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The Bulletin of Integrative Psychiatry tries to continue the tradition initiated at "Socola" Hospital in 1919, when a group of intellectuals, medical doctors and personalities from other professions founded the Society of Neurology, Psychiatry and Psychology in Iaşi. Even from its beginnings, the Society edited a journal entitled "Bulletins et Mémoires de la Société de Neurologie, Psychiatrie et Psychologie de Iassy", the first publication of the kind in Romania, which was unique also by its vision and opening towards biology, psychology, sociology and philosophy and by its prestigious board of editors: C. I. Parhon, Gh. Preda, Constantin Fedeleș, Arnold Stocker, P. Andrei, Corneliu Popa-Radu, I. A. Scriban, well known personalities, some of them being physicians of great culture and scientific qualification.

Starting from 1920, the Association and its Bulletin, born and edited at "Socola", due to their remarkable scientific activity have contributed to the organization of 18 congresses, which are mentioned in the description of "Socola" Hospital activities.

In 1947, the last number of "The Bulletin of the Society", edited in French, was banned as a result of the interdictions imposed by extremist tendencies. From its first number in 1919 and until 1947, "The Bulletin of the Society" published 2,412 articles.

The journal or "The Bulletin of the Society" has appeared under several titles: "Bulletin et Mémoires de la Société de Neurologie, Psychiatrie et Psychologie de Iassy" (between 1919 and 1922), then "Bulletin de l'Association des Psychiatres Roumains" and from 1923 it has changed its title several times.

After the year 1947, all publications at "Socola" Hospital were included in the "Medico-Surgical Journal of the Society of Physicians and Naturalists in Iaşi", another prestigious scientific journal which has been published without interruption since 1886.

Starting from 1994, Professor Dr. Tadeusz Pirozynski, Professor dr. Petru Boișteanu, Professor dr. Vasile Chiriță, Conf. dr. Radu Andrei and Dr. M. E. Berlescu have revived the tradition of publications at "Socola" Hospital, editing the new "Bulletin of Integrative Psychiatry".

At the end of 2014, "Socola" Hospital became the "Socola" Institute of Psychiatry, which has increased its responsibilities regarding medical assistance, scientific research, didactic activity, professional training and also the development of editorial activity.

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BPI Bulletin of Integrative Psychiatry
Buletin de Psihiatrie Integrativă

Editorial

BPI Bulletin of Integrative Psychiatry
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Interdisciplinary Reference Points in Psychiatry Considerations on the Socola Summer School, 2019 edition

Roxana Chiriță, Elena-Rodica Popescu

Roxana Chiriță - Professor, M.D., Ph.D., senior psychiatrist, "Grigore T. Popa" University of Medicine and Pharmacy, Iaşi, "Socola" Institute of Psychiatry Iaşi
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The year 2019 marks the 114th anniversary of the inauguration of the Asylum for the mentally alienated Socola in Iasi on October 12, 1905 by Dr. Alexandru Brăescu. In that year, Socola was the first modern psychiatric hospital in Romania, where psychiatric assistance was set up to the standards of the major European hospitals in France, England, Scotland, Switzerland, Belgium or Austria, and a new place of higher education and scientific research. Following the initiative of C.I. Parhon in 1912, the Society for Neurology, Psychiatry, Psychology and Endocrinology was founded, and started editing the *Bulletin et Memoires de la Société de Neurologie, Psychiatrie et Psychologie de Iassy (June 1919)*, being the first such publication in the country, both through multidisciplinary approach and it's cultural and scientific information. The effort and the spirit of transmitting high-quality scientific information at European standards has been maintained over the years among Psychiatry and Medicine specialists and researchers to the pages of the current number of the Bulletin of Integrative Psychiatry, completing the fundamental concept of the Socola School through holistic and psychosocial approaches of the psychiatric disorders.

Already crystallized as a tradition, the National Symposium of Psychiatry with International Participation marks every year the efforts made to share psychiatric novelties and to restore the frontiers of knowledge in this complex medical field in order to understand the most recent pragmatic aspects of the specialized assistance. As an extension of the Symposium, with a broad target audience, the Summer School-Interdisciplinary Reference Points in Psychiatry, organized at the Socola Institute Psychiatry, reached its 4th edition this year. Continuing the tradition of high-level scientific

communication, what has been, is, and will be a continuously representative process of scientific communication through sessions presented in a way outside of the classic didactic sphere, backed by important personalities of the medical world, multidisciplinary national participations, workshops, and interactive case presentations. Specialist physicians, young resident doctors, PhD students, students of the “Grigore T. Popa” University of Medicine and Pharmacy and more, are encouraged to assign and bring their knowledge up to date, in an interactive way with practical applications in a free spirit of exchanging and accumulating information.

In this way, the Summer School maintains its consecrated title, Interdisciplinary Reference Points in Psychiatry, and it will be organized once more by the “Socola” Institute of Psychiatry from 13th to 15th of June 2019. This scientific event received much gratitude in its anterior editions and the unfolding of the event was possible thanks to the collaboration between the “Socola” Institute of Psychiatry, the Department of Psychiatry of the “Grigore T. Popa” University of Medicine and Pharmacy, Iași and the Romanian College of Physicians, Iași. Thus, for three days, various multidisciplinary and specific psychiatric themes will be addressed, involving practical aspects of the daily life of the psychiatrist. The courses, workshops, interactive presentations proposed for this edition present a wide range of subjects, and they will try to address, through other sciences, new ways of knowing the human psyche.

Among this year's novelty, which include the poster session, concretized through a competition for young resident doctors from Socola Institute of Psychiatry, through which they are encouraged to find and consolidate new ways of transmitting scientific information. The resident doctors will also be involved through a digest of their weekly scientific contributions. In addition, considering the motto of the Summer School, we will discuss the importance of the psychiatrist in assisting the functional gastroenterological diseases, the ethical aspects as the foundation of the medical sciences, the diagnostic challenges and highlighting the importance of perception disorders, and the clinical management of the risks. This edition will be marked by and interactive session designated towards sharing the practical experiences of the young specialists who graduated from Socola School of Psychiatry.

The 2019 edition of the Socola Summer School aims to consolidate the boundaries and interferences of psychiatric diagnoses through presentations, debates, courses, and interactive sessions, addressing mental illness through the interdisciplinary perspective, as this represents the reality of modern medicine and the most desirable approach of current psychiatric practice.

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Articles

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Physiological effects of static Qigong meditation: a systematic review

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ABSTRACT
Background: Qigong meditation has been rooted in Traditional Chinese Medicine where it is perceived as a form of intervention which results in enhancing the mind and body connection. The main purpose it is to simultaneously exercise the mind and the body for treating various chronic diseases and moreover, promoting healthy life.
Objectives: The main aim of the present review sits in emphasizing the benefits of static qigong since the majority of studies focused on the benefits of qigong practice without differentiating between the dynamic and static form.
Method: The research was conducted according to the Preferred Reporting Items of Systematic Reviews and Meta-analyses (PRISMA) guideline by consulting various medical and non-medical data-bases were for identifying the publications of interest.
Results: Nine studies met the selection criteria totalizing 458 participants. The main outcome measures included physiological measures by using EEG and/or heart signals with major implications for focus and relaxation in six cases. One study investigated stress related markers (e.g. cortisol, adrenaline, endorphins etc.), while another study investigated various hormones related to the immune capacity. The preference for various meditation techniques, among which static qigong, was also investigated.
Conclusion: The present research emphasized a highly positive relationship between static qigong, as a mind-body therapy, and various psychophysiological effects. Specifically, this review shows that static qigong can improve people's health by positively altering indicators like heart rate signals, EEG monitored brain waves, cortisol and immunity related markers.

KEYWORDS:
Static qigong, meditation, physiological effects, review

INTRODUCTION

Alternative therapies have proven their usefulness in the last decade (1), especially in promoting physical and psychological well-being (2). By incorporating different practices such as meditation and relaxation strategies into specific psychotherapeutic protocol could lead to positive outcome. Traditional qigong practice or simply put, Chi meditation is a practice of aligning breath, movement, and awareness for various purposes such as exercise, healing, and meditation. Rooted in Chinese medicine, martial arts, and philosophy, qigong is traditionally viewed as a practice to balance qi (Chi) or what has been translated as intrinsic life energy. Generally, a qigong practice is fairly complex, involving various rhythmic breathing, coordinated with various slow repetition of fluid movement, and a calm mindful state (3). For the Traditional Chinese Medicine theory the concept of qi is central. It adopts a world view that can be considered qi monism. If it were to compare with other concepts in modern science, the most similar to qi is energy. Qi in Traditional Chinese Medicine can therefore be likened to the modern scientific concept of energy. This assumption becomes the foundation of the rationale that the human body contains an energy system. To some, this comparison can be considered simplistic since the concept of qi may be wider than that of energy (4). Qigong practice is a widely enjoyed Chinese meditation exercise (5). Regarding the terminology, qi is related to invisible energy while gong stands for the level of accomplishment in an area of endeavor (6). The Chinese qigong practice must not be confused with transcendental meditation or Yoga Gong. The qigong is a complex system of exercises consisting of deep-breathing exercises for prevention or treatment purposes. The complete practice consists of deep-breathing exercises along with conscious control of mind in order to mentally relax, in combination with the harmonious and slow movements of limbs (7).

Although qigong consists of a sequence of various styles of practice that can be divided into two forms, static and dynamic (8). The static form is purely meditative without the exercise component similar to Zen meditation. On the other hand, the dynamic form refers to the collection of a variety of qigong styles that involve a movement or exercise component (9). However, some scholars (10) found differences in brain function between qigong static meditation and Zen meditation. It is suggested that internal qigong is a semiconscious process that involves some awareness and activity, whereas Zen meditation is a neutral process that releases the meditator from all concerns. Perhaps this is why qigong is considered a healing art, whereas Zen is generally not (11). The qigong static meditation or visualization method (also known by the name of Microcosmic Orbit from the Taoist tradition) is an attention focused practice. This involves a concentrative focus on a specific object of meditation to the exclusion of all other experiences. This meditation method uses a self-generated auditory and/or visual object. The qigong static meditation method uses the dynamic image of a thin column of light rising from the base of the spine up to the top of the head with the inhale, and then descending down the front midline of the body to the perineum with the exhale. The tip of the tongue lightly touched the palate during the practice (12).

PROVED EFFECTS OF QIGONG

In Traditional Chinese Medicine, qigong has been perceived as a form of intervention, enhancing the mind-body connection. In the sense that it simultaneously exercises the mind and the body for treating various chronic diseases and moreover, promoting healthy life (13). Free flow of qi energy within the meridian system is essential for good health whereas blockage would result in illness. Qigong practice provides the free flow of energy. When the internal qi is strengthened or balanced, it improves health and wards off or slows down the progress of diseases. However, the physiological effects of qi are still a subject of debate. It has been stated that qi might be a form of vibration energy derived from rhythmic body movements, and can be usually identified at acupressure points (14). For a good health, was important that this form of vibration energy to work in resonance with the heart beats for a good blood circulation. This also explains partially the close relationship between qi and blood within the Traditional Chinese Medicine context (9).

Recent meta-analysis results shows that Qigong practice has many health related benefits such as, improved quality of life, better sleep quality, balance, handgrip strength, flexibility, systolic and diastolic blood pressure, and resting heart rate (2). The studies in the cited paper demonstrated that Qigong may be beneficial for a variety of populations on a range of psychological well-being measures, including mood, anxiety, depression, general stress management, quality of life, and exercise self-efficacy. The Qigong practice includes movements that are relatively easy to learn, if compared to other mind body traditions. Therefore, there are many reasons for which people from diverse backgrounds practice qigong such as exercise, recreation, well-being, self-healing, meditation, self-cultivation, and training for martial arts. There is great potential for qigong practice to be integrated for the prevention purposes or treatment of various chronic illnesses (15).

Regarding cancer patients research, results have shown that qigong practice had positive effects in decreasing inflammatory markers and cortisol level. Reduction of inflammatory markers may indicate that qigong may be beneficial in improving the immune function of cancer patients. Many of the cancer patients suffer from immune deficiency, consequently improving their immune function by practicing qigong could have a significant therapeutic effect. Nevertheless, the research in this field could benefit for better designed and more rigorous studies which are required to confirm that qigong therapy can improve cancer patients' immune functions. Moreover, it could be clarifying to examine the possible underlying mechanisms of how it improves the immune function of cancer patients (16). It seems that qigong also has positive effects on blood pressure regulation (17). According to endorphin theories, an enhancement of parasympathetic system and a reduction of sympathetic activity are manifested by the decrease of blood pressure, levels of stress hormones, anxiety, and stress levels after short-term practice of qigong (18, 19, 20). The significant lower levels of cortisol, blood pressure, stress, and anxiety symptoms of qigong subjects when compared with non-practitioners provides empirical support for parasympathetic regulation after qigong. Studies have also shown that practicing qigong regularly brings improvement in psychological well-being, relaxation, physical ability, as well as relieving psychosomatic and stress-related health conditions (21, 22, 23).

Many qigong researchers consider that qigong's effect on the body is systemic, and does not affect one element in particular, such

as blood pressure. However, a study showed that qigong was not more effective than conventional muscle relaxation in reducing blood pressure, but has advantages when it comes to the holistic status of patients, such as sleep quality, and feeling energized (24). Another study showed that how long-term practice of qigong with drug therapy may have encouraging preventive effects for cardiovascular diseases, superior to the effects of drug therapy alone (25).

Some evidences support the idea that the practice of Qigong has some antidepressant and anxiolytic effects. But again, more rigorous designed studies are needed to discount design and sampling bias and to verify whether the observed effects differ according to various participant characteristics and different levels of qigong exposure (26).

Considering the substantial number of research produced over the years regarding the health benefits of practicing qigong, it may be valuable for the scientific community to have access to a comprehensive review of static qigong. Many therapists could implement static qigong in different therapeutic protocols, since they are already familiarized with relaxation techniques or other forms of guided imagery. The previous reviews on the topics were mainly focused on the effectiveness of qigong practice which included exercises and body movements (2, 26). However, a comprehensive review has not been conducted yet to specifically evaluate the physiological response or other health-related outcomes of static, meditative qigong in healthy or special populations. Therefore, we conducted a systematic review to investigate the effectiveness of static qigong for different health outcomes.

METHOD

SEARCH STRATEGY

The review was conducted according to the Preferred Reporting Items of Systematic Reviews and Meta-analyses (PRISMA) guidelines (27). Various medical and non-medical data-bases were searched for identifying the publications, such as Medline, Qigong Institute Database, Google Scholar, PsycINFO, ResearchGate, ScienceDirect, Springer, Taylor & Francis, ProQuest and EBSCO. English keywords were used for the search such as ‘‘Qigong Meditation’’ or ‘‘Qigong Visualization’’ or ‘‘Static qigong‘‘. Only intervention studies published in peer-reviewed journals were considered for the review. Citations of the listed articles were also searched for any potential studies that were initially missed in the data-base search.

ELIGIBILITY CRITERIA

The intervention could be in individual or self-practice, group-based practice with or without a complementary home program or following along audiovisual training materials. Trials comparing any type of internal qigong with any type of control intervention were included. Those using internal qigong as an adjunct to conventional treatment were excluded along with trials with qigong as a part of a complex intervention. Studies that used both internal and external qigong, as well as studies that included any type of exercise or body movement were also excluded. The main focus was on static, internal qigong.The focus of the current review was on static forms of qigong, which is purely meditative in nature and does not involve an exercising element. The employed outcome measures included biomarkers or physiological parameters (e.g. EEG, blood pressure, etc.), and questionnaire or survey.

DATA EXTRACTION AND QUALITY ASSESSMENT

Data were extracted independently by two of the authors, using a specifically designed data extraction form. For each study details of treatment and control procedures, main outcome measures, and main results were extracted. Discrepancies were resolved by discussion between the reviewers and, if needed, by seeking the opinion of the third. However, there was no disagreement between the two reviewers during the data extraction.

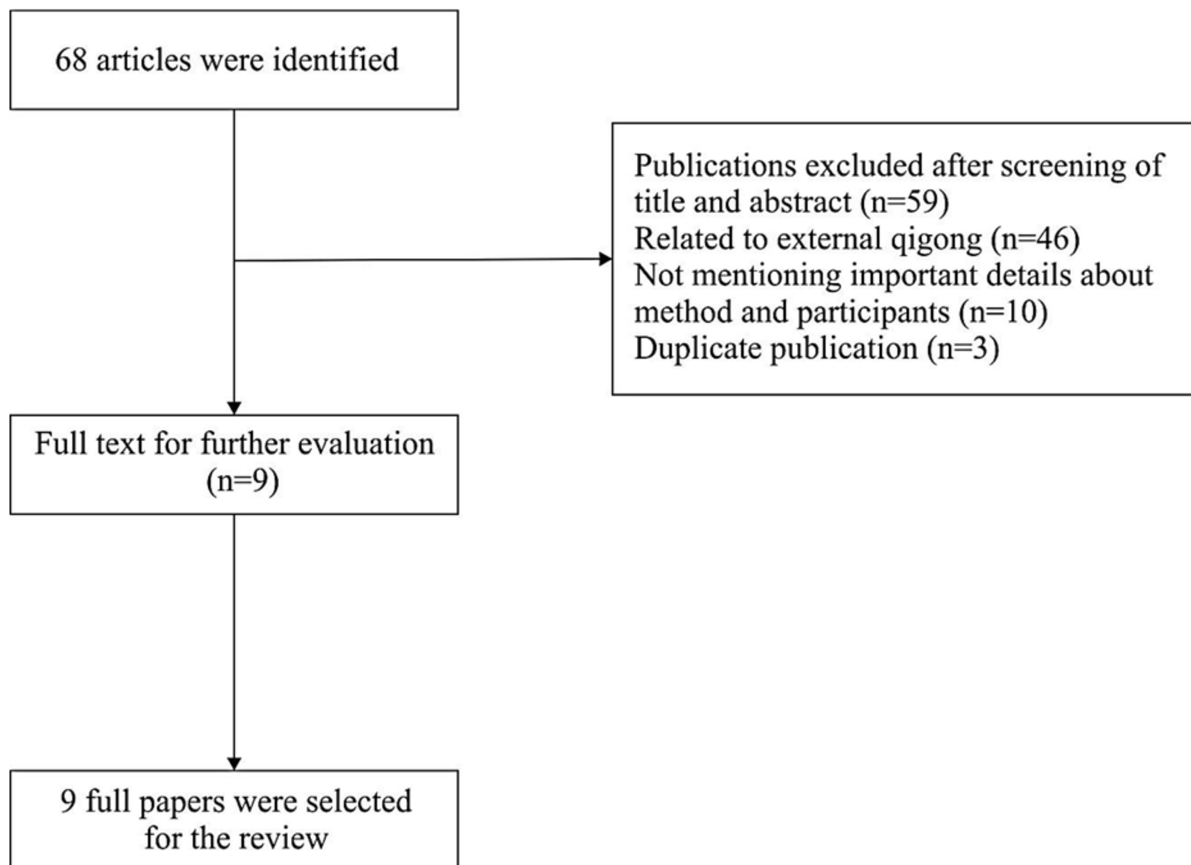

Fig. 1. Flowchart showing the retrieval of studies for review

RESULTS

DESCRIPTION OF INCLUDED STUDIES

A total of nine studies with 458 participants were included in this review. Of these nine investigations, outcome measures included physiological measures by using EEG and/or heart signals with major implications for focus and relaxation in six cases. One study investigated stress related markers (e.g. cortisol, adrenaline, endorphins etc.), one investigated various hormones related to the immune capacity, while the last one assessed the preferences for various mediation techniques, among which, static qigong. The main characteristics of these studies are summarized in Table I. The majority of the studies had an extremely small sample size, but this trend for qigong studies was observed also by previous research (Zeng, 2014). The interventions lasted from 40 minutes to a maximum of 7 months.

Study	Design	Participants	Intervention	Outcome measures	Results
Shi *et al.*, 1991	Within-subjects design	47 experienced practitioners	Brain function during qigong was monitored	EEG	During EEG monitoring the peak frequency of alpha waves became slower
Zhang *et al.*, 1993	Between-group design/Experiment	37 patients without neurological disorders – experimental group 11 subjects – control group	Novice and Qigong practitioners were exposed to auditory stimulus.	The functional state of the cerebral cortex was investigated with flash visual evoked potentials (F-VEPs) recorded from the occipital scalp.	Qigong meditation may have facilitative or inhibitory effect on the visual cortex depending on the level of expertise regarding qigong meditation.
Yu *et al.*, 1998	Between-group design	80 subjects practicing qigong at different levels	The brain activity was monitored during a long term period.	EEG	After 3-7 months of practicing Qigong, both the concentration degree and tranquilization degree improved.
Higuchi *et al.*, 2000	Pretest- posttest design	6 experienced practitioners	The subjects were exposed to 40 minute meditation protocol.	Before and after a 40 minute meditation, the levels of cortisol, adrenaline, noradrenaline, dopamine, and beta-endorphin in venous blood were simultaneously measured to study changes.	Immediately after practicing this static Qigong and also 40 minutes later, plasma adrenaline decreased significantly. The other items did not show significant changes. Based on the results, we believe that the level of sympathetic nerve activity declines and this affects endocrine changes.
Higuchi *et al.*, 2000	Pretest- posttest design	6 experienced practitioners	The subjects were exposed to 40 minute meditation protocol	Before and after a 40-minute meditation, the levels of Natural Killer (NK) cell activity and Interleukin (IL)-2 in venous blood were simultaneously measured to	The levels of NK cell activity and IL-2 showed a significant increase when compared to the findings achieved from a study conducted on a group of subjects who had no experience in

				study changes.	qigong meditation. It became clear that Qigong Cosmic Orbit Meditation was effective in enhancing the level of immune capacity
Litscher *et al.*, 2001	Case studies	2 experienced practitioners	Brain function during qigong was monitored.	Transcranial Doppler Sonography	The peak frequency of EEG alpha rhythm is slower during qigong than in the resting state. A marked suppression of the activity in the alpha-band of compressed spectral array was observed.
Peng *et al.*, 2004	Observational study/Within-subjects design	10 experienced practitioners	The subjects were exposed to three different protocols of breathing during the qigong practice.	Heart rate oscillation amplitude measured using EEG signals and respiratory rate.	The meditation techniques resulted in low heart rate oscillations associated with slow breathing.
Goshvarpour & Goshvarpour, 2012	Within-subjects design	12 experienced practitioners	The subjects were exposed to qigong and kundalini meditation protocols.	Poincare plots, Lyapunov plots and Hurst exponents of heart rate variability signals.	The results show that heart rate signals become more periodic and their chaotic behavior was decreased in both forms of meditation.
Burke, 2012	Within-subjects design	247 undergraduate students	Participants learned four meditation techniques among which qigong.	Ranking of the subjective preference of meditations practiced.	Significantly more subjects preferred other meditations techniques to the detriment of qigong.

Table 1. Summary of the 9 studies of static qigong meditation

All four studies that monitored the brain activity (28, 29, 30, 31) concluded that the peak frequency of the alpha rhythm is slower during static qigong than in resting state. One study suggested that both concentration degree and tranquilization degree went up after long term usage of qigong meditation (29). Alpha brain waves signify non-arousal. This types of waves are slower, and higher in amplitude. A person who is in resting phase or in a meditation phase is often in an alpha state. Two of the previous mentioned studies (28, 29), observed short burst in theta waves indicating that qigong is an unusual state of excitation, not a state of consciousness between wakefulness and sleep. Theta brain waves, are typically of greater amplitude and slower frequency indicating a state of absorption. A recent study recorded next to the mentioned modifications of the alpha rhythm, a significant increase in the blood velocity (31).

Two of the nine studies included in the systematic review investigated the heart rate oscillations and heart rate variability signals (32, 3) on a two samples of experienced practitioners. Both studies held similar results, the meditation techniques resulted in low heart rate oscillations associated with slow breathing also heart rate signals became more periodic and their chaotic behavior decreased during meditation.

One study (33) examined the evolution of cortisol levels before and after qigong practice. Immediately after practicing this static Qigong adrenaline and cortisol levels decreased significantly. Based on these results, is generally believed that the static qigong lead to declines of sympathetic nerve activity and this affects endocrine changes. The same author was interested in examining the blood levels of Natural Killer (NK) cell activity and Interleukin (IL)-2 before and after static qigong in a small sample of experienced practitioners; both markers showed a significant increase when compared to the findings achieved from a study conducted on a group of subjects who had no experience in qigong meditation. Only one study investigated participants' preferences towards different methods of meditation. When compared to Zen meditation, mindfulness and mantra, qigong was among the least preferred methods (34).

DISCUSSION

Static qigong as a mental practice includes a significant degree of internalized attention that correlates with theta activity. Psychological and physiological states of wakefulness or arousal as measured in terms of activation of particular EEG frequency bands are frequently associated with different self-reported experiences of the Qigong state in experienced practitioners. In general, an increase in alpha activity is related to increased relaxation and well-being. An increase of EEG frontal theta activity is associated to mindfulness, an attentive state which is one of the reaching objectives in Buddhist meditation. To conclude, systematically effects of Qigong meditation on EEG brain activity can be resumed with most results reaching a consensus in the sense that they observed an increase in frontal theta and posterior alpha activity as a neurophysiological correlate for a relaxed and attentive mind. Some results suggest that static, as well as dynamic Qigong practice, increases alpha activity and therefore induces a relaxed state of mind. In addition, mental practice of Qigong entails a higher degree of internalized attention that correlates with theta activity (35).

Regarding the heart rate variability analysis it must be stressed that it has become an important tool in cardiology, because its measurements are noninvasive and easy to perform, have relatively good reproducibility and provide the great information;

information was found directly linked to health and prognostic information on patients with heart disease. The results of the reviewed studies are in line with other studies that showed how qigong practice has physiological effects that indicate stabilization of the cardiovascular system. Specifically, the heart rate, respiratory rate and systolic blood pressure were significantly decreased during qigong training (22). The results of the two mentioned studies are in line with previous research extending the effects to the static qigong practice.

As it was shown, static qigong may be effective in enhancing the level of immune capacity, although static qigong might not be the only meditation technique that holds this effect. A recent review (36) showed that mindfulness meditation modulates various immune parameters in a manner that suggests a healthier immune profile. Specifically, mindfulness meditation appears to be associated with reductions in proinflammatory processes, increases in cell-mediated defence parameters, and increases in enzyme activity that guards against cell aging. Another study underlines the positive effect of visual imagery and meditation on various dermatological conditions (37). For long-term effects it is necessary that regardless of the meditation technique used, to be practiced frequently and integrated in the daily routine. As was showed by previous studies, the benefits of meditation increase over time. Therefore, by selecting a method that motivates sustained practice is a critical objective if therapeutic effects are to be achieved (12).

This review emphasized a highly positive relationship between static qigong, as a mind-body therapy, and various psychophysiological effects. Whether these results can be applied to a larger population or if they remain stable regardless of the experience in practicing this type of meditation remains unestablished, but might be useful for further investigation. In addition, the present review shows that static qigong can improve people's health by affecting several indicators like heart rate signals, EEG monitored brain waves, cortisol, immunity related markers and so on. One of the main limitations of the reviewed studies consists of the small samples and in general experienced practitioners. Finally, the success of safe, small cost mind-body therapy can justify larger studies on populations with various conditions.

Another limitation is related to the qigong practice in general. Being based on the energetic system the qigong practice different characteristics are those of a material system. Specifically, it is difficult to directly observe the energy, having no clear boundaries or measuring scales (sunspot activity affects the processes of the human body). Also, it can be induced by consciousness, for example the Microcosmic Orbit and Macrocosmic Orbit of Qigong practice. The two orbits are two paths through which energy or the internal qi is moved (4). For the reasons mentioned above, the experimental methods used to study material and structural systems are difficult to be directly applied to the study of energetic systems. Moreover, without the hypothesis of an energy system, it is hard to exploit any new research directions and fields.

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REFERENCES

1. Leung JC, Liu KP, Fong SS. Effects of qigong training on physical and psychosocial well-being of breast-cancer survivors: a systematic review. Nursing and Palliative Care. 2016;2(1):1-7.
2. Zou L, SasaKi JE, Wang H, Xiao Z, Fang Q, Zhang M. A systematic review and meta-analysis of Baduanjin Qigong for health benefits: Randomized controlled trials. Evidence-Based Complementary and Alternative Medicine.2017.
3. Goshvarpour A, Goshvarpour A. Chaotic behavior of heart rate signals during Chi and Kundalini meditation. International Journal of Image, Graphics and Signal Processing. 2012;4(2):23.
4. Liu T. The scientific hypothesis of an “energy system” in the human body. Journal of Traditional Chinese Medical Sciences. 2018;5(1):29-34.
5. Mackenzie ER, Rakel B, editors. Complementary and alternative medicine for older adults: A guide to holistic approaches to healthy aging. Springer Publishing Company; 2006.
6. Liu GL, Cui RQ, Li GZ, Huang CM. Changes in brainstem and cortical auditory potentials during Qi-Gong meditation. The American journal of Chinese medicine. 1990;18:95-103.
7. Jian-Zhou Z, Jing Z, Qing-nian H. EEG findings during special psychical state (Qi Gong state) bymeans of compressed spectral array and topographic mapping. Computers in biologyand medicine. 1988;18(6):455-63.
8. Tsang HW, Cheung L, Lak DC. Qigong as a psychosocial intervention for depressed elderly with chronic physical illnesses. International journal of geriatric psychiatry. 2002;17(12):1146-54.
9. Ng BH, Tsang HW. Psychophysiological outcomes of healthqigong for chronicconditions: a systematicreview. Psychophysiology. 2009;46(2):257-69.
10. Kawano K, Kushita KN. The Function of the Brain using EEGs during Induced Meditation. Journal of International Society of Life Information Science. 1996;14(1):91-6.
11. Sancier KM. Medical applications of qigong. Alternative therapies in healthand medicine. 1996;2:40-6.
12. Burke A. Comparing individual preferences for four meditation techniques: Zen, Vipassana (Mindfulness), Qigong, and Mantra. Explore: The Journal of Science and Healing. 2012;8(4):237-42.
13. Tsang HW, Cheung L, Lak DC. Qigong as a psychosocial intervention for depressed elderly with chronic physical illnesses. International journal of geriatric psychiatry. 2002;17(12):1146-54.
14. Wang WG. The Musical Movements of ‘‘Qi.’’. Taipei: Locus Publishing Company. 2002.
15. Wang F, Man JK, Lee EK, Wu T, Benson H, Fricchione GL, Wang W, Yeung A. The effects of Qigong on anxiety, depression, and psychological well-being: a systematic review and meta-analysis. Evidence-Based Complementary and Alternative Medicine.2013.
16. Zeng Y, Luo T, Xie H, Huang M, Cheng AS. Health benefits of qigong or tai chi for cancer patients: a systematic review and meta-analyses. Complementary therapies in medicine. 2014;22(1):173-86.
17. Zhang E. Diagnostics of TraditionalChinese Medicine. Publishing House of Shanghai University of Traditional Chinese Medicine. bothChineseand English. 1990.
18. Jones BM. Changes in cytokine production in healthysubjects practicing Guolin Qigong: a pilot study. BMC complementary and alternative medicine. 2001;1(1):8.
19. Lee MS, Lee MS, Kim HJ, Moon SR. Qigong reduced blood pressure and catecholamine levels of patients with essential hypertension. International Journal of Neuroscience. 2003;113(12):1691-701.
20. Lee MS, Kang CW, Lim HJ, Lee MS. Effects of Qi training on anxietyand plasma concentrations of cortisol, ACTH, andaldosterone: a randomized placebo controlled pilot study. StressandHealth. 2004;20(5):243-8.
21. Hui PN, Wan M, Chan WK, Yung PM. An evaluation of two behavioral rehabilitation programs, qigong versus progressive relaxation, in improving the quality of life in cardiac patients. Journal of Alternative &Complementary Medicine. 2006;12(4):373-8.
22. Lee MS, Ryu H, Chung HT. Stress management by psychosomatic training: effects of Chun DoSun Bup Qi training on symptoms of stress: a crosssectional study. Stress Medicine. 2000;16(3):161-6.
23. Shin YI, Lee MS. Qitherapy (externalqigong) for chronic fatigue syndrome: case studies. The American journal of Chinese medicine. 2005;33(01):139-41.
24. Ritter C, Aldridge D. Qigong Yangsheng as a therapeutic approach for th etreatment of essential hypertension in comparison with a western muscle relaxation therapy: a randomised, controlled pilot study. Chin Med. 2001;16:48-63.
25. Guo X, Zhou B, Nishimura T, Teramukai S, Fukushima M. Clinical effect of qigong practice on essential hypertension: a meta-analysis of randomized controlled trials. The Journal of Alternative and Complementary Medicine. 2008;14(1):27-37.

26. Yin J, Dishman RK. The effect of Tai Chi and Qigong practice on depression and anxiety symptoms: a systematic review and meta-regression analysis of randomized controlled trials. Mental Health and Physical Activity. 2014;7(3):135-46.
27. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Systematic reviews. 2015;4(1):1.
28. Shi MM, LuanLY, Kawano K, Shinagawa Y. Difference in EEG between meditation and chinese qigong. Jpn J Phisiol.1991;41,191.
29. Zhang W, Zheng R, Zhang B, Yu W, Shen X. An observation on flash evoked cortical potentials and Qigong meditation. The American journal of Chinese medicine. 1993;21:243-9.
30. Yu X, Wang Y, Xu J, Qian A, Yu X. Quantitative EEG analyses to the concentration and tranquilization in static qigong. 7th IntSymp on Qigong.1998.
31. Litscher G, Wenzel G, Niederwieser G, Schwarz G. Effects of QiGong on brain function. NeurologicalResearch. 2001;23(5):501-5.
32. Peng CK, Henry IC, Mietus JE, Hausdorff JM, Khalsa G, Benson H, Goldberger AL. Heart rate dynamics during three forms of meditation. International journal of cardiology. 2004;95(1):19-27.
33. Higuchi, Y., Kotani, Y., Higuchi, H., Yu, Y, Momose, S. Endocrine changesduring cosmic orbit meditation of qigong. Journal of International Society of Life Information Science.2000;18 (1):158-9.
34. Higuchi, Y., Kotani, Y., Higuchi H. Immune changes during Cosmic Orbit Meditation of Qigong. Journal of International Society of Life Information Science. 2000;18(2):352-354.
35. Henz D, Schöllhorn WI. EEG Brain Activity in DynamicHealthQigong Training: Same Effects for Mental Practice and Physical Training? Frontiers in psychology. 2017;8:154.
36. Black DS, Slavich GM. Mindfulness meditation and the immune system: a systematic review of randomized controlled trials. Annals of the New York Academy of Sciences. 2016;1373(1):13-24.
37. Collins MP, Dunn LF. The effects of meditation and visual imagery on an immune system disorder: Dermatomyositis. Journal of Alternative & Complementary Medicine. 2005;11(2):275-84.

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The quality of life for a patient with an autoimmune diseas

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ABSTRACT

Autoimmune diseases involve altering the immune response with loss of tolerance to the person itself long before the onset of symptoms. Among pathologies with autoimmune determinism, scleroderma is remarkable by infallible prognosis and a reduced life expectancy, being a disease with many unknowns. The incomplete elucidated mechanisms and often the lack of an effective treatment to stop the evolution of the disease, the disabling character, and not in the least the pain and skin lesions, have a significant impact on the quality of life of the patient with autoimmune disease. The identification of functional and psychological deficiencies can guide optimal interventions on a target dysfunction. This study proposes a review of existing data in the literature on the functional impact of autoimmune diseases and, in particular, of systemic scleroderma, impairment of daily activities and care, work capacity and psychological impact on the patient It is necessary to optimize the management of autoimmune diseases, a complex approach of the disease in the psycho-social and

therapeutical plan and to pay more attention to the relationship between the patient and the practitioner, aiming at improving the quality of life related to health in this category of patients.

KEYWORDS:
Systemic slerosis, scleroderma, autoimmune disease, quality of life, morphea

INTRODUCTION

Autoimmune diseases involve the alteration of the immune response by producing autoantibodies directed against their own structures and activation of B and T lymphocytes long before the onset of the symptomatology (1). It was observed an association between the autoimmune diseases and cutaneous amyloidosis (2). The autoimmune pathology affects all organs and tissues and involves a complex immunological disruption as a result of interaction between the environmental factors and the preexistent genetic terrain, leading to an excessive immune activation with loss of self-tolerance (3). Autoimmune diseases, especially systemic scleroderma (SCS), associate severe multiorganic impairment often with functional disabilities that reduce significantly the ability to work and self-care and implicit it lowers the quality of life. At an economic level, inclusion in disability groups raises the costs of psychosocial assistance (4).

An important functional impact, social and on the patient's quality of life, is the skin damage (5). Chronic inflammation of systemic scleroderma is characterized by an autoimmune determinism in which self structures are no longer recognized and are considered non-self in the context of a disruption of the immune system. The auto-antibodies which are generated secondary to immune dysfunction trigger microvasculopathy and extensible cutaneous fibrosis that leads to visceral fibrosis.The specific clinical manifestations of the Scs induce discomfort, affect quality of life and reduce life expectancy (6).

MATERIAL AND METHOD

I analysed and reviewed 24 studies from the literature to assess the impact of autoimmune diseases, in particular, of systematic scleroderma, on the quality of life, the psychological consequences and the life expectancy of these patients, opportunities to manage symptoms and how they affect dailly activities and work capacity in the patients with autoimmune disease.

There were developed multiple tools for the quantification of the life quality, questionnaires assessing general health , the degree of fatigue and the disability index, the index of quality of dermatological life for children and adults and also the impairment score of the daily routine and work capacity.

RESULTS AND DISCUSSIONS

Scleroderma is a rare disorder more common in women than in men with a 1:4 ratio between sexes (7). Assessing the quality of life with the Short-Form questionnaire 36 Medical Outcomes (SF-36) on a batch of 795 patients with systemic scleroderma with a witness lot of 1154 healthy peoplehas shown that in the systematic sclerodoma disease the quality of life is affected in all aspects physical, emotional and psychological compared to the group of healthy people. As a result of these observations, it is recommended to pay special attention to the overall health with a favorable outlook on quality of life (8). There were conducted numerous studies to evaluate the limitations of the autoimmune disease. WPS-RA (the

study made on the patient's work capacity with rheumatoid arthritis) was also used to assess work productivity in systemic scleroderma, their ability to engage in family activities, household and recreational activities. Of the 162 patients included in the study, 37% were employed in the workplace and showed a work incapacity of 2.6 days per month with a fall in work productivity of 2.5 days per month. The 102 patients without employment, presented 8 days a month in which the manifestations of the disease did not allow them to carry out their domestic activities and a low productivity of 6 days per month (43). All the symptoms of depression are assessed using the Short-Form Scale of Light Depression in the Center for Epidemiological Studies (CESD-10).The fatigue scale, The FACIT-Fatigue scale (The Functional Assessment of Chronic Illness Therapy – Fatigue Scale) evaluates the degree of fatigue and the way in which the patient's activities with autoimmune disease are affected. All of the 162 patients had low FACIT-Fatigue scores that indicated a high degree of fatigue, and 39 of the patients were disabled. The overall health status is assessed by the patient using the unique question questionnaire (9). Cruz-Domínguez and his associates (2017) adapted and translated the quality of life questionnaire for scleroderma (SySQ) into Spanish and later used it as a tool for assessing the severity of the disease and the quality of life in Spanish patients, and they later used it as a tool for assessing the severity of the disease and the quality of life on a group of 70 Spanish patients aged between 17 and 78 years of which 65 were women (10). McMahan and his associates (2018) used the quality of life questionnaire for reflux and dyspepsia (QOLRAD) to monitor the improvement of gastrointestinal symptoms after treatment on a batch of 116 systemic sclerosis patients with gastroesophageal reflux disease. The Medsger severity score was significantly increased in patients with cardiac, pulmonary or joint impairment and in accordance with the quality of life questionnaire (11). With the help of the Cochin Hand Function Scale (CHFS), the hand function was assessed in the presence of Raynaud's phenomenon, digital ulceration and small joint contractions comparative on a group of 1193 patients with systemic scleroderma, rheumatoid arthritis and myositis. Patients with SCS experienced a significant impairment of hand function by the presence of digital ulcers and contractions of small joints (12).

Systemic rheumatic autoimmune diseases (SARDs), particularly rheumatoid arthritis, myositis, erythematosus lupus and systemic scleroderma affect 5% of the population, are more common in women and their common aspects such as Raynaud's phenomenon, arthritis, the presence of anti-nuclear antibodies, pulmonary affection, have a considerable impact on the quality of life of patients. Thus, in a study in patients with autoimmune inflammatory rheumatic diseases of which 118 were part patients with systemic lupus erythematosus, 108 patients with SCS, 64 patients with rheumatoid arthritis and 25 patients with idiopathic inflammatory myopathies, it was observed that patients with myositis at onset have the lowest health-related quality of life index both mentally and physically (13). Johnson and his associates noted in a 2006 study that 28 patients with systemic scleroderma assessed using the Health Assessment Questionnaire Disability Index (HAQ-DI) and Short Form-36 Health Survey (SF-36) had poorer scores than groups with 74 patients with systemic lupus erythematosus, 42 patients with rheumatoid arthritis and 82 patients with psoriatic arthropathy. The joint pain of patients with ScS was more severe than the one suffered by those with psoriatic arthropathy (14).

Neuropathic pain, accompanied by sensililitate disorders was similar in patients with rheumatoid arthritis and systemic scleroderma, however their features affected more the psychological status and the functional status and overall the quality of life in patients with rheumatoid arthritis in a study of 54 patients with ScS of which 23 have presented neuropathic pain and 53 patients with rheumatoid polyarthritis of which 24 with neuropathic pain (15). Ardalan and his associates studied the predictors of quality of life (QoL) in children with localized scleroderma. In a study (2017) on a batch of 80 pediatric patients aged between 4 and 16 years, with a localized form of scleroderma they note that extraarticular manifestations and females have a greater impact on quality of life than damage skin and the extraarticular manifestations were monitored especially contraction articular and hemifacial atrophy, assessed by CDLQI score > 1 (the dermatological index of children's quality of life) (16). They noticed that a longer initial visit had a positive impact on the quality of life. Identifying patients at risk of unfavorable evolution with the help of life quality predictors is useful for rehabilitating treatment and their psychological counseling (3). In a recent study (2018) conducted on 101 patients with morphea, Bali and the team took into consideration the quality of life related to health (HRQoL) in the context of localized morphology using the dermatological quality index (DLQI) and quantified it using the severity index of scleroderma localized modified (mLoSSI) and the index of localized scleroderma locomotor (LoSDI) (17). They have noted the psychological impact of morphea especially when it is located in sensitive and exposed areas. The most common accusations were related to digital ulceration, pain, and skin pruritus with significant impact on the dermatological quality of life index (DLQI). HRQoL appears to be more affected in female sex, in generalized morphea, or when hands and feet are involved, and in high-grade disease-rated forms assessed by the PGA-A score (the overall assessment of activity by the physician). The feeling of embarrassment frequently encountered in these patients implies the need for psychological counseling (17). Systemic scleroderma is associated with sometimes severe malnutrition, with a prevalence of 10.9% in a study of 129 patients with ScS. A MUST score (The Malnutrition Universal Screening Tool) ≥2 expresses malnutrition with impact on quality of life (18). Morphea, a localized form of scleroderma, can be triggered by infections.There were quoted cases of morphea caused by Borrelia burgdorferi infection (19) and morphea lesions that have evolved in the context of Toxopalasma gondii infection (20).

Scleroderma scarring reduces productivity at work and in the household, and disability accounts for nearly 40% of scleroderma patients (9). Bretterklieber and his study team (2014) assessed the quality of life on a batch of 41 patients with scleroderma compared to other dermatological diseases (pemphigus, psoriasis, ichthyosis, vitiligo and dermatological lupus) and concluded that the slow progressive and unhealed progression of scleroderma significantly decreased quality of life in the scleroderma patient requiring psychosocial and spiritual support with favorable impact on depression and generally mental health (21). As it is in case of scleroderma, fatigue in systemic lupus erythematosus significantly reduces work capacity, reduces physical strength by installing disability. It is anticipated that effective tiredness control in these patients can increase work productivity and increase individual performance (22).

A study of 419 argentinean patients with lupus erithematosus indicated a prevalence of

24,3% of work incapacity is favored by precarious socio-economic status, sedentarism, a low quality of life index, and being conditioned by the ethnic factor (the mestizo population) (23). Morrisroe and his study team (2018) correlated the results from the questionnaire on impairment of capacity and quality of life related to health (HRQoL) and showed that a lowering quality of life also causes a decline in work productivity. They included in the study 476 patients with systemic scleroderma, of which only 55.2% were employed under the age of 65, and observed that 16% of the active active patients reported lack of work and 22% had a reduced working capacity. The authors of the study concluded that the reduced work capacity of the patient with systemic scleroderma decreases labor productivity and, in parallel with the installation of disability, increases the costs of socio-economic support (24). The microstoma of scleroderma facies, oropharyngeal and gastrointestinal disease, have an impact on the comfort of these patients, not least on aesthetics, nutrition, and quality of life (25). Systemic scleroderma commonly associates sarcopenia with decreased physical strength and work capacity, similar to the elderly sarcopenia, but without age and duration differences (26). A group of 42 pediatric patients of North America diagnosed with systemic scleroderma were enrolled in a study on the characteristics of the disease and the impact on quality of life, and concluded that the most common clinical manifestations were cutaneous, followed by vascularization and musculoskeletal damage, but with the greatest impact on quality of life remains gastrointestinal dysfunction, 38% of these patients presenting 4 types of damage (27).

Okiyama and her study team (2018) assessed the impairment of daily activities using the ADL score in 177 Japanese adult patients with localized scleroderma-like form in which the inflammation of the skin is not accompanied by inflammation and visceral fibrosis. They tracked the 8 items of the ADL performance scale in using the phone, preparing food, washing clothes, doing household cleaning, using public transport, shopping, the ability to buy things and to use the money. Their study also used the Barthel incapacity scale, which appreciates the day-to-day performance of another person's help in "assisted independent" and "quasi-independent" categories, and showed the importance of these additional assessments over the Life Quality Index (DLQI) in appreciation of the degree of disability.

They noted that the addition of foot lesions significantly lowers the ADL score compared with lesions of other body segments (28). Hand injuries impose the need for a medical gymnastics program needed to maintain the functionality of this segment. A group of researchers applied a set of hands exercises to a group of 22 patients with scleroderma (of which 19 women, 16 limited and 6 diffuse forms) at which pain was assessed periodically using the Visual Analog Scale (VAS) and hand function using the Cochin Hand Function Scale, Raynaud's phenomenon, digital ulceration, prehension, finger mobility. After 8 weeks there was an improvement in hand function with favorable outcomes on quality of life (29). The function of the hand is additionally affected in systemic scleroderma in case of the association of favorable conditions: smoking, overweight, enlargement to the diffuse form of scleroderma and the association of other autoimmune diseases (rheumatoid arthritis, myositis). Female sex is also associated with lower scores on the Cochin Scale of Hand Function (12).

Leite and Maia (2013) studied a batch of 128 Brazilian patients with ScS and noted that half of them presented anxiety, and two-thirds of them had a deformed image on their own

body (30). The scleroderma facies and other changes in the skin aspect assessed using the anxiety scale on the social aspect (SAAS) can induce anxiety and depression, dissatisfaction with the appearance of their own body and social phobia (31). Seravina and his team (2017) concluded that all of the 110 patients with scleroderma included in the study had cognitive impairment, 90% of them associated psychiatric disorders and 3/4 of the patients had recurrent depressive episodes. They used as measurement tool the Montgomery-Asberg Depression Scale, the Hamilton's Anxiety Scale and some Memory and Attention Tests (32). The dissatisfaction with the image of their own body was also identified in African-American patients with diffuse ScS form more than in those with limited ScS regarding pigmentary skin lesions and digital ulceration in a study of 98 patients with systemic scleroderma, of which 27% were African-Americans (33). In a study of 2327 patients with systemic scleroderma, Guillevin and his team (2013) have shown that personal care and daily activities are limited in proportion to the number of digital ulcers and they are requiring support from close relatives (34). The presence of digital ulcerations accompanied by pain, complicated with extensive infections sometimes up to the bone, gangrene and necrosis, calcinosis, limits daily activities, installs disability and lowers the quality of life. In a study of 282 patients with systemic scleroderma, of which 254 were women, 84% were limited systemic scleroderma and 16% diffuse forms of scleroderma, 55% had complicated digital ulceration in 67.3% of cases, 19,2% complicated with osteomyelitis and 16% with gangrene, and 11.5% of patients required amputation. The therapeutic interventions in recent years are able to improve the functional status and maintain a reasonable level of the quality of life for these patients (35).

The Raynaud phenomenon has as a substrate the peripheral microvasculopathy common to several autoimmune diseases and is present in over 95% of patients with scleroderma. Managing it requires high costs for hospitalization and medical care. To improve the quality of life score, a batch of 30 patients was included in a physical exercise program with 2 sessions of 45 minutes per week for 12 weeks accompanied by serial Doppler evaluations of vascular tone and fluximetry. Medical gymnastics program improved digital microvasculature and physical capacity of hands (36).

A study team led by Gonzales-Ericsson (2018) described a case of morphea developed post-radiotherapy in the context of breast cancer. Skin lesion has erythematous appearance with sclerosis and tegument retraction and requires histopathological confirmation from cutaneous biopsy. Radiotherapy rarely complicates with morphea and has an adverse impact on quality of life (37). Smith and Argobi (2018) observed that pruritus occurs in several collagenases with autoimmune determinism: systemic scleroderma and systemic lupus erythematosus, Sjogren's syndrome, dermatomyositis as an indicator for the activity of the disease. Pruritus in the autoimmune diseases may have causes that exclude the activity of the disease. But whatever the cause, pruritus affects the quality of life. As a measuring instrument, the authors used the VAS visual analogue scale to assess the intensity of pruritus with scores ranging from 1 to 10, on a batch of 70 patients with dermatomyositis and quantified the intensity of pruritus with grade 4 on the VAS scale, with higher intensity than in systemic and cutaneous lupus erythematosus and for efficient intervention it is essential to identify trigger factors (38). Patients with scleroderma associated and lowering plasma cortisol below the lower limit of normal values have a

lower pain threshold and depressive symptoms. Targeted management of deficiencies is useful for increasing the quality of life score (39).

80-90% of patients with systemic scleroderma show erectile dysfunction due to microangiopathy. Cavernous body fibrosis and intimate proliferation of small vessels limit blood flow through the penis. There were obtained minimal results by administration of phosphodiesterase-5 inhibitors or prostaglandin E1 injections into the corpus cavernosum (40). Sampaio-Barros and his associates (2000) noted that 37% of the 150 sexually active Brazilian patient, diagnosed with scleroderma presented dyspareunia that affected their quality of their sexual life (41). Recent studies have shown that haematopoietic stem cell transplantation (HSCT) in systemic scleroderma patients, despite the risk of association with other autoimmune diseases, has the advantage of decreasing skin induration and improving microvascularisation with a beneficial effect on quality of life related to health. However, HSCT has limited indications of advanced visceral damage (42).

The prognosis of pulmonary arterial hypertension secondary to scleroderma is reduced compared to idiopathic arterial hypertension and involves low resistance to exercise, a certain degree of work incapacity and a low quality of life index. Studies on this issue recognize the need for multidisciplinary care essential to survival rates (43). At international level, Australia is remarkable with a large and growing prevalence of systemic scleroderma, although there is access to health care.

There is a need of new ways to manage immune dysfunction that improves health-related quality of life (HRQoL), starting with the evaluation of all aspects of the disease (44). Although no treatment for scleroderma is known, medical care through the participation of various medical specialties can improve the general condition of the patient with autoimmune disorder and increase the quality of life related to health (45). The divergent results on the quality of life index in various autoimmune disorders impose the need for further studies to better define the impact of autoimmune disorder on daily activities and work capacity. Effective disease management is useful in identifying possible obstacles and "improving health care strategies" (46). The multitude of unknowns related to this disease leads to the patients' lack of trust in the therapeutic and applied care plan, anxiety-generating attitude and depression with image impairment and isolation (47). Comparative studies prove useful for a complex approach to psycho-social and therapeutic disease, aiming at improving the quality of life in this category of patients (13).

The patient with autoimmune disease needs multidisciplinary care: medical and social care, psychological counseling and psychiatric consultation if needed, physiotherapy, kinetotherapy and occupational therapy, spiritual counseling (21). The concept of multidisciplinary care is supported by other authors. Constantin and his colleagues (2018) support team management of pediatric patients with systemic scleroderma. Collaboration between pediatricians, rheumatologists and dermatologists is designed to make care for systemic juvenile scleroderma more efficient (48). The reduced effectiveness of the medical treatment applied in scleroderma implies the need for optimization of the management by means of medical recovery measures according to the individual needs with a favorable effect on the quality of life and prophylactic on disability (49).

CONCLUSIONS

Autoimmune diseases have a considerable impact on the patient on all levels. Digital ulceration and Raynaud's phenomenon, fingers with flexion blockage present in systemic scleroderma, limits professional and household activities and, in the end, daily activities of care and nutrition, favors the installation of disability, which necessitates the support of another person in everyday life. Facies scleroderma, all physical limitations imposed by the disease affects the psychological structure of the patient and even the depression. Also, psoriasis and morphea, dermatomyositis and systemic lupus erythematosus can induce anxiety and depression. Multi-systemic damage to autoimmune diseases: cardio-pulmonary and renal, gastrointestinal and musculoskeletal decreases the quality of life in the presence of symptoms, especially in the presence of pain, increases the cost of health care, social assistance and psychological support.

In order to quantify the degree of organic damage and the limitations of the disease, numerous questionnaires for assessing the quality of life and determining disability scores have been developed. These are useful tools for identifying functional and psychological deficiencies to guide optimal interventions on target dysfunction.

The multiple pathogenic unknowns, incomplete etiology, make the autoimmune diseases and especially the systemic scleroderma, chronic diseases with a reduced life expectancy through various organic complications, which once installed evolve ineluctably. These considerations make it opportune to investigate the numerous facets of autoimmune diseases, detailed analysis of all aspects, to improve the quality of life and psychological comfort of patients.

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REFERENCES

1. Baglaenko Y, Chang NH, Johnson SR, Hafiz W, Manion K, Ferri D, Noamani B, Bonilla D, Rusta-Sellehy S, Lisnevskaia L, Silverman E, Bookman A, Landolt-Marticorena C, Wither J. 2018. The presence of anti-nuclear antibodies alone is associated with changes in B cell activation and T follicular helper cells similar to those in systemic autoimmune rheumatic disease. Arthritis Res Ther. 2018 Nov 29;20(1):264.
2. Andrese E, Vâţă D, Ciobanu D, Stătescu L, Solovăstru LG. 2015. The autoimmune constellation in lichen amyloidosis. Rev Med Chir Soc Med Nat Iasi. 2015 Oct-Dec;119(4):1045-50.
3. Jin F, Hu H, Xu M, Zhan S, Wang Y, Zhang H, Chen X. 2018. Serum microRNA Profiles Serve as Novel Biomarkers for Autoimmune Diseases. Front Immunol. 2018 Oct 16;9:2381.
4. Hudson M, Steele R, Lu Y, Thombs B, Baron M. Work disability in systemic sclerosis. J Rheumatol. 2009;36(11):2481–6.
5. Asano Y. 2016, Recent advances in animal models of systemic sclerosis, J Dermatol. 2016 Jan;43(1):19-28.
6. Sakkas LI, Simopoulou T, Daoussis D, Liossis SN, Potamianos S. 2018. Intestinal Involvement in Systemic Sclerosis: A Clinical Review. Dig Dis Sci. 2018 Apr;63(4):834-844.
7. Furst DE, Fernandes AW, Iorga SR, etal. Epidemiology of systemic sclerosis in a large US managed care population. J Rheumatol.2012; 39:784-786.
8. Li L, Cui Y, Chen S, Zhao Q, Fu T, Ji J, Li L, Gu Z. 2018. The impact of systemic sclerosis on health-related quality of life assessed by SF-36: A systematic review and meta-analysis. Int J Rheum Dis. 2018 Nov 14.
9. Singh MK, Clements PJ, Furst DE, Maranian P, Khanna D. 2012. Work productivity in scleroderma: analysis from the University of California, Los Angeles scleroderma quality of life study. Arthritis Care Res (Hoboken). 2012 Feb;64(2):176-83.
10. Cruz-Domínguez MP, Casarrubias-Ramírez M, Gasca-Martínez V, Maldonado García C, Carranza-Muleiro RA, Medina G, García-Collinot G, Montes-Cortes DH. 2017. The Systemic Sclerosis Questionnaire (SySQ): Validation of the translation of the original German version into Spanish and its relationship to the disease and to quality of life. Reumatol Clin. 2017 Dec 11. pii: S1699-258X(17)30239-5.
11. McMahan ZH, Frech T, Berrocal V, Lim D, Bruni C, Matucci-Cerinic M, Smith V, Melsens K, Proudman S, Zhang J, Mendoza F, Woods M, Khanna D. 2018. Longitudinal Assessment of Patient-reported Outcome Measures in

Systemic Sclerosis Patients with Gastroesophageal Reflux Disease - Scleroderma Clinical Trials Consortium. J Rheumatol. 2018 Nov 15. pii: jrheum.180004.
12. Kwakkenbos L, Sanchez TA, Turner KA, Mouthon L, Carrier ME, Hudson M, van den Ende CHM, Schouffoer AA, Welling JJKC, Sauvé M, Thombs BD and the SPIN Investigators. 2018. The association of sociodemographic and disease variables with hand function: a Scleroderma Patient-centered Intervention Network cohort study. Clin Exp Rheumatol. 2018 Jul-Aug;36 Suppl 113(4):88-94.
13. Greenfield J, Hudson M, Vinet E, Fortin PR, Bykerk V, Pineau CA, Wang M, Bernatsky S, Baron M; Canadian Scleroderma Research Group and Canadian Inflammatory Myopathy Study Group. 2017. A comparison of health-related quality of life (HRQoL) across four systemic autoimmune rheumatic diseases (SARDs). PLoS One. 2017 Dec 19;12(12):e0189840. doi: 10.1371/journal.pone. 0189840.
14. Johnson SR, Glaman DD, Schentag CT, Lee P. 2006. Quality of life and functional status in systemic sclerosis compared to other rheumatic diseases. J Rheumatol. 2006 Jun;33(6):1117-22.
15. Cengiz G, Erol K, Gok K, Ozgocmen S. 2018. Comparison of Pain Characteristics in Patients with Rheumatoid Arthritis and Systemic Sclerosis with Particular Reference to Neuropathic Pain Component: Cross-Sectional Study. Med Princ Pract. 2018 Sep 5.
16. Ardalan K, Zigler CK, Torok KS. 2017. Predictors of Longitudinal Quality of Life in Juvenile Localized Scleroderma. Arthritis Care Res (Hoboken). 2017 Jul;69(7):1082-1087.
17. Bali G, Kárpáti S, Sárdy M, Brodszky V, Hidvégi B, Rencz F. 2018. Association between quality of life and clinical characteristics in patients with morphea. Qual Life Res. 2018 Jun 19.
18. Preis E, Franz K, Siegert E, Makowka A, March C, Riemekasten G, Cereda E, Norman K. 2018. The impact of malnutrition on quality of life in patients with systemic sclerosis. Eur J Clin Nutr. 2018 Apr;72(4):504-510.
19. Morariu SH, Badea M, Capreanu P, Vartolomei M, Cotoi OS. 2013. Morfeea in placi ca manifestare a infectiei cu Borrelia burgdorferi. DermatoVenerol. (Buc.), 2013 Sept 58: 183-190.
20. Solovăstru L, Amălinei C. 2003. (Morphea associated with toxoplasmosis). Rev Med Chir Soc Med Nat Iasi. 2003 Jul-Sep;107(3):646-9.
21. Bretterklieber A, Painsi C, Avian A, Wutte N, Aberer E. 2014. Impaired quality of life in patients with systemic sclerosis compared to the general population and chronic dermatoses. BMC Res Notes. 2014 Sep 2;7:594.
22. Basta F, Margiotta DPE, Vadacca M, Vernuccio A, Mazzuca C, Picchianti Diamanti A, Afeltra A. 2018. Is fatigue a cause of work disability in systemic lupus erythematosus? Results from a systematic literature review. Eur Rev Med Pharmacol Sci. 2018 Jul;22(14):4589-4597.
23. Pisoni CN, Muñoz SA, Tamborenea MN, García M, Curti A, Cappuccio A, Rillo O, Imamura PM, Schneeberger E, Ballent M, Cousseau ML, Velasco Zamora J, Saurit V, Toloza S, Danielsen MC, Bellomio VI, Graf C, Paira S, Cavallasca J, Pons Estel B, Moreno JLC, Díaz M, Alba P, Verando M, Tate G, Mysler E, Sarano J, Civit EE, Risueño F, Álvarez Sepúlveda P, Larroude MS, Méndez MF, Conforti A, Sohn D. 2018. Work disability in Argentinian patients with systemic lupus erythematosus is prevalent and it is due to ethnic, socioeconomic and disease-related factors. Int J Rheum Dis. 2018 Apr 2.
24. Morrisroe K, Sudararajan V, Stevens W, Sahhar J, Zochling J, Roddy J, Proudman S, Nikpour M. 2018. Work productivity in systemic sclerosis, its economic burden and association with health-related quality of life. Rheumatology (Oxford). 2018 Jan 1;57(1):73-83.
25. Smirani R, Truchetet ME, Poursac N, Naveau A, Schaeverbeke T, Devillard R. 2018. Impact of systemic sclerosis oral manifestations on patients' health-related quality of life: A systematic review. J Oral Pathol Med. 2018 Oct;47(9):808-815.
26. Siegert E, March C, Otten L, Makowka A, Preis E, Buttgereit F, Riemekasten G, Müller-Werdan U, Norman K. 2018. Prevalence of sarcopenia in systemic sclerosis: assessing body composition and functional disability in patients with systemic sclerosis. Nutrition. 2018 Nov;55-56:51-55.
27. Stevens BE, Torok KS, Li SC, Hershey N, Curran M, Higgins GC, Moore KF, Egla Rabinovich C, Dodson S, Stevens AM; and the Childhood Arthritis and Rheumatology Research Alliance Registry Investigators. 2018. Clinical Characteristics and Factors Associated With Disability and Impaired Quality of Life in Children With Juvenile Systemic Sclerosis: Results From the Childhood Arthritis and Rheumatology Research Alliance Legacy Registry. Arthritis Care Res (Hoboken). 2018 Dec;70(12):1806-1813.
28. Okiyama N, Asano Y, Hamaguchi Y, Jinnin M, Motegi SI, Koizumi H, Hasegawa M, Ishikawa O, Sato S, Takehara K, Yamamoto T, Fujimoto M, Ihn H. 2018. Impact of a new simplified disability scoring system for adult patients with localized scleroderma. J Dermatol. 2018 Apr;45(4):431-435.
29. Landim SF, Bertolo MB, Marcatto de Abreu MF, Del Rio AP, Mazon CC, Marques-Neto JF, Poole JL, de Paiva Magalhães E. 2017. The evaluation of a home-based program for hands in patients with systemic sclerosis. J Hand Ther. 2017 Nov 29. pii: S0894-1130(17)30025-X.
30. Leite CC, Maia Â. 2013. Symptoms of disease and psychological adaptation in Brazilian scleroderma patients. Rev Bras Reumatol. 2013 Sep-Oct;53(5):405-11.
31. Mills SD, Kwakkenbos L, Carrier ME, Gholizadeh S, Fox RS, Jewett LR, Gottesman K, Roesch SC, Thombs BD, Malcarne VL and the Scleroderma Patient-centered Intervention Network Investigators. 2018. Validation of the Social Appearance Anxiety Scale in Patients With Systemic Sclerosis: A Scleroderma Patient-Centered Intervention Network Cohort Study. Arthritis Care Res (Hoboken). 2018 Oct;70(10):1557-1562.

32. Seravina OF, Lisitsyna TA, Starovoytova MN, Desinova OV, Kovalevskaya OB, Veltishchev DY. 2018. (Chronic stress and mental disorders in patients with systemic scleroderma: Results of an interdisciplinary study). Ter Arkh. 2017;89(5):26-32.
33. Nusbaum JS, Gordon JK, Steen VD. 2016. African American race associated with body image dissatisfaction among patients with systemic sclerosis. Clin Exp Rheumatol. 2016 Sep-Oct;34 Suppl 100(5):70-73.
34. Guillevin L, Hunsche E, Denton CP, Krieg T, Schwierin B, Rosenberg D, Matucci-Cerinic M; DUO Registry Group. 2013. Functional impairment of systemic scleroderma patients with digital ulcerations: results from the DUO Registry. Clin Exp Rheumatol. 2013 Mar-Apr;31(2 Suppl 76:71-80.
35. Giuggioli D, Manfredi A, Lumetti F, Colaci M, Ferri C. 2018. Scleroderma skin ulcers definition, classification and treatment strategies our experience and review of the literature. Autoimmun Rev. 2018 Feb;17(2):155-164.
36. Mitropoulos A, Gumber A, Crank H, Akil M, Klonizakis M. 2018. Investigating the effectiveness and feasibility of exercise on microvascular reactivity and quality of life in systemic sclerosis patients: study protocol for a feasibility study. Trials. 2018 Nov 21;19(1):647.
37. Gonzalez-Ericsson PI, Estrada MV, Al-Rohil R, Sanders ME. 2018. Post-irradiation morphoea of the breast: a case report and review of the literature. Histopathology. 2018 Jan;72(2):342-350.
38. Smith GP, Argobi Y. 2018. Pruritus in Autoimmune Connective Tissue Diseases. Dermatol Clin. 2018 Jul;36(3):267-275.
39. Bagnato G, Cordova F, Sciortino D, Miceli G, Bruno A, Ferrera A, Sangari D, Coppolino G, Muscatello MRA, Pandolfo G, Zoccali RA, Roberts WN. 2018. Association between cortisol levels and pain threshold in systemic sclerosis and major depression. Rheumatol Int. 2018 Mar;38(3):433-441.
40. Jaeger VK, Walker UA. Erectile Dysfunction in Systemic Sclerosis. Curr Rheumatol Rep. 2016 Aug;18(8):49.
41. Sampaio-Barros PD, Samara AM, Marques Neto JF. Gynaecologic history in systemic sclerosis. Clin Rheumatol. 2000;19(3):184-7.
42. Walker UA, Saketkoo LA, Distler O. 2018. Haematopoietic stem cell transplantation in systemic sclerosis. RMD Open. 2018 Jun 17;4(1):e000533.
43. Humbert M, Singh M, Furst DE, Khanna D, Seibold JR. 2017. Pulmonary hypertension related to systemic sclerosis: points to consider for clinical trials. Rheumatology (Oxford). 2017 Sep 1;56(suppl_5):v33-v37.
44. Morrisroe K, Stevens W, Proudman S, Nikpour M. 2017. A systematic review of the epidemiology, disease characteristics and management of systemic sclerosis in Australian adults. Int J Rheum Dis. 2017 Nov;20(11):1728-1750.
45. Almeida C, Almeida I, Vasconcelos C. 2015. Quality of life in systemic sclerosis. Autoimmun Rev. 2015 Dec;14(12):1087-96.
46. Mouthon L, Alami S, Boisard AS, Chaigne B, Hachulla E, Poiraudeau S. 2017. Patients' views and needs about systemic sclerosis and its management: a qualitative interview study. BMC Musculoskelet Disord. 2017 May 30;18(1): 230.
47. Sumpton D, Thakkar V, O'Neill S, Singh-Grewal D, Craig JC, Tong A. 2017. "It's Not Me, It's Not Really Me." Insights From Patients on Living With Systemic Sclerosis: An Interview Study. Arthritis Care Res (Hoboken). 2017 Nov;69(11):1733-1742.
48. Constantin T, Foeldvari I, Pain CE, Pálinkás A, Höger P, Moll M, Nemkova D, Weibel L, Laczkovszki M, Clements P, Torok KS. 2018. Development of minimum standards of care for juvenile localized scleroderma. Eur J Pediatr. 2018 Jul;177(7):961-977.
49. Maddali-Bongi S, Del Rosso A. 2016. Systemic sclerosis: rehabilitation as a tool to cope with disability. Clin Exp Rheumatol. 2016 Sep-Oct;34 Suppl 100(5):162-169.

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Validation of the Romanian version of the personality disorder test in the context of the alternative model of DSM-5

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ABSTRACT
DSM-5 with "DSM-5 Alternative Model for Personality Disorder Model" provides a new hybrid approach to the diagnostics of personality disorder, both dimensional and categorical, and proposes a model for conceptualization of personality disorders in which they are characterized by impairment of personality functioning and pathological personality traits. Personality inventory for DSM-5 (PID-5) is a self-report measure designed to assess the presence and severity of maladaptive personality traits. The long form of PID-5 consists of 220 self-assessment items used to measure 25 maladaptive personality facets, which are included in five broad domains of higher order. The adaptation and validation of the Romanian version of PID-5 for the Romanian population in the Republic of Moldova was carried out on a sample of 225 participants. The results have provided evidence that the Romanian version of PID-5 can be used to assess reliably and validly the maladaptive personality traits described in the alternative model of the DSM-5.

KEYWORDS:
DSM-5, Alternative Model DSM-5 for Personality Disorder, PID-5, Romanian version PID-5

INTRODUCTION

Each person has certain personality traits. Some of these may be so dysfunctional that it is difficult to justify a resolute diagnosis of personality disorder. Personality disorder is considered to be different from mental illness because it is more persistent during adulthood, while mental illness results from a morbid process of a certain type and has a more recognizable onset and evolution. There are two major systems for diagnosing personality disorders: ICD-10 Classification of Mental and Behavioral Disorders (World Health Organization, 1992), used in European countries and the Diagnostic and Statistical Manual of Mental Disorders DSM-IV (American Psychiatric Association, 2000), used in the USA. For over thirty years, the Manual of Diagnosis and Statistics of Mental Disorders (DSM) has used a firm and discreet model to characterize individual differences in phenotypic manifestations of personality disorders.

The new Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5) included many and important changes in the category of personality disorders. The assessment and diagnosis of personality disorders and personality in general are formulated here. It is desired to change the clinician's focus from an overall assessment and general typology of personality disorders to a detailed look at the personality traits. Thus, the "Alternative DSM-5 Model for Personality Disorders" chapter provides (1):

- a new approach to personality disorders, namely, according to the DSM-5 alternative model, "personality disorders are characterized by impairment of personality functioning and pathological personality traits."
- a new concept that presents itself by appreciating the level of personality functioning through a quantitative scale (Levels of Personality Functioning Scale-Self Report), from lack of impairment (normal functionality, level 0) to extreme impairment (level 4) which assesses the level of personality functioning on two dimensions: self (identity and self-direction) and interpersonal (empathy and intimacy);
- a complex way of describing and evaluating the pathological personality traits that are organized in five broad domains: Negative Affect, Detachment, Antagonism, Disinhibition and Psychoticism. Within these five broad domains of features, there are 25 facets of traits (specificity of second order). These five high personality domains comprise four or more facets of second-order facets. Examples of facets of the Disinhibition domain are: Impulsivity, Distractibility, Risk Taking, Irresponsibility, and Rigid Perfectionism (the absence of this facet denotes a low level of Disinhibition).
- only six types of specific personality disorders: Antisocial, Avoidant, Borderline, Narcissistic, Obsessive-compulsive, and Schizotypal. Each personality disorder is defined by typical disturbances in personality functioning(2).

In this context, the DSM-5 provided an alternative model for diagnosing personality disorders, where assessment of personality functioning and pathological personality traits are central diagnostic criteria. It includes an experience-based support that sustains the three-dimensional model of a personality disorder (3, 4), which is assessed through the Personality Inventory for DSM-5 (PID-5). It. The proposed questionnaire provides for the personality traits to be evaluated in 5 broad domains, each including four or more recognized facets of the 25 facets of the traits. With this dimensional approach, the new classification system gives clinicians and researchers the opportunity to describe the patient in more detail than was possible. Full and in-depth revision of PID-5 can be found in June 2013 (2, 4).

The Personality Inventory for DSM-5 is a self-assessment, designed to evaluate 25 facets of personality traits. These facets were designed to be used in combination with other diagnostic criteria to diagnose personality disorder (PD) and are presented in Section III of the 5th Edition of the Diagnostic and Statistical Manual of Mental Disorders DSM-5; American Psychiatric Association, 2013), describing a new hybrid approach to PD diagnosis, both dimensional and categorical (4, 5, 6, 7). Thus, the fifth edition of the DSM is a reference point in the history of official

classification systems of PD, as it is the first DSM to present an empirical model based on maladaptive personality traits. The traits of the patients with personality disorders were discussed by the DSM-5 working group in the chapter "Personality Disorders" and then operationalized and refined in an empirical project underlying the construction of the Personality Inventory for DSM-5 (PID-5) (8).

As such, PID-5 characterizes the personality according to five superior domains of personality trait, focusing on maladaptive traits in these areas: Negative Affect, Detachment, Antagonism, Disinhibition, and Psychoticism. Indeed, a large number of scientific papers sustains the validity of the pathological personality traits represented in PID-5 (3, 5, 7, 8, 9, 10, 11, 12).

Despite numerous studies using this inventory (13, 14, 15, 16), more than 30 papers in 3 years following the publication of the DSM-5 (17), none of them has used a Romanian version. Therefore, the main objective of this paper is to present the stages of Romanian translation of the Personality Inventory for DSM -5 in its complete form with 220 questions (PID-5) (4, 8).

The present paper aims at introducing into the Romanian scientific circuit an assessment tool of PD in compliance with the International Test Commission's translation, adaptation and validation rules and with the consent of the authors, this tool being applied on a sample of 225 participants, considering the need for such an instrument, adapted to the Romanian population in the Republic of Moldova.

PERSONALITY INVENTORY FOR DSM-5 (PID-5). STRUCTURE AND CONTENT.

The Personality Inventory for DSM-5 is a questionnaire containing 220 items of self-rated personality trait assessment, used to measure the maladaptive personality traits, characterized in DSM-5. Responses are selected on a four-point scale, from 0 ("Very False or False") to 3 ("Very True or Often True").

Thus, the PID-5 offers scores on a 4-point scale for 25 facets of personality traits. Each facet includes 4 to 14 items. These facets correspond to the maladaptive personality traits and are included in the five domains of higher rank described in Section III of DSM-5: Negative Affect, Detachment, Antagonism, Disinhibition, and Psychoticism. Score 2 and greater is a quantitative index of one of the 6 types of PD: Antisocial, Borderline, Schizotypal, Avoidant, Obsessive-compulsive, and Narcissistic.

PROCEDURE

Translation and cultural adaptation of PID-5

The protocol adopted for the translation and cultural adaptation of PID-5 followed, relatively faithfully, the protocol described by Knudsen (18), Hambleton (19, 20, 21), Geisinger (22) and Beaton (23).

Deviations from the original protocol will be discussed below.

1. Translation of the inventory from the source language (English) into the target language (Romanian).
2. Discussionof the translation inside a small research group. First revision of the data; compilationof the list of problematic/disputed items.
3. Retroversion.
4. Comparisonof the retroversion with the original version. Second revision of the data; revision of the list of problematic items.
5. Setting up a group of experts. Discussion of the list of problematic items within the expert group.
6. Discussionof the results of the group of experts in the initial research group. The last (third) revision and confirmation of the final version.
7. Assessment of the internal validity of the final version (Cronbach coefficient).
8. Verification of the psychometric qualities (stability and validity) of the Romanian version of the inventory.

Steps 1-8 will be briefly presented below, and the 8th step will be the subject of a separate article in the future.

Translation of the inventory. The first version of the translation

The translation of inventory from the source language into the target language was done, taking into account the criterion of the degree of conceptual overlap between the source

culture and the target culture. Conceptual overlap is given by the extent to which a concept has the same meaning in both languages.
According to the four-level differentiation developed by Sartorius and Kuyken (24), the translation of the inventory was carried out in the context of the pragmatic approach, which involves a considerable conceptual overlap between the source culture and the target culture. There is a significant conceptual overlap of patient assessments, mental health servicesand costs in the European space; therefore, the pragmatic approach was considered to be the most appropriate for the creation of the Romanian version of the inventory. The aim of the translation is to maintain, as much as possible, the semantic and linguistic equivalence, as well as the conceptual and technical equivalence between the English and Romanian versions of the inventory (18, 23, 25).
The translation of the inventory into Romanian was done by two English-certified translators (Romanian native speakers), experienced in the field of mental health care and treatment (psychologist with formation in assessment and psychodiagnosis, respectively, psychiatrist , both with psychotherapy training), as well as in the use of English in specialist practice (clinical context - patient interview - English language training programs, creation and editing of English materials (research papers, funding projects).

Discussion group. Revision of the first translation
The next step, the two versions were confronted, and the differences were discussed and a first version in Romanian was finalized. Following the original protocol, the first version of translation was discussed in a small research group made up of the two translators, plus other specialists in mental health (medical psychologist, neurologist, neurophysiologist), experienced in translating from English. The discussions led to the first revision of the material and to the compilation of a list of problematic/disputed items.
The issues on which the discussions focused were related both to the content and applicability of the content of the items in the Romanian socio-cultural context, as well as to the linguistic formulations (26).

Performing the retroversion
Retroversion is a verifying process to ensure that the translated version reflects the same content item as the original version. However, the accordance between the retroversion and the original version does not guarantee a satisfactory translation, it simply ensures a consistent translation (23).
Retroversion was carried out by a licensed professional translator who retranslated the Romanian version back to English, then the authors checked, if there were differences of interpretation and discrepancies between the two variants. Subsequent changes were made with the agreement of both parties. Comparison of the retroversion with the original version led to the second revision of the material and the list of problematic items. Retroversion is just a type of validation, which highlights gross expressions or conceptual errors in translation.

Expert group
The next step was to form the expert group whose role is to deal with all versions of the inventory in order to reach a consensus on any discrepancy. Decisions taken by this committee will allow for equivalence between source and target version (23, 27).
During the sessions the final list of problematic items was discussed. The results of the expert group led to the last (third) revision and the final version of the inventory (see Annex). In order to achieve the purpose of the study, we decided to keep the structure of the inventory faithfully, but we also took into consideration the suggestions of all members regarding the formulation or reformulation of some expressions on an understandable level.

Validity testing
To determine the reliability indicators of the inventory, the internal consistency of the inventory was analyzed. For this purpose, we have calculated the Cronbach’s alpha coefficient of the internal consistency which measures the extent to which the test items are intercorrelated. For a proper correlation of

items, a value of at least 0.7 is needed (27). Table I shows the results of internal consistency for the Romanian version of PID-5. Following these results, namely - 0.972 in men and 0.969 in women - we can conclude that the test is reliable. Cronbach's alpha coefficient is dependent on the number of inventory items, and in this case we have a very high coefficient.

	Cronbach's alpha	**No of items**
Men	0.972	
Women	0.969	
		220

Table I. Cronbach's alpha for PID-5

Subjects

The study implied the use of the PID-5 inventory by 300 subjects. Out of 300 applied questionnaires, only 225 sets of answers (N = 225) were completed and used in later analysis (validity analysis). The final group included 225 volunteers, while the retest, after 2 weeks, was taken by 178 people.

The demographic data of participants in validation study of the PID-5 in Romanian are included in Table II.

	Test				**Retest**			
	N	Min	Max	Mean ± SD	N	Min	Max	Mean ± SD
Women	166	18	56	22,61±0,55	130	18	48	22,39±0,62
Men	59	18	52	22,34±0,92	48	18	52	22,57±1,02
Total	225				178			

Table II. Demographics of the participants in the study

The test-retest correlation indicates the extent to which a participant can obtain similar results at different times of measurement. We tested the same people again and calculated the correlation of the coefficients in the two measurements. The longer the time goes, the correlation is weaker. This phenomenon happens not only because the tool is not a stable one, but mostly because behavior can also change over time.

ASSESSMENT OF THE PSYCHOMETRIC QUALITIES OF THE ROMANIAN VERSION OF THE INVENTORY.

The participants completed the questionnaire individually without time limit. For the stability check, after a 2-week interval, the questionnaire was used again to determine the stability of the results over time. After comparing the responses to the 220 items, we obtained the following results: 10 subjects, representing 5.6% of the total number of participants, responded identically to all 220 items, 29 subjects (16.3%) presented only one difference in answers in the test / retest, 56 subjects (31.5%) - 2 differences, and 28 subjects (15.7%) had not the same in answer to 3 items. Overall, 68% of subjects had from 0 to 8 differences in the answers to the 220 elements, and from 18 to 166 different answers to the same item were registered in one subject (0.6%) or two subjects (1.1%).

In the next stage, each item was analyzed, namely, how many people had the same answer in the test / retest and if it has changed, then by how many points. We present two examples, item 93 (Table III) with the highest difference in answers in the test / retest, and item 153 (Table IV) with the lowest incoherence. Thus, it was possible to highlight the most problematic items that were to be reviewed in the last edition.

Element No. 93		***N of subjects***	***%***
Answer to the item	Same	154	86,5
	Changed by1 point	14	7,9
	Changed by2 points	10	5,6
	Total	178	100,0

Table III. Examples of item with the highest deviation in the test / retest.

ORIGINAL

I often worry that something bad will happen due to mistakes I made in the past.

Item description

Deseori îmi fac griji că ceva rău se va întâmpla din cauza greşelilor făcute în trecut.

I often worry that something bad will happen because of mistakes made in the past.

Accepted after last editing
Deseori îmi fac griji că s-ar putea întâmpla ceva rău din cauza greșelilor făcute în trecut.
I often worry that something bad could happen because of mistakes made in the past

Element No. 153		***N of subjects.***	***%***
Answer to the item	Same	173	97,2
	Changed by 1 point	1	0,6
	Changed by 2 points	4	2,2
	Total	178	100,0

Table IV. Examples of item with the lowest deviation in the test / retest

ORIGINAL
I don't care if my actions hurt others.

Item description
Nu-mi pasă dacă acţiunile mele rănesc pe alţii.
I do not care if my actions hurt others.

Accepted after last editing
Mie nu-mi pasă dacă acţiunile mele îi rănesc pe alţii.
I do not care if my actions hurt others.
Even in items with multiple differences in answers no radical changes were made, the translation being exact (Table III, IV). These deviations may be explained by the subjects' tendency to respond according to the mood at the moment; and we have noticed that a large number of people who committed differences in their answers were at the level of social introversion or hypochondria.

CONCLUSIONS

Thus, we have followed PID-5 validation steps: translation, adaptation, retroversion, validity.
The result of the described work is the Romanian version of the PID-5 inventory. We can say, it is the first Romanian tool, adapted for the population of the Republic of Moldova, which proposes a methodical evaluation of people with a mental health problem. Performing the translation, with the assurance of conceptual overlapping, is the first step in testing stability of this tool by the test-retest method and in calculating the Cronbach's coefficient of internal consistency (inercorrelations between items).
This translation provides sufficient consistency and validity for use in future studies. These empirically valuable results sustain the trustworthiness of the translated tool to assess individual differences and personality traits. The results also require further studies in more representative groups, focusing on clinical caseswith personality disorders.

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REFERENCES

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (DSM–5). https://www.psychiatry.org/psychiatrists/practice/dsm
2. Alternative DSM-5 Model for Personality Disorders https://doi.org/10.1176/appi.books.9780890425596.AlternatePersonalityDisorders
3. Anderson, J., Snider, S., Sellbom, M., Krueger, R., Hopwood, C.: A comparison of the DSM-5 Section II and Section III personality disorder structures. Psychiatry Res 2014; 216: 363–372
4. Markon, K. E., Quilty, L. C., Bagby, R. M., Krueger, R. F.: The development and psychometric properties of an informant-report form of the Personality Inventory for DSM-5 (PID-5). Assessment 2013; 20: 370–383
5. Hopwood, C. J., Wright, A. G., Krueger, R. F., ș. A.: DSM-5 pathological personality traits and the Personality Assessment Inventory. Assessment 2013; 20: 269–285
6. Krueger, R. F., Derringer, J., Markon, K. E., Watson, D., Skodol, A. E.: Initial construction of a maladaptive personality trait model and inventory for DSM-5. Psychol Med. 2012; 42: 1879–1890
7. Thomas, K. M., Yalch, M. M., Krueger, R. F., Wright, A. G., Markon, K. E., Hopwood, C. J.: The convergent structure of DSM-5 personality trait facets and five-factor model trait domains. Assessment 2013; 20: 308–311

8. Krueger, R. F., Markon, K. E.: The role of the DSM-5 personality trait model in moving toward a quantitative and empirically based approach to classifying personality and psychopathology. Annu Rev Clin Psychol. 2014; 10: 477-501
9. De Fruyt, F., de Clercq, B., de Bolle, M., Wille, B., Markon, K., Krueger, R. F.: General and maladaptive traits in a five-factor framework for DSM-5 in a university student sample. Assessment 2013; 20: 295–307
10. Few, L. R., Miller, J. D., Morse, J. Q., s.a.: Examining the reliability and validity of clinician ratings on the Five-Factor Model Score Sheet. Assessment 2010; 17: 440–453
11. Quilty, L.C., Ayearst, L., Chmielewski, M., Pollock, B. G., Bagby, R. M.: The psychometric properties of the Personality Inventory for DSM-5 in an APA DSM-5 field trial sample. Assessment 2013; 20: 362–369
12. Suzuki, T., Griffin, S. A, Samuel, D. B.: Capturing the DSM-5 alternative personality disorder model traits in the five-factor model's nomological net. J Pers. 2017; 85 (2): 220-231
13. Aluja, A., García, L. F., Cuevas, L., Lucas, I.: Dimensional Pathological Personality Predicting Personality Disorders: Comparison of the DAPP-BQ and PID-5 Shortened Versions in a Spanish Community Sample. J Psychopathol Behav Assess 2018; 40: 1-14
14. Combaluzier, S., Gouvernet, B., Menant, F., Rezrazi, A.: Validation of a French translation of Krueger's personality inventory for DSM-5 in its brief form (PID-5 BF). Encephale 2018; 44(1): 9-13
15. Pires, R., Sousa Ferreira, A., Guedes, D.: The psychometric properties of the Portuguese version of the Personality Inventory for DSM-5. Scand J Psychol. 2017; 58 (5): 468-475
16. Thimm, J. C., Jordan, S., Bach, B.: Hierarchical Structure and Cross-Cultural Measurement Invariance of the Norwegian Version of the Personality Inventory for DSM-5. J Pers Assess 2017; 99 (2): 204-210
17. Al-Dajani, N., Gralnick, T. M., Bagby, R. M.: A psychometric review of the personality inventory for DSM-5 (PID-5): current status and future directions. J Pers Assess 2016; 98(1): 62-81
18. Knudsen, H. C., Vazquez-Barquero, J. L., Welcher, B., ș. a.: Translation and cross-cultural adaptation of outcome measurements for schizophrenia. EPSILON Study 2. European Psychiatric Services: Inputs Linked to Outcome Domains and Needs. Br J Psychiatry Suppl. 2000; 39: 8-14
19. Hambleton, R. K., Patsula, L.: Adapting tests for use in multiple languages and cultures. Social Indicators Research 1998; 45: 153-171
20. Hambleton, R. K.: Guidelines for adapting educational and psychological tests: a progress report. European Journal of Psychological Assessment 1994; 10: 229-244
21. Hambleton, R. K.: The next generation of the ITC test translation and adaptation guidelines. European Journal of Psychological Assessment 2001; 17 (3): 164-172
22. Geisinger, K. F.: Cross-cultural normative assessment: translation and adaptation issues influencing the normative interpretation of assessment instruments. Psychological Assessment 1994; 6: 304-312
23. Beaton, D. E., Bombardier, C., Guillemin, F., Ferraz, M. B.: Guidelines for the process of cross-cultural adaptation of self-report measures. Spine 2000, 25 (24): 3186–3191
24. Sartorius, N., Kuyken, W.: Translation of Health Status Instruments, In: Orley, J., Kuyken, W., editors. Quality of Life Assessment: International Perspectives. Berlin, Springer-Verlag Berlin Heidelberg, 1994, 3-18
25. Lupu, I. R., Opre, A. N., Lupu, V.: Validarea versiunii în limba română a South Oaks Gambling Scale Revisited for Adolescents – scala pentru jocurile de noroc south oaks –revizuită pentru adolescenţi (SOGS-RA). Revista de Neurologie şi Psihiatrie a Copilului şi Adolescentului din România 2015; 21 (2): 19-27
26. Casian, D., Gutsu, E., Culiuc, V.: Validation of the Romanian translated ABC-V (Assessment of Burden in Chronic - Venous Disease) questionnaire. Chirurgia 2013; 108 (3): 381-384
27. Mihai, C., Bojincă, M., Chircu, J., ș.a.: O variantă românească a Chestionarului de evaluare a stării de sănătate adaptat pentru pacienţii cu sclerodermie sistemică (shaq). Revista română de reumatologie 2011; 20 (3): 156-163

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Depression and anxiety manifestations in Irritable Bowel Syndrome

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ABSTRACT
Irritable Bowel Syndrome is a gastrointestinal disorder characterized by abdominal pain and which is accompanied by altered bowel habits. Just like with other functional medical disorders, there is no current identifiable physical, neurological or metabolic cause for IBS. IBS has a very increased prevalence rate all over the world, with an approximately 6 to 15% incidence in Canada and USA. In addition, besides the specific gastro-intestinal manifestations described in the Rome IV criteria, lately there is also an increased interest in the psychological and psychiatric comorbidities from the complex and multifactorial Irritable Bowel Syndrome pathophysiology. Thus, in the present mini-report we will focus our attention on the anxiety and depression-related manifestations of the Irritable Bowel Syndrome in both humans and animal models studies.

KEYWORDS:
Irritable Bowel Syndrome, depression, anxiety

INTRODUCTION
Irritable Bowel Syndrome (IBS) is a gastrointestinal disorder characterized by abdominal pain that is accompanied by altered bowel habits. Just like with other functional medical disorders, there is no identifiable physical, neurological or metabolic cause for IBS(1). IBS has a prevalence rate of approximately 6-15% in Canada and USA (2,3). In addition, besides the specific gastro-intestinal manifestations described in the Rome IV criteria, lately there is also an increased interest in the psychological and psychiatric comorbidities from the complex and multifactorial Irritable Bowel Syndrome pathophysiology. Thus, in the present mini-report we will focus our attention on the anxiety and depression-related manifestations of the Irritable Bowel Syndrome in both humans and animal models studies.

PSYCHIATRIC COMORBIDITIES IN IRRITABLE BOWEL SYNDROME

As mentioned above, it is already suggested that patients with Irritable Bowel Syndrome are exhibiting comorbidities such as anxiety-related psychopathology.

Thus, in order to observe the role anxiety plays in the maintenance and the exacerbation of IBS, the links between IBS and body vigilance and discomfort intolerance were previously examined by various research groups, in relation to the depressive symptoms or focusing entirety of anxiety itself.

In this way, up to 50 to 90 % of the individuals with IBS meet the criteria for a psychiatric disorder (4), with depression and anxiety disorders being the most common conditions (1).

In addition, patients diagnosed with IBS reported increased levels of worry, distress, neuroticism and somatization (2,5,6). Also, these patients are more likely to report that their anxiety symptomatology preceded the development of IBS (7). In this way, these findings are validating the significance of anxiety symptoms in the IBS pathophysiology.It has also been suggested that anxiety disorders and IBS could actually share common etiological factors (8). In this way, existing data are pointing out that patients with IBS are exhibiting anxiety and a variety of related psychological risk factors. To offer an example, it was previously reported that patients with IBS are showing elevations in anxiety sensitivity (5).

Thus, anxiety sensitivity and all things regarding anxiety symptoms and automatic arousal are a well-established psychological risk factor that predicts the development of panic attacks and anxiety disorders (e.g. when we talk about the body vigilance, we refer to the extent to which individuals monitor the internal body sensations) (9, 10). In addition, it was previously shown that patients with panic disorder reported increased vigilance to bodily sensations in the attempt to identify any potential signals of an impending panic attack (11, 12)

Also, new data are showing that the individual's tendency to selectively attend physical sensations mediates the commonly noted relationship between negative affectivity and increased reporting of physical symptoms (11).

Moreover, individuals that have panic disorder reported elevated vigilance to bodily sensations in an attempt to identify any potential signals of an impending panic attack, as previously described (12).

Thus, in a very similar way with patients having panic disorder, individuals with IBS may be more likely to scan their bodies for potential internal indicators of an impending IBS episode.

Even more, for the individuals with IBS, the hypervigilence to internal cues may appear to be proactive to prepare oneself to manage an IBS episode, but selectively attending to these physical symptoms that could actually result in an exacerbation of symptoms. For example, among those with panic disorders, heightened vigilance to internal sensations is associated with increased reactivity to those sensations and increased anxiety-like symptomatology (12).

In this way, hypervigilence to internal sensations could result in a similar positive feedback loop in IBS by making the individual more aware to the symptoms and more fearful of the symptoms (e.g. exacerbating the symptoms instead).

This also seems to be a secondary anxiety-related construct that might play an integral role in IBS. Discomfort intolerance consists in the experience of both physically painful and uncomfortable sensations that represents a broader concept, as compared to pain tolerance alone (13). Keeping in mind that, we can conclude that discomfort intolerance is characterized by the inability to tolerate and desire to avoid physically uncomfortable sensations.

Also, as above mentioned, anxiety sensitivity was linked with other anxiety relevant risk factors, including body vigilance and discomfort intolerance (13). Also, recent studies showed that women had significantly higher scores on anxiety levels, as compared to males (14).

It was also previously showed that both anxiety and depression were elevated in subjects who reported abdominal pain vs. those who did not (14).

In addition, anxiety and depression scores seem to correlate positively with pain perception. Thus, subjects with abnormal anxiety and depression scores had higher abdominal pain.

As discussed, the relationship between elevated anxiety and depression levels vs. abdominal pain was reported to be more prominent in women. In addition, it has been observed that defecatory symptoms were significantly associated with anxiety and depression scores (14). It was also showed by Aro and coworkers on a gastroscopy– based population study that anxiety was associated with uninvestigated dyspepsia, functional dyspepsia, suggesting that there is a causal link between the mechanistic of the upper gastrointestinal symptoms and anxiety.

There is also a current interest in the association between subjects having abdominal pain and elevated anxiety and depression levels It has been for example demonstrated that anxiety and depression independently predicted pain reporting, with women having a higher lifetime rate of anxiety disorders, as compared to men (e.g. approximately 30% as compared to 19%, respectively). This could be also related to the fact that women have also a higher prevalence for IBS and somatoforms symptoms (14). Also, as previously described there were consistent correlations between more defecatory symptoms and higher ratings in anxiety and depression-related state.

ANIMAL MODELS STUDIES

We can also describe shortly that our group has also some previous work on this matter, with aforementioned reports stating anxiety and depression (as studied in various behavioural specific tasks such as elevated plus maze task and forced swimming test) in an IBS rat models based on very mild stressful situations such as isolation mild stress, contention mild stress, or using such mild stressors for a short amount of time in 6 consecutive days (15,16).

CONCLUSIONS

It seems that anxiety and depression are linked to functional abdominal pain at patients with IBS, this being also the case some healthy people with mild similar symptoms as those described above.

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REFERENCES

1. North C. S., Hong, B. A., Alpers, D. H.2007. Relationship of functional gastrointestinal disorders and psychiatric disorders: Implications for treatment. World Journal Gastroenterology, 13, 2020 – 2027.

2. Hazlett – Stvens H., Craske M. G., Mayer E. A., Chang, L., Naliboff, B. D.2003. Prevalence of Irritable Bowel Syndrome among university students. The roles of worry, neuroticism, anxiety sensitivity and visceral anxiety. Journal of Psyhosomatic Research, 55, 501, 505.

3. Norton, G. R., Norton, P. J., Asmundson, G. J., Thompson, L. A., & Larsen, D. K. 1999. Neurotic butterflies in my stomach: The role of anxiety, anxiety sensitivity and depression in functional gastrointestinal disorders. Journal of Psychosomatic Research, 47, 233 – 240.

4. Lydiard, R. B. 2001. Irritable Bowel Syndrome, anxiety and depression: What are the links? Journal of Clinical Psychiatry, 62, 38 – 47.

5. Gros, D. F., Antony, M. M., McCabe, R. E., Swinson, R. P. 2009. Frequency and severity of the symptoms of Irritable Bowel Syndrome across the anxiety disorders and depression. Journal of Anxiety Disorders, 23, 290 – 296.

6. Koloski, N. A., Talley, N. J., Boyce, P. M. 2003. Does psychological distress modulate functional gastrointestinal symptoms and health care seeking? A prospective community cohort study. American Journal of Gastroenterology, 98, 789 – 797.

7. Sykes M. A., Blanchard E. B., Lackner J., Keefer L., & Krasner S.2003. Psychopatology in Irritable Bowel Syndrome: Support for a psychophysiological model.

8. Goddard, E.R., Barth, K.S., Lydiard, R.B.2007. Disorders which frequently overlap with Irritable Bowel Syndrome:

Can a shared neurobiology can explain a frequent association ? Primary Psychiatry,14,69-73
9. Hayward C., Killen, J. D. Kraemer, H. C. Taylor, C. B.2000. Predictors in panic attacks in adolescents. Journal of the American Academy of Child and Adolescent Psychiatry, 39, 207 -214.
10. Schmidt N. B., Zvolensky M. J., Maner J. K.2006. Anxiety sensitivity: Prospective perspective on panic attacks and axis I pathology. Journal of Psychiatric Research, 40, 691 – 699.Journal of Behavioral Medicine, 26, 361 – 372.
11. Kolk H., S. Gijsbers van Wijk 2003. A symptom perception aproach to common physical symptoms. Social Science Medicine, 57, 2343 – 2354.
12. Schmidt, N. B., Lerew, D. R., Trakowski, J. H.1997. Body vigilance in panic disorder: Evaluating attention to bodily perturbations. Journal of Consulting and Clinical Psychology, 65, 214 – 220.
13. Schmidt, N. B., Richey, J. A., Fitzpatrick, K. K. 2006. Discomfort intolerance: Development of a construct of measure relevant to panic disorder. Journal of Anxiety Disorders, 20, 263 – 280.
14.R.O. Cojocariu, A. Ciobica, D. Timofte, The current state of knowledge on the link between the human microbiome and some neuropsychiatric disorders, Bulletin of Integrative Psychiatry, 2018, 2, 27-38.
15. R. Lefter, A. Ciobica, S. Guenne, M. Compaore, M. Kiendrebeogo, C. Stanciu, A. Trifan. A Complex Behavioral Characterisation of a Rat Model of Irritable Bowel Syndrome generated by Chronic Stress Contention, Neurophysiology, 2018, 50(4), 266-277.
16. R. Lefter, A. Ciobica, D. Timofte et al. A new biological approach in generating an irritable bowel syndrome rat model -focusing on depression in sucrose splash test and body weight change, Romanian Biotechnological Letters.2019.DOI: 10.26327/RBL2018.208.

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Absinthe and *Período Azul* in Pablo Picasso

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ABSTRACT
Creative genius, Pablo Ruiz y Picasso was the most brilliant artistic personality of the 20th century. Lesser-known, like other great painters, Picasso was an absinthe consumer, alcoholic liquor that inspired his creation.

Keywords:
Absinthism syndrome, Pablo Picasso, melancholy, chromatopsia, cyanopsia

Figure 1. Pablo Picasso (1881-1973), Revista Vea y Lea, Argentina (1962) (public domain)

Pablo Ruiz y Picasso (1881-1973) (Figure 1) was, without a doubt, the most brilliant artistic personality of the 20th century. Andalusian and Catalonian, Spanish and French, Picasso was a painter of genius who experienced with all the artistic movements of the 20th century, i.e. surrealism, expressionism and neoclassicism, to become one of the undisputed masters of modern art.

Lesser-known, however, is that, like other great painters such as Vincent van Gogh, Edgar Degas, Paul Gauguin or Édouard

Manet, Picasso was also an absinthe consumer, an liquor that inspired his creation.

ABSINTHE IN THE 19TH CENTURY FRANCE

Pablo Picasso lived in France for most of his life, a country in which absinthe had been popular liquor since the 1840s, especially among the French military personnel. In the beginning, this liquor was mostly used to prevent malaria. Originally formulated in Switzerland, absinthe quickly rose to popularity in the neighbouring country as well, France, towards the end of the 19th century. Thus, from 1875 until 1913, the consumption of this liquor increased fifteen-fold (1).

Also called the *green fairy*, absinthe was initially fervently consumed among the rich. It then became known and used by the poorer social classes as well, including the painters. It thus became an icon of la vie de bohème and, in many bars and cafes in Paris, l'heure verte (the green [cocktail] hour) was a daily event (2).

Although this spirit was forbidden at the beginning of the 20th century even in Picasso's country of origin, Spain, he was careful to procure it in his frequent travels between Barcelona and Paris. Picasso was not an excessive drinker; he consumed absinthe occasionally, without destroying his health like van Gogh, who was an avid drinker of absinthe (3).

PICASSO'S BLUE PERIOD

The great Picasso is also known for his *Blue Period* (Spanish: *Período Azul*), the period from 1901 to 1904 in which he painted his monochromatic paintings in shades of blue, dark blue and blue-green and only occasionally warmed up by other colours. This *Blue Period* in Picasso's creation expresses loneliness, suffering and poverty, reflecting a melancholy mood or even a possible transient cyanopsia-type dyschromatopsia (chromatopsia). As an alcohol and absinthe drinker (4, 5), Picasso might have suffered a possible cyanopsia secondary to an acute toxic optic neuropathy due to the consumption of absinthe and other alcoholic liquors.

Although Picasso encountered difficulties in selling his blue paintings at that time, nowadays they became some of his most popular works of art. The themes of his paintings in this period were drunkards, beggars or prostitutes. Moreover, Picasso was prompted to choose cold shades of blue by the suicide of his close friend Carlos Casagemas in 1901. He himself said that "I started painting in blue when I learned of Casagemas's death" (6).

Picasso's pleasure for this liquor was also illustrated in at least six of his paintings, which he entitled*: The Absinthe Drinker* (1901 and 1902) (Figure 2), *The Absinthe* (1921), *The Absinthe Lover* (1901), *Drunk Woman is Tired* (1902) or *Woman Drinking Absinthe* (1901) (7). Picasso later became interested in absinthe as a theme, therefore, his paintings *Glass of Absinthe* (1911) and *Bottle of Pernod* (1912) were followed by the bronze sculpture *The Absinthe Glass* (1914) (8).

ABSINTHE

The absinthe-based spirit was traditionally made of dried wormwood (*Artemisia absinthium*), anise and fennel, stored overnight in 85% ethanol. The next day, the preparation was boiled and distilled, completed by adding Roman wormwood (*Artemisia pontica*) extract, lemon balm and hyssop. It was then filtered and a green liqueur of 74% alcohol (2) was obtained. The main ingredient, *Artemisia absinthium*, containing the toxic monoterpene thujone (9), contributed to its flavour, fragrance, unique taste, and not least to its toxicity (10).

Figure 2. Pablo Picasso, La buveuse assoupie (The Absinthe drinker) (1902), Kunstmuseum Bern (public domain)

The first medical studies on the side effects of absinthe were published around 1870. They concluded that absinthe abuse could cause convulsions, respiratory or kidney disorders (11). Later studies showed that a long abuse of absinthe could produce *absinthism syndrome*, characterized by auditory and visual hallucinations, tremors, paralyses (8, 11, 12) as well as metabolic effects such as hypernatremia, hypokalemia, rhandomyolysis with acute renal failure and hypobicarbinaemia (8). The visual or auditory hallucinations were explained by researchers by the fact that the toxin thujone blocks brain receptors for gamma-aminobutyric acid (GABA), a natural inhibitor for nerve impulses, and when GABA is blocked, neurons fire too easily and brain signals go out of control (13). Moreover, these visual hallucinations were described as being terrifying and vivid (11, 12).

Within the absinthism syndrome, optic neuritis, amblyopia and even xanthopsia-type chromatopsia were reported as ophthalmic pathologies (14, 15). The toxic effects were caused by the alcohol in the drink, by the thujone ketone in *Artemisia absinthium* and especially by the combination of these two substances (2).

ABSINTHE AND TOXICITY

α-Thujone is thought to be the principal active ingredient of wormwood oil and toxic principle in absinthe. α-Thujone is neurotoxic in rats, and ingestion of wormwood oil containing α-thujone recently resulted in human poisoning.

A study conducted in by Hold *et al.* concluded that α-thujone modulates the GABA A receptor. They compared α-Thujone with picrotoxinin, a classic GABA A receptor antagonist, and the result was that they had similar poisoning signs. Also, in both cases, the toxicity could be trated with diazepam, phenobarbital and ethanol (16).

Wormwood oil and absinthe also contain other toxic components, such as β-thujone and ethanol. The two main toxicants in mouse neurotoxicity are α-thujone and its 7-hydroxy metabolite .7-hydroxy can be found in the brain at higher doses than α-thujone, suggesting that a in situ conversion might occur, meaning that one or both of them could contribute to absinthe toxicity.

A number of studies were conducted in animals in order to prove that thujone, a component of warmwood, which is structurally an isomer of camphor, was responsible for causing absinthism, especially seizures. When exposed to a high dose of α-thujone (45 mg/kg), mice had a tonic convulsion that led to death in 1 minute, whereas at 30-45 mg/kg they presented tail-raising, flexion of the trunk and clonic activity in the forelimbs followed by tonic/clonic convulsions that finally resulted in recovery or death. When intraperitoneal diazepam or phenobarbital was administered 15 minutes before α-Thujone, all mice survived the potentially lethal dose. The same result was obtained when ethanol was administered in pretreatment (1g/kg).

Therefore, it has been proven that α-Thujone is indeed a convulsant (16).
The toxicology of thujone, both acute and chronic, was reviewed by WHO Food Additives Series (17) followed by Scientific Committee on Food of the European Commission (18). These organisations concluded that the mechanism of toxicity is a result of GABA type A modulation (α-Thujone neurotoxicity and convulsant effects) and porphyrogenicity (in chick embrio liver cell cultures). Also, the behavioral effects are thought to be related to 5-HT3 receptor modulation, studied by Deiml et al. They were looking at 5-HT3 receptor as a site for the psychotropic effect of α-thujone. In the homomeric receptors, it increased the channel-blocking potency of the 5-HT natural ligand; in the heteromeric receptors, it engaged an additional component for channel-blocking in the agonist, meaning that there is indeed a reduction in the 5-HT3 receptor activity (17, 18).
Thujone is also the main constituent of essential oils and derives from a number of plants, including sage, tansy, clary, or white cedar. These plants are used as ingredients in essential oils, as fragrances or as flavouring in alcoholic drinks all around the world. Thujone can be toxic, and the presence of alpha- or beta-thujone in food or beverages is managed according to the laws in several countries. In the United States, thujone as a solo ingredient is banned from being added to food. Even wormwood itself is oftenly used for flavoring vodka in Sweden, whereas vermouth and chartreuse contain small ammounts of thujone. Sage oil contains 20-30% thujone and is used for flavoring as well, but for sausages, other type of meats, sauces or spices (19). Thamm I et. al conducted a study that quantified α-thujone and its metabolites (4-OH and 7-OH) in human urine after consuming a sage infusion. The result was that candidates with a faster metabolism had a smaller ammount of the toxine detected and a faster excretion of hydroxythujones, therefore proving an effective detoxification in humans (20).
At normal levels, the potential for toxicity is quite low. Nevertheles, the possibility of an idiosyncratic response still exists. After being prohibited for almost a century in most european countries, absinthe is back in the market, reviving the legends and myths of previous centuries, during which it inspired the artistic and literary personalities of the “belle epoque’’.
Picasso turned his life into a legend. After the years spent among the bohemians in Montmartre, after eighty years of artistic activity, he became the most renowned painter of the 20th century due to his genius and innovative spirit.

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REFERENCES

1. Schmidt H: L'absinthe-l'aliénation mentale et la criminalité. (Rapport fait au nom de commission d'hygiène publique de la chambre des députés). Annales d'Hygiène Publique et de Médicine Légale 1915; 23: 121133.
2. Strang J, Arnold WN, Peters T: Absinthe: what's your poison? Though absinthe is intriguing, it is alcohol in general we should worry about. British Medical Journal 1999; 319: 1590-1592.
3. Lanier D: Absinthe - The Cocaine of the Nineteenth Century: A History of the Hallucinogenic Drug and Its Effect on Artists and Writers in Europe and the United States. McFarland: McFarland & Company, 2004.
4. Charles V: Pablo Picasso. New York: Parkstone International, 2011.

5. Blocker JS, Fahey DM, Tyrrell IR: Alcohol and Temperance in Modern History: An International Encyclopedia, volume I. Santa Barbara: ABC-CLIO, 2003.

6. Wattenmaker R, Distel A: Great French Paintings from the Barnes Foundation: Impressionist, Post-impressionist, and Early Modern. New York: Little, Brown and Company, 1993.

7. Arnold WN. Vincent van Gogh: Chemicals, Crises and Creativity. New York: Springer Science & Business Media, 2013.

8. Bradley RJ, Adron Harris R, Hardbound PJ: The Neurobiology of Painting: International Review of Neurobiology. Waltham: Academic Press, 2006.

9. Lachenmeier DW, Walch SG, Padosch SA, Kröner LU: Absinthe-a review. Critical Reviews in Food Science and Nutrition 2006; 46(5): 365-377.

10. Arnold WN: Absinthe. Scientific American 1989; 260: 112-117.

11. Magnan V: On the comparativc action of alcohol and absinthe. Lancet 1874; 2: 410-412.

12. Sollmann T: A manual of pharmacology and its applications to therapeutics toxicology. Philadelphia: W.B. Saunders Company, 1948.

13. Collman JP: Naturally Dangerous: Surprising Facts about Food, Health, and the Environment. University Science Books, 2001.

14. Arnold WN, Loftus LS: Xanthopsia and van Gogh's yellow palette. Eye 1991; 5: 503-510.

15. Wood CA: The American encyclopedia and dictionary of ophthalmology. Chicago: Cleveland Press, 1919.

16. Höld KM, Sirisoma NS, Ikeda T, Narahashi T, Casida JE: α-Thujone (the active component of absinthe): γ-Aminobutyric acid type A receptor modulation and metabolic detoxification. Proc Natl Acad Sci USA 2000; 97:3826-3831.

17. WHO Thujone. Toxicological Evaluation of certain food additives WHO food additives series 16. 1981.

18. Scientific Committee on Food of the European Commission. Opinion of the Scientific Committee on Food on Thujone. https://ec.europa.eu/food/sites/food/files/safety/docs/fs_food-improvement-agents_flavourings-out162.pdf

19. Dolan LC, Matulka RA, Burdock GA. Naturally occurring food toxins. Toxins (Basel) 2010; 2(9):2289-332.

20. Thamm I, Tiefenbacher K, Rychlik M. Quantification of α-Thujone and Its Metabolites in Human Urine after Consumption of a Sage Infusion Using Stable Isotope Dilution AssaysToxins (Basel) 2018; 10(12): 511, in press.

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Epidemiological study of drug addiction, psychological disorders and the incidence of the B/C Virus Hepatitis on an imprisoned population from district of Moldavia

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ABSTRACT

The bulk of the subject population was made of 211 (39%) prisoners of the 20-29 age group, 148 prisoners of the 30-39 age group (27%), with a precarious marital status and having a low level of education. The frequency of the subjects who administer drugs by injection shots was significantly higher at the VHB/C group (10,2%), as compared to the witness group (2,4%), a frequency which is statistically significant (p=0,001). The intake of cocaine as *crack* was small in both investigated groups (7,4% *vs* 4,2%), as the frequency differences were statistically insignificant (p=0,264). Based on the type of aggression, by drawing the ROC curve it is confirmed that self-aggression is an important risk factor. Physical aggression was present with 57,1% of the subjects (57,1% *vs* 42,9%) with previous criminal records, sexual aggression with 73% (73% *vs* 27%), whereas self-aggression with (58,5% *vs* 41,5%,). Incarcerated individuals suffer from a consistent psychiatrically and somatically pathology, as

compared to the general population. It needs specific, multi-disciplinary measures. The psychotherapy component plays an important part in preventing the spread of the disease.

KEY WORDS:

Imprisoned population, viral hepatitis B, C, drug addiction

INTRODUCTION

Prisoners all over the world are known as a population with a high risk of transmitting viral liver diseases (Hepatitis with the B and the C Virus – HVB, HVC), HIV or BTS (1,6), the risky behaviour of this population which lives at the margin of society and includes many risk factors among which the use of injectable drugs (2,5), homosexual relationships, tattoos, etc., determine the significantly-increased sero-positivity for these categories, as compared to the general population (7,4). The use of injectable drugs (3) and the transfusion of infected blood or sanguine products were the most common transmission paths for the VHC infection. (8).

CASES AND RESULTS

The bulk of the subject population was made of 211 (39%) prisoners of the 20-29 age group, 148 prisoners of the 30-39 age group (27%), with a precarious marital status: only 97 were married (18%), whereas 38,5% (205/533) were concubines and having a low level of education. More than 64% of them dropped secondary school without graduating, more than 40% had no occupation, whilst among those with a job 50% had been working on a daily basis, without a stable, permanent job. The profile of the prison new-comer shows that 58,34 % of the prisoners included in the studied subject lots have penal antecedents, they are recidivists. All the subjects had fulfilled an informed consent. The study was approved by Ethical Commission of University “Gr. T. Popa” Iasi.

The demographic characteristics do not influence the lots significantly from the statistical viewpoint. The average age of the patients from the VHB/C lot was slightly higher (35,41 *vs* 33,19 years old), with a weight of the subjects with ages under 35 of 56,5% (p=0,272), for the subjects from the VHB/C lot, the rural provenance determined a relative risk of over 2 of viral liver infection (p=0,045), for subjects coming from orphanages there were no significant differences between the investigated lots (13,9 *vs* 11,5%) (p=0,612), the reduced educational level was one criterion for over 86% of the lot of subjects infected with the hepatic virus B&C, but the frequency was not significantly increased as compared to the witness group (p=0,342), the professions with contact risk to biological products, including blood, presented reduced frequencies with both of the groups (2,8% *vs* 6,4%) (p=0,228). One can only spot the increased weight at the HVB/C group, especially at the age-group of 50-59. The prison environment represents an increased risk for all transmittable diseases. This is well-expressed statistically when we compare the epidemiological data which are influenced by the ***demography of the prison***: the length of the detention, the number of imprisonments, etc.: the detention period which is longer than 5 years leads to a relative risk of infection with a B/C virus of over 7 (RR=7, 21), the number of over 15 individuals in a room present a relative risk of RR=3, 36 of infection with a hepatic B/C virus. At the VHB/C group, the contact with individuals infected with B or C represented a relative risk of infection with HVB/C of 3,58, the contact with people with AgHBs positive represented a relative risk of over 7 of infection with a B or C hepatic virus for the subjects in the VHB/C group, as compared to the witness group (RR=7,87), for the subjects infected with a B or C hepatic virus, the intra-

family contact presented a relative risk of approximately 4 (RR=3,94). This data highlights the fact that there are risk factors which keep their weight irrespective from the prison environment. (Table 1)

Table I. Risk factors showed comparatively on study lots

Risk Factor	VHB/C Group (n=108)		Witness Group (n=425)		Weight		RR	IC95%
	n	%	n	%	χ^2	P		
Medical Risk Factors								
Surgeries	46	42,6	146	34,4	2,19	0,139	1,24	0,96÷1,60
Frequent hospitalizations	9	8,3	36	8,5	0,02	0,882	0,98	0,49÷1,98
Blood transfers	18	16,7	19	4,5	17,99	**0,001**	3,73	2,03÷6,86
Empirical Treatment	12	11,1	18	4,2	6,39	**0,011**	2,62	1,30÷5,27
Dental Treatment	39	36,1	115	27,1	3,01	0,083	1,33	0,99÷1,79
Accident	17	15,7	48	11,3	1,20	0,273	1,39	0,84÷2,32
Non-medical risk factors								
Common use of syringes	11	10,2	10	2,4	11,97	**0,001**	4,33	1,89÷9,93
Cosmetic treatment	9	8,3	30	7,1	0,06	0,804	1,18	0,58÷2,41
Tattoos	70	64,8	220	51,8	5,40	**0,020**	1,25	1,06÷1,48
Piercing	49	45,4	98	23,1	20,36	**0,001**	1,97	1,50÷2,58
Common personal objects	40	37,0	78	18,4	16,37	**0,001**	2,02	1,47÷2,77
Intake of toxic substances								
Daily intake of alcohol	70	64,8	216	50,8	6,23	**0,013**	1,28	1,08÷1,51
Injectable drugs	11	10,2	10	2,4	11,97	**0,001**	4,33	1,89÷9,93
Cocaine intake	8	7,4	18	4,2	1,25	0,264	1,75	0,78÷3,91
Antalgic medication	32	29,6	82	19,3	4,87	**0,027**	1,54	1,08÷2,18
Medication against tuberculosis	11	10,2	46	10,8	0,04	0,986	0,94	0,50÷1,75
Medication containing hepatotoxic substances	19	17,6	66	15,5	0,14	0,707	1,13	0,71÷1,80
Accidental intoxication	13	12,0	14	3,3	11,93	**0,001**	3,65	1,77÷7,54
Psychiatric treatment	23	21,3	85	20,0	0,03	0,869	1,06	0,71÷1,60
Aggression								
Sexual	2	1,9	12	2,9	0,05	0,820	0,66	0,15÷2,89
Physical	20	18,5	68	16,0	0,23	0,628	1,16	0,74÷1,82
Self-inflicted aggression	42	38,9	100	23,5	9,62	0,002	1,65	1,23÷2,21

It is to be mentioned that only 28.6 % of the drug users were without previous criminal record, the other lot of 71.4 % came from the population which had previously served time. Concerning the use of toxic substances, one can notice that 64,8% of the subjects from the VHB/C group and 50,8% of the witness group declared their daily intake of alcohol, these are significant percentage differences from a statistical viewpoint (p=0,013). The daily intake of alcohol was insignificant as quantity, over 60 g/day for 62, 9% of the VHB/C group and for 53,7% of the witness group (Figure 1 and 2).

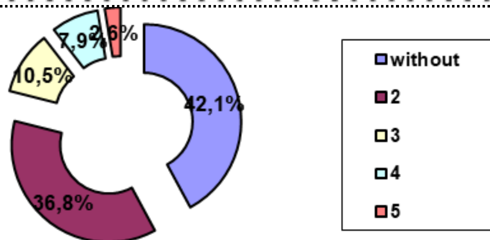

Fig. 1. Distribution of prevalence of non-medical risk factors

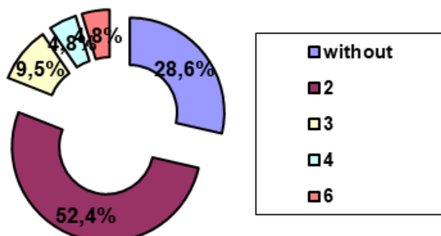

Fig. 2. Distribution of subjects using common syringes

The frequency of the subjects who administer drugs by injection shots was significantly higher at the VHB/C group (10,2%), as compared to the witness group (2,4%), a frequency which is statistically significant (p=0,001). Based on the declarations of the subjects, the intake of cocaine as *crack* was small in both investigated groups (7,4% *vs* 4,2%), as the frequency differences were statistically insignificant (p=0,264). (Figure 3)

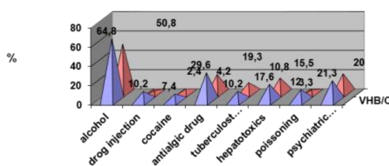

Fig. 3. The distribution of the subjects according to the intake of toxic substances

The distribution of the subjects shows that 57,9 % of the consumers of injectable drugs and 73,1% of those who sniffed cocaine come from the group of prison population with previous criminal records.

Concerning the types of aggression and their association with sero-positivity VHB/C, the following information is to be noted:

- 1,9% of the subjects in the VHB/C and 2,8% of the witness group declared they were sexually abused, the percentage differences between the study groups were insignificant from a statistical viewpoint (p=0,820),
- Physical aggression was acknowledged in proportion of 18,5% at the VHB/C group and 16% in the witness group, without significant frequency differences from a statistical viewpoint between the investigated groups (p=0,628),

Self-aggression was significantly more frequent at the VHB/C group (38,9%) as compared to the witness group (23,5%) (p=0,002) (Figure 4 and 5).

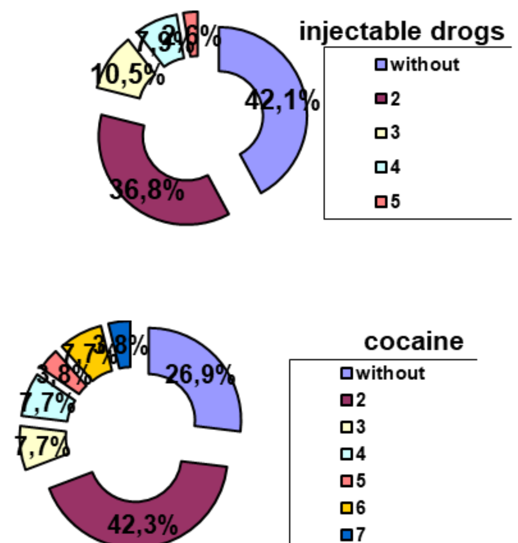

Fig. 4. The distribution of the subjects using injectable drugs or cocaine as crack, based on the number of incarcerations

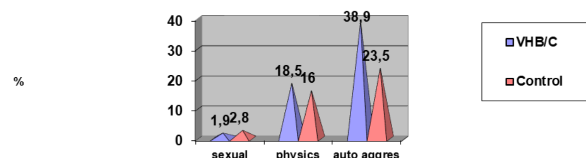

Fig. 5. The distribution of the subjects according to the aggression type

Based on the type of aggression, by drawing the ROC curve it is confirmed that self-aggression is an important risk factor (Figure 6).

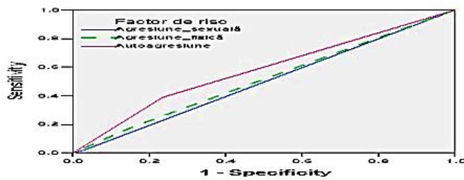

Fig. 6. The specificity of aggression as a risk factor

Physical aggression was present with 57,1% of the subjects (57,1% *vs* 42,9%) with previous criminal records, sexual aggression with 73% (73% *vs* 27%), whereas self-aggression with (58,5% *vs* 41,5%,) (Figure 7).

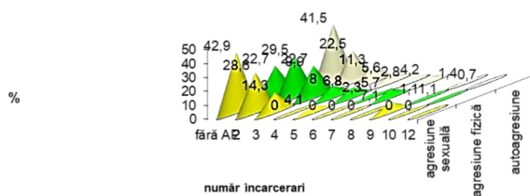

Fig. 7. The distribution of the sexually-, physically- or self-abused subjects, according to the number of incarcerations

DISCUSSIONS

The main hepatic chronical diseases found in the prison environment were: chronical hepatitis with VHB, chronical hepatitis with VBC, toxic alcoholic chronical hepatitis and medicine-induced toxic hepatitis. Of all the non-medical risk factors, the invasive manoeuvres connected to the injection of drugs and the common use of syringes by several individuals, tattoos and piercings were significant ways of infection with VHB/VHC. Thus, the common use of syringes represented, for the VHB/VHC group, a risk factor of over 4 (RR=4,33), the tattoo induced a relatively low risk factor (RR) of 1.25 for the VHB/VHC group, the piercing represents a risk factor which is twice as high with patients having an VHB/VHC infection (RR=1,97), the common use of personal objects represented for the VHB/VHC group a risk factor which is twice as high (RR=2,02). The opioid drug over-use/addiction in the prison environment is an international problem, which was preponderantly noticed in the U.S.A. Urine tests designed to spot opioid toxicology at the admission in prison was proved to be positive for both males and females, with values ranging from 12% - 25% and 13% - 23% respectively, in 2003 (*17*). In France, 30% of the prisoners were heroin-addicted (2005), in Germany, 13% of the prisoners inject mainly heroin (2007), in Australia, 59% of the interviewed subjects report having injected drugs (9). On the one hand, drug-addicts have a higher risk of mortality during the first two weeks after release from prison, but on the other hand, the institutionalised prison environment offers the opportunity of joining treatment programs which can continue in the community after the release from prison (17).

An overview analysis on several observational studies which showed a greater rate of incidence/prevalence of HVC with individuals who did not report any commonly-shared use of syringes for injecting drugs can be explained by the lack of homogeneity of the studies and by the inexact reports (10). Dolan K and his collaborators (11) highlight in 1995 the presence of the over-infection with HIV with all the drug addicts who use shared syringes. Within the category of toxic substances intake, the injectable drug induced a relative risk of infection with a B or C virus of over 4 with the VHB/C group (RR=4,33), even if the frequency of the cocaine consumers (those who sniff crack) from the VHB/C group was not significantly increased as compared to the witness group (7,4% *vs* 4,2%), the relative

risk of infection with hepatic viruses which was calculated was of 1.75 for the VHB/C group. The distribution of the subjects shows that 57, 9 % of the injectable drug consumers and 73, 1% of those who sniffed cocaine are convicts with previous criminal records. As for the aggression models which are to be found in prisons and the risk of contamination with HVB/C, for the subjects coming out of the VHB/C group, self-aggression represented a risk factor which was 1.65 times stronger as compared to the witness group. Aggressions and self-aggressions were risk factors which were specific to prisons, as they were being used with the aim of obtaining material advantages, or even a higher position in the internal hierarchy of the prisoners. In very many cases, this is a protest form for the detention conditions, but also a way of impressing or blackmailing the prison staff. The individuals who use or have used intravenous drug shots (16), as well as those which were involved in the circuit of illegal drug supply were much more exposed to infection with hepatitis C (5), because they can share the needles or other tools used by drug addicts (including the heating plates, the cotton, the spoons, the water, etc.), which can all contain blood which is contaminated with the virus of hepatitis C (12). It is estimated that 60% up to 80% of all the users of injectable drugs in the United States were infected with VHC. Strategies to reduce the risk were encouraged in many countries, in order to hinder the spread of hepatitis C, through education, the free furnishing of needles and syringes and the promotion of secure injection techniques (13). The mortality which is attributed to the drug use reaches a percentage of about 3% of the total deaths of the adult population under 40 years of age. In Europe there are 7,000 to 8,000 deaths, the majority being the cause of overdose (18). In Romania, because of the unclear definition of the concept of death determined by drugs, only the deaths which occur shortly after the administering the substance come to light and are thus quantified. These cases are connected to the material effect of the drug: overdose or acute reaction (18). There is no concrete tri-dimensional relationship *drug-consumption – Hepatitis C – death*. The spread of VHC could be possible through nose-inhaling of illegal drugs such as cocaine and methamphetamine crystals (14), when the straws (with traces of mucus and blood) were shared between the users (14).

Imprisoned individuals present, both psychiatrically and somatically, a consistent pathology as compared to the general population. The most of the statistical data comes from highly-developed countries. Since many years there were debates organized in order to discuss about the care and treatment of prisoners, such as capital punishment for the psychologically-ill patients in some countries (15). The differences of health status between the imprisoned and the general population were attributed to the socio-economic conditions and to behaviours which are typical in prison environments: the high rate of intravenous drug use which leads to a high risk of infection, alcohol intake and smoke. These habits also generate an increase in the risk of cardiovascular diseases and of some forms of cancer (17). This is the reason why specific, multidisciplinary measures are necessary, the psychotherapy and individual as well as group communication/therapy play a central role.

CONCLUSIONS

Incarcerated individuals suffer from a consistent psychiatrically and somatically pathology, as compared to the general population.

The addiction manifested through drug addiction and alcohol intake, but also aggression/self-aggression forms have epidemiological, social and pathological particularities.

The common ground of the addiction in prison environment and the prevalence of the viral B and C hepatitis are intensely studied.

From the category of the toxic substance intake, the injectable drug induced a relative risk of infection with a B or C virus of over 4 for the VHB/C group (RR=4, 33),

Self-aggression represented a risk factor of 1, 65 higher as compared to the witness group.

57.9% of the users of injectable drugs and 73.1% of those who sniffed cocaine are prisoners with a previous criminal record.

It needs specific, multi-disciplinary measures. The psychotherapy component plays an important part in preventing the spread of the disease.

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REFERENCES

1. Hull HF, Lyons LH, Mann JM, Hadler SC, Steece R, Skeels MR. Incidence of hepatitis B in the penitentiary of New Mexico. American Journal of Public Health. 1985,75: 1213–1214.
2. Agnello C K, Lewis J, Tracy S L, Spelman T, Bowden D S, Bharadwaj M, et al.- High incidence of hepatitis C virus reinfection in a cohort of injecting drug users. Hepatology, 2008 48:1746-1750.
3. Grebely J, Conway B, Raffa J D, Lai C, Krajden M,Tyndall M W. Hepatitis C virus reinfection in injection drug users. Hepatology 2006,44:1139.
4. Khan AJ, Simard EP, Bower WA, Wurtzel HL, Khristova M, Wagner KD, et al.. Ongoing transmission of hepatitis B virus infection among inmates at a state correctional facility. American Journal of Public Health. 2005,95:1793–1799.
5. Micallef J M, Macdonald V, Jauncey M, Amin J, Rawlinson W, Kaldor J M, et - High incidence of hepatitis C virus reinfection within a cohort of injecting drug users. Journal of Viral Hepatitis 2007, 14:413-417.
6. Andrus JK, Fleming DW, Knox C, McAlister RO, Skeels MR, Conrad RE, et al.. HIV testing in prisoners: is mandatory testing mandatory? American Journal of Public Health. 1989,79:840–842.
7. Solomon L, Flynn C, Muck K, Vertefeuille J. Prevalence of HIV, syphilis, hepatitis B, and hepatitis C among entrants to Maryland correctional facilities. Journal of Urban Health. 2004,81:25–37.
8. Houghton M- Discovery of the hepatitis C virus. Liver International 2009,29 (1):82-87.
9. Stallwitz A, Stover H. The impact of substitution treatment in prisons—a literature reviews. International Journal of Drug Policy 2007, 18: 464–74.
10. Palmateera N, Hutchinsona S, Innesa H, Schniera C, Wuc O, Goldberga D, et al.- Review and meta-analysis of the association between self-reported sharing of needles/syringes and hepatitis C virus prevalence and incidence among people who inject drugs in Europe. International Journal of Drug Policy 2013, 24:85– 100.
11. Dolan K, Wodak A, Penny R. AIDS behind bars: Preventing HIV spread among incarcerated drug injectors. AIDS 1995,9:825–832.
12. Hagan H. Hepatitis C transmission dynamics in injection drug users. Substance Use & Misuse 1998,33:1197—1212.
13. Hutin YJ, Hauri AM, Armstrong GL. Use of injections in healthcare settings worldwide, 2000: literature review and regional estimates. British Medical Journal 2003,8(327):1075.
14. Fox RK, Currie SL, Evans J, et al.. Hepatitis C virus infection among prisoners in the California state correctional system. Clinical of Infectious Disease 2005, 41: 177–86.

15. Assadi SM, Noroozian M, Pakravannejad M, et al.. Psychiatric morbidity among sentenced prisoners: prevalence study in Iran. The British Journal of Psychiatry 2006, 188: 159–64.
16. Laar T J, Molenkamp R, Schinkel J, Beld M G, Prins M, Coutinho R A, et al. - Frequent HCV reinfection and superinfection in a cohort of injecting drug users in Amsterdam. J. Hepatol. 2009,51:667.
17. National Institutes of Hearth Consensus Development Conference on Management of Hepatitis C: 2002.
18. Vicol M C1, Bulgaru-Iliescu D, Ioan B, Astărăstoae V- Drogodependentul: pacient sau prizonier? Romanian Journal of Legal Medic 2009,4: 309 – 312.

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A mini-review through the main behavioral animal models of depression and their metabolic relevance

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ABSTRACT
Depression is now one of the most important and prevalent psychiatric disease worldwide. It is believed that depression will represent the second leading cause of disability worldwide by 2020. One of the most important ways to further investigate the pathophysiological mechanisms and possible treatments for this psychiatric disorder (as for most diseases in general) could be represented by the usage of the animal models. Besides the important ethical aspects of the issue, it should be also mention that until now, there is no perfect animal model for any neuropsychiatric disorder, which are mainly developed to mimic one of the related mechanism of the specific disorder (e.g. behavioral modifications, gene alterations, affected neurotransmitter functioning). Thus, we describe in this mini-report the model of helplessness learned, chronic mild stress model and social defeat stress. Since there is also an increased awareness regarding the metabolic component for most of the neuropsychiatric disorder including depression, we will focus here on the latest aspect regarding the relevance of some metabolic modifications in depression pathophysiology and possibly in designing the animal models of depression.

KEYWORDS:
Depression, metabolism, model

INTRODUCTION

Depression is one of the most important mood swings and affects up to 20% of the global population (1, 2, 3). The World Health Organization predicts that major depression will be the second leading cause of disability worldwide by 2020 (4). In addition, the economic burden caused by depression is estimated to be 83$ billion a year in the United States (5). Although there has been a significant development since the first introduction of antidepressant drugs (AD) around 1950, there are still many patients whose this disease cannot be attenuated by these drugs, including tricyclic antidepressants (ACT), monoamine oxidase inhibitors (MAOI), and selective serotonin and/or norepinephrine reuptake inhibitors (SSRI and / or SNRI). Also, in the case of the response, the improvement of mood begins only after three to six weeks of AD administration. These unmet medical needs require more efforts in finding new and effective strategies to treat depression.

IMPORTANCE OF ANIMAL MODELS FOR DEPRESSION

Despite the prevalence of depression and its serious effects, studies on the pathogenesis of depression are still preliminary, as compared to those on the pathogenesis of other chronic and potentially fatal multifactorial conditions such as diabetes or Parkinson's disease(6). The main obstacle in this case is choosing the animal model because for that is a limited the availability. Firstly, an ideal animal model provides an opportunity to understand the molecular, genetic and epigenetic factors that can lead to depression. By using animal models, the molecular changes underlying them and the causal relationship between genetic or environmental changes and depression can be examined, which would allow a better understanding of the pathology of depression. Because it was not identified any "depression gene" to generate depressive symptoms in mice, stress remains a risk factor for depression(7). Secondly, improved animal depression models are indispensable for identifying new depression therapies(8).

Ideally, a suitable animal model of human depression should meet as much as possible the following criteria: strong phenomenological similarities and similar pathophysiology (validity facade), etiology comparable (construct validity) treatment (predictive validity) (9, 10, 11, 12, 13). Unfortunately, depression is a heterogeneous disorder (14) and its multiple symptoms (depressed mood, feeling of worthlessness and recurrent thoughts of death or suicide) are difficult to imitate in laboratory animals. Several models of depression fully fit on these validation criteria, and most of the models currently used are based either on known antidepressant actions or on stress responses (14). It is not necessary that an animal model of "ideal" depression show all anomalies of depression-related behaviors, just as patients do not show any possible symptom of depression. In fact, anhedonia is the main symptom of depression (15), and most current models mimic only anhedonia. It should be noted that there is a difference between a model and a test. A model can be defined as a nonhuman body or a particular state of a body that reproduces aspects of human pathology, providing a certain degree of predictive validity. A test, on the other hand, provides only a behavioral or physiological measure designed to assess the effect of genetic, pharmacological or environmental manipulation (15). In this paper, animal models of depression commonly used are summarized, and their advantages and disadvantages are discussed individually. Many authors have proposed validity criteria for animal depression models, those proposed

by McKinney and Bunney in 1969, over 40 years ago, still being the most cited. These authors propose that the validity of an animal model can be determined by the extent to which it is "reasonably analogous" to human disorder in its manifestations or symptomatology, there exist a change of behavior that can be objectively monitored, behavioral changes observed should be reversed by the same treatment modalities that are effective in humans and the system should be reproducible between the experiments.

Further, the relative importance of the individual criteria of animal depression models was viewed differently. It is important to note the pragmatic criterion of Geyer and Markou. They propose that the only criteria that are necessary and sufficient for the initial use of an animal model to be a paradigm with strong predictive validity (broadly defined) and that reading behavior be reproducible within the same laboratory but also between different laboratories (16). These authors suggest that satisfying other criteria, such as constructive or discriminatory validity, is also desirable but not essential for the initial use of a model in both basic neurobiological research and drug discovery. Moreover, it becomes clear that the most useful strategy in animal models is to evaluate unique endophenotypes (clearly observable behavior) relevant to the disease stage rather than reflecting the entire spectrum of symptoms (17).

Similar efforts have been made to dissect the DSM IV criteria of different psychiatric disorders into specific endophenotypes and to use this modified classification as a basis for investigating new treatments and underlying genes for specific endophenotypes in humans (18, 19, 20).

Also, since lately there is an ever-increasing interest in the metabolic component of most of the neuropsychiatric disorders and the importance of various metabolic changes in the pathophysiology of neuropsychiatric deficiencies, we will also focus here some of our attention to the latest information regarding the relevance of the metabolic modifications in depression.

In fact, our group recently demonstrated that for example the laparoscopic sleeve gastrectomy (e.g. an important surgical tool against obesity) is associated with reduced depressive symptoms in a one-year follow-up study, which was mainly based on the fact that the point prevalence of depressive disorders decreased significantly after surgery ($p<0.01$) (21).We also showed at that time that “the score on the depression scale we used significantly decreased after the laparoscopic sleeve gastrectomy”(21).

Thus, while our findings spoke “in favor of a considerable improvement in a psychological aspect such as depressive symptoms in the course of the 1st year after the laparoscopic sleeve gastrectomy”(21), previous data also showed similar results.

For example the Lutter group showed in 2009 that depression is associated of course with obesity, metabolic syndrome, insulin-dependent diabetes mellitus type II and death after myocardial infarction, while also focusing their attention on leptin and ghrelin molecules and their importance in this context(22).In the same way, the relation between the metabolic syndrome and depression was reviewed and meta-analyzed by Ghanei group in 2016, with significant results referring mainly to a number of 31880 patients (23).

Even more, it was recently demonstrated that focusing on the metabolic matter of the patients with depression will even result in a significant positive outcome of the depression and its suicidal aspects their self, as the Pan group showed in 2017 in a study with 33 patients having a refractory response to antidepressants (e.g. treatment-refractory

depression). Thus, the aforementioned group focused their attention in treating the aforementioned patients with sapropterin, a tetrahydrobiopterin analogue, based on the very little attention that is focused on the incidence of metabolic abnormalities contributing to treatment-refractory depression (24). In this way, in the present paper we will shortly describe the model of helplessness learned, chronic mild stress model and social defeat stress, while further leaving place to speculations regarding their possible usage in the following metabolic-related studies. In addition, our future studies will focus on the tail suspension test and other related aspects.

THE MODEL OF HELPLESSNESS LEARNED

Stressful life events can be the main reason for some types of human depression. The vulnerable people with these stressors can develop clinical depression. In this case, stress can be a similar symptom to induce depression in rodents. One well-validated animal model is that of learned helplessness, in which the depressed state of animals is induced by an uncontrollable and unpredictable electrical shock (25 ,26, 27, 28, 29). The helpless learning was noticed for the 1960's when Richard L. Solomon, a graduate student of Dr. Mowrer, tried the two processes of Pavlov's classic conditioning. He noticed that animal experiences related to uncontrollable traumatic events lead to unexpected changes in behavior. Further, Overmier and Seligman found that exposure to an uncontrollable traumatic event for a total of three to five minutes distributed over two hours led to dramatic deficits in behavioral choices, associative learning and emotional expression and called these "helpless learning". According to protocols in different laboratories, helpless learning is induced in a day or after several days of repeated exposure (30). Helpless behavior is assessed by analyzing the performances in an active escape paradigm, such as the latency to press a lever or a switch of a door (28). For this model, we should take care at the difference between mice and rats. The transfer box paradigm is commonly applied to mice (31), while in rats the experiment incorporates the lever pres s (32). Animals with learned helplessness shows some changes autonomic reminiscent of depression, such as changing the REM sleep (33) weight loss, decreased sexual behavior (34) and increased releasing factor corticotrophin (CRF) and corticosterone (35). By selectively reproducing animals that have learned the helpless behavior of animals that did not learn this behavior, two different rows of rats could be established: rats experiencing congenital learning helplessness (cLH) and rats with resistance to learning helplessness (cNLH) (36). The cLH rats shows helplessness learned without suffering uncontrollable shocks and has anhedonia and/ or anergy under the initial conditions. On the other hand, cNLH rats are resistant to the effects of inevitable shock (37). Establishing cLH rats is a validation of the congenital strain of helpless behavior and serves as a useful model for studying mechanisms underlying depression (16). Currently, studies have shown that repeated administration of AD (anti-depressive) (38) or electroconvulsive therapy (ECS) (39) reduces latency and decreases the number of animals experiencing the helplessness learned. The specificity of this response appears to be very high, and at present no clinically effective compound has succeeded in reversing the learned helplessness (40). In contrast, a wide range of compounds (including benzodiazepine anxiolytics, typical neuroleptic chlorpromazine and psychostimulants, caffeine, amphetamine, phenobarbital and ethanol) are not effective in improving helplessness, suggesting that

learned helplessness has predictive validity at least as a model of action anti-depressants (38). An advantage of the learned helplessness model paradigm is that its symptoms are similar to those of major depression and that most of them can be reversed by treatment of acute (sub-chronic) AD (usually 3-5 days) (42). In addition, cognitive outcomes (learning) and other behaviors (neurovegetative abnormalities) seem to be correlated, thus contributing to the understanding of depressive symptomatology in humans. These values of predictive validity make helplessness learned an interesting model to explore the pathophysiology of depression (40). In addition, this model can also be generally used to measure the escape performance of different labyrinths of mice with different mutations in which target depression genes may affect the vulnerability to develop a condition similar to human depression (31, 43).

However, the major drawback of this model is similar to most of the symptoms of depression that did not persist after discontinuation enough uncontrollable shock (19). In addition, the paradigm can be performed in different ways in various laboratories (44). Moreover, different breeds of rats have different sensitivities to the helplessness learned after the uncontrollable shock. For example, the Kyoto and Charles River Holtzmann lines are the most sensitive to learned helplessness, and Harlan Sprague-Dawley is the intermediary, while Lewis, Brown Norway, Fischer F-344 and Sasco Holtzman are almost resistant to the effects of inevitable shock (45). For mice, the uncontrollable foot shock induces performance deficiencies marked in some breeds only (BALB / cByJ and C3H / HeJ), while in other strains the interference is modest (C57BL/ 6J, DBA/2J and CD -1) or totally absent (A / J) (46).

CHRONIC MILD STRESS (CMS) MODEL

As is well known, repeated exposure to the same stressor usually leads to an adaptation, however, can be prevented by providing a variety of stress in an unpredictable sequence. In this way, the chronic stress model was developed. The Chronic Mild Stress paradigms want to provide a model of a chronic depressive state that develops over time and gradually in response to stress and can provide a more natural inducement of this state. The first paradigm of mild chronic stress was introduced by Katz et al, and which was further developed by Willner (47, 48, 49, 50). That being a basis for the most paradigms which are used nowadays. Initial protocols included three weeks of exposure to electrical shocks, cold water immersion, immobilization, light/dark cycle reversal, and a variety of other stressors (47). These series of stress factors could lead to an increase in plasma corticosteroid levels and a reduction in preference for sucrose (51), suggesting that chronic stress can cause anhedonia. The preference for sucrose is used as an indicator of anhedonia (lack of interest in rewarding stimuli) that is present in some forms of affective disorder, including depression. In this task, the animal's interest in looking for a sweet drink rewarding for regular drinking water is assessed. A tendency towards sweetened beverage is typical, failure to do so indicates anhedonia/depression. However, this protocol has rarely been used in the original series of publications (47, 48, 51, 52, 53), mainly due to serious ethical issues. The pattern of mild chronically stress is then developed in an attempt to achieve the same final results but in an ethically more acceptable manner. This revised procedure involves a relatively continuous exposure of rats (54) or mice (55) to a variety of mild stress factors, such as periods when animals are free of water or food, mildly low ambient

temperature, changing cage colleagues and other easy but unpredictable manipulations of this kind. In a period (usually three weeks) of chronic exposure to this type of mild stress, the preference for sucrose is gradually attenuated (preference for sucrose is calculated as the proportion of sucrose consumption in total fluid consumption)(56), and the condition of the fur is damaged (the state of the layer is calculated as the sum of the scores of seven body areas: head, neck, back, stomach, tail, and back). Each area is marked 0 if it is in good condition (the fur is smooth and brilliant, without pinned areas), 0,5 if it is in moderate bad condition (the fur is a little ruffled with areas where the fur is spiky) and 1 in poor condition the fur is dirty and ruffled on most of the body, with slight spots) (57). According to subsequent studies, these deficits may persist a few weeks after the stress has ceased (58). Moreover, the slight chronic stress causes many other symptoms of depression, such as a decrease in sexual, aggressive behaviors and a decrease in locomotor activity. It is important to note that, in contrast, mild chronic stress does not induce an "anxious" profile in two behavioral tests of anxiety: Elevated Plus Maze and the Social Interaction Test, suggesting that behavioral changes are specific to depression (50).

Reducing preference for sucrose and other symptoms induced by mild chronic stress can be gradually reversed by chronic treatment but not acutely with a wide variety of antidepressants (59). It is important to note that these antidepressants do not alter the rewarded behavior in control animals that have not been subjected to stress. In addition, the duration of the therapeutic improvement observed in this model closely reflects the clinical action of these drugs (usually two to five weeks). The advantages of this model are predictive validity good (behavioral changes are reversed by chronic treatment with a wide variety of antidepressants), the validity of the facade (almost all symptoms demonstrable depression were reproduced) and construct validity (model chronic mild stress causes a decrease in general reactivity to rewards comparable to anhedonia, the main symptom of depression) (50). Therefore, chronic mild stress model is currently probably available the most valid and the most widely used animal model of depression.

However, the pattern of mild chronic stress has two major drawbacks. The first would be the practical difficulty of experimenting with this model. The actual experiments using the easy chronic stress model require a lot of work, lots of space, and stretch over long periods of time. The second possible disadvantage would be that the procedure can be difficult to set up in a new laboratory setting, and the data may be difficult to replicate in other laboratories (59).

SOCIAL DEFEAT STRESS

Although both of the above-mentioned paradigms are capable of inducing long-term behavioral, neuroendocrine and neurobiological effects, they are non-social nature. Because most stress stimuli that lead to psychopathological changes are of a social nature in humans (60), research on the consequences of social stress on experimental animal models is crucial. Rodent models are the most commonly used for the social stress paradigm (61, 62, 63 ,64). Firstly, male experimental animals are introduced into the territory of aggressive male congener. Intruders are quickly investigated, attacked and defeated by residents. To ensure the desired outcome of the social conflict, residents are familiar with the fighting and usually have a higher body weight. These usually belong to a line with a relatively high level of aggression (65). After a few minutes of physical interaction, residents and intruders are usually separated by a plastic divider with

holes, allowing visual, olfactory and auditory contacts for the remainder of the 24 hours period. Every experimental model have to be exposed for several days to a different resident or aggressor (61, 62, 63, 64, 65). According to our and other laboratory studies, this procedure can induce many behavioral changes compared to control, such as the decrease in social interaction (61, 62 ,63, 64) and anhedonia (66), accompanied by the physiological, neuroendocrine and neurobiological consequences of social stress. These changes can be interpreted as signs to identify certain aspects of human depression (65). It is noteworthy, however, that long-term effects are only observed in the animals housed alone, but not in the case of animals housed in groups (65, 66).

Lately, most studies has clearly demonstrated that pharmacological and behavioral tools in treating human depression can be also beneficial for reducing behavioral, physiological, neuroendocrine and neurobiological changes after social defeat.

Sleep deprivation (67), antidepressants such as clomipramine (68), imipramine and fluoxetine (61, 62, 63, 64) and social interaction (67) can prevent many of the consequences of social stress. To this end, stress of social defeat is generally interpreted as a model of human depression. In addition, this model provides another validity that chronic antidepressant but not acute treatment can reverse social aversion (69).

However, this model has two major drawbacks. One is that a pattern applied over the shorter period is more likely to result in anxiety phenotype (70), as studies indicate that 20 days of social stress are needed to develop depression (71). The other is that this model can be used only for male rodents, as female rats or mice do not struggle with each other in a confrontation like resident-intruders (72).

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REFERENCES

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders, fourth ed. American Psychiatric Press, Washington, DC 1994.Anon, 1994.
2. Jones I. Blackshaw JK. An evolutionary approach to psychiatry. Aust N Z J Psychiatry 2000; 34: 8–13.
3. Nesse RM. Is depression an adaptation?. Arch Gen Psychiatry 2000; 57:14–20.
4. Dubrovsky B. Evolutionary psychiatry. Adaptationist and nonadaptationist conceptualizations. Prog Neuropsychopharmacol Biol Psychiatry 2002; 26: 1–19.
5. McLoughlin G. Is depression normal in human beings? A critique of the evolutionary perspective. Int J Ment Health Nurs 2002; 11: 170–173.
6. Berton O, Nestler EJ. New approaches to antidepressant drug discovery: beyond monoamines. Nat Rev Neurosci 2006; 7: 137-151.
7. Nestler EJ, Barrot M, DiLeone RJ, Eisch AJ, Gold SJ, Monteggia LM. Neurobiology of depression. Neuron 2002; 34: 13-25.
8. Krishnan V, Nestler EJ. The molecular neurobiology of depression. Nature 2008, 455: 894-902.
9. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study. Lancet 1997; 349: 1498-1504.
10. Han D, Wang EC. Remission from depression: a review of venlafaxine clinical and economic evidence. Pharmacoeconomics 2005; 23: 567-581.
11. Willner P, Mitchell PJ. The validity of animal models of predisposition to depression. Behav Pharmacol 2002; 13: 169-188.

12. Anisman H, Matheson K. Stress, depression, and anhedonia: caveats concerning animal models. Neurosci Biobehav Rev 2005; 29: 525-546.
13. Vollmayr B, Mahlstedt MM, Henn FA. Neurogenesis and depression: what animal models tell us about the link. Eur Arch Psychiatry Clin Neurosci 2007; 257: 300-303.
14. Cryan JF, Markou A, Lucki I. Assessing antidepressant activity in rodents: recent developments and future needs. Trends Pharmacol Sci 2002; 23: 238-245.
15. Urani A, Chourbaji S, Gass P. Mutant mouse models of depression: candidate genes and current mouse lines. Neurosci Biobehav Rev 2005; 29: 805-828.
16. McKinney WTJ, Bunney WEJ. Animal model of depression. I. Review of evidence: implications for research. Arch Gen Psychiatry 1969; 21: 240–248.
17. Geyer MA, Markou A. Animal models of psychiatric disorders. In: Bloom, F.E., Kupfer, D.J. (Eds.), Psychopharmacology: The Fourth Generation of Progress. Raven Press, New York 1995; 787–798.
18. Hyman SE, Medicine Fenton WS. What are the right targets for sychopharmacology?. Science 2003; 299: 350–351.
19. Inoue K, Lupski JR. Genetics and genomics of behavioral and psychiatric disorders. Curr Opin Genet Dev 2003; 13: 303–309.
20. Gottesman II, Gould TD. The endophenotype concept in psychiatry: etymology and strategic intentions. Am J Psychiatry 2003; 160: 636–645.
21. Timofte D, Ciuntu B, Bulgaru Iliescu D, Hainarosie R, Pantea Stoian A, Mocanu V. Laparoscopic Sleeve Gastrectomy is associated with Reduced Depressive Symptoms: a One-Year Follow-Up Study. Revista de Cercetare si Interventie Sociala 2018; 61: 147-154.
22. Lutter M, Elmquist J. Depression and metabolism: linking changes in leptin and ghrelin to mood. F1000 Biol Rep. 2009; 1:63.
23. Ghanei Gheshlagh R, Parizad N, Sayehmiri K. The Relationship Between Depression and Metabolic Syndrome: Systematic Review and Meta-Analysis Study. Iran Red Crescent Med J. 2016; 18(6).
24. Pan LA, Martin P, Zimmer T et al. Neurometabolic Disorders: Potentially Treatable Abnormalities in Patients With Treatment-Refractory Depression and Suicidal Behavior. Am J Psychiatry 2017; 174(1):42-50.
25. Overmier JB, Seligman ME. Effects of inescapable shock upon subsequent escape and avoidance responding. J Comp Physiol Psychol 1967; 63: 28-33.
26. Hitzemann R. Animal models of psychiatric disorders and their relevance to alcoholism. Alcohol Res Health 2000; 24: 149- 158.
27. Willner P. The validity of animal models of depression. Psychopharmacology (Berl) 1984; 83: 1-16.
28. Seligman ME, Maier SF. Failure to escape traumatic shock. J Exp Psychol 1967; 74: 1-9.
29. O'Neil MF, Moore NA. Animal models of depression: are there any? Hum Psychopharmacol 2003; 18: 239-254.
30. Nestler EJ, Gould E, Manji H et al. Preclinical models: status of basic research in depression. Biol Psychiatry 2002; 52: 503-528.
31. Chourbaji S, Zacher C, Sanchis-Segura C, Dormann C, Vollmayr B, Gass P. Learned helplessness: validity and reliability of depressive- like states in mice. Brain Res Brain Res Protoc 2005; 16: 70-78.
32. Vollmayr B, Henn FA. Learned helplessness in the rat: improvements in validity and reliability. Brain Res Brain Res Protoc 2001; 8: 1-7.
33. Adrien J, Dugovic C, Martin P. Sleep-wakefulness patterns in the helpless rat. Physiol Behav 1991; 49: 257-262.
34. Dess NK, Raizer J, Chapman CD, Garcia J. Stressors in the learned helplessness paradigm: effects on body weight and conditioned taste aversion in rats. Physiol Behav 1988; 44: 483-490.
35. Greenberg L, Edwards E, Henn FA. Dexamethasone suppression test in helpless rats. Biol Psychiatry 1989; 26: 530-532.
36. Henn F, Edwards E, Muneyyirci J. Animal models of depression. Clin Neurosci 1993; 1: 152-156.
37. Vollmayr B, Bachteler D, Vengeliene V, Gass P, Spanagel R, Henn F. Rats with congenital learned helplessness respond less to sucrose but show no deficits in activity or learning. Behav Brain Res 2004; 150: 217-221.
38. Sherman AD, Sacquitne JL, Petty F. Specificity of the learned helplessness model of depression. Pharmacol Biochem Behav 1982; 16: 449-454.
39. McKinney WT. Electroconvulsive therapy and animal models of depression. Ann N Y Acad Sci 1986; 462: 65-69.
40. Vollmayr B, Henn FA. Stress models of depression. Clin Neurosci Res 2003; 3: 245-251.
41. Fadda P, Pani L, Porcella A, Fratta W. Chronic imipramine, Lsulpiride and mianserin decrease corticotropin releasing factor levels in the rat brain. Neurosci Lett 1995; 192: 121-123.

42. Takamori K, Yoshida S, Okuyama S. Availability of learned helplessness test as a model of depression compared to a forced swimming test in rats. Pharmacology 2001; 63: 147-153.
43. Ridder S, Chourbaji S, Hellweg R et al. Mice with genetically altered glucocorticoid receptor expression show altered sensitivity for stress-induced depressive reactions. J Neurosci 2005; 25: 6243-6250.
44. Mitchell PJ, Redfern PH. Animal models of depressive illness: the importance of chronic drug treatment. Curr Pharm Des 2005; 11: 171-203.
45. Henn FA, Vollmayr B. Stress models of depression: forming genetically vulnerable strains. Neurosci Biobehav Rev 2005; 29: 799-804.
46. Anisman H, Merali Z. Rodent models of depression: learned helplessness induced in mice. Curr Protoc Neurosci 2001; Chapter 8: Unit 8 10C.
47. Katz RJ, Roth KA, Carroll BJ. Acute and chronic stress effects on open field activity in the rat: implications for a model of depression. Neurosci Biobehav Rev 1981; 5: 247-251.
48. Katz RJ, Roth KA, Schmaltz K. Amphetamine and tranylcypromine in an animal model of depression: pharmacological specificity of the reversal effect. Neurosci Biobehav Rev 1981; 5: 259- 264.
49. Willner P, Towell A, Sampson D, Sophokleous S, Muscat R. Reduction of sucrose preference by chronic unpredictable mild stress, and its restoration by a tricyclic antidepressant. Psychopharmacology (Berl) 1987; 93: 358-364.
50. Willner P. Validity, reliability and utility of the chronic mild stress model of depression: a 10-year review and evaluation. Psychopharmacology (Berl) 1997; 134: 319-329.
51. Katz RJ. Animal model of depression: pharmacological sensitivity of a hedonic deficit. Pharmacol Biochem Behav 1982; 16: 965-968.
52. Katz RJ, Baldrighi G. A further parametric study of imipramine in an animal model of depression. Pharmacol Biochem Behav 1982; 16: 969-972.
53. Katz RJ. Animal model of depression: effects of electroconvulsive shock therapy. Neurosci Bio0behav Rev 1981; 5: 273-277.
54. Willner P, Muscat R, Papp M. Chronic mild stress-induced anhedonia: a realistic animal model of depression. Neurosci Biobehav Rev 1992; 16: 525-534.
55. Monleon S, D'Aquila P, Parra A, Simon VM, Brain PF, Willner P. Attenuation of sucrose consumption in mice by chronic mild stress and its restoration by imipramine. Psychopharmacology (Berl) 1995; 117: 453-457.
56. Pothion S, Bizot JC, Trovero F, Belzung C. Strain differences in sucrose preference and in the consequences of unpredictable chronic mild stress. Behav Brain Res 2004; 155: 135-146.
57. Stemmelin J, Cohen C, Yalcin I, Keane P, Griebel G. Implication of (beta)3-adrenoceptors in the antidepressant-like effects of amibegron using Adrb3 knockout mice in the chronic mild stress. Behav Brain Res 2010; 206: 310-312.
58. Zhu XH, Yan HC, Qu HD et al. Antidepressant effects of intermittent hypoxia by promoting hippocampal neurogenesis in adult rats. Annual Meeting of the Society of Neuroscience 2009, Chicago.
59. Willner P. Chronic mild stress (CMS) revisited: consistency and behavioural-neurobiological concordance in the effects of CMS. Neuropsychobiology 2005; 52: 90-110.
60. Brown GW, Prudo R. Psychiatric disorder in a rural and an urban population: 1. Aetiology of depression. Psychol Med 1981; 11: 581-599.
61. Yan HC, Qu HD, Sun LR et al. Fuzi polysaccharide-1 produces antidepressant-like effects in mice. Int J Neuropsychopharmacol 2010; 13: 623-633.
62. Berton O, McClung CA, Dileone RJ et al. Essential role of BDNF in the mesolimbic dopamine pathway in social defeat stress. Science 2006; 311: 864-868.
63. Krishnan V, Han MH, Graham DL et al. Molecular adaptations underlying susceptibility and resistance to social defeat in brain reward regions. Cell 2007; 131: 391-404.
64. Tsankova NM, Berton O, Renthal W, Kumar A, Neve RL, Nestler EJ. Sustained hippocampal chromatin regulation in a mouse model of depression and antidepressant action. Nat Neurosci 2006; 9: 519-525.
65. Buwalda B, Kole MH, Veenema AH et al. Long-term effects of social stress on brain and behavior: a focus on hippocampal functioning. Neurosci Biobehav Rev 2005; 29: 83-97.
66. Von Frijtag JC, Reijmers LG, Van der Harst JE, Leus IE, Van den Bos R, Spruijt BM. Defeat followed by individual housing results in long-term impaired reward- and cognition-related behaviours in rats. Behav Brain Res 2000; 117: 137-146.
67. Meerlo P, Overkamp GJ, Benning MA, Koolhaas JM, Van den Hoofdakker RH. Long-term changes in open field behavior following a single social defeat in rats can be reversed by sleep deprivation. Physiol Behav 1996; 60: 115-119.

68. Fuchs E, Kramer M, Hermes B, Netter P, Hiemke C. Psychosocial stress in tree shrews: clomipramine counteracts behavioral and endocrine changes. Pharmacol Biochem Behav 1996; 54: 219-228.
69. Cryan JF, Slattery DA. Animal models of mood disorders: Recent developments. Curr Opin Psychiatry 2007; 20: 1-7.
70. Kalueff AV, Avgustinovich DF, Kudryavtseva NN, Murphy DL. BDNF in anxiety and depression. Science 2006; 312: 1598- 1599.
71. Kudryavtseva NN, Bakshtanovskaya IV, Koryakina LA. Social model of depression in mice of C57BL/6J strain. Pharmacol Biochem Behav 1991; 38: 315-320.
72. Bjorkqvist K. Social defeat as a stressor in humans. Physiol Behav 2001; 73: 435-442.

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Students' perception regarding behavioral patterns used in doctor-patient relationship

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ABSTRACT
Background. Communication is a process of generating meaning by sending and receiving verbal or nonverbal symbols and sings; a process of transmitting and receiving messages (verbal and nonverbal); the transfer or exchange of information from a sender to a receiver. Students' perception, in the context of work, represents the position, opinion of the students towards of a set behavioral patterns used in doctor-patient relationship. Objective. Evaluation of students' perception regarding behavioral patterns used in the doctor-patient relationship. Methods. It was used a set of behavioral patterns used indoctor-patient relationship. Students were asked to evaluate on a scale with five ratios (1 = very important, 5 = very little important) behavioral patterns presented. Subjects. The research was attended by a number of 60 students, second year of study, Faculty of Dental Medicine, Bucharest. Results.Analysis of the results reveals a hierarchy of behavioral patterns used in doctor-patient relationship in relation to the intensity of the students surveyed attitudes evaluated towards them. Conclusion.The hierarchy obtiained the following behavioural patterns use in the doctor-patient relationship occupying high places.

KEYWORDS:
The doctor patient relationship, patterns behaviors, descriptive and inferential statistics

INTRODUCTION

Communication is a process of generating meaning by sending and receiving verbal or nonverbal symbols and sings; a process of transmitting and receiving messages (verbal and nonverbal); the transfer or exchange of information from a sender to a receiver. The attitude, in the context of work, represents the

position, opinion of the students towards a set of behavioral patterns used in doctor-patient relationship.

The doctor–patient relationship has been and remains a keystone of care: the medium in which data are gathered, diagnoses and plans are made, compliance is accomplished, and healing, patient activation, and support are provided (1). The three functions are gathering information, developing and maintaining a therapeutic relationship, and communicating information. These three functions inextricably interact (1).

The doctor–patient relationship is central to the delivery of high quality medical care and has been shown to affect patient satisfaction and a variety of other biological, psychological, and social outcomes (3).

A doctor's communication and interpersonal skills encompass the ability to gather information in order to facilitate accurate diagnosis, counsel appropriately, give therapeutic instructions, and establish caring relationships with patients (3,4). These are the core clinical skills in the practice of medicine, with the ultimate goal of achieving the best outcome and patient satisfaction, which are essential for the effective delivery of health care (5, 6).

Basic communication skills in isolation are insufficient to create and sustain a successful therapeutic doctor-patient relationship, which consists of shared perceptions and feelings regarding the nature of the problem, goals of treatment, and psychosocial support (4,7).Interpersonal skills build on this basic communication skill. Appropriate communication integrates both patient- and doctor-centered approaches.

The main goals of current doctor-patient communication are creating a good interpersonal relationship, facilitating exchange of information, and including patients in decision making (3, 8). Effective doctor-patient communication is determined by the doctors' "bedside manner," which patients' judge as a major indicator of their doctors' general competence (9).

Good doctor-patient communication has the potential to help regulate patients' emotions, facilitate comprehension of medical information, and allow for better identification of patients' needs, perceptions, and expectations (3, 10). Patients reporting good communication with their doctor are more likely to be satisfied with their care, and especially to share pertinent information for accurate diagnosis of their problems, follow advice, and adhere to the prescribed treatment (11, 12, 13). There are many barriers to good communication in the doctor-patient relationship, including patients' anxiety and fear, doctors' burden of work, fear of litigation, fear of physical or verbal abuse, and unrealistic patient expectations (14).

Physicians have been found to discourage patients from voicing their concerns and expectations as well as requests for more information. Lack of sufficient explanation results in poor patient understanding, and a lack of consensus between doctor and patient may lead to therapeutic failure (15).

A majority of the literature frequently uses patient satisfaction and adherence to determine the efficacy of the doctor-patient relationship (7, 16).

The research highlights the following qualities of doctor for an efficient communication with patients (qualities of a great health care professional): communication skills; stable emotionally; empathy; flexibility; good attention to detail; interpersonal skills; physical endurance; problem solving skills; respect; time management skills; the ability to separate work from their personal life; dedication to patients' confidentiality; honesty; sobriety; humane.

Objectives

Evaluation of students' perception regarding the behavioral patterns of behavioral used in doctor-patient relationship.

Material and method

It was used a set of behavioral patterns used in doctor-patient relationship. Students were asked to evaluate on a scale with five ratios (1 = very important, 5 = very little important) behavioral patterns presented.

The research was attended by a number of 80 students, second year of study, Faculty of Dental Medicine, Bucharest.

Results and discussions

In table 1 are presented patterns of behavioral used in doctor-patient relationship and how they were assessed by student. Also, are presented descriptive statistics values (averages and standard deviations) of these ratings.

Behavioral patterns in the doctor-patient relationship	m	s
1. Physical examination of body parts that are relevant for the suffering	4.18	.90
2. Explain the nature of medication and treatment	4.53	.69
3. The evaluation in a calm, relaxed	4.71	.46
4. Ensuring patient communication through listening and encouragement	4.42	.90
5. Develop with the own words of the patient's symptoms	4.47	.76
6. Encouraging the patient on a request for information about the diagnosis, treatment, prognosis	3.84	1.05
7. Explain the nature of the disorder, suffering (disease)	4.58	.60
8. Information on the situation and problems of subsequent social	3.97	.85
9. Understanding the emotional reaction in disease	4.08	.91
10. Information on what and how the patient has understood about their own disease	4.03	1.10
11. The evaluation of the compliance of the patient	3.58	.68
12. Stressing the importance of medical indications and recommendations	4.18	.77
13. The use of words and sentences short	3.50	.86
14. The formulation of clear sentences	4.63	.75
15. Repeat referrals	3.84	1.05
16. The provision of factual information, precise, detailed	4.53	.60
17. Real communication of information in difficult situations regarding diagnosis, the effectiveness of interventions, treatment, prognosis	4.29	.96
18. The provision written information	3.21	.78
19. The duration of the consultation	2.97	.82
20. Compliance with programming in any situation	3.21	1.07

Table 1. Descriptive statistics values (averages and standard deviations)

Analysis of the data in table 1 indicate that some of the behaviors register values of the averages higher than others. Standard deviation values indicate differences concerning the assessments made by the respondents.

Patterns of behavior that register the highest values of the averages are follows: the evaluation in a calm, relaxed (m = 4.71); the formulation of clear sentences (m = 4.63); explain the nature of the disorder, suffering (m = 4.58); explain the nature of medication and treatment (m = 4.53); the provision of factual information, precise, detailed (m = 4.53); develop with the own words of the patient's symptoms (m = 4.47); ensuring patient communication through listening and encouragement (m = 4.42).

Patterns of behavior that records the lowest values of the averages are as follows: the duration of the consultation (m = 2.97); compliance with programming in any situation (m = 3.21); the provision written information (m = 3.21); the use of words and

sentences short (m = 3.50); the evaluation of the compliance of the patient (m = 3.58); repeat referrals (m = 3.84); encouraging the patient on a request for information about the diagnosis, treatment, prognosis (m = 3.84).

In table 2 are presented the values of the test for assessing the significance of the differences between the averages obtained for behavioral patterns studied (t-test).

Behavioral patterns in the doctor-patient relationship	**t**	**p**
1. Physical examination of body parts that are relevant for the suffering	28.78	.000
2. Explain the nature of medication and treatment	40.60	.000
3. The evaluation in a calm, relaxed	63.18	.000
4. Ensuring patient communication through listening and encouragement	30.64	.000
5. Develop with the own words of the patient's symptoms	36.20	.000
6. Encouraging the patient on a request for information about the diagnosis, treatment, prognosis	22.48	.000
7. Explain the nature of the disorder, suffering (disease)	47.14	.000
8. Information on the situation and problems of subsequent social	28.70	.000
9. Understanding the emotional reaction in disease	27.57	.000
10. Information on what and how the patient has understood about their own disease	22.51	.000
11. The evaluation of the compliance of the patient	32.30	.000
12. Stressing the importance of medical indications and recommendations	33.67	.000
13. The use of words and sentences short	25.03	.000
14. The formulation of clear sentences	38.04	.000
15. Repeat referrals	22.48	.000
16. The provision of factual information, precise, detailed	46.24	.000
17. Real communication of information in difficult situations regarding diagnosis, the effectiveness of interventions, treatment, prognosis	27.66	.000
18. The provision written information	25.48	.000
19. The duration of the consultation	22.35	.000
20. Compliance with programming in any situation	18.51	.000

Table 2. The values of the test for assessing the significance of the differences between the averages obtained for behavioral patterns studied (t-test)

Analysis of the data of table 2 indicates that there are significant differences between students on the assessment of behavioral patterns used in doctor-patient relationship (p = .000).

CONCLUSIONS

Patterns of behavior that register the highest values of the averages are follows: the evaluation in a calm, relaxed (m = 4.71); the formulation of clear sentences (m = 4.63); explain the nature of the disorder, suffering (m = 4.58);explain the nature of medication and treatment (m = 4.53); the provision of factual information, precise, detailed (m = 4.53); develop with the own words of the patient's symptoms (m = 4.47); ensuring patient communication through listening and encouragement (m = 4.42).

Patterns of behavior that records the lowest values of the averages are follows: the duration of the consultation (m = 2.97); compliance with programming in any situation (m = 3.21); the provision written information (m = 3.21); the use of words and sentences short (m = 3.50); the evaluation of the compliance of the patient (m = 3.58); repeat referrals (m = 3.84); encouraging the patient on a request for information about the diagnosis, treatment, prognosis (m = 3.84).

Analysis indicates that there are highly significant differences between students on the assessment of behavioral patterns used in doctor-patient relationship.

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REFERENCES

1. Lazare A, Putnam SM, Lipkin M., Jr.The Medical Interview: Clinical Care, Education, and Research, New York, NY, Springer-Verlag 1995: 3–19.
2. Simpson M, Buckman R., Stewart M. et al.Doctor–patient communication: the Torontoconsensus statement BMJ 1991;303:1385–1387.
3. Brédart A., Bouleuc C., Dolbeault S. Doctor-patient communication and satisfaction with care in oncology, Curr Opin Oncol.2005;17(14):351–354.
4. Duffy F. D., Gordon G. H., Whelan G., et al. Assessing competence in communication and interpersonal skills: the Kalamazoo II report, Acad Med.2004;79(6):495–507.
5. Brinkman W. B., Geraghty S. R., Lanphear B. P., et al. Effect of multisource feedback on resident communication skills and professionalism: a randomized controlled trial,, Arch Pediatr Adolesc.2007;161(1):44–49.
6. Henrdon J., Pollick K. Continuing concerns, new challenges, and next steps in physician-patient communication. J Bone Joint Surg Am.2002;84-A(2):309–315.
7. Mechanic D, Schlesinger M. The impact of managed care on patients' trust in medical care and their physicians, JAMA 1996;275(21):1693–7.
8. Lee S. J., Back A. L., Block S. D., Stewart S. K.Enhancing physician-patient communication, Hematology Am Soc Hematol Educ Program2002;1:464–483.
9. Hall J. A., Roter D. L., Rand C. S.Communication of affect between patient and physician, J Health Soc Behav.1981;22(1):18–30.
10. Platt F. W., Keating K. N.Differences in physician and patient perceptions of uncomplicated UTI symptom severity: understanding the communication gap, Int J Clin Prac. 2007;61(2):303–308.
11. Alazri M. H., Neal R. D. The association between satisfaction with services provided in primary care and outcomes in Type 2 diabetes mellitus. Diabetes Med.2003;20(6):486–490.
12. Kindler C. H., Szirt L., Sommer D., Häusler R., Langewitz W.A quantitative analysis of anaesthetist-patient communication during the pre-operative visit, Anaesthesia2005;60(1):53–59.
13. Tongue J. R., Epps H. R., Forese L. L.Communication skills for patient-centered care: research-based, easily learned techniques for medical interviews that benefit orthopaedic surgeons and their patients, J Bone Joint Surg Am.2005;87:652–658.
14. Fentiman I. S.Communication with older breast cancer patients, Breast J.1981;13(4):406–409.
15. DiMatteo M. R.The role of the physician in the emerging health care environment, West J Med.1998;168(5):328–333.
16. Harms C., Young J. R., Amsler F., Zettler C., Scheidegger D., Kindler C. H.Improving anaesthetists' communication skills, Anaesthesia2004;59(2):166–172.

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The aggressiveness- suicide risk correlation in depressed patients - an observational study

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ABSTRACT
More than 800,000 people worldwide die each year by suicide, this figure representing 1.4% of global deaths. Aggressiveness has been proven to be a strong predictor of suicidal behaviour. The serotonergic hypofunction has been suggested as a possible source of comorbidity among people with depression and has been associated with impulsive aggressiveness. In this study we aim to analyse the correlation between suicidal risk and aggressiveness in patients diagnosed with depression. The subject group consists of 113 patients from the Socola Institute of Psychiatry, Iasi with an even gender distribution and an average age of 41.85 years. Depending on the suicidal risk, we have divided the patients into two subgroups. From an aggressiveness standpoint, the results are more significant in the suicide risk group when compared to the group without suicide risk.

KEYWORDS:
Depression, suicide risk, aggressive behaviour

BACKGROUND

Depression and aggressiveness

In the scientific literature, aggressiveness is linked to depression, as well as to violent acts (1, 2). Forty-four percent of those diagnosed with major depressive disorder have physically or verbally attacked another individual (3). Furthermore, the severity of the major depressive disorders has been associated with anger attacks (4).

Serotonergic hypofunction has been suggested as a possible source of comorbidity among people with depression and has been associated with impulsive aggressiveness. For example, research results indicate that prolactin response to fenfluramine, an indicator of serotonergic activity, is low in patients with depression (5) and in individuals with an impulsive aggressive behaviour (2). Pharmacological research has shown that symptoms of aggression and depression have been reduced by the administration of fluoxetine, a selective serotonin reuptake inhibitor (6). These results indicate that serotonin disfunction has been identified as the link between aggression and depression and may, in part, contribute to the comorbidity of these conditions.

Suicide and aggressiveness

Aggressiveness has been proven to be a strong predictor of suicidal behaviour (7). Moreover, individuals who have had suicidal behaviour in the past demonstrate more impulsive and aggressive features (8; 9). The suicidal ideation has been linked to impulsivity and irritability in a sample of 625 people (10). In addition, in a study conducted on people with a mood disorder diagnosis, those with a history of suicidal behaviour had a higher level of impulsivity and hostility than those without a history of suicidal behaviour, even though the authors controlled the variables, such as the severity of depression and duration of the disease (11). More specifically, the violent behaviour of suicide had been linked to high levels of impulsivity and aggressiveness, those being identified as consistent variables (12).

It is known that a poor serotoninergic function plays an important role in the high comorbidity between aggression and suicide (13). Low serotonin activity is associated with high-lethality suicide attempts (14), also with impulsive and aggressive behaviours (15). In addition, several studies have reported strong associations between poor serotoninergic function and violent suicide attempts (14, 15). Brain imaging studies suggest that people who exhibit suicidal behaviour may have typical brain dysfunctions common to individuals with aggressiveness and impulsivity. In vivo and post-mortem studies report an association between suicide and poor serotoninergic function in the ventral prefrontal cortex (13). According to a post-mortem imaging study, serotonergic abnormalities were localized in the ventral and ventrolateral prefrontal cortex of those who committed suicide (16). In addition, high-lethality suicide attempts show dysfunctional serotoninergic activity in the ventromedial prefrontal cortex when compared to low lethal suicide attempts (17). Subsequently, Kamali and Associates (13) argued that the source of impulsive and aggressive behaviours can be explained by the deficient inhibitory capacities of the ventral prefrontal cortex due to serotonergic hypofunction, which can lead to impulsive aggressiveness or suicide in the context of significant stressful life factors. The comorbidity of aggressiveness and suicidal behaviour suggests a common neurological mechanism generating a predisposition to these types of behaviours that may be associated with a poor serotoninergic function in the ventral prefrontal cortex.

METHODS

We have analysed a sample of 113 patients from the Socola Institute of Psychiatry, Iaşi, Romania. 53 of the patients are male and 60 females, and the median age is of 41.85 years. The inclusion criteria in the subject group consists of patients diagnosed with depression and the age range between the 18 and 65 years. The exclusion criteria are: mental deficiency, affective disorders of organic nature, dementia, psychotic disorders,

Parkinson's disease and other somatic disorders not stabilized by treatment.

The study has been conducted with the approval of the Research Ethics Commission of the University of Medicine and Pharmacy "Grigore T. Popa" Iasi.

Patients have been investigated by applying psychometric tests. Considering the parameters proposed for analysis in our study, we have chosen to use the Colombia suicide risk scale and the Buss & Perry aggressiveness questionnaire.

To perform a comparative analysis, we have divided the patients into two subgroups: with suicidal risk and without suicidal risk.

RESULTS

Analysis of demographic data of patients with suicide risk / without suicide risk based on Colombia scale

The biological gender

Regarding the biological gender of patients without suicide risk, 53.13% of them are men and the rest of 46.88% are women.

The ratio has changed when we have analysed the distribution among those at risk of suicide. In this case, women have a higher percentage of 55.56%, while the remaining 44.44% are men.

Age

The distribution by age group of those without suicidal risk is as follows: 0% <20 years, 9.38% 20-29 years old, 9.38% 30-39 years old, 59.38% 40-49 years old, 21.88% 50 -59 years old, 0%> 60 years old.

Regarding the age group distribution of patients with suicide risk we have found: 1.23% <20 years old, 20.99% 20-29 years old, 28.4% 30-39 years old, 19.75% 40-49 years old, 16.05 % 50-59 years old, 13.58% age group> 60 years old.

Subjects' Origin Community

In terms of the community of origin, patients in our sample who have not been at risk of suicide have had a perfectly equal distribution: 50% are from the rural area - 50% from the urban area.

However, the distribution is different for the sample consisting only of patients at risk of suicide. Most of these, namely 79.01%, come from the urban area, while only 20.99% come from the rural area.

Educational level

From the perspective of educational level, the distribution of patients without suicidal risk illustrates a majority percentage of 90.63% and is made up of those with higher education, followed by those with middle education 6.25%, and only 3.13% with primary education.

Again, distribution changes completely for those at risk of suicide. In this sample, the majority is represented by those with middle education 62.96%, followed by those with higher education 25.93%, while 11.11% have only primary education.

Civil status

The distribution by civil status of patients without suicidal risk has as majority of 90.63% married, followed by 9.37% divorced. (while 0% of those divorced did not have suicidal risk)

Regarding the distribution by civil status of those with suicidal risk, 75.31% are married, 17.28% are unmarried and 7.41% are divorced.

Occupational status

The distribution by occupational status of patients without suicidal risk is formed exclusively by those employed 100% while 0% of those without suicidal risk are unemployed.

The distribution by occupational status of those with suicidal ideation is made up of 91.36% of those who have a job, and 8.64% are unemployed.

APPLYING THE BUSS & PERRY AGGRESSIVENESS EVALUATION SURVEY

The Buss & Perry Aggressiveness Scale consists of 4 components: Physical Aggression, Verbal Aggression, Anger, and Hostility. The total score for aggressiveness is the sum of the scores of the four components.

PHYSICAL AGGRESSION SUBSCALE

Regarding the physical aggression subscale of the Buss & Perry scale, the results of the test show statistically significant differences between the group without suicide risk and the group with suicide risk $p < 0.001$. Patients at risk of suicide have a significantly higher score than patients without suicide risk (Figure 1).

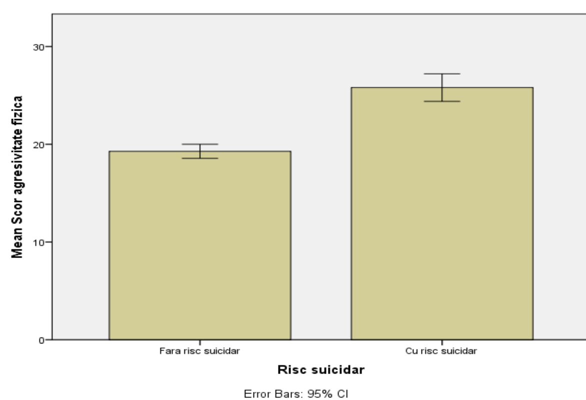

Fig. 1. Significant differences between patients with suicidal risk and patients without suicidal risk, in terms of physical aggression subscale score $p < 0.001$.

VERBAL AGGRESSION

Concerning the second subscale of the test, verbal aggression, the statistical analysis reveals statistically significant differences between the group of patients with suicidal risk and the group of patients without suicidal risk $p < 0.001$. Patients at risk of suicide have significantly higher scores than patients without suicidal risk in the verbal aggression subscale (Figure 2).

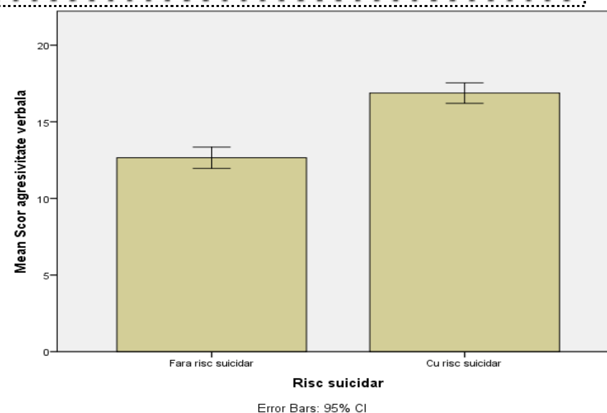

Fig. 2. Significant differences between patients with suicidal risk and patients without suicidal risk, in terms of verbal aggression subscale score $p < 0.001$.

ANGER SUBSCALE

When analysing the third subscale, which measures the level of anger, the statistical analysis shows significant differences in terms of this subscale score between patients with suicidal risk and patients without suicidal risk $p = 0.015$. This difference revealed by statistical analysis is that patients without suicidal risk have significantly higher anger scores compared to patients with suicidal risk (Figure 3).

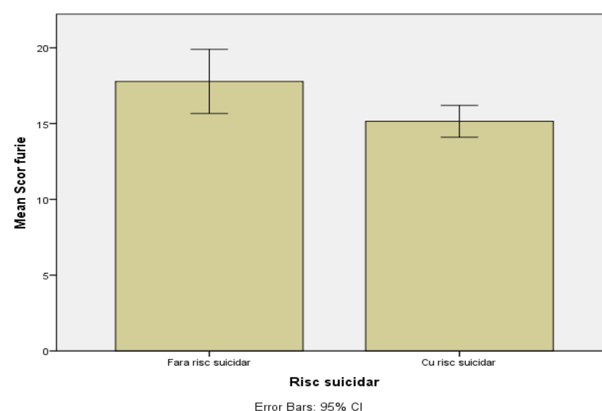

Fig. 3. Significant differences between patients with suicidal risk and patients without suicidal risk, in terms of anger subscale score $p < 0.001$.

HOSTILITY SUBSCALE

The statistical analysis of the last subscale of the survey, a subscale which measures the

level of hostility, reveals significant differences between the two groups of patients in terms of the subscale score $p < 0.001$. These statistically significant differences are represented by the fact that patients with suicidal risk score higher on the subscale that measures the level of hostility when compared to patients without suicide risk (Figure 4)

Fig. 4. Significant differences between patients with suicidal risk and patients without suicidal risk in terms of hostility subscale score $p < 0.001$.

TOTAL SCORE

Regarding the overall aggressiveness scale score, the statistical analysis reveals that there are significant differences in terms of the overall score, in relation to the scale that measures aggressiveness between the group with suicidal risk and those without suicide risk $p < 0.001$. This major difference between the two groups can be interpreted as that patients without suicidal risk have a lower total score when compared to patients with suicidal risk (Figure 5).

Fig. 5. Significant differences between patients with suicidal risk and patients without suicidal risk in terms of the total score of aggressiveness scale $p < 0.001$.

DISCUSSIONS

More than half of people with clinical depression have suicidal ideation, major depressive disorder and bipolar disorder; these are the most commonly psychiatric disorders associated with suicide (18). Some symptoms of depression have been identified as being of particular importance for the risk of suicidal behaviour: loss of hope, feelings of guilt, loss of general interest, insomnia and low self-esteem (19). Effective prevention and treatment of mood swings could reduce the number of severe suicide attempts, given that most depressed patients are inadequately treated at the time of the suicide attempt (18). Thus, active and intensive treatment of patients with suicidal depression could provide an effective way of preventing suicidal behaviour.

Studies show that those who have suicidal attempts have higher levels of aggressiveness than those with no attempts, among the population suffering from major depression (20). More than 800,000 people worldwide die each year by suicide (21), this figure representing 1.4% of deaths worldwide. Suicide can occur at any time in life, being the second most common and, in some

countries, the very leading cause of death among young people aged 15-24 (21).

Evidence from research literature shows that the suicidal ideation is linked to an increased risk of suicide attempt, especially when there has been a previous attempt. (22) The suicidal ideation is, however, much more frequent than suicide attempts. In a well-known study, Smith and Crawford (23) found that 63% of high school students reported suicidal ideation, while actual suicide attempts made up 8%. Consequently, we may conclude that suicidal ideation has a limited value as a risk factor for suicide in the general population (24). This is one of the reasons why we chose to use in our study the Columbia scale for the severity of suicide risk, because this scale which is validated in countless studies, measures not only the level of suicidal ideation, but also the suicidal risk per se.

The study published by Malone KM et al in 1995 shows that people with suicide attempts have a higher aggressiveness when compared to those without attempts, amongst the population suffering from major depression (20). The results obtained in our research come in support of this data, proving an association between suicidal risk, aggressiveness and depression.

CONCLUSIONS

The presence of suicide risk in depressed patients, evaluated by the Columbia scale, has a statistically significant correlation with the level of increased aggression measured by the Buss & Perry scale. Patients at risk of suicide have a significantly higher score at this scale than patients without suicide risk. Also, statistically significant results were acquired for the scores obtained in case of each of the 4 components of the scale in the group of patients with suicide risk.

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REFERENCES

1. Mammen OK, Kolko DJ, Pilkonis PA. Negative affect and parental aggression in child physical abuse. Child Abuse and Neglect 2002;26:407–24.

2. Newman ME, Shapira B, Lerer B. Evaluation of central serotonergic function in affective and related disorders by the fenfluramine challenge test: a critical review. International Journal of Neuropsychopharmacology 1998;1:49–69.

3. Fava M, Bless E, Otto MW et all. Dysfunctional a attitudes in major depression. Changes with pharmacotherapy. Journal of Nervous and Mental Disease 1994;182:45–9.

4. Tedlow J, Fava M, Uebelacker L et all. Outcome definitions and predictors in depression. Psychotherapy and Psychosomatics 1998;67:266–70.

5. Mulder RT, Porter RJ, Joyce PR. The prolactin response to fenfluramine in depression: effects of melancholia and baseline cortisol. Journal of Psychopharmacology 2003;17:97–102.

6. Zanarini MC, Frankenburg FR, Prachini EA. A preliminary, randomized trial of fluoxetine, olanzapine, and the olanzapine-fluoxetine combination in women with borderline personality disorder. Journal of Clinical Psychiatry 2004;65:903–7.

7. Dumais A, Lesage AD, Alda M et all. Risk factors for suicide completion in major depression: a case-control study of impulsive and aggressive behaviors in men. American Journal of Psychiatry 2005a;162:2116–2124.

8. Carballo JJ, Oquendo MA, Giner L et all. Impulsive-aggressive traits and suicidal adolescents and young adults with alcoholism. Internation Journal of Adolescent Medicine and Health 2006;18:15–9.

9. Turecki G. Dissecting the suicide phenotype: the role of impulsive-aggressive behaviours. Journal of Psychiatry and Neuroscience 2005;30:398–408.

10. Conner KR, Meldrum S, Wieczorek WF et all. The association of irritability and impulsivity with suicidal ideation among 15- to 20-year-old males. Suicide and Life-Threatening Behavoir 2004;34:363–73.
11. Michaelis BH, Goldberg JF, Davis GP et all. Dimensions of impulsivity and aggression associated with suicide attempts among bipolar patients: a preliminary study. Suicide and Life Threatening Behavior 2004;34:172–6.
12. Dumais A, Lesage AD, Lalovic A et all. Is violent method of suicide a behavioral marker of lifetime aggression? American Journal of Psychiatry 2005b;167 (7):1375–1378.
13. Kamali M, Oquendo MA, Mann JJ. Understanding the neurobiology of suicidal behavior. Depression and Anxiety 2001;14:164–76.
14. Mann JJ, Malone KM. Cerebrospinal fluid amines and higher-lethality suicide attempts in depressed inpatients. Biological Psychiatry 1997;41:162–71.
15. Asberg M, Traskman L, Thoren P. 5-HIAA in the cerebrospinal fluid. A biochemical suicide predictor? Archives of General Psychiatry 1976;33:1193–1197.
16. Arango V, Underwood MD, Mann, JJ. Postmortem findings in suicide victims. Implications for in vivo imaging studies. Ann. N. Y. Acad. Sci. 1997;836: 269–287.
17. Oquendo MA, Placidi GP, Malone KM et all. Positron emission tomography of regional brain metabolic responses to a serotonergic challenge and lethality of suicide attempts in major depression. Archives of General Psychiatry 2003;60:14–22.
18. Oquendo MA, Currier D, Mann JJ. Prospective studies of suicidal behavior in major depressive and bipolar disorders: what is the evidence for predictive risk factors? Acta Psychiatr Scand. 2006;114:151–158.
19. Lonnqvist J. Major Psychiatric disorders in suicide and suicide attempts. In: Wasserman D, Wasserman C, editors. Oxford Textbook of Suicidology and Suicide Prevention: a Global Perspective. Oxford: Oxford University Press; 2009;275–286.
20. Malone KM, Haas GL, Sweeney JA, Mann JJ. Major depression and the risk of attempted suicide. J Affect Disord. 1995;34(3):173–l85.
21.WHO. First WHO report on suicide prevention. https://www.who.int/mediacentre/news/releases/2014/suicide-prevention-report/en/
22. Kuo WH, Gallo JJ, Tien AY. Incidence of suicide ideation and attempts in adults: the 13-year follow-up of a community sample in Baltimore, Maryland. Psychol. Med. 2001; 31(7): 1181–1191.
23. Smith K, Crawford S. Suicidal behavior among ‘‘normal’’ high school students. Suicide Life Threat. Behav. 1986;16(3): 313–325.
24. Busch KA, Fawcett J, Jacobs DG. Clinical correlates of inpatient suicide. J. Clin. Psychiatry 2003;64(1): 14–19.

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Case Reports

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Case report. Late onset manic episode: evolution and management of the elderly patient

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ABSTRACT
This article synthesizes the psychopathological aspects of the manic episode in terms of the particularities of the studied case : late onset in a senior patient, associating psychotic elements, in the case of a woman with no history of psychiatric disorders, rather showing features of an accentuated personality such as exaltation and boisterousness, who also fell under a non-conformist, jolly, uninhibited lifestyle. Therapeutic adherence is very important in controlling and reducing the severity of the symptoms and to prevent the occurrence of new episodes. In this respect, besides the social support network, the doctor-patient relationship plays a crucial role, especially when communicating the diagnosis.

KEYWORDS:
Manic episode, management of the elderly patient, differential diagnosis

INTRODUCTION

Affective disorders along with schizophrenia are the two pillars of classical psychiatric nosography. The main nosographic entities of affective psychoses - mania and melancholy - represent two of the six types of "madness" described by Hippocrates in the fourth century B.C. The correlation between mania and melancholy has been outlined since the second century by Areteus of Cappadocia. The clinical picture of mania was complemented by Galen, who described the moment patients evolved towards depression, becoming "shy and taciturn"(1).

Given the major impact of affective disorders on the functionality of individuals, physicians have been preoccupied with the related therapeutic aspects since ancient times. For example, 1500 years ago, Aurelianus used to address „manic madness" with alkaline water from certain mineral springs, which are known today for being lithium-rich. Both the treatment of a single manic episode and of the bipolar affective disorder involve higher costs than in the case of hypertension, primarily due to the long duration of hospitalizations and the frequent relapses(2, 3).

More than 75% of patients with mania suffer at least one manic episode during their lifetime(4,5). Moreover, current research in the field of psychiatry certify that both single manic episode and also bipolar affective disorder can be associated with a high risk of developing cardiovascular diseases. Physical and emotional stress has been shown to cause hemodynamic changes in haematocrit, haemoglobin, total plasma protein and plasma viscosity values(6). During mood swings related to bipolar affective disorder, although hematological parameters remained within the normal range, manic and depressive episodes were associated with the redistribution of body fluids. In this context, mania was correlated with fluid retention and hemodilution, whereas depression was associated with hemoconcentration (7).

In the case of patients with mania or severe depressive episodes at their first presentation or when they are not able to provide their medical history, it is useful to apply the HLC-32 Questionnaire (Hipomania Checklist), which may help the physician framing the episode in a bipolar affective disorder(8). Moreover, this questionnaire can also be used as a screening method for teenagers, for the early detection of tendencies towards developing manic episodes, cyclothymia or any bipolar affective disorder(9).

Reason for admission at the hospital

A 65-year-old patient from Brasov presents herself with her family for admission to the Socola Psychiatry Institute of Iasi in July 2018 for a manic syndrome described by: elevated mood, pressured speech, lack of censorship, grandiose delusions, impulsivity, irritability, mixed insomnia, spontaneous hyperprosexia, marked distraction, verbal aggression towards the daughter, dromomania tendencies.

PAST PERSONAL MEDICAL HISTORY AND FAMILY HISTORY - noncontributory.

Regarding life and work conditions it should be mentioned that she lived by herself in a two-room apartment, in urban settings, she graduated high school, she's been divorced for the past 30 years, she has never worked, she is of Orthodox Christian faith. The patient's relatives stated that she has obsessive-compulsive traits (she collects bags).

HISTORY OF PRESENT ILLNESS

The family reports that over the years the patient has shown extrovert, uninhibited behaviors, the symptoms being aggravated in the last year before the presentation, amid domestic conflicts.

On admission, the patients presented psychomotor agitation and psychotic elements, thus the following treatment was initiated:Bromazepam 1,5 mg x 3/day,Acid valproic 500 mg x 2/day, Risperidone 1mg/day.The evolution was favorable, the psychotic elements gradually diminishing, thus we decided to stop the anti-psychotic treatment and to reduce the anxiolytic dosage, the new regimen being: Bromazepam 1,5 mg x 2/day, Acid valproic 500 mg x 2/day.

THE PHYSICAL EXAM did not lead to any pathological findings.

THE PSYCHIATRIC EXAM

Appearance and General Behavior **:**

- Attitude: cooperative, curious, arrogant, psychomotor restlessness;
- Clothing: neat, sometimes wearing excessive jewelry, inadequate for the hospital environment, good hygiene status;
- Voice: accelerated verbal flow, voice of medium tonality and increased intensity, emotionally modulated, the contents corresponding to the perturbation of thoughts;
- Look: expressive, establishes and maintains visual contact with the examining physician;
- Facies: mobile
- Mimics and pantomime: gestural activity slightly increased

Cognitive functions:

- Sensation: slight hyperaesthesia.
- Perception: she does not present hallucinatory phenomena;
- Attention: spontaneous hyperprosexia, marked distraction;
- Memory: selective evocation hypermnesia for events related to the patient's personal life
- Thinking unfolds in a disorganized, accelerated rhythm, presenting pressured speech, racing thoughts, delusions of grandiosity, prejudice and pursuit, and showing somatic concerns of hypocondrial tinge.
- Imagination: without disturbances

Affective and motivational functions:

- Mood: elevated;
- Aggressive behavior and negative emotions towards the family.
- Feelings: inadequate, showing appreciation and sympathy for inappropriate persons;
- Passions: insufficiently structured;
- Motivation: periods of delay in initiating activities;
- Instincts:
  - eating – diminished;
  - preservation – denies autolytic ideation;
  - sexual – exacerbated.

Executive functions:

- Volition: high spontaneity, but with low involvement in activities, hasty decision making and initiation of actions, with inability to complete the desired acts, due to the multitude of tasks that she proposes to fulfill
- Motor activity: self conduct and self care abilities maintained;
- Verbal activity: increased spontaneous verbal communication – pressured speech;
- Behavior: uninhibited;
- Sleep: decreased need for sleep;

Judgment and Insight :

- Conscience: orientation in space, time, and person preserved;
- Insight over illness: absent;
- Intellect: in accordance with educational background
- Character: inappropriate attitude towards the examiner; no censorship during discussions

Psychological examination: manic configuration with elevated mood, accelerated thought processes and eccentric aspect, instability traits, integrative and relational deficiency.

MRS (The Bech-Rafaelsen Mania Rating Scale)= 35 points. (Studies have shown that the overall score of the 11 elements of this scale is enough for the evaluation of mania's intensity. The sum of the 11 elements of the MRS was standardized in the following way: a score below 15 indicates hypo-mania, a score above 15 but below 28 indicates moderate mania and a score above 28 indicates severe mania).

The MMSE Test (Mini Mental State Examination) = 28 points (a score below 10 points indicates severe dementia, 11-19 points moderate dementia, 20-24 points mild dementia).

POSITIVE DIAGNOSIS: Manic episode with psychotic symptoms.

DIFFERENTIAL DIAGNOSIS:

1. Organic affective disorders (organic manic disorder); we eliminated somatic diseases and the consumption of drugs for somatic diseases;
2. Unspecified dementia with psychotic symptoms - the cognitive impairment may be accompanied by altered emotions, social behavior or motivation. In the submitted case we excluded this diagnosis because neither the results of the imagistic investigations nor the applied tests, the MMSE (Mini Mental State Examination), showed any suggestive changes for dementia.
3. Bipolar affective disorder – in order to claim that the patient suffers from bipolar affective disorder there must be at least 2 episodes of modified mood in the medical history, of which at least one must be of depressive/hypo-manic/manic or mixed type. Due to the fact that this was her first presentation to our hospital and her full medical history was not available to us, this diagnosis cannot be totally excluded, the evolution still having to be tracked over time.
4. Psychotic disorders, primarily delusional - as it can be found in literature, the symptoms of this disorder have an abrupt onset, with no prodromal phase, usually caused by a traumatic event and the symptoms are connected thematically with the stressful situation; this aspect is disproved in here, the patient's delusions being mainly of grandeur.
5. Psychotic disorders induced by certain life conditions or by substance abuse.
6. Schizotypal disorder – a person showing symptoms which meet the criteria for this category could be said to present ideas of reference, odd beliefs with mystical or paranormal influences, observations that could not be made in the case of our subject.
7. Persistent delusional disorders include a multitude of pathologies for which the clearest characteristic is the presence of delusions in the long term, for at least 3 months, diagnosis which cannot be excluded because the patient is at her first presentation.
8. Antisocial personality disorder - the main characteristics of this disorder are represented by the lack of respect towards other people and their rights, rights which sometimes are broken, and the incapacity to adapt to social and legal norms, symptoms which we could not find in the case of this patient, neither from her behavior, nor from the statements of her family.
9. Schizoaffective disorder is a pathology in which both affective and schizophrenic symptoms can be found during the same episode, diagnosis that cannot be confirmed in this case,

the patient not showing any schizophrenic symptoms.

During hospitalization the patient was under strictly supervised treatment, showing a good progress, with a visible improvement of her mental and physical state. The psycho-motor activity was reduced and she did not present pressured speech anymore. She reestablished her nycthemeral rhythm, her mood became more tempered and she did not show uninhibited behavior nor sexual exacerbation anymore. Both the therapeutic treatment and the family support played a major role in the good evolution of the disorder.
The prognosis remains reserved, even though the progress during hospitalization was good, due to the fact that the symptoms were just partially remitted and that the disease has a debilitating character.
Positive prognosis factors:

- social support network;
- good adherence to the current treatment;
- absence of a family history of psychiatric diseases;

Negative prognosis factors:

- the civil status: divorced;
- deficits in social relationship skills

DISCUSSIONS

One peculiar aspect of the case was the differential diagnosis between an endogenous manic disorder with onset in the elderly and an organic affective disorder, which would have been statistically more probable for this age. Another special feature was the obsessive-compulsive disorder that the patient developed in the last year before presenting herself to the doctor.
In a study by Karishma and his collaborators in India in 2018, investigating the evolution of bipolar affective disorder, after a first manic episode, it was found that the vast average of the first manic episode in men was 27 years. 38% of patients had a history of depressive episodes. 54% of patients reported a manic episode in the next 6 months. The 5-year follow-up revealed a double number of manic but depressive decompensations, especially for patients aged between 40 and 60 years (10).
It is estimated that by 2030, more than 20% of the US population will be over 65 years old. Many of these people will need psychiatric care. Unfortunately, the needs of the patient with bipolar affective disorder are not well studied. According to research in the field, standard treatments for mania are less effective in elderly patients and they have more noisy symptoms in terms of anger and rate of decompensation.
Given the global demographic changes as well as the financial and humanitarian aspects of the diagnosis of bipolar affective disorder, there is an urgent need for research in this domain.

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REFERENCES

1. D. Prelipceanu.Clinical Psychiatry. The Medical Publishing House, București, 2011
2. Cloutier M, Greene M, Guerin A, Touya M, Wu E. The economic burden of bipolar I disorder in the USA in 2015. J. Affect. Disord. 2017.226, 45–51.
3. Bergeson JG, Kalsekar I, Jing Y, You M, Forbes RA, Hebden T. Medical care costs and hospitalization in patients with bipolar disorder treated with atypical antipsychotics. Am. Health Drug Benefits 2012.5(6), 379–386.

4. Tingjian Y, Mallik G, E Chang, Maelys Touya, M.S Broder. Impact of initiating long-acting injectable antipsychotics on hospitalization in patients with bipolar I disorder, J_Comp Eff Res. 2018 Aug 21. doi: 10.2217/cer-2018-0068

5. Gonda X, Rhmimer Z, Prediction of response to lamotrigine treatment in bipolar outpatients: a multicentric, 6-month, prospective, observational study, Neuropsychopharmacologia Hungarica, 2018; 20(2): 40–45

6. Se-Hoon Shim, Jonghun Lee, Jye-Heon Song, Beomwoo Nam et al.Screening with the Korean Version of the Mood Disorder Questionnaire for Bipolar Disorders in Adolescents: Korean Validity and Reliability Study, Clinical Psychopharmacology and Neuroscience 2018;16(3):316-323

7. Hochman E, Weizman A, Valevski A, Fischel T, Krivoy A. Association between bipolar episodes and fluid and electrolyte homeostasis: a retrospective longitudinal study. Bipolar Disord 2014;16:781-789.

8. Mert DG, Terzi H. Mean platelet volume in bipolar disorder: the search for an ideal biomarker. Neuropsychiatr Dis Treat 2016;12:2057-2062

9. Tevfik Kalelioglu, Murat Kocabiyik, Burcu Kok, Pelin Unalan, Sule Sozen, Ozge Yuksel, Nesrin Karamustafalioglu, Does Blood Flow Change according to Mood? Blood Rheology in Bipolar Disorder, Clinical Psychopharmacology and Neuroscience 2018;16(3):310-315

10. Karishma R, Preethy V, Shyam S, Kesavan M, Course and naturalistic treatment seeking among persons with first episode mania in India: A retrospective chart review with up to five years follow-up, Journal of Affective Disorders Volume 240, November 2018, 183-186

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Time according to Lucian Blaga: eternity

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In the night, somewhere, there is everything that was and is no longer, what has moved away, what has been lost from the living time, from the mute time.
Lucian Blaga

ABSTRACT
Creators of values and time – Eminescu, Blaga, Stănescu –shared between them the eternity of their own time: time according to Eminescu was highly used by Blaga, time according to Blaga was a source of inspiration for Stanescu, who, on his turn, passed it on to the future creators to prevent *deterioration* of time. Lucian Blaga is of the opinion that time is an "ascending ladder for the idea in its historical embodiments" or even the "path of Divinity towards itself". With a correct intuition and visionary spirit, Lucian Blaga transforms *time without homeland* into *transcendental time*. Being part of *the first Romanian generation unconditioned by a previous historical objective that had to be fulfilled,* the thinker from Lancram tried to make the best of the short historical peace after the Great Union in Romania and created the philosophical system of *the time of Romanian culture*. These *"possible perspectives*" of time according to Blaga represent that *beneficent suffering* experienced by Blaga in his way towards another century, towards immortality.

KEY WORDS:
Creators of time, river-time, waterfall-time, Blaga's self, living time, mute time, the horizon of mystery, immortality

From the perspective of creating his own time, *acknowledged by itself in its light* (Poem), having the meaning of *eternity* or *immortality*, Lucian Blaga unfolds his philosophical program regarding not the abstract time, but time in all its dimensions: *the time of yesterday, the time of today, the time of tomorrow.* Involved in *the moving image of eternity (Plato), the time* that was the focus of Blaga was not so much the *time of his life*, but the *time of his immortality*. In fact, this is target of every man of culture

throughout his whole life: he creates his time of immortality, which lasts according to his talent, his perseverance , his chosen objectives, being based on the importance of his message to the future generations, where, although the author does not belong, his work (that is the author's actions) already lives.

Understood as *an interval of the universe* or as *an interval of all things,* as it was defined by the Pythagorean Archytas de Tarentum (Lucretius, *De rerum natura*, 1, 459), the eternal time of a culture is a space with no beginning and no end, where the time of *one* or *several* creators of values, *creators of time,* belong. The time created by the lyrical philosopher and diplomat has the value of his work, being either the time flowing through decades, even though centuries, or the time stunned in the admiration of Blaga's monumental work.

Creators of values, and of time – Eminescu, Blaga, Stanescu - shared between them the eternity of their time: time according to Eminescu was greatly used by Blaga, time according to Blaga was a source of inspiration for Stanescu, who at his turn, passed it to the future creators in order to stop the *deterioration* of time. Couldn't it be *preparation, anticipation, intention of eternity*? In this way a collective soul, a nation is created. Even if he was excluded from public life, Lucian Blaga was aware that he was present in the culture of the nation, sensing *the space* and *time* in which his philosophical messages and his metaphors would have to travel.

Using metaphors like "water fall", "artesian fountain", "river", the philosopher speaks about the time in which "he can breathe, he can live and hope". Time according to Blaga is "a horizon open to far away experiences directed mainly to the future"[1,p.73]. It is in this context, the "artesian-fountain-time" that the soul, described by the author, has the "definite and straightforward essence placed in the dimension of future". And, it has "the significance of a continuous departure in relation to an initial point, which has been endowed with a supreme value", which, in Blaga's opinion, "neither the present nor the past can enjoy " because this type of time " is lived and understood by itself". The soul that experiences it will find out that time "has the gift to continuously raise the level of existence", *being a creator of higher and higher values* [1, p.74]. Could Blaga have spoken about immortality? Evolutionism and Hegel, understanding the evolution as being "a progress from chaos to a more organized cosmos", which means that they considered it to be a transition from "a lower level of equilibrium to a superior one". Therefore, it would mean that the world is "the more heterogeneously organized in established and balanced systems the more advanced in time it is"[1,p.76]. In other words, the Romanian philosopher ascertained that *time is given creative virtues.*

"River-time" is focused on perpetual present. "The present of yesterday, of today and of tomorrow is ever considered as existing for itself, self-sufficient", as Blaga stated in the *Trilogy of Culture* ,being "neither a step towards something higher that is to come, nor a stage of dissolution of something higher that was already". In other words, this time is wholly included in the present moment, but, at the same time, in everything that was or can become a present moment". And "no moment exists only as a transition towards the next moment, but it is an aim in itself and for itself" [1,p.74] An aim in itself and for itself may be the immortality of a personality, which has become a cultural patrimony of a nation, why not even the immortality of this nation conceived as a people.

The "water-fall time", a horizon of "some feelings whose supreme values based on the dimension of the past", is given by the philosopher "the significance of a continuous departure from an initial point, endowed with the highest value"[1,p.75]. In this *short and vain flight* through life, man can discover himself, understand himself, and to create and the chosen ones, to be able to return into the cosmos, becoming by their immortality a song, "penetrated by eternity calls", which could remain in the patrimony of the nation where it was born:

"Hallelujah, my eyes can see the birds and the wind,
I do not owe a single thought to life,
But I owe it my whole life"
……………………
From the leaves of the village I come out
As from a biblical tent.
Hallelujah, today, as never before,
I am the tired brother
Of the sky below
And of the smoke coming down from the hearth.
(*Fallen smoke*)

Accepting Hegel's theory, according to which *time creates the conditions for ideas and for Divinity to reach the dialectical achievement in the historical context*, Lucian Blaga asserts that time is " an ascending ladder of the idea in its historical embodiments" or even " Divinity's path to itself" [1,p.76]. As *no moment is an end in itself*, *any second being dominated by the following one*, the lyrical philosopher ascertains that *the past and the present are only stages, fulfillment will be achieved in the future. By definition, time means a growing enhancement, a continuous amplification of values. It goes without saying that this "artesian –fountain time" is also the unconscious substratum of all progressive ideas* [1,p.77].

Exegetes move from an *objective* silence regarding the universe to a *subjective* silence, the poet's personal, inner silence. It is also to be noted" the existence of a mute quietness and a musical quietness" [2, p. 125]. Being "a person of departures and interrogations" [3, p.90], man in Blaga's view adapts himself to the *abyss of sleep* because he experiences all the nuances of the abyss, passes through all the stages created by the philosopher in his research and in his essays gathered in trilogies. Unlike Jung, Blaga considers the abyss from the height or from depth of the *creative power*, which is in itself an endless abyss of ideas, preoccupations, boldness and essence of a well delineated aim, an achievement leading to a fertile posterity. Blaga's ego goes along "this path from the solitude of restlessness to the solitude of his human being confronted with destiny":"In my solitude, I, the earthly being in tears,/ I stay awake close to my hearth of passions./
A soul fallen in loam like between pillows-/ no tidings –can give me rest./
(Close to the Hearth)

This is proof that Blaga, making the *Ego of the creating power*, was creating the time of the future, the *time of immortality* means that *despair* is not found in his poems (neither in dramaturgy: Zamolxe enjoys his death, Master-Builder Manole buries Ana in the wall). Blaga's ego cannot be *perplexed* - it builds itself, it rises, creates itself having all the most powerful possible qualities "whatever cannot burn, cannot be destroyed, it is the self" [2,p.104] – or even more obvious: *self consciousness* of absolute power: in the night, somewhere, there is everything that was and is no longer/ that has moved away, that is lost/from the living time, from the silent time./(*In the night, somewhere, it is*). While a piece of work by Blaga "has been taken away by the wind" [4. P.14], as the poet's daughter remarks with sadness,

because in the literary world "Blaga played a role model [4, p. 19), his monumental work was carefully taken care of, with responsibility to protect it from that "wind" of hard times. While "all the dead go away/ somewhere, each of them / . Going away with close eyes / They turn off their light/ (*Their Path*).

Having the talent to penetrate the most remote cosmic depths, the least known soul corners, Lucian Blaga (the man and scholar) is aware that: " each and every corner of our soul has so much resonance of everything going on in ourselves, that, quite often it seems to me that each idea has its heart beating for something – and every feeling has a mind to think" [1. P.38]. Pointing out several important relationships, the philosopher, in fact, finds what he has already discovered for a long time. The poet picks up an idea, the philosopher only gives it a name, he puts into light relationships which he, later on, admires : an intensified *mystery*. Being placed between the "horizon of mystery" and the "idea that comes back with a changed role", opposing the "metaphorical nebulosity", by limitation defeating limitation, the philosopher opens up towards what is universal, the *Mioritic space* being the work by which " this Romanian man has fallen at great honour", says Constantin Noica, adding "in Blaga's vision". Mioritic: Romanian geographic space with mountains and valleys, good for shepherding; a spiritual Romanian universe whose matrix is represented by the Romanian geographic space. The mioritic space, a term created by Lucian Blaga, refers to the Romanian soul connected to a deep spatial horizon looking like a wavy plan alternating between hills and valleys)

Rising up by *falling at great honour,* Lucian Blaga was looking for the art "which was not yet foreseen by artists", while he would enlarge the mioritic space according to the necessities of the *creative power* preventing it from stifling. Academician Mihai Cimpoi asserts that, in this context," Blaga expresses his pleading". And if *expressionism* was the impulse and the urge for him to *Europenize*, no less visible is the *stylistic matrix of the diplomatic space* in which Lucian Blaga lived, while he was creating his time or his *immortality* or the eternity of the *Mioritic space.* Making use of expressionism, his admiration for Goethe and Dostoevsky will not quench his *longing for* his country, which meant for him the most lasting material out of which the *creative power* emerged, beingthe foundation,even the *stylistic matrix* on which an edifice was rising right in the *centre* of the seismic zones. His philosophical search will not be an obstacle in his he career of a diplomat. Led by a formative appetite, by the high passion of becoming, the horizon is a circle which changes its centre and circumference, it is a circle that explodes. The idea in it continuously undergoes a mutation and a permutation: it is subject to all becoming avatars, so that, it cannot be equated, as Kant did, to its *a priori* function. In this period of time, Blaga's great appreciation for Brancusi or Titulescu is not accidental. Lucian Blaga's genial intuition could easily identify a personality, especially one with a creative power like his, no matter what domain of activity such a person could have, he could sense the *historical personality* from the space of eternity. That is because *Man is the being placed in the "horizon of mystery" for revelation by means of cultural creations*. (Anthropological aspects). The lyrical philosopher says that even "history does not achieve final conquests". In the *Trilogy of culture* and in his poems, Blaga warns about his coming back.

"I would grasp the hand of time to feel
Its pulse with its scarce seconds.
What would be going on on the Earth now?

May the same stars fall like flocks on its forehead
And are the swarms of bees still fly
From my bee hives?"
(*Thoughts of a dead man*)

Engrossed in the *time of his life*, especially concerned with the *time of his immortality*, the lyrical philosopher from Lancram will seek in his philosophical essays and in his lyrical poetry to find the right place for several essential categories, which refer not so much to time, but more to the immensity of time: " Only in trees the rings of age/ are enlarging ./In my body time grows slowly/ weaker from one day to the next one, under the celestial vault." (*Ecce tempus*)

Personally involved in the dialogue with time, the poet creates in his first books a *time of transition,* of *dispelling* … in other words, it is *the time seen as the great transition towards measuring the unraveling*, (The Great Transition, 1924, motto: *Stop the transition. I know that where there is no death, there is no love- nevertheless, I pray: Please God, stop the clock with which you measure our unraveling).* In the poems written in the second part of his life, time according to Blaga is overflowing (On the Great Water Divide) it becomes space, eternity and steps to infinity. Convinced that "never an end will be" (Clock) and time goes beyond the limits of the earth, becoming space, becoming deeds, becoming a human being … concluding, becoming *living time.* The lyrical work written by Blaga is most likely to produce *living time.*

In a number of exegeses regarding Blaga's work up to 1989, the **mute time** was discussed in the most simple way, even in a simplistic manner, starting from Blaga's silence in his early years of life. Now, in the third millennium, studying the poem from which we quote: *"Lucian Blaga/in his country is/ mute like a swan*", we find out that this verse is not a confession about his early years in life, this poem is a call, the philosopher's great sadness who conveys to the future the fact that the philosopher is banned, that he is intimidated morally and physically by the system, that he lives a mute time, he himself being the time .Even more, Blaga feels himself to be that **time without homeland:**

"Time without homeland: river without water,/drought in the river bed and under my eyelids.
Time without homeland: hearts defeated,/sterile ages, extinct senses.
Time without homeland: grayish story,/ roar of the black fir-tree branches over the top of mountains.
Time without homeland: un ploughed land,/ dead lights and burned souls.
Time without homeland: extinguishing the torch,/ unfriendly vault, the bell of fate.
Time without homeland: bitter love,/ rivers longing for rivers and wax."
(*Time without homeland*)

With a correct intuition and a proving to himself his visionary spirit, Lucian Blaga transforms the *time without homeland into transcendental time,* moving into another century in which, he, the creative essence, as *"an anvil acquires with time all the strength of all hammers that has knocked it"*[5,p.161]. Merging into the endless history-time, into the time of immortality of the next century: "Of all things, time makes us think the most", the philosopher discovers that the "Time", *the fairy tale element of reality,*, being after Blaga "one of the greatest secrets of time (relativity)", which he discovered from fairy tales before discovering it from Einstein" [5,p.226].
Endless time, the logical dimension which can be immortality or even eternity itself, this

"*immense world",* with everything that has been going on in a lifetime *"with its autumn and its evening*", presented by the poet, we find that it is life itself with its past, its present and its future *"grafted on my being"* – this is the time faccording to Lucian Blaga. *Time* according to Blaga*,* present in each of his poems, has the most various spaces, "unlimited" in the shortest or endless span of time, during an *autumn* or during an *evening* and all this time is *grafted upon the* human *being* of the creative power:

"A stray wind wipes away its cold tears/ on windows. It rains.
Obscure sadness comes upon me, but all/ pain/ that I feel I do not feel it inside me,
In my heart, in my chest, but in the drops of rain that fall.
And grafted upon my being the immense world/ with its autumn and its evening
Hurts me like a wound. Clouds with full udders go towards mountains.
And it's raining."
(*Melancholy*)

Assessing the "spiritual dimension" of the *creative power as being the absolute power,* Lucian Blaga also found the dimension of time, and the dimension of metaphorical space and the dimension of communication between conscious and unconscious and the dimension of the eternal moment for the necessity of the dimension of transcendence which cuts across "limitless space" because "the centre of the universe is in each Self" [2, p.34]. Belonging to *the first Romanian generation not previously conditioned to achieve a historical objective* (Mircea Eliade), the lyrical philosopher from Lancram makes ample use of *the short historical respite* after the Great Union and creates the philosophical system of the *time of the Romanian culture.* As the collective memory points out, time distributes everything in the right place.

"We find ourselves contemporary with those from the future", prophesies the young Lucian Blaga as a 120 year old wise man would have said. This vibrant and lucid conscience " in a permanent dialogue with his epoch and the spirit of his time", Lucian Blaga started to make himself a *creative power* from his first poems and philosophical pamphlets, then, with his articles and essays even with his trilogies, which quite often are called philosophical essays. The *accountable negligence* of the "river-tine" regarding a great Man of culture, statesman, diplomat, philosopher, poet, publicist, Ambassador of the Great Romania, justifies us, who do not come from the domain of letters, to contribute to capitalize the immense amount of the cultural and philosophical patrimony of the greatest value. By this research we express the truth that we consider ourselves to be *contemporary* with Lucian Blaga, not only because we have a *past times to unearth,* but also because we see ourselves to be *contemporary with those belonging to the future.*

Those aspects which "will be connected with the plastic elements of the substance of the soul are also linked to the unconscious horizon of the creator" as the philosopher asserts in *Horizon and Style*. And no matter "how abstract the metaphysical conception may be, it is always penetrated by the veins of lyricism proper to the human soul". Lyricism and metaphysical spirit, each having its own paths, "sometimes are closely connected due to the unconscious horizons of the soul". Speaking about the difference existing between lyricism in a metaphysical conception in the perspective of "waterfall-time" and the metaphysical conception from the "artesian-fountain-time" perspective, Lucian Blaga exclaims: "What a latent, troubled, underground melancholy resides in one; what explosions possible of trust and joy,

what a seed of light in the other one"[1, p.85]. To *trust Time* is the "most mysterious extension of our being" (*Patience* from the "Island's Elan") These "*possible perspectives"[*1, p. 84] of Time according to Blaga are that " beneficial suffering experienced by Blaga in his progress towards another century, towards eternity.

Conclusion

We live the time of Blaga's immortality. Starting from beyond the time in which the young man from Lancram experiences a "violent intellectual curiosity", satisfied through "the most amazing passion for reading", reaching the time in which his creative power builds its posterity, we can see how the philosopher of today created his immortality. Eternity was born in the countryside as Blaga says and he, the creator, creates his way in life. He expresses his world, he "subdues the world" and skillfully transforms it into "the image of his soul" by which he expresses himself even today. Being a creative power of life, of the "praise of existence", Lucian Blaga has chosen to create a work which can maintain his immortality. Even the idea of the "devouring time" is unbearable for the lyrical philosopher and he will "restore" the direction of time creating by his lyrical and philosophical work a perpetual recovery of his time, eternity.

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REFERENCES

1. Blaga L. Trilogia culturii. Bucureşti, Humanitas, 2011.
2. Popa I. Glose blagiene II, Târgu Mureş, Ardealul, 2005.
3. Einstein A. Cum văd eu lumea. Teoria relativităţii pe înţelesul tuturor. Bucureşti, Ed. Humanitas, 1996.
4. Blaga D. Tatăl meu, Lucian Blaga. Bucureşti, Humanitas, 2012.
5. Blaga L. Aforisme. Bucureşti, Humanitas, 2008.

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Mother of god in bulgarian healing rituals

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ABSTRACT

This paper deals with healing rituals in the Bulgarian traditional culture, in which theMother of God plays the central role. Her image is very different from the Christian canonical one. One of the differences is that in the healing incantations, Mother of God is presented together with God as a couple. Additionally, according to the folk beliefs, Mother of God is a patron of some healers and some of them also claim that she has taught and has been guiding them in conducting properly the healing rituals. The healing incantations speak of her as a mistress of the elements, ruler of the forest nymphs called samodivi. She appears on crossroads when she hears the cry of the sick. All these functions and other special features bring her closer to the ancient notion of the Great Mother Goddess than to the Mary of the Bible.

KEYWORDS:
Healing rituals, magic, Goddess, Mother of God

The concept of the divine in the image of the Great Mother Goddess is attested in South - Eastern Europe and especially on Bulgarian territories from prehistoric times (at least from 8-7millennium BCE). This concept may have its origin in the prehistoric epochs, but in time it was developed by various peoples and cultures, which were present at different times on the territory of modern day Bulgaria. So, for example, in the Thracian culture this prehistoric veneration continued and subsequently passed to other newly arrived ethnicities like Slavs, proto-Bulgarians etc., who, on their turn, enriched it with beliefs and rituals of their own. The substratum of ideas and practices have not prevented the survival of the old ones and in some cases turns out to be a favourable ground for the existence of many archaic rituals and beliefs, which have typological parallels in the corresponding geographical region. Coming and going religious structures have given a different configuration of these ideas. So, the primordial, all-embracing Great Goddess has been named in various ways and was evoked in different ritual manifestations. These names or better say ‘namings’ and images changed in time. The local Thracian epithets of the Goddess during the Hellenistic and the Roman age were ‘translated’ according to their pantheon conformities. Thus, on the monuments from this age she was known as –

Artemis, Diana, Cybele, Hekate, Aphrodite, Demeter etc. (1). Later on, the Slavs called her Mokosh, Ladaamong other names. From the Slavs and their pantheon, we have got only scarce information, primarily from the written tradition, but this material is very limited. From the literary sources we understand that the ancient authors also identified the Goddesses worshiped by the Slavs with their ancient counterparts. As an example, we mention the relationship existing between the Slavic Goddess Mokosh and the Goddess Hekate (2). Most likely, proto-Bulgarians also brought with themselves their own concept, which was later connected with the image of the Great Goddess they found on these territories.

With the adoption of Christianity, the ancient images and concepts of the Goddess assumed new names (3). People kept their far-off beliefs and rites, but transformed them once again in order to preserve them. It is unlikely that this process was conducted deliberately and on purpose. More likely, the natural admiration and the necessity of unity with nature were the reasons for seeking ways of preserving the rituals and beliefs, which offered the possibility to interact with it. There is some evidence regarding the way pre-Christian rituals were performed after the adoption of Christianity (4). It is of a particular interest some information from the hagiography of St George the Hagiorite in the 10th-11th century CE regarding a village in the Rhodope Mountains where, at that time (5), a marble statue (6) of the Goddess was worshipped by the local population and the saint George the Hagiorite broke it into pieces in order to enforce Christianity. This evidence confirms once more the strength of people's inner necessity of having their Goddess. The marble image might be broken down to pieces, but the sacred springs, the sacred caves, the sacred home hearths, remain and continue to be the places, where, to the present day, the proximity of this power, which the ancient people sometimes just called the Great Goddess, keeps on being sought and experienced. In ancient times she was called Bendis, Hekate, Zerynthia, Cotyto, Cybele, Artemis, Demeter and in numerous other ways, now she is called Maria, Marina, Helen or even in a different way. But, today, the Goddess continues to be present and venerated in rituals, because in this way the Christian female saint remains a Goddess.

The magical rituality including the healing rites is a very conservative type of folk knowledge. One other reason for the preservation of so many very archaic features is that it is kept in secret and the influence of the so called official culture is not as strong as that of other types of rituals and beliefs, which are open to the public. As a result of that, in this paper I will give some examples of how the image of the Virgin Mary is perceived in a very different way in comparison with the Christian canon. In the magical rituals and especially in the healing rites, the Virgin Mary is at first anonymous. She is called 'the Mother of God' as it is usual in the Bulgarian folk tradition, i.e. it is important to point out her function as Mother and as divine Genetrix. It is a common fact that she is invoked together with God as a couple. In some cases she appears alone being the only support for a sick person.

In the ancient ritual texts, as in the Hittite ones (but not only there), the Great Mother Goddess was invoked for help in various diseases. She was the force, who brought order and restored good health. At the same time, the Great Goddess was believed to have power over all supernatural forces and, so, she was the mediator who could get help from the benevolent ones and to chase away the malicious ones. So, in the Hittite myth and in

conjuration of fire, the following description is to be found:

„They have sent:
…
they have sent the illness,
they have sent the illness of the eyes,
they have sent the illness of the feet,
they have sent the illness of the hands,
they have sent the illness of the head,
to disappear from it the warmth
and it has cried out.
The sea has asked it:
Why are you crying?
The fire answered:
The warmth has disappeared from me…“ (7)

Almost the same structure and meaning are to be found in the following incantation against the evil eye from the Bulgarian traditional folk-magic:

„…they have strocked (the name of the person),
they have cried out, they have screamed;
they have taken the dream,
they have taken the face,
they have taken the eyes,
they have taken the head,
they have taken the body,
they have taken the feet,
they have taken the eating,
they have taken the drinking.“ (8)

In the cited Hittite ritual the fire cried out and this cry was heard by the sea, but after that, the fire asked for help fromthe Goddess Kamrusepa. It is a similar case in the Bulgarian healing rituals, but there, the role of the Great Goddess is played by Mother of God:

„…(name of the sick person) has cried out.
The cry was heard by Mother of God…“ (9)

This is one of the most widespread motifs in the Bulgarian healing incantations – the sick person cries as he suffers from some disease and pain and Mother of God hears this cry and comes to help. Here I will present one such incantation, which is interesting because it has a very clear ancient counterpart.

INCANTATION AGAINST THE MODRITSA (10, 11)

Mother of God was on her way,
(she met) the Modritsa coming towards her,
she asked her: “Where are you going?”
– I am going into the mountain.
– I will send you,
I will send you away from (the name of the sick person),
here is no place for you,
here they cannot take care for you,
they cannot make up the bed for you,
they cannot cover you.
There in the green forest,
there are seventy wives,
seventy unmarried young women,
seventy unmarried young men,
there they will take care for you,
there they will make the bed up for you,
there they will sing for you,
there they will dance a ring dance for you.
There are seventy apostles,
they will take care for you,
all the heavenly saints will do that.
Just as the fair disperses,
so shall the misfortune disperse,
just as the market disperses,
so shall the misfortune disperse,
just as the salt put in water disperses,
so shall the misfortune disperse.

The first part of this incantation is almost the same as in an ancient healing incantation inscribed on a silver lamella dated in 1-2 century CE, where instead of Mother of God there appears the ancient goddess Artemis of Ephesos, also a Great Mother Goddess (12).

> For The 'Half-Head' [Migraine): Antaura came out of the sea. She shouted like a hind. She cried out like a cow.
> Artemis of Ephesos met her (saying): "Antaura, where are you going?"
> (Antaura): "Into the half-part of the head."
> (Artemis): "No, do not [go] into the [half-part of the head ...]. "
> Left edge: ... for the reliefs (?) ... .

One of the better preserved versions of this spell, commented on by R. Kotansky (13), has more common features with the Bulgarian folk spell.

> Migraine-prayer against the headache:
> Migraine came out from the sea rioting and roaring,
> and our Lord Jesus Christ came to meet it and said to it:
> "Where are you going, O headache and migraine and pain in the skull and
> In the eyes and inflammation and tears and leukoma and dizziness?"
> And the Headache answered our Lord Jesus Christ:
> "We are going to sit down in the head of the servant of God, So-and-So."
> And our Lord Jesus Christ said to it:
> "Look here, do not go into my servant, but be off altogether and go into
> The wild mountains and settle in a bull's head. There you may eat flesh,
> There drink blood, there ruin the eyes, there darken the head, seat and wriggle. But if you do not obey me, I shall destroy you there on the burning mountain where no dog barks and cock does not crow."
> You who have set a limit to the sea stop headache and migraine and the pain
> In the skull and between the eyes and on the lids and from the marrow from
> The servant of the Lord, So-and-So.

The difference is that, while in the Bulgarian spell Mother of God is the successor of Artemis, and Jesus is the one who helps instead of Artemis. The further part of the incantation describes the way in which sickness is sent into the forest, i.e. to the mountain and where the spirit of the disease has food and drink etc.

The next ritual to be discussed here is a complex rite including the use of herbs and other materials (leaves from nine kinds of fruit trees etc.), actions and incantation addressing Mother of God.

HEALING HERBAL BATH (14)

In the region of the town Slivent there was an old man, Stoyan Yordanov Sabev, 86 years old, living in the village of Zhelyo Voyvoda, who was very famous as a healer. Sick people also from North Bulgaria, used to ask him for help, because his ritual baths made with various herbs helped a lot of people with all kinds of sickness. In the past, it was a common fact to see more than 40 carts loaded with sick people waiting in front the house of the old man Stoyan. After 1927, he started to heal, when his mother died, who was also a folk healer. In his healing procedures he used baths to cure fear affecting for more than 3000 people. The way of making the ritual bath is as follows:

He was taking 41 species of herbs (15) as for example, burning bush (16), elecampane (17), valerian (18), lemon balm (19),

coltsfoot (20), hart's-tongue 21), commontoadflax (22), bathurstburr (23), male fern (24), St John`s wort (25), cross gentian (26), wild tulip, also leaves from nine kinds of fruit trees – pear-tree, apple-tree, plum-tree, common toothwort (27) and others. The herbs were boiled in water by the old man Stoyan and after that the herbal infusion was to be put outside in the garden, under the stars. Before having the herbal bath, the sick person was told to undress and the herbal infusion was poured onto him. The bath was done on Wednesdays and on Fridays, early in the morning, at about 5-6 o'clock and in the evenings at about 9 o'clock. While the patient was having the bath the old man Stoyan used to say the following incantation:

> Evil hour, evil harm,
> Mother of God has gathered them all, seventy seven,
> different faiths (i.e. spirits) unbaptized, unanointed (i.e. unblessed),
> there where there is nothing to eat,
> and nothing to drink,
> where there is also nothing good:
> Mother of God has brought them into the church,
> has sorted them out into various kinds and
> has set them free into the woods and
> has set them free as the she-wolf sets her wolf-cubs free.

After 20 days, they could find out if the bath had helped or not. After that, the healer used to give a second herbal bath. For these baths the old man Stoyan used also some other magical things– a hub from a horse cart, a wolf`s skull, a horn from a snake. These things were to be put on the head of the sick person at the time he was having the bath, while pouring the herbal infusion on him. The dirty water from the herbal bath was to be collected in a vessel and to be thrown away in some place, where nobody had stepped before.

As already mentioned, the ritual includes different elements – herbs, actions, magical attributes, time prescriptions, incantation. The only supernatural authority called for help here is Mother of God. She is called not only by the incantation, but also with the other ritual utensils. The herbs used in this ritual, especially some of them, as burning bush, elecampane, valerian, male fern, common toothwort and gentian are strongly connected with the samodiva, i.e. the forest nymphs. Boiling the herbs and then leaving the infusion under the open sky, under the stars, are very archaic elements in the ritual, known since ancient times and frequently attested in the ancient sources. The liminal time for doing the ritual before sunrise and after sunset has a symbolical meaning also connected with the idea of liminality and passing from one condition (illness) to another (health). Mother of God is the most impressive image in the incantation, because she is described as a ruler over all kinds of spirits, she gathers them and imposes order so that they cannot be harmful anymore. She chases away the spirits of the diseases into the woods, far away from the human world and from the cultural space. In the last sentence of the incantation, this action of Mother of God is compared with the notion of how the she-wolf takes her wolf-cubs into the woods. Here is something interesting to be mentioned, that, according to the folklore tradition, three ‘Mothers of God’ are worshipped – the Little, the Middle and the Big (28). The Middle is honored on November 21-st and is considered to be the mistress of wolves – “This Mother of God gives orders to the wolves” (29). According to the folk belief, these three ‘Mothers of God’ are sisters (30). The Triple Mothers of

God are strange because their presence is unacceptable from the perspective of the Christian canon, but in the folklore tradition there is no obstacle to rule out their existence (31).

INCANTATION AGAINST EVIL EYE (32)

Three lumps of sea salt are taken. The healer (female or male) stands in front of the ill person. The lump is taken with the right hand and whirled around the head of the person while saying:

God's mother sat at the crossroad,
tucked up her white sleeves,
began to spin a black tow and said:
-Wild samodivi,
cross over nine forests,
over nine cold waters –
to bring our child a cure.
If it comes from a male –
From the male let curse of the evil eye burst forth.
If it comes from a female –
From the female let the curse of the evil eye burst forth.
If it comes from a male –
Let his left testicle burst;
if it comes from a female –
left breast burst.
As the people
scatter from church,
soshall the evil eye scatter
from the waist,
from the heart,
from the little nails.
As the line dance scatters,
So shall the evil eye scatter
from the waist,
from the heart,
from the little nails.
Yesterday three brothers were born,
Yesterday they were born,
yesterday they began to walk,
yesterday they began to speak
and they took fast horses,
and went into the Tilileyan forest (i.e. a mythical far away forest)
to cut a tree –
from the top down,
from the roots up.
When it happens
this child to sit
under that tree,
only then can it
be cursed by the evil eye.

In this healing rite, that aims to remove the influence of the evil eye, the divine support is again Mother of God, but she is described veridically as an ancient Goddess. So, she is invoked and makes her divine appearance at the crossroad. The Goddess is invoked using one of her signs – the salt, which in the Ancient Rome was honoured also as another Goddess called Salus. In the incantation, the dual nature of the Goddess is designated by the white and black and, thus, she resembles more the image of the Thracian goddess Bendis, who was called in Ancient Greek **dilonchos**– the one with the double spear, the lexicographers explained that the Goddess was honoured both from the earth and from the sky. The Goddess is asked to reorganize the Cosmos both on the horizontal level – represented by the crossroad, and on the vertical level– represented by the spinning. The spinning itself again directs us to the image of Bendis being described as a spinner (33). With her spinning the Goddess creates the connections and threads in the Cosmos, i.e. she connects (34) it and generates its unity, unifying the vertical and the horizontal. In the healing incantation-charm the Goddess gathers around her the samodivi, these successors of the ancient nymphs, which in folklore are believed to be healers as well. So she acts as their leader and mistress and in this function.

After resorting to the healing nymphs (the samodivi) in the incantation, there follows a segment based on the principle of associative magic – 'as-so'. The spoken destruction of the sex characteristics of the person causing the illness has also the goal of destroying the effect of his deeds. The sex characteristics in this case represent the power of the person causing the illness – the testicles of the man, the breast of the woman.

In the last part of the commented incantation the three brother riders appear, who are sent to the world beyond with the charm to bring a tree, under which the ill person should sit and only then could he be harmed again, i.e. the last part of the incantation is for the future protection of the patient.

CONCLUSION

The traditional societies, such as the Balkan ones, including the Bulgarian society, until the middle of the last century, have maintained the connection of the ritual with the cultural tradition despite the official religious doctrine (Christianity or Islam). Keeping this connection and performing the rites, as they were done for centuries, have enabled the preservation of powerful archaic ritual practices. They refer to the mythical concept of a force, which appears as mother of All, as a healer, a zealous mother-guardian. Speaking about the above practices, we see that the Christian female saint remains a Goddess in the ritual. She is still invoked as a main figure to bring health to the body and soul to those who pray to her.

REFERENCES

1. **Fol, V. Popov, D.** TheDeities of theThracians. Sofia, 2010, 66-68.
2. See Sermon of St Gregory the Theologian (893 y.): "Goddess Ekatia (Hekate) for virgin they proclaim her and Mokosh they venerate...." online: http://liternet.bg/publish/akaloianov/slovo.htm<20.10.2011>.

For the traces of the cult of Hekate in Bulgaria see **Mladenova**, **Y.** Images of Hekateinourlands. // Archeologymagazine 1961, b. 3.

Many scholars comment and think of an explanation for the Thraco-phrygian origin of the cult to Hekate, because she is perceived by the Hellenes as a foreign deity, bearing strange features and rituality and was perceived as a barbarian goddess, see **Zeleny**, **K.** Die GöttinHekate in den Historiae Deorum Gentilium des LiliusGregoriusGyraldus (Basel 1548) unterbesondererBerücksichtigung der RezeptionHekates in humanistischen Handbüchern und Kommentaren des 16. Jahrhunderts, Wien, 1999, 12; **Ronan, St.** The Goddess Hekate: Studies in Ancient Pagan and Christian Religion & Philosophy, Vol. 1. Hastings 1992, 23-24.

3. For such examples see **Kraemer, R.** Women´sreligions in the Greco-RomanWorld.New York/Oxford 2004, 85-86.
4. SeealsoNikolova, M. Pagan and Christian motifs in the Christmas song about the birth of the "Young God". // Crypto-Christianity and religiouss yncretism in theBalkans.Sofia 2002, 69-76.
5. This happens about two centuries after the adoption of Christianity in the First Bulgarian State in 864.
6. **Gerasimov, T**. Information about a marble idol among the Bulgarian Slavs in theThessalonikiregion. // Linguistic-ethnographic researches in memoriam Acad. St. Romanski.Sofia, 1960, 557-561.
7. Translated into English by Georgi Mishev from the German publication of the Hittite text by F. Fuscagni (ed.), accessed at: hethiter.net/:CTH 457 (TRde 05.02.2013).
8. **Pirgova**, **I**. Traditional healing rituals and magical practices. Sofia, 2003, 150.
9. Ibid., 353.
10. Collection of Bulgarian Folklore and FolkStudies 11. Sofia, 1894, 87.
11. Modritsa is called the spirit, which causes pain felt over the entire body, also joint and muscle pain.
12. The text and the image are cited after Kotansky, R. Greek magical amulets: the inscribed gold, silver, copper, and bronze lamellae. Text and commentary by RoyKotansky. [In Zusammen arbeit mit derArbeitsstelle für Papyrus forschung im Institut fürAltertums kunde der Universität zu Köln].(Abhandlungen der Rheinisch-Westfalischen Akademieder Wissenschaften: SonderreihePapyrologicaColoniensia; Vol. 22), 60.

13. The text is cited by Kotanksy (Ibid. 61).
14. **Yanakieva, Zh.** Folk healing in the region of Sliven. Sliven, 1980, 4-5.
15. The identification of the herbs is my suggestion, because in the ethnographical record there are some unclear names of some of the mentioned herbs.
16. Dictamnusalbus.
17. Inulahelenium.
18. Valerianaofficinalis.
19. Melissa officinalis.
20. Tussilagofarfara.
21. Phyllitisscolopendra.
22. Linaria vulgaris.
23. Xanthium spinosum.
24. Dryopterisfelix-mas.
25. Hypericumperforatum.
26. Gentiana cruciate.
27. Lathraeasquamaria.
28. The Wolf Mother of God is considered to be the middleone, because the other two celebrations dedicated to Mother of God are respectively Little Mother of GodonSeptember 8, i.e. the birth of St Mother of God and Big Mother of God on August 15, i.e. her Assumption. Thus theWolf Mother of God is the middle one, because she is situated between the other two, i.e. between her birth and her death.
29. For the continuity of this calendar cycle and the in formation about the Wolf Mother of God see **Marinov**, D. Religious folk customs – selected works in 5 volumes, v. I, part 2.Sofia, 2003, 397-402.
30. Ibid. 398.
31. The double and triple images of saints are an interesting phenomenon in the folk beliefs and usuallyit is due to strong pre-Christian groundings of the worship, in this connections ee **Popov**, R. Twin Saints in the Bulgarian Folk Calendar.Sofia, 1991.
32. **Pirgova, I**. Traditional healing rituals and magical practices.Sofia, 2003, 139-140.
33. As a whole, the image of the Goddess in her function of a Mistress of Fate is commonly connected with knitting. This image is known from the Hittite ritual texts, see **Bossert, H.** DieSchicksalsgöttinnenderHethiter. // DieWeltdesOrients.Bd. 2, H. 4. 1957, 349-359.
34. It is likely that the name Bendis can be interpreted as originating from the Indo-European bhendh “to connect” exactly in his sense as the One, who connects and unifies the elements and thec osmic forces.

BPI Bulletin of Integrative Psychiatry
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Book Review

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Buletin de Psihiatrie Integrativa

The Italian experiment, fruit of Italian experiment

Author: Mario Di Fiorino
Review signed by Prof. Vasile Chiriță, Ovidiu Alexinschi

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Ovidiu Alexinschi-MD, senior psychiatrist, Socola Institute of Psychiatry Iasi, Romania

Nowadays, Mario Di Fiorino is well-known not only for the peculiarity of Psychiatric Reform Law in Italy, but also for having framed the Italian deinstitutionalization in the history of ideas, the thought of Italian psychiatrists. Also abroad Franco Basaglia is known for the radicalism of the reform that inspired.

The new book allows us to grasp the specificity of this operation, which has been very different from similar processes in the USA and the United Kingdom.

In fact, in Italy the ideology weighed, the reform of 40 years ago was born from a compromise between the Anti-psychiatry movement and a leadership of the Italian Psychiatric Society, accustomed to give up not to lose, and to survive in every regime.

"If we want everything to remain as it is, everything must change" the conviction of Tancredi Falconeri, nephew of the Prince of Salina in "The Leopard", has marked the choices of the ruling group of Italian psychiatrists, who grossed with the law 180 the entry of Psychiatrists in the General Hospital, however, at the price of renouncing the presence of a psychiatric institution for the most serious mental disorders.

So the Italian Psychiatric Reform over a few years, has closed all psychiatric hospitals, also preventing the construction of new hospitals. Deinstitutionalization has led to the massive transfer of severely mentally ill persons out of institutional care in favor of community psychiatry. According to a realistic estimate from the years 70s to 2000, public psychiatric hospital beds dropped from 207 to 21 beds per 100,000 persons (Manderscheid et al. 2004).

To understand the cultural climate of deinstitutionalization we must start from the Counterculture of the 1960s, an anti-establishment cultural phenomenon that developed first in the United Kingdom (UK) and the United States (US), expression of culture that Alexander Mitscherlich appointed *“Auf dem Weg zur vaterlosen Gesellschaft” Society Without the Father :* the Civil Rights Movement, with claims of experimentation with psychoactive drugs, the rejection of

conventional social norms regarding human sexuality, women's rights.

In Italy the attack launched against psychiatric discipline and institutions had meaningful success, when the ideas and the anti-institutional struggles reached the goal of inspiring the Reform Law with a radical closure and dismantling of the mental hospitals in the whole country. It was one of the most radical attempts in history to abolish the practise of custodial psychiatry using legislation (Pycha et Al., 2011).In May 1978. Franco Basaglia inspired Psychiatric Reform Act (Law 180), and the anti-psychiatric Utopia came to power. In December 1978 the law merged in Law 833, that introduced National Health Law.

The duty to protect is the task of the psychiatrist as is now testified by the sensitivity of the judiciary and legislative power. In this context they must enroll the rights of the sufferer, on the side of respect for the dignity of his person, and of his right to care and protection. For the alienists, the psychiatric hospital, the Asylum, constituted the typical building of raison, the result of a medical thought impregnated with utopia and strong social values.

The "Hospitals for fools " were conceived to function as a "healing tool", great pedagogical institutions, effective machines against madness, to be entrusted in the hands of a psychiatrist capable The "Machine to heal" is a kind of poisoned fruit of the Enlightenment, the Century of *Raison* that we are accustomed to consider as a positive moment of the history of mankind for the scientific emphasis and the utopian urges, elements that soon however spoil themselves with respect to the intentions of those who conceived them, and not only in kindergarten.

As the Horkheimer and Adorno argue, authoritative exponents of the Frankfurt School, in the Dialectic of the Enlightenment (1947), that Enlightenment is a century full of good intentions for the good of mankind that ends up producing great distortions. In the Enlightenment, in the very idea of being able to control and bend nature to human reason, the worst totalitarian regimes of the twentieth century are rooted. And in this there is no different experience of the birth of Asylum: conceived as a "machine to heal", before the advent of drugs, become a concentration universe for chronic patients.

Foucault did not want to see the constructive aspect, albeit of utopistic matrix, the thrust to the construction of an ideal world governed by *Raison* and sees the institutions as emanations of power, who want to control, supervise and punish the diversity and deviance. The thought of Foucault, which has permeated the anti-psychiatric movement, has represented in Italy, for decades, a sort of unique thought, of soft dictatorship.

The Foucaultian Franco Basaglia has exercised in a charismatic way a cultural primacy in large sectors of Italian society, unimpeded to any criticism. And that this has assumed an almost religious dimension testifies to that sort of secular pilgrimage carried out by a papier-mâché horse, "The animal of good conscience", dragged through Italy in a visit to all the Forensic hospitals (OPG) before their closure, with the culmination of the awarding of the medal to Marco Cavallo, officiating the President of the Italian Republic Napolitano.

With the proposal of bill (Senate Act 656), which has as its first signatory the senator Raffaella Marin (2018), Italy would standardize its legislation to that of the countries of Europe and North America where, after a first period linked to the emergency conditions, the extension of the limitation of liberties (with the obligation of hospitalization and the obligation to undergo treatment) is ordered or validated by the judge. Within 6 months of the promulgation, the Regions will have to identify psychiatric

hospitals for the hospitalization of 40- 50 patients. The new proposal for an Italian Reform, at Mario De Fiorino proposal and signed by senator Marin reclaims society's obligation to provide adequate care and treatment - and, when necessary, asylum, to persons with severe mental illness. According to De Risio (2019) “in this view, the possibility to add to the existent network of community services a group of specialized units for a protracted hospital stay in the most severe cases of acute mental disorders (Di Fiorino et al., 2018) would help in containing the severity of symptoms. Such a unit of offer would arrest the derangement induced by the ‘crisis model’ in large urban contexts, where the patients are still today mainly entrusted to their relatives. The persistence of a virtuous course of care will be maintained only if the unit of offers for the mentally ill patients will differentiate, so as to allow the support of them in an individualized style apt to let them pursue a satisfactory and profitable interior experience.”

In synthesis, the book is a reference work, which combines information, biographies, magistral notes and comments skillfully comprising both history and future, making possible the new reality of today - the pendulum, after having carried out its oscillation towards the pole of the defense of the rights of freedom of choice even of those who are not able to choose, returns to reconsider, in key beneficiary, the pole of the right to care and protection.

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