2.Distribution of patients in study group according to gender

One of the objectives of this study was to verify the existence of statistically significant quantitative changes according to sex for the two groups - study and control. In table 10 are presented the results of the descriptive statistics of the analyzed parameters for the two batches according to gender.

Table 10. Descriptive statistics of the analyzed parameters in both group according to gender

Descriptive Statistics

Lot	Sex		N	Minimum	Maximum	Mean	Std. Deviation
Control	Masculin	K(mEq/l)	15	4,20	5,80	4,9067	,54833
		Na(mEq/l)	15	113	146	132,93	7,778
		Ca(mg/dl)	15	7,80	9,80	8,5867	,49981
		Mg(mg/dl)	15	1,86	2,70	2,3887	,26465
		Fe(microg/dl)	15	98	128	114,80	10,073
		P(mmol/l)	15	4,20	5,20	4,6133	,30675
	Feminin	K(mEq/l)	15	4,30	5,90	4,9800	,51575
		Na(mEq/l)	15	118	142	131,73	6,974
		Ca(mg/dl)	15	6,80	9,20	8,4333	,64660
		Mg(mg/dl)	15	1,54	2,80	2,4147	,35615
		Fe(microg/dl)	15	89	108	99,87	5,986
		P(mmol/l)	15	3,73	5,40	4,8153	,44652
Studiu	Masculin	K(mEq/l)	15	2,80	6,90	4,7867	1,07959
		Na(mEq/l)	15	113	142	133,67	7,158
		Ca(mg/dl)	15	5,70	10,40	8,0000	1,28230
		Mg(mg/dl)	15	1,30	3,80	2,2933	,64083
		Fe(microg/dl)	15	30	154	94,47	31,135
		P(mmol/l)	15	3,76	6,44	4,7260	,96079
	Feminin	K(mEq/l)	15	2,80	5,80	4,3133	,89432
		Na(mEq/l)	15	110	142	128,53	10,113

	Ca(mg/dl)	15	6,20	9,60	8,5867	1,06962
	Mg(mg/dl)	15	1,40	2,80	2,0453	,45541
	Fe(microg/dl)	15	48	132	86,20	24,015

In all cases, between the average values of the variables under study for Male and Female groups, separately for each plot (study and control), there are no significant differences p 0.05 >. This finding allows the study of the Control and Study Group no more split each side into groups according to gender.

Another objective of this study was the development of the statistical correlations between the values of the analyzed parameters.

a) serum total Calcium - serum magnesium correlation

From the data presented in table 11 for the correlation of serum calcium and serum magnesium it follows that r = 0.662, p< 0.001, and correlation is significant at the 0.01 level (2-tailed). Figure 3 displays the graphical representation of this positive correlations.

Table 11. The results of the correlation between serum calcium/ serum magnesium

Correlations

		Ca total (mg/dl)	Mg (mg/dl)
Ca total (mg/dl)	Pearson Correlation	1	**.662****
	Sig. (2-tailed)		.000
	N	30	30
Mg (mg/dl)	Pearson Correlation	.662**	1
	Sig. (2-tailed)	.000	
	N	30	30

. **Correlation is significant at the 0.01 level (2-tailed).

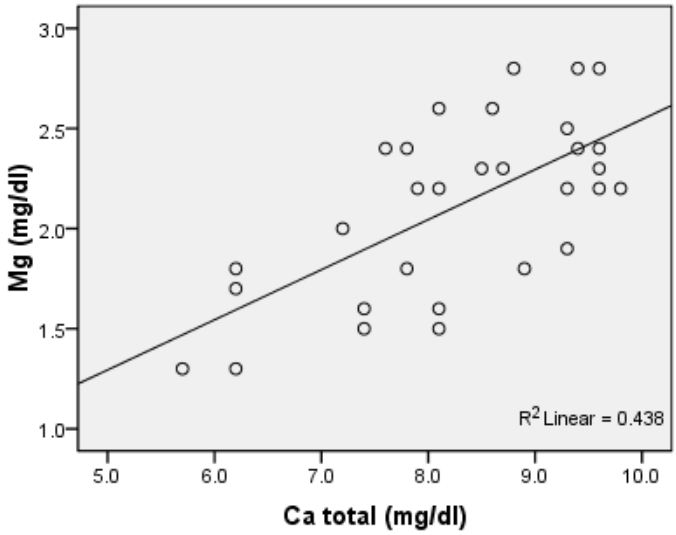

Fig.3. Graphical representation of the correlation between serum total calcium / serum magnesium in study group

b) Correlation serum total calcium / serum inorganic phosphate

The calculated values for the Pearson correlation between serum magnesium and inorganic phosphate in serum are shown in table 13 and they show that r = 0.450, p = 0.012, and the correlation is significant at the 0.05 level (2-tailed). Graphical representation of this correlation is illustrated in Figure 4.

Table 13. Serum magnesium / serum inorganic phosphate correlation

Correlations

		Mg (mg/dl)	P (mmol/l)
Mg (mg/dl)	Pearson Correlation	1	-.450*
	Sig. (2-tailed)		.012
	N	30	30
P (mmol/l)	Pearson Correlation	-.450*	1
	Sig. (2-tailed)	.012	
	N	30	30

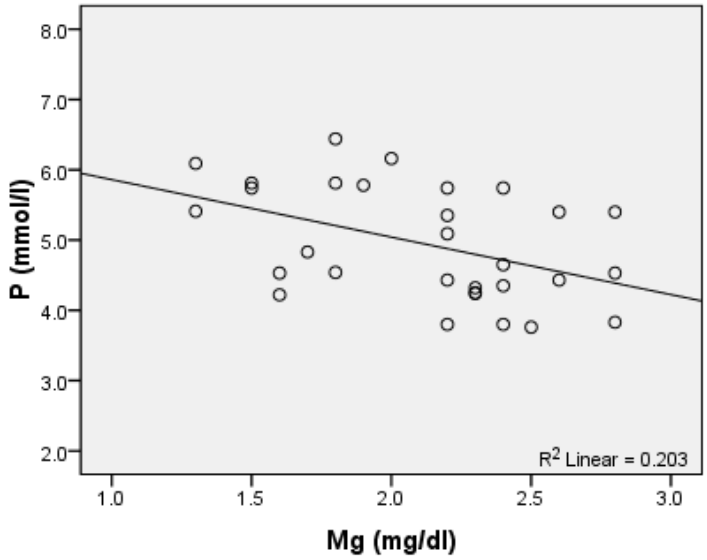

Fig .4. Graphical representation of the correlation between serum magnesium and serum inorganic phosphate

c) serumNa- serum K correlation

Correlation Pearson Results of sodium and potassium in serum are presented in table 14 and the graphical representation of this correlation is illustrated in Figure 5.

Table 14. Results of serum Na- serum correlation

Correlations

Lot			Na(mEq/l)	K(mEq/l)
Control	Na(mEq/l)	Pearson Correlation	1	,253
		Sig. (2-tailed)		,177
		N	30	30
	K(mEq/l)	Pearson Correlation	,253	1
		Sig. (2-tailed)	,177	
		N	30	30
Studiu	Na(mEq/l)	Pearson Correlation	1	**,579****
		Sig. (2-tailed)		**,001**
		N	30	30
	K(mEq/l)	Pearson Correlation	,579**	1
		Sig. (2-tailed)	,001	
		N	30	30

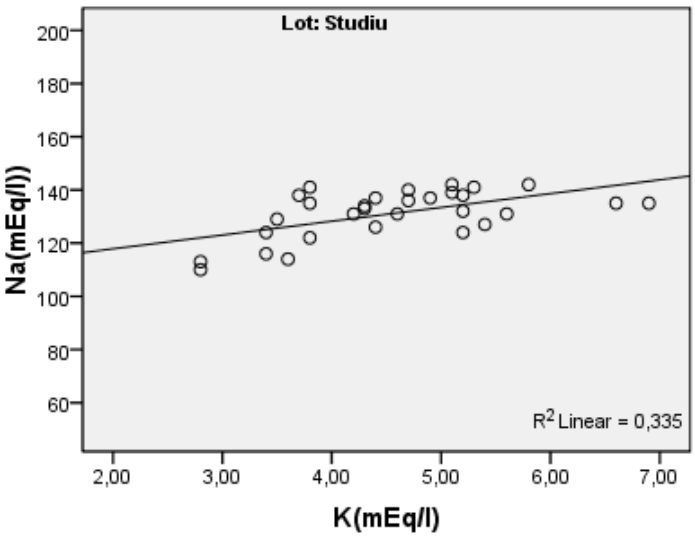

Fig. 5 Graphical representation of the correlation between serum sodium and serum potasium in study group

d) Serum inorganic phosphate- serum iron correlation

Correlation Pearson results of inorganic phosphate and serum iron are presented in table 15, and graphical representation of this correlation is illustrated in figure 6.

Tabel 15. Results of serum inorganic phosphate- serum iron correlation

Lot			P(mmol/l)	Fe(microg/dl)
Control	P(mmol/l)	Pearson Correlation	1	-,035
		Sig. (2-tailed)		,855
		N	30	30
	Fe(microg/dl)	Pearson Correlation	-,035	1
		Sig. (2-tailed)	,855	
		N	30	30
Studiu	P(mmol/l)	Pearson Correlation	1	**,509****
		Sig. (2-tailed)		**,004**
		N	30	30
	Fe(microg/dl)	Pearson Correlation	,509**	1
		Sig. (2-tailed)	,004	
		N	30	30

. **Correlation is significant at the 0.01 level (2-tailed).

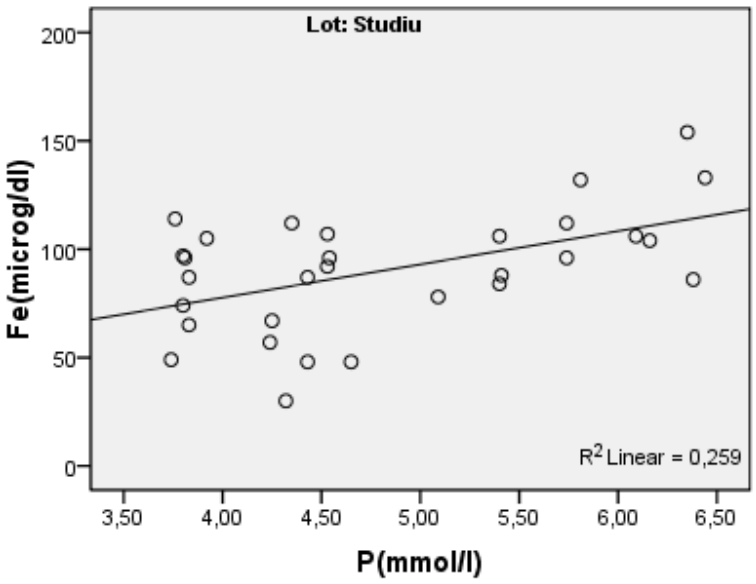

Fig.6 Graphical representation of the correlation between serum inorganic phosphate and serum iron in study group

Conclusions

Depressive disorders are characterized by complex, but reversible changes of neuronal excitability and a therefore arenecessary both the determination of electrolytes and the investigation of hidrolelectrolitic balance at the cellular level as well as within the whole organism, including biological fluids (blood, serum, plasma, cerebrospinal fluid, urine).

The ionic hypothesis of cell excitability is the hypothesis that explains how the Ionic balances shall be established and the manner in which they are used by cells in order to attend their physiological functions.

- ✓ The positive serum Na- serum K correlation obtained by calculating the coefficient Bravais-Pearson can explain some of the symptoms of clinical depression, such as: decreased ability of physical and intellectual effort, adinamia, changes in neuromuscular activity and this confirms the third hypothesis of this study.

Fluctuations in the levels of sodium in the body can affect the mood and it may be useful an increased sodium intake through the diet. Understanding the effects of sodium on the activity of the central nervous sistem and behavioral changes can help to elucidate the biochemical causes of various diseases such as affective disorders, adictions, memory and learning problems.

Potassium is an essential element for nerve activity and mental health, thanks to its role in maintaining the electrical conductivity of nerve and the share in the transmission of nerve impulses. Also, K + is involved in the transport of serotonin, the neurotransmitter that regulates emotional States like joy, positive mood. For these reasons, it follows that, in order to maintain emotional equilibrium, it is essential to maintain the homeostasis of the internal environment and a balance of Na-K in the body anis appropriate to the determination of the two cations on in patients with moderate or severe depression.

- ✓ Positive correlation – statistically significant – between serum total calcium and serum magnesium reflects the idea of the determination in the same time of the concentrations of these two electrolytes in patients with affective depressive disorder and so the results confirm the first hypothesis of this study It has to be mentioned that this correlation was obtained in a group inside which 40% from its patients had low values of serum total calcium and 60% normal values of this parameter.
- ✓ Negative correlation between serum total calcium and serum inorganic phosphorus confirms the data from the literature that mention an inverse relation of the serum levels of these two parameters and the existence of a normal ratio Ca: P of 1:2.5 under an adequate diet and an appropriate hormonal control.
- ✓ It is known that, in the case of affective depressive disorder, the body is subjected to a prolonged stress or even progressively accentuated and that the body is becoming increasingly vulnerable to its action and effects. Positive correlation between serum inorganic phosphate and serum magnesium confirms the second hypothesis of the study and supports the idea that apathy, weight changes, lack of appetite, decreased ability of concentration, confusion, disorientation as clinical signs of depression can be explained as a result of quantitative changes of these electrolytes.
- ✓ The statistical analysis of the obtained results for some of electrolytes led to getting some negative correlations, which shows that not all types of electrolytes are changed simultaneously in depression and that these results are part of the orientation of the data in the literature that there is no unified theory on quantitative changes of the level of electrolytes in patients diagnosed with mild or moderate depression.
- ✓ Results confirms the assumption that some signs of depression materialized through somatic complaints may be the consequence of the cumulative imbalances of electrolytes and, therefore, it is appropriate to determine them in parallel in order to give a consistent interpretation of the obtained values. Also, their interpretation must take into account the existence, in patients from the study group, both of an acute physical and psychic stress and of the differences related to the physical condition of the patients, their fields of activity and the environments in which they arise.
- ✓ If the results obtained and their statistical analysis have led to getting some negative correlations such as between serum Fe serum inorganic phosphate, than it is indicated a multidisciplinary approach to the problems posed by quantitative changes in blood electrolytes which can be performed on a greater number of subjects in the study group in

order to clarify the role of these elements in the emergence of depressive symptomsand in maintaining or reinforcing them.

Study 3

Determination of certain parameters of oxidative stress in patients with affective disorder depressive type

Oxidative stress is a biochemical and physiological process in which, as in the case of mental stress, the body's response is often inadequate. Mental and emotional stress may increase oxidative stress, as it can be reduce by relaxation. There are studies that show that oxidative stress is one of the mechanisms involved in the occurrence of depression, and reactive oxygen species may play a role in the occurrence of neuropsychiatric disorders. Research shows that the activation of immuno-inflammatory processes followed by increasing catabolism rate of monoamines in the brain and changing of cerebral lipid level can cause overproduction of reactive oxygen species and – at the same time-of antioxidant enzymes and lipid peroxidation and these phenomena can be linked to the patophyisiology of depression, particularly of the major one (BILICI et al, 2004).

There are also researches that focused on the correlation of electrolytes with oxidative stress parameters. Thus, a deficiency in magnesium and oxidative stress have been identified as pathogens factors both of the aging process and of neurodegenerative disorders characterized by lawsuits or accompanied by neural biochemical imbalances at. (BEGOÑA et al., 2000; SAMARGIU et al., 2012).

Study assumptions:

1. Oxidative stress is characterized by the presence in the body of an imbalance between reactive oxygen species actions and defensive mechanisms with an antioxidant role. Under the terms of a long-term oxidative stress that includes processes that takes place in chain and can amplify one another and the most exposed system to this type of stress is the nervous system, it is assumed that the action of reactive oxygen species may reflect or may influence changes of the values of blood parameters analyzed in patients with affective disorder depressive type.
2. The emergence and rise of symptoms of depression may be associated with the existence of statistically significant differences according to sex between the values of the parameters analyzed.
3. Taking into account the fact that magnesium is a natural calcium antagonist, supposedly – amid a prolonged oxidative stress – changes of the values of these two electrolytes can cause maintenance of specific depressive syndrome clinical signs and that these values correlate with those of TAS (mmol\l).
4. Because the role of the non-enzymatic antioxidants of certain biochemical parameters is already known it is presumed that between their values in patients from the study and those of patients from the control group there are statistically significant differences that may explain the influence of oxidative stress in the occurrence of depression and its impact on the evolution of this emotional disorders.

Material and methods

The Study Group was made up of 30 patients with moderate and severe depression. These were diagnosed according to the diagnostic criteria from DSM-IV and in accordance with the application scores Hamilton scale for depression. Of this batch were excluded people with bipolar disorder and none of them received calcium, magnesium or other minerals.

• The control Group was composed of 30 patients without electrolyte and affective disorders in antecedents-free; the control group was the same as in study 2.
• Distributions of the study patients according to age and sex are shown in figures 7 and 8.

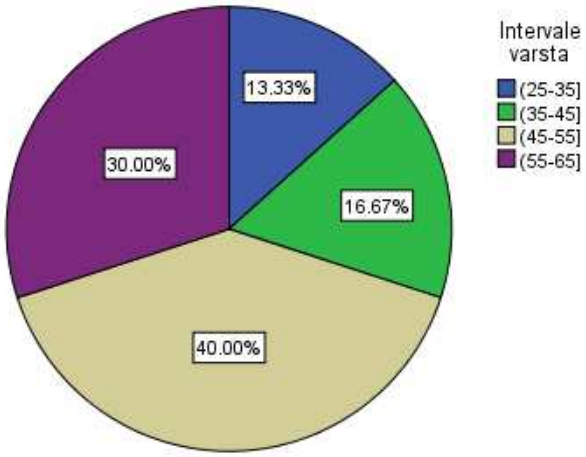

Fig. 7 Distribution of patients in study group according to age

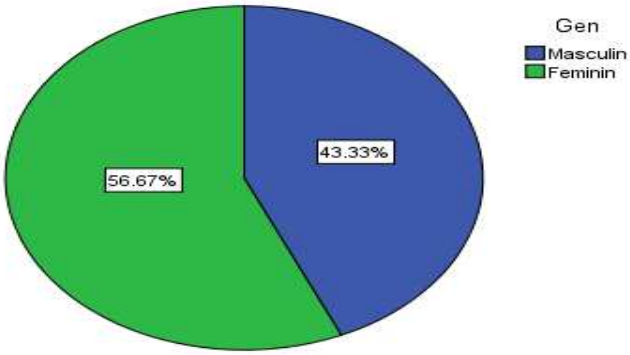

Fig 8. Distribution of patients in study group according to gender

Results and discussions

In tables 16 and 17 reflects the distribution of values of the parameters analyzed for both groups – the study and the control.

Table 16. Distribution of the results in both groups

One-Sample Kolmogorov-Smirnov Test

Lot			GR (U/L)	TAS (mmol/l)	Acid uric (mg/dl)	Ca (mg/dl)	Mg (mg/dl)	SOD (U/l)
Studiu	N		30	30	30	30	30	30
	Normal Parameters[a,,b]	Mean	56,6583	1,8107	4,2700	8,9067	2,3933	128,2667

		Std. Deviation	10,05374	,29752	,92295	,69029	,22581	36,21672
	Most Extreme Differences	Absolute	,133	,197	,133	,135	,204	,091
		Positive	,090	,154	,133	,135	,204	,091
		Negative	-,133	-,197	-,102	-,121	-,129	-,082
	Kolmogorov-Smirnov Z		,727	1,079	,727	,740	1,118	,499
	Asymp. Sig. (2-tailed)		,667	,195	,666	,643	,164	,964
Control	N		30	30	30	30	30	30
	Normal Parameters[a,,b]	Mean	55,6910	1,7680	4,6900	8,5100	2,4017	196,9667
		Std. Deviation	9,94894	,27770	1,44302	,57316	,30858	16,70532
	Most Extreme Differences	Absolute	,098	,187	,098	,191	,171	,171
		Positive	,078	,187	,098	,173	,100	,171
		Negative	-,098	-,107	-,086	-,191	-,171	-,072
	Kolmogorov-Smirnov Z		,539	1,027	,537	1,044	,936	,936
	Asymp. Sig. (2-tailed)		,933	,242	,936	,226	,345	,345

a. Test distribution is Normal.

b. Calculated from data.

Tabel 17. Distribuția rezultatelor obținute pe ambele loturi

One-Sample Kolmogorov-Smirnov Test

Lot			GPx (U/l)	Glicemie (mg/dl)	Proteine totale (g/dl)	BT (mg/dl)	Fe seric (ug/dl)
Studiu	N		30	30	30	30	30
	Normal Parameters[a,,b]	Mean	4344,7333	96,7333	6,7127	,5840	91,8000
		Std. Deviation	1579,58080	28,75453	,52400	,37655	24,41791
	Most Extreme Differences	Absolute	,084	,240	,085	,180	,075
		Positive	,084	,240	,082	,180	,060
		Negative	-,072	-,143	-,085	-,174	-,075
	Kolmogorov-Smirnov Z		,458	1,316	,468	,985	,409
	Asymp. Sig. (2-tailed)		,985	,063	,981	,286	,996
Control	N		30	30	30	30	30
	Normal Parameters[a,,b]	Mean	4922,2000	89,1000	6,6200	,5893	101,0333
		Std. Deviation	1232,44544	9,27864	,65517	,18975	4,94440

Most Extreme Differences	Absolute	,121	,114	,117	,137	,092
	Positive	,121	,114	,092	,118	,064
	Negative	-,118	-,091	-,117	-,137	-,092
Kolmogorov-Smirnov Z		,663	,624	,641	,753	,506
Asymp. Sig. (2-tailed)		,771	,832	,806	,623	,960

a. Test distribution is Normal.

b. Calculated from data.

Sig. (2-tailed) sau p > 0.05 - All the variables under study are normally distributed.

Comparison of the mean values of the parameters analysed between batches and Control Study was made by the t test and the values are listed in table 18.

Table. 18. The statistical analysis by independent samples test results for both groups

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
GR (U/L)	Equal variances assumed	,016	,901	,375	58	,709	,96733	2,58237	-4,20184	6,13651
	Equal variances not assumed			,375	57,994	,709	,96733	2,58237	-4,20185	6,13652
TAS (mmol/l)	Equal variances assumed	,052	,820	,574	58	,568	,04267	,07430	-,10607	,19140
	Equal variances not assumed			,574	57,727	,568	,04267	,07430	-,10609	,19142
Acid uric (mg/dl)	Equal variances assumed	6,455	,014	-1,343	58	,185	-,42000	,31274	-1,04601	,20601
	Equal variances not assumed			-1,343	49,325	,185	-,42000	,31274	-1,04836	,20836
Ca (mg/dl)	Equal variances assumed	2,550	,116	2,421	58	,019	,39667	,16381	,06876	,72457
	Equal variances not assumed			2,421	56,104	,019	,39667	,16381	,06853	,72481
Mg (mg/dl)	Equal variances assumed	,909	,344	-,119	58	,905	-,00833	,06981	-,14808	,13141
	Equal variances not assumed			-,119	53,137	,905	-,00833	,06981	-,14835	,13168

SOD (U/l)	Equal variances assumed	14,668	,000	-9,435	58	,000	-68,70000	7,28175	-83,27601	-54,12399
	Equal variances not assumed			-9,435	40,806	,000	-68,70000	7,28175	-83,40793	-53,99207
GPx (U/l)	Equal variances assumed	2,582	,114	-1,579	58	,120	-577,46667	365,78670	-1309,66830	154,73496
	Equal variances not assumed			-1,579	54,761	,120	-577,46667	365,78670	-1310,59139	155,65806
Glicemie (mg/dl)	Equal variances assumed	7,979	,006	1,384	58	,172	7,63333	5,51639	-3,40892	18,67558
	Equal variances not assumed			1,384	34,974	,175	7,63333	5,51639	-3,56582	18,83249
Proteine totale (g/dl)	Equal variances assumed	2,811	,099	,605	58	,548	,09267	,15317	-,21393	,39927
	Equal variances not assumed			,605	55,328	,548	,09267	,15317	-,21425	,39958
BT (mg/dl)	Equal variances assumed	2,793	,100	-,069	58	,945	-,00533	,07698	-,15943	,14877
	Equal variances not assumed			-,069	42,836	,945	-,00533	,07698	-,16060	,14994
Fe seric (ug/dl)	Equal variances assumed	31,798	,000	-2,030	58	,047	-9,23333	4,54856	-18,33826	-,12840
	Equal variances not assumed			-2,030	31,374	,061	-9,23333	4,54856	-18,50570	,03903

In figures 9 and 10 are presented the values of the SOD and serum calcium, and the results obtained reveals that between them there is a statistically significant difference between the two groups – study and control.

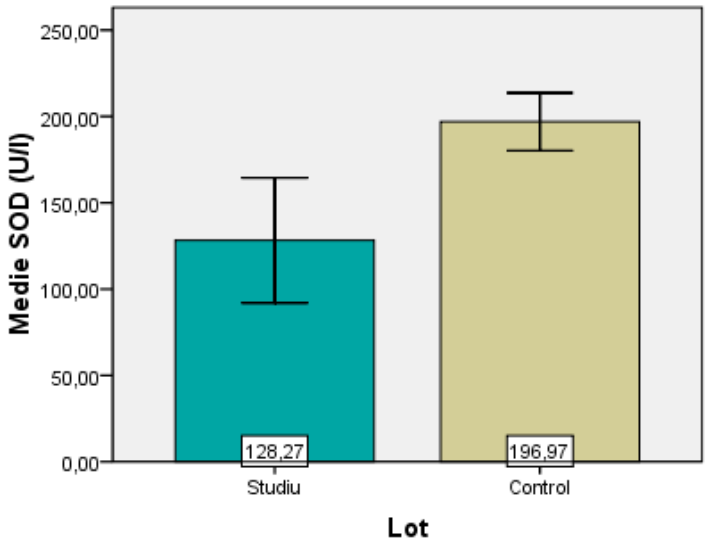

Fig.9 Graphical representation of the average values of SOD between the two groups
Between the average values os SOD of those two groups Study and Control (M_{Studiu} = 128.66U/L and $M_{Control}$ = 196.966 U\L) there are significant differences: t = 9.435; df = 40.806; Mdiff = 68.70; p = 0.000 < α = 0.05; 95% confidence interval of the difference = (83.40-53.99)

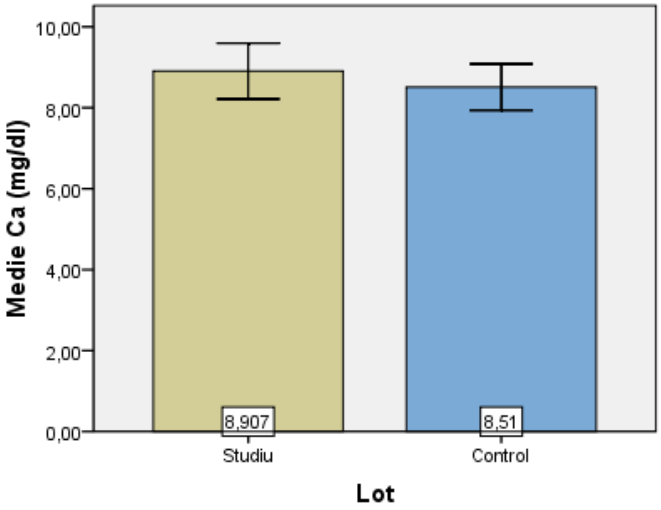

Fig.10 Graphical representation of the average values of serum total calcium between the two groups

Between the average values of serum calcium corresponding to those two groups Study and Control (MStudiu = 8.9067 mg\/dl and MControl = 2.4017 mg\/dl) are significant differences: t = 2.421; df = 58;Mdiff = 0.39667; p = 0.019 > α = 0.05; 95% confidence interval of the difference = (0.06876,-0.724757).

It was also found that in all cases, between the average values of the variables under study for Male and Female groups, separately for each plot (and study), there are no significant differences p> 0.05.

This finding has allowed the study of the Control and Study Groups no more split each side into groups according to gender.

Checking the third hypothesis required of Bravais-Pearson correlations between the parameters involved, the data analysis being presented in tables 19, 20, 21, 22, 23, 24, 25, 26, 27 and in figures 11 and 12.

Table 19. TAS – serum magnesium correlation

Correlations

		TAS (mmol/l)
Mg (mg/dl)	Pearson Correlation	.690**
	Sig. (2-tailed)	.000
	N	30

****. Correlation is significant at the 0.05 level (2-tailed).**

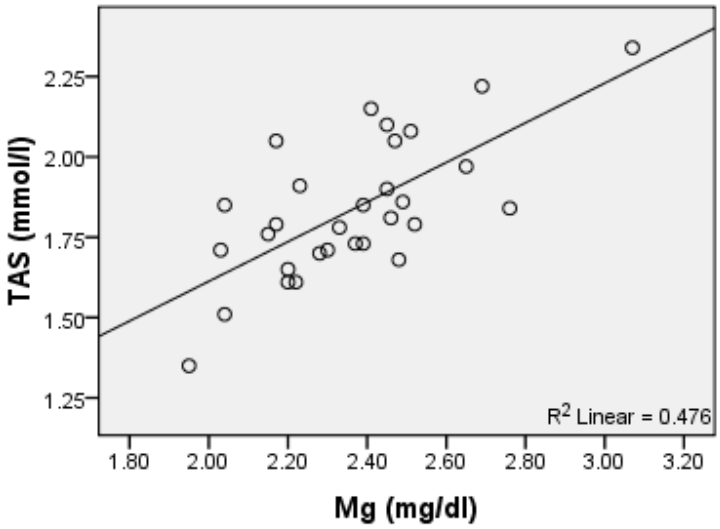

Fig. 11. Graphical representation of TAS – serum magnesium correlation

The two variables correlate at **r = .690, p < 0.001, α = 0.05**

Tabel 20 TAS – serum total calcium correlation

Correlations

		TAS (mmol/l)
Ca (mg/dl)	Pearson Correlation	.770**
	Sig. (2-tailed)	.000
	N	30

. **Correlation is significant at the 0.05 level (2-tailed).

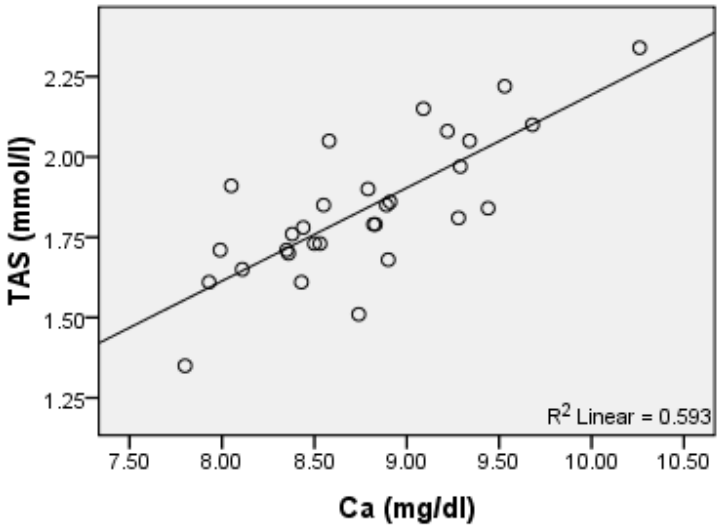

Fig. 12. . Graphical representation of TAS – serum total calcium correlation

The two variables correlate at **r = .770, p < 0.001, α = 0.05.**

Tabel 21. Results of SOD – GPx correlation

Correlations

		SOD (U/l)	GPx (U/l)
SOD (U/l)	Pearson Correlation	1	-,171
	Sig. (2-tailed)		,367
	N	30	30
GPx (U/l)	Pearson Correlation	-,171	1
	Sig. (2-tailed)	,367	
	N	30	30

Tabel 22. Results of SOD – GR correlation

Correlations

		SOD (U/l)	GR (U/L)
SOD (U/l)	Pearson Correlation	1	-,006
	Sig. (2-tailed)		,974
	N	30	30
GR (U/L)	Pearson Correlation	-,006	1
	Sig. (2-tailed)	,974	
	N	30	30

Tabel 23. Results of GPx - GR correlation

Correlations

		GPx (U/l)	GR (U/L)
GPx (U/l)	Pearson Correlation	1	,242

	Sig. (2-tailed)		,197
	N	30	30
GR (U/L)	Pearson Correlation	,242	1
	Sig. (2-tailed)	,197	
	N	30	30

Tabel 24. Results of SOD – serum iron correlation

Correlations

		SOD (U/l)	Fe seric (ug/dl)
SOD (U/l)	Pearson Correlation	1	,066
	Sig. (2-tailed)		,728
	N	30	30
Fe seric (ug/dl)	Pearson Correlation	,066	1
	Sig. (2-tailed)	,728	
	N	30	30

Tabel 25. Results of SOD – serum total calcium correlation

Correlations

		SOD (U/l)	Ca (mg/dl)
SOD (U/l)	Pearson Correlation	1	-,259
	Sig. (2-tailed)		,167
	N	30	30
Ca (mg/dl)	Pearson Correlation	-,259	1
	Sig. (2-tailed)	,167	
	N	30	30

Tabel 26. Results of serum total calcium – serum total proteins correlation

Correlations

		Ca (mg/dl)	Proteine totale (g/dl)
Ca (mg/dl)	Pearson Correlation	1	,015
	Sig. (2-tailed)		,939
	N	30	30
Proteine totale (g/dl)	Pearson Correlation	,015	1
	Sig. (2-tailed)	,939	
	N	30	30

Tabel 27. Results of serum total bilirubin – serum iron correlation

Correlations

		BT (mg/dl)	Fe seric (ug/dl)
BT (mg/dl)	Pearson Correlation	1	,083
	Sig. (2-tailed)		,662
	N	30	30
Fe seric (ug/dl)	Pearson Correlation	,083	1
	Sig. (2-tailed)	,662	
	N	30	30

Statistical analysis results recorded in the tables above show that there no are statistical correlations between these sets of parameters.

Conclusions

- ✓ Total antioxidant status and individual antioxidants enzymatic and non-enzymatic had normal values, with the exception of five patients (16,66%) in which the TAS values were slightly larger than those considered physiologically normal. The results do not support the first hypothesis, which may lead to the idea that not all parameters analyzed suffer quantitative significant alterations in patients with affective disorder depressive type.
- ✓ For all biochemical parameters analyzed in this study, between their mean values in male and female groups, separately for each plot (study and control), there are no statistically significant differences at $p > 0.05$. This finding has allowed the study of the Control and Study Groups no more split each side into groups according to gender.
- ✓ Survey results have shown that there are significant statistical differences between serum calcium and SOD values between the two groups, which reflects the fact that oxidative stress lead to quantitative changes in case of enzymatic antioxidants and electrolytes. These results confirm the third hypothesis of the study and support the idea that free radicals are implicated in the etiopathogenesis of depressive disorder and they can produce some neurodegenerative changes.
- ✓ It is known that, in the case of affective disorder depressive type, the body is subjected to a prolonged stress or even progressively accentuated and that the body is becoming increasingly vulnerable to its action and effects. Positive correlation serum Mg-TAS and TAS –calcium total serum serum – confirm the third hypothesis of the study and claim the idea that apathy, weight changes, lack of appetite, decreased ability of concentration, confusion, disorientation as clinical signs of depression can be explained as a result of changes in quantity of these electrolytes and amid a prolonged oxidative stress (in major depression, symptoms persist and and emphasizes regardless of sex).
- ✓ It is known that the main energetical substrate of the brain is glucose and that the brain uses only 20% of the total quantity of oxygen in the body. This underlines the importance of an efficient cerebral blood circulation and of free radicals with protective effect, but both of them may be affected in different psychiatric conditions like dementia, schizophrenia, affective disorders.
- ✓ There are different tests that can measure the levels of plasmatic antioxidants in humans, as well as the possible presence in the body of the resulting products through oxidation. Interpretation of the results of these tests will depend on the conditions in which the

measurements are done, because they are dynamic, evolutionary systems whose effects on the state of physical and mental health become visible over time.

An increase in the oxidant capacity of the plasma is not necessarily a favorable condition because it can reflect a reaction to a possible oxidative stress. Also, any decrease in antioxidant capacity is not necessarily a negative aspect, because it can reflect the reduced production of reactive oxygen species. Basically, in order to be properly interpreted and correlated assessments must be complex and repeated.

- ✓ Oxidative stress can be considered an important pathogenic link to human body and studying this phenomenon in the future can bring new necessary items and can develop an in-depth understanding of the various types of disorders.

GENERAL CONCLUSIONS

Based on data obtained by performing the three studies in this work as well as on appraisals, comments and conclusions for each study individually, there results the following general conclusions:

Affective disorder depressive type has many causes, from being determined entirely by a biochemical change in inherited, passed up to be exclusively the result of psychological or environmental factors. The majority of cases diagnosed falling between the two extremes and involves simultaneous action of biochemical, psychological and environmental factors.

Knowledge of depression, both as regards its neurobiological foundations and the therapeutic profile has made remarkable progress. Today there are sufficient arguments that claim the involvement of the structures and anatomofunctional circuits, of monoamines, cytokines and axis of the hypothalamic-pituitary-adrenal gland. In this context, this disorder must be analyzed integrative, multidimensional, and pharmacological interventions must attain the objectives of etiopatogenice therapy".

Neuronal monoamine-based systems are located in the brainstem, where it designs in other areas of the brain and, therefore, these locations represent areas of interest to psychiatric, electrophysiological and biochemical researches, bearing in mind that any amendment of them, any imbalance may result in changes to multiple plans, cognitively, emotionally and behaviorally, versus the anterior level of functioning of the individuals.

Research upon biochemical changes in affective disorder of depressive type began in the late 1950s and today they are in a continuous development. Studies on the mechanisms of action of antidepressants determined the foundations for the development and study of various hypotheses on the biochemical changes in depressive syndrome, in all its forms of manifestation and have led to fundamental discoveries about neurobiology of the central nervous system.

Neurotransmitters interact with specific receptors in order to be able to exert their effects. Data from the literature sustain that changes in biochemical and physiological properties of these receptors may be involved in the mechanisms of action of antidepressants and in the patophysiology of depression. These influences are, at present, the objectives of the study of continuous research in medical and research laboratories all around the world.

Many of the studies of neurophysiology and biochemistry have as objective the determination of different biochemical parameters in blood plasma, serum, cerebrospinal fluid, erythrocytes, platelets, tissues – in order to identify subtypes of depressive disorder.

Because the clinical heterogeneity and biological substrate of depressive disorder is recognized, it is considered from the outset that the focus on catecholamine metabolism was a major simplification of complex biological mechanisms underlying affective disorders.

The researches in this field support the idea that the pathophysiology of depressive disorder is not strictly linked to abnormal functioning of the central nervous system.

Depressive affective disorder must be conceptualized and addressed as a complex of neuroendocrinometabolic changes affecting various organs and systems within the body.

Differentiation of biological subtypes of this disorder can, when the changes are statistically significant and relevant in terms of neurobiochimical aspects, separate groups of patients who appear to be similar, but who present different biochemical changes. Highlighting the existence of these subtypes may have important clinical implications.

Pharmacological agents, such as antidepressants and other types of stimuli in the environment can act either for the purposes of remission of depressive symptoms, either in the sense of interneuronal-mediated chemical alteration, taking into account the fact that the body may respond differently to the same type of treatment, or may present particular side effects. Neurophysiological and neurochemical changes can influence the biological vulnerability with the emergence of depressive episodes or may even precipitate the emergence of such an episode or a relapse. Therefore, there may be no clear dividing line between pure depression caused by genetic or environmental factors and depressed caused by biological or psychological modifications.

Mentally and emotional factors can lead to an increase in the absorption and excretion of mineral elements. It is appropriate to recognize that powerful or chronic emotional reactions will produce neurological, hormonal or nutritional disturbances represented by metabolic changes that can be quantified through various types of Clinical Biochemistry determinations.

Determination of biochemical parameters of lipid metabolism – the total lipid serum total cholesterol, LDL-cholesterol, HDL-cholesterol and triacilgliceroli (TAG) – was carried out in order to establish correlations between quantitative changes of these parameters and the severity of symptoms of depression, marked by severity scores obtained from applying the scale for depression Hamilton. The results showed that lipid metabolism parameters values do not correlate with the severity of depression and did not differ statistically significant between men and women in both groups, the study and control

Serum Mg^{2+} correlate or are influenced by levels of Ca^{2+}, PO_4^{3-}, K^+, Na^+. Low values of blood electrolytes-calcium, magnesium, sodium, potassium, iron, inorganic phosphate causes some of the clinical signs of depressive disorder such as confusion, fear, disorientation, irritability, crying. At the same time, magnesium is removed from processed food, solid which may lead to impaired functioning of the nervous system. Therefore, it is appropriate to balance the food intake of both minerals and natural antioxidants.

Considering these findings, it appears that:

- ✓ in investigating the causes of the depression is important the biochemical determination of these concentrations and accompanying elements in order to deepen the knowledge of the biochemical causes of depression;
- ✓ in medical practice, if the meaning of these changes and the correlation between them are known, specialists can act for therapeutic rebalancing of body electrolyte and for the prevention of complications of depression.

Oxidative stress can be considered an important pathogenic link to human body and studying this phenomenon in the future can bring the necessary items in order to develop in-depth the understanding of the various types of diseases. Cumulative injuries of free radicals on the various cellular structures could, over time, degrade, quantitative and qualitative the functions of neurotransmitters and, ultimately, to produce behavioral changes, partially solvable by administration of antioxidants.

The results for the activity of SOD in patients from the study and the fact that there have been achieved statistically significant differences between the average values of the enzyme between the two groups reflects the fact that the antioxidant system is not balanced during a

depressive episode in patients diagnosed. We can consider that nutritional supplements of antioxidants may have therapeutic benefit in the treatment of unipolar depression, because they can diminish the effects of free radicals, allowing improvement of depressive symptoms and delaying or avoiding relapse.

Further research in this area will contribute to the discovery of new correlations or interconnections between the complicated emotional and mental disorders. It is already known that many types of diseases have an emotional component. There is increasingly more the idea that emotions are caused by biochemical changes which, in turn, may cause symptoms of affective disorders emphasis. For example, the most well represented correlation in this sense, is the one between the type of behaviour and the incidence of heart diseases.

Investigation of biochemical changes in the brain is a scientific approach quite difficult, primarily owing to the complexity of the technological means required for such investigations and then because of the sensitivity of the central nervous system influences or predisposing factors or disruptive of the external environment.

In practice, the investigation of blood biochemical markers in the study of depressive disorder has several major advantages:

- ✓ uses technology less complex and less expensive;
- ✓ quantitative changes of blood biochemical parameters can be evaluated, in part, by enzymatic methods or endpoint that are fast and thAT use very small and small amounts of biological material (plasma, serum saguin);
- ✓ the subjects of such studies are not subjected to tough investigations that might have imprevizibilie effects in cognitive, emotional, or behavioural plans.

Numerous tests in Biochemistry and neurophysiology laboratories are currently used in Psychiatry and it is considered that, in the future, these tests will have a very important role in the evaluation, diagnosis and treatment of patients with depressive disorders. The results obtained from these studies contribute to the widening of the existing knowledge of depressive disorder regarding the neurochemical balances and outlines new directions for deepening the study of these issues through further research.

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