

ASILUL DE ALIENATI
SOCOLA IAȘI
INSTALAT ȘI S'A DESCHIS DE
DOCTOR AL. BRĂESCU
MEDIC PRIMAR ȘI DIRECTOR
IN ANUL 1903 OCTOBRE 12

1-ère Année. Juin 1919. No. 1.

Bulletins et Mémoires de la Société
DE
Neurologie, Psychiatrie et Psychologie
DE
→ JASSY ←

SOMMAIRE :

Séance du 9 Septembre 1918.
Constitution de la Société et Statuts.

Séance du 7 Octobre 1918.
M. G. Préda : Remarques psychologiques sur notre guerre etc.
M. A. Stocker : La cholestérine dans la thérapie de l'épilepsie.
M. I. Scriban : L'involution de la queue du têtard et les myopathies.
MM. C. Parhon, Isanos et M-me H. Alistar : Contribution à l'étude de la démence sénile avec quelques remarques sur la vieillesse en général.

Séance du 4 Novembre 1918.
MM. G. Préda et J. Constantinesco : Un cas de sclérose latérale amyotrophique.
MM. C. Parhon et A. Stocker : Trois cas d'adénomes cortico-surrénaux.
M. P. Andrei : Psychologie du mensonge en temps de guerre.
M. G. Préda : Remarques psychologiques sur notre guerre etc. (suite)
M. D. Marinesco : Deux cas de tumeurs cérébrales.
M. C. Parhon : Essais de graphologie scientifique.

Séance du 2 Décembre 1918.
M. G. Préda : Suppléances dans les troubles neuro-psychiques.
MM. G. Préda et J. Constantinesco : Recherches sur le liquide céphalo-rachidien dans l'actuelle épidémie de grippe (dite espagnole).
M. C. Parhon : Remarques critiques sur un travail de M. Pitulesco.
MM. C. Popa-Radu et Jacques Goldner : Recherches sur les sourcils des aliénés.

Jassy.—Imprimerie «Progresul» A. Grünberg rue Stefan cel Mare 4.

Bulletin of Integrative Psychiatry. Buletin de Psihiatrie Integrativă

New series of “Bulletins et Mémoires de la Société de Neurologie, Psychiatrie et Psychologie de Iassy”, edited by “Socola” Hospital of Psychiatry Iași from 1919 to 1946

Serie nouă a “Bulletins et Mémoires de la Société de Neurologie, Psychiatrie et Psychologie de Iassy”, editat de Spitalul de Psihiatrie „Socola” Iași în perioada 1919 – 1946

Redacția/Editorial Board: Institutul de Psihiatrie „Socola” Iași / “Socola” Institute of Psychiatry Iași

Adresa/Address: Șoseaua Bucium nr. 36, cod poștal 700282, Iași, România

Telefon/Phone: +40 232 430 920

E-mail: buletindepshiatrice@yahoo.com; Web: www.buletindepshiatrice.ro

Images on the first page represent: *Inaugural board of “Socola” Hospital of Psychiatry Iași*

The cover of the first number of “Bulletins et Mémoires de la Société de Neurologie, Psychiatrie et Psychologie de Iassy”

The image on the first cover represents the main building of “Socola” Institute of Psychiatry Iași

Imaginile de pe pagina întâi reproduc: *Placa inaugurală a Spitalului de Psihiatrie „Socola” Iași*

Coperta primului număr din “Bulletins et Mémoires de la Société de Neurologie, Psychiatrie et Psychologie de Iassy”

Imaginea de pe coperta I reproduce clădirea principală a Institutului de Psihiatrie „Socola” Iași

ISSN: 1453-7257

Copyright © 2017 INSTITUTUL DE PSIHIATRIE „SOCOLA” Iași, România

The papers published in “The Bulletin of Integrative Psychiatry” are protected by copyright. Their full or partial publication in other journal is allowed only with the written approval of “SOCOLA” Institute of Psychiatry Iași, Romania.

Toate drepturile asupra prezentei ediții sunt rezervate Institutului de Psihiatrie „SOCOLA” Iași. Reproducerea parțială sau integrală a textelor, prin orice mijloc, fără acordul scris al Institutului de Psihiatrie „SOCOLA” Iași, România, este interzisă și se va pedepsi conform legislației în vigoare.

Published by “Socola” Institute of Psychiatry Iași, Romania

Publicație a Institutului de Psihiatrie „Socola” Iași, România

editura
doxologia

Revistă apărută sub egida Editurii DOXOLOGIA

Str. Cuza-Vodă, nr. 51, 700038, Iași

Tel.: 0232-216693, fax: 0232-216694

E-mail: editura@doxologia.ro; edituradoxologia@gmail.com

www.edituradoxologia.ro

Serie Nouă | New Series
An XXIV nr. 1 (76) | Year XXIV No. 1 (76)
Martie 2018 | March 2018
Frecvență Trimestrială | Frequency: Quarterly

BPI | **Bulletin of Integrative Psychiatry**

Buletin de Psihiatrie Integrativă



Official Publication of
"SOCOLA" INSTITUTE OF PSYCHIATRY
Iași, Romania

PUBLISHER: "SOCOLA" INSTITUTE OF PSYCHIATRY IAȘI

EDITORIAL BOARD:

Editor in Chief	VASILE CHIRIȚĂ, M. D., Ph. D., Prof., Honorary Member of the Romanian Academy of Medical Sciences
Deputy Editors	ROXANA CHIRIȚĂ, RADU ANDREI, CĂLINA GOGĂLNICEANU, LAURA PRICOP, CRISTINEL ȘTEFĂNESCU, ALEXANDRA BOLOȘ
Associated Editors	OVIDIU ALEXINSCHI, ANAMARIA CIUBARĂ, ROMEO P. DOBRIN, IOAN MIHALACHE
Editorial Secretary	ANA CATERINA CRISTOFOR, DANIA RADU, IRINA SĂCUIU, ILINCA UNTU
Designer	ELENA POPESCU

ADVISORY BOARD:

J. F. ALLILAIRE (France)	PETER KAMPITS (Austria)
VASILE ASTĂRĂSTOAE (Romania)	BERNARD KNIGHT (USA)
CONSTANTIN BĂLĂCEANU-STOLNICI (Romania)	MIRCEA LĂZĂRESCU (Romania)
VLADIMIR BELIȘ (Romania)	MARCEL LEPEE (Croatia)
MARIN BURLEA (Romania)	DRAGOȘ MARINESCU (Romania)
VASILE BURLUI (Romania)	ANATOL NACU (Republic of Moldavia)
GAVRIL CORNUȚIU (Romania)	AUREL NIREȘTEAN (Romania)
NICOLAE COSMOVICI (Romania)	BRIAN NISHARA (Canada)
ION COȘCIUG (Republic of Moldavia)	JASUJA OM PRAKASH (India)
ION DAFINOIU (Romania)	VALENTIN OPREA (Republic of Moldavia)
MICHAEL DAVIDSON (Israel)	FRANCESCO PIANI (Italy)
POMPILIA DEHELEAN (Romania)	DAN PRELIPCEANU (Romania)
MARIO DI FIORINO (Italy)	ELENA PRUS (Republic of Moldavia)
TUDOREL DIMA (Romania)	MIRCEA REVENCO (Republic of Moldavia)
VIRGIL ENĂTESCU (Romania)	DAN RUJESCU (Germany)
LIANA FODOREANU (Romania)	CĂLIN SCRIPCARU (Romania)
IOSIF GABOȘ-GRECU (Romania)	RENE STOCKMAN (Belgium)
MARIETA GRECU-GABOȘ (Romania)	MASATOSHI TAKEDA (Japan)
SIMON HABOT (Israel)	<u>GHEORGHE TALĂU (Romania)</u>
MIHAI HOTINEANU (Republic of Moldavia)	<u>TUDOR UDRIȘTOIU (Romania)</u>
ADINA HULUBAȘ (Romania)	DUARDE NUNO VIEIRA (Portugal)
	ALLAN H. YOUNG (UK)

PEER REVIEW

All manuscripts intended for publication will be subject to peer-review by a committee of experts which assesses the scientific and statistical correctness of submitted articles. Submitted manuscripts are screened for completeness and quality of files and will not enter the review process until all files are satisfactory.

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 Iași. 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 Iași”, 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.



În conformitate cu Decizia nr. 2 din 23 ianuarie 2009 din cadrul Programului Național de Educație Medicală Continuă și în temeiul art. 406, 414 și 431 din Legea nr. 95/2006 privind reforma în domeniul sănătății, Consiliul Național al Colegiului Medicilor din România a decis ca articolele științifice publicate în reviste de specialitate clasificate CNCS, grupa B, să fie punctate cu 80 credite/articol.

Redacția

**Revistă cotate B+ CNCS, indexată BDI Index Copernicus, DOAJ, Erih Plus, Gale Cengage
Journal B+ CNCS and Indexed IDB by Index Copernicus, DOAJ, Erih Plus, Gale Cengage**

Editorial contact:

- Alexandra BOLOȘ: bolalexandra@gmail.com
- Irina SĂCUIU: irina_sacuiu@yahoo.com

Distribution and subscription:

- Ioan MIHALACHE: ioanmihalache@yahoo.com
Tel.: +40 745 528 849

Publisher contact:

- Editura DOXOLOGIA
Tel.: 0232-216693, fax: 0232-216694
E-mail: editura@doxologia.ro; dituradoxologia@gmail.com
-

Summary

Editorial / 9

Community Psychiatry - A Modern Approach of the Mental Health Care / 11

Andreea S. Szalontay, Mihaela Miron

Articles / 15

Intellectual modifications in patients with schizophrenia / 17

Valentin Oprea, Ecaterina Ojog

The importance of exercising in the pathological manifestations of some psychiatric disorders such as autism or schizophrenia / 23

Andrei Ciobică, Cezar Honceriu, Alin Ciobică, Vasile Chiriță, Romeo Dobrin, Irina Dobrin, Florin Trofin, Daniel Timofte

The effects of antipsychotics, antidepressants and mood stabilizer medication over the cardiovascular disease in patients with schizophrenia, depression and mood disorders / 31

Maria-Magdalena Leon-Constantin, Ovidiu Mitu, Cristina Furnică, Alexandra Maștaleru, Ștefan Paviliu, Florin Mitu

Parents against autism spectrum disorders / 39

Mihaela Grasu

Dietary supplements and their influence on our mental health / 49

Antoneta Dacia Petroaie, Adriana Cosmescu, Elena Adorata Coman, Alexandra Bolos

Deep brain stimulation versus transcranial magnetic stimulation in psychiatric pathology / 57

Frîncu Raluca Mihaela, Gavril Radu, Lușșa Livia Andreea, Pădurariu Manuela, Băluță Cezar Valeriu, Cristinel Ștefănescu

Multidisciplinary contributions / 67

The metaphor - a means of communication between the conscious and the unconscious world / 69

Dan Verejanu

The Phenomenon of Translation in Terms of Psycholinguistics / 75

Metleaeva (Luchiancova) Miroslava

Case reports / 81

Phenotypic variability and genetic susceptibility of schizophrenia-evidence from a family study / 83

Adina Cramă, Marina Buzut, Marcel-Alexandru Găină, Vasile Chirita, Alexandra Boloș, Roxana Chiriță

Clinical and diagnostic features of a case of dissociative motor disorder / 95

Anca Bradu, Cosmin-Adrian Ungureanu, Oana-Mihaela Nantu, Irina Sacuiu, Roxana Chiriță

Book review / 103

Managing Pharmacological Dependencies, Guide for Students, Residents and Psychiatric Narcotics Specialists (Gestionarea dependentelor farmacologice, Ghid pentru student, rezidenti si specialist psihiatri-narcologi) / 105

Ilinca Untu, Vasile Chiriță

In memoriam / 109

Psychiatry community in mourning / 111

Editorial

Community Psychiatry - A Modern Approach of the Mental Health Care



Andreea Silvana SZALONTAY



Mihaela MIRON

Andreea Silvana SZALONTAY – MD, PhD, lecturer, senior psychiatrist, Gr.T.Popa University of Medicine and Pharmacy Iasi

Mihaela MIRON – MD, senior psychiatrist, Socola Institute of Psychiatry Iasi

In 2001, the World Health Organization recommended in the World Health Report the partial transfer of psychiatric hospital services and psychiatric care services to the mental health services provided in the community. The aim was to increase the quality of life of the psychiatric patient by changing the pattern of care in a framework that respects their rights and also has economic benefits for long-term by reducing care costs and social pressure. The effect will be that a

large proportion of these patients will be rehabilitated so that they can provide a useful activity to society, even in a protected system and this will increase their self-esteem and well-being.

When it comes to reform mental health, this involves several steps:

- developing mental health services in the community;
- mental health services provided in primary care units;

– focusing on rehabilitation and recovery services.

Studies show that the exclusively hospital approach or exclusively community-based approach is not effective. A balanced psychiatric care between the community services and the hospital services is recommended.

In addition, reforming the system requires a clear vision and a sufficient time for implementation. The experience of other countries that have shut down psychiatric hospitals without providing alternative community services has only aggravated the situation of these patients and this will not have to be repeated. The community system of psychiatric services requires interconnection with social assistance and involves financial efforts, including the establishment of sheltered housing, as an integral part of social rehabilitation. Professional and vocational rehabilitation, which adds value to society and increases patient self-esteem, refers to the establishment of social enterprises, like paid workplaces, especially for people with mental health problems.

In this context, the work of mobile psychiatric and psychosocial care teams aims at increasing the accessibility of mental health services. At the same time, the mobile team is a model of service with a high degree of community integration, thus participating in the destigmatization of the psychiatric patient and the transformation of the psychiatric units into open institutions towards the community, while offering the community the chance to get involved in the activity of the hospital unit. The purpose of these teams is to move the specialized psycho-social service at the patient's home, based on the legislation in force and detached from the current psychi-

atric practice because it has been found that a considerable proportion of patients remain outside the mental health care system because of their physical or mental disability to access these services, reaching a late-stage psychiatric hospital with a high chance of becoming a hospital addict.

Thus, a multidisciplinary team specialized in providing medical and social community-based services, in according with european standards can be created with a visible service offer at the level of local communities, developing a formal and informal network of people trained in community assistance. So there are several types of services that can be provided:

- Mobile mental health team that provides and coordinates a wide range of interventions in different locations, interacting and collaborating with other health service providers (general practitioners, other specialties) or other competent structures;
- Support team providing mobile support and treatment for people with severe or chronic psychiatric disorders, including those with forensic implications;
- Crisis and home care team providing immediate and short-term treatment or social support to resolve crisis situations to avoid or reduce the period of hospitalization (crisis intervention).

The relationship with other types of psychiatric services contributes to increasing the quality of community life in the context of respecting the lives of all people. Although in the Romanian legislation (Order 375/2006) it is stipulated this, the implementation of this type of service is difficult due to the lack of financing and the lack of legislative correlation. The desire of mental health profes-

sionals to diversify the range of services offered, tailored to the needs of mental health service users, can not materialize without a firm action plan for health decision-makers and unblocking of legal and financial pathways, which requiring also the policy will.

REFERENCES

1. World Health Organization. Mental Health Action Plan 2013 – 2020. http://www.who.int/mental_health/publications/action_plan/en/
 2. Strategia de reforma a sanatatii mintale propusa Ministerului Sanatatii de un grup de lucru al Asociatiei Psihiatrice Romane si al Ligii Romane pentru Sanatate Mintala. Proiectul de sanatate mintala al Pactului de Stabilitate pentru tarile din Sud-Estul Europei. <http://www.romjpsychiat.ro/article/strategia-in-domeniul-sanatatii-mintale-a-ministerului-sanatatii-din-romania>
 3. T. Udristoiu, C. Marcean, C.M. Zaharescu. Manual de instruire a personalului din cetrele de sanatate mintala in psihiatria comunitara elaborat in cadrul programului national de sanatate mintala si profilaxie in patologia psihiatrica al Ministerului Sanatatii pentru Spitalul Clinic de Neuropsihiatrie Craiova
 4. Ordinul MS 375/2006 privind înființarea, organizarea și funcționarea centrelor de sănătate mintală
 5. <http://cnsm.org.ro>
 6. Strategia Nationala de Sanatate 2014-2020. <http://www.ms.ro/strategia-nationala-de-sanatate-2014-2020/>
-

Articles

Intellectual modifications in patients with Schizophrenia

Valentin OPREA, Ecaterina OJOG

Valentin OPREA – MD PhD Associate Professor, State University of Medicine and Pharmacy, Chair of Psychiatry, Narcology and Medical Psychology.

Ecaterina OJOG – psychiatry resident, State University of Medicine and Pharmacy, Chair of Psychiatry, Narcology and Medical Psychology.

ABSTRACT

Background: Many studies tried to find a connection between schizophrenia and intelligence, it being a vastly stigmatized chronic disease did not raise that type of questions. Either there a cognitive decline after the onset of the pathology or the changes in cognition that accompany the disease prevent the individual from manifesting one's intelligence. Even if there are certain modifications in the measured intellect it does not necessarily mean that schizophrenia is a disease that leads to an inevitable dementia. It is not clear whether that decline is due to the pathological process of schizophrenia or an existent low premorbid IQ.

Materials and methods: The articles that were found on the internet via PubMed up to 01.10.2016, via GoogleScholar up to 01.10.2016. The key words used in the search were: („schizophrenia”, “IQ”, “dementia”, “cognition”, “intelligence”, “intellect”, “neuropsychology”). The titles and abstracts were examined and evaluated thoroughly in order to determine whether they meet the necessary criteria and information. Additional findings were obtained through manual search and cross referencing.

Conclusions: At this point there is no neurobiological, psychometrical or clinical proof of intellectual decline in schizophrenia. The patients manifest difficulty of expressing the intelligence rather than losing the intellectual potential. However, further studies and investigations are required to confirm these findings.

KEYWORDS:

schizophrenia, intellect, intelligence, IQ, dementia.

Introduction

Several contemporary studies have attempted to link intelligence to schizophrenia, which has been a vastly stigmatized pathology, has not risen these questions for a long time. We have set ourselves the goal of analyzing the existing data and answering to some fundamental questions. Either there a cognitive decline after the onset of the pathology or the changes in cognition that accompany the disease prevent the individual from manifesting one's intelligence. Even if there are certain modifications in the measured intellect it does not necessarily mean that schizophrenia is a disease that leads to an inevitable dementia. It is not clear whether that decline is due to the pathological process of schizophrenia or an existent low premorbid IQ. It is well established, therefore, that some adults with schizophrenia have low results in general intellectual function tests. However, it is not clear whether this deficit reflects a decline that can be attributed to the pathological process of the disease or is better thought to have a premorbid deficiency that increases the risk of the disease. The theory of intellectual deterioration is widespread in history. For example, the introduction and use by Kraepelin of the term „dementia praecox“ when describing schizophrenia, which means continuous cognitive decline.

In order to answer the questions asked, we need to deepen our terminology and history. William Stern (1914) defined intelligence as the general ability of the individual to adapt to the new requirements and conditions of life; the general mental capacity involved in calculating, reasoning and perceiving relationships and analogies, rapid learning, sto-

ring, classification, generalization and access to information, using a fluent language (1).

Raymond Cattell believed that intelligence can be divided into two fundamental parts. Fluid ability and Crystallized ability. Fluid capacity is considered to be the innate capacity to make decisions through rationalization. While the crystallized intelligence is the information and skills that are gained through experience in a cultural environment. Many of these concepts are puzzling, and we have considered that they must be correctly understood and interpreted before they reach the results and discussions. Intelligence is the ability to know and rationalize. Intelligence is the practical manifestation of knowledge to think in a complex and innovative way. So, the intellect is the ability to know many things, while intelligence is the ability to use its knowledge in innovative, analytical and practical ways (2).

IQ - Intelligence Quotient was introduced by W. Stern (1914), is a concept and score derived from various standardized tests that attempt to measure intelligence. The average human intelligence coefficient is 100, the maximum score is 240, $IQ = \text{mental age} / \text{chronological age} \times 100$ (1).

Charles Spearman (1904) considered that there is a certain factor that can reflect our level of intelligence regardless of the individual's knowledge. He called it Factor G (General Intelligence, General Intellectual Capabilities) - a construct formed in the psychometric investigations of cognitive abilities and human intelligence. It is a variable that sums the positive correlations between different cognitive requirements, reflecting that individual performance in one type of pregnancy can be compared to the results of this person in another type of

cognitive task (3).

Over time, psychologists have decided that intelligence cannot be measured by such a simplistic method. LL Thurstone (1935) used 56 different tests to test abilities. And he classified intelligence into 7 main groups. Though Spearman's and Thurstone's ideas did not coincide, they founded psychometrics. Which has evolved much since then. Analytical, creative and emotional intelligence has been introduced. F.Glatton used the principles of Darwin's natural selection and applied them to the intelligence, he hypothesized that smart people should only reproduce with smart people, in order to create a superior race of geniuses - eugenics.

As we have already mentioned, the cognitive deficits in schizophrenia have been thoroughly studied since the time they were described by Kraepelin. It has also been investigated the association of a low IQ and a possible eventual development of schizophrenia. But the question: „Does the overall intelligence decrease over time?“ Has not been sufficiently investigated. Initially, cognitive disorders were thought to be caused by deficits of precursors to intelligence: memory and attention. Mental operations and the actions of a schizophrenic patient are kept intact, his memory and attention is not affected, but he is unable to synthesize correct, independent conclusions.

Individuals in acute psychosis with an overbearing chaos of thoughts, stupor, mentism, ideatory inhibition, are incapable of smart displays but do not lack intellect. Patients accuse lack of attention, memory issues „it is not as it once was ...“. In reality, they hardly concentrate on a subject and read mechanically, not focusing on the essential, but they

are tempted to permanently obsess on the main process of “work”, and instead of doing something productive, they ultimately end up focusing on their sensations and not on the task. Eventually, they miss the essence. So it is a particular, peculiar productivity of the thinking process, with a tendency to resonate, rather than an intellectual deficit (4).

Although this „complicated mechanism“ evades the subject's attention, it does not destroy the integrity of learning nor the logical course of thought and conclusions. The patient's efforts are directed to the attempts to compensate, to permanently seek the support on which the integrity of the perception and the logic of the intellectual process of the patient are based. The increased tendency of the patient to resonate and correct his or her actions makes it harder for the cognitive process to perform and is interrupting it (5).

The mental capacities of the patient with schizophrenia remain intact and all the changes occurring are caused by the personality alteration in general. We detect memory disorders or of other precursors of the intellect in such patients, as well as the loss of knowledge and of thinking abilities, and the occurrence of modifications of behavior that looks like “hebephrenic bizarreness”. There is also the inability to separate the essential from unessential, or simply what is considered essential in the social empirical real world (4).

Objectives

The analysis of contemporary scientific literature on the issue of intellectual changes and the level of intelligence in patients with

schizophrenia. Intelligence versus cognitive deficits in endogenous processes. Establishing and evaluating the bi-directional influence of schizophrenia and intelligence.

Material and methods

A systematic research was conducted to identify the change in IQ in schizophrenia. The literature used is included in the bibliography. We used the articles that were found on the internet via PubMed up to 01.10.2016, via GoogleScholar up to 01.10.2016. The key words used in the search were: („schizophrenia”, “IQ”, “dementia”, “cognition”, “intelligence”, “intellect”, “neuropsychology”). The titles and abstracts were examined and evaluated thoroughly in order to determine whether they meet the necessary criteria and information. Additional findings were obtained through manual search and cross referencing.

Results

Some early studies (Schwartzman A 1962; Albee G 1963) that were examining the stability of intelligence in schizophrenia reported a decline when they compared the premorbid IQ and postmorbid IQ. This studies were highly criticized because the majority of them set a time limit to the tests, which is not suitable for a patient that undergoes treatment with antipsychotic medication – the reason why they cannot be tested like the healthy population (6). Hamilin R. et al (1969) examined 49 patients with schizophrenia and did not succeed proving the concept of intellectual decline. The patients that have a better management of

their symptoms and a better social function shower an improvement of the results (7).

It is well established that a low IQ is associated with a bad outcome of the disease, and a high IQ serves as a protective factor and predicts a benign evolution of schizophrenia and is associated with a high social functioning. The paranoid type tends to accumulate higher scores than non-paranoid – type (8). Heaton et. Al noticed that the patients with schizophrenia have a higher verbal IQ than the healthy control lot (9). Vinogradov et. Al reported a decrease of speed and precision IQ in the patients’ lot (10).

According to the longitudinal studies, Jones et al (1994) used the data from the British national study that followed those born in the same week, March 1946. These 5362 individuals were investigated at equal intervals from birth. 30 of them who developed schizophrenia had lower IQ than their peers at the age of 8, 11, 15 - long before the onset of psychosis. In the general population, the lower the IQ in childhood, the higher the chances of a possible onset of schizophrenia (11). The same result was also achieved by another study (1995) that followed a cohort of 1958 (12). David et al also found a low premorbid IQ when examining the score for 50,000 young people enrolled in the army who eventually received a diagnosis of schizophrenia compared to their non-psychotic fellows (13).

A cross-sectional study carried out by Hyde et. Al (1994) concluded that „there is no intellectual decline in patients with chronic schizophrenia higher than could be expected from the effects of aging“ (14, 18).

In his study, Alisa J Russel et al. (1997) concluded that adults with schizophrenia

accumulated a lower score than the healthy group but it is unclear whether this deficit of -10 points in the environment is attributable to the pathology concerned or a low IQ at the premorbid stage. It is not clear whether IQ decreases or continues to decline in patients with schizophrenia vs control lot (15).

Hedman et. Al reported a moderate difference between groups. The mean baseline IQ was set at 97.20 for patients and 109.26 for control. The increase in mean IQ per year was 0.33 for patients and for control 2.08. Cognitive impairment in patients with schizophrenia is expressed as a lower increase in the score at repeated testing compared to healthy subjects. Thus, schizophrenia is characterized by a relative lack of accumulation of new cognitive abilities at a global level over time, not

the loss of already accumulated capacities (16). Some time ago schizophrenia was considered to be a neurodegenerative pathology resulting in the deterioration of intelligence and intellect. However, extensive studies have shown that all neurological changes that occur are a consequence of treatment or other factors. Robert B. Zipursky et al (2012) concluded that there is no direct evidence of the toxic effect of psychosis on brain tissue and is the consequence of antipsychotic medication, alcohol, cannabis use, smoking, hyper cortisol and low physical activity contributing to changes in cortical volumes and ventricular. Their importance lies in the fact that at least some of the consequences can be reversible (17).

Discussions

At this point there is no neurobiological, psychometrical or clinical proof of intellectual decline in schizophrenia. The patients manifest difficulty of expressing the intelligence rather than losing the intellectual potential. The G factor would be the most useful tool in appreciating the IQ level of the individual with schizophrenia. The mental processes of the patient, but the mechanism of elaborating individual conclusions is biased. However, further studies and investigations are required to confirm these findings.

ACKNOWLEDGEMENTS AND DISCLOSURES

The authors state that they are no declared conflicts of interest regarding this paper

REFERENCES

- 1.Stern W. 1914 The Psychological Methods of Testing Intelligence
- 2.Cattell, R. B. (1963). Theory of fluid and crystallized intelligence: A critical experiment. *Journal of Educational Psychology*, 54, 1-22.
- 3.Spearman, C.E. (1904). „General intelligence’, Objectively Determined And Measured“
- 4.Jaspers Karl. *General Psychopathology*
- 5.Zeigarnik Bluma 1965 The pathology of thinking
- 6.Hamlin R: The stability of intellectual function in chronic schizophrenia. Hyde TM et. Al Is there cognitive decline in schizophrenia? 1994;164:494-500
- 7.Schwartzman A, Douglas V: Intellectual loss in schizophrenia, part I. *Can J Psychiatry* 1962; 16:1-10

- 8.Heaton R et al. Neuropsychological deficits in schizophrenics. Relationship to age, chronicity, and dementia Psychiatry 51:469-476.
- 9.Vinogradov S, Adcock RA, Fischer A, Poole JH (2000) Neurocognitive findings in schizophrenic subjects with above average IQ. Biol Psychiatry 47:23S.
- 10.Jones et al: Child development risk factors for adult schizophrenia in the British 1946 birth cohort. Lancet 1994; 344:1398-1402
- 11.Crow TJ, Done DJ, Sacker A: Childhood precursors of psychosis as clues to its evolutionary origins. Eur Arch Psychiatry Clin Neurosci 1995; 245:61-69
- 12.David, A., van Os, J., Jones, P., Fahy, T., Harvey, I. & Forster, A. (1995). Insight and the course of psychiatric illness: cross-sectional and longitudinal associations. British Journal of Psychiatry 167, 621-626
- 13.Hyde TM, Nawroz S, Goldberg TE, Bigelow LB, Strong D, Ostrem JL, Weinberger DR, Kleinman JE: Is there cognitive decline in schizophrenia? a cross-sectional study. Br J Psychiatry 1994; 164:494-500
- 14.Ailsa J. Russell et. al Schizophrenia and the Myth of Intellectual Decline Am J Psychiatry 1997; 154:635-639
- 15.Anna M. Hedman et. al. IQ change over time in schizophrenia and healthy individuals: A meta-analysis. Schizophrenia Research 146 (2013) 201-208
- 16.Robert B. Zipursky et.al The Myth of Schizophrenia as a Progressive Brain Disease doi:10.1093/schbul/sbs135
- 17.Goldberg, T. E., Hyde, T. M., Kleinman, J. E. & Weinberger, D. R. (1993a). Course of schizophrenia: neuropsychological evidence for a static encephalopathy. Schizophrenia Bulletin 19, 797-804.

Correspondence:

Valentin OPREA,

MD PhD Associate Professor, Chair of Psychiatry, Narcology and Medical Psychology,
E-mail: dr.valentin.oprea@gmail.com

Submission: 27 nov 2017

Acceptance: 22 jan 2018

The importance of exercising in the pathological manifestations of some psychiatric disorders such as autism or schizophrenia

Andrei CIOBICĂ, Cezar HONCERIU, Alin CIOBICĂ, Vasile CHIRIȚĂ, Romeo DOBRIN, Irina DOBRIN, Florin TROFIN, Daniel TIMOFTE

Andrei CIOBICĂ - Student, Alexandru Ioan Cuza University, Iasi, Romania

Cezar HONCERIU - Associate Professor, Alexandru Ioan Cuza University, Iasi, Romania

Alin CIOBICĂ - Researcher II, Department of Research, Faculty of Biology, Alexandru Ioan Cuza University, Iasi, Romania, Academy of Romanian Scientists, Bucuresti, Romania, Center of Biomedical Research, Romanian Academy, Iasi, Romania

Vasile CHIRIȚĂ - Acad., MD, PhD, senior psychiatrist Socola Institute of Psychiatry Iasi, Romania

Romeo DOBRIN - MD, PhD, senior psychiatrist, associate professor "Gr. T. Popa" University of Medicine and Pharmacy, Iasi, Romania

Irina DOBRIN - MD, PhD, psychiatrist, assistant professor, "Gr. T. Popa" University of Medicine and Pharmacy, Iasi, Romania

Florin TROFIN - Assistant Professor, Alexandru Ioan Cuza University, Iasi, Romania

Daniel TIMOFTE - Associate Professor, "Gr. T. Popa" University of Medicine and Pharmacy, Iasi, Romania

ABSTRACT

Recent studies are showing that together with obesity, low diet quality and smoking, reduced physical activity belongs to the combination of lifestyle factors being responsible for up to 55 % of deaths worldwide. Thus, an increased number of reports are suggesting some mental health-related benefits of resistance training, manifested as a decrease in depression-like manifestations, an increase in self-esteem and physical self-concept, as well as improved cognitive abilities. Even more, as we will show in the present mini-review, exercising has been used to reduce the stereotypic behaviour of autistic individuals, as well as to enhance psychological and general well-being in schizophrenic patients, while also reducing the positive and negative symptoms. Moreover, large-scale meta-analytic and narrative reviews are offering some compelling evidences to support the use of exercising in order reduce anxiety, depression and stress reactivity, while also improving the cognitive functioning. Thus, in the present report we focused our efforts in understanding the main results and mechanisms related to a possible protective effect of exercising in the pathological manifestations of two important psychiatric disorders, such as schizophrenia and autism. In this way, we are demonstrating here that patients with autism and schizophrenia could use resistance training as an important and low-cost therapeutic tool for improving their physical, functional and mental health.

KEY WORDS

autism, schizophrenia, exercising.

INTRODUCTION

Lately, prospective epidemiological studies are showing that together with obesity, low diet quality and smoking, reduced physical activity belongs to the combination of lifestyle factors being responsible for up to 55 % of deaths worldwide [1].

In this way, an increased number of reports are suggesting some mental health benefits of resistance training, manifested as a decrease in depression-like manifestations, an increase in self-esteem and physical self-concept, as well as improved cognitive abilities [2].

Even more, as we will show in the present mini-review, exercise has been used to reduce the stereotypic behaviour of autistic individuals, as well as to enhance psychological and general well-being in schizophrenic patients, while also reducing the positive and negative symptoms [3].

Moreover, large-scale meta-analytic and narrative reviews offer some compelling literature to support the use of exercise to reduce anxiety [4], depression [5] and stress reactivity [6], while also improving cognitive functioning [7].

In this way, to this date, although not one causal mechanism has been identified, there are several mechanisms that are commonly believed to be responsible for the beneficial changes in mental health, as a result of physical activity. These mechanisms are typically categorized as either psychiatric or physiological-related (e.g. endorphin hypothesis, serotonin hypothesis) or cognitive (e.g. expectancy hypothesis, mastery hypothesis).

Thus, in the present report we focused our efforts in understanding the main results and mechanisms related to a possible protective

effect of exercising in the pathological manifestations of two important psychiatric disorders: schizophrenia and autism.

EXERCISING VS. AUTISM

Autism spectrum disorders (ASDs) are a group of multisystem neurodevelopmental disorders characterized by impairments in social interactions and lack of communication skills and the presence of repetitive and stereotypical behaviours and interests [8]. Children with ASDs have impairments in social communication domains characterized by behaviours such as reduced eye contact, problems with social reciprocity, and verbal and nonverbal communication delays [9]. Stereotypical behaviours and interests in children with ASDs may include adherence to inflexible routines and motor stereotypes such as hand flapping or body rocking [10].

In addition to these main diagnostic impairments, children with ASDs may have a large range of impairments in cognitive-behavioural and perceptuomotor domains. Cognitive and behavioural impairments may include attention problems, intellectual delays, anxiety, depression, aggression, temper tantrums, and self-injurious behaviours [11,12]. In terms of sensorial related impairments, children with autism may have difficulties in modulating tactile, auditory, visual, and vestibular inputs, with either hyper responsiveness or hypo responsiveness to sensory stimuli [13].

Children with ASDs could also have pervasive gross motor impairments such as poor visuo-motor and bilateral coordination, as well as postural impairments in static and dynamic balance [14,15]. In addition, many children

with ASDs have systemic comorbidities such as gastrointestinal disorders and food sensitivities [16]. Overall, ASDs are complex multi-system disorders characterized by a vastness of impairments in several domains.

In relations to exercising in this disorder and regarding the obesity in children with ASDs an alarming analysis showed that the prevalence of obesity in children with ASDs is 30.4% compared with 23.6% in age-matched children without ASDs [17]. Even more, among children with chronic disabilities, the prevalence of obesity is greater in children with ASDs, as compared to children with other developmental disabilities, including Attention Deficit Hyperactivity Disorder (ADHD) and learning disabilities [18].

It is also known that obesity in general population is associated with long-term physical and psychosocial consequences, including diabetes, stroke, osteoarthritis, increased cardiovascular risk, stigma, and depression [19]. Moreover, obesity is a significant comorbidity in individuals with ASDs, and it serves as a call for clinicians, such as physical therapists, occupational therapists, and physical educators to address issues related to overweight and obesity in their patients with ASDs.

It is generally believed that there are four potential factors contributing to obesity in individuals with ASDs: the main one is low physical activity levels, followed by a poor nutrition, medication use and metabolic abnormalities, plus a lack of knowledge or awareness regarding a healthy lifestyle [20]. In this way, daily physical activity levels and nutrition directly affect the balance between energy expenditure and intake and contribute to obesity in both children who are developing typically and those with disabili-

ties. Additional indirect contributions to obesity in individuals with ASDs could also come from the intake of specific medications, metabolic and hormonal abnormalities, as well as certain autism-specific impairments. Thus, regarding the connections between cardiovascular exercising and autism, there are previous studies in children with ASDs, which have received a variety of exercise interventions in an effort to reduce autism-specific impairments, such as problem behaviours, stereotypical behaviours and inattention, as well as in order to improve academic performance, social responding, peer relations and motor skills.

Moreover, a variety of exercises were used, including swimming, jogging, cycling, weight training, walking and horseback riding [21]. In addition, a meta-analysis of 16 studies suggested that, on average, cardiovascular exercise interventions led to a 37% improvement in overall symptomatology of autism, with best results in behavioural and academic improvements [22].

Also, in terms of behavioural skills of children with ASDs, vigorous intensity exercises such as jogging, roller-skating, hydrotherapy exercises and exergames (e.g. video games that are also a form of physical exercise) have been used to reduce the frequency of stereotypical behaviours [23], aggressive or self-injurious behaviours and hyperactivity [24]. In addition, another study found that in terms of academic performance, physical exercise preceding classroom lessons led to an increase in academic responding and on-task behaviours, while reducing disruptive behaviours in class children with ASDs [25]. Moreover, the amount of time spent in physical activity is in some studies positively

correlated with the engagement in class activities [26].

Also, in terms of addressing social skills, aquatic and equine therapies have been used to reduce antisocial and aggressive behaviour and improve social responding and relations in children with autism [27].

Lastly, recreational pool exercises [28] and horseback riding [29] have been used to facilitate gross motor coordination and balance in children with autism. Overall, there is considerable evidence that cardiovascular exercise interventions are effective in improving motor, social, and behavioural skills of individuals with ASDs [30].

Moreover, when it comes to the relations between strength training and autism, much of the investigations have focused on resistance training exercises, as an intervention for individuals with autism.

In fact, the purpose of these researches was to conduct exercise-training programs following standard guidelines with individuals with autism, in order to stimulate future researchers to implement such programs.

Thus, in a study by Lochbaum et al. aerobic and muscular strength training programs (MST) were conducted on patients suffering from ASDs. In this way, aerobic fitness increased 33%, 50%, and 33% for the 3 participants. Moreover, for the MST, bench press increased 19% and 28%, low row increased 47% and 21%, and leg press increased 29% and 12% for the 2 participants. Following such results, future directions are discussed with regard to using exercise-training programs not only to enhance physical health, but also the psychological well-being of individuals with autism [31].

In summary, past research examining the

effects of physical activity on stereotypic behaviours and the known physiological and psychological benefits of physical activity presents a promising outlook for individuals with autism.

This promising outlook is greatly needed, given the recently declared international emergency regarding the number of annually diagnosed individuals with autism that is projected to annually cost in 10 years a staggering \$50 to \$300 billion in the US (Autism Society of America, 2002).

Thus, future research should examine the effects of physical activity–training programs that will reduce stereotypic behaviours in individuals with autism and promote a healthy lifestyle, necessary for productive participation in all aspects of society that require a certain degree of physical stamina such as work, self-care or recreation.

EXERCISING VS. SCHIZOPHRENIA

Schizophrenia is a severe mental disorder with prevalence in the range of 0.7–1 % of the population [32], which in the majority of cases already starts at a young age [33]. Negative symptoms like alogia, blunted affect, anhedonia, avolition and apathy occur early in prodromal states and remain persistent during the course of the illness, responding poorly if at all to antipsychotic treatment [34].

In this way, firstly it should be mentioned that patients with schizophrenia tend to live a less healthy lifestyle [35]. Moreover, due to medication [36] and genetic liability [37] they also run a high risk for developing a metabolic syndrome, diabetes and cardiovascular diseases [38]. This risk might be increased in combination with reduced physical activity [39].

According to the DSM-IV, this disease is associated with social and work dysfunctions [40]. Patients with schizophrenia demonstrate a blunted affect and also typically sedentary behaviour, which can contribute to deterioration of symptoms and increase the risk of comorbidities [41].

For example, a recent systematic review demonstrated that patients with schizophrenia who participate less in physical activities have experience more negative symptoms, antipsychotic side effects, low self-efficacy and other unhealthy lifestyle habits [42].

Even more, physiological adaptations to regular physical exercise afford a certain amount of time. Investigations in sport science led to the development of a model, which proposes that after approximately 6 weeks of training, a new level of adaptation is reached [43]. Subsequently, training intensity should be modified accordingly. Physical exercise according to the continuous method with no changes in intensity needs neither warming up nor cooling down and is feasible even with cognitively impaired patients [44]. Thus, high-intensity interval training seems to be very promising as well, especially concerning the improvement of peak oxygen uptake levels [45]. In this way, training durations of at least 30 minutes could provide stimuli for metabolic, as well as neurologic, muscular and cardiovascular systems [46].

In addition, 30 minutes are well tolerated by the patients [47]. As experiences from current studies show, even patients only accustomed to shorter continuous physical activity are able to exercise for 30 minutes after a short habituation phase.

However, there are indications that longer training sessions show an even greater

positive effect on positive and depressive symptoms in schizophrenia [48].

In this way, it seems that after having been neglected as a therapeutic intervention, despite its cost-effectiveness for a long time, exercising is back in the focus as therapeutic add-on in various psychiatric disorders [49]. This could be quite relevant especially considering that in the beginning, the effects of exercising on schizophrenia were seen mainly with regards to physiological changes like obesity or metabolic syndrome [3], while psychological alterations, not to mention the neurobiological changes, were being ignored. Also, in regards to the connections between cardiovascular exercises and the schizophrenic manifestations, in a randomized controlled trial, Beebe et al. [50] were able to show reductions of positive and negative symptoms in chronically ill schizophrenia patients after aerobic exercise, though the differences did not reach statistical significance.

Another study in chronically ill schizophrenia patients with aerobic exercise (indoor cycling), as compared to a patient control group and healthy controls found a reduction in the severity of total symptoms of up to 9 % in the cycling group, while non-exercising patients presented a total symptom increase of 13 % measured by the positive and negative symptom scale (PANSS), but then again the findings did not reach statistical significance most likely due to small sample sizes [51].

In fact, in regards to obesity, very well-known studies from the literature are showing that almost 40-80% of patients on antipsychotics have weight gain that exceeds ideal body weight by 20% or more [52].

In addition, obesity rates among persons with schizophrenia could range from 40% to

62% and are especially high in women [53]. This could be additionally explained perhaps by estrogen-related effects, while also menopause has been cited in this context [54]. Moreover, when it comes to the correlations between the strength training and schizophrenia, we have to mention that although resistance exercises improve aspects of mental health, their effects remain relatively unknown among adults with schizophrenia, for whom training variables (e.g., volume and intensity) are controlled, antipsychotic medications are monitored, and psychiatric scales are blinded. In addition, few studies have evaluated IGF-1, IGFBP-3, and BDNF after resistance or concurrent training among this population.

However one study on 47 adult males with a DSM-IV diagnosis of schizophrenia, evaluated the effects of 20 weeks resistance exercising on psychotic and depressive symptoms and quality of life outcomes [55]. In this way, the intervention exercises focused on the large muscle groups that are important for activities of daily living, and included the leg press, leg curl, vertical traction, chest press, arm extension, arm curl, and abdominal crunch. Moreover, two sessions per week with progressive loading could be sufficient to produce some benefits mentioned above.

Thus, the 20-week resistance training signifi-

cantly improved the symptoms of patients with schizophrenia. Moreover, after 10 and 20 weeks of exercise, patients in the intervention group exhibited reductions in psychotic symptoms (positive, negative, and total scores) as measured by the PANSS. In addition, an improvement in quality of life outcomes was also observed in the intervention group. Another pilot study assigned patients with schizophrenia to a maximum strength-training program for their legs to investigate whether this type of training would improve the mechanical efficiency of walking. The intervention protocol consisted of four sets of four repetitions of 85 to 90% 1RM leg-press exercises three times a week over 8 weeks, with the final results suggesting that patients with schizophrenia can safely participate and benefit from resistance training. Even more, the program did improve the mechanical efficiency of walking [56].

CONCLUSIONS

In this way, it seems that the results of these studies are suggesting that patients with schizophrenia and autism should use resistance training as an important and low-cost therapeutic tool for improving their muscle strength and their physical, functional and mental health.

ACKNOWLEDGEMENTS AND DISCLOSURES

The authors state that they are no declared conflicts of interest regarding this paper

REFERENCES

1. van Dam RM, Li T, Spiegelman D, Franco OH, Hu FB. Combined impact of lifestyle factors on mortality: prospective cohort study in us women. *BMJ*. 2008; 337:1440-1445.
2. Ciobica A, Lefter R, Paulet M, Trofin F, Honceriu C, Antioch I, Ababei D, Anton E, Timofte D, 2015. Physical exercising is reducing anxiety, depression and memory deficits associated with a MPTP-induced rat model of Parkinson's disease. *Neurodegener Dis*; 2015:1918-1919.

3. Honceriu C, Sandu L, Ciobica A, Trofin F, Lefter R, Timofte D, Mini-review: The relevance of body mass index and obesity in schizophrenia, *Bulletin of Integrative Psychiatry* 2016; 68:17-24.
4. Landers D, Petruzzello S, 1994. Physical activity, fitness, and anxiety. In C. Bouchard, R. J. Shepard, & T. Stephens (Eds.), *Physical activity, fitness, and health*, 868-881.
5. Mutrie N. The relationship between physical activity and clinically-defined depression. In S. J. H. Biddle, K. R. Fox, & S. H. Boutcher (Eds.), *Physical activity, mental health, and psychological well-being*, 2000:46-62.
6. Taylor A. Physical activity, anxiety, and stress. In S. J. H. Biddle, K. R. Fox, & S. H. Boutcher (Eds.), *Physical activity, mental health, and psychological well-being*, 2000:10-45.
7. Etnier J, Salazar W, Landers D, Petruzzello S, Han M, Nowell, P. The influence of physical fitness and exercise upon cognitive functioning: A meta-analysis. *Journal of Sport & Exercise Psychology* 1997; 19:249-277.
8. *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR)*. 4th ed Washington, DC: American Psychiatric Association; 2000.
9. Dawson G, Toth K, Abbott R. Early social attention impairments in autism: social orienting, joint attention, and attention to distress. *Dev Psychol* 2004; 40: 271-283.
10. Richler J, Bishop S, Kleinke J, Lord C. Restricted and repetitive behaviors in young children with autism spectrum disorders. *J Autism Dev Disord*. 2007; 37:73-85.
11. Williams DL, Goldstein G, Minschew NJ. Neuropsychologic functioning in children with autism: further evidence for disordered complex information-processing. *Child Neuropsychol*; 12:279-298.
12. Lecavalier L. Behavioral and emotional problems in young people with pervasive developmental disorders: relative prevalence, effects of subject characteristics, and empirical classification. *J Autism Dev Disord*. 2006; 36:1101-1114.
13. Tomchek SD, Dunn W, 2007. Sensory processing in children with and without autism: a comparative study using the short sensory profile. *Am J Occup Ther*; 61:190-200.
14. Fournier KA, Hass CJ, Naik SK. Motor coordination in autism spectrum disorders: a synthesis and meta-analysis. *J Autism Dev Disord*; 40:1227-1240.
15. Bhat A, Landa R, Galloway JC, 2011. Perspectives on motor problems in infants, children, and adults with autism spectrum disorders. *Phys Ther*; 91:1116-1129.
16. Buie E, Campbell DB, Fuchs GJ, 2010. Evaluation, diagnosis, and treatment of gastrointestinal disorders in individuals with ASDs: a consensus report. *Pediatrics*; 125:1-18.
17. Curtin C, Anderson SE, Must A, Bandini L, 2010. The prevalence of obesity in children with autism: a secondary data analysis using nationally representative data from the National Survey of Children's Health. *BMC Pediatr*; 10:11-18.
18. Chen AY, Kim SE, Houtrow AJ, Newacheck PW, 2009. Prevalence of obesity among children with chronic conditions. *Obesity*; 18:210-213.
19. Tyler CV, Schramm SC, Karafa M, 2011. Chronic disease risks in young adults with autism spectrum disorder: forewarned is forearmed. *Am J Intellect Dev Disabil*; 116:371-380.
20. Rimmer JH, Rowland JL, Yamaki K, 2007. Obesity and secondary conditions in adolescents with disabilities: addressing the needs of an underserved population. *J Adolescent Health*; 41:224-229.
21. Lang R, Koegel LK, Ashbaugh K, 2010. Physical exercise and individuals with autism spectrum disorders: a systematic review. *Res Autism Spect Dis*; 4:565-576.
22. Sowa M, Meulenbroek R, 2012. Effects of physical exercise on autism spectrum disorders: a meta-analysis. *Res Autism Spect Dis*; 6:46-57.
23. Anderson-Hanley C, Tureck K, Schneiderman RL, 2011. Autism and exergaming: effects on repetitive behaviors and cognition. *Psychol Res Behav Manag*; 4:129-137.
24. McGimsey J, Favell J. The effects of increased physical exercise on disruptive behavior in retarded persons. *J Autism Dev Disord*; 18:167-179
25. Rosenthal-Malek A, Mitchell S, 1997. Brief report: the effects of exercise on the self-stimulatory behaviors and positive responding of adolescents with autism. *J Autism Dev Disord*; 27:193-202.
26. Nicholson HK, Bray TJ, Heest MA, Van J, 2011. The effects of antecedent physical activity on the academic engagement of children with autism spectrum disorder. *Psychol Schools*; 48:198-213.
27. Pan C-Y, 2010. Effects of water exercise swimming program on aquatic skills and social behaviors in children with autism spectrum disorders. *Autism*; 14:9-28.
28. Pan C-Y, 2011. The efficacy of an aquatic program on physical fitness and aquatic skills in children with and without autism spectrum disorders. *Res Autism Spect Dis*; 5:657-665.
29. Wuang YP, Wang CC, Huang MH, Su CY, 2010. The effectiveness of simulated developmental horse-riding program in children with autism. *Adapt Phys Activ Q*; 27:113-126
30. Sowa M, Meulenbroek R, 2012. Effects of physical exercise on autism spectrum disorders: a meta-analysis. *Res Autism Spect Dis*; 6:46-57
31. Lochbaum M, Debbie Crews, 2003. Viability of Cardiorespiratory and Muscular Strength Programs for the Adolescent with Autism. *Complementary Health Practice Review*; 8:225-229.
32. McGrath J, Saha S, Chant D, Welham J, 2008. Schizophrenia: a concise overview of incidence, prevalence, and mortality. *Epidemiol Rev*; 30:67-76.

33. Kendler KS, Gallagher TJ, Abelson JM, Kessler RC, 1996. Lifetime prevalence, demographic risk factors, and diagnostic validity of non-affective psychosis as assessed in a US community sample. The national comorbidity survey. *Arch Gen Psychiatry*; 53:1022–1031.
34. Hasan A, Falkai P, Wobrock T, Lieberman J, Glenthøj B, Gattaz W, 2012. World federation of societies of biological psychiatry (WFSBP) guidelines for biological treatment of schizophrenia, part 1: update 2012 on the acute treatment of schizophrenia and the management
35. Brown S, Inskip H, Barraclough B, 2000. Causes of the excess mortality of schizophrenia. *Br J Psychiatry*; 177:212–217.
36. Goff DC, Sullivan LM, McEvoy JP, Meyer JM, Nasrallah HA, Daumit GL et al., 2005. A comparison of ten-year cardiac risk estimates in schizophrenia patients from the catie study and matched controls. *Schizophr Res*; 80:45–53.
37. van Welie H, Derks EM, Verweij KH, de Valk HW, Kahn RS, Cahn W, 2013. The prevalence of diabetes mellitus is increased in relatives of patients with a non-affective psychotic disorder. *Schizophr Res*; 143:354–357.
38. Brown S, Birtwistle J, Roe L, Thompson C, 1999. The unhealthy lifestyle of people with schizophrenia. *Psychol Med*; 29:697–701.
39. Chamove AS, 1986. Positive short-term effects of activity on behaviour in chronic schizophrenic patients. *British J Clin Psychol/British Psychol Soc*; 25:125–133.
40. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR)*, 2000. Arlington: American Psychiatric Publishing.
41. Lindamer LA, McKibbin C, Norman GJ, Jordan L, Harrison K, Abeyesinhe S, 2008. Assessment of physical activity in middle-aged and older adults with schizophrenia. *Schizophr Res*; 104:294–301.
42. Vancampfort D, Knapen J, Probst M, Scheewe T, Remans S, De Hert M, 2012. A systematic review of correlates of physical activity in patients with schizophrenia. *Acta Psychiatr Scand*; 125:352–62.
43. Neumann NU, Frasch K, 2008. New aspects regarding physical exercise in psychiatry-clinical and scientific basics. *Dtsch Z Sportmed*; 59:28–33.
44. van Uffelen JG, Chinapaw MJ, Hopman-Rock M, van Mechelen W, 2009. Feasibility and effectiveness of a walking program for community-dwelling older adults with mild cognitive impairment. *J Aging Phys Activity*; 17:398–415.
45. Helgerud J, Hoydal K, Wang E, Karlsen T, Berg P, Bjerkaas M et al., 2007. Aerobic high-intensity intervals improve vo₂max more than moderate training. *Med Sci Sports Exerc*; 39:665–671.
46. Neumann G, Schuler KP, 1994. *Diagnostics in sports medicine*. Johann Ambrosius Barth Verlag, Leipzig Berlin Heidelberg.
47. Pajonk FG, Wobrock T, Gruber O, Scherk H, Berner D, Kaizl I et al. Hippocampal plasticity in response to exercise in schizophrenia. *Arch Gen Psychiatry* 2010; 67:133–143.
48. Scheewe TW, Backx FJ, Takken T, Jorg F, van Strater AC, Kroes AG. Exercise therapy improves mental and physical health in schizophrenia: a randomised controlled trial. *Acta Psychiatr Scand* 2013; 127:464–473
49. Roine E, Roine RP, Rasanen P, Vuori I, Sintonen H, Saarto T. Cost-effectiveness of interventions based on physical exercise in the treatment of various diseases: a systematic literature review. *Int J Technol Assess Health Care* 2009; 25:427–454.
50. Beebe LH, Tian L, Morris N, Goodwin A, Allen SS, Kuldau J. Effects of exercise on mental and physical health parameters of persons with schizophrenia. *Issues Mental Health Nurs* 2005; 26:661–676.
51. Pajonk FG, Wobrock T, Gruber O, Scherk H, Berner D, Kaizl I et al. Hippocampal plasticity in response to exercise in schizophrenia. *Arch Gen Psychiatry* 2010; 67:133–143.
52. Mitchell A, Malone D. Physical health and schizophrenia. *Current Opinions in Psychiatry* 2006; 19:432–437.
53. Anisman H, Ravindran A, Griffiths J, Merali Z. Endocrine and cytokine correlates of major depression and dysthymia with typical or atypical features. *Mol Psychiatry* 1999; 4:182–188.
54. Lovejoy J. The menopause and obesity. *Prim. Care* 2003; 30:317–325.
55. Silva B, Ricardo C, Cassilhas, Cecília Attu. A 20-week program of resistance or concurrent exercise improves symptoms of schizophrenia: results of a blind randomized controlled trial. *Rev. Bras. Psiquiatr* 2015;1-10.
56. Heggelund J, Morken G, Helgerud J, Nilsberg GE, Hoff J. Therapeutic effects of maximal strength training on walking efficiency in patients with schizophrenia. *BMC Res Notes* 2012; 5:344–348.

Correspondence:

Romeo P. DOBRIN

MD, PhD, senior psychiatrist, lecturer,

Gr. T. Popa” University of Medicine and Pharmacy, 16 Universitatii Street, 700115,

Iasi, Romania,

E-mail: romeodobrin2002@gmail.com, 0744693053

Submission: 08 jan 2018

Acceptance: 03 feb 2018

The effects of antipsychotics, antidepressants and mood stabilizer medication over the cardiovascular disease in patients with schizophrenia, depression and mood disorders

Maria-Magdalena LEON-CONSTANTIN, Ovidiu MITU, Cristina FURNICĂ,
Alexandra MAȘTALERU, Ștefan PAVILIU, Florin MITU

Maria-Magdalena LEON-CONSTANTIN - "Grigore T Popa" University of Medicine and Pharmacy - Iasi, Romania, Faculty of Medicine, Department of Medical Specialties (I), address: University street nr 16, Iasi, Romania; Clinical Rehabilitation Hospital - Cardiovascular Rehabilitation Clinic, address: Pantelimon Halipa street nr 14, Iasi, Romania e-mail: leon_mariamagdalena@yahoo.com

Ovidiu MITU - "Grigore T Popa" University of Medicine and Pharmacy - Iasi, Romania, Faculty of Medicine, Department of Medical Specialties (II), address: University street nr 16, Iasi, Romania; Sf. Spiridon Hospital - Cardiology Clinic, address: Piata Universitatii street nr 1, Iasi, Romania - e-mail: mituovidiu@yahoo.co.uk

Ștefan PAVILIU - "Grigore T Popa" University of Medicine and Pharmacy - Iasi, Romania, Faculty of Medicine, Department of Medical Specialties (I), address: University street nr 16, Iasi, Romania; Clinical Rehabilitation Hospital - Cardiovascular Rehabilitation Clinic, address: Pantelimon Halipa street nr 14, Iasi, Romania

Cristina FURNICĂ - "Grigore T Popa" University of Medicine and Pharmacy - Iasi, Romania, Faculty of Medicine, Department of Morphofunctional Sciences I, address: University street nr 16, Iasi, Romania; Forensic Medicine Institute, address: Buna Vestire street nr 2, Iasi, e-mail cristinafurnica@yahoo.com

Alexandra MAȘTALERU - "Grigore T Popa" University of Medicine and Pharmacy - Iasi, Romania, Faculty of Medicine, Department of Medical Specialties (I), address: University street nr 16, Iasi, Romania; Clinical Rehabilitation Hospital - Cardiovascular Rehabilitation Clinic, address: Pantelimon Halipa street nr 14, Iasi, Romania

Correspondent author: Alexandra Mastaleru - email: alexandra.mastaleru@gmail.com

Florin MITU - "Grigore T Popa" University of Medicine and Pharmacy - Iasi, Romania, Faculty of Medicine, Department of Medical Specialties (I), address: University street nr 16, Iasi, Romania; Clinical Rehabilitation Hospital - Chief of Cardiovascular Rehabilitation Clinic, address: Pantelimon Halipa street nr 14, Iasi, Romania - e-mail: mitu.florin@yahoo.com

ABSTRACT

Introduction: Patients with severe psychiatric disease have a mortality rate of 2-3 times higher than the general population, possible due to the psychiatric disease, unhealthy life style but also to the adverse reactions of the administered medication.

Objectives: The risk of developing cardiovascular disease like hypertension, metabolic disease, myocarditis, torsades de pointes, prolonged QT interval is higher in patients with depression and bipolar disorder treated with antipsychotic medication.

Results and conclusions: From the antidepressant medication, venlafaxine is most frequently associated with high blood pressure, while mirtazapine is associated with hypertension in a lower rate compared to tricyclic antidepressants. A meta-analysis reported that old adults that use first generation antipsychotic medication have no significant statistical risk of myocardial infarction compared to the one treated with second generation antipsychotics. The risk of cardiovascular events varies with each of the second generation antipsychotics, being

decreased for aripiprazole and ziprasidone. For the first generation antipsychotics, patients that are at the debut of schizophrenia have a higher risk for mortality from cardiovascular cause in the ones treated with levomepromazine. A cohort study shows that in the first year of treatment with second generation antipsychotics, the patients have a high risk to develop hypertension, diabetes mellitus, hypertensive cardiomyopathy, stroke, coronary heart disease, hyperlipidemia compared to the ones who was administered antidepressant medication. Myocarditis can appear after the treatment with clozapine and imposes electrocardiographic monitoring. First generation antipsychotics with high risk of prolonged QTc are thioridazine (the highest risk), pimozide, droperidol, mesoridazine and haloperidole and from the second generation are sertindole, amisulpride and ziprasidone. A meta-analysis reported the fact that SSRIs have a risk of increased QTc dependent on the dose. The most potent effect seems to be associated with citalopram.

KEY WORDS:

antipsychotic, antidepressant, hypertension, myocarditis, metabolic syndrome.

INTRODUCTION

Patients with severe psychiatric disorders, especially schizophrenia, bipolar disorder and recurrent major depression have a 2-3 times higher mortality rate compared to general population, corresponding to a cut life expectancy by 10-25 years (1, 2). The most common cause of death at these patients is somatic disorders.

Factors related to the psychiatric pathology, unhealthy life style, discrepancies in the provision of the medical assistance and addressability to the physician lead to a reserved prognostic in psychiatric patients. Using psychotropic medication can increase the risk of somatic complications (3).

Therefore, it is necessary a thorough knowledge of the side effects of the psychotropic medication that is frequently used in the somatic state in patients with severe psychiatric disorders (4).

HIGH BLOOD PRESSURE

Even if antipsychotics have as a side effect gaining weight and are associated with

obesity, the effect over the blood pressure is less pronounced, most probably due to the action of blocking the alpha-1 receptor, which can decrease the blood pressure. In the same time, the criteria for metabolic syndrome are met more often in patients with schizophrenia than in the general population (OR = 1.36, 95% CI: 1.21-1.53) and in chronic patients with schizophrenia under antipsychotic treatment (39,7%) compared to the patients with a first psychotic episode (30,4%) or without medication (24,3%) (2). There has been observed a high risk of developing pathologies like high blood pressure and metabolic syndrome in patients with depression and bipolar disorder, pronounced in the ones treated with antipsychotics (5).

From the antidepressant medication, venlafaxine is most frequently associated with high blood pressure, while mirtazapine is less associated with it compared to tricyclic antidepressants (6). Mood stabilizers have no effect over the blood pressure, with the exception of chronic renal insufficiency induced by lithium.

CORONARY HEART DISEASE AND STROKE

Actual data suggest that patients with schizophrenia, bipolar disease and recurrent major depression have a significant higher risk of cardiovascular morbidity and mortality compared to general population. The risk is approximately 1,5-3 times higher in patients with schizophrenia and bipolar disorder and only 1,5 times higher in recurrent major depression. Moreover, cardiovascular disease is the most frequently cause of death in patients with severe psychiatric disease, with a 10 times higher risk compared to suicide (7, 8). The literature that talks about the cardiovascular prognostic regarding the antipsychotics is insufficient and the data are contradictory.

Even if some studies reported a high risk of cerebrovascular disease in patients that received antipsychotic treatment, others had inconclusive results. In case-control studies on old patients, the probability of stroke on the ones that received antipsychotic treatment compared to the ones without medication was approximately 1,3-2 times higher. The risk of cerebral infarction is increased in the first weeks of treatment. A meta-analysis of 20 cohort studies has concluded that old people (≥ 65 years) that are treated with first generation antipsychotic medication have no statistical significant increased risk (RR = 1.4; 95% CI: 0.81-1.91) of myocardial infarction compared to the ones treated with second generation antipsychotics (9).

Few studies have analyzed the association between antipsychotics and myocardial infarction, being a controversial topic because of the clinical and methodological different approaches. Some studies have reported a

higher risk of myocardial infarction in old people (≥ 66 years) with or without dementia or in patients with severe psychiatric disease treated with antipsychotics compared to control subjects (RR = 1.15-6.2) (10). In a study conducted by Lin et al. on a significant number of patients with schizophrenia, affective disorders or dementia, AOR for the risk of acute myocardial infarction was 2,52 (95% CI: 2.37-2.68) for antipsychotics in general, 2,32 (95% CI: 2.17-2.47) for the first generation ones and 2,74 (95% CI: 2.49-3.02) for the second generation ones (11). A meta-analysis reported an increased risk of myocardial infarction in old people (≥ 65 years) treated with first generation antipsychotics (RR = 1.2; 95% CI: 1.16-1.23), compared to the ones treated with second generation. Instead, some studies haven't found an association between the exposure to antipsychotic medication and the risk of myocardial infarction (12).

The risk of cardiovascular events varies with each of the second generation antipsychotics, being reduced for aripiprazole and ziprasidone. For the first generation antipsychotics, a 5 year follow-up study on patients at the debut of schizophrenia detected a high cardiovascular mortality risk in patients treated with levomepromazine (OR = 2.68; 95% CI: 1.37-5.25, $p = 0.004$) (13).

Literature data regarding cardiovascular safety of the second generation antipsychotics in young people are limited. In a cohort study (N = 48.625), the risk of major cardiovascular events (cardiovascular mortality, acute coronary syndrome or ischemic stroke) in adult psychiatric patients (18-64 years) that are ambulatory monitored was similar for risperidone, olanzapine and

quetiapine in the first year of treatment. In another cohort study were enrolled 284.234 patients with ages between 18 and 65 years old; the ones with second generation antipsychotic treatment that was started less than one year had an higher risk of developing high blood pressure (adjusted HR, AHR = 1.16, 95% CI: 1.12-1.21), diabetes mellitus (AHR = 1.43, CI: 1.33-1.53), hypertensive cardiomyopathy (AHR = 1.34, CI: 1.10-1.63), strokes (AHR = 1.46, CI: 1.22-1.75), coronary heart disease (AHR = 1.17, CI: 1.05-1.30) and hyperlipidemia (AHR = 1.12, CI: 1.07-1.17) compared to the ones exposed to antidepressant medication (14).

In obese patients, the ones with psychiatric pathology have a significant higher cardiovascular risk. It is possible that, additional to the weight gain and the mechanisms correlated with obesity, to be a direct effect of the antipsychotics over the cardiovascular risk. For example, an autonomic nervous system dysfunction triggered by schizophrenia could be exacerbated by the antipsychotic treatment by blocking the peripheral dopamine receptors, increasing the sympathetic activity. A direct effect of antipsychotic treatment over the insulin resistance that induces impaired glucose tolerance can be another mechanism that leads to the increase of the appearance of cardiovascular disease (15).

Potential cardiovascular side effects of the tricyclic antidepressants are well known. They can cause orthostatic hypotension, lower cardiac conduction, increase heart rate, meaning that they should be avoided as much as possible in patients with preexistent cardiovascular disease. SSRIs (e.g. citalopram) seems like having a superior cardiovascular safety, still in patients with high risk it can be

associated a slight QTc interval prolongation. Serotonin-norepinephrine reuptake inhibitors are associated with a slightly increased incidence of the cardiovascular side effects (hypertension, tachycardia and orthostatic hypotension), but they do not prolong QTc interval at therapeutic doses. Even if lithium can have side effects over cardiac conduction, it can generally be used in patients with cardiovascular disease (16).

MYOCARDITIS

Myocarditis can appear after the treatment with clozapine, being diagnosed mostly at the beginning of the treatment and in young patients. Therefore, routine electrocardiographic monitoring in the first 4 weeks of treatment and interrupting clozapine if the myocarditis appears can prevent death. However, case reports suggest that gradually resuming clozapine may have success in most of the cases (15).

CARDIAC ARREST

Patients with schizophrenia have 2-4 times higher risk of cardiac arrest compared to general population. Even if the causes of this high risk remain unclear, the individual susceptibility (e.g. coronary heart disease) and an increase prevalence of Brugada electrocardiographic anomalies seem relevant. Important additional risk factors include unhealthy life style and psychotropic medication.

The association between cardiac arrest and specific psychotropic medication has been explained by the prolonging of the ventricular depolarization (prolonged QTc), that

predisposes to life-threatening ventricular tachyarrhythmia (e.g. torsades de pointes). There is a consensus that the values of $QTc > 500$ ms or an absolutely increase with ≥ 60 ms compared to the basal values without medication includes the patient at a significant risk of torsades de pointes and cardiac arrest. However, even if there is a bond between QTc and torsades de pointes, this is not direct. Torsades de pointes can appear at therapeutic doses with antipsychotics or antidepressants with a QTc interval < 500 ms (17, 18).

Patients under treatment with first or second generation antipsychotics have an increased risk of cardiac arrest compared to the ones without treatment, with or without psychiatric disease, from 1,5 to 5,8 times higher according to the type on antipsychotic and the defining criteria of the cardiac arrest that we take into consideration. The largest study until now (459.614 patients treated with antipsychotics) has reported an incidence of cardiac arrest of 3,4 at 1000 persons/year (19). First generation antipsychotics with an increased risk of QTc prolonging include thioridazine (the highest risk), pimozide, droperidole, mesoridazine and haloperidole with intravenous administration (total cumulative dose > 2 mg) and from the second generation sertindole, amisulpride and ziprasidone. QTc prolonging for lurasidone and aripiprazole is not clinically significant and the one associated with asenapine and iloperidone is comparable with risperidone, olanzapine and quetiapine (20).

A meta-analysis reported the fact that SSRIs have a statistical significance association (but insignificant clinically) and dose dependent with the increasing QTc interval (+6.10 milliseconds; 95% CI: 3.47-8.73, $p < 0.001$)

compared to placebo. The most potent effect seems to be with citalopram. Tricyclic antidepressants prolong the QTc with a factor > 2 compared to SSRIs. Studies that correlate antipsychotic and antidepressant medication with an increased risk of cardiac arrest suggest a dose dependent relationship (18).

Cases of torsades de pointes have been reported for antipsychotics, tricyclic antidepressants and SSRIs. The ARITMO project (Arrhythmogenic Potential of Drugs) classified beside ziprasidone five other second generation antipsychotics (amisulpride, clozapine, olanzapine, quetiapine and risperidone) as having a high risk of developing torsades de pointes. However, these antipsychotics (with the exception of amisulpride and possibly quetiapine) have generally been associated with a relatively low potential of prolonging QTc interval. SSRIs determine very rarely torsades de pointes, with a small number of reported cases. The association between SSRIs and second generation antipsychotics determine exceptional torsades de pointes. There haven't been reported cases of torsades de pointes induced by lithium (21). We don't have to forget that coronary heart disease are underlying to most of the cardiac arrests. The actual recommendations don't suggest routinely electrocardiographic monitoring for the initiation of the antipsychotic treatment in the absence of the cardiovascular risk factors, but only if the prescribed antipsychotic has a high risk of torsades de pointes or cardiac arrest (20).

CONCLUSIONS

Patients with severe psychiatric disorders have a high risk of cardiovascular disease and

in consequence an increased mortality rate. Additional to the factors regarding the psychiatric disorder, like the discrepancies in the access and in the use of healthcare and the unhealthy life style, the psychotropic medication can contribute to the development or aggravation of the cardiovascular disease. We summarized the existing evidence over the antipsychotic, antidepressants and mood stabilizers medication side effects in the somatic state of the patients with schizophrenia, recurrent major depression and bipolar disorder. Generally, the side effects regarding the health are pronounced for antipsychotics, followed by mood stabilizers, tricyclic antidepressants and new generation antidepressants. Increased doses, polymedication and the treatment of the vulnerable persons (young or old) seem to be associated with a more pronounced effect over most of the cardiovascular disease.

Even if the antipsychotic medication has a high potential to affect the physical condition of the patients, it is important to retain that a number of large studies that obtained data

that could be generalized suggest that mortality has higher rates in schizophrenic patients without antipsychotic medication (2, 22). Moreover, clozapine, antidepressants, lithium and antiepileptic medication have a low mortality rate through suicide. Thus, the potential risk of antipsychotic, antidepressants and mood stabilizer medication should be compared to the risk of the psychiatric diseases for which they are used and to the long term potential benefit induced by the medication.

In the same time, there should be paid more attention to the possible impact of the psychotropic medication and its side effects over the cardiovascular system in patients with severe psychiatric diseases. This could help the medical staff in selecting the optimal treatment for each and every one of the patients. Moreover, information regarding the side effects for some of the medication might be useful in implementing an adequate monitoring and strategies in order to improve prognosis both somatically and psychiatrically.

ACKNOWLEDGEMENTS AND DISCLOSURES

The authors state that they are no declared conflicts of interest regarding this paper.

REFERENCES

1. Brown S, Kim M, Mitchell C, Inskip H. Twenty-five year mortality of a community cohort with schizophrenia. *Br J Psychiatry*. 2010 Feb; 196(2): 116–121.
2. Vancampfort D, Wampers M, Mitchell AJ et al. A meta-analysis of cardio-metabolic abnormalities in drug naïve, first-episode and multi-episode patients with schizophrenia versus general population controls. *World Psychiatry*. 2013 Oct;12(3):240-50.
3. Tiihonen J, Lönngqvist J, Wahlbeck K et al. 11-year follow-up of mortality in patients with schizophrenia: a population-based cohort study (FIN11 study). *Lancet*. 2009 Aug 22;374(9690):620-7.
4. Tiihonen J. Real-world effectiveness of antipsychotics. *Acta Psychiatr Scand*. 2016 Nov; 134(5): 371–373.
5. Emul M, Kalelioglu T. Etiology of cardiovascular disease in patients with schizophrenia: current perspectives. *Neuropsychiatr Dis Treat*. 2015; 11: 2493–2503.
6. Stahl SM, Grady MM, Moret C, Briley M., SNRIs: their pharmacology, clinical efficacy, and tolerability in comparison with other classes of antidepressants. *CNS Spectr*. 2005 Sep;10(9):732-47.
7. Laursen TM, Munk-Olsen T, Vestergaard M. Life expectancy and cardiovascular mortality in persons with schizophrenia. *Curr Opin Psychiatry*. 2012 Mar;25(2):83-8.

8. Kisely S, Preston N, Xiao J, Lawrence D, Louise S, Crowe E., Reducing all-cause mortality among patients with psychiatric disorders: a population-based study. *Can Med Assoc J.* 2013 Jan 8; 185(1): E50–E56.
9. Shapiro PA, Psychiatric Aspects of Heart Disease (and Cardiac Aspects of Psychiatric Disease) in Critical Care. *Crit Care Clin.* 2017 Jul;33(3):619-63.
10. Brauer R, Smeeth L, Anaya-Izquierdo K et al. Antipsychotic drugs and risks of myocardial infarction: a self-controlled case series study. *Eur Heart J.* 2015 Apr 21;36(16):984-92.
11. Lin ST, Chen CC, Tsang HY et al. Association between antipsychotic use and risk of acute myocardial infarction: a nationwide case-crossover study. *Circulation.* 2014 Jul 15;130(3):235-43.
12. Rehm J, Roerecke M. Cardiovascular effects of alcohol consumption. *Trends Cardiovasc Med.* 2017 Jun 10. pii: S1050-1738(17)30078-6.
13. Cipriani A, Hawton K, Stockton S, Geddes JR. Lithium in the prevention of suicide in mood disorders: updated systematic review and meta-analysis. *BMJ.* 2013 Jun 27;346: f3646.
14. Correll UC, Joffe B, Rosen LM, Sullivan TB, Joffe RT. Cardiovascular and cerebrovascular risk factors and events associated with second-generation antipsychotic compared to antidepressant use in a non-elderly adult sample: results from a claims-based inception cohort study. *World Psychiatry* 2015 Feb; 14(1): 56–63.
15. Nielsen J, Correll CU, Manu P, Kane JM. Termination of clozapine treatment due to medical reasons: when is it warranted and how can it be avoided? *J Clin Psychiatry.* 2013 Jun;74(6):603-13.
16. Beach SR, Kostis WJ, Celano CM et al. Meta-analysis of selective serotonin reuptake inhibitor-associated QTc prolongation. *J Clin Psychiatry.* 2014 May;75(5):e441-9.
17. Hasnain M, Vieweg WV. QTc interval prolongation and torsade de pointes associated with second-generation antipsychotics and antidepressants: a comprehensive review. *CNS Drugs.* 2014 Oct;28(10):887-920.
18. van Haelst IM, van Klei WA, Doodeman HJ et al. QT interval prolongation in users of selective serotonin reuptake inhibitors in an elderly surgical population: a cross-sectional study. *J Clin Psychiatry.* 2014 Jan;75(1):15-21.
19. Leonard CE, Freeman CP, Newcomb CW et al. Antipsychotics and the Risks of Sudden Cardiac Death and All-Cause Death: Cohort Studies in Medicaid and Dually-Eligible Medicaid-Medicare Beneficiaries of Five States. *J Clin Exp Cardiol.* 2013; Suppl 10(6):1-9.
20. Shah AA, Aftab A, Coverdale J. QTc prolongation with antipsychotics: is routine ECG monitoring recommended? *J Psychiatr Pract.* 2014 May;20(3):196-206.
21. Hazell L, Raschi E, De Ponti F et al. Evidence for the hERG Liability of Antihistamines, Antipsychotics, and Anti-Infective Agents: A Systematic Literature Review From the ARITMO Project. *J Clin Pharmacol.* 2017 May;57(5):558-572.
22. Lange C, Deutschenbaur L, Borgwardt S, Lang UE, Walter M, Huber CG. Experimentally induced psychosocial stress in schizophrenia spectrum disorders: A systematic review. *Schizophr Res.* 2017 Apr;182:4-12.

Correspondence:

Alexandra Mastaleru,

“Grigore T Popa” University of Medicine and Pharmacy – Iasi, Faculty of Medicine Department of Medical Specialties (I), Discipline of Medical Semiology, Department of Medical Specialties (II), Discipline of Cardiology 3 – Department of Morphofunctional Sciences I, Discipline of Anatomy,
E-mail: alexandra.mastaleru@gmail.com

Submission: 18sep 2017
Acceptance: 21 dec 2017

Parents against autism spectrum disorders

Mihaela GRASU

Mihaela GRASU - Ph. D., teacher for students with special needs, Special School "Constantin Păunescu" Iași, 11-15 C. A. Rosetti Street

ABSTRACT

Autism spectrum disorders have a wide variety of clinical manifestations. The central elements are the isolation and indifference to others, delays in expressive language development and repetitive behaviors, stereotyped, rigid or self-and heteroaggression. Having a child with autism spectrum disorders is one of the biggest challenges for parents, because autism spectrum disorders do not heal. Obvious improvement in symptoms and increasing social integration occur when therapeutic intervention was early and intensive. This study is based on a field investigation conducted in the period January 2015 - November 2016 in several centers in Iasi offering psychosocial services to children with autism: a special school, Department of Child Protection and Social Welfare and two non-governmental organizations. Interviews were conducted with a number of 25 professionals and parents. Analysis of data obtained show that in addition to the difficulties of acceptance disorder and behavioral problems of children, the parents are faced with the lack of intervention services and social stigmatization. This article proposes a series of measures to help improve services for children with autism spectrum disorders and their families.

KEYWORDS:

autism spectrum disorders, field investigation, diagnostic and therapy services for children with autism spectrum disorders, social stigma.

INTRODUCTION

Discovered in 1943 by psychiatrist Léo Kanner, autism spectrum disorders (ASD) have a wide variety of clinical manifestations. The central element is the isolation or indifference to the others, people with ASD prefer-

ring instead the world of objects. Delays in expressive language development is another observed characteristic of children with ASD. Typically, children with ASD may seem deaf, although audiometry tests are normal. Thirdly, repetitive behaviors, stereotypes motor rigidity and self-movements and heteroagre-

sive are distinguished. Other disorders such as food or sleep problems are among the most common. While some people with ASD show a delay cognitive function, 10% of them were isolated skills in certain areas, such as music, drawing, memory for specific information numeracy skills, sophisticated construction, puzzle etc. (6).

If for clinicians and scientists ASD is a mystery for families is a painful experience. More research points to high levels of stress in mothers of children with ASD, fear of future and depressive symptoms compared with mothers who have not children with developmental disorders (4) or parents of children with Down syndrome, fragile X syndrome or severe intellectual disability (1). If the severity of symptoms associated with ASD is higher, the mothers have higher levels of depression and stress (3). The inclusion of children in early intervention programs focused on developing communication, social skills and academic prevent repetitive behaviors and inadequate determine both increase the chances of social integration of children with ASD (22) and a reduction in levels of stress and depression experienced by mothers (4), (13). The couples raising a child diagnosed with TSA work better if they receive external social support (10), (20).

The aim of this study is to identify the main difficulties faced by parents of children with ASD in Iasi, expressed by parents or reflected by professionals. The study also proposes a series of measures to facilitate family functioning where there is a child with ASD.

METHOD

The research took place in Iasi, in January 2015-November 2016. The research method used was semi-structured interview based on an interview guide. 25 interviews were conducted with eight professionals from two non-governmental organizations (two managers, a social worker, a pedagogue, four psychologists), eight teachers from the Special School *C. Păunescu*, four specialists from the Department of Child Protection and Social Welfare (DCPSW) and five parents of children with ASD. The questions concerned the parents: the child disorder history, institutional route followed, difficulties and expectations from institutions and professionals. Professionals were asked about their working with the parents of children with ASD, the difficulties they encounter in relation to various institutions, the expectations they have of the specialists. Participants in the research were informed about the purpose of research, the method of collection the information and were guaranteed anonymity. Interviews were audio recorded with the consent of the subjects. After transcribing the interviews followed the analysis, identifying significant elements, then grouping them into themes and subthemes.

RESULTS

The analysis of the interviews shows that parents of children with ASD face the following problems: 1) the difficulties of acceptance of the disorder; 2) difficulties of managing problematic behaviors of the child; 3) lack of intervention services; 4) social stigmatization.

THE DIFFICULTIES OF ACCEPTANCE OF CHILD DISORDER

Most parents noticed the first signs of concern in children, but not always immediately go to the specialists. They are going through an intense kneading process until they have the courage to go to an assessment with the child. In many cases, early diagnosis of child postponement was caused by lack of knowledge of family physician who advised parents to wait because the development is different from child to child:

I always knew that the girl has problems. It was a fussy baby from the beginning, she became rigid when I take in my arms. (...) All in the family encouraged me, she is beautiful, smart, she will speak. Family physicians assured me it was okay, she'll talk, she's spoiled. (...). Then the encouragement helped me, I did not want to accept that trouble. I went with the girl to the doctor neuropsychiatrist at 3½ years, and only when she was diagnosed (interview no. 23, parent).

I went to the physicians and I told him that the girl does not speak and said that other children talk later In the end I went and asked reference to neuropsychiatry. And I took her to the neuropsychiatrist to 3 years and 9 months (interview no. 21, parent).

Sometimes parents are dismayed by physicians who confused ASD with hearing loss. In other cases, even neuropsychiatrists were reserved and delayed diagnosis of ASD, which involved have not immediate intervention (interview no. 15, DCPSW specialist).

After receiving the diagnosis, parents closely

in denial, blame, depression, especially when they realize that autism is a disorder for life. Until they can be able to balance and mobilize to begin the therapy with the child, it may take a long time:

After the child was diagnosed with autism we said let's go and to other specialists and we went to all neurologists and psychiatrists in Iasi, then we arrived in Bucharest and they all gave us the same diagnosis (interview no 22, parent).

The question is *how the parents learn to live with autism, which is not easy. (...) Some parents have no resources, no solutions, they do not have the power to do something for it, and then automatically passed on to the child and the family relations* (interview no. 16, DCPSW).

Finally, the parents seek help for children, but for themselves it's hard to do, although they pass through the confusion, discomfiture or depression. It reaches even to family breakdown, because one parent does not accept that it has a child with ASD and he give him another full responsibility of bringing up child:

Nobody gives parents advice, guidance, help, they have to deal with a problem that will last a lifetime, have a wide range of emotions and no one pays attention (interview nr. 18, DCPSW specialist).

The difficulties of acceptance of child disorder may manifest in the form of higher expectations for the child. When the child's progress is less visible, especially in developing the language, parents fall into depression.

For this reason the specialists explain to parents from the beginning that progress can occur very hard, many hours of therapy and help parents to recognize that have to be completed all stages of development, can not jump over them. It takes time and overcome some phases that parents can see the child as it is and to give him what he needs to develop to the fullest possibilities:

parents (...) waiting for healing, expects to see progress (...) they put a lot of heart in what they do and expect child's progress (...) There are severe cases that evolve very, very hard, but the mother wants a miracle (interview no. 7 specialist NGOs).

There are parents who do not see realistic problem ... the child is 8 months cognitive stage, but the parent asks when the child starts to speak ... he will be enrolled in regular school. It is hard for parents to accept that we teach to use the toilet, eat alone, to bathe themselves (interview no. 3 specialist NGOs).

THE DIFFICULTIES IN MANAGING CHILD PROBLEM BEHAVIORS

Range of children's problem behavior is varied from agitation, self- or hetero-aggressive behavior, oppositional behavior, refusal to change to insomnia and eating problems.

Children with ASD may become agitated or aggressive in the face of situations that seem new or difficult. They refuse change because they have a fear of what is unpredictable or uncontrollable:

When we have to leave home and I have to, dress her, she beginning to cry. (...) She started

to hit, she has an aggressive behaviour (interview no 21, parent)

The parents of children with ASD are constantly in a state of vigilance and feel the need to always supervise. They have learned to anticipate their needs, especially where children are not expressed verbal:

We communicate in looks, gestures, she moves her lips, I know he is hungry or thirsty, rubs his ear, I know he is sleeping, when she yells I have to try and see what's missing and what she wants. When she does not want to eat, no water, not sleepy at some point say, bye, that would ride or start and cry and cry, let's go to the kids, until you try all the variants to see, maybe she misses her teeth, maybe she has a stomach ache, maybe she has something she can not say and then and then we learn to be patient and try to find out what she has (interview no 25, parent).

Sometimes the children suffer from insomnia and the parents are forced to resort to drugs, which in turn can have other adverse effects.

LACK OF INTERVENTION SERVICES

After diagnosing the child, parents should receive post-diagnostic counseling and guidance services for network intervention. But in many cases, the specialists who evaluate the child and give the diagnosis, provide little information for parents. Few of them guiding them toward therapy services, on the contrary, they transmit the idea of parents that for ASD can not do anything:

I received the diagnosis from a doctor, a paper and so, I was not told where to go. After I re-

covered a little I started looking (interview no. 20, parent).

Governments of Romania adopts the same passive attitude in front of ASD. They providing benefits to families who have a child with ASD framed in degree disability, without creating free services that can be accessed by parents. Also, do not settle educational therapies, although in 2010 was adopted Law no. 151 (12) on services for people with autistic spectrum disorders. Moreover, the procedure for obtaining financial aid by the state is quite laborious and it must be repeated annually:

I have to go to the Commission in July and I have to start documents in May. You need a medical certificate from the specialist physician, psychological evaluation, social inquiry at the city hall and all sorts of other documents (interview no. 21, parent).

Once parents aware of child's diagnosis and realize the need for specific action, they seek solutions to starting of therapy. At the local level there are few specialized intervention services to children with ASD. Some of them are extra cost, and some parents are unable to access them because they can not make face the expenses, especially since some mothers gave up work to care for the child:

I took the girl to a private kindergarten, but as I was left service and tax was higher than the salary of a personal assistant, I have not coped expenses (interview no. 23, parent).

We do not have specialized institutions. Should a day center where the child to stay from 7 am to 5 pm for parents to be able to go to work (interview no. 22, parent).

In the Special School *C. Păunescu* and DCPSW children with disabilities can be included in intervention and recovery programs, but parents of children with ASD turn to them only when no other alternative. They look for services that offer specific therapy by a trained, because goodwill is not enough to work with these children:

Special Kindergarten 7-8 years ago received both children with autism and mental deficiency were together and then I have not wanted to give and we went to Ancora Salvării Foundation which really only work with autistic children. They were the same age, I looked, it was educational stimulation and the boy went there (interview no. 22, parent).

The staff must receive initial training and continue to have appropriate materials and to deal with an optimal number of children. Large groups of children are not effective, because ASD involve an individual work, for training and practicing basic skills:

In Iași there are several private and state initiatives for children with autism, in contrast there is no service for adults with autism. This leads parents of children with autism to look into the future with fear and wonder what will happen to their child when they are no longer. Creation of services for adults with autism, as existing models in other countries, is a real priority. In this way, the investment in schooling of children with ASD would be found in sheltered workshops where people with ASD should carry out paid work (interview no 12, Special School specialist).

Also after the age of 18, the state withdrew financial support. This was before 2013, when

the diagnosis of ASD was not recognized in adulthood and was changed to schizophrenia. Order 692 of 23 May 2013 the Minister of Health (15) has regulated this issue, the diagnosis of ASD in adulthood is recognized and classified in degree disability.

SOCIAL STIGMA

Besides issues related developmental delay or child's challenging behaviors the parents must overcome and externalizing behavioral reactions of others to the child. Lack of information about ASD, the contrast between the physical appearance of the child showing no signs of any disabilities and behavior perceived as abnormal or strange are his parents to go through the embarrassing predicament. Child behavior is often seen as a symptom of lack of education or parental indulgence. In this way parents perceive themselves stigmatized and misunderstood by others:

She screamed loud when it came to go by bus or on the street and people convict me (interview no. 24, parent).

With regard to inclusive education of children with ASD are big problems. From the legal point of view, parents of children with ASD can choose between special and inclusive schools. In fact, some parents refuse special school because they are afraid that children there will not progress and that they may be abused. In mainstream school, the numerous and heterogeneous collectives of pupils put the teacher into difficulty:

I took her to kindergarten than a few days, she had episodes of self-harm and scare those other children and the teacher accepted her, but I was constantly stay with her (interview no 22, parent).

DISCUSSIONS

Following this research were revealed the main categories of difficulties faced by parents of children with ASD in Iasi on which I proposed several measures to help improve services for children with ASD and their families.

The main categories of difficulties resulting from this study parents are accepting disorder, child behavior problems, lack of intervention services and social stigmatization.

Parents find it difficult to accept that they have a child with a disease for which there is no cure and go on to different specialists hoping refute the diagnosis. The fact that this diagnosis is made based on the descriptions of behavioral and clinical observation and that there is no medical test to determine definitely whether or not a person has ASD, as in Down syndrome, parents create greater confusion. And other researches have revealed that behavioral problems associated with ASD, self- and hetero-aggression, sleep difficulties, fixation on certain objects etc. are a source of stress for parents of children with ASD (16) (14), (20).

Altieri and Von Kluge (2) found five challenges that emerged from the family's experiences of children with ASD: Development, Questioning, Devastation, Solutions and Growth. First of

.....

all, parents are worried about delays in language development. They begin to ask questions, like: is my child different? What's wrong with him? Usually from pediatrician they expecting answers to these questions. Every parent described the confusion that resulted from their child's behavioural presentat and the feelings of loss and devastation that occurred after discovering their child has ASD. Finally, parents will mobilize all their possible resources to help their child, sometimes in any possible way. After Scorgie et al. (18), the parents passes through three stages after the child is diagnosed. In the early stages following diagnosis, parents are confronted with a number of critical emergent questions: Who is my child? Who can he/she become? What is my life going to be like, now and in the future? Secondly, the parents try to mak sense of the diagnosis and its impact on their lives: Why did this happen to us? How can I make sense of it? Finally, the parents wondering themselves how they are going to manage life: How am I going respond? What options are available to me and my family?

Limited access to medical services or educational intervention is another difficulty faced by parents of children with ASD (21), (16). A common frequently applied solution is the formation of parents to become the child's therapists (13), (5).

Lack of understanding, support and involvement from the State leads parents to accumulate a series of negative experiences (19) analysis of online media in Romania show that parents feel frustrated because the state is not involved in creation free services for people with ASD (7). In addition, parents are thinking with concern the future, given the dependence of children and lack of services for adults with ASD (19), (7). And other research results that parents of autistic children feel misunderstood and stigmatized by society (16), (11) and that they live in a world of its own, because their life is programmed as ABA therapy, are isolated from friends and extended family and are without support from the institutions (21).

Ryan and Runswick Cole (17) believes that, in general, the parents of children with disabilities take on the role of an advocate because they have to facilitate contact with the other children, they face other parents, notify organizations, authorities or interact with professionals. Among these parents there are the parents whom he calls activists, who do not focus only on their child, but they fight for the cause of several children.

Also the problem of integrating children with ASD in mainstream schools is a subject frequently reported through press articles on the theme of ASD (7). For a successful integration of students with ASD need to reach a certain level of development, so as to be accepted by peers, participate in group activities. On the other hand, inclusive schools in Romania are insufficiently prepared to accept children with special educational needs. Pupils missing school programs tailored to their needs and the number of support teachers and school counsellors is very low (9). Teachers working in inclusive classes feel this as a "double constraint", having to choose between to be attentive to children with SEN or other students in the class. Thus, teachers resort to a series of secondary coping mechanisms, such as neglect of children with SEN, their indiscriminate treatment to her classmates, use of inappropriate punishment (8).

DISCUSSIONS

Following this research were revealed the main categories of difficulties faced by parents of children with ASD in Iasi on which I proposed several measures to help improve services for children with ASD and their families.

The main categories of difficulties resulting from this study parents are accepting disorder, child behavior problems, lack of intervention services and social stigmatization.

Parents find it difficult to accept that they have a child with a disease for which there is no cure and go on to different specialists hoping refute the diagnosis. The fact that this diagnosis is made based on the descriptions of behavioral and clinical observation and that there is no medical test to determine definitely whether or not a person has ASD, as in Down syndrome, parents create greater confusion. And other researches have revealed that behavioral problems associated with ASD, self- and hetero-aggression, sleep difficulties, fixation on certain objects etc. are a source of stress for parents of children with ASD (16) (14), (20).

Altieri and Von Kluge (2) found five challenges that emerged from the family's experiences of children with ASD: Development, Questioning, Devastation, Solutions and Growth. First of all, parents are worried about delays in language development. They begin to ask questions, like: is my child different? What's wrong with him? Usually from pediatrician they expecting answers to these questions. Every parent described the confusion that resulted from their child's behavioural presentat and the feelings of loss and devastation that occurred after discovering their child has ASD. Finally, parents will mobilize all their possible resources to help their child, sometimes in any possible way. After Scorgie et al. (18), the parents passes through three stages after the child is diagnosed. In the early stages following diagnosis, parents are confronted with a number of critical emergent questions: Who is my child? Who can he/she become? What is my life going to be like, now and in the future? Secondly, the parents try to mak sense of the diagnosis and its impact on their lives: Why did this happen to us? How can I make sense of it? Finally, the parents wondering themselves how they are going to manage life: How am I going respond? What options are available to me and my family?

Limited access to medical services or educational intervention is another difficulty faced by parents of children with ASD (21), (16). A common frequently applied solution is the formation of parents to become the child's therapists (13), (5).

Lack of understanding, support and involvement from the State leads parents to accumulate a series of negative experiences (19) analysis of online media in Romania show that parents feel frustrated because the state is not involved in creation free services for people with ASD (7). In addition, parents are thinking with concern the future, given the dependence of children and lack of services for adults with ASD (19), (7). And other research results that parents of autistic children feel misunderstood and stigmatized by society (16), (11) and that they live in a world of its own, because their life is programmed as ABA therapy, are isolated from friends and extended family and are without support from the institutions (21).

Ryan and Runswick Cole (17) believes that, in general, the parents of children with disabilities

take on the role of an advocate because they have to facilitate contact with the other children, they face other parents, notify organizations, authorities or interact with professionals. Among these parents there are the parents whom he calls activists, who do not focus only on their child, but they fight for the cause of several children.

Also the problem of integrating children with ASD in mainstream schools is a subject frequently reported through press articles on the theme of ASD (7). For a successful integration of students with ASD need to reach a certain level of development, so as to be accepted by peers, participate in group activities. On the other hand, inclusive schools in Romania are insufficiently prepared to accept children with special educational needs. Pupils missing school programs tailored to their needs and the number of support teachers and school counsellors is very low (9). Teachers working in inclusive classes feel this as a “double constraint”, having to choose between to be attentive to children with SEN or other students in the class. Thus, teachers resort to a series of secondary coping mechanisms, such as neglect of children with SEN, their indiscriminate treatment to her classmates, use of inappropriate punishment (8).

CONCLUSION

This study provides a true picture of the difficulties that parents of children with ASD live. It is limited to Iasi, so the results can not be generalized. From this research appear some practical implications:

First, parents need information on child disability peculiarities, but also in terms of the services dealing with people with ASD.

Secondly there is a need for setting up services for people with ASD, for all palettes age from early intervention services, to services for adults with ASD to support them in their social integration.

Development centres providing support to the entire family is also essential. Parents are assisted throughout intervention on the child, help him understand, to learn how they can help you develop, how to react in the face of difficult behaviors, to express emotions and personal feelings, solve problems that arise.

ACKNOWLEDGEMENTS AND DISCLOSURE

This paper is a result of a research made possible by the financial support of the Sectoral Operational Programme for Human Resources Development 2007-2013, co-financed by the European Social Fund, under the project POSDRU/159/1.5/S/ 132400 – “Young successful researchers – professional development in an international and interdisciplinary environment”.

The author states that there are no declared conflicts of interest regarding this paper.

REFERENCES

1. Abbeduto, L., Seltzer, M. M., Shattuck, P., Krauss M. W., Orsmond, G., Murphy, M. M. Psychological Well-Being and Coping in Mothers of Youths With Autism, Down Syndrome, or Fragile X Syndrome. *Am J Ment Retard.* 2004; 109 (3): 37–254.
2. Altieri, M. J., Von Kluge, S. (2009). Searching for acceptance: Challenges encountered while raising a child with autism. *Journal of Intellectual and Developmental Disability* 2009; 34 (2): 142-152
3. Athari, P., Ghaedi, L. et al.: Mothers' depression and stress, severity of autism among children and family income. *Int. J. Psychol. Res.* 2013; 6 (2): 98-106.
4. Baker-Ericzén, M. J., Brookman-Frazee, L. and Stahmer, A. Stress Levels and Adaptability in Parents of Toddlers With and Without Autism Spectrum Disorders *RPSD* 2005; 30 (4): 194-204.
5. Corsello, C. M., Early Intervention in Autism. *IYC* 2005; 18(2): 74-85.
6. Guillery-Girard, B., Eustache, F. Fonctionnement mnésique dans l'autisme: un paradoxe. *La Lettre des Neurosciences Bulletin de la Société des Neurosciences* 2011; 41: 15-16
7. Grasu, M.: Challenges parents of children with autism in local and national press. *Communication, Context, Interdisciplinarity, Studies and Articles. Vol. III, Section Psychology and Sociology*, Boldea, I. Târgu-Mureş: Petru Maior University Press; 2014: 370-375.
8. Grasu, M. *Sociologia câmpului de intervenție profesională. Incluziunea copiilor cu cerințe educative speciale în învățământul de masă (Sociology of the field of intervention. Inclusion of children with special educational needs mainstream education)* Iași: University Publishing House Al. I. Cuza, 2013.
9. Grădinaru, C. *Analiza serviciilor de sănătate mintală pentru copiii din România (Analysis of mental health services for children in Romania)* 2010, Save the Children
10. Harper, A., Dyches, T. T., Harper, J., Roper, S. O.; and South, M., Respite Care, Marital Quality, and Stress in Parents of Children with Autism Spectrum Disorders. *JADD* 2013; 43 (11): 2604-2616
11. Heiman, T.: Parents of Children With Disabilities: Resilience, Coping and Future Expectations. *Journal of Developmental and Physical Disabilities* 2002; 14: 159-171.
12. Law no. 151/2010 on integrated specialized health, education and social services for persons with autistic spectrum disorders and associated mental health disorders. *Official Gazette of Romania*, I (483): 14.07.2010.
13. McConachie, H, Diggle, T. Parent implemented early intervention for young. *RJLM* 2007; 15 (2): 127 – 134
14. Neely-Barnes, S., Dia, D.: Families of Children With Disabilities: A Review of Literature and Recommendations for Interventions. *JEIBI* 2008; 5 (3): 93 – 107.
15. Order no. 692/982/2013 on the modification of chapter. 1 of the Annex to the Order of the Minister of Labor, Family and Equal Opportunities and of the Minister of Public Health no. 762/1992/2007 for the approval of the medical-psychosocial criteria on the basis of which it is established the degree of handicap, published in the *Official Gazette of Romania*, I (313): 30.05.2013.
16. Pisula, E. Parenting Stress in Mothers and Fathers of Children with Autism Spectrum Disorders. Mohammadi, M-R. (Ed.), *A comprehensive book on autism spectrum disorders* Rijeka: Publiches by InTech, 2011; 87-106
17. Ryan, S., Runswick Cole, K. From Advocate to Activist? Mapping the Experiences of Mothers of Children on the Autism Spectrum. *JARID* 2009; 22: 43–53
18. Scorgie, K, Wilgosh, L., Sobsey, D. The experience of transformation in parents of children with disabilities: Theoretical considerations. *DDB* 2004; 32 (1): 84-110.
19. Ștefănescu, F., Oșvat, C. Socioeconomic Implications of Autism Case Study on Realities. *Revista de Asistență Socială* 2011; 2:79-88.
20. Weiss J.A. et al. Family hardiness, social support, and self-efficacy in mothers of individuals with Autism Spectrum Disorders. *RASD* 2013; 7: 1310–1317
21. Woodgate, R. L., Ateah, C., Secco, L. Living in a World of Our Own: The Experience of Parents Who Have a Child With Autism. *QHR* 2008; 18 (8): 1075-1083.
22. Zwaigenbaum, L. et all. Early Intervention for Children With Autism Spectrum Disorder Under 3 Years of Age: Recommendations for Practice and Research. *Pediatrics* 2015; 136 (1): S60-S81

Correspondence:

Mihaela Grasu

Ph. D., teacher for students with special needs,
Special School "Constantin Păunescu" Iași, 11-15 C. A. Rosetti Street,
zip code 700141, tel 0721665057, fax 0232-277269,
E-mail: grasumihaela73@gmail.com.

Submission: 17 nov 2017
Acceptance: 10 jan 2018

Dietary supplements and their influence on our mental health

Antoneta Dacia PETROAIE, Adriana COSMESCU,
Elena Adorata COMAN, Alexandra BOLOȘ

Antoneta Dacia PETROAIE - MD, PhD, assistant of professor, Discipline of Family Medicine, Department of Preventive Medicine and Interdisciplinarity, Gr.T.Popa University of Medicine and Pharmacy Iasi

Adriana COSMESCU - MD, PhD, senior pediatrician, pediatric diabetology, lecturer, Discipline of Family Medicine, Department of Preventive Medicine and Interdisciplinarity, Gr.T.Popa University of Medicine and Pharmacy Iasi

Elena Adorata COMAN - MD, PhD, senior internist, lecturer, Discipline of Family Medicine, Department of Preventive Medicine and Interdisciplinarity, Gr.T.Popa University of Medicine and Pharmacy Iasi

Alexandra BOLOȘ - MD, PhD, lecturer, senior psychiatrist, Gr.T.Popa University of Medicine and Pharmacy Iasi

ABSTRACT

The general practitioner is the first one that contributes to our health, having a major role in promoting and maintaining health, as well as in the detection of various diseases. Psychiatric pathology is considered to be a major health problem lately, as the number of mental disorders is becoming higher. In our everyday practice, we interact with patients of all ages that complain of the symptoms of anxiety or depression. The family doctor, through its direct and frequent contact with the patient and due to effective collaboration with the psychiatrist, is able to prevent or even pinpoint this type of disorders. In this context, we ask whether particular food can influence the clinical evolution of an anxious or depressed patient. This article tries to centralize the results from published studies and to find out a possible link between diet and this pathology.

KEYWORDS:

Nutrition, anxiety, depression

The statement, released by the International Society Nutritional Psychiatry Research (ISNPR) highlights the fact that there is epidemiological and clinical evidence to show that diet, especially certain nutrients, both influences the risk and the evolution of mental health disorders: "The changes in our diet, globally, have resulted in a tsunami of ill

health across the globe, and an unhealthy diet is understood to be the greatest cause of early mortality, mental health disorders, neurodegenerative disorders, and possibly neurodevelopmental disorders"(1).

Even though the outcomes achieved by current treatments of mental disorders are "suboptimal," little attention is paid to pre-

vention. As such, diet and nutrition are modifiable targets for the prevention of mental disorders and play a key role in promoting mental health. From this perspective, I believe that the family doctor, in close collaboration with the psychiatrist, could contribute effectively to dispensing the patient suffering from mental disorders, as the preventive medicine is one of the most important parts of the family medicine. Furthermore, ISPNR states that “evidence-based nutritional change should be regarded as an efficacious and cost-effective means to improve mental health.” (1). As a result, changing dietary habits should be done in the context of a partnership between the patient, the family doctor and the psychiatrist. First of all, the patients should be available to discuss their problems with some specialized persons and also aware of the benefits of a healthy diet in relieving his illness. Modern nutrition counseling needs to be as individualized as possible and every advice, every piece of information has to suit patients’ needs and their possibilities to follow them.

At this point, the influence of **dietary patterns** of cognitive changes is not very well known and very precise. A survey conducted in Norway in 2011 on 5731 adults, women and men, suggests that the modern global diet (western-type diet) has been correlated with an increased risk of anxiety, about 25%, compared to a healthier diet (High-Quality diet) that is less susceptible to such disorders (2). More research suggests that adherence to a Mediterranean-style diet (fruit, vegetables, monounsaturated fatty acids: olive oil or avocado, polyunsaturated fatty acids: fatty acids) may be protective towards the aging brain, the risk of developing depression is

significantly reduced.

Possible mechanisms by which these foods may boost brain function include neuronal membrane stabilization and anti-inflammatory effects(3). There are increasing debate and evidence regarding the crucial role that certain nutrients play in brain health: **choline, S-adenosyl methionine, omega-3 fatty acids, probiotics, and magnesium.**

Choline is a dietary component essential for normal function of all cells. In 1998, the National Academy of Sciences from USA issued a report identifying choline as a required nutrient for humans and recommended daily intake amounts(4). The adequate intake is 425 mg/day for women, 450 mg/day for pregnant women and 550 mg/day for men and for women during lactation(5). There is a significant variation of the need for choline, which can be explained mainly by a genetic polymorphism. Nutrigenetics and nutrigenomics have contributed to demonstrating that choline needs vary among individuals; genetic polymorphisms, genes, estrogenic status, and intestinal microbial composition, influencing optimal intake levels.

The currently recommended daily intake does not take into account these genetic variations that are in fact a modulator of dietetic requirements. When the daily dose was established in 1998, it was assumed that less than 5% of the population would be affected by choline deficiency. It is now clear that up to 50% of the population may have genetic polymorphisms that increase the need for methyl from food, a major source for this being choline. It is good to know that the foods with the highest total choline concentration (mg/100g) are: beef liver (418), chicken liver (290), egg (251), wheat germ

(152), bacon (125), soybean (160), pork meat (103) (6).

Despite its importance in the central nervous system as a precursor for acetylcholine and membrane phosphatidylcholine, the role of choline in mental disorders has been little studied. In tissues and foods, there are several choline compounds that contribute to the total choline concentration (choline, glycerophosphocholine, phosphocholine, phosphatidylcholine and sphingomyelin). Although there is a pathway for endogenous choline synthesis, its deficiency may affect cognitive function and anxiety. A prospective study published in 2009, which included 5918 patients with symptoms of anxiety and depression, showed that low plasma levels of choline may increase the risk of anxiety disorders by up to 33% without influencing the symptoms of depression(7). Patients were evaluated using the Hamilton scales for anxiety and depression, used both to detect anxiety and depression, and to assess their severity (8).

As a conclusion, given the importance of choline in the development and functioning of the central nervous system, as well as the consequences of suboptimal dietary intake, nutritional recommendations should encourage the consumption of food rich in choline to improve mental health.

Betaine, a metabolite of choline, is the main source of methyl groups in the diet. Foods with the highest betaine concentration (mg/100g) are wheat bran (1339), wheat germ (1241), spinach (645), pretzels (237), shrimps (218) and wheat bread (201). By methylation of homocysteine, methionine is formed, of which S-adenosyl methionine is synthesized in the presence of magnesium

and adenosine triphosphate (ATP). This enzyme participates in the synthesis of neurotransmitters: L-dopa, dopamine, serotonin, adrenaline, noradrenaline and acetylcholine. The specialised literature emphasize that S-adenosyl methionine (SAME) has antidepressant efficacy and is used as an additional treatment for subjects with mild to moderate depression that have poorly responded to other antidepressants. However, there is some concern about the possible impact of SAME therapy on homocysteine levels, hyperhomocysteinemia associated with an increased risk of cardiovascular disease and venous thrombosis. Betaine is known both to counteract the high level of homocysteine in plasma and to increase liquor and plasma levels of SAME, thus potentiating its effect.

A randomized controlled trial that enrolled 46 subjects with a diagnosis of mild-to-moderate depression and a suboptimal control of their symptoms according to the Beck Depression Inventory evaluated the role played by betaine, administered along with SAME, in potentiating the antidepressant role played by SAME administered as such. The combination of SAME and betaine statistically demonstrated greater efficacy after a 90-day treatment than SAME alone, although both treatments have improved symptom relief such as anxiety, psychomotor agitation, feelings of helplessness and lack of value, physical efficiency and somatization (9).

Concerns about the evaluation of SAME effects in relation to placebo or antidepressant medication are increasing, but in order to benefit from strong evidence and conclusions, future research should include large controlled, randomized, high-quality clinical studies.

In recent years, there has been a growing debate about bowel-brain connection and intestinal microbial influence on mental health, the use of probiotics and fermented foods in patients with anxiety and depression becoming a topic of great interest.

Relatively new research strategies have deepened the understanding of psychiatric illnesses and their connections with certain disorders of the gastrointestinal tract. It has been demonstrated the existence of bi-directional communication between the brain and the intestine and an increasing number of clinical evidence support the hypothesis that cognitive and emotional processes are influenced by the brain-intestinal axis. On the other hand, the microbiota can influence brain function and even behavior, giving to specific microorganisms a psychobiotic potential (10).

There are studies showing that **probiotics** can have an anxiolytic and protective effect against the symptoms of social anxiety for those with higher genetic risk (11). It is suggested that certain probiotics, such as Bifidobacterium and Lactobacillus, would alleviate stress response, depressive disorder, stemming from the interaction between susceptibility genes and environmental events, particularly stressful events. A randomized, double-blind, placebo-controlled study, published in 2016, which included 40 patients with a diagnosis of depression, concluded that probiotics had beneficial effects on them. Probiotic capsules consisted of three viable and lyophilized strains: Lactobacillus acidophilus, Lactobacillus casei, and Bifidobacterium bifidum. After eight weeks of treatment with probiotic supplements, the total scores of the Beck Depression inventory decreased

significantly (-5.7 ± 6.4 vs -1.5 ± 4.8 , $P = 0.001$) compared to placebo(12). In 2013, in a study conducted by researchers from the University of California, Los Angeles and France, two fermented dairy products, kefir and yogurt were analyzed, with a significant influence on neural circuits related to somatic emotions (13). Modification of the microbiota leads to increased intestinal permeability and irritable bowel syndrome which is a typical phenotypic phenomenon of psychological stress, manifested and developed in patients with depressive disorder (14).

All these results lead us to the conclusion that recommending probiotics or fermented foods to patients with anxiety and depression (kefir, yogurt, unpasteurized pickled cabbage) is beneficial, as their intestinal microbiota would be enriched and in the same time their mental health would be positively influenced.

Omega-3 fat must be taken into account when talking about mental health and nutritional psychiatry. There is sufficient evidence that the deficiency of these fats in the diet is involved in the etiology and pathophysiology of depressive disorders. Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are two long-chain omega-3 polyunsaturated fatty acids (PUFA), EPA having more antidepressant and anti-inflammatory effects than DHA. PUFAs are essential macronutrients that our body cannot synthesize, so they can only be obtained from the diet. The primary source of omega-3 fatty acids (EPA + DHA) is fat fish oil (herring, sardine, anchovies, trout, salmon, mackerel, cod, tuna), fish oil and edible seaweed supplements.

Several cross-over studies have investigated the relationship between regular fish/fish oil consumption and depression rates in the

general population. For example, a 2007 transversal study on 21.835 adult and elderly subjects in Norway found that subjects who ate daily cod liver oil (EPA: about 300-600 mg/day, DHA: about 300-600 mg/day) were 30% less likely to have depressive symptoms than non-consumers(15). It has also been shown that patients who are in an acute depressive episode (especially in those with comorbid anxiety), omega-3 PUFA levels are lower than those in remission or who are healthy (16).

There are currently concerns about the efficacy of omega 3 when it comes to speaking about pregnant women with depression. A pilot study conducted in 2017 showed that the administration of 1800 mg of omega 3 containing 1206 mg of eicosapentaenoic acid and 609 mg of docosahexaenoic acid for 12 weeks modify the Hamilton scale for depression, improving depressive symptoms of future mothers. Randomized controlled studies and additional investigations are needed to support the beneficial effects of omega 3 in preventing and monitoring depression during pregnancy and immediately after the birth.

Therapies in depressive disorders for children are still unclear and represent a subject of study worldwide. Although literature data are limited to have solid conclusions, results on the use of omega-3 in children with depressive disorder are positive and encouraging. As the onset of depressive disorders occurs frequently during adolescence, it is relevant that low intake of omega-3 fatty acids in adolescents is associated with increased depressive symptoms.

Depression and inflammation combine with each other, inflammation playing a key role in

the pathogenesis of depression. A certain lifestyle (inappropriate diet, sedentaryism), depressive symptoms or stress factors can cause frequent and long-lasting inflammatory responses, with negative consequences on mental and physical health(18). Because of the fact that proinflammatory cytokines production is increasing, it has been hypothesized that administration of omega-3 PUFA supplements to healthy subjects would lead to a decrease in this production. We present the results of a double-blind randomized controlled clinical trial conducted in 2011 on 68 medical students who received for 12 weeks, omega 3 capsules with a 7/1 EPA / DHA ratio (2,5 g/day, 2085 mg EPA and 348 mg DHA) or placebo capsules. They provided blood samples for less stressful periods, as well as a few days before a requesting exam. Compared to the witnesses, those students who received omega-3 fat showed a 20% reduction in anxiety scores without a significant change in depression scores(19). This study suggests that EPA might be more effective than DHA in preventing anxiety under stress. At the same time, interleukin-6 levels were also analyzed and a significant reduction of up to 14% was observed.

The American Psychiatric Association adopted the recommendations of the American Heart Association consensus for a dose of 1 g/day of a 2:1 ratio considered most effective in the treatment of depressive symptoms (20). Although additional studies are required to determine the optimal dose of omega 3, the existing evidence suggests that an initial dose of 1 g / day of EPA + DHA is safe and well tolerated by children, teenagers and adults suffering from psychiatric disorders. Hence, in depressive and anxious disorders,

the low level of omega-3 fat is a modifiable risk factor. In this sense, I would say that a lot of patients would benefit from an EPA + DHA treatment and a dietary supplementation with oily fish or fish oil recommended by the family doctor or psychiatrist.

Magnesium, the second most important intracellular cation, is involved in a number of biochemical processes crucial for the proper functioning of the human body and acts as a metabolic cofactor for over 300 enzymatic reactions. Among its different roles, magnesium modulates the entry and release of calcium from the sarcoplasmic reticulum and adjusts ATP pumps in the neuron, thus adapting neuronal excitability. It also plays a vital modulating role in brain biochemistry, influencing several neurotransmission pathways associated with depression. The lack of magnesium in the brain seems to reduce serotonin levels, while antidepressants produce an increase in magnesium in the brain. That is the reason why it is assumed that magnesium treatments could be beneficial to almost all depressive syndromes.(21) Even if a few experimental and clinical studies were made, the results showed a relationship between magnesium and depression and/or anxiety, but not specifically between the magnesium intake and the incidence of these disorders. Since the extracellular concentration of magnesium ions may not reflect their intracellular level, none of the current methods of evaluating magnesium status are regarded as satisfactory. It appears that magnesium supplementation is well-tolerated and enhances the efficacy of conventional antidepressant treatments (22). A randomized controlled trial was carried out in 2016 on 126 adults (mean age 52; 38%

men) diagnosed with mild to moderate depressive symptoms on PHQ-9 questionnaire, showed that daily supplementation with 248 mg elemental magnesium for 6 weeks leads to a significant decrease in the symptoms of depression and anxiety, regardless of age, gender, initial severity of depression, or use of antidepressant medication(23). The relief of symptoms was observed within a few weeks, and the effect was diminished within two weeks after stopping administering supplements due to a relatively fast clearance. Long-term efficacy is unknown and longer studies are required. As a result, magnesium supplements can be a fast, safe, easy and affordable alternative to initiating or increasing the dose of antidepressants.

Thus, we can consider that magnesium is a variable of interest in depressive disorders, just like omega 3 fat. The best sources of magnesium are green leafy vegetables, oleaginous fruits (nuts, almonds, pistachios, sunflower seeds), black chocolate, fat fish, whole grains, avocados, bananas. There are authors who claim that a diet low in magnesium would alter the intestinal microbiota, which in turn generates an anxious behavior (24). Magnesium (Mg) status is associated with subjective anxiety, which leads to the idea that Mg supplementation can alleviate the symptoms of anxiety (25). Controlled, randomized, large-scale studies are needed to identify the potentially protective role of magnesium ion against depression and / or anxiety (26).

Conclusions

Recent studies provide more and more valuable information on the implications and

role of certain nutrients in psychiatric disorders, particularly in depression and anxiety. Strengthening the relationship between the family doctor, psychiatrist and patient would lead us to a favorable outcome, if we start thinking that primary prevention is the best strategy to maintain the health of our patients. Regarding this, promoting a beneficial diet for brain health, as well as using certain supplements (SAME, probiotics, polyunsatu-

rated Omega 3 fatty acids, and minerals) would greatly help high-risk individuals, would influence the onset and clinical evolution of the disease and may even increase the therapeutic effect of antidepressants and anxiolytics. We can positively influence mental health through diet, which is not yet sufficiently and efficiently used, and research on this topic must be continued for deeper and clearer understanding.

ACKNOWLEDGEMENTS AND DISCLOSURES

The authors state that they are no declared conflicts of interest regarding this paper

REFERENCES

1. Liam Davenport. Dietary Change Key to Improving Mental Health, Experts Say. *World Psychiatry*. 2015;14:370-371.
2. Jacka FN; Mykletun A; Berk M; Bjelland I; Tell GS. The association between habitual diet quality and the common mental disorders in community-dwelling adults: the Hordaland Health study. *Psychosom Med*. 2011;73(6):483-90.
3. Pauline Anderson. New 'Brain Food' Scale Flags Best Nutrients for Depression. *Medscape Medical News*, May 26, 2016.
4. Zeisel SH. Choline: needed for normal development of memory. *J Am Coll Nutr*. 2000 Oct;19(5 Suppl):528S-531S.
5. Steven H. Zeisel. Choline. *Adv Nutr* vol.1: 46-48, 2010.
6. Zeisel SH, Mar MH, Howe JC, Holden JM. Concentrations of choline-containing compounds and betaine in common foods. *J Nutr* 2003;133:1302-7.
7. Bjelland I, Tell GS, Vollset SE, Konstantinova S, Ueland PM. Choline in anxiety and depression: the Hordaland Health Study. *Am J Clin Nutr*. 2009;90:1056-1060.
8. Steven H. Zeisel, M.D., Ph.D. and Kerry-Ann da Costa, Ph.D. Choline: An Essential Nutrient for Public Health *Nutr Rev*. 2009 Nov; 67(11): 615-623.
9. Di Pierro F, Orsi R, Settembre R. Role of betaine in improving the antidepressant effect of S-adenosyl-methionine in patients with mild-to-moderate depression. *J Multidiscip Healthc*. 2015 Jan 16;8:39-45.
10. Vlainić JV; Šuran J; Vlainić T; Vukorep AL. Probiotics as an Adjuvant Therapy in Major Depressive Disorder. *Curr Neuropharmacol*. 2016; 14(8):952-958.
11. Hillmire MR, DeVlyder JE, Forestell CA. Fermented foods, neuroticism, and social anxiety: an interaction model. *Psychiatry Res*. 2015;228:203-208.
12. Akkasheh G; Kashani-Poor Z; Tajabadi-Ebrahimi M; Jafari P; Akbari H; Taghizadeh M; Memarzadeh MR; Asemi Z; Esmailzadeh A. Clinical and metabolic response to probiotic administration in patients with major depressive disorder: A randomized, double-blind, placebo-controlled trial. *Nutrition*. 2016; 32(3):315-20.
13. Tillisch K; Labus J; Kilpatrick L; Jiang Z; Stains J; Ebrat B; Guyonnet D; Legrain-Raspaud S; Trotin B; Naliboff B; Mayer EA. Consumption of fermented milk product with probiotic modulates brain activity. *Gastroenterology*. 2013; 144(7):1394-401, 1401.e1-4.
14. Kunugi H. Depressive Disorder and Gut-brain Interaction. *Brain Nerve*. 2016; 68(6):641-6.
15. Robert K. McNamara. Role of Omega-3 Fatty Acids in the Etiology, Treatment, and Prevention of Depression: Current Status and Future Directions *J Nutr Intermed Metab*. 2016 Sep; 5: 96-106.
16. Thesing CS, Bot M, Milaneschi Y, Giltay EJ, Penninx BWJH. Omega-3 and omega-6 fatty acid levels in depressive and anxiety disorders. *Psychoneuroendocrinology*. 2017 Oct 6;87:53-62.
17. Vaz JDS, Farias DR, Adegboye ARA, Nardi AE, Kac G. Omega-3 supplementation from pregnancy to postpartum to prevent depressive symptoms: a randomized placebo-controlled trial. *BMC Pregnancy Childbirth*. 2017 Jun 9;17(1):180.
18. Kiecolt-Glaser JK, Derry HM, Fagundes CP. Inflammation: depression fans the flames and feasts on the heat. *Am J Psychiatry*. 2015 Nov 1;172(11):1075-91.
19. Kiecolt-Glaser JK; Belury MA; Andridge R; Malarkey WB; Glaser R. Omega-3 supplementation lowers inflammation and anxiety in medical students: a randomized controlled trial. *Brain Behav Immun*. 2011; 25(8):1725-34.
20. Kuan-Pin Su, Yutaka Matsuoka and Chi-Un Pae. Omega-3 Polyunsaturated Fatty Acids in Prevention of Mood and Anxiety Disorders *Clin Psychopharmacol Neurosci*. 2015 Aug; 13(2): 129-137.
21. Serefko A, Szopa A, Poleszak E. Magnesium and depression. *Magnes Res*. 2016 Mar 1;29(3):112-119.

22. Młyniec K, Davies CL, de Agüero Sánchez IG, Pytka K, Budziszewska B, Nowak G. Essential elements in depression and anxiety. Part I. Pharmacol Rep. 2014 Aug;66(4):534-44.
23. Tarleton EK, Littenberg B, MacLean CD, Kennedy AG, Daley C. Role of magnesium supplementation in the treatment of depression: A randomized clinical trial. PLoS One. 2017 Jun 27;12(6):e0180067.
24. Pyndt Jørgensen B, Winther G, Kihl P, Nielsen DS, Wegener G, Hansen AK, Sørensen DB. Dietary magnesium deficiency affects gut microbiota and anxiety-like behaviour in C57BL/6N mice. Acta Neuropsychiatr. 2015 Oct;27(5):307-11.
25. Boyle NB, Lawton C, Dye L. The Effects of Magnesium Supplementation on Subjective Anxiety and Stress-A Systematic Review. Nutrients. 2017 Apr 26;9(5).
26. Jacka FN, Overland S, Stewart R, Tell GS, Bjelland I, Mykletun A. Association between magnesium intake and depression and anxiety in community-dwelling adults: the Hordaland Health Study. Aust N Z J Psychiatry. 2009 Jan;43(1):45-52.

Correspondence:

Antoneta Dacia Petroaie

MD, PhD, assistant of professor,
University of Medicine and Pharmacy Gr.T.Popa Iasi,
str. Universitatii 16, 700115,
E-mail: pantoneta@yahoo.com,
+40744454703

Submission: 20 dec 2017

Acceptance: 02 feb 2018

Deep brain stimulation versus transcranial magnetic stimulation in psychiatric pathology

Raluca Mihaela FRÎNCU, Radu GAVRIL, Livia Andreea LUPȘA, Manuela PĂDURARIU, Cezar Valeriu BĂLUȚĂ, Cristinel ȘTEFĂNESCU

Raluca Mihaela FRÎNCU - M. D., Ph. D. Student, Specialist psychiatrist, "Socola" Institute of Psychiatry, Iași, Romania

Radu GAVRIL - M. D., Resident in Psychiatry, "Socola" Institute of Psychiatry, Iași, Romania

Livia Andreea LUPȘA - M. D., Resident in Psychiatry, "Socola" Institute of Psychiatry, Iași, Romania

Manuela PĂDURARIU - M. D., Ph. D. Student, Specialist psychiatrist, "Socola" Institute of Psychiatry, Iași, Romania

Cezar Valeriu Băluță - M. D., Resident in Nephrology Dr. C. I. Parhon Clinical Hospital, Iași, Romania

Cristinel ȘTEFĂNESCU - Professor, MD, PhD, senior psychiatrist, Gr.T.Popa University of Medicine and Pharmacy Iasi

ABSTRACT

Psychiatric and neuropsychiatric disorders continue to represent a major challenge for healthcare professionals, both through the direct risks they pose to the individual's life and society as a whole and because of the costs of treatment. Thus, an imperative need for new therapeutic approaches exists. Transcranial magnetic stimulation is a new technique that might just open new horizons in this field. Starting from the physical mechanism described two centuries ago, deep brain stimulation (DBS) has found its place among the therapeutic options targeting a multitude of psychiatric pathologies including obsessive compulsive disorder, depression and Alzheimer's disease. However, shortcomings such as the need for surgery, limited battery life, selecting the optimal brain target, along ethical arguments, reveal some of DBS technique's limitations. Addressing these issues, a new technique - transcranial magnetic stimulation (TMS) emerged in the current therapeutic arsenal. Considering the promising preliminary results, TMS proves to be worth more in depth exploration and research for potential applications in psychiatric practice.

KEYWORDS:

deep brain stimulation, transcranial brain stimulation, Alzheimer's disease, depression, obsessive compulsive disorder

Psychiatric and neuropsychiatric disorders influence all aspects of a patient's life, from basic physical functions, to thinking, memory, affectivity, and interpersonal relationships. Research on methods of therapeutic intervention in psychiatry is constantly increasing in volume, given the scale of the phenomenon

and its social and financial consequences. In view of the high rate of relapse as well as the suicidal risk related to mental disorders, new treatments and in-depth studies are needed. Currently, in addition to drug therapy and psychological support, in conditions refractory to treatment, some patients may opt for

brain stimulation methods that have proven efficacy in certain pathologies.

Transcranial magnetic stimulation (TMS) is a modern and non-invasive technique used both for diagnostic and therapeutic purposes in neurology and psychiatry. It is a currently accepted clinical method to obtain action potentials in the human body. In other words, transcranial magnetic stimulation of the brain is commonly used to activate the motor cortex and obtain evoked motor potentials. It relies on a magnetic field that modulates the excitability of the cerebral cortex. Unlike electroshock, it can only stimulate a certain area through an induction coil that will generate a magnetic field, thus not provoking mnemonic disturbances or seizures. It is mainly used for the treatment of psychiatric disorders such as obsessive-compulsive disorder, depression and, recently, in the cases of cerebral trauma (1). Depending on the shape of the induction coil, different types of magnetic fields can be induced. For example, the circular coil, which is the most commonly used, will induce a magnetic field of circular shape, depolarizing, a larger surface. Although it has the advantage of easier use, it has the disadvantage of not providing precise information on the delineation of the stimulated area. Butterfly-shaped induction coils generate a particular magnetic field with a maximum of intensity at the intersection of the two spirals. It is frequently used in clinical research and in cases where an accurate information on the delineation of the investigated area is desired (2).

This technique is widely applied to approach some important neuropsychiatric conditions, including: treatment resistant depression, schizophrenia, smoking cessation, post-

stroke motor sequelae and aphasia, migraines, Parkinson's disease, multiple sclerosis, or dystonia (3). The method is also used experimentally in conditions such as: Tourette's syndrome, eating disorders, post traumatic stress disorder and autism (4).

Magnetic stimulation is based on the principle of electromagnetic induction, first shown experimentally by M. Faraday in 1831, consisting in the occurrence of an electromotive voltage in an electric circuit traversed by variable magnetic flux over time. Magnetic fields can induce an electric field at the level of the nerve tissue by placing a coil that is traversed by variable electrical current near a nerve fiber (5).

The principle of magnetic stimulation of peripheral nerve fibers is based on theoretical mathematical models that show how nervous excitation occurs. These theoretical models were originally tested on in vitro models and subsequently on human subjects (6).

Since ancient times, electrical stimulation has been used to modulate the nervous system and treat some neurological disorders. Scribonius Largus, the physician of Roman Emperor Claudius, in his text "Compositiones medicorum" suggested the application of electrical stimuli on the skull surface as a remedy for headache. More specifically, he referred to the use of *Torpedo torpedo* and *Torpedo nobiliana* fish, which are known to be capable of producing an electric discharge that kills their prey. "Electric" fish have later been used in the treatment of epileptic seizures, depression and pain (7).

The first mention in literature for the use of deep brain stimulation in treatment of mental disorders is represented by a 2002 Lancet report that discusses the method as a pos-

sible treatment for obsessive-compulsive disorder and transient tic disorder (8).

The first report suggesting that DBS could treat depressive disorder was published in 2005 (9). DBS has been authorized for the treatment of epilepsy and OCD in Europe and the US (10). This approval increased research and promoted the development of DBS, particularly with regard to vagus nerve stimulation mechanisms (11).

Deep brain stimulation procedure consists of implanting two two-threaded electrodes with the end under the skin of the neck, having a pacemaker-like principle of action, but involving electrical discharge into a specific brain area. The component parts are: an implanted pulse generator powered by a battery, a stimulation probe and the extension – an insulated wire that descends from the skull to the side of the neck towards the pulse generator, which is placed subcutaneously behind the collarbone. Deep brain stimulation is a reversible procedure, can be adapted according to disease progression, is performed with the aid of local anesthesia surgery and intraoperative checkings for the effects. Approximately 80,000 people have undergone DBS treatment worldwide, with a reported mortality rate of 0-0.4% (12).

Potential complications are represented by intracranial haemorrhage, which has a prevalence of 0.4-1.3% and irreversible brain damage, with a prevalence of 0.8%, wound infection in 3-5%, infection involving the areas stimulated by the electrodes, electrode fracture, battery inefficiency, electrodes displacement during surgery (13). There is also the risk of developing psychiatric symptoms other than those for which the intervention is performed (transient aggression, hypoma-

nia, mania, depression, anxiety, apathy and even suicide). The most common side effect is postoperative delirium (15.6%), followed by depression and hypomania (14).

In what concerns DBS treatment of Parkinson's disease, for example, the most severe side effect is an increased risk of suicide, especially when the target region is in the subthalamic nucleus and globus pallidus internus. Suicidal risk assessment is therefore necessary for patients undergoing DBS intervention (15).

In the case of dyskinesias, predominantly mild side effects were observed. Since its first uses, the advantages of DBS technology have been highlighted, among which good specificity, and the reversible inhibitory effect on the thalamic motor nucleus. These advantages are particularly important given that there are currently not many effective therapeutic options available to people with mental disabilities. Unlike neurosurgical treatments, DBS is fully reversible, representing a therapeutic technique void of the risk of major permanent damage (16).

It should be noted that there are currently no large, double-blind randomized studies able to determine the long-term impact of DBS on personality, cognitive function, attention and self-awareness. Generally, the side effects of DBS are much less common and less severe than those of stereotactic surgery and there are fewer post-surgical complications associated with DBS. Furthermore, if severe side effects occur during treatment, electrodes may be shut down in order to prevent other damage (17).

Theoretical basis of DBS is used in examining the target areas (18). Therefore, information derived from clinical experience, brain ima-

ging and pathophysiological knowledge of various diseases is contributing in selection the target areas for therapy of mental illness (19). Psychiatric disorders are typically not the result of simple pathological changes in a single brain structure, and different brain structures may have different roles in the progression of the disease and its symptoms. It is also possible that, target areas displaying similar anatomical structures or functional relationships, such as neural networks, may generate overlapping effects. Therefore, different target regions may be able to regulate the same pathological network in different ways. It has been established that the target regions have the ability to modulate the symptoms of psychosis (20).

DBS technology has been experimentally used to stimulate the Brodmann cg25 region under the cingulate cortex, which plays an essential role in regulating negative emotions. It has been shown that stimulation of this region can have an antidepressant effect. For instance, Lozano et al. reported a 55% decrease in depressive symptomatology, assessed using the Montgomery-Asberg in 20 depressed patients who underwent DBS (21). Accumbens nucleus septi (NAcc) is the target of DBS for depression, being able to effectively improve the underlying symptom of the disorder (loss of interest in daily activities) due to the effects of NAcc on the reward system. Bewernick and colleagues followed 11 patients with NAcc-DBS for 4 years, showing that 5 patients (45%) presented beneficial long-term effects (22).

The ventral capsule / ventral striatum (VC / VS) are also considered targets for the treatment of depression and may be associated with neural network regulation of the reward

system. Malone et al. reported that out of 15 patients with chronic, severe, refractory depression treated with DBS on VC / VS areas, 40% reported positive curative effects 6 months after the procedure (23).

Sartorius and Henn first proposed habenula as a target of DBS treatment of depression. This region controls nerve fibers that activate serotonin, dominating the raphes dorsalis nucleus and the noradrenergic nerve that regulates the ceruleus nucleus. Sartorius and Henn deduce that the excessive activation of the habenula nucleus is associated with depression, and the lower thalamus neck links the nonspecific thalamus system to the orbitofrontal cortex. Dysfunction of the non-specific thalamic system appears to play an important role in the development of depression. Bilateral stimulation of the lower side of the thalamus neck may also lead to a decrease in the degree of depression, assessed by the Hamilton Depression Rating Scale, from a score of 42 to 10, and the curative positive effect is maintained for up to 24 months (24).

Obsessive Compulsive Disorder (OCD) has different potential target areas, as the orbital frontal cortex and anterior cingulate cortex are part of the OCD circuit. Unfortunately, these regions are very large; so the size of the cortex region that needs to be modulated would be too big (25). Most studies on this matter have indicated unilateral or bilateral stimulation of the anterior limbs of the internal capsule as a treatment target, reporting promising results, from partial improvement to complete remission of symptomatology. Regarding the side effects, several researchers (26) have identified that hypomania, which may occur with direct stimulation,

completely disappeared after a decrease in stimulus intensity. The *acies thalamus optica-zona incerta* was also investigated in three patients with Parkinson's and OCD, and the corresponding reports indicate an improvement in obsessive-compulsive symptoms. Also, a patient with OCD and comorbid depression has entered remission after DBS treatment targeting NAcc and the caudal nucleus (27).

Tourette's syndrome (TS) is a neuropsychological disorder characterized by repetitive stereotyped involuntary movements, and motor and vocal tics, with a prevalence rate of 1% (28). TS is related to a series of psychiatric disorders, among which, obsessive-compulsive disorder is fairly frequent (29, 30).

Standard treatment for TS includes drug therapy and behavioral psychotherapy, but only 1/3 of patients benefit from total improvement; 30-40% of patients experience exacerbations and approximately 5% of patients develop a form of disability (31).

Researchers have previously tried to perform surgical nerve resection in TS patients, with mixed results; the central thalamus complex tract has been shown to be the most effective target after various attempts. Based on the results for the treatment used in OCD and in dyskinesias, the researchers have speculated that the internal globus pallidus (IGP) segment in which DBS is applied may also be effective in treating refractory TS (32).

A study of 18 patients showed positive preliminary results at follow-ups at 3 and 18 months, and the 2-year evaluation demonstrated by that the severity of spasms, obsessive-compulsive disorder, anxiety, and depression fell remarkably (33). A case study

also reported that IGP and VC/VS DBS may have potential curative effects in patients with severe TS (34).

In 1999, Vandewalle and colleagues reported the case of a 42-year-old patient with TS whose movement tics were eliminated one year after the implantation of a double-lateral electrode in the thalamus nuclei (35). In the 1960s, Hassler and Dieckmann destroyed the thalamic nuclei in 3 subjects with TS (36); since then, considerable research has been done on the efficacy of DBS treatment by implanting electrodes into thalamic nuclei or other targets, such as globus pallidus. These studies reported significant improvements in motion scores, although some patients experienced a variety of side effects including decreased energy, fatigue, bradyphasia, decreased motility and decreased libido. However, the maximum sample size investigated so far only included 18 subjects and few randomized double-blind studies were performed. Current evidence, however, is sufficient to support the large-scale randomized clinical trials of DBS for TS in order to clarify the underlying pathological mechanism (37).

Alzheimer's disease (AD) is a neurodegenerative condition with a 1-2% prevalence in America (38). More than 10% of people past 65 years of age have AD and primary therapies available today are drugs that slow down rather than prevent subsequent cognitive decline (39). A case study described hypermnesia in a patient with obesity treated with DBS of the fornix (40). Based on this report, Laxton et al. started a trial involving 6 elderly AD patients treated with fornix DBS. After a follow-up of 1 year, the parietal lobe's glucose metabolism was significantly improved. Two of these patients demonstrated

a significant slowdown in cognitive decline and an improvement in clinical symptomatology without obvious side effects. The underlying mechanisms of action are not fully elucidated; however, it is believed that activation of axons in fornix also activates the regions of the downstream brain involved in memory. The efficacy of this treatment for AD supports the use of electrical stimulation therapy for other neurodegenerative diseases including Parkinson's, AD, myodistonia, OCD, TS and depression (41).

Repetitive transcranial magnetic stimulation (rTMS) is a relatively new noninvasive method of focal cortical stimulation widely used to investigate cortical plasticity and cortical excitability in humans. Research has shown that localized and reversible changes in the brain tissue produced by rTMS exert antidepressant properties in both humans and animal models. Moreover, the beneficial effects of rTMS on cognitive function have been demonstrated in healthy individuals, older adults with mnemonic disorders, Alzheimer's disease and brain trauma (42).

Brain trauma is a major global health problem, the main cause of brain damage in children and young adults, and is the most common cause of prolonged disability in Europe. In the United States, more than 1.7 million people suffer brain injuries annually, representing the cause of 52,000 deaths per year (43). Brain injury triggers pathological reactions that can damage brain cells through excessive calcium intake in the neurons, excitotoxicity and free radical formation, thus promoting neuroinflammation, neuronal death and neurological dysfunction. Strategies and neuroprotective treatments aim at improving neurological recovery by allevia-

ting these secondary lesions (44).

Pape et al. used rTMS in a patient who had been in coma for 287 days after a traumatic brain injury and for two other patients with severe brain trauma. The authors did not report adverse effects and showed slight neuro-behavioral improvements (45).

A study by Verdugo-Diaz and his collaborators analyzed the effect of intermediate frequency rTMS (2 Hz) on behavioral and histological recovery after cerebral trauma in rats. Wistar male rats were divided into six groups: three groups without brain damage (no manipulation, movement restriction plus partial rTMS and motion restriction plus rTMS) and three groups subjected to brain trauma (trauma only, trauma plus movement restriction and partial rTMS and trauma plus motion restriction and rTMS). Movement restriction groups were included so that rTMS could be applied without anesthesia. The results indicate that restriction of motion and rTMS per se promotes recovery, measured using a neuro-behavioral scale, although rTMS has been associated with a faster and higher recovery. It has also been observed that the trauma caused changes in CA1 and CA3 subregions of the hippocampus, which are partially restored by motion restriction and rTMS. The results showed that motion restriction prevents damage caused by cerebral trauma and that intermediate frequency rTMS promotes behavioral and histological recovery after trauma (46).

Applying repetitive transcranial magnetic stimulation (rTMS) in major depressive disorder as an augmentation of the therapeutic strategy for treatment-resistant patients has been extensively investigated over the past decades. In rTMS, a magnetic coil is placed at

a specific location on the scalp to alter brain targets by applying magnetic impulses and inducing an electrical current in the base of the cortex (47). The efficacy of rTMS on the dorsolateral prefrontal cortex (DLPFC) has been largely established in multicenter randomized controlled trials and meta-analyses and thus it's considered an evidence-based treatment for major depressive disorder (48).

These studies highlight the clinical significance of rTMS for the treatment of patients with major depressive disorder. Currently, rTMS is usually applied either as a monotherapy in adjunction to pharmacotherapy. Although the response to this approach is positive, a large portion of patients do not respond to treatment. Therefore, it is important to optimize the protocol so that the results improve. Such enhanced effect was observed in studies combining psychotherapy with pharmacotherapy and rTMS with pharmacotherapy (49).

Even more powerful additional effects can be expected from rTMS and psychotherapy as both neuroplasticity targets act similarly in different ways. Furthermore, psychotherapy may be preferable as an adjuvant to rTMS, as many patients would be willing to give up medication. The main disadvantages of pharmacotherapy consist of undesirable side

effects, cumulated with high drop-out rate and lack of response in a significant portion of patients. This has been demonstrated in a randomized clinical trial that enrolled patients with major depressive disorder without psychotic elements treated at various stages of the disease (50), named the Sequenced Treatment Alternatives to Relieve Depression (STAR * D).

DBS has some advantages compared to destructive and disruptive surgical techniques, higher efficacy and more indications than TMS; however, the treatment process is slow and still requires invasive surgery. The popularization and application of DBS technology is hampered by battery life limit, the need for adjustment of stimulus parameters, the need for selecting the optimal target area, patient selection criteria, and ethical arguments. Exploitation of new pharmacological agents and targets, more precise focal stimulation devices, and extracranial neuromodulation devices aiming deep brain structures (which are more efficient than transcranial magnetic stimulation) can lead to improvements in DBS technology. The development of other non-invasive effective stimulants, including photosensitive manipulation of visual purple and halorhodopsin, also deserves attention.

ACKNOWLEDGEMENTS AND DISCLOSURES

The authors state that there are no declared conflicts of interest regarding this paper.

REFERENCES

1. Wassermann E. M., Epstein C. M., Ziemann U., Walsh V., Paus T., Lisanby S. H. (2008). Oxford Handbook of i Stimulation. New York: Oxford University Press;
2. Epstein CM, Davey KR. Iron-core coils for transcranial magnetic stimulation. J Clin Neurophysiol 2002;
3. Donxing Wang, Xuejun Liu, Bin Zhou. Advanced research on deep brain stimulation in treating mental disorders, Exp Ther Med. 2018 Jan; 15(1): 3-12. Published online 2017;
4. Figeet M, Bervoets C, Denys D, Deep brain stimulation in psychiatry, Tijdschr Psychiatr. 2017;

5. Maccabee PJ, Nagarajan SS, Amassian VE, Durand DM, Szabo AZ, Ahad AB, Cracco Q, Lai KS, Eberle LP. Influence of pulse sequence, polarity and amplitude on magnetic stimulation of human and porcine peripheral nerve. *The Journal of Physiology* 1998;
6. Taday EC, Olree KS and Horch KW. Differential activation of nerve fibers with magnetic stimulation on humans. *BMC Neuroscience* 2006;
7. Rossi U. (2013). "The history of electrical stimulation of the nervous system for the control of pain," in *Electrical Stimulation and the Relief of Pain*, ed. Simpson B. A., editor. (Amsterdam: Elsevier B.V.);
8. Mallet L, Mesnage V, Houeto JL, Pelissolo A, Yelnik J, Behar C, Gargiulo M, Welter ML, Bonnet AM, Pillon B, et al. Compulsions, Parkinson's disease, and stimulation. *Lancet*. 2002;
9. Mayberg HS, Lozano AM, Voon V, McNeely HE, Seminowicz D, Hamani C, Schwab JM, Kennedy SH. Deep brain stimulation for treatment-resistant depression. *Neuron*. 2005;
10. Müller UJ, Voges J, Steiner J, Galazky I, Heinze HJ, Möller M, Pisapia J, Halpern C, Caplan A, Bogerts B, Kuhn J. Deep brain stimulation of the nucleus accumbens for the treatment of addiction. *Ann N Y Acad Sci*. 2013;
11. Schlaepfer TE, Frick C, Zobel A, Maier W, Heuser I, Bajbouj M, O'Keane V, Corcoran C, Adolfsson R, Trimble M, et al. Vagus nerve stimulation for depression: Efficacy and safety in a European study. *Psychol Med*. 2008;
12. Müller UJ, Voges J, Steiner J, Galazky I, Heinze HJ, Möller M, Pisapia J, Halpern C, Caplan A, Bogerts B, Kuhn J. Deep brain stimulation of the nucleus accumbens for the treatment of addiction. *Ann N Y Acad Sci*. 2013;
13. Laxton AW, Tang-Wai DF, McAndrews MP, Zumsteg D, Wennberg R, Keren R, Wherrett J, Naglie G, Hamani C, Smith GS, Lozano AM. A phase I trial of deep brain stimulation of memory circuits in Alzheimer's disease. *Ann Neurol*. 2010;
14. Houeto JL, Mesnage V, Mallet L, Pillon B, Gargiulo M, du Moncel ST, Bonnet AM, Pidoux B, Dormont D, Cornu P, Agid Y. Behavioural disorders, Parkinson's disease and subthalamic stimulation. *J Neurol Neurosurg Psychiatry*. 2002;
15. Benabid AL, Torres N. New targets for DBS. *Parkinsonism Relat Disord*. 2012;
16. Holtzheimer PE, Mayberg HS. Deep brain stimulation for psychiatric disorders. *Annu Rev Neurosci*. 2011;
17. Saint-Cyr JA, Trépanier LL, Kumar R, Lozano AM, Lang AE. Neuropsychological consequences of chronic bilateral stimulation of the subthalamic nucleus in Parkinson's disease. *Brain*. 2000;
18. Sudhyadhom A, Haq IU, Foote KD, Okun MS, Bova FJ. A high resolution and high contrast MRI for differentiation of subcortical structures for DBS targeting: The fast gray matter acquisition T1 inversion recovery (FGATIR) Neuroimage. 2009;
19. Wider C, Pollo C, Bloch J, Burkhard PR, Vingerhoets FJ. Long-term outcome of 50 consecutive Parkinson's disease patients treated with subthalamic deep brain stimulation. *Parkinsonism Relat Disord*. 2008;
20. Schlaepfer TE, Bewernick BH. Deep brain stimulation for psychiatric disorders-state of the art. *Adv Tech Stand Neurosurg*. 2009;
21. Lozano AM, Mayberg HS, Giacobbe P, Hamani C, Craddock RC, Kennedy SH. Subcallosal cingulate gyrus deep brain stimulation for treatment-resistant depression. *Biol Psychiatry*. 2008;
22. Bewernick BH, Kayser S, Sturm V, Schlaepfer TE. Long-term effects of nucleus accumbens deep brain stimulation in treatment-resistant depression: Evidence for sustained efficacy. *Neuropsychopharmacology*. 2012;
23. Malone DA, Jr, Dougherty DD, Rezai AR, Carpenter LL, Friehs GM, Eskandar EN, Rauch SL, Rasmussen SA, Machado AG, Kubu CS, et al. Deep brain stimulation of the ventral capsule/ventral striatum for treatment-resistant depression. *Biol Psychiatry*. 2009;
24. Sartorius A, Henn FA. Deep brain stimulation of the lateral habenula in treatment resistant major depression. *Med Hypotheses*. 2007;
25. Jiménez F, Velasco F, Salin-Pascual R, Hernández JA, Velasco M, Criales JL, Nicolini H. A patient with a resistant major depression disorder treated with deep brain stimulation in the inferior thalamic peduncle. *Neurosurgery*. 2005;
26. Damiaan Denys, Mariska Mantione, Deep brain stimulation in obsessive-compulsive disorder, *Progress in Brain Research*, Volume 175, 2009;
27. Servello D, Porta M, Sassi M, Brambilla A, Robertson MM. Deep brain stimulation in 18 patients with severe Gilles de la Tourette syndrome refractory to treatment: The surgery and stimulation. *J Neurol Neurosurg Psychiatry*. 2008;
28. Swain JE, Scahill L, Lombroso PJ, King RA, Leckman JF. Tourette syndrome and tic disorders: A decade of progress. *J Am Acad Child Adolesc Psychiatry*. 2007;
29. Mink JW, Walkup J, Frey KA, Como P, Cath D, DeLong MR, Erenberg G, Jankovic J, Juncos J, Leckman JF, et al. Patient selection and assessment recommendations for deep brain stimulation in Tourette syndrome. *Mov Disord*. 2006;
30. Mink JW. Clinical review of DBS for tourette syndrome. *Front Biosci (Elite Ed)* 2009;
31. Dong S, Zhuang P, Zhang XH, Li JY, Li YJ. Unilateral deep brain stimulation of the right globus pallidus internus in patients with Tourette's syndrome: Two cases with outcomes after 1 year and a brief review of the literature. *J Int Med Res*. 2012;
32. Servello D, Porta M, Sassi M, Brambilla A, Robertson MM. Deep brain stimulation in 18 patients with severe Gilles de la Tourette syndrome refractory to treatment: The surgery and stimulation. *J Neurol Neurosurg Psychiatry*. 2008;
33. Mink JW. Clinical review of DBS for tourette syndrome. *Front Biosci (Elite Ed)* 2009;
34. Vandewalle V, van der Linden C, Groenewegen HJ, Caemaert J. Stereotactic treatment of Gilles de la Tourette syndrome by high frequency stimulation of thalamus. *Lancet*. 1999;
35. Hassler R, Dieckmann G. Stereotaxic treatment of tics and inarticulate cries or coprolalia considered as motor obsessional phenomena in Gilles de la Tourette's disease. *Rev Neurol (Paris)* 1970;
36. Servello D, Porta M, Sassi M, Brambilla A, Robertson MM. Deep brain stimulation in 18 patients with severe Gilles de la Tourette syndrome refractory to treatment: The surgery and stimulation. *J Neurol Neurosurg Psychiatry*. 2008;
37. Hamani C, McAndrews MP, Cohn M, Oh M, Zumsteg D, Shapiro CM, Wennberg RA, Lozano AM. Memory enhancement induced by hypothalamic/fornix deep brain stimulation. *Ann Neurol*. 2008;
38. Burns A, Iliffe S. Alzheimer's disease. *BMJ*. 2009;338:b158. doi: 10.1136/bmj.b158
39. Hamani C, McAndrews MP, Cohn M, Oh M, Zumsteg D, Shapiro CM, Wennberg RA, Lozano AM. Memory enhancement in-

- duced by hypothalamic/fornix deep brain stimulation. *Ann Neurol.* 2008;
- 40.Remy C, Marret E, Bonnet F. Effects of acetaminophen on morphine side-effects and consumption after major surgery: Meta-analysis of randomized controlled trials. *Br J Anaesth.* 2005;
- 41.Maas A. I., Stocchetti N., Bullock R. Moderate and severe traumatic brain injury in adults. *The Lancet Neurology.* 2008;7(8):728-741. doi: 10.1016/s1474-4422(08)70164-9.
- 42.Cotelli M., Manenti R., Cappa S. F., et al. Effect of transcranial magnetic stimulation on action naming in patients with Alzheimer disease. *JAMA Neurology.* 2006;
- 43.Faul M., Wald M. M., Wu L., Coronado V. G. Traumatic brain injury in the United States : emergency department visits, hospitalizations, and deaths, 2002-2006. *Centers for Disease Control and Prevention.* 2010;
- 44.Kabadi S. V., Faden A. I. Neuroprotective strategies for traumatic brain injury: Improving clinical translation. *International Journal of Molecular Sciences.* 2014;
45. Pape T. L.-B., Rosenow J. M., Patil V., et al. RTMS safety for two subjects with disordered consciousness after traumatic brain injury. *Brain Stimulation.* 2014;
- 46.Leticia Verdugo-Diaz, Francisco Estrada-Rojo, Aron Garcia-Espinoza, Eduardo Hernandez-Lopez, Alejandro Hernandez-Chavez, Carlos Guzman-Urbe, Marina Martinez-Vargas, Adan Perez-Arredondo, Tomas Calvario, David Elias-Viñas, Luz Navarro, Effect of Intermediate-Frequency Repetitive Transcranial Magnetic Stimulation on Recovery following Traumatic Brain Injury in Rats, *Biomed Res Int.* 2017; 2017: 4540291. Published online 2017;
- 47.Ridding MC, Rothwell JC. Is there a future for therapeutic use of transcranial magnetic stimulation? *Nat Rev Neurosci* 2007;
- 48.Lefaucheur J-P, Andre-Obadia N, Antal A, Ayache SS, Baeken C, Benninger DH, et al. Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rtms). *Clin Neurophysiol* 2014;
- 49.Berlim MT, Van den Eynde F, Daskalakis ZJ. High-frequency repetitive transcranial magnetic stimulation accelerates and enhances the clinical response to antidepressants in major depression: a meta-analysis of randomized, doubleblind, and sham-controlled trials. *J Clin Psychiatry* 2013;
- 50.Warden D, Rush AJ, Trivedi MH, Fava M, Wisniewski SR. The STAR*D project results: a comprehensive review of findings. *Curr Psychiatry Rep* 2007;

Correspondence:

Gavril Radu

M. D., Resident in Psychiatry,
"Socola" Institute of Psychiatry, Iași, Romania,
E-mail: gavriltradu25@gmail.com,
Tel: 0755 535 172

Submission: 05 jan 2018
Acceptance: 04 feb 2018

Multidisciplinary contributions

The metaphor – a means of communication between the conscious and the unconscious world

Dan VEREJANU

DAN VEREJANU -Institute of Philology - Academy of Sciences of the Republic of Moldova

ABSTRACT

The study entitled **THE METAPHOR – A MEANS OF COMMUNICATION BETWEEN CONSCIOUS AND UNCONSCIOUS** analyzes the relation between the conscious and the unconscious sides in Lucian Blaga's lyrical and philosophical works. We are referring to the poems and treaties written by Blaga during his diplomatic activity, when he created the well-known philosophical and cultural concepts of "stylistical matrix", "metaphysical sadness", "panism" (expressionism), "creative power", "metaphorical" and "personal entity".

Also under analysis are the possible connections with the philosophical systems of Freud, Adler, Jung, which lay stress on unconscious matters. The key concept of the metaphor as communication between the conscious and the unconscious is convincingly illustrated in his poems included in *Praise of Sleep* and *At the Courtyard of Yearning*.

KEYWORDS:

plasticizing metaphors, revealing metaphors, metaphysical sadness, communication, conscious, unconscious, sleep, dream, vegetative conscience, Trilogy of culture, Trilogy of knowledge

Opening the shortest possible way towards Divinity, Lucian Blaga observed, according to his personal inner experience, that realization of a metaphor, actually the essence of creation, involved precisely a most productive communication between the conscious and the unconscious, or it is, perhaps, the very result of such a communication. The philosophers of Antiquity defined this commu-

nication as *inspiration*. The contemporary poets called it: *the fifth season*. Our investigations were urged by "the most powerful reasons which create art and science", which "drive the sensitive man away from his personal life towards the world of objective contemplation and understanding" [1, p. 33]. The profound revelation of the lyrics and philosophy of Blaga came from the belief in the pre-

eminence of the metaphor, generated by the *communication between the conscious and the unconscious*, a conception to be developed in the following.

Starting from the *plasticizing metaphors and revealing metaphors* proposed by Lucian Blaga in **The Trilogy of Culture**, or from **The Metaphor - communication between the conscious and the unconscious**, viewed as a gnoseological function and a key concept in the present study, one can easily grasp the *existentialistic mystery, understood as a "center" of philosophy*. In the numerous philosophical essays forming his trilogies, in *Genesis of the metaphor and the meaning of culture*, Blaga considers himself entitled to develop his analysis both vertically and horizontally, and to sincerely disclose his German education and the sympathies he proposes – over time – to the generations to come: "In the universal literature, it is only with great difficulty to find a second, so clearly perceptible example, illustrating with the same power what we have here asserted on the metaphoric character of the poetic language in itself and viewed as a whole, than the poetry of Hölderlin". According to the ravishing opinion of the Romanian poet on his German colleague, the poetry of Hölderlin "contaminate" and enter, by their "physics", by their "rhythm and position of the word within the sentence, by their unusual syntactic construction", as these verses "suggest with an irresistible force and an unique power the spiritual melancholy, the suffering and the sublimated wisdom of the poet". Analysis of the poetic work of the German writer reveals the position Lucian Blaga assumed at the level of his own conscience, and its acknowledgement at the level of his own *creative power*. Appreciating "the spell

and prestige" of Hölderlin, while discussing on the philosophy of existence and spirit of the century [4, p. 44], Lucian Blaga actually talks about Lucian Blaga. Attempting at a radiographic analysis of the philosophical work of Blaga, focus being laid on the intention of the author of extending the significance of the *metaphoric side*, the author of the study has tried to update such a perception. The intentions of Blaga – to be traced exactly in *The trilogy of culture* and *The trilogy of knowledge* [1, p.3, 2, p.7] have become highly actual along the time.

Particularly of the hour is the assertion of Blaga that "the metaphor was created simultaneously with the creation of the human being", as far as man has accepted his "humanity" as a lasting structure and as an immutable manner of being in the world; "the metaphor exists with the same persistent intensity, with the same professed stringency as the human being himself" [1, p.357]. Or, the genesis of the metaphor coincides with the genesis of man.

According to some critics, issuing of a "final edition" permitted a higher appreciation of the "exceptional importance of the posthumous lyrical work of Lucian Blaga", which "may be considered as equal to the one published during the life of the author" [2, p.19]. As a matter of fact, the poetry published during his life in the six volumes, *The Poems of Light* (1919), placed under the sign of "expressio-nistic panism", *The Paces of the Prophet* (1921), characterized by the existentialistic "shout" of an enormous gesticulation, *During the great passage* (1924), the lyrics of Blaga get darker, whereas, in the volumes written during his diplomatic period: *Praise to sleeping* (1929) and *At the Watershed* (1933), the

poems wrap themselves up in a sort of "metaphysical sadness", recognized as irremediable, being only slightly brightened up in the images created in *At the Courts of the Great Longing* (1938). Also pervaded by *metaphysical sadness* is the life of the creator, who discloses his essence through the beings represented by *sleeping*.

This relation between the *conscious* and the *unconscious*, defined as the communication which creates the *metaphor*, may receive different names from different specialists. Possibly, academician Mihai Cimpoi assumed the same communication, by an implicit correspondence: "With Blaga, one may notice a tacit correspondence between the cosmic increased and the psychic increased world, between the phenomenological cryptic and fanatic and the fanatic of the soul" [5, p.64]. Taking as a stylistic matrix "the lofty heaven of the transcendent one is looking for", the poet examines his most intimate thoughts, up to the most curious roots, smashing the hard rocks of the unconscious "with a life older than the history of humanity", so that: "The most obscure depths are brought into light, being exposed in a most ostentatious manner; the spiritual yielding its position to the biological side, to the voice of blood, to the living power submitted to blind forces, as under a universal spell" [5, p.64].

"A fundamental sadness" accompanies the lyrical creation of Blaga in the poems written and published during his years of diplomatic activity (to paraphrase here Eugen Simion), while "*prophetic falls will come*", and "*words die in blood*", and, somewhere, "*the cloth of the vanquished one is cast lots*"...; in most of the poems from the volume *Praise of sleep, the stylistic matrix* is not hopeless, so that the

message is not a desperate one. Each poem appears as a mode of "taking upon oneself", an "embrace", a particular "philosophy". Lucian Blaga attempts at transmitting to his readers the novelties he knows from his diplomate colleagues at other embassies, where, as early as 1929, one used to speak about extraterrestrial life, about "cars riding under the earth", about certain houses on which "antennae fondle spaces/with other language and other lives", about "intercontinental electric rumours" (something in a way similar to our present-day Internet) ... yet, in spite of all these diplomatic information, it is the "wild pigs" living in the forests of Lancrăm the ones which "open the springs". The roots of Blaga's poems, descending from "depths of sadness", communicate permanently and maintain a close contact with "the lofty and spiritual azure". One may observe in the poems of Blaga that the profoundest depths are to be found in the souls whose roots come from hundreds and hundreds of generations, in the common soul of the generations. It is exactly at such depths that the communication between the conscious and the unconscious occurs: metaphysical communication, transcendental communication. It is exactly at such depths that the most crystalline and profound spiritual springs – the metaphors of Blaga are created. Here, they gather together and are born under "the lofty vault of the transcendental world". With all its roots deeply descending up to these springs of collective memory, the work of Blaga includes no moment in which the *creative life* permits any type of "self-sacrifice". Creative life imposes its own objectives, establishes the route to be followed, looks for its roots, thus granting its strength and firmness, in

one word – the depths of consciousness. Viewing them as a *demonism of roots*, Lucian Blaga observes: “Comparatively with a plant, the root has a demonic aspect. Its form shows beyond any doubt that it is exclusively the organ of effort. The root represents the struggle with the substances, adhering to them and eliminating them” [2, 94].

The poet recognizes he lives in an uninterrupted quest: “I am looking for something, I do not know what am I looking for”, and, on expecting a response from the part of the sky, Lucian Blaga will resume the *leit-motiv*, in a melancholic atmosphere of a monotonous routine work, or during his walkings through Bern, as he used to do each day: „*Caut, nu știu ce caut. Caut / Un cer trecut, ajunul apus. Cât de-aplecată / E fruntea menită-nălțărilor altădată! / Caut, nu știu ce caut. Caut / Aurore ce-au fost, țâșnitoare, aprinse / Fântâni – azi cu ape legate și-nvinse. / Caut, nu știu ce caut. Caut / O oră mare rămasă în mine fără făptură / Ca pe-un urcior mort o urmă de gură. / Caut, nu știu ce caut. Subt stele de ieri, / Subt trecutele, caut / Lumina strânsă pe care-o tot laud.*” (The light of yesterday)

Belonging to the “few thinkers who believe in the exceptional destiny and position of the human being”, an assertion made in *The uniqueness of the human being* [1, p.491], we will ask ourselves, together with the philosopher of Lan crăm: “is it not the creative destiny, with its sacred, abyssal roots, the very impressive launching of revealing intentions in the “Non-immediate”, followed by the transcendent obstacles opposing it, something highly human, quite different from the characteristics of all other creatures?” [1, 492].

The poet Lucian Blaga, occupying a diplomat

position, used to write in the newspapers of that time that... even if the *fire is spent away in its sheath, the soul remains a firing sword*, even if it does not hurt, it does not attack anyone, only remaining in its sheath, it is still a *sword, a sword made of fire*, above all.

The philosophical discoveries of Lucian Blaga about the metaphor and about its role in the communication between the conscious and the unconscious would have had “a significance accompanied by intense resonance of an astounded «wakening up»”. Possibly, this astonished wakening was not complete, as the Second World War was already launched, followed by a totalitarian regime not interested at all in recognizing the actions of Lucian Blaga, and wholly incapable of experiencing astounded wakening.

Lucian Blaga suggests and transmits to his readers his conviction that “the discovery of the **unconscious side** appears as a victory, especially for the *philosophy of nature*, embraces with incomparable enthusiasm several Romantic thinkers”, such as Schelling, Carus, or poets-philosophers as Goethe, and others, from the same epoch [1, p. 28].

Having a profound knowledge on the philosophic system of Freud, Adler, Jung, Lacan, who – as physicians and psychoanalysts - provided a most convincing image of the unconscious, Lucian Blaga will elaborate a new philosophic system, proposing a wholly different approaching of the unconscious. The Romanian philosopher states that “the unconscious is an independent domain, with its own structure and dynamics, as well as with categories and cognitive forms of its own”, [1, p.29], providing, therefore, “a knowledge of its own type”. In the opinion of C.G Jung, the unconscious is “a menu differ-

ent from the conscious" [3, p. 48]. To better understand our thoughts, to be able to think to the things we have to do, we resort to inner dialogue, as Socrate intended. We deliberated with our own self, as Lucian Blaga, many years later, intended to do, discovering the **unconscious**, structured on incalculable levels and depths, some of them close to the surface, others deeper, others extremely profound, still preserving "a memory of the whole humanity". Jung defines this type of thoughts and ideas as **Archetypes**. In their turn, both Blaga and Jung consider that the source of our **conscious** activities is properly the **unconscious**. Blaga insists upon the permanent dialogue between the conscious and the unconscious, on the continuous and constant communication which the philosopher-to-become grasped several times, once he

defined it as a *personance*.

"There exists in the unconscious a still undiscovered magma, a magma of attitudes and manners of logical reaction, different yet not less important than that of the conscious condition, an inner rhythm, consolidated as a secrete feeling of destiny, a primary appetite for forms, an enthusiasm of the imagination which gives meaning to the world, a bunch of initiatives capable of breaking any obstacle ... All such attitudes, horizons, initiatives come to light, in spite of the pressure exercised upon them by conscience" [1, p.48]. Unique communication, the communication between the conscious and the unconscious is, according to the vision of Lucian Blaga, **the metaphor**, even if "*Lucian Blaga e mut ca o lebădă. / În patria sa/ (Autoportret/Self-portrait)*).

ACKNOWLEDGEMENTS AND DISCLOSURES

The authors state that they are no declared conflicts of interest regarding this paper

REFERENCES

1. Blaga, Lucian. *Trilogia culturii*. București: Humanitas, 2011
2. Blaga, Lucian. *Trilogia cunoașterii*, București: Humanitas, 2013
3. C.G. Jung, *Puterea sufletului*, București: Anima, 1994
4. Martin Heidegger, *Originea operei de artă*, București: Univers, 1982
5. Cimpoi, Mihai. *Lucian Blaga, Paradisiacul, Lucifericul, Mioriticul*, Iași: Princeps Edit, 2012

Correspondence:

Dan Verejanu

Institute of Philology,
Academy of Sciences of the Republic of Moldova,
E-mail: danverejanu@yahoo.com

Submission: 10 jan 2017

Acceptance: 20 sep 2017

The Phenomenon of Translation in Terms of Psycholinguistics

Miroslava METLEAEVA (LUCHIANCICOVA)

Miroslava METLEAEVA (LUCHIANCICOVA) - Researcher The institute of Philology, Academy of Sciences of the Republic of Moldova

ABSTRACT

In the process of translation “conflict” situations between the author and the translator often arise. In this situation temporal environment, double nature of translation, fundamental differences between the process of the creation of a literary text and its translation must be taken in consideration.

The so called *translation- research* is a specific and experimental method to understand the process of forming the structure of the text in target language. *Translation- research* also helps to perform a translation with saving specific features of the original text (in source language). To understand the process that takes place in translator’s mind, *translation- research* approach pays special attention to the psychological aspects of translation on the basis of introspective observation.

KEYWORDS:

double nature of translation, temporal environment, translation-research, psychology, experiment, introspective observation.

From August Schlegel, one of the first who tried to give a theoretical foundation to the impossibility and incapacity to transpose faithfully literary works into another language, up to the present day, the idea of untranslatability is accepted by many, discussed in the whole European literary world, approaching mainly poetry. Translation was relatively late included in the domain of linguistics, because the structuralist approach,

denying the study of semantics, ignored the matter of traductology, creating the conditions for the development of the so-called *theory of intractability*, according to which translation in general is impossible to achieve. A paradoxical situation has occurred: the century old practical activity appeared to be impossible to be made and, indirectly, inexistent.

The post-war informational development led

to essential transformations in traductology and the *Theory of intraductology* suffered a strong blow, the linguistic factors creating not only complications for translations, but also the conditions to surpass them, because, at the basis of the structure and usage of any language, there is one and the same principle, which makes their relationship in the process of translation possible. "Regardless of the validity of any hypothesis, there is no doubt about the presence in all languages of certain universal essential features. This universality is an important premise for the success of translation from one language into another one." [1, p.17]

It is to be noted, that in the domain of contemporary translation, there is an interest in the less studied theory of the artistic translation, especially regarding the influence of psychology and of national mentality upon the activity of the translator. The experimental traductology based on ethno-social linguistics is confronted with a theoretical problem regarding the subjectivity of the translator; his vision upon the national image of the world in terms of the dialogue between two literatures and cultures.

As Iuri Krivoturov pointed out "Translation is a complicated communicative phenomenon made up of elements of the physiological – psychological (anthropological) way of life, of the linguistic systems of language (language-source and language – target) and of the relationships, quite often antagonistic, between these systems, but, also including the result of cancelling these contradictions after having chosen the best variant of transmitting the text from the "source –language" to the "target-language". [2, p. 125].

Bogdan Ghiu speaks about the major role of

the author in transmitting the idea to the reader in the framework of the source-language (the origin) and the problem of the translator, in the case of valuable theoretical texts, which may come close to the artistic ones, showing the way of creating in the target-language a proper complex language for the works of such masters as Deleuze, Derrida, Foucault, Bourdieu.

Here we come to an important idea: "Authors are the first to translate, translation begins long before the real inter-linguistic translation, by which we do nothing more than to transplant, to relaunch a relatively intraductible singularity from one language into another one, that is, from a space of translation of singular idioms into another one. There exist translation because there is already translation, it is possible to translate because, from the very beginning, in a mysterious way, where only thinking-translation can progress, one can translate." [3,p.2].

At this stage, we can speak about *decoding, interpretation, translation of the "language" of the author's way of thinking in order to express what he intends to transfer to the receptor (reader)*.

In this context we will identify and analyze the difficulties encountered by translator in the process of translation of the text from the language-source into the language-target in order to *render the understanding of the author's way of thinking, taking into account all the difficulties in understanding the original text in close connection with recoding the language-source into language-target, having in view its code and decoding the author's way of thinking and taking into account the translator's way of thinking*.

Each group of communication belongs to an

individual culture and language and, therefore, has its own mentality, national psychology, ideology and vision upon the world. Nevertheless, we do not fully agree on Ricoeur's thesis regarding the *absence of an absolute criterion for a good translation* resulting from an arbitrary interpretation of the source.

In our opinion, such a criterion is the *initial source* of translation – the *original*, but indicating – a *comparative analysis* of the existing translations of the original source: the author's text. According to Ricoeur's thesis. We can understand that any translation can be declared to be the equivalent of the best translation of a text. Thus, leveling the results of translation is based mainly on the "opportunity" of a certain historical moment.

The consequences of such an attitude towards translation are presented by Nicolae Rambu in the article *Barbarism of interpretation. Remarks upon the hermeneutics of Schleiermacher*, where he emphasized the aspect of *misuse of interpretation*: "The association between barbarism and interpretation might sound strange, but it is about a terrible phenomenon which made numerous victims.

The researcher, relying on some axiomatic rules, considers the author of the original text and the translator to be essentially creators. At the same time, Krivoturov says that in the process of creation between the two may occur conflicting relationships. "The text itself, reflected in the translator's consciousness, is a phenomenon of the psychic and inevitably subscribes to the ideal, spiritual, material level (the material substratum)". [2, p. 127]

There are opinions supporting the idea that

the translated work belongs half to the author and half to the reader or, in our case, to the translator, establishing the aim of the translator in his work regarding the original text: to transmit by his art the authorial individuality. In this context, we can place the contradictory definition "translator-co-author".

It is necessary to have a clear idea about the essential feature of the process of creation of a literary work and the same thing should be applied in the process of transferring the original text into the adoptive language. Let us put into light only the more important and the fundamental factors of the interaction of the two creative individualities, being the two psycho-social and ethno-linguistic systems in the creation and recreation of the work.

First, we will speak about the "*temporal environment*", a notion we propose in the present study. It is our opinion that this notion – the "*temporal environment*"- includes *a totality of ethno-social, historical, cultural, mental and psychological factors present in the development, existence and creative activity of the personality of creation*. Well known contemporary psychologists point out the mutual relationship between the rules of psychology and the most important aspects of everyday life.

One of the founders of social psychology, Kurt Levin, a long time ago, developed a simple equation: behavior depends on two variables – the unique personality of the individual and the situation in which he accomplishes the facts.[4,p.51].

Both the author and the translator cannot avoid or ignore all these, because of the acknowledged importance of individual uniqueness in the sphere of influence, which, nevertheless, is under the action of the

second component of influence – *the force of situation (the force of the moment)*. From the point of view of the *temporal environment*, which is part of the social-psychological factor, this refers to the whole literary process. To understand translation, which is important for the national and universal culture, without a synthetic and comprehensive perception and considering it to be a concise product made up of social, psychological, moral, confessional, esthetic, political-ideological, technical- scientific, economic, cultural and other factors of the same spatial-temporal category, we cannot perceive correctly the original text and its author. In order to identify the synthesis towards an interdisciplinary analysis of the creative process of “author-translator”, we propose the generalizing term “*temporal environment*”. This aspect was also approached by the Russian structuralists in the 20s of the last century. Mentioning the so-called co-paternity “translator-coauthor”, we see that it ignores the notion of *temporal environment*. The problem becomes more complicated, when the translator distances from the temporal parameters of the work he translates into another language. Even when he is a contemporary of the author, the translator should observe the *temporal environment* in which the original was created and which is prior to the translation. It is also important to have in view, the temporal environment of the translator and his capacity to deal with it as if it were his own subjectivity, and also to consider his action upon the *actual temporal environment*. In this way, we realize the *secondary status* of the act of translation. From this point of view, the problem of co paternity “author-translator” is out of question.

Co paternity is a common creation with equal rights of the persons adhering to the same idea, and translation is a “post-factum” process, a process of transposing an original literary work into a foreign cultural-informational space and into the realm of another language. But this *secondariness* of translation is *paradoxical* because the whole paradox is reduced to the fact that, by its cultural-informational essence *any integral transposition of the literary original is primary, having no analogy in the initial language*, in spite of the fact that there are some other translations of the same original text. *The cause of this paradoxical situation is the fact, that each translation carries the mark of the personality of a real translator and, at the end of the day, of his temporal environment.*

The essence of the activity of translation resides in its *double nature*: on the one hand it is secondary, on the other hand – it is primary. The cause should be looked for in the analogies and differences of the process of creating the original and the translation. The main differences between the activities of creation and translation, on a creative-psychological level are expressed by a) the author’s psychic energy goes to the creative materialization of his *own* imaginary object in his native linguistic space; b) the translator’s psychic energy goes to the materialization of a real object, but *foreign* in a different ethno-linguistic and cultural space; c) the author is *free* in his process of creation; d) the translator *depends* on the original and the quality of his work is directly proportional with *empathy*, that is, his capacity to live again the emotions experienced by the author in the process of creating his work and, in addition, to become familiar with the

author's temporal context. In other words, the translator should embody three types of empathy:

- *emotional*, based on the mechanism of projection and imitation of another person's reactions;
- *cognitive*, based on intellectual processes: comparison, analogy etc;
- predictive manifesting itself by the prevision of another person in certain situations [5'p. 951-952]. It is this moment that is linked to the author's motivation and to his characters from the work lying on the translator's table.

Now, let us speak in more details about the *resemblance and difference of creative imagination of the author and of the translator.* It is to be noted p 7.

In the process of their activity both the author and the translator have an active imagination, that is, a combination between abstract thinking and images which get a special shape during the further activity, represented by the desired image or dream as a necessary condition for a long term achievement. Nevertheless, the above mentioned couple "author-translator" have different types of imagination:

- *creative* - in the case of the author it is about the independent creation of images occurring in new and original works, without analogies, in which novelty can be objective, when images and ideas do not retake what could be the experience of

other people and subjective, when previous works are repeated, but for the present author they are new and original;

- *reproductive* - in the case of the translator everything develops on the material already described," being based on the creation of one or other image, corresponding to the description". [5, p.103-105]. Therefore, the translator reconstructs the initial material in another ethno linguistic environment with his own imaginative resources (the arbitrary and involuntary imagination) which he personally has. We point out that the *arbitrary imagination* is characteristic to the achievement of the commented artistic tasks, and the *involuntary* one is specific to dreams and profound reflections. Here, we include *intuition, heuristic thinking*. In this way, we come across various types of creative imagination, a fact which does not diminish the creative potential the reconstitutive imagination of the translator.

The similitude of the creative process in the case of the author and translator is mainly evident in the domain of stylistics and on the lexical and grammatical level.

All the nuances in the search of the necessary word, the transmission of his own contextual and inter contextual semantics, the whole process of restoring the original text in syntactic, stylistic, metric even phonetic systems of the language of translation correspond to the creative aspiration of the author.

Conclusion: translation is focused on the text which is the aim, object and result of translation. This process can be considered to be the transformation into the **second material reality** of the original poetic work, dressed in the attire of another language, but, which has preserved the spirit and, considering the possibilities, the artistic value of the original.

ACKNOWLEDGEMENTS AND DISCLOSURES

The authors state that they are no declared conflicts of interest regarding this paper

REFERENCES

1. Комиссаров В.Н., *Перевод как объект лингвистического исследования*. Ст. в Хрестоматии *Проблемы переводческой интерпретации текста в трудах российских лингвистов конца 20-го, начала 21-го веков*. Изд. Лингва, Ереван, 2009. с.5-21.
2. Кривотуров, Юрий. Интерпретационные стратегии в лингвистике, переводе и дидактике/dir.-publ.: Ana Guțu; red.șt.: Elena Prus [et al.]; Univ.Liberă Intern. Din Moldova, Inst.de Cercet.Filologice și Interculturale. – Chișinău: ULIM, 2015. 145 p.
3. Ghiu, Bogdan. *Europa este traducere*, interviu consemnat de Matei Martin. În: *Dilema veche*. 2015, nr. 586, p. 7-13. Disponibil la: <http://dilemaveche.ro/sectiune/zi-cultura/articol/europa-este-traducere-interviu-bogdan-ghiu> (văzut la 13.10.2015).
4. Зимбардо Ф., Ляйппе М. Социальное влияние. – СПб. Изд. «Питер», 2000. – 448 с.
5. Головин С.Ю. *Словарь психолога-практика*. – 2-е изд., перераб. и доп. – Мн.: Харвест, М., АСТ, 2001.- 976 с.

Correspondence:

Metleaeva (Luchiancova) Miroslava
Researcher The institute of Philology,
Academy of Sciences of the Republic of Moldova,
E-mail: mira@imperativ.mldnet.com

Submission: 20 feb 2017
Acceptance: 10 dec 2017

Case Reports

Phenotypic variability and genetic susceptibility of schizophrenia-evidence from a family study

Adina CRAMĂ, Marina BUZUT, Marcel-Alexandru GĂINĂ, Vasile CHIRIȚĂ,
Alexandra BOLOȘ, Roxana CHIRIȚĂ

Adina CRAMĂ -Resident in Psychiatry,"Socola" Institute of Psychiatry,Iași,Romania

Marina BUZUT -Resident in Psychiatry,"Socola" Institute of Psychiatry,Iași,Romania

Marcel-Alexandru GĂINĂ - Resident in Psychiatry,"Socola" Institute of Psychiatry, Iași, Romania

Vasile CHIRIȚĂ - Acad., M.D., Ph.D.,Senior Psychiatry, "Socola" Institute of Psychiatry Iași, Romania

Alexandra BOLOȘ -M.D., Ph.D.,Senior Psychiatry,Lecturer,"Grigore T. Popa" University of Medicine and Pharmacy Iași, Romania

Roxana CHIRIȚĂ - M.D., Ph.D.,Senior Psychiatry, professor,"Grigore T. Popa" University of Medicine and Pharmacy Iași, Romania

ABSTRACT

In ICD 11, schizophrenia will be treated in Chapter 5 05 B: "Schizophrenia and Primary Psychotic Disorders", and in the same way that DSM-5 eliminated subtypes, we will most likely encounter this change in ICD 11, in an attempt to harmonize the two manuals.

Anamnestic interviewing of the S.I. patient along with his two brothers, S.V. and S.C. who have addressed the Socola Institute of Psychiatry in 2017, determined us to further study the archives of the Institute in order to realize a complex overview of this family and the psychiatric disorders. Throughout retrospective documentation of over 143 different admissions of their family members, we revealed a high degree of agglutination of psychosis spectrum disorders within the S family.

The results reveal that there was no known relative of the S. family without a psychiatric disorder throughout history and far as we could trace the archives, we managed to study the genealogy up to their grandparents. Furthermore our study reveals a 100% percent risk of developing a psychotic spectrum disorder among the third genealogic branch of the members of the family, through a family psychogenogram through which we also identified a consanguineous relationship between their parents, determining they are second degree cousins.

Therefore, we were determined to engage a field study in order to warn the parents S.V. and S.C. about the possibility that their children develop such a disorder. Furthermore we believe that early observation and further investigation of the four children of two of the brothers represents an important step towards the good management of an eventual early debut.

We emphasize on the importance of a family psychogenogram in the understanding of these genetically imbued cases.

KEYWORDS:

schizophrenia, familial aggregation, psychogenogram, consanguinity

INTRODUCTION

The nosographic classification of current mental disorders began at the end of the nineteenth century, with the publication of a section on mental disorders (Section V) in the sixth revised edition of the International Classification of Diseases and Health Problems (ICD-6) in 1949 and in the first edition of the Manual of Diagnosis and Statistical of Mental Illness (DSM-I) in 1952. In later revisions of these manuals (ICD-7 to ICD-10 and DSM-II to DSM-V) substantial changes have been made to the diagnostic criteria, but the basic structure has been retained (1).

Schizophrenia represents one of the most important categories of diagnosis in both manuals, still being framed as a mental disorder at the border between disorder and syndrome in the absence of elucidation of a set of clear etiopathogenic mechanisms underlying this condition.

Since the first definition realized by Kraepelin in 1896, using the term “dementia praecox” and after that, Bleuler, who introduced the term schizophrenia in 1911, the definitions and the boundaries of this disorder have undergone various changes, in the last century. In ICD-11, schizophrenia is described in Chapter 5 05 B “Disorders of the Spectrum of Schizophrenia and Primary Psychotic Disorders”, where the term “primary” having the role of distinguishing them from psychotic disorders generated by medical conditions or by psychoactive substances. In the past, one attempted to explain the heterogeneity of this disorder by defining the classical subtypes of schizophrenia paranoid, disorganised, catatonic, undifferentiated and simple, but since these subtypes did not bear any clinical or re-

search utility, only two subtypes, the paranoid and undifferentiated ones, being used more frequently in medical practice, they have been removed from the DSM-5 classification system and will be removed from the ICD-11 system also, with the intention to simplify the clinical description of schizophrenia. The revisions suggested in DSM-5 and the changes from ICD-11 attempt to harmonize the criteria of diagnostic for schizophrenia in both manual, in terms of evolutionary stages and heterogeneity, but some differences remain as regards the conceptual orientation (2,3,1).

Schizophrenia is a major psychiatric condition whose multifactorial etiopathogenesis is still of great interest, not only in the field of psychiatry, but also in medicine, in general. At present, biological factors play a major role in the etiopathogenesis of the disorder, leaving behind the role of psychological and social factors. The assessment of the genetic risk is based on three categories of studies that attempt to determine the relative contribution of heredity and of the environment to its etiopathogenesis: family aggregation studies, twin studies, and studies of adopted children. Globally, research via family aggregation studies highlights the increased prevalence of schizophrenia in relatives of subjects diagnosed with schizophrenia, as compared to those found in relatives of the control group or to the prevalence in the general population. In addition, relatives of subjects with schizophrenia present an increased risk of developing other group of disorders from the schizophrenia spectrum disorders (paranoid, schizoid, schizotypal personality disorders) and also they feature an increased risk of developing a schizophrenic-type disorder (4,2).

Studies realized by Gottesman and Bertelsen show that the morbid risk of schizophrenia varies during lifetime, depending on the degree of genetic kin. If the overall risk is 1% for the general population, a family history of schizophrenia correlates with a higher risk to develop this disorder, as follows: in third-degree relatives the risk is 2%, in second degree relatives between 2% and 6% and for the first degree relatives it is between 6% and 17%, with high percentages in monozygotic twins with 48%, and children with both parents suffering from schizophrenia, 46%. Dizygotic twins have a 17% risk, similar to the risk of a child with a single parent with schizophrenia (5,2).

CLINICAL CASE

The clinical cases discussed below began with patient S.I., a 46-year-old male, living in the city, currently retired for medical reasons. The patient was diagnosed with paranoid schizophrenia in February 1988, his evolution being traced and medicated at the Socola Institute of Psychiatry from Iasi. The anamnesis revealed the existence of an association of pathologies from the spectrum of psychoses within the family. This is what drove us to study the characteristics of family aggregation through retrospective documentation and compilation of family psychosocial genogram.




Personal pathological history: it features the following somatic disorders: first degree obesity, mixed dyslipidemia, liver steatosis, mixed polyneuropathy.

The collateral hereditary history reveals the existence of schizophrenia disorders in the family. Thus, S.V.'s mother was diagnosed in

1987 with "Delusional melancholy with autolytic risk" and the father, S.C. was diagnosed with "Asthenic-depressive syndrome", both of whom also had a degree of consanguinity being second-degree cousins. The maternal uncle, S.I., was diagnosed with "discordant psychosis with asthenic-dysthymic residual evolution." The other two brothers of the patient were also hospitalised at the Institute being diagnosed with "Paranoid Schizophrenia" (S.C.) and with "Hypomanic Episode" (S.V.). Their sister, S.E., was diagnosed in the infantile neuropsychiatry clinic with "Depressive episode" and later, in the adult period, the patient was diagnosed with "Schizophrenia Hebephreno-Catatonic type".

Living and working conditions: The patient lives with his brother S.C. (Table I), is a non-smoker and does not consume alcohol. (Table II)

Medical history: the patient has been registered at the Institute since 1988, being admitted for a symptomatology manifested by psychomotor agitation, irritability, delusional-hallucinatory behaviour, delusional ideation of persecution and surveillance. The second hospitalization took place at Obregia Hospital, in Bucharest in 2004, the patient presented symptoms such as a delusional ideas with mystical and grandiose themes ("I thought I was Jesus' messenger on earth", "I had the power to communicate with the animals"), delusional-hallucinatory behaviour, bizarre behaviour ("I thought I was an animal and I behaved like an animal", "I feel the need to hold people in my arms"). In 2006, the patient also presented a suicidal attempt by hanging and later on, multiple psychotic relapses which required changes of the therapeutic plan, several times.

LIVING AND WORKING CONDITIONS	S.V.	S.C.	S.I.
Residence	"Protected home" Social project		"Protected house" Social project
Education	10 classes	10 classes	12 classes (repeats twelfth grade for medical reasons)
Marital status			Unmarried
Religion	Orthodox Christian Weekly practitioner	Orthodox Christian Weekly practitioner	Orthodox Christian Practicing yoga for eleven years, since the debut of the disorder
Professional route	Shepherd for 2 years (forced) Animal caretaker	Welder- 28 years Medically retired (since 2010)	Soldier - 11 ani Guard- 2 ani Medically retired (since 2006)

(Table I – Living and working conditions)

	S.V.	S.C.	S.I.
Addictive behaviours	Declares alcohol consumption in the past (~1l wine/daily)	Declares alcohol consumption in the past	Declares alcohol consumption in the past
	Smoker in the past (~28 packs/year)	Smoker in the past (~15 packs/year)	Non-smoker

(Table II- Addictive behaviours)

Psychiatric examination highlights:

The psycho-diagnosis of the expression: the patient has a cooperative attitude, mimics and gestures diminished in amplitude; he initiates and maintains intermittent visual contact with the examiner, medium intensity and tone of voice, untidy clothes, poor hygienic state (table III)

Cognitive functions (table IV):

Sensation - the patient manifests hypoesthe-

sia characterized by irritability and anger.

Perception - he currently denies the existence of psychotic features, but he mentions the existence of complex verbal auditory hallucinations with an imperative character in the past. The patient manifests voluntary and spontaneous hypoprosexia, as well as fixation hypomnesia. Instead, he manifests selective hypermnesia regarding events with a negative impact from the past. Thinking process takes place in a slow rhythm, he shows weak

(Table III - Psychodiagnosis of the expression)

	S.V.	S.C.	S.I.
ATTITUDE	cooperative	cooperative	cooperative
CLOTHING AND OVERALL ASPECT	Poor aspect	Good aspect	Good aspect
VOICE TONE	High tone	Low tone	Low tone
GESTURAL EXPRESSION	Over expressed	Lowered amplitude	Lowered amplitude

	S.V.	S.C.	S.I.
SENSATION	Hyperesthesia	Hypoesthesia	Hypoesthesia
PERCEPTION	Isolated visual hallucinations (in the past)	Imperative auditory hallucinations (in the past)	Visual and auditory hallucinations (in the past)
ATTENTION	Spontaneous hyperproxia Voluntary hypoprosexia	Voluntary and spontaneous hypoprosexia	Voluntary and spontaneous hypoprosexia
MEMORY	Fixation hypomnesia Evocation hypermnesia	Evocation and fixation hypomnesia	Evocation and fixation hypomnesia

(Table IV – Cognitive functions)

ideological associations, prevalent mystical ideas, suspicion. His imagination is exulted. Affective and motivational functions: the patient's disposition is dysthymic with a severe reduction in the intensity of affective expression. Motivation is diminished. His passions are predominantly for topics of philosophy and religion. He manifests eating disorders in the form of an increased appetite. Defense and sexual instincts are diminished. Effectors functions: communication displays verbal output disorders-verbal hypoactivity with bradylalia, bradyphemia and low intensity voice. Also, he manifests speech dysfunc-

tions, such as delayed or monotonous speech. His volition is characterized by hypobulia and motor behaviour by hypokinesia, motor stiffness, bizarre behaviour. The sleep disorders are represented by the mixed insomnia type. Synthesis functions: the patient is temporal-spatially oriented, auto and allopsychic. The insight is partially preserved. He manifests a melancholic temperament with a personality characterized by indifference, detachment, isolation tendencies. Also, he presents major difficulties in social adaptation, integration to public and family environment. A holistic view of these 7 cases allowed us to

observe the phenotypic variation of the pathological genotype under different environmental factors, in order to highlight be-

havioral features and common clinical aspects of these brothers (Figure 2).



(Figure 2 - Diagram of shared symptomatology aspects)

The positive diagnosis of paranoid schizophrenia has been established according to the ICD-10 criteria.

Treatment: From the onset of the disorder until now, the patient received treatment with antipsychotics, mood stabilizer, anxiolytics and hypnotic inducers. In 2014, the patient asked for an evaluation of the therapeutic plan due to the significant weight gain; at the time he was undergoing treat-

ment with Olanzapine and Valproic acid. Thus, one advocated for the initiation of treatment with Aripiprazole while preserving the mood stabilizer. Next, one switched to depot administration of the new antipsychotic, Aripiprazole. In 2015, the patient presented a relapse of the psychotic symptoms, occurring in the context of the non-compliance to psychotropic medication, in 2016 the treatment with Paliperidone was initiated.

DISCUSSIONS

The importance of genetic factors in the determinism of schizophrenia is now widely accepted, evidence of hereditary transmission, at least of the predisposition or risk for schizo-

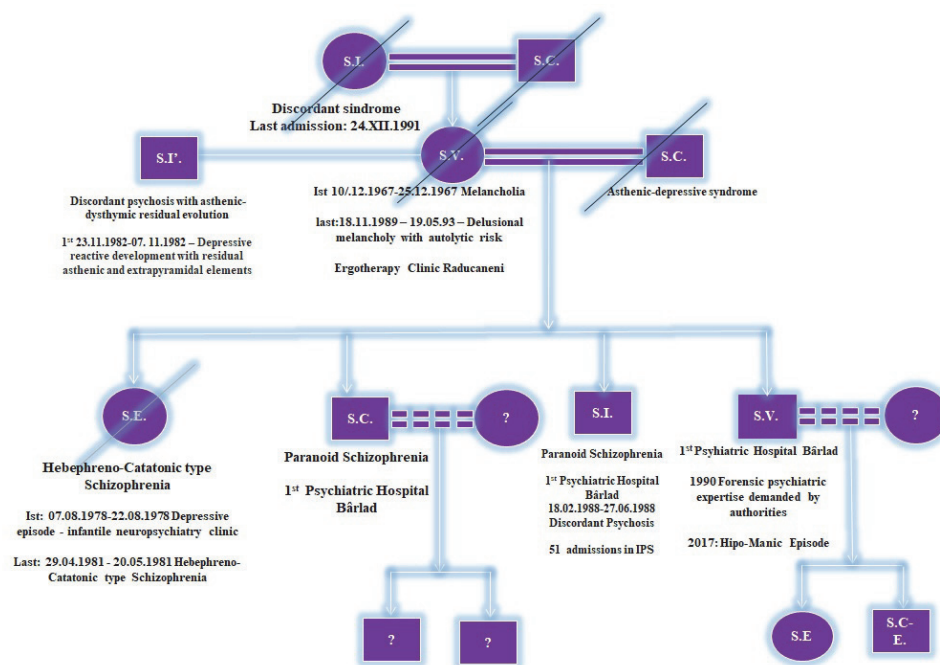
phrenia, becoming increasingly consistent and widely accepted.

Schizophrenia is still a psychotic disorder with variable phenotypic expression that implies a major genetic contribution. But, the finding that some of the biological abnormalities are also observed in unaffected relatives, suggests that in addition to familial genetic propensity, additional exposure to environmental factors is required to explain the schizophrenic phenotype. It was demonstrated that the percentage of heredity contribution is estimated at 83% and the impact of environmental factors at 17% (6,7).

The family concentration of this pathology is not influenced only by genetic factors, but also by the presence of identical environmental factors or by the stress involved by the long contact with a psychiatric patient. These factors accumulate over time, created a background vulnerability that is accentuated at certain moments of the ontogenesis. Because the genetic risk of a child from a family with a schizophrenic parent is well known, it is necessary to identify this disorder as soon as possible, while considering a degree of prevention (Figure 2).

Early therapeutic intervention becomes a favorable prediction factor for the subsequent clinical development. Although the two children of patient S.C. manifest a risk of approximately 17% according to Gottesman's studies, it should be noted that for a subject, the risk of schizophrenia is not the only possible progression and that having genes associated with schizophrenia does not imply a certainty of diagnosis, trigger factors being also necessary most of the times. Bearden et al. argue that diathesis-stress models of schizophrenia suggest that environmental stress can interact with genetic vulnerability in triggering psychotic symptoms, exacerbating them during the disorder and relapse (8).

The molecular overlap between schizophrenia and bipolar disorder was confirmed by a family study conducted in Sweden by Lichtenstein. This study showed that the risk of recurrence of



(Figure 2 - Family psychogenogram)

schizophrenia in children of a schizophrenic parent is of 10%, and the risk for bipolar disorder in the same children is of 5.2%. The risk of bipolar disorder in children of a bipolar parent is 6.2% and the risk of schizophrenia in these children is 2.4%. The fact that the same parent with schizophrenia or bipolar disorder may have children who can be diagnosed with any of the two disorders, although with different probabilities, indicates the presence of overlapping genetic vulnerability of schizophrenia and bipolar disorder (9,2).

Consanguinity is an important risk factor in psychiatric pathology, with a significant positive correlation with psychiatric disorders and a higher risk of developing schizophrenia in descendants of consanguineous couples. Thus, a population survey conducted between January 1996 and December 2013 revealed an increased consanguinity rate of 41.3% among schizophrenic patients as compared to 28.7% among non-schizophrenic patients. The diagnosis of schizophrenia is more common in consanguineous families, a family history of schizophrenia being correlated with a higher risk of developing the disorder, but also mood disorders or other disorders belong to the psychotic spectrum.

In the S. family one can speak of consanguinity given that the two spouses S.V. and S.C. were second-degree cousins (Figure 2), which confirmed and determined the major risk of psychiatric disorders from the spectrum of psychosis in their children. The results of studies on consanguineous families highlight the need for genetic counseling in communities or families at risk, and the importance of implementing preventive measures, as well as informing the population with regard to the risks of consanguinity (10,11).


According to some studies conducted in pediatric psychiatry clinics, early onset of schizophrenia is characterized by genetic susceptibility, the severity of the progression and a reserved prognosis caused by the insidious onset of the disorder, poor family support, the presence of psychiatric history, social retirement and school dropout, the presence of positive and negative symptoms, associated neurological symptomatology and multiple recurrences (12,13).

These factors of negative prognosis are encountered in the case of S.I. with an early onset of symptomatology at the age of 18, with an oscillating progression, with multiple psychotic relapses and side effects of the psychotropic medication, which required frequent changes in therapy.

At the last hospitalization of patient S.I., the symptoms were characterized by: high psychomotor agitation, disinhibited behavior, non-systematized delusional ideas, trivial language and impulsive-explosive manifestations.

The other two brothers who had an onset of mental disorders at an older age show a favorable evolution, with rare relapses and a good compliance with the treatment (Table V)

The main therapeutic option in schizophrenia is represented by antipsychotics, which can cause many side effects. However, the long-term administration of antipsychotic medication has proven to be the most effective strategy to improve the prognosis of schizophrenia (14). These undesirable, but inevitable effects in their frequency and intensity are an important component of pharmacological therapy which significantly reduces therapeutic compliance.

	S.V.	S.C.	S.I.
EVOLUTION	Favorable; improvement and reintegration	Improvement	Improvement
Prognostic +	Good compliancy to treatment; receptivity, trust in physicians "doctors are not human, they are angels" 		
-	The presence of a family history of schizophrenia Civil Status (Unmarried / Divorced)		

(Table V – Evolution and prognostic)

Thus, in 2014 patient S.I. required a change in treatment due to a significant weight gain (35 kg in 11 months). Also, the abdominal ultrasound performed at that time reveals the presence of liver steatosis, and laboratory tests reveal a dyslipidemic syndrome. Additionally, one year later, the patient describes unilateral right-handed tremor for which neurological evaluation and imaging exploration via native cranial-cerebral scan is recommended, revealing fine atheromatous calcifications in the cavernous segments of internal carotid arteries.

It should be noted that 50% of patients who followed a long-term treatment with neuroleptic developed Parkinsonian tremor and stiffness, akathisia, postural instability and late dyskinesia. The onset occurs within two to four weeks after the initiation of the treatment, sometimes earlier, sometimes with increasing doses. It is the consequence of occupying D2 receptors from the striate by neuroleptics with high dopamine blocking potency (2).

Clinical manifestations of neuroleptic Parkinsonism are classically characterized by bilateral and symmetrical tremor without resting tremors. However, about half of these patients exhibit asymmetric and resting tremor, making it difficult to differentiate idiopathic Parkinson's disease from neuroleptics-induced Parkinsonism (Table VI).(15). During the evolution of the disorder, various therapeutic plan have been approached/used: Haloperidol, Risperidone, Olanzapine, Aripiprazole, drugs frequently causing parkinsonism(15).The reasons for each change in the medication regimen included poor tolerability, insufficient response at the maximum tolerated dose, worsening symptoms and ceasing the treatment. Due to the lack of improvement with other antipsychotics, the patient was started on Paliperidone.

Some studies have reported several cases of the coexistence of schizophrenia and idiopathic Parkinson's disease and the management of concurrent psychosis and parkinsonism has been considered as quite difficult as even atypical antipsychotics may worsen parkinsonism; conversely L-dopa may worsen psychosis (16,17). In patients requiring continued antipsychotic medication, it is preferred to use atypical antipsychotics with a lower risk of extrapyramidal syndromes due to stronger antagonism of 2A serotonin receptors as compared to dopamine receptors and to faster dissociation from D2 receptors after blocking them (15). The findings support the hypothesis that the nigrostriatal and mesolimbic dopaminergic path-

Table VI. Clinical features of drug-induced Parkinsonism and Parkinson's disease (15)

Variables	Drug-induced parkinsonism	Parkinsonism
Symptoms at onset	Bilateral and symmetric or asymmetric	Unilateral or asymmetric
Onset	Acute or subacute	Chronic
Course with appropriate treatment	Regressive	Progressive
Response to anticholinergic drugs	Evident	Mild to moderate
Response to levodopa	Poor	Marked
Akathisia	Present	Absent
Other associated features	Oro-buccal dyskinesia and rabbit syndrome	Motor fluctuations
Incidence of rest tremor	More evident	Less evident
Gender	More in females	More in males
Freezing	Uncommon	Common

ways largely function independently, suggesting that patients with schizophrenia are not necessarily less likely than other patients to develop idiopathic Parkinson's disease at this age. Thus, the number of schizophrenic patients with comorbid idiopathic Parkinson's disease will increase in aging patients with schizophrenia(16,17).

CONCLUSIONS

The clinical case presented highlights that a positive family history of schizophrenia is one of the most potent risk factors for the development of this pathology. It is necessary to achieve an overview of the family psychosocial genogram for a better understanding of psychiatric pathology in the context of family aggregation and consanguinity.

We want to emphasize the major impact of social rehabilitation measures for patients as well as their inclusion in 'sheltered home' projects, as is their case, which will result in improving the quality of life for these patients by facilitating their treatment through the increase of addressability in the context of possible relapses, as well as an adequate, multidisciplinary management of cases.

ACKNOWLEDGEMENTS AND DISCLOSURES

The authors state that they are no declared conflicts of interest regarding this paper

REFERENCES

1. Bucci P. ICD11 draft diagnostic guidelines open to input by mental health professionals, **World Psychiatry** 2017 Feb; 16(1): 115-116.
2. Prelipceanu D. Schizofrenia. In: Psihiatrie clinică. Ed. Medicală, București, 2015; 351-453.
3. Wolfgang G. Status of Psychotic Disorders in ICD-11. **Schizophrenia Bulletin** vol. 38, 2012; 895-898.
4. Chou I.J., Kuo C.F., Huang Y.S. et al. Familial Aggregation and Heritability of Schizophrenia and Co-aggregation of Psychiatric Illnesses in Affected Families. **Schizophrenia Bulletin** vol. 43, 2017; 1070-1078.
5. Canavan J. The Role of the Family in Schizophrenia. **The Trinity Student Medical Journal** vol. 1, May 2000; 31-39.
6. Henriksen M., Nordgaard J., Jansson L. Genetics of Schizophrenia: Overview of Methods, Findings and Limitations. **Frontiers in Human Neuroscience** vol. 11, June 2017; 1-9.
7. Svrakic D., Zorumski C., Svrakic N. et al. Risk architecture of schizophrenia: the role of epigenetics. **Current Opinion in Psychiatry** vol. 26, March 2013; 188-195.
8. Ienciu M., Romoșan F., Lăzărescu M. Schizofrenia și tulburările de spectru. Ed. Brumar, Timișoara, 2012.
9. Lichtenstein P., Yip B.H., Bjork C. et al. Common genetic determinants of schizophrenia and bipolar disorder in Swedish families: a population-based study. **Lancet**, January 2009.
10. Bener A., Dafeeah E., Samson N. The Impact of Consanguinity on Risk of Schizophrenia. **Psychopathology**, 2012; 399-400.
11. Jaber A., Halpern G. Consanguinity and Susceptibility to Common Diseases. In: **Consanguinity-Its Impact, Consequences and Management**. Bentham Science Publishers, 2014; 75-94.
12. Racos-Zzabo E., Szava I. Evolutional and prognostic particularities in early onset schizophrenia. **Rom journal of psychiatry** vol. XVII, December 2015; 131-134.
13. Jablensky A. The diagnostic concept of schizophrenia: its history, evolution, and future prospects. **Dialogues in Clinical Neuroscience** vol. 12, 2010; 271-287.
14. Teodorescu R., Rancas E., Feller G., Prelipceanu D. A non-interventional study to observe real-life usage of atypical antipsychotics in the acute inpatient management of schizophrenia in Central and Eastern Europe. **Rom journal of psychiatry** vol. XVII, September 2015; 68-77.
15. Shin H., Chung S. Drog-Induced Parkinsonism. **Clinical Neurology**, 2012; 8: 15-21
16. Law R.W. Chronic schizophrenia and idiopathic Parkinson's disease. **Can. J. Psychiatry** 1993; 38: 75-77.
17. Winter C., Juckel G., Protkin M., Jeahaus L., Kupsch A. Paranoid schizophrenia and idiopathic Parkinson's disease do coexist: A challenge for clinicians. **Psychiatry Clin. Neurosci.** 2006; 60: 639.

Correspondence:**Marcel-Alexandru GĂINĂ**

M.D., Resident in Psychiatry, "Socola" Institute of Psychiatry,
sos. Bucium 36, Iași, Romania,
E-mail: gaina_alex@yahoo.com

Submission: 04 dec 2017

Acceptance: 15 jan 2018

Clinical and diagnostic features of a case of dissociative motor disorder

Anca BRADU, Cosmin-Adrian UNGUREANU, Oana-Mihaela NANTU,
Irina SĂCUIU, Roxana CHIRIȚĂ

Anca BRADU – MD, Psychiatry Resident at „Socola” Institute of Psychiatry in Iasi, Romania
Cosmin-Adrian UNGUREANU – MD, Psychiatry Resident at „Socola” Institute of Psychiatry in Iasi, Romania
Oana-Mihaela NANTU – MD, Psychiatry Resident at „Socola” Institute of Psychiatry in Iasi, Romania
Irina SĂCUIU – MD, PhD, Psychiatry Consultant at „Socola” Institute of Psychiatry in Iasi, Romania
Roxana CHIRIȚĂ – MD, PhD, Professor of Psychiatry at „Socola” Institute of Psychiatry in Iasi, Romania

ABSTRACT

Dissociative motor disorder is part of a larger group of psychiatric disorders characterized by loss or alteration of movements or sensations, called dissociative disorders of movement and sensation. The patient appears to have a somatic problem, but the cause to explain the symptoms cannot be found. In this paper we present a case of a patient with a broad neurological history and multiple admissions for a polymorphic and fluctuating symptomatology, but without a certain etiological factor. This symptomatology is accompanied by psychiatric manifestations, resulting in a controversial case with a difficult differential diagnosis.

KEYWORDS:

dissociative motor disorder, depression, diagnostic challenge

INTRODUCTION

The study of the dissociative disorders began at the end of the 18th century, and although they do not appear in the first edition of DSM (Diagnostic and Statistical Manual of Mental Disorders), the second edition mentions them as a subcategory of hysterical neurosis(1). The DSM-III gave up using the term “hysteria”, being too imprecise and having various definitions, and the features of this

pathology made up different diagnoses: dissociative disorders, somatoform disorders (conversion disorder and somatization disorder), posttraumatic stress disorder in the anxiety disorders section, histrionic personality disorder and borderline personality disorder (1).

While ICD-10 (International Classification of Mental and Behavioral Disorders) treats dissociative and conversion disorders as being the same entity, having similar underlying

mechanisms, the DSM-5 considers them two separate conditions(1). Conversion disorder (functional neurological symptom disorder) appears as a subtype of somatic symptom and related disorder (former somatoform disorder in DSM-IV), a category defined on the basis of positive signs and symptoms (distressing somatic symptoms plus abnormal thoughts, feelings and behaviors in response to these symptoms), rather than an absence of a medical explanation for somatic symptoms (2). These divergences in diagnosis, as well as the debates between mentalists and behaviorists, between psychodynamically oriented and biologically oriented clinicians, between cognitive researchers and clinical researchers and practitioners, demonstrate the controversial nature of these dissociative disorders (1).

ICD-10 clearly states that the term “hysteria” should be avoided due to lack of precision(3). In ICD-10 dissociative (conversion) disorders include: dissociative amnesia, dissociative fugue, dissociative stupor, trance and possession disorder, and dissociative disorder of movement and sensation, subclassified in dissociative motor disorder, dissociative convulsions, dissociative anesthesia and sensory loss, mixed dissociative disorders and other dissociative disorders (Ganser’s syndrome, multiple personality disorder, transient dissociative disorders) (3).

Dissociative motor disorder is characterized by the loss of ability to move the whole or a part of a limb or limbs, the paralysis being complete or partial, with weak and slow movements(3). Variable degrees of incoordination (ataxia) may be evident, resulting in a bizarre walk or inability to stand unaided (astasia-abasia), or there may be exaggerated

trembling or shaking of the extremities or the whole body, resembling almost any variety of ataxia, apraxia, akinesia, aphonia, dysarthria, dyskinesia, or paralysis (3).

Dissociative motor disorders are especially common in children and women, associated with past stressful elements (4).

CASE REPORT

Reasons for admission

Patient T.G., a woman of 70 years old from the rural area, is at her first admission to “Socola” Institute of Psychiatry Iasi, and comes to the hospital accompanied by her family, at the neurologist indication, for a symptomatology manifested by: negative hyperthymic mood, marked irritability, irascibility, reduced tolerance to minor frustrations, psycho-emotional lability, feelings of uselessness and despair, low self-esteem, diffuse anxiety, mixed insomnia, mnesic and prosexic disorders, interpretative ideation with mystical-religious theme in the patient’s cultural context, volunteer laryngeal stridor, facial hemispasm, tremors of the extremities, paraparesis, various somatizations, marked difficulties in adapting, integrating and relating in the socio-familial environment.

Personal pathological and illness history

The patient had three previous admissions to the second Neurology Clinic, at “Prof. Dr. N. Oblu” Emergency Clinical Hospital in Iasi, where the following diagnoses have been established: cerebral lacunarism, bulbar palsy, right temporal meningioma (with no indica-

tion for surgical treatment), trigeminal neuralgia, stage two hypertension, carotid atheromatosis, bilateral chronic serous otitis, chronic hypertrophic rhinitis.

First admission in Neurological Clinic was in September 2016 when the patient was transferred from the Emergency Hospital in Barlad, for an intense pruritus on the left side of the face and scalp, a sensation which occurred in crisis, triggered even by touch or by “the wind breeze”, a symptom which appeared three weeks prior to admission, and which was accompanied later by difficulties in swallowing solids. The pneumological consultation and ENT examination did not reveal any organic etiology for the swallowing difficulties.

The second admission took place after two months of chronic home treatment with neurotrophic, antihypertensive, antiaggregant, anxiolytic and antalgic drugs. In December 2016, the patient suddenly installed a motor deficit in the left lower limb, which extended within three days to the right lower limb. Multiple transient cerebral attacks were suspected, but the investigations carried (EKG, laboratory tests – hematology and biochemistry, cranio-cerebral scan, CSF analysis, chest X-ray) ruled out any cause for the paraplegia. But the evolution was favorable, the patient being released with possible walking, with mild hypertonia.

The third admission was in March 2017 when the patient returned to the Neurology Clinic because of the worsening of her left facial paresthesia, difficulties swallowing solids and fluids, phonation difficulties, vertigo, static and dynamic equilibrium difficulties, installed a week earlier. During admission, the patient developed a facial hemispasm and

a laryngeal stridor with hyperpnea and desaturation ($\text{SaO}_2=62\%$). The stridor calmed down spontaneously, but was increased by emotions. The paraclinical investigations and the neurology, pulmonology and ENT consultations again excluded an organic pathology.

Physical examination

The physical examination notices left axillary enlarged lymph nodes, the presence of the laryngeal stridor, the facial hemispasm, vertigo, a decrease in visual and auditory acuity, hypotonia, hypotrophy and bradykinesia, impossible walking, the patient presenting paraparesis.

Psychosocial evaluation

The patient comes from a rural area. She’s an Orthodox Christian married woman, with three children, and currently retired.

Psychiatric examination

At the psychiatric examination, the patient has a psychomotor agitation, with a demanding attitude, the cooperation is difficult due to her difficulties in breathing (the laryngeal stridor), she doesn’t keep eye contact, responds with simple and short phrases when questioned, vocabulary limited to simple and concrete notions, reduced gestures.

Negative hyperthymic mood, marked irritability, irascibility, reduced tolerance to minor frustrations, feelings of helplessness (the departure of the children, the distance from her husband), uselessness, low self-esteem, culpability, marked anxiety, vegetative manifestations (tremor, profuse sweats).

Coherent thinking, with slow flux of the ideas, interpretative ideation with mystical-religious theme in the patient's cultural context (a religious person from a rural area) ("I was possessed by devil", "while admitted at the Neurology Clinic the priest there tried to exorcise me", "the nurses where talking about me, saying I am a great sinner").

Hypomnesia of fixation, voluntary hypoprosexia, selective hyperprosexia (focused on health). Liminal intellect. She is oriented in time and space, auto and allo-psychic. At the time of examination the insight is partially present, but she had marked difficulties in adapting, integrating and relating to others in the socio-familial environment.

Psychological examination

The psychological exam reveals: Vocabulary QL=70 (knowledge level consistent with the level of education – 8 classes); MMSE=22points; WM: depressive tendencies 280 (psychic strain, sad mood, melancholia, increased affective status, reactions that paralyze the psychic energy and will), mental fatigue 245 (lack of psychic energy, nervousness, indecision, depression, pessimism, doubt), anxiety and interpretative tendencies 212, irritability 216, unstable tendencies 260 (instinctive actions in which the effect prevails, voluntary actions uninhibited by reason, irresistible morbid training, lacking inhibitory control), emotiveness 280 (abnormal reactions to even minimal affective demands); HAM-D=42 – severe depression. Severe depressive configuration with anxious-interpretative aggravation, specific integrative-relational deficit, psychosomatization.

Paraclinical investigations and interdisciplinary consultations

The neurological examination and laboratory tests (hematology, biochemistry) were repeated and a consult of physical medicine and recovery was performed, strengthening the following diagnoses: sciatic popliteal nerve palsy, cerebral lacunarism, non-surgical right temporal meningioma, facial hemispasm, intermittent laryngeal stridor.

Differential diagnosis

The early stages of progressive neurological disorders, such as multiple sclerosis and systemic lupus erythematosus, can be misdiagnosed with dissociative disorders (3). Isolated dissociative symptoms may occur during major mental disorders such as schizophrenia or severe depression (3). Multiple and ill-defined somatic complaints can be classified under somatoform disorders or neurasthenia (3).

In this case, the diagnoses of sclerosis and systemic lupus erythematosus were ruled out, the patient is presenting other somatic disorders which cannot explain the psychiatric symptoms. The neurological symptoms could be determined by the right temporal meningioma, although the actual scan of the brain excludes this possibility. Imaging follow-up of the brain tumor remains as a recommendation to eventually see the possible connections with other cerebral structures. Another possible neurological diagnosis would be a functional paresis, but it would not explain the patient's entire symptomatology.

Since all paraclinical investigations and interdisciplinary examinations (neurological,

pneumological, ENT) exclude an organic etiology for the somatic symptoms (swallowing difficulties, laryngeal stridor, facial hemiparesis, fluctuating paraparesis) and that during admission it is seen that the patient's degree of incapacity varies depending on the number of persons present in the room, we can discuss about a psychiatric causality. The patient does not exhibit a histrionic behavior, nor does she oppose to various medical investigations and procedures, thus excluding a somatoform disorder or hypochondria. Trance and possession disorder is ruled out by the fact that the idea of possession is more influenced by the patient's beliefs and culture, and that it appears and intensifies on a background of affective depressive disorder. The onset of dementia may also be considered, given the age of the patient, but the cranio-cerebral scan does not reveal any characteristic changes for ischemia or cerebral atrophy.

Positive diagnosis

For a positive diagnosis there should be no evidence of physical disorder and sufficient must be known about the psychological and social setting and personal relationships of the patient, to allow a convincing formulation of the reasons for the appearance of the disorder (3).

Positive diagnosis:

- Dissociative motor disorder

DISCUSSIONS

A search on PubMed for "dissociative motor disorder" has revealed few examples of such cases in the scientific literature. A female patient had sensory paralysis that involved the right

The patient meets the criteria for the diagnosis of dissociative motor disorder: no evidence to explain the somatic symptoms and the presence of disturbing events and disturbed relationships in the family (children leaving home, the distance from her husband).

- Severe depressive episode

The mood changes, the considerable suffering, the feelings of uselessness and despair, the low self-esteem, the interpretative idea which involves the idea of sin ("the nurses and people around are saying I am a great sinner") are characteristic of a severe depressive episode.

Treatment and evolution

The psychiatric treatment consisted of: Duloxetine 60 mg/day, Quetiapine 100 mg/day, Lorazepam 1 mg/day, Gabapentin 300 mg x 3 times/day, and psycho-social counseling. The evolution of the patient was oscillating, with periods was calm and rest, alternating with periods of exacerbation of symptoms, depending on the patient's emotions and on the number of people present in the room. The patient is discharged with an improved mood, with possible walking, with an improvement regarding the laryngeal stridor, and with the recommendation to continue the psychiatric treatment and eventually to attend psychotherapy sessions, as far as it's possible, given the age and the educational level of the patient.

half of the body, a motor deficit consisting of permanent contracture in flexion of fingers 2-5 of the right hand, homonymous hemianopia and amblyopia, depression and a history of gynecological disorders (5). A 10 year-old child had his right knee extended and foot in the equinus position (6), and a 13 year-old girl was unable to walk and stand unaided in the absence of motor weakness or sensory loss (7).

In a descriptive study of 100 patients with dissociative disorders, study conducted in 2010 at Dhaka Medical College Hospital, dissociative motor disorders ranked third as incidence (19%), being preceded by mixed dissociative disorders (34%) and dissociative convulsions (33%) (8). In another study conducted in the same year at a psychiatric institute in India, dissociative motor disorders had the highest incidence (43.3%) (9), compared to Western countries where dissociative identity disorder is the most prevalent. Female preponderance was seen across most subtypes of dissociative disorder (9). Functional weakness or psychogenic paralyses are other terms used in the literature to describe dissociative motor disorder (10, 11).

Depression is commonly associated (84%) (12) and cognitive-behavioral psychotherapy has good results in treating patients with dissociative disorder (13).

CONCLUSION

The particularity of the case is the rich and fluctuating neurological symptomatology, without a clear etiology, and accompanied by behavioral changes and psychiatric manifestations, concluding a psychological causality and a difficult and probably controversial diagnosis.

ACKNOWLEDGEMENTS AND DISCLOSURES

The authors state that they are no declared conflicts of interest regarding this paper

REFERENCES

1. Sadock BJ. *Kaplan and Sadock's Comprehensive Textbook of Psychiatry*. 9th edition. Lippincott Williams & Wilkins, 2009. p: 1965.
2. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)*. Arlington, VA, American Psychiatric Association, 2013. p: 309.
3. *The ICD-10 Classification of Mental and Behavioral Disorders. Clinical descriptions and diagnostic guidelines*. Geneva: World Health Organisation, 1992. p: 122-128.
4. Jith A, Narayanan D. *Dissociative Motor Disorder*. Indian J Psychol Med. 2017 Jan-Feb; 39 (1): 99-101.
5. Oregon Garcia F. *A case of conversion disorder analyzed from a psychodynamic, psychophysiologic, and morphodynamic perspective*. Arch Neurobiol (Madr). 1991 May-Jun; 54 (3): 111-21.
6. Tripathy SK, Mishra BR, Mishra S, Mohapatra D. *Psychogenic limp in a child: are we are of it?* J Pediatr Orthop B. 2014 Jul; 23 (4): 343-5.
7. Stankovic M, Kostic J, Grbesa G, Tosic T, Stankovic S. *Astasia-Abasia and Ganser Syndrome in a Preadolescent Girl: A Case Report*. Srp Arh Celok Lek. 2015 Jul-Aug; 143 (7-8): 446-50.
8. Ahsan MS, Mullick SI, Sobhan MA, Khanam M, Nahar JS, Salam MA, Ali R, Islam M, Kabir MS. *Subtypes of dissociative (conversion) disorder in two tertiary hospitals in Bangladesh*. Mymensingh Med J. 2010 Jan; 19 (1): 66-71.
9. Chaturvedi SK, Desai G, Shaligram D. *Dissociative disorder in a psychiatric institute in India – a selected review and patterns over a decade*. Int J Soc Psychiatry. 2010 Sep; 56 (5): 533-9.

10. Stone J, Warlow C, Sharpe M. *The symptom of functional weakness: a controlled study of 107 patients*. Brain. 2010 May; 133 (Pt 5): 1537-51.
11. Stone J, Warlow C, Sharpe M. *Functional weakness: clues to mechanism from the nature of onset*. J Neurol Neurosurg Psychiatry. 2012 Jan; 83 (1): 67-9.
12. Alvi T, Minhas FA. *Type of presentation of dissociative disorder and frequency of co-morbid depressive disorder*. J Coll Physicians Surg Pak. 2009 Feb; 19 (2): 113-6.
13. Moene FC, Hoogduin KA, Van Dyck R. *The inpatient treatment of patients suffering from (motor) conversion symptoms: a description of eight cases*. Int J Clin Exp Hypn. 1998 Apr; 46 (2): 171-90.

Correspondence:

Anca Bradu

"Socola" Institute of Psychiatry
No. 36 Bucium, 700282, Iasi, Romania
E-mail: anca_bradu@yahoo.com

Submission: 12 dec 2017
Acceptance: 19 jan 2018

Book Review

Managing Pharmacological Dependencies, Guide for Students, Residents and Psychiatric Narcotics Specialists (Gestionarea dependentelor farmacologice, Ghid pentru student, rezidenti si specialist psihiatri-narcologi)

Ilinca UNTU, Vasile CHIRIȚĂ

Ilinca UNTU – M.D., PhD, senior psychiatrist, “Socola” Institute of Psychiatry, Iași, Romania
Vasile CHIRIȚĂ – Prof., M.D., Ph.D., “Socola” Institute of Psychiatry, Iași, Romania

The work *Managing Pharmacological Dependencies, Guide for Students, Residents and Psychiatric-Narcotics Specialists (Gestionarea dependentelor farmacologice, Ghid pentru student, rezidenti si specialist psihiatri-narcologi)*, belonging to the authors Anatol Nacu, Igor Nastas, Jana Chihai, Liliana Fiodorova, Ina Tcaci and Larisa Boronin appeared in Chisinau in 2016 and was conducted within the Psychiatry Discipline, Narcology and Medical Psychology of *Nicolae Testemitanu* University of Medicine and Pharmacy, Chisinau .

The present book emerged from the need to benefit from a clear, synthetic and up-to-date working tool that addresses psychopharmacological dependencies from a clinical and diagnostic point of view as well as from a multidisciplinary therapeutic perspective.

On the 106 pages, this book is divided into four chapters focusing on the Basics of Dependence, Types of Dependencies, Population Groups and Comorbidity Management Strategies and Dependent Care. Also, at the end of the paper there are a number of annexes that include specific scales of assessment of abuse, dependence and withdrawal phenomena in the context of onyphilitis or drug addiction. The last item of the table is a test of evaluation of the knowledge gained after the text, highlighting the teacher’s teaching structure and making a synthesis instead of a conclusion, personalized for each reader.

The first chapter refers to the bases of addiction, defining in turn the notion of psychoactive substance, classifying psychoactive substances in general and depending

on their mechanisms of action on the central nervous system. The chapter further exposes, according to the scientific field, the diagnostic criteria DSM V for addictive pathology. After the synthetic and clear setting of the general theoretical framework, the authors present a series of screening tests for addictions, then to bring into question a fundamental problem associated with this nosological category, namely the ethical and legislative implications in the dependencies. At the end of the chapter, the main coordinates of the therapeutic approach of addictive pathology - overdose management and psychosocial care, fundamental for the reinsertion and support of the patient included in this category of diagnostics are drawn.

The second chapter reviews the types of addictions, starting with alcohol and reaching up to benzodiazepine, barbiturates, cannabinoids, opiates, volatile substances, amphetamines / methamphetamines, cocaine and hallucinogens, including lysergic acid diethylamide, psilocybin, mescaline, phencyclidine, ketamine, colinoblocks, antihistamines, anti-parkinsonianes, mifepridone, synthetic cannabinoids and the very current and controversial, synthetic-ethnobotanic drugs. For each potentially addictive substance in the list the clinical effects / acute intoxication status, as well as withdrawal phenomena and their implications are exposed. In addition, for each major category of substances that lead to addictions, short and long term intervention methods are synthesized. This chapter is extremely rich in information, clearly formulated and has an operational character that confirms the book's quality of guidance. The complexity of information is constant, moving from the clinical-diagnostic

elements to the multidimensional and multidisciplinary therapeutic benchmarks.

The third chapter deals with particular situations of somatic comorbidity in the outline of addictive pathology, specifying information for HIV/AIDS patients, HCV/HBV viral hepatitis and for patients with pulmonary tuberculosis. Subsequently, the authors report on the main psychiatric disorders that may have substance-dependent comorbidity - depression, bipolar affective disorder and schizophrenic disorder.

The final chapter focuses on multidimensional care in dependence, referring to primary care filtered through emergency medical services and other specialized services, daycare centers for therapeutic communities materialized in short and long-term rehabilitation programs and outreach workers' work. At the same time, the importance of psychotherapeutic interventions is also mentioned.

In addition, community-based therapeutic resources are exposed and, at the end of the chapter, the specialized care levels of patients with addictions. The bibliography is made up of both classical references, fundamental to the field of addictions, as well as current articles and works. Thus, the present book is an updated work that relates to the classical theoretical markers of the domain of addictions. The bibliographic references are individualized on chapters, being presented as reading recommendations. Thus, the quality of the guide is once again certified, by pushing it to deepen and expand the information.

Managing pharmacological dependencies (Gestionarea dependentelor farmacologice , Ghid pentru student, rezidenti si specialist

psihiatry-narcologi) is a work that targets a real, ever-expanding public health issue. Its purpose is to increase the level of knowledge and understanding of this issue, the systematization of the neurobiological, etiopathogenic and social factors that compete with the occurrence of addictive pathology and the elucidation of drug treatment principles with all their interdisciplinary implications. The

book is built as a guide for students, residents in psychiatry, as well as psychiatrists specializing in narcology.

The concise, synthetic form, schema-related information, and the presence of assessment tools recommend this paper as a very effective working tool in current practice on addictive pathology.

In memoriam

The psychiatrist doctors from “Socola” Institute of Psychiatry Iasi are thinking with great respect of the late **Prof. Tudor Udristoiu, Prof. Ghiorghe Talau** and **Dr. Constantin Barabolschi**, great personalities of Romanian Psychiatry.

May they rest in peace!

Psychiatry community in mourning



Prof. Tudor Udristoiu was born on 2nd January 1946. He graduated from the Faculty of Medicine, the University of Medicine and Pharmacy “Carol Davila” in Bucharest in 1969 and became consultant in Psychiatry in 1974. He undertook further specialist training at the National Institute of Neurology and Psychiatry in Bucharest, and also in France, Holland and Norway.

In 1995 he became university professor, and from 2003 he was PhD supervisor at the University of Medicine and Pharmacy in Craiova. In the period of time 1993 – 2004, he was Head of Neuropsychiatry Department at the University of Medicine and Pharmacy in Craiova, and between 2000- 2008 was Vice Rector at the same university. Between 1994

and 1996, he was President of the National Board of Psychiatry, and between 2003 and 2006, he was President of the Romanian Association of Psychiatry. From 2008, he was President of the Romanian Society of Biological Psychiatry and Psychopharmacology. He was hospital director in Negoii, Dolj, 1970-1977 and director of “Victor Babes” Clinical Hospital in Craiova between 1993 and 1995. Between 2004 and 2006, he was president of the Council of the Clinical Hospital of Neuropsychiatry in Craiova, and from 2006 until 2008 he was manager in the same hospital. He was member of prestigious national and international scientific societies: “Romanian Psychiatric Association”, “American Psychiatric Association”, “World Federation of Societies of Biological Psychiatry Task Force on Eating Disorders”, “European College of Psychopharmacology”, “International Society for Bipolar Disorders”, “Association Medico- Psychologique de France”, as well as the Founding Editor of the Romanian Journal of Psychopharmacology. He chaired national Conferences of Psychiatry in 2001, 2004, and 2006, he was awarded the Prize of Excellence “Eduard Pamfil” of the Romanian Association of Psychiatry in 2003, 2005, 2006 and was Honorary Member of the Romanian Academy of Medical Sciences. He published more than 200 papers, two chapters in the Treatise of Psycho-Pharmacology, 4 university courses and over 10 volumes in the speciality. *Professor Tudor Udristoiu* died in Craiova on 28th January 2018.

**The Institute of Psychiatry “Socola”
Iasi, February, 2018**



Prof. Ghiorghe Talau was born at Zatrani, Valcea county on 8th February 1948 and died on 27th January 2018. He graduated from the

Faculty of Medicine in 1973 and from the same year he worked in Hospital in Gradistea, Calarasi. In the period of time 1974-1976, he worked in the Town Hospital Horezu, Valcea, and between 1976 and 1980 he trained as a psychiatric doctor at "Socola" Clinical Hospital Iasi (at present the Institute of Psychiatry "Socola" Iasi).

In 1980, by competitive admission he joined the Clinical Hospital of Psychiatry in Sibiu, and was its director in the period of time 1997-2000. In 1997 he was lecturer and then university professor at the Faculty of Medicine at "Lucian Blaga" University in Sibiu.

He was member of the Romanian Association of Psychotherapy, of the Romanian Association of Psychiatry and of the World Association of Psychiatry. In his didactic, medical and research activity as well as chief of the service he got remarkable results. He organized and took part in national and international scientific events and published articles in journals in Romania and abroad and wrote chapters in the Treatise of Psychiatry.

Professor Ghiorghe Talau, who trained at the School of Psychiatry at "Socola" in Iasi, was a prestigious personality in the Romanian psychiatry, with a performance and results on the level of European standards.

On 8th February he would have been 70 years old, he but passed away after a long fight with suffering on 27th January 2018.

**The Institute of Psychiatry "Socola"
Iasi, February, 2018**



Dr. Constantin Barabolschi (01.11.1943-18.01.2018) finished school at “C.Negruzzi” High School in Iasi, the capital of Moldavia, then, he enrolled as a student at the Faculty of Medicine, “Gr.T. Popa” University of Medicine and Pharmacy –Iasi, Pediatrics.

He chose to specialize in pediatric psychiatry, his internship was in Bucharest, under the guidance Professor Dr. Academician Stefan Milea. Dr. Constantin Barabolschi opted for pediatric psychiatry starting from several questions (some of them without an answer even today): what is going on in the mind of a mentally ill child; what are the mechanisms that induce the disease and how can we help such a child? After passing the required exams, he became consultant, head of division and led the Laboratory of Mental Health at “Socola” hospital Iasi.

Following retirement, he continued clinical practice until 2014 at “Socola” Hospital in Iasi, due to lack of specialists in pediatric psychology. In the last years, including 2018, he worked in a private clinic. Out of the 50 years of medical activity, he dedicated four decades

to psychiatry, striving until the last minute to help. Dr. Constantin Barabolschi did not have a limited number of working hours, his working day was over when there was no patient waiting for him. Dr. Barabolschi’s personality had something of a paradox; he was jovial, always ready for a joke, always on the move; but, at the same time he was an excellent professional, a very good diagnostician; he made a difficult diagnosis with ease and spontaneity, **from the age of 8 months one can make the diagnosis of autism in a child**”, he used to say.

He loved people, animals, nature, books and travelling. In his courtyard, he had stray dogs and cats, he spoke about each of them as about friends, admiring their intelligence and loyalty. He was a keen gardener and grew fruit trees. He had an already famous fig tree in his garden, and made jam with its fruit which gave to his friends.

All Dr. Constantin Barabolschi activities aimed to do GOOD. He did GOOD discretely without humiliating anyone. He used to give his patients sweets, clothes, money, doing this naturally, with joy. He had Christian Orthodox conviction and was always ready to help.

For more than 20 years I was on call with Dr. Constantin Barabolschi. Everything seemed simple and natural with him and he helped his colleagues with a good sense of humour. When I had a difficult case in my department, I always looked for Dr. Barabolschi’s advice. I learned pediatric psychiatry from him. He was a fluent speaker in French, he had friends in France and in other francophone countries. An alert spirit, he practiced his profession until the last day of his life. This sudden loss deeply saddened his colleagues, friends and patients.

“All departures create opportunities for reunions.”

Brandusa Vornicu
MD, PhD, senior psychiatrist
The Institute of Psychiatry “Socola”

Instructions for authors

***Bulletin of Integrative Psychiatry* accepts for publication the following types of works (articles): reviews, updates, meta analysis, original papers, case report.**

Fields of research: psychiatry correlated with philosophy, ethics, metaethics, bioethics, aesthetics, economy, sports, nutrition, law, forensic medicine, political sciences, communicational sciences, sociology, social assistance, anthropology, cultural anthropology, literature, religion, etc.

Manuscript Criteria and Information

Manuscripts and all attached files should be submitted in electronic form and on paper.

The electronic form should be submitted, either on compact disk or by e-mail (see at end). It is preferable that two copies (in English and Romanian) of the manuscript, printed on one side of A4 paper format, single-spaced, with 2 cm margins, be also submitted to the same address. The manuscript should be accompanied by **a cover letter** including the statement on authorship responsibilities form, the statement on ethical considerations and the statement on financial disclosure (For more information please see directions on website.).

Authorship

All named authors should meet the criteria for authorship as stated in the "Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication" issued by the International Committee of Medical Journal Editors (www.icmje.org).

Ethical considerations

If the scientific project involves human subjects or experimental animals, authors must state in the manuscript that the protocol has been approved by the Ethics Committee of the institution within which the research work was undertaken. All authors are responsible for adhering to guidelines on good publication practice.

Financial Disclosure

The manuscript should be accompanied by a **cover letter** including the statement on financial disclosure. The statement on conflicts of interest will be published at the end of the paper. Please submit all requested signed documents by regular mail to the Secretariat. Scanned copies sent electronically and fax submissions are not acceptable.

Corrections

Scientific fraud is rare events; however, they have a very serious impact on the integrity of the scientific community. If the Editorial Board uncovers possible evidence of such problems it will reserves the right to take all steps it considers necessary for the elucidation of the situation, including possibility to publish errata, corrigenda, or retractions.

Copyright

The papers published in the *Bulletin* and protected by copyright. Their full or partial publication in other journal is allowed only with the written approval of the publisher.

Manuscript Preparation

- Romanian authors should send both the *Romanian* and *English* version of the article, including title, abstract and keywords. Foreign authors should send the English version of the article.
- Manuscripts must be prepared in conformity to the “Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication” issued by the International Committee of Medical Journal Editors (www.icmje.org).
- Articles must be written in Microsoft Word, Style: *Normal + Justify*, Font: *Times New Roman*, size: 12. All manuscripts must be typed single-spaced. Original source files (not PDF files) are required. In text editing, **do not use** spacing with spacebar, or paragraph mark, use only *Enter* or *Tab* key.
- Subheadings of the article should be left-justified, typed with capital letters, Font: *Times New Roman*, size: 12.
- The abstracts and keywords must be written in Microsoft Word, Style: *Normal + Justify*, Font: *Times New Roman*, size: 12.
- Use as few formatting commands as possible:
 - input your text continuously (without breaks);
 - do not use different types of fonts to highlight your text;
 - any word or phrase that you would like to emphasize should be indicated throughout the text by underlining;
 - use only the *Enter* key to indicate the end of the end of paragraphs, headings, lists, etc.;
 - do not use the *Space Bar* to indicate paragraphs, but only the *Tab* key.
- Figures must be cited in order in the text using Arabic numerals (e.g., fig. 2). Their width should be max. 13,5 cm. The figures have to satisfy the following conditions:
 - Black and white photographs with good contrast, with recommended size;
 - Scanned photograph with a resolution of minimum 300 dpi and edited on a computer, original file (*.JPG);
 - Illustrations (drawings, charts) created on a computer, cited in the text, original file (*.XLS, *.CDR). Every figure should be accompanied by a title and a legend.
 - Tables, numbered consecutively with Latin numerals (e.g., Tab. II), should have a width of max. 13,5 cm. Every table should be also accompanied by a title and a legend. The distribution of tables and figures in the text should be balanced.
 - Please do not import tables or figures into the text document, but only specify their insertion in text (e.g., Table no. III insertion). They have to be sent in separate files. Files should be labelled with appropriate and descriptive file names.
 - Abbreviations shall be avoid. If used, will occur preceded by the full term at their first apparition in text. A list of all used abbreviations shall be made at the end of the article.
 - Separate pages: tables, graphics, pictures and schemes will appear on separate pages.
 - You may use a common compression program: ARJ, RAR or ZIP.

Manuscript organization

Article title: titles should be short, specific, and descriptive, emphasizing the main point of the article. Avoid a 2-part title, if at all possible. Do not make a declarative statement in the title. Title length, including punctuation and spaces, ideally should be under 100 characters and must not exceed 150 characters.

Manuscript Size

- Original paper – 8 pages/3500 words;
- Review and update – 8 pages/3500 words;
- Case report – 4 pages/1700 words;
- Clinical notes – 3 pages/1300 words;
- Letters to editor, information scientific reunions – one page/450 words.

Author(s). First name, middle initials and surname of the authors, without any scientific, didactic or military degrees (e. g., Mircea A. Popescu, Aura Vasilescu, **not Popescu M. A., Vasilescu A.**).

Footnote that specifies the authors' scientific titles, professional title, name and address of their workplaces (institution and department) for each author; contact details of the corresponding author (full address, telephone number, fax number, e-mail address) and the address of the institution and department where the study has been carried out. Contact details will be published unless otherwise requested by the author.

Abstracts in English and Romanian should have max. 300 words. For original articles is advisable to include five paragraphs, labelled Background, Objective(s), Method(s), Result(s), and Conclusion(s).

Keywords: maximum of 6 keywords (minimum of 3). Keywords should not repeat the title of the manuscript.

Original papers organized in:

- **Introduction** (no more than 25 % of the text), material and methods, results, comments or discussions and acknowledgements.
- **Material and methods** have to be described in enough detail to permit reproduction by other teams. The same product names should be used throughout the text (with the brand name in parenthesis at the first use).
- **Results** should be presented concisely. Tables and figures should not duplicate text.
- **Discussions** should set the results in context and set forth the major conclusions of the authors.
- Information from the Introduction or Results should not be repeated unless necessary for clarity. The discussion should also include a comparison among the obtained results and other studies from the literature, with explanations or hypothesis on the observed differences, comments on the importance of the study and the actual status of the investigated subject, unsolved problems, questions to be answered in the future.
- **Acknowledgements** section must disclose any substantive conflicts of interest in addition to the customary recognition of non-authors who have been helpful to the work described.
- **References.** References should be numbered consecutively **in the order in which they are first mentioned in the text.** Identify references in text, tables, and legends by Arabic numerals in parentheses. The reference list will include only the references cited in the text (identified by Arabic numerals in parentheses, **not in square brackets and not bold**). All authors should be listed when four or less; when five or more, list only the first three and add "*et al.*" (Popescu I., Popescu I., Vasile V. *et al.*). The name of the Journals cited in the References should be abbreviated according to ISI Journal Title Abbreviations.

It is absolutely imperative that references to be entered in the text!!

Examples:

- **Reference to a journal publication:**

Amura SG.: Neurotransmitter transporter: recent progress. *Ann Rev Neurosci* 1993; 16; 73-93.

Tonis PJ, von Sandick JW, Nieweg OE, *et al.*: The hidden sentinel node, in breast cancer. *Eur J Nucl Med* 2002; 29: 305-311

- **Reference to a book:**

Ashcroft FM.: Ion channels and disease, San Diego, London: Academic Press, 2000, pp. 26-52.

- **Reference to a chapter in an edited book:**

Article title: titles should be short, specific, and descriptive, emphasizing the main point of the article. Avoid a 2-part title, if at all possible. Do not make a declarative statement in the title. Title length, including punctuation and spaces, ideally should be under 100 characters and must not exceed 150 characters.

ACKNOWLEDGMENTS AND DISCLOSURE

Authors: An “author” is generally considered to be someone who has made substantive intellectual contributions to a published study, and biomedical authorship continues to have important academic, social, and financial implications (1). *An author must take responsibility for at least one component of the work, should be able to identify who is responsible for each other component, and should ideally be confident in their co-authors’ ability and integrity.*

We strongly encourage developing and implementing a contributor ship policy, as well as a policy on identifying who is responsible for the integrity of the work as a whole.

Disclosure: The authors must declare if they have or not a potential conflicts of interest to disclose.

Acknowledgments: All contributors who do not meet the criteria for authorship should be listed in an acknowledgments section. Authors should declare whether they had assistance with study design, data collection, data analysis, or manuscript preparation. If such assistance was available, the authors should disclose the identity of the individuals who provided this assistance and the entity that supported it in the published article. Financial and material support should also be acknowledged.

PEER REVIEW PROCESS

All manuscripts intended for publication will be subject to peer-review by a committee of experts which assesses the scientific and statistical correctness of articles submitted. The committee receives the manuscripts without knowing the authors name and proposes possible changes, which will be transmitted to the authors by the medium of Editorial Board. The authors have the obligation to oversee the text in English language with the help of a professional translator.

When submitting a paper, a confirmation email is automatically sent back to the author. It contains a unique registration number used as a referral in further correspondence.

Initially, the editorial team verifies whether the manuscript complies with the editing instructions. If the paper does not meet the necessary requirements, it is rejected and the corresponding author is notified to correct the errors. If all instructions for editing have been followed accordingly, the editor selects two reviewers that will independently evaluate the paper. They have high expertise in the “peer-review” system and are well-known specialists in the field. The reviewers have all academic affiliations and may be already accredited by the Journal or specifically contacted for certain papers. Their affiliation is usually different from the one of submitting authors.

The editor sends the paper in both electronic and printed format to each reviewer with the invitation to evaluate it within 15 days. The reviewers will analyze the paper from several perspectives such as clarity, objectivity of data, scientific quality and relevance. A scale from 1 to 5 is used, where 5 is excellent and 1 is poor. The reviewers score the paper accordingly and issue a recommendation.

The existence of a manuscript under review is not revealed to anyone other than peer reviewers and editorial staff. Peer reviewers remain anonymous and are expected to maintain strict confidentiality. After the review process has been completed, authors will be informed by mail of the Editor’s decision.

It is absolutely imperative to fill and send “Cover letter for submission of manuscript” and “Declaration of Interests and disclosure form”, which you can download from the website of *Bulletin of Integrative Psychiatry* (www.buletindepsihiatrie.ro).

Address to send the manuscripts:

Buletin de Psihiatrie Integrativă

Institutul de Psihiatrie „SOCOLA” Iași

Assistant Prof. Alexandra BOLOȘ

Institutul de Psihiatrie „SOCOLA” Iași

Șos. Bucium nr. 34, cod 700282, Iași, jud. Iași

Phone/Fax: +40 232 233 549; +40 232 236 200

E-mail: bolalexandra@gmail.com

Contact person:

Assistant Prof. Alexandra BOLOȘ

E-mail: alex_andra_bolos@yahoo.com

Assistant Prof. Irina SĂCUIU

E-mail: irina_sacuiu@yahoo.com

