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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 Iaşi. Even from its beginnings, the Society edited a journal entitled "Bulletins et Mémoires de la Société de Neurologie, Psychiatrie et Psychologie de Iassy", the first publication of the kind in Romania, which was unique also by its vision and opening towards biology, psychology, sociology and philosophy and by its prestigious board of editors: C. I. Parhon, Gh. Preda, Constantin Fedeleş, Arnold Stocker, P. Andrei, Corneliu Popa-Radu, I. A. Scriban, well known personalities, some of them being physicians of great culture and scientific qualification.

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

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

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

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

Starting from 1994, Professor Dr. Tadeusz Pirozynski, Professor dr. Petru Boişteanu, Professor dr. Vasile Chiriţă, 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 Naţional de Educaţie Medicală Continuă şi în temeiul art. 406, 414 şi 431 din Legea nr. 95/2006 privind reforma în domeniul sănătăţii, Consiliul Naţional al Colegiului Medicilor din România a decis ca articolele ştiinţifice publicate în reviste de specialitate clasificate CNCS, grupa B, să fie punctate cu 80 credite/articol.

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BPI Bulletin of Integrative Psychiatry
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Editorial

DSM-5 – Between the good and the bad

Roxana CHIRIȚĂ, Ilinca UNTU

Roxana CHIRIȚĂ – Prof., M. D., Ph. D., "Socola" Institute of Psychiatry, Iași, Romania
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The 1980 launch of the DSM-3 represented the trigger of revolutionary changes in the field of psychiatry and of related sciences. Thus, the classification of mental diseases turned into a partially arbitrary endeavour, within a well-determined system, with criteria delimited for each disease. The introduction of a classification system of psychiatric conditions has made psychiatry, clinical psychology and other related fields evolve from the level of modest scientific acknowledgement and even from the status of pseudo-science, at times, to the highest level in terms of healthcare research. The immediate consequence of these radical transformations was precisely a deeper insight into the proper therapeutic options for patients within a certain nosological category.

The latest edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) is the product of over 10 years of efforts made by hundreds of internationally renowned experts in diverse fields of mental health. The outcome is precisely a volume that has become an authority in the field, which defines and classifies psychiatric disorders with the final purpose of optimizing diagnostic and therapeutic strategies and of opening new research directions at the same time.



Addressed to both clinicians and scientists, as main diagnostic and classification instrument for psychiatric disorders, the DSM-5 comprises concise but explicit criteria, in order to facilitate a more objective approach to symptoms and to the entire array of manifestations – most of the times polymorphic and heterogeneous – of mental conditions. At the same time, DSM-5 aims to categorize disorders more precisely, by the severity of symptoms, considering the need of therapeutic home care, in conditions of hospitalization or partial hospitalization or outpatient care, thus delimiting more accurately the needs of mental patients.

The most apparent characteristic of the DSM-5 is precisely the elimination of diagnostic axes, previously promoted by the DSM-4, which forced clinicians to assess each patient by criteria that often deviated from their main psychiatric diagnostic. In the same multiaxial context of the DSM-4, there was an artificial association on axis II of mental deficiency and of personality disorders, because all the other disorders were on axis I. Another shortcoming solved by the DSM-5 is the categorization of other mental disorders of childhood – a collection of unrelated disorders that "originated in childhood" (but not "mental retardation") – within a common section, not taking into account the symptomatic particularities. The DSM-5 places all psychiatric disorders in section II, thus replacing the first three axes, while axis IV was replaced by significant psychosocial and contextual features. Axis V, concerning Global Assessment of Functioning, known as GAF, was removed altogether. Therefore, the elimination of diagnostic axes represents, at least apparently, a positive element of the DSM-5, which clarifies a series of nosological categorisation confusions. The new version of the DSM also replaces the NOS categories with two options: other specified disorder and unspecified disorder to increase the utility to the clinician, the first allowing the clinician to specify the reason that the criteria for a specific disorder are not met and the second allowing the clinician the option to forgo specification. Another beneficial change of the DSM-5 is that "mental retardation" is no longer being used as a diagnosis but is being replaced by "intellectual disability," which makes DSM-5 consistent with established practices in the field. Moreover, other diagnostics with potentially stigmatizing names were modified, including Hypochondriasis, now called "Illness Anxiety Disorder" and the Paraphilias, now called "Paraphilic Disorders", and the list goes on. At the same time, autistic disorders were eliminated and replaced by "autistic spectrum disorder", which is a more operational name. These terminological modifications go beyond the authors' wish for political correctness: they aim to find more accurate names for psychiatric disorders. Other disorders – previously included artificially within larger nosological categories – were re-categorized, such as Obsessive Compulsive Disorder, which is now independent, not included within anxiety disorders, and PTSD, which is now included within "Trauma and Stressor-Related Disorders". One must also highlight the disambiguation and liberation of schizophrenia from too-limited forms: currently, they focus on more precise means for assessing the severity of symptoms. Guidelines for evaluating suicidality are also being included in DSM-5, providing clinicians with greater structure in assessing individuals who may present a risk to themselves.

Aside from these strong points of the DSM-5, which endow the classification of mental disorders with a clear, diagnostic-adapted style and which tend to destigmatize mental patients, the manual has also received its fair share of criticism, concerning the perfectible aspects of the latest diagnostic and classification system. For instance, the inclusion of "Mild Neurocognitive Impairment" has the very real potential to pathologize the normal age-related changes in cognition that many people experience. This extends to an apparent trend of pathologizing normal human re-

actions, thus altering the concept of bereavement for instance.

The Diagnostic and Statistical Manual-5 (DSM-5), published in May 2013, represents the materialisation of years-long efforts, of clinical trials, debates and tests conducted by hundreds of scientists who activate in the field of psychiatry and in related domains. Called the *Bible of psychiatry,* the DSM-5 includes almost all possible variations of human behaviour. Beyond the strong and weak points of the DSM-5, it represents a step forward, a change saluted by some and detested by others, but which definitely clarifies certain diagnostic aspects dominated by ambiguity in the past. Only time will decide how these changes promoted by the DSM-5 will impact mental health and the evolution of psychiatry in both clinical and research fields.

BPI Bulletin of Integrative Psychiatry
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Articles

BPI Bulletin of Integrative Psychiatry
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An overview of the most important side effects of the psychotropic medication

Alexandra BOLOŞ, Dumitriţa GAFENCU-SAVLOVSCHI, Andreea Silvana SZALONTAY

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ABSTRACT

This paper is a review of several of the most concerning side effects of psychotropic medications, because their use entails a difficult trade-off between the benefit of alleviating psychiatric symptoms and the risk of troubling, sometimes life-shortening, adverse effects. It is well known that people with severe mental disorders have a considerably shorter lifespan than the general population. This excess mortality is mainly due to physical illness. Next to mental disorders, related factors, unhealthy lifestyle, and disparities in health care access and utilization, psychotropic medications can contribute to the risk of physical morbidity and mortality. Updating the information about the principal side effects of the psychotropic medication can lead to a better therapeutic management of the patient.

KEYWORDS

psychotropic medication, side effects, antipsychotics, antidepressants, mood stabilizers

People with severe mental disorders have a considerably shorter lifespan than the general population. This excess mortality is mainly due to physical illness. Next to mental disorders, related factors, unhealthy lifestyle, and disparities in health care access and utilization, psychotropic medications can contribute to the risk of physical

morbidity and mortality. Updating the information about the principal side effects of the psychotropic medication can lead to a better therapeutic management of the patient.

I. ANTIDEPRESSIVE DRUGS
TRICYCLIC ANTIDEPRESSANTS

- *Cardiovascular side effects*

Various aspects of the cardiotoxicity of tricyclic antidepressants have been reviewed, including direct myocardial actions and hypotension. Tricyclic antidepressants are highly concentrated in the myocardium; this may account for the vulnerability of the heart as a target organ, as well as for inconsistently and inconclusively reported relations between plasma drug concentrations and specific manifestations of cardiac toxicity.

These drugs can interfere with the normal rate, rhythm, and contractility of the heart through actions both on the nerve and the muscle, that are mediated by at least four different mechanisms (singly, in combination, or due to imbalance), including an anticholinergic action, interference with reuptake of catecholamines, direct myocardial depression, and alterations in membrane permeability due to lipophilic and surfactant properties.

Changes in conduction and repolarization cause prolongation of the PR, QRS, and QT intervals and flattening or inversion of T-waves on routine electrocardiograms; conduction delay occurs distal to the atrioventricular node and appears as a prolonged HV interval (the time from activation of the bundle of His to contraction of the ventricular muscle).

As many as 20 % of patients taking adequate doses of a tricyclic antidepressant, experience marked postural hypotension. This effect is not consistently correlated with plasma concentrations and tolerance does not develop during treatment [1] [2] [3]. The mechanism for this effect is uncertain; it has been attributed to a peripheral antiadrenergic action, to a myocardial depressant effect, and to an action mediated by alpha-adrenoceptors in the central nervous system [4] [5] [6].

- *Respiratory side effects*

There has been one case report of reduced ventilatory response to hypercapnia after nortriptyline in a woman with chronic obstructive pulmonary disease [7].

- *Nervous system side effects*

Miscellaneous symptoms that have been attributed to the tricyclic antidepressants include fatigue, weakness, dizziness, headache, and tremor; patients are likely to fall because of these disturbances [8].

Several organs are the target for the anticholinergic (antimuscarinic) activity of the tricyclic antidepressants. They constitute the most common and troublesome adverse effects of the tricyclic antidepressants, but the peripheral anticholinergic actions can also be put to therapeutic use in conditions such as irritable bowel syndrome, premature ejaculation, and nocturnal enuresis.

Regarding the extrapyramidal side effects, tricyclic antidepressants are often listed among the many drugs that can produce buccofaciolingual or choreoathetoid movements [9].

- *Metabolism and endocrine side effects*

The tricyclic antidepressants (TCAs) can lead to increased weight, and this is primarily due to increased appetite and carbohydrate craving, that are likely the result of blocking histamine and 5-HT2 receptors in the brain. TCAs can also raise

serum cholesterol and triglycerides; however, it is not clear if those effects are secondary to the weight gain [10].

- *Gastrointestinal side effects*

This treatment can cause simple a bowel disturbances or more serious complications like paralytic ileus, which can be life-threatening, especially in the elderly [11].

The incidence of gastroesophageal reflux disease has been reported to be higher in depressed patients (14.2 per 1000 person per year; 95 % CI¼ 13.6, 14.8) compared with controls (8.3 per 1000 person per year; 95 % CI ¼ 1.60, 1.85) in a large cohort study; the hazard ratio was 1.72 (95 % CI ¼1.34, 2.20) [12] and the researchers speculated that the anticholinergic effects of tricyclic antidepressants may reduce lower esophageal sphincter pressure, leading to more frequent episodes of reflux [5].

- *Hematologic side effects*

Occasional cases of blood dyscrasias, agranulocytosis or non-thrombocytopenic purpura have been associated with this treatment [13] [14] [15] [16].

- *Psychiatric side effects*

Musical hallucinations have been reported in association with clomipramine [17] and it is widely believed that there is a significant risk that tricyclic antidepressants can precipitate mania or rapid cycling in up to 10 % of patients, and that various factors increase this possibility, including being female or younger, having an earlier onset of illness, and having a positive first degree family history. [18]

SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS)

- *Nervous system side effects*

In a case-crossover study there was an association between antidepressant drug use and an increased risk of stroke (AOR ¼ 1.48) [19]. An excess risk of stroke with antidepressant use was more apparent for ischemic strokes (AOR ¼ 2.52) than with hemorrhagic strokes (AOR ¼ 1.92). SSRIs were associated with the highest risks for all strokes and ischemic strokes (AOR ¼ 4.22 and 4.11 respectively), and other antidepressants (SNRIs, Trazodone and Venlafaxine) for hemorrhagic stroke (AOR ¼ 5.40, SSRIs 4.24). [20]

- *Cardiovascular side effects*

The SSRIs appear to have a better cardiovascular safety. Only Citalopram may be associated with QTc prolongation. The effect of Citalopram on the QTc interval has been confirmed in a cross-sectional study using ECG and clinical data from electronic health records [21]. In that study, the relationship between dosage of a number of antidepressants and QTc was examined in 38 397 patients who had an ECG following prescription of an antidepressant. [22]

- *Metabolic and Endocrine side effects*

Uguz *et al.* examined weight gain in patients taking SSRI in a cross-sectional study of 362 consecutive psychiatric patients taking antidepressants for 6 to 36 months. Over half of the patients studied (55.2 %) gained weight with 40.6 % gaining 7 % or more of their initial weight. Citalopram, Escitalopram, Sertraline, Paroxetine, Venlafaxine, Duloxetine and Mirtazapine, but not Fluoxetine, were all associated with significant weight gain. Blumenthal *et al.* identi-

fied 22 610 adult patients who had commenced an antidepressant and for whom weight data were available in a regional health care system, assessing the association between individual antidepressants and weight change, over 12 months after treatment initiation. They found the greatest weight gain in patients taking Mirtazapine and Paroxetine, which was similar in magnitude to that observed with Citalopram. Compared with Citalopram, a significantly decreased rate of weight gain was observed in patients treated with Bupropion, Amitriptyline and Nortriptyline. Noting limited empirical data on antidepressant use and weight change in younger patients, Cockerill *et al.* performed a historical cohort study assessing change in BMI (body mass index) associated with antidepressant use in overweight adolescents with a depressive disorder. They found that BMI was significantly increased only in those adolescents treated with SSRIs. [23]

Treatment with SSRIs and SNRIs was associated with an increased risk of hyperprolactinemia (reporting odds ratio, ROR ¼ 3.3) in a study using data from the French Pharmacovigilance Database; the risk was particularly increased with fluvoxamine (ROR ¼ 4.5), Citalopram (ROR ¼ 3.9), and Fluoxetine (ROR ¼ 3.6); Sertraline, Duloxetine, and Milnacipran were not associated with an increased risk. [24]

- *Hematologic side effects*

Bleeding abnormalities associated with antidepressants are becoming more commonly reported, leading to questions about the safety and appropriateness of these medications in a number of relevant clinical scenarios and patient populations. Over the last decade or so there have been a number of reports of increased risk of bleeding associated with selective serotonin reuptake inhibitors (SSRI), like gastrointestinal bleeding, postpartum hemorrhage, brain hemorrhage or perioperative hemorrhage [25] [26] [27] [28] [29]. Although there have been numerous reports concerning antidepressants and bleeding, relatively few have examined direct in vitro platelet effects, with most examining effects on platelet aggregation. A small study examined the effect of two SSRIs (Sertraline and Citalopram), Venlafaxine and Reboxetine on both platelet adhesion and plasma coagulation (activated partial thromboplastin time (APTT) and prothrombin time) [30]. This study found that both SSRIs, but not Venlafaxine, significantly inhibited platelet adhesion to both collagen and fibrinogen in a concentration - dependent fashion. None of the drugs studied had a significant effect on plasma coagulation. [31]

- *Reproductive system (pregnancy, development and infancy) side effects*

There has been ongoing controversy and uncertainty about the possible contribution of antidepressants to spontaneous abortion, pre-eclampsia, congenital malformations and neonatal development. But the majority of the studies concluded that only the Fluoxetine and Paroxetine should be avoided during the first trimester and in those at risk of unplanned pregnancy. [32] [33]

- *Musculoskeletal side effects*

The most recent meta-analysis (237 studies), which pooled results from 13 qualifying cohort and case-control studies, found that SSRIs were associated with a significantly increased risk of fractures (RR51.72, 95 % CI: 1.51 – 1.95, $p < 0.001$). This increased risk was also observed in studies that adjusted for depression (RR51.74, 95 % CI: 1.28 – 2.36, $p < 0.001$) and for BMD

(RR51.70, 95 % CI: 1.28 – 2.25, p < 0.001) [34].

SEROTONIN AND NORADRENALINE REUPTAKE INHIBITORS (SNRIS)

- *Cardiovascular side effects*

Serotonin-norepinephrine reuptake inhibitors (SNRIs) are associated with a small, but increased incidence of cardiovascular adverse events (hypertension, tachycardia and orthostatic hypotension), while at therapeutic doses they do not seem to cause QTc prolongation [6].

- *Nervous system side effects*

Serotonin syndrome with rabdomiolysis occurred in a patient with Parkinson's disease after he had taken Venlafaxine 75 mg/day for depression for two weeks [35]. Previous reports of serotonin syndrome with Venlafaxine have been related to overdose [36]. Parkinsonism or drug – drug interactions with the antiparkinsonian medications may have predisposed this patient to serotonin syndrome at such low doses of Venlafaxine. Bruxism has been not infrequently associated with SSRIs, but there have been few reports associated with other antidepressants. Bruxism apparently related to Venlafaxine 150 mg/day has been reported in a 31-year-old woman after one week of treatment [37]. She had experienced similar symptoms previously with the Escitalopram and Fluoxetine. The symptoms resolved with Buspirone 20 mg/day, and she was able to continue taking Venlafaxine.

- *Reproductive system (pregnancy, development and infancy) side effects*

Galactorrhea and metrorrhagia have been attributed to Venlafaxine at therapeutic doses [38]. There have been reports of neonatal withdrawal symptoms with SSRIs, but little is known of this phenomenon with other antidepressants. When seven mother – child pairs exposed to Venlafaxine from the second trimester, were studied [39], five of the neonates had a withdrawal syndrome, including tachypnea and respiratory distress; the changes corresponded to falling plasma Venlafaxine concentrations. The neonate exposed to the highest maternal dose of Venlafaxine (300 mg/day) had the most severe and most persistent signs. [40]

II. ANTIPSYCHOTICS

- *Neurologic side effects*

A study comparing somnolence determined by Asenapine, Olanzapine, Risperidone and Haloperidol relative to placebo evaluated ten clinical trials of patients with schizophrenia or bipolar disorder [41]. The duration and incidence of somnolence was the greatest for Asenapine and Olanzapine (maximal for olanzapine) and with shorter time to onset than the other antipsychotics and placebo; patients with bipolar disorder were the most sensitive. [42]

Even if the second generation antipsychotics, compared with the first generation antipsychotics, carry a much lower risk to develop neurological symptoms, both classes can induce within hours of initiation of antipsychotic treatment, dystonic reactions, including torticollis, oculogyric crisis (upward deviation of the eyes) and life-threatening laryngospasm, or after weeks of treatment they can induce rigidity, akinesia, bradykinesia, tremor and akathisia, symptoms that are collectively known as "extrapyramidal side-effects". [43]

A retrospective case analysis of 55 pediatric emergency department patients re-

ported presentations due to drug induced dystonic reactions with first generation of antipsychotics (Haloperidol, Chlorpromazine), second generation of antipsychotics (Risperidone) and antiemetics with antidopaminergic activity (Metoclopramide). [44]

A literature review identified Amisulpride, Flupenthixol, Haloperidol, Levopromazine, Sulpiride, Thioridazine, Zuclopenthixol and second generation antipsychotics at higher doses (Aripiprazole, Olanzapine, Risperidone) as high risk of inducing Parkinson symptoms. [45] Ziprasidone was identified as intermediate risk. [42]

- *Metabolic and endocrine side effects*

Most SGAs, and a part of FGAs, have been shown to cause weight gain and other metabolic syndromes, including dyslipidemia, and hyperglycemia (leading to type two diabetes mellitus). Specifically, dyslipidemia includes hypertriglyceridemia and low high-density lipoprotein levels. The SGAs are divided into high – Olanzapine, Clozapine, moderate – Quetiapine, Risperidone, and low – Ziprasidone, Aripiprazole risk classes for weight gain and metabolic side-effects according to a consensus statement by the American Diabetes Association and American Psychiatric Association in 2004. Possible mechanisms for weight gain include histaminic or serotonergic antagonism, or insulin resistance. Monitoring recommendations include measurement of waist circumference, fasting glucose, triglycerides, high density lipoprotein, and blood pressure routinely in patients taking SGAs (Nasrallah and Smeltzer, 2003; Rosenbaum *et al.*, 2005; Marder and Wirshing, 2009). [43] [46] Weight gain with SGAs typically occurs within the first four to twelve weeks of treatment and may or may not reach a plateau after one year [47].

Thus, an increase in the natural mortality rate of 1.5e2-fold as compared to the general population was reported for depressed, bipolar and schizophrenic patients (Brown, 1997; Harris & Barraclough, 1998; Joukamaa *et al.*, 2001; Angst *et al.*, 2002; Saha *et al.*, 2007, Laursen *et al.*, 2007) [48] which appears to be mainly due to an increased comorbidity for metabolic and cardiovascular illness that significantly worsens the incidence of mortality in this subpopulation. (Musselman *et al.*, 1998; Osby *et al.*, 2000; Cohn and Remington, 2003; McEvoy *et al.*, 2005; Van der Kooy *et al.*, 2007, Birkenaes *et al.*, 2007). In addition, several studies reported a higher prevalence of metabolic syndrome in various psychotic disorders including bipolar and schizophrenic patients as compared to the general population (Birkenaes *et al.*, 2007; Correll *et al.*, 2008; Fiedorowicz *et al.*, 2008; Sicras *et al.*, 2008; Van Winkel *et al.*, 2008), and this can be because of overweight or frank obesity, dyslipidemia, hypertension, hyperglycemia (impaired fasting glucose tolerance) but also smoking habits (Compton *et al.*, 2006), poor diet and sedentary lifestyle (Brown *et al.*, 1999). These are all aspects of medical concern which are predominant among individuals with major mental disorders. This legitimates the consideration of a cluster of factors identifiable as cardiometabolic disease risk (Newcomer, 2007). [48, 49]

A study of prolactin levels in 268 patients treated for schizophrenia with Olanzapine, Risperidone, Aripiprazole, Quetiapine or Perospirone in monotherapy found lower levels with Aripiprazole. [50, 51] Both Olanzapine and Risperidone were associated with higher levels as was female sex and higher dose [42] A study of 100 men with

psychotic disorders found that the rate of sexual dysfunction was highest for Risperidone, followed by Trifluoperazine and Olanzapine, measured on three different scales [52]. Rates of sexual function varied according to the scale used; decreased libido was the most prevalent except for orgasmic disorders for Risperidone on the ASEX scale. [42]

- *Cardiovascular side effects*

Many of the conventional antipsychotics have shown an increased risk in cardiac dysrhythmias, specifically with prolongation of the QRS or QTc intervals. This can lead to life-threatening ventricular arrhythmias such as torsade de pointes or ventricular fibrillation. The SGAs have prolonging effects on the QTc interval, much like some of the FGAs, but are often not clinically significant [43]. A retrospective cohort study of elderly (over 65 years old) patients did not find that SGAs were associated with a significantly greater risk of cerebral-vascular events, cardiac arrhythmia and congestive heart failure compared to FGAs [53]. Overall, there was a lower risk of mortality, but higher risk of myocardial infarction for SGAs compared to FGAs. [42]

- *Gastrointestinal side effects*

In the case of FGA anticholinergic side-effects lead to constipation, nausea, vomiting, and dry mouth. In severe cases, this can lead to paralytic ileus. Treatment should include regular use of stool softeners and bulking agents to promote regular bowel function. A rare hypersensitivity reaction has been described with the aliphatic phenothiazines, specifically Chlorpromazine. The incidence of cholestatic jaundice is approximately 0.1 % and often develops in the first one or two months of treatment. Symptoms include nausea, fever, malaise, pruritus, abdominal pain, and jaundice, and signs include elevation of bilirubin and alkaline phosphatase (Nasrallahand Tandon, 2009) [43]. For SGA transient elevation in liver enzymes may occur with Olanzapine early in treatment, but often resolves in nine or ten weeks. Anticholinergic effects with Olanzapine, Clozapine, and Quetiapine can result in constipation. [43]

- *Reproductive system (pregnancy, development and infancy) side effects*

All SGAs are rated as category C by the FDA, which means there are few or no animal or human data to indicate absence of teratogenicity. Only Haloperidol, an older neuroleptic with 40 years of use, has been deemed safe in pregnancy, but its neurological side-effects to the mother and the fetus are a major drawback.

III. MOOD STABILIZERS

Lithium

- *Nervous System side effects*

Tremor is a classic and common side effect caused by lithium, with an estimated rate of 27 %. While usually benign, this adverse effect may lead to nonadherence or, in some cases, it may be an initial sign of lithium toxicity. Commonly, it presents in the hands or upper limbs at rest, oscillating at 8 – 12 Hz, and worsens during activity. Compiled results from a literature search on this side effect reveal that it usually manifests upon initiation of lithium, it is not progressive, and decreases over time. Other characteristics include its symmetric nature and correlation with dose. Its mechanism has never been closely examined but may be related to effects on brainstem serotonergic neurons. [54] [55]

- *Endocrine side effects*

Nephrogenic diabetes insipidus is a common adverse effect of lithium [56]. Out of 56 patients who took lithium for an average of 11 years, 39 had urine volumes that exceeded three l/day, of whom 30 spontaneously reported polyuria and 35 reported that the polyuria had caused some dysfunction in their daily routine [57]. The duration of psychiatric disorder, the duration of lithium treatment, and the total number of episodes, particularly depressive episodes, all correlated positively with the polyuria.

Major side effects of the chronic use of lithium medication also include hypothyroidism and goiter (Aral and Vecchio-Sadus, 2008; Grandjean and Aubry, 2009; Kibirige *et al.,* 2013). A recent meta-analysis showed a 5.8 fold increase in the prevalence of clinical hypothyroidism among patients taking Lithium compared with those given placebo. Lithium treatment was also associated with increased levels of serum thyroid-stimulating hormone (TSH), calcium, and parathyroid hormone (McKnight *et al.,* 2012). Consistent with these observations, alterations in thyroid function were also reported in populations consuming drinking water with high Lithium concentrations. [58]

- *Cardiovascular side effects*

Several cases of lithium related cardiotoxicity have been reported. These include a case of fatal sudden cardiac death [59]; sinus node dysfunction at therapeutic concentrations (0.94 and 1.06 mmol/l) [60] and moderately raised concentrations (2.32 mmol/l) [61]; and atrioventricular block at therapeutic concentrations in a patient who was also taking Clozapine [62]. Two cases of Mobitz type II block were associated with subtherapeutic lithium concentrations (0.4 and 0.2 mmol/l) [63], but since no information establishing possible causality was presented, it seems unlikely that lithium was causal in those cases. [64]

ANTICONVULSANTS

Of all the anticonvulsant mood stabilizers, the most used in psychiatry and with the most adverse effects is Valproic acid.

- *Cardiovascular side effects*

Very rarely, valproate-induced carnitine deficiency adversely affects cardiac function. Some studies attributed hypotension [65] and carotid artery intima media thickness to this treatment [66]. One study measured carotid artery intima media thickness and serum lipids in 44 children with epilepsy taking Valproic Acid and 40 healthy children. Although there was no difference in serum lipid profiles, the intima media of the common carotid artery was significantly thicker in those who took valproic acid [66]. This finding may be due to epilepsy and not to the drug.

- *Gastrointestinal side effects*

Gastrointestinal symptoms, such as nausea, anorexia, vomiting, gastritis, and diarrhea, occur in 36 % of patients [67], although over 20 % of them may be affected at high dosages [68]. Stomatitis, parotid gland enlargement, and gingival hyperplasia are exceedingly rare [69] [70] [71]. In a retrospective survey, gastrointestinal adverse effects were less common in 150 patients taking valproate semisodium than in an equal number taking valproic acid 15 *versus* 29 %), despite the fact that serum valproic acid concentrations were comparable in the two groups [72]. Patients taking valproate semisodium were less likely

to discontinue medication because of gastrointestinal adverse effects (4 *versus* 13 %). The difference was ascribed to the enteric-coated formulation of valproate semisodium. The suggestion that Divalproex (valproate semisodium) causes fewer gastrointestinal adverse reactions than valproate [73] has been challenged [74]. In other cited studies Divalproex was associated with a higher risk of gastrointestinal effects. [75]

- *Reproductive system (pregnancy, development and infancy) side effects*

A study found an association with Valproate exposure and the risk of developing autism spectrum disorder and childhood autism. The 14-year absolute risk is 1.53 % (95 % CI, 1.47 – 1.58 %) for autism spectrum disorder and 0.48 % (95 % CI, 0.46 – 0.51 %) for childhood autism. Maternal valproate exposure was associated with a 2.9 fold increase (95 % CI, 1.7 – 4.9) in autism spectrum disorder and a 5.2 fold increase (2.7 – 10.0) in childhood autism adjusted for multiple factors. This association was not found with other antiepileptics [76]. A retrospective study reviewing fetal malformations and valproic exposure demonstrated a dose-dependent correlation and risk of abnormalities at birth. Spina bifida and hypospadias were associated with maternal exposure of 2 000 and 2 417 mg daily doses, respectively. Other malformations were associated with significant lower doses of 740 – 1 527 mg. Furthermore, mean maternal daily exposure decreased over time with a corresponding decrease in spina bifida and hypospadias, but not in other malformations. Of note, direct correlation cannot be inferred from the above findings. However, the authors did notice that the correlation may be stronger with spina bifida than hypospadias because 85 % of spina bifida cases were associated with Valproic Acid [77] [78]. A meta-analysis from pooled data looking at Valproic Acidum and various malformations by Jentink (2010) concluded that there was statistically significant evidence of associations between VPA exposure and spina bifida, atrial septal defect, cleft palate, hypospadias, polydactyly, and craniosynostosis. Similar significant associations were found by Vajda (2013) except in relation to cleft palate and hypospadias and by Werler (2011) in relation to neural tube defects, oral clefts, and hypospadias. Typically for Valproic Acid, there is primarily an up to 20 fold increased risk for spina bifida and other neural tube defects if the mother received treatment between the 17th and 28th day after conception (Dansky, 1991). This indicates that about 1 – 2 % of exposed children will be affected. [79]

- *Nervous system side effects*

There have been several further reports of valproate induced hyperammonemic encephalopathy [80] [81] [82] [83]. In one case, it was associated with central pontine mielinolysis and coma in a patient with Sjogren's syndrome who had taken long-term Valproic Acid for a psychiatric disorder [84]. Encephalopathy has been studied in 63 adults who had taken Valproate for a minimum of at least two years in a retrospective analysis [85]. Long duration of Valproate treatment did not correlate with the risk of encephalopathy. In seven cases, temporary administration of lactulose alone was effective and valproate was not withdrawn. The authors also concluded that this complication is relatively common. In one patient, there was a possible synergistic interaction of Valproic Acid and Topiramate with respect to the

emergence of hyperammonemic encephalopathy [86]. The authors speculated that inhibition of carbonic anhydrase by Topiramate might be the basis of this, since HCO is used in the synthesis of carbamoylphosphate in the urea cycle. In a young child, valproate-induced stupor was unusually associated with an electroencephalographic pattern of increased fast activity [87]. The authors speculated that this effect of valproate was related to an interaction of valproate with GABA metabolism and GABA neuronal networks. Tremor is seen in 15 % of patients taking Valproate [88], although its incidence can increase to over 60 % at serum drug concentrations in a high range (80 – 150 mg/ml) [89]; it is clinically reminiscent of essential tremor and responds to dosage reduction. Asterixis has been associated with intoxication by most anticonvulsants, but with Valproate it can occur at therapeutic drug concentrations [75] [90].

- *Metabolic side effects*

Valproic acid can cause weight gain [91], insulin resistance, hypertriglyceridemia, and other components of metabolic syndrome [92]. It decreases production of adiponectin, which is an adipocytokine that enhances insulin sensitivity [92]. Valproic acid also increases the likelihood of PCO [93], which is a syndrome of insulin resistance, obesity, infertility, and mood disorder. Slow release forms of Valproic acid may be more benign.[10]

The effect of valproate on body weight and hormones has been studied in 52 healthy adults who were randomized to valproate or placebo in a double-blind protocol [95]. Weight increased significantly with Valproate but not placebo. Those who took Valproate also had increased cravings for fast food and reduced glucose concentrations compared with placebo. Physical activity, hunger, binge eating, depression, and GLP-1 were increased by Valproate. The authors concluded that Valproate associated weight gain is probably due to reduced glucose concentrations and an increased motivation to eat in association with increased body size [96]. Weight gain during Valproate treatment occurs during the first three months of therapy, and women are more susceptible than men. The mechanism is not known.

From the results of a systematic review of ten epidemiological studies, about 50 % of patients would be expected to have significant weight gain during treatment for two or more years [97]. The authors suggested that body weight should be measured before starting Valproate and that if body weight increases by two kg in the first consideration should be given to using another antiepileptic drug. [75]

CONCLUSIONS

Side effects can vary greatly among individual patients, not only depending on the doses, or on the medicine itself, but also because of the vulnerabilities that one can have. Polypharmacy, higher dosages and the treatments of those vulnerabilities can be associated with a great effect on the lifespan of the psychiatric patients.

Of course, a greater attention to the possible impact of the psychotropic medications on the physical health can aid clinicians in selecting appropriate treatments. The biggest

effects on physical health are those caused by antipsychotics, followed by mood stabilizers, tricyclic antidepressants and newer antidepressants. Knowledge of these side effects, in tight balance with a well understanding of the patients' needs and vulnerabilities, will aid the full recovery of the psychiatric patients, without affecting the physical health. An appropriate management and monitoring strategy must be implemented also, with the sole objective to serve at the improving both the physical and the mental health of these generally disadvantaged populations.

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Pathophysiological mechanisms in post-stroke depression. Psychosocial and economic implications of patient rehabilitation

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ABSTRACT

A stroke is an acute loss of cerebral function caused by the stenosis, occlusion or rupture of an artery in the brain, resulting from a variety of predisposing factors. Depression and fatigue are the most common psychiatric complications after stroke, many researchers associating the two. Furthermore, if norepinephrine, serotonin and dopamine are functionally altered, the nervous system is also affected, contributing to changes in emotional regulation and the pathogenesis of depression.

Regarding the localization of the lesions, infarcts of the basal ganglia, the corona radiata and the internal capsule were randomly associated with the emergence of fatigue at three months after the stroke, while injuries that occurred in the cerebellum showed no association with it.

Inflammation, cognitive disturbances and depression are distinctive characteristics that occur after a stroke. To alleviate their clinical expression, many researchers have studied ways to control these phenomena. The inflammatory hypothesis stipulates that depression is associated with the increase of pro-inflammatory cytokines and acute phase proteins. The presence of depressive symptoms is not only a negative prognostic factor in patients with known cardiovascular disease, but may also precipitate cardiovascular dis-

turbances in healthy individuals. Moreover, several other elements, such as the vascular endothelial growth factor (VEGF), the fibroblast growth factor-2 (FGF-2) and insulin-like growth factor-1 have been associated with the onset of major depressive disorder. The vascular hypothesis posits that the small lesions that disrupt important neural pathways can also precipitate the occurrence of depression.

Considering that stroke is a condition that implies neurological dysfunctions of various impact degree, coping mechanisms, and an early recognition and management of depression become key psychological resources in the process of recovery.

KEYWORDS

post-stroke depression, inflammatory markers, neurotransmitters, neurotrophic and growth factors, orexins

INTRODUCTION

A cerebrovascular accident (CVA or stroke) is an acute loss of brain function, with a sudden onset, that occurs after a disorder of the blood supply to the brain. It can be caused by stenosis, occlusion or the rupture of an artery in the brain, and can result from a variety of predisposing factors. The clinical manifestations of the stroke indicate the installation of a temporary or permanent brain dysfunction (1). In most cases, patients who become physically disabled following a stroke will also suffer from other of its complications (2).

Worldwide, 15 million people are affected by CVA each year. For at least 5 million people, the stroke is fatal, and another third remain with post-stroke sequelae (3). Over half of the 10 million survivors have reported an overwhelming fatigue and a permanent lack of energy (4). Decreased vitality, as a general consequence, will weaken the patients' ability to regain lost functions. Similarly, most of these patients have depressive elements (post-stroke depression) that considerably affect their quality of life (5).

POST-STROKE DEPRESSION

Depression is a disabling psychiatric condition, characterized by negative hyperthythmic mood, anhedonia, hypobulia, fatigue, attention an memory deficits, feelings of worthlessness and guilt, decreased vitality and personal efficiency, and minimum involvement in daily activities, associated or not with suicidal ideation (6).

Many researches in the field have associated fatigue with post-stroke depression. In a study conducted in Sweden, 49 % of patients with fatigue at 1 year after a stroke developed depression, compared with 39 % in the control group (7). Similarly, a study done in Korea found out that 34 % of the patients diagnosed with depression were among those presenting fatigue about 15 months after the stroke (8).

In a research conducted by Changjuan and his collaborators, 368 patients were included for a first interview 14 days after they suffered a stroke. The second interview took place at three months after the stroke. The diagnosis of depression was established in the case of 19.3 % of patients upon admittance to study and of 23.6 % of them at three months after the stroke. For 23 of the 71 patients who developed depression in the acute phase of

the stroke the symptoms disappeared, while for the other 48 of them depression persisted at three months after the stroke. Fatigue was documented for 23.4 % of the patients admitted in the study and for 29.6 % of them at three months from the stroke. Of the 86 patients who experienced fatigue during the acute phase of stroke, 28 returned to their original state, but for 58 of them the symptoms persisted. Moreover, 75.6 % of the patients who initially developed fatigue were diagnosed with depression at three months after the stroke and 53.5 % of those who initially experienced depression had developed fatigue at three months after the stroke. Depression has been associated with fatigue for 10.9 % of patients upon admittance and for 12.2 % of them at three months after the stroke (9). In the case of these patients, social support and adaptation mechanisms are considered important factors in the rehabilitation process.

MONOAMINE NEUROTRANSMITTERS

The cerebral neurotransmitters, norepinephrine, serotonin and dopamine are biogenic amines which transmit information between nerve cells or between neurons and effector cells, integrating the overall coordination of body functions. If these neurotransmitters are functionally impaired, the nervous system is also affected, leading to depression. In the pathogenesis of depression, the function and content of these three neurotransmitters may be altered and affect the patient's disposition and emotional regulation in varying degrees (10).

Serotonin (5-HT) acts as a hormone and a neurotransmitter, being involved in mitogenic induction. In 1918, at the time of its discovery, 5-HT was considered to be a vasoconstrictor stored in platelets, therefore it was called “serotonin”, after the Latin word “serum” and the Greek one “tonic”. In 1937, 5-HT has been found in the enterochromaffin cells of the gastrointestinal tract, and was named *enteramine* because of its believed implications in the intestinal smooth muscle contraction. Scientists assigned a neurotransmitter role to serotonin in 1952 and associated it with mood, behaviour, sleep-wake regulation cycle and appetite (11).

Norepinephrine is the second neurotransmitter discovered, after acetylcholine, and was originally named *sympathetin,* because it was produced by the stimulation of the sympathetic nervous system and because it had acetylcholine-antagonism effects on the myocardium. Noradrenaline secretion is stimulated by stressful events, as well as by low blood pressure. As a result, heart rate is increased and blood is redirected to the muscles, with increased glycemic levels to ensure a greater supply of energy to the cells (10).

Dopamine, discovered in 1958, has numerous functions, including controlling, triggering and executing voluntary movements and the postural adjustment associated with them, and controlling emotional behaviour, pleasure, the brain's reward system, cognitive functions and short-term memory (12).

Dopamine and serotonin are considered to be responsible for the appearance of fatigue in Parkinson's disease. Regarding the localization of cerebral lesions, infarcts of the basal ganglia, the corona radiata and the internal capsule appeared to be randomly related to the emergence of fatigue at three months after the stroke, while

injuries that occurred in the cerebellum showed no association with it. Previously, the dopaminergic neurons that take action over the rewarding system and are located in the ventral tegmental area were found to project fibres at the striatum Venti level (13). Experiments on animals have shown that the profuse serotonergic fibres of the raphe nuclei, located in the brainstem – from which fibres leave both upward and downward, affecting many areas of the brain, especially the cortex, the limbic system, the thalamus and the hypothalamus – are projected in the basal ganglia and in the cerebellum (14).

Coping mechanisms refer to the patient's cognitive and behavioural efforts to manage the internal and external demands in the social environment. Keeping in mind that stroke is considered a particular physical condition, involving neurological dysfunctions of varying impact degree, the coping mechanism can be considered a key psychological resource in the recovering process of the patient's quality of life (4).

EXPERIMENTAL MODELS ON ANIMALS

In another study, Xiao and his colleagues induced a cerebral vascular accident on mice, adopting the method of occluding the left cerebral artery. The cerebrovascular physiopathological changes in the brain of those mice, as a result of the procedure, were similar to the clinical manifestations of stroke. The mice were divided in two groups: the reference group, that had post-stroke depression, and the control group, which had only suffered a stroke. The post-stroke depression has been induced by applying a mild chronic stress to each animal in the experiment. They observed a significant reduction in the levels of serotonin, norepinephrine and dopamine in the frontal cortex and in the hippocampus of mice with post-stroke depression, compared to the control group. These results can be associated with the direct division of the pathways involving serotonin and norepinephrine following a stroke (15). Neuronal cell bodies are located in the brainstem and their axons reach the frontal cortex and the hippocampus, passing through the thalamus and the basal ganglia, which play an important role in the regulation of emotions and dispositions. Damage on the paths involving serotonin and norepinephrine induce a decrease in the level of these neurotransmitters, resulting in the emergence of post-stroke depression (16).

THE INFLAMMATORY HYPOTHESIS

The inflammatory hypothesis stipulates that depression is associated with the activation of the innate immune system, with the increase of pro-inflammatory cytokines and acute phase proteins. In support of this hypothesis, numerous studies have detected significantly elevated levels of inflammatory markers, more importantly IL-6 and IL-1b interleukins, alpha tumour necrosis factor (TNF-α) and C-reactive protein, in patients diagnosed with depression compared to healthy groups (17).

The presence of depressive symptoms is not only a negative prognostic factor for patients with known cardiovascular disease, but it is also a risk factor for developing cardiovascular disturbances in the case of healthy individuals. However, the underlying mechanisms are not fully known yet. Several explanations have been proposed, including changes at the level of clotting factors, genetic factors that increase the risk of having both depressive and cardio-

vascular disease symptoms, and changes in the metabolism of glucose. Inflammation is a physiological mechanism often mentioned in studies regarding the underlying processes of developing depressive symptoms in the evolution of cardiovascular diseases (18).

NEUROTROPHIC AND GROWTH FACTORS

Several neurotrophic and growth factors, such as the vascular endothelial growth factor (VEGF), the fibroblast growth factor-2 (FGF-2) and the insulin-like growth factor-1 have been implicated in the etiopathology of major depressive disorder. Particular attention was paid to brain-derived neurotrophic factor (BDNF), which is a molecule with a wide range of biological activities. Numerous studies have reported low levels of BDNF at the hippocampal level in various stressful situations (19). Moreover, after analyzing post-mortem brains of patients, low levels of BDNF were found, especially in the case suicidal patients and those with depressive mood disorders. Stress and hypercortisolism would induce the atrophy of the hippocampus and reduced synaptic plasticity, by shortening the dendrites. Chronic antidepressant treatment increases the effect of neurotrophic factors, neurogenesis and the hippocampal volume, which would explain the several weeks long latency for the antidepressant effect to appear (20).

The fibroblast growth factor plays an important role in the development of the neocortex and in the survival and growth of neurons in adults. The essential role that FGF occupies in the brain is regulating neuronal proliferation, and the migration, differentiation and survival of glial cells. Precursors of neural plate cells have the capacity to differentiate into dopaminergic and serotonergic neurons, and are believed to be associated with neural plasticity. The abnormal expression of FGF may cause depression (21). FGF-2 protects ischemic tissue by activating the anti-apoptotic protein (22). Although experiments on mice showed an association between post-stroke depression and low levels of monoamine neurotransmitters and FGF-2, the link between FGF and depression is not clearly established yet (16).

Finally, a stroke involves neurodegeneration. The vascular hypothesis posits that even the small lesions that disrupt important neural pathways can precipitate the occurrence of depression. For example, ischemic brain injuries may directly disrupt upward monoamine projections from the midbrain and the brainstem. In addition, the gradual accumulation of multiple vascular lesions may eventually pass a critical threshold, beyond which the risk of depression occurrence is very high (23).

In 1980, Robinson and his colleagues demonstrated for the first time that there is a correlation between a high depression score, calculated using the Hamilton and Zung scales, and left-frontal injuries, indicating that there is an association between the specific location of an injury and mood fluctuations in the case of patients who suffered a stroke (24, 25).

Psychopharmaceutic therapy provides an effective treatment for post-stroke depression. New clinical trials suggest that treatment with a selective serotonin reuptake inhibitor, applied in the subacute phase, can have multiple beneficial effects, that extend far beyond mood fluctuations, in recovering from a stroke. For example, the FLAME multicenter study demonstrated

that the early prescription of fluoxetine (starting five to ten days after the CVA) to patients with ischemic stroke and moderate to severe motor deficit, but with no form of depression, significantly accelerated motor recovery after three months. Moreover, double-blind studies have reported an increase in the survival rate of both patients with depression and the control group who followed an antidepressant treatment for a period of 12 weeks during the immediate recovery phase (26).

OREXINS

Inflammation, cognitive disturbances and depression are distinctive elements that appear after a stroke. To alleviate their clinical expression, many researchers have studied ways to control these phenomena.

Orexins – also known as hypocretins, are neuropeptides synthesized in the posterolateral hypothalamus, and are represented by Orexin A and Orexin B. They have widespread projections and implications in regulating metabolism and the sleep-wake rhythm. Three remarkable roles of orexins have been described after stroke: 1) they control the inflammation by regulating the expression of immune mediators, such as pro-inflammatory cytokines; 2) they improve memory, promote hippocampal neurogenesis and protect the neural pathways from damage caused by post-stroke oxidative stress; 3) they alleviate depression by accelerating the secretion of neurotrophic factors. Although studies on the post-stroke role of orexins are still in the preliminary stages, further research may reveal their clinical value as effective therapeutic modulators, given their preventive role over the emergence of new, secondary strokes.

DEPRESSION AND APHASIA

Aphasia has a prevalence of 31 % in the case of a first stroke and persists in a proportion of 60 % at 12 months after it. As a consequence, important psychosocial and lifestyle changes occur, such as reduced professional performance or even the inability to work, impaired relationships with others and social withdrawal. The incidence of depression after aphasia is estimated to be at 62 % – 70 %, which is higher than in the case of stroke survivors who don't develop aphasia. Family members of patients with aphasia are also prone to develop depression, as well as to suffer a variety of psychosocial consequences. Due to communication difficulties, people with aphasia have reported difficulties in accessing existing mental health services, interventional programs or support groups that could meet their needs (27).

Patients older than 55, females and those with poor lifestyle choices have been identified as demographic categories with increased risk factors in the onset of depression. In support of the need to improve the quality of life of patients with aphasia in the long term, an intervention program called Aphasia Action Success Knowledge (Aphasia ASK) has been developed. It addresses patients that are within 6 months after the stroke, and includes explanatory concepts regarding the stroke and aphasia, elementary communication strategies regarding the management of mood fluctuations and strategies for creating social support networks. Preliminary results showed a significant improvement in the quality of life and a lower incidence of depression among participants and their family (28).

CONCLUSIONS

Patients with stroke show constant changes regarding their mood, ranging from simple emotional reactions, such as low motivation, indifference and frustration, to more severe depressive symptoms, such as appetite loss, insomnia and feelings of being useless.

Depression is the most common psychiatric problem encountered after a stroke, and can occur from few days up to several months post-CVA. Several risk factors for the occurrence of post-stroke depression have been identified, such as age, sex, social background, but also patients' comorbidities and the presence of aphasia.

The diagnosis of post-CVA depression, however, is still a challenge, the symptoms often remaining unrecognized or untreated. The families of these patients are also at risk of developing depression, which leads to important consequences, from both a social and an economical point of view.

The physiological mechanisms involved in the onset of post-stroke depression haven't been fully elucidated yet. On the other hand, preliminary studies in this field seem to open up new ways in developing more efficient therapeutic strategies.

Finally, it is widely accepted that early recognition and management of depression is an important aspect at any stage of post-stroke rehabilitation. Thus, the development of support groups, educational, preventive, and interventional programs play a key role in the recovery process of these patients and in their social reintegration.

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The loss of sadness of the human being: the beginnings of psychosurgery (Part I)

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„Doctors are different by nature. One kind adheres to the old principle: first, do no harm (primum non nocere); the other one says: it is better to do something than do nothing (melius anceps remedium quam nullum). I certainly belong to the second category."

Gottlieb Burckhardt, the father of psychosurgery (1836 – 1907)

ABSTRACT

The history of psychosurgery has been written since its prehistoric beginnings until its sad culmination in the 19th century, based on suffering and agony. The neurosurgical treatment of mental illnesses imagined by mankind has a long and controversial history. This paper aims to trace the key moments in the history of psychosurgery, from antiquity until the period of Antonio Egas Moniz, the Portuguese neurologist who was considered to be the father of psychosurgery as a branch of medicine.

KEYWORDS

psychosurgery, trepanation, lobectomy, lobotomy

FROM ANCIENT TREPANATION TO WERNICKE AND BROCA'S COGNITIVE FUNCTIONS

The history of psychosurgery is as old as the history of neurosurgery, and the trepanation holes discovered in the prehistoric human skull are living testimony to the fact that these surgeries have been performed since ancient times.

There is no doubt that trepanation is one of the oldest surgical procedures, as well as the oldest neurosurgical intervention made by humans (1). The practice of trepanation has evolved from its mystical and ritualistic content from primitive African and later pre-Columbian Mesoamerican cultures, to a potentially therapeutic destination in the Egyptian, Greek and Roman civilizations, who left behind tools and instructions to perform them (1, 2).

This wide-spread surgical practice since the Mesolithic (3) is certified by the trepanation procedures discovered throughout the world, including in Europe and the Mediterranean Sea, North America, Africa and Australia, the most common practice being found in archaeological sites from Andes and Mesoamerica (4).

The first obvious signs of skull trepanation dates from 5 100 years B. C. ago and was found in 1996 in Alsace, France. Although the reason for which this intervention was performed is unknown, the bone scarring around the craniectomy is a sign of the fact that the patient survived the surgery (5, 6). The skull has two burr holes, one smaller, located at the level of the frontal bone, close to the coronal suture, and one larger, located posteriorly, with an extension at the level of both parietal bones. Moreover, the first neurosurgical trepanation of the skull, performed for psychosurgical purposes, was carried out in 1 500 B. C., "to let out a spirit imprisoned in the body" and "sooth pains and melancholy or release demons" (7).

The reason for which these trepanations were carried out is still somewhat unclear, as several causes can be speculated (5). Brothwell suggests four reasons for which trepanations were performed in the prehistoric era: as a surgical treatment for a head injury (especially for skull fractures), as a treatment for mental illness, headache and epilepsy, to promote longevity and to obtain roundels that were later used as amulets (8).

The anthropological studies have highlighted the fact that the frontal bone, followed by the parietal bone and the occipital bone were the most common locations for burr holes (9). This suggests that our ancestors anticipated that the human mental activity mainly occurred in the frontal lobes.

Brothwell also states in his studies that even though trepanation maneuvers were carried out in poor conditions in a time when the aseptic and antisepsis principles were not yet anticipated, almost half of the cases of trepanation found in human skull remains attest to a complete cure. In his work, *Digging up bones. The excavation, treatment and study of human skeletal remains,* Brothwell notes: "if the edges of the hole are rounded and the exposed diploic spaces of the spongy inner tables shows signs of closing or have closed" (8).

Hippocrates of Kos (460 – 355 B. C.), considered to be the father of rational medi-

cine, because he applied logic and observation in the medical practice, offered, in his treatise *On injuries of the head,* coherent information on the anatomy of the skull and classifications of skull fractures, proposing a methodical management of head trauma. Moreover, Hippocrates provided amazing technical details of the trepanation technique (10), being considered to be among the first who supported the use of this procedure only from pure medical reasons, not mystical or spiritual ones, thus separating medicine from theology and philosophy (11, 12).

Hippocrates's followers, however, sought to find a treatment for mental illnesses in trepanation, from antiquity until the early Middle Ages. Therefore, in the 1170s, the Italian surgeon ***Rogerius of Parma (1140 – 1195)*** used trepanation as a treatment for mental illnesses. In his work, *Practica Chirurgiae*, he wrote: "for mania or melancholy a cruciate incision is made in the top of the head and the cranium is penetrated, to permit the noxious material to exhale to the outside. The patient is held in chains and the wound is treated as above, under treatment of wounds" (13). It was only in late 19th century, once with the development of the European schools of neuroanatomy and neurology, the scientists started to look for logical explanations for the trepanation procedures. Thus, the most important observations about the clinicopathological correlations of neural destruction, with an impact on cognitive functions, such as language, were made by the physicians ***Paul Broca (1824 – 1880)*** and ***Carl Wernicke (1848 – 1905)*** (14, 15).

THE MOST BEAUTIFUL "EXPERIMENT OF NATURE"

The most famous "experiment of nature" was, without a doubt, Phineas Gage's dramatic and strange accident from 1848, aged 25, the foreman of a railway constructions team from the obscure country town of Cavendish, USA. After an explosion, a 109 cm long and 3 cm thick iron bar penetrated his orbit and brain, coming out of his skull, into the air. The consequences of this accident were downright surprising: from an intelligent patient and an upright citizen, the patient became an uninhibited rogue (16). His physician, ***John Martyn Harlow (1819 – 1907),*** referred to the destruction of "the equilibrium or balance, so to speak, between his intellectual faculty and animal propensities", but his friends were much more convincing when they said that "Gage was no longer Gage" (17). Moreover, Dr. Harlow correlated Gage's behavioural changes with the cerebral area in the frontal region, which was assumed to have been destroyed by the iron bar when it penetrated the skull. 150 years later, Damasio and his collaborators published a study on Gage's exhumed skull and proposed a trajectory of the injury through the left hemisphere, through the anterior half of the orbitofrontal cortex (Brodmann areas 11 and 12), through the anterior mesial frontal cortices (Brodmann areas 8 to 10, 32) and the most anterior region of the cingulate gyrus (Brodmann area 24). Damasio correlated these injuries with the symptoms of a lot of patients with a similar neuropathology (18).

THE BIRTH OF MODERN PSYCHOSURGERY

Modern psychosurgery was born once with the Swiss psychiatrist ***Gottlieb Burckhardt (1836 – 1907)***, who is considered to be the first modern psychosurgeon (19) because he attempted to practice a systematic psychosurgery. He operated on 6 patients with intractable psychiatric illness and aggressive behaviour, five of whom were suffering from "primare Verrucktheit", a clinical category equivalent to schizophrenia (20) in chronic patients hospitalized at the Swiss Préfargier Asylum, managed by Burckhardt. In a small room on the grounds of the asylum (21), Burckhardt bilaterally removed different parts of the frontal and temporal cerebral cortex of his patients, regions responsible for pathological behaviour in relation with the neuroanatomical and functional models of the time (22), surgical interventions which he then called *topectomies*.

The German ***Friedrich Goltz (1874)***, who demonstrated that the total removal of the neocortex in dogs made them more hyperactive and angry, while the ablation of the temporal cortex made them gentler and calmer than usual (23, 24, 25), was the one who influenced Burckhardt. The latter thought that such procedures would also have calming effects on his patients, stating that "none of the cases operated upon was of traumatic origins, the indications for the operation were therefore purely psychiatric" (9). Therefore, in 1890, Burckhardt started to perform surgeries on his patients. After removing the skull, using a scalpel, he excised the cerebral cortex (26). Of the 6 patients operated by Burckhardt, three showed improvements, being easier to manage; one died after a week due to seizures (24); one committed suicide; and for one patient, the surgery produced no results (26).

One of his patients, a painter aged 26, suffering from schizophrenia and auditory and visual hallucinations, who painted a nose and a mosquito in a corner of all his paintings, Burckhardt excised 4.6 g of cortical tissue from portions from Wernicke's area (the posterior half of the first and second temporal circonvolution from the left hemisphere) in a surgical procedure, performed on 5 June 1889, which lasted approximately 4 hours. One week after the surgery, mild aphasic symptoms occurred and the visual and auditory hallucinations persisted, which displeased Burckhardt, who decided to intervene again, this time on Broca's area (19, 20).

In a surgical procedure which lasted two hours and a half, he resected 2.5 grams of cortex, excising both pars opercularis and pars triangularis of the inferior frontal gyrus of the left hemisphere. This time, the surgery was successful, diminishing hallucinations without the occurrence of postoperative motor aphasia deficits (19). The patient's mother stated that the patient became quieter and better behaved (20). Although impressed by the possibilities made available by psychosurgery, Burckhardt stopped, because in 1890 – 1891, when he presented his results before the *Académie française*, he shocked the medical world who considered him to be irresponsible and reckless. They ridiculed and ignored him in the academic medical world (27). In 1891, Burckhardt wrote with a heavy heart: *"Doctors are different by nature. One kind adheres to the old principle: first, do no harm (primum non nocere); the other one says: it is better to do something then do nothing (melius anceps remedium*

quam nullum). I certainly belong to the second category". (20, 28)

After Burckhardt, neuroresearchers continued to investigate frontal lobe resection. For this purpose, the Estonian neurosurgeon ***Ludovicus Puusepp (1875 – 1942)*** performed frontal lobotomies, but without much success (29), destroying the association fibres between the frontal and parietal cortex, in 3 maniac depressive patients (29), while the American neurosurgeon ***Wilder Penfield (1891 – 1976)*** described the relief of psychiatric symptoms in patients after the resection of lesions replacing the space at the level of the frontal lobe (30).

1935 was an important moment in the history of psychosurgery. At the Second World Congress of Neurology held in London, the American physiologist ***John F. Fulton (1899 – 1960***) presented his experiment: following the resection of the frontal cortex in two chimpanzees, they became "devoid of emotional expression", and the resection of the anterior frontal association cortex succeeded in calming behavioural changes (31). Fulton and his collaborator Carlyle Jacobson brought the two chimpanzees at the Congress and demonstrated to the symposium that the animals were no longer able to evoke "experimental neuroses" and that they lacked all signs of anxiety and frustrational behaviour (22). Among the participants at the Congress there were two Portuguese neuro-researchers, ***Antonio Egas Moniz (1874-1955),*** a neurology professor at the University of Lisbon and his collaborator, the neurosurgeon ***Almeida Lima (1903 – 1985***), as well as the American neurologist ***Walter Freeman (1895 – 1972),*** who have greatly influenced the practice of frontal lobotomies in psychosurgery (31, 32).

CONCLUSION

The neurosurgical treatment of mental illnesses imagined by mankind has a long and controversial history, which began since antiquity, and was built on fame and infamy. Throughout the centuries, neurologists, neurosurgeons and psychiatrists have attempted to find a treatment for mental illness in psychosurgery, which laid the foundation of modern psychosurgery involving structures such as amygdala, hippocampus, thalamic and hypothalamic nuclei, as well as the orbitofrontal and prefrontal cortex and cingulate gyrus. The most common modern psychosurgical procedures are limbic leucotomy, capsulotomy, cingulotomy and subcaudate tractotomy and involve a close collaboration between psychiatrists and neurosurgeons.

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The insight of clinicians regarding the psychiatric health service (legal and ethical aspects)

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ABSTRACT

The insight of clinicians regarding the psychiatric health service implies numerous ethical and legal discussions. The social destigmatization of the psychiatric patient is currently a challenge for Romania, a member of the European Union. The current research aims to evaluate the clinicians' standpoint regarding the legal and ethical aspects within the psychiatric health service.

Materials and methods – this is a prospective study that was undertaken on medical staff involved in the psychiatric aid of the mentally ill. Thus, the study encompassed a studied population of 50 clinicians (e.g., neurology, neurosurgery, cardiology, intensive care) involved in the medical aid of the psychiatric patient from different medical centres (e.g., Iasi, Botoșani, Vaslui, Suceava). The study is descriptive, questionnaire type and was done from July 2012 to July 2013.

***Results* – A high percentage of clinicians consider that professional and social reinsertion of the psychiatric patient would be compromised if the personal information of the patient wouldn't be kept confidential.**

Conclusions **– Stigma is a phenomenon which delivers important disadvantages to the patient via discrimination and social drawback. The discrimination of the psychiatric patient, when compared to other patients, comes first of all from the medical staff.**

KEYWORDS

clinicians, mental disease, ethical

INTRODUCTION

Mental health is of important concern not only in Romania, but also in the whole world. On a global level the World Health Organization estimates an alarming increase of mental disorders, highlighting that one out of four patients who addresses a health service provider has a mental or a personality disorder.

Mental health legislation is necessary to a society in order to protect the socially vulnerable individuals with mental disorders. In psychiatry, as in other medical fields, ethical problems are encountered both in research and in clinical practice. Within the psychiatric service there are two different ways of admission: with consent (voluntary) and without consent (non-voluntary). In the last 50 years radical changes have arose in many countries. From a psychiatric health service point of view, the changes draw in new ethical problems. At the present day psychiatric patients have the same rights as the patients suffering from other non-psychiatric diseases, including the right to a confidential patient-doctor relationship.

A good understanding and appreciation of the main ethical aspects that appear in the medical practice of a psychiatrist ingrain him with ethical conduct from a professional perspective. A therapeutic relationship built on ethical grounds leads to a better valorisation of the psychiatric patient as a human being with rights and obligations, feelings, failures and accomplishments, without us being guided by protocols.

Apart from the legal and ethical aspects regarding non-voluntary admissions, there are many different opinions regarding the problems concerning voluntary admissions, implicitly the way of obtaining a valid informed consent. Informed consent is a formal act of agreement, free and undamaged, given by a person with judgement.

Discriminated persons and groups of persons are attested in the oldest written documents of humanity (1). Social stigma is a relational and dynamical process (2). The traits of social stigma depend on the society and the time in which they appear. Some forms are obvious (e.g. obesity, skin colour), others are relatively hidden (homosexuality, mentally ill persons) (3). The social stigma process (4) arises when the individual is deviant, process which implies numerous negative stereotypes. Social media bears an important role regarding this process, due to its power to associate mental illness with notions like: incompetence, violence, guilt. Frequently, through stigma, the patient is discriminated against and harmed (5). Mass-media plays an important role in the process of stigmatization of the mentally ill, especially through informational broadcasts, which erroneously highlight criminal behaviour, unpredictability, and dangerousness (6). In our society this category of patients at-

tracts the highest level of social stigma, thus rendering them to social pressure.

According to Crocker, the process of stigmatization is oriented on three dimensional axes within the social relations and interactions: perspective, identity and reaction. Perspective refers to the perception of the society or the mentally ill patients regarding stigmatization. Identity implies affiliation to a group and reaction is the result of stigma (7). Moreover, the characteristics of stigma (visibility, suggestibility and impact) are important aspects in the process of stigmatization (8).

Stigmatization, which is a complex process within society, has multiple ethical implications (9). The stigmatized patient can have difficulties upon employment (10), is discriminated against, and one's access to health services is hindered. Although multiple studies show that mentally ill persons do not have more antisocial acts than non-mentally ill persons, the former are unjustly socially rejected (11). Society's perception about the mentally ill is saturated with fear, rage, disgust and hostility. These negative emotions materialize in social discrimination (9). Stigma and mental illness form together an important barrier in achieving an efficient mental health service (6). The existing preconceptions about the mentally ill contribute to their social withdrawal, henceforth generating discrimination and labelling (12). Mass-media's image about the mentally ill is thus exaggerated, these individuals being portrayed as dangerous and unpredictable (6).

Medical confidentiality is an obligation in medical ethics. Respecting confidentiality is a strong and well kept tradition within medical service. Thus, in the present day, a strong accent is put on the intimacy of information. Medical information can be divulged only with the written consent of the person, thus respecting one's autonomy. In international documents, the confidentiality of the individual is protected by law (13, 14, 15). The term confidentiality appears in most of the codes of ethics. Both a theoretical principle and a practical obligation, medical confidentiality is a stringent requirement in medical care (16). As an ethical ideal of medical care, confidentiality is the cornerstone of the medic-patient relationship (17). By breaking the rules of confidentiality, the integrity of the medical relationship is cleaved, thus leaving the patient vulnerable (13).

Confidentiality, as an old medical tradition, is a practice protected by the law (16), both in medical research and in medical service (18). The medic is frequently subjected to ethical tension and to interferences to violate the medical confidentiality (16). In the medical care, confidentiality (19) is of the utmost importance, and in the psychiatric service it is essential for the development of the medic-patient relationship (20). While in certain medical fields confidentiality is absolute (21), in psychiatry there are some legal regulations that allow, in certain conditions, the disclosure of medical information. In psychiatry, confidentiality can be relative under certain situations, as seen in the non-voluntary admission and the mandatory treatment. These situations imply circumstances that refer to aggression towards others (either verbally or physically), aggression towards oneself (suicide, attempted suicide, or suicidal ideation) or psychotic symptoms. All of these, according to some authors, justify the breaking of confidentiality. In these situations the pa-

tient is informed about the possibility of a future broken confidentiality.

MATERIALS AND METHODS

This is a questionnaire-type, prospective study applied to the medical staff involved in the psychiatric aid of the mentally ill. The study was carried out between July 2012 and July 2013 and encompassed an examined population of 50 clinicians involved in the psychiatric aid of the mentally ill from medical centres located in Iaşi, Suceava, Botoşani and Vaslui. The questionnaires cover questions regarding mental health legislation, stigma, discrimination, confidentiality and informed consent.

The questionnaires covered all the steps ranging from pretesting, reviewing and validation to their application in their final form. The results were statistically processed for every item individually. Afterwards, the correlations between the answers to the questions and the different traits of the studied lots were obtained. The Cronbach alpha value was of 0.730, thus offering an acceptable result in comparison with the 0.70 threshold and also a validation needed for the further usage of the questionnaire on the examined medical population.

The questionnaires were applied in a direct manner, anonymity was preserved and confidentiality was respected, these being important aspects regarding the psychiatric aid of the mentally ill.

RESULTS AND DISCUSSIONS

Statistical analysis

- Two independent groups**:** χ 2 – it is a nonparametric test that compares two or more frequency repartitions from the same population; it is applied when the events exclude one another

- For more than two independent samples: the Kruskal Wallis test

Demographical characteristics

In the clinicians' lot the analysis of the frequency distribution based on medical specialization shows the predominance of residents (54.0 %), followed by primary doctors (24.0 %). The use of the Kruskall-Wallis nonparametric intergroup test revealed significant statistical differences between the doctor's specializations (Figure 1).

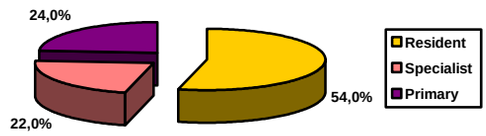


Figure 1. *The distribution of clinicians based on specialization*

The distribution of the lots depending on gender reveals the predominance of female doctors with a frequency of 72 % (Figure 2).

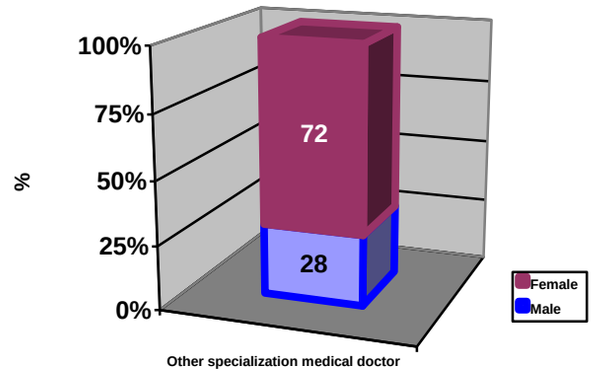


Figure 2. *Clinicians' repartition based on gender*

The distribution based on age

The distribution based on age reveals a greater statistical weight regarding the subjects aged between 30 and 39 years (46.0 %) but a frequency of 32.0 % has to be noticed in the less than 30 years old subject group (Figure 3).

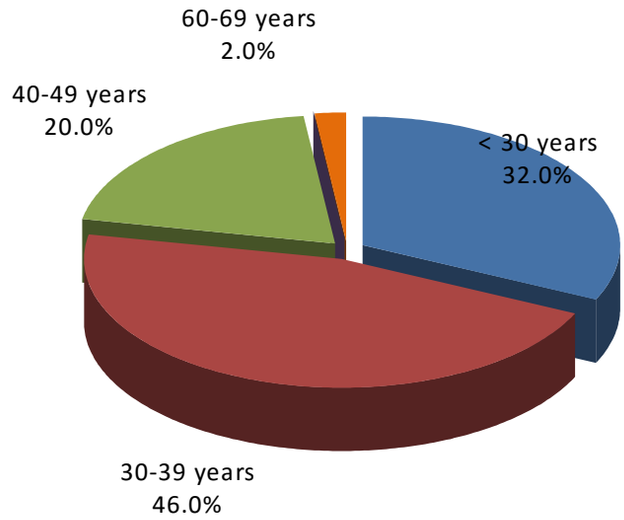


Figure 3. *The clinicians' distribution based on age*

Questionnaire

Question 1: The law concerning mental health and the protection of the mentally ill is:

a. *Law 487/2002;*
b. *Law 129/2012;*
c. *Law 487/2002 and Law 129/2012;*
d. *I don't know.*

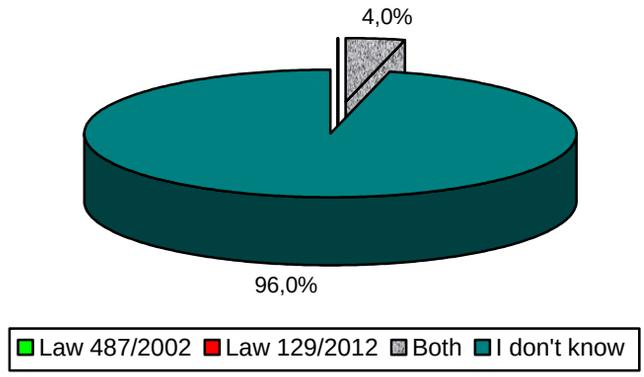


Figure 4. *The distribution of the answers of the non-psychiatric clinicians*

Based upon the studied lot, the answer regarding the active legislation concerning the protection of the mentally ill reveals unawareness of the law in 96.0 % of cases, this percentage representing the vast majority of the clinical staff involved in aiding of the psychiatric patient (Figure 4).

Question 2: Do you consider that before starting treatment, the mentally ill should be informed regarding the benefits and the adverse effects of the treatment?

a. Yes, the psychiatric patient has the right to an adequate informed consent that must be respected;

b. In the particular case of the psychiatric patient, minimum disclosure is enough;

c. The psychiatric patient must not be informed;

d. I don't know.

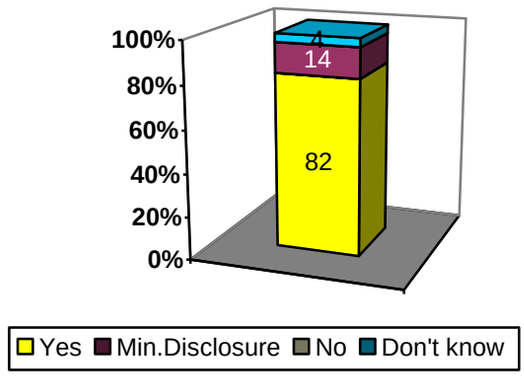


Figure 5. *The clinicians' answer distribution regarding the treatment informing of the psychiatric patient*

Regarding the answers to question number 2, compared on studied lots, the results show a predominance of affirmative answers.

Question 3: "In your opinion, the social attitude towards the mentally ill is one of":

a. Acceptance and/or tolerance;

b. Discrimination and/or intolerance;

c. Other.

Erving Goffman considers stigmatization to be a form of social disgrace of one's reputation and behaviour (9). The branded patient can come across difficulties on employment (10), can be morally casted out of society and access to health service can be hindered.

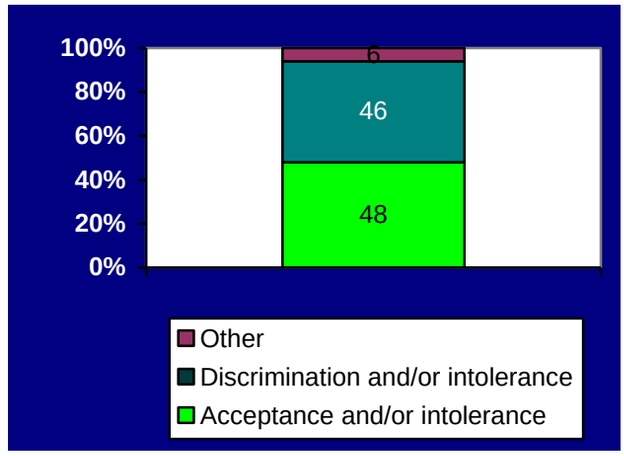


Figure 6. *The clinicians' answer distribution regarding social attitude towards mentally ill persons*

The answers to these questions have highlighted significant statistical differences in percentages between the study groups. 48.0 % of the clinicians considered that social attitude regarding the psychiatric patient is one of acceptance and/or tolerance. Yet, 46 % of clinicians considered that the social attitude is one of discrimination and/or intolerance (Figure 6).

Question 4: Supposing that the personal information of the psychiatric patient would not be kept confidential and would be therefore disclosed, do you think that the patient would be harmed?

a. The patient would not be harmed;

b. Yes, but without major harm;

c. Yes. Social and professional reinsertion would be compromised;

d. I don't know.

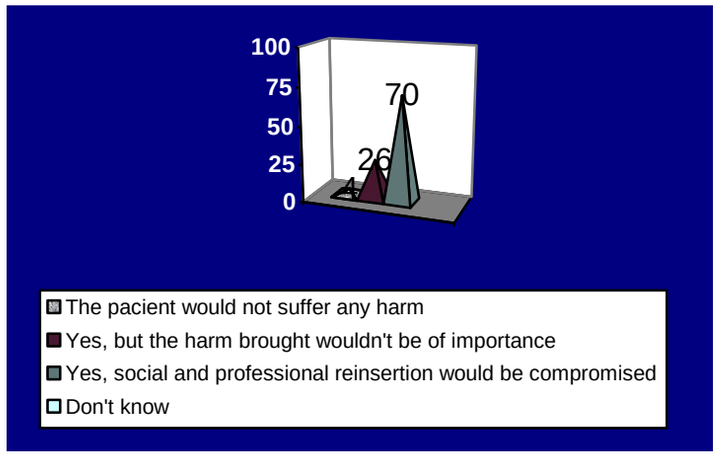


Figure 7. *The non-psychiatric clinicians' answer distribution regarding the harm brought to the mentally ill in case of lack of confidentiality*

The answers recorded to question number 4 shows a predominance of affirmative answers on all of the studied lots. 70.0 % of the clinicians consider that social and professional reinsertion would be compromised if the personal information of the psychiatric patient would be disclosed (Figure 7).

Medical confidentiality is an important principle in health service and the protection of it is a form of respect that should be offered to every person (13).

Question 5: The personal information of the psychiatric patient can be disclosed in certain situations to the medical team within the health service in conjunction with:

a. Family/legal representative;

b. Police/legal body (e.g., Court);

c. Other alternative;

d. I don't know.

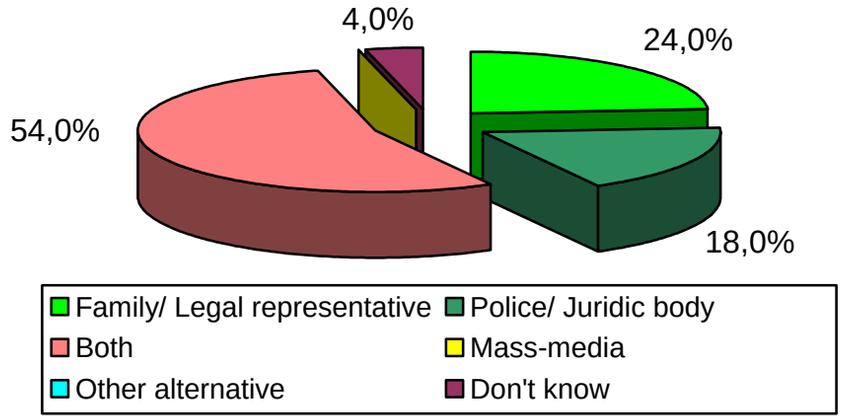


Figure 8. *The answer distribution of non-psychiatrics clinicians regarding the permission to break confidentiality*

Regarding the answers to question number 5, a percentage of 54.0 % of clinicians consider the disclosure of information is to be allowed in conjunction with family and/ or with the police/legal body (Figure 8).

Question 6: Do you consider that the law should force any psychiatric patient to admission to a hospital and to non-voluntary treatment?

a. Yes, because it is desirable to treat the patient and an authoritarian attitude (paternalistic) coming from the psychiatrist is mandatory in this situation;

b. No, the law should force the psychiatric patient to compulsory admission and treatment only in case of psychiatric emergency (e.g., aggression, violence);

c. No, this would defy the patient's right to decide for himself. Hence, non-voluntary admission and compulsory treatment will reduce the patient's demand for psychiatric aid;

d. I don't know.

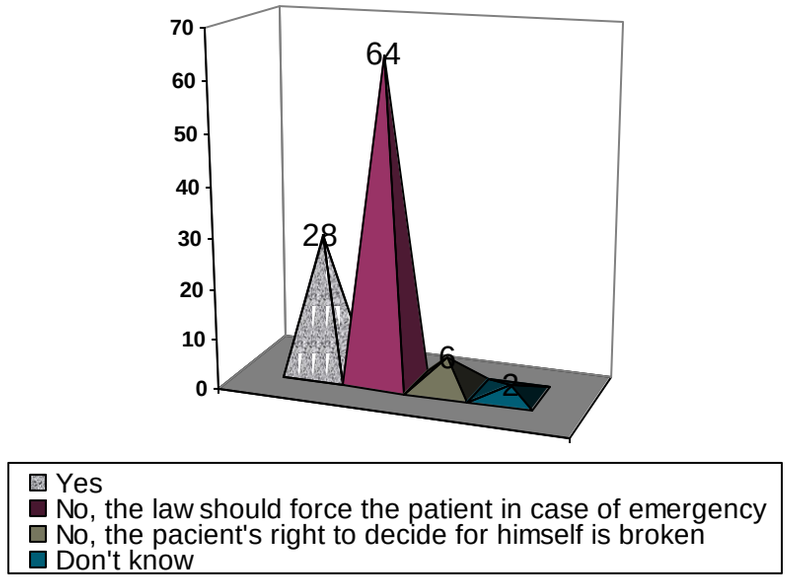


Figure 9. *The non-psychiatric clinicians' answer distribution regarding the informing of persons about psychiatric treatment*

The answers recorded from question number 6 show the following results:

- with proportions that fluctuate from 64.0 %, clinicians implicated in the aid of the mentally ill consider that the law should force the patient to compulsory admission and treatment only in case of psychiatric emergency (e.g., aggression, violence). Yet, a percentage of 26 % consider that the law should force any psychiatric patient to compulsory admission (Figure 9).

Question 7: Do you consider that the psychiatric patient is more discriminated compared with other patients?

a. Yes, they are discriminated;

b. No, they are not discriminated;

c. I don't know.

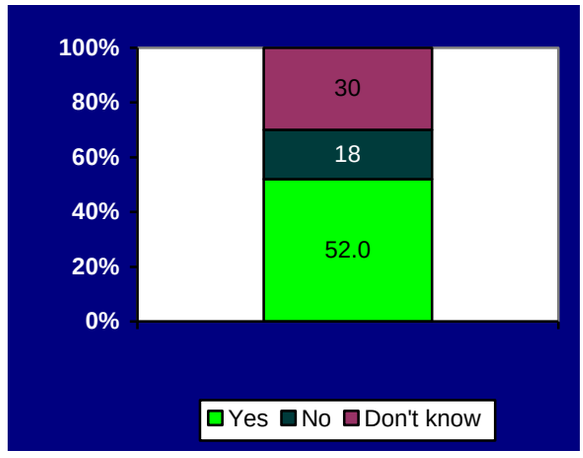


Figure 10. *The non-psychiatric clinicians' answer distribution regarding the discrimination of the mentally ill compared with other patients*

The answers to this question highlighted significant percentage differences from a statistical standpoint between medical residents, specialists and primary doctors. 52 % of clinicians consider that the psychiatric patient is discriminated compared to other patients (Figure 10).

CONCLUSIONS

Mental health legislation differs significantly from one country to another. The legal psychiatric system appeared with the purpose to protect the vulnerable mentally ill.

Social stigma and labelling are a violation of human dignity and freedom. The subject of non-discrimination is an ambitious challenge in Romania (an EU country). Within the framework of social services, stigma is an important problem within the modern psychiatric health service.

Although absolute confidentiality is an ethical principle hard to accomplish, the psychiatrist has the obligation to protect it however possible. In mass-media, medical care, and in medical research, the boundaries of medical confidentiality present themselves as an ethical challenge for the 21st century.

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James Joyce: aspects of psychology, psychoanalysis and Irish nationalism intertwined with alcohol consumption

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ABSTRACT

In this report we will describe how alcohol played an important role throughout James Augustine Aloysius Joyce's work, even though the Irishman has never been clinically diagnosed as being an alcoholic. In this way, while for some of his readers it might come as a shock to find out that he was a binge drinker, Joyce not only admitted to his drinking habits, but he claimed that drinking made for an excellent writing aid. He is also said to have believed that liquor heightened feelings and he could not write as well without the drinking process. Another link that brings its contribution to the chaining of alcohol to Joyce's work from a literary point of view is the presence of Irish nationalism. Thus, the nationalist fervour depicted in his literary work seems to always be accompanied by alcohol consumption, self-pity and the reminiscences of the greater times, all dominated by a sense of sarcasm conducted by the author.

KEYWORDS

James Joyce, psychology, psychoanalysis, Irish nationalism, alcoholism

INTRODUCTION

James Joyce, the scion of a Dublin family, was the eldest of ten children. Given every advantage during upbringing, by his adoring father, to realize his potential and regarding himself from an early age as somewhat a genius, Joyce chose to become a novelist after briefly flirting with the idea of doing medicine. He was a brilliant student when he chose to excel, a prodigy; and, despite the family's relentless downward spiral, John Joyce wasted a considerable inheritance, himself being a heavy drinker, he received a serious education at Jesuit schools.

Later on in life, rejecting both church and state, Joyce eloped to Europe with his long time life partner, Nora Barnacle. They drifted round the Mediterranean for years, sometimes in dire poverty, staying in Pola, Trieste and Rome. Their two children were born during this time, Giorgio [George] and Lucia. Regardless of circumstances, Joyce was unrelenting in his dedication to his art and in 1914 began the novel that was to be known as 'Ulysses' and would gain international acclaim. Uprooted by the turmoil of the First World War, the Joyces moved to Zurich and later to Paris, where they lived for the next two decades. 'Ulysses' was published in 1921 to general acclaim and Joyce attracted wealthy sponsors to relieve his chronic poverty. Success, however, seem not to aid in anyway his life. Illness and family problems weighed heavily on him and he suffered considerably. After years of health problems, aided by heavy drinking, Joyce died in Zurich in 1941 after surgery for a perforated duodenal ulcer.

"A man of small virtue, inclined to extravagance and alcoholism" is how Joyce described himself to Carl Jung, rather in a humbled manner as he has been depicted as an enormously disciplined artist. No single word entered his sentences without much deliberation and he would go to considerable lengths to ensure that he was satisfied with the final result. Despite all the problems encountered, he never lost control of his work. There is a circulating anecdote from Frank Budgen, one of his biographers, that proves so, in which Joyce is described saying he had been working hard all day, but only writing two sentences. 'You were seeking the right words?' asked Budgen. 'No,' replied Joyce, 'I have the words already. What I am seeking is the perfect order in the sentence.'

In early adulthood, he was devastated by his mother's death from cancer. Psychologists have argued that maybe this may be one of the episodes that triggered his alcoholism in the first place. He drank excessively and could be an extremely difficult person. For a large part of his life, he had severe eye problems and was close to blindness. To cope, he drank more, used denial, refused to follow medical advice and changed doctors in the hope of finding something close to a magical cure. Driven to desperation by his daughter's psychotic illness, he believed he could save her by the sheer power of his love. Yet he never stopped writing and continued to produce literature of the highest order

In a most simplistic sense, Joyce fits this profile of the Irish traumatized individual; his family was not native to Dublin but moved there from Cork in 1874 or 1875, thereby placing him in the gre famine's

reach. His life, no matter how hard he tried to avert it, follows a stereotypical Irish profile. Richard Ellmann, in his comprehensive biography, notes in the introduction: 'It is not easy, either, to enter into his life with the abandon of comradeship'. Joyce described himself to Louis Gillet, the French Academician who wished to exalt him, by saying, 'Don't make a hero out of me. I'm only a simple middle-class man'. (Ellmann, 5)

Inevitably and almost needless to say, Joyce is a product of his father, John, who is a character in his own right: reckless, talented, convinced that he was the victim of circumstances, never at a loss for a riposte, fearfully sentimental and acid, drinking, spending, talking, singing; he became identified in his son James's mind with something like the life-force itself. John Joyce's direct literary equivalent is obviously Simon Dedalus, but his influence goes beyond Stephen's father. Touches of John reside in Leopold Bloom and Joyce's own life, a life never substantially separated from his writing.

JOYCE'S CLASHES WITH PSYCHOLOGY & PSYCHOANALYSIS

The general view is that Joyce's relation to psychoanalysis was antagonistic. It is known he had copies of Freud's study on Leonardo da Vinci, Jones' on Hamlet and Jung's 'The Father in the Destiny of the Individual' and it is clear that he had been reading the influential names of psychoanalysis early in his career. But Joyce's preference seems to be at its best echoed in the smiling and slightly critical remarks of his Stephen Dedalus:

'Saint Thomas, Stephen smiling, said whose gorbellied works I enjoy reading in the original, writing of incest from a standpoint different from that of the new Viennese school Mr. Magee spoke of likens it in his wise and curious way to an avarice of the emotions' (Joyce)

Joyce will continue with negative comparisons to Freud throughout his life. Among the testimonials, is the somewhat spiteful comment to Budgen: '... why all this fuss and bother about the mystery of the unconscious, what about the mystery of the conscious?'(Budgen).

Not only did Joyce maintain that Freud had been anticipated by Vico, he remarked to the Danish writer Tom Kristensen: 'I don't believe in any science, but my imagination grows when I read Vico but it doesn't when I read Freud and Jung'.(Ellmann)

Jung and Joyce had previously clashed at a distance over the former's introduction to the German edition of 'Ulysses'. Jung rudely claimed that it could be read backwards or forwards. Joyce, perplexed, asked his publisher why Jung was so rude to him. What he had done to psychoanalysis? 'Translate your name into German,' was the response [Freud's name, in English translation, is a near-homophone of Joyce.]. Jung later dropped some of his antagonism, being especially impressed with Molly Bloom's soliloquy in the last chapter, which he described as 'a string of psychological peaches' (Ellmann, 675). He, somewhat unexpected, found "Ulysses" disturbing and perplexing. He had a hard time getting through it, and he wrote an essay, in 1932, in which he tried to sort through his reaction to the book:

"What is so staggering about 'Ulysses,'" he wrote, "is the fact that behind a thousand veils nothing lies hidden; that it turns neither toward the mind nor toward the world, but, as cold as the moon looking on

from cosmic space, allows the drama of growth, being, and decay to pursue its course." (Brown)

Taking Lucia on as a patient, Jung was unimpressed with her father. The period spent with her resulted in the observation that Joyce's daughter had become a something of a muse for him, and thus confirmed a suspicion which Joyce had formed many years earlier when interpreting a dream of Nora Barnacle: that his daughter was a kind of sacrifice for his own genius. He made the now-famous comment that Lucia and her father 'were like two people going to the bottom of a river, one falling and the other diving'. (Ellmann, 680)

Lucia was unsuitable for psychoanalysis and Jung failed to keep her in treatment. Jung's final observation on Joyce, even after a quasi-apologetic correspondence, is that his psychological style is definitely schizophrenic, the difference being that an ordinary patient cannot help himself talking and thinking in such a way, whereas Jung states Joyce wished this to be so.

It seems that the only nonconflictual connection with the psychoanalysts' society was established with Lacan, with whom Joyce seemed to share a number of theories and beliefs. Later on, the French philosopher and psychoanalyst held seminars dedicated to the process of decrypting, in a way, the Irishman's literary work and also gave birth to the 'sinthome' concept, redefining the psychoanalytic symptom in terms of his topology of the subject while exploring Joyce's literary work. In his seminar "L'angoisse" (1962 – 63) he states that the symptom does not call for interpretation "the symptom can only be defined as the way in which each subject enjoys (jouit) the unconscious in so far as the unconscious determines the subject" (Lacan), but a pure form of enjoyment not really addressed to no one

IRISH NATIONALISM INTERTWINED WITH ALCOHOL CONSUMPTION

'Ulysses', famously set on June 16, 1904, captures an image of Ireland that links nationalism, masculinity, and alcohol and manages to skilfully weave the fabric of Irish life. Rendering from the most spiritual actions such as remembering the dead to one of the most profane one as requesting a pint amongst friends, a representational portrait of Dublin is created through the text. But perhaps the most stereotypical activity in the Irish society is considered to be drinking, which seems to be the triggering factor when both producing and reproducing a nationalist rhetoric comes into consideration.

'Ulysses' is not a novel solely concerned with alcohol or nationalism but those two concerns weighed heavily on the collective Irish political conscious of the time. Joyce uses the template of Dublin, 1904, as the background for the text and although Dublin did not face the same destruction as the western counties, its population was not left unaffected by the famine.

In this Irish colonial space, drinking was a result of poverty; poverty was a result of the famine, and the countless deaths of the famine a symptom of English indifference and oppression. This made the call for a free and independent Ireland to grow louder and favoured its nourishment by alcohol. Alcoholism was universal and it served, as already mentioned when discussing the artistic minds, as a liberating agent even for the masses. Thus, scenes of a dark pub filled with men scorned by his-

tory inevitably filled with political demagogy and rebel calls can be discovered throughout Joyce's work.

The meeting of drinking and nationalist fervour is best portrayed in the "Cyclops" episode of 'Ulysses'. This type of drinking in the novel is mostly culturally normative and not necessarily abusive, a fact emphasized by Joyce's choice of language in the "Hades" episode:

"Expect we'll pull up here on the way back to drink his health. Pass round the consolation. Elixir of life" (Joyce, 430)

This particular description embodies many of the elements of the alcoholic stereotype. The Irish men view alcohol as the natural outlet for mourning and death. In the original Irish, the word 'usquebeagh' is in fact the "waters of life", or "elixir of life". Also, that space of death and misery in the larger historical context has always, arguably, related drinking culture.

Joyce slips a fair amount of irony in this episode, firstly by underlining the fact that the narrator of the scene and his companion, Joe, did not attend Paddy Dignam's funeral but they still decide to join the group, whether is because they associate drinking to a memorial tribute, or they see it as a good opportunity of cultural normative drinking.

It seems that in the moment of beverage exchange, little else matters to the men. Their insults and nationalism disappear during it. They become easy and free, void of any hatred or fiery language that may have preceded the offer. This is sustained by the fact that the first exchange follows a quick jab from the Citizen upon the narrator's entrance, "What's your opinion of the times?" (Joyce, 133). But after a brief response, the prospect of a drink shortens any new comment:

'— Arrah, give over your bloody coddling, Joe, says I. I've a thirst on me I wouldn't sell for half a crown.

— Give it a name, citizen, says Joe.

— Wine of the country, says he.

— What's yours? says Joe.

— Ditto MacAnaspey, says I.

— Three pints, Terry, says Joe. And how's the old heart, citizen? says he' (Joyce, 141-147).

The scene, taking place in Barney Kiernan's pub, speaks frankly about the Irish condition, the constant presence of alcohol, the nationalistic discussion that intensifies with every drink, and depicts Leopold Bloom as the "rank outsider" in any Irish space.

Here, is where Bloom stands out probably the most, far outside from this society. It is enough that he is a Jew, an easy target in a country struggling to find an identity, this identity being defined as "Irish Ireland", a "pure" Irish race. This definition comes for the man who seems to rule this particular space, the Citizen, a Catholic, working-class man, drunk in the middle of the day. This character seems to embody all of Joyce's ironies and his sarcasm regarding the Irish nationalists.

The anger towards the protagonist does not begin in all seriousness and the insults don't start to flow, however, until Bloom refuses to drink with the men, despite the offer of a free drink:

"So they started arguing about the point, Bloom saying he wouldn't and he couldn't and excuse him no offence and all to that and then he said well he'd just take a cigar"(Joyce, 436).

From this moment forward, there is no chance of acceptance or respect for Bloom. The reality of this scene, a scene that Bloom knows all too well from living in Dublin for his entire life, is that without drinking with these men and without not buying them a drink in turn, he is opening himself to endless ridicule.

As Rosenzweig explains, the social custom of 'standing' (treating): 'Provided the nineteenth century Irishman with a crucial means of declaring his solidarity and equality with his kin and neighbours' (Davies, 53); to refuse a drink was tantamount to insult.

Furthermore, Richard Stivers in his study of pub culture in Ireland has discovered that aggressive male jockeying for position is a part of how younger men were socialized for adulthood in 'bachelor groups' within the pub, overtly in opposition to familial roles that are 'remapped' onto the male alternate 'family' in the pub.

In such situations, older men set the pattern for the younger men to emulate, this suggestion was also corroborated by Robert F. Bales and it seems to be rendered both in this episode with Bloom and in 'A Portrait of the Artist as a Young Man' in the Cork bar scene with Stephen and his father.

Alcohol acts as a true social lubricant in this 'Ulysses' episode because it not only provides the men with a ritual, but also fuels their rants and offers some sort of justification for displacement of their pain through drinking. But these are men underemployed, or unemployed even, who waste time in pubs in the middle of the day discussing the same things their fathers did before them and yet the act of drinking is heroicized and labelled Irish; and despite the thoughts of the narrator, who often disagrees with the Citizen, the other men allow him to perorate because it is perceived as decidedly male behaviour.

Interestingly, Stivers's analysis of Dublin pub cultural practices notes that the male role was constructed according to rules guiding male behaviour while in the pub, not according to rules of adulthood external to the pub.

There are small lapses in the drinking but the process's pace is continuous. As these men talk, they drink and only wait till someone decides to buy another round, an inevitable event in this pub:

'And lo, there entered one of the clan of the O'Molloy's, a comely hero of white face yet withal somewhat ruddy, his majesty's counsel learned in the law, and with the prince and heir of the noble line of Lambert.

— Hello, Ned.

— Hello, Alf.

— Hello, Jack.

— Hello, Joe.

— God save you, says the citizen.

— Save you kindly, says J. J. What'll it be, Ned?

— Half one, says Ned.

— So J.J. ordered the drinks' (Joyce, 1011)

This makes a greater comment on Ireland. The forced disruption of the drinking, the repetition of entrances in the pub seems sometimes even exaggerated, is meant to interrupt the narrative and to emphasize the abusive nature of alcohol.

A frequent topic of discussion at Barney Kiernan's is the inevitable purchase of drinks. If these men had their society that they wished to, they might have no such convention as money, especially when it came to alcohol, but someone must pay

eventually. In a typically male fashion, in this scene, Joe decides to use his income for drink, a decision too often made in Ireland after the famine, Brian Baillie observes.

Joyce displays the vulgarity of this scene by showing the joy that this act induces to the men:

'So anyhow Terry brought the three pints Joe was standing and begob the sight nearly left my eyes when I saw him land out a quid. O, as true as I'm telling you. A good looking sovereign.

— And there's more where that came from, says he.

— Were you robbing the poorbox, Joe? says I.

— Sweat of my brow, says Joe. 'Twas the prudent member gave me the wheeze.

— I saw him before I met you, says I, sloping around by Pill lane and Greek street with his cod's eye counting up all the guts of the fish' (206).

Repeatedly, the ordering of drinks and their consumption, both elements of a normative Irish social gesture, interrupts the hyperbolized literary narrative. The centre of this parody is the uselessness of these characters. They fill the pub in the middle of the day and obtain free drinks from men who are, at best, acquaintances.

Cathy Caruth, in 'Trauma: Explorations in Memory', mentions events like famine as a locale of the directly traumatic event, a period that leads to wide-scale depression and an entirely changed society. Her definition is as follows: 'trauma describes an overwhelming experience of sudden, or catastrophic events, in which the response to the event occurs in the often delayed, and uncontrolled repetitive occurrence of hallucinations and other intrusive phenomena' (Caruth). The "intrusive phenomena" in this case is drinking, which is often abusive and detrimental not only to the individual, but to the collective Irish consciousness; becoming in Irish culture the vehicle of traumatic memory. 'Although there is a logical series of historical events leading to the omnipresence of alcohol consumption, the progression is better understood through trauma theory and subsequently, the concept of social memory' (Caruth, 38). The trauma that Caruth outlines is somewhat understandable considering the impact of a famine like the one that Ireland faced in the mid-nineteenth century. But drinking and reminiscence do not solve any political, social, or economic issues; if anything they merely intensify those same issues, not only in realistic terms but also in the fantastical ideals of nationalism. Thus, the "Cyclops" episode is a perfect embodiment of this condition.

On the same note, "History", Stephen states," is a nightmare from which I am trying awake" (Joyce, 377), and Caruth seemingly mirrors his thoughts in her paper, "the traumatized carry an impossible history within them, or they become themselves the symptom of a history they cannot entirely possess." (39)

The men, aside from the abstainers, such as Bloom, are the human results of the famine and their futile nationalism is wasted.

Emer Nolan notes the moment that involves the unemployment issue; as the employed and useful men who enter the pub side with Bloom, this may be the only time when this takes place, and agree, "that political progress might be made in Ireland if England's guilt were internationally recognized through peaceful actions and campaigns" (101).

In this discourse, sobriety and responsibility become joined with the peaceful and thoughtful veins of Irish nationalism, whereas unemployment and drunken idleness propagate racism and violence.

There are other scenes in 'Ulysses' that render perfectly the relationship between alcohol and Irish nationalism. For example, the drinking of absinthe is first mentioned in 'Ulysses' in the 'Proteus' episode, during Stephen's meditations on the beach at Dublin Bay. He recalls making the acquaintance of the Irish nationalist Kevin Egan in Paris, 'sipping his green fairy' (Joyce, 36), foreshadowing the following episode.

Earle notes in his article titled "Green eyes, I see you. Fang, I feel": The Symbol of Absinthe in "Ulysses" that 'absinthe's colour has clear political overtones in the text' (699). Absinthe is a drink symbolic of early nineteenth-century counterculture and by drinking it straight so that it retains its green colour, which is culturally symbolic of Ireland, Kevin Egan comes to represent the drawbacks of Irish nationalism. Exiled in Paris, Egan, in Stephen's description, seems to have become an alcoholic whose plans for rebellion have been reduced to his rolling 'gunpowder cigarettes' (Joyce, 36). Perhaps Stephen's consumption of absinthe in 'Circe' episode, after recalling their meeting earlier in the day, represents the younger man's support of Egan's cause.

Set in Dublin's red-light district, Nighttown, the events that are described during the 'Circe' episode reveal the psychological impact that absinthe has on Stephen. Inside Bella Cohen's brothel, Stephen's first appearance in the chapter features him 'standing on a piano carrying on an intellectual conversation about ancient Greek music' (Gifford and Seidman, 487) with his inanimate interlocutor 'The Cap', which belongs to his friend Lynch. At another moment in 'Circe' Stephen's comparison to a seminarian, provokes the young man's vision of himself as a Roman Catholic cardinal wearing a rosary made out of corks, perhaps an allusion to drinking as religious ritual in Irish culture. Once Bloom takes an intoxicated Stephen into his care by holding onto his money for him, they both look into a mirror and although it is unclear whether the reflection is being described from Stephen or Bloom's point of view, the image of an antlered William Shakespeare appears in the glass with them. During the climactic scene of the episode, Stephen is presented with a vision of his dead mother, whom he tries to ward off with his walking stick and accidentally smashes the chandelier. Joyce's description of Stephen's mother morphing into a 'green crab with malignant red eyes' (475) suggests that absinthe has brought about Stephen's hallucinations and is the reason for his irrational behaviour, as Bloom confirms to the English soldiers:

'BLOOM: (to the privates, softly) He doesn't know what he's saying. Taken a little more than is good for him. Absinthe. Greeneyed monster. I know him. He's a gentleman, a poet. It's all right' (Joyce, 483).

The interweaving process between alcohol consumption and Irish nationalism can be observed through a strictly linguistic point of view, as well, as there seem to be so many equivalent Irish phrases and terms to the not so few alcoholic beverages mentioned in 'Ulysses'.

In order to exemplify better the focus will fall upon the 'Cyclops' episode once more.

This chapter emphasizes the Irish gift of language like no other scene can manage to do.

The movement towards the pub follows from initial paragraphs introducing the new narrator:

'— Are you a strict t.t.? says Joe.

— Not taking anything between drinks, says I.

— What about paying our respects to our friend? Says Joe.

— Who? says I. Sure, he's out in John of God's off his head, poor man.

— Drinking his own stuff? says Joe.

— Ay, says I. Whiskey and water on the brain.

— Come around to Barney Kiernan's, says Joe. I want to see the Citizen' (Joyce, 52-57)

There is constant language that describes alcohol as organically Irish, similar to the 'autochthonous qualities of the potato.' (Baillie)

The phrase "Wine of the country" is symptomatic of the informal descriptions of drinking and was also a phrase used by Joyce himself once he began drinking. The suggestive nature of the English translation of the Irish word 'usquebeagh' as the "waters of life" is also pinpointing, whiskey, in particular, but also other beverages, as representative of the Irish landscape but also as a thriving part of daily life. Such a colloquial translation from an ancient language reveals the embedded role of alcohol in the Irish everyday life.

Throughout the episode, the men offer Bloom drinks which he repeatedly declines. The difference in their choice of language is starkly contrasted in this constant refusal. The speech associated with drinking is casual yet ritualized and every word that Bloom articulates after refusing offends the men more:

'— Could you make a hole in another point?

— Could a swim duck? says I.

— Same again, Terry, says Joe. Are you sure you won't have anything in

the way of liquid refreshment? Says he.

— Thank you, no, says Bloom. As a matter of fact I just wanted to meet Martin Cunningham, don't you see, about this insurance of poor Dignam's. Martin asked me to go to the house. You see, he, Dignam, I mean, didn't serve any notice of the assignment on the company at the time and nominally under the act of the mortgagee can't recover on the policy.

— Holy Wars, says Joe, laughing, that's a good one if old Shylock is landed. So the wife comes out top dog' (Joyce, 756-766).

Joyce's nationalism seems to be difficult to define, as well as his relationship with alcohol. Some portion of this novel is a very literal and autobiographic discussion of Joyce's life and only by reading Richard Ellmann's work this fact becomes obvious. In this episode, as with many others, there are evident biographical narrative intrusions. He is not overtly the unnamed narrator in this episode, but there are moments where we see Joyce's nationalism emerge, one that is founded in the mode of an Emmet or a Parnell, two men who recur frequently in his literary work.

These men, in some way spokespersons of Ireland in the chapter, are caricatures of masculinity, the stereotypical Irish peasant, individuals who only manage to become cruel when drunk.

Joyce answers the question of the failure of Irish intellect and talent in a very simple

statement in the middle of this episode, "Ireland sober is Ireland free" (692). The same statement comes within, reconfigured of this quote in 'Finnegans Wake', "Ireland sober is Ireland stiff"(1.7)

CONCLUSIONS

In this way, it can be confirmed that alcohol played an important role throughout James Augustine Aloysius Joyce's work, even though the Irishman has never been clinically diagnosed as being an alcoholic. However, for some of his readers it might come as a shock to find out that he was a binge drinker. But Joyce not only admitted to his drinking habits, he claimed that drinking made for an excellent writing aid. He is said to have believed that liquor heightened feelings and he could not write as well without the drinking process. Another link that brings its contribution to the chaining of alcohol to Joyce's work from a literary point of view is the presence of Irish nationalism. The nationalist fervour depicted in his literary work seems to always be accompanied by alcohol consumption, self-pity and the reminiscences of the greater times, all dominated by a sense of sarcasm conducted by the author. As a country that has suffered throughout history, (the great famine, the British invasion) Ireland and her inhabitants seem to be bound to a state of melancholia that can be drowned only by 'the waters of life'. Those who are not able to comply and participate are categorized as outcasts and will never be able to gain the respect or friendship of the representatives of this society.

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The XXIst century and the signs of a significant social change

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ABSTRACT

In recent years, when analyzing the defining characteristics of the XXIst century, several specialists in sociology, politology or philosophy have observed that its social «scene» comes to be more and more dominated by the game of alternatives, by free thinking and a large diversity of possible interpretations. In their opinion, it goes without saying that, under the new historical conditions, a life style centered upon discontinuity, relativism and dynamism will prevail. Within such a context, individualism, egalitarianism, universalism and progressivism will most probably appear as landmarks for the attitudes to be adopted and also for the main lines of actions to be followed.

KEYWORDS

liberalism, social conflict, fundamental social change

F. Fukuyama, whose name represents a character in contemporary American politology [1], is the one who, more than twenty years ago, oriented the interest of numerous people in a polemic which, according to several specialists – especially D. Bercea [2] –, *is continuously extending, no signs appearing that it will be solved too soon*.

Launched by the study entitled *The End of History and Last Man?* [3], this controverse brings into discussion an extremely important issue — namely, the ever increasing incapacity of large masses of people of avoiding the impression that *«something of crucial importance»* is in progress in their world.

According to the anticipations of Fukuyama, a declared enemy of any reductionist approach (especially in relation with the concepts of *policy of force and eco-*

nomic determinism), the XXth century appears as a terrible tedious stage, a *sign of decline towards a climax of ideological violence*, a *period setting up dangerous conditions for the manifestation of/favouring of the possible final apocalypse of a nuclear war*.

No matter how drastic and relentless would it appear, this century can by no means symbolize *the end of civilization*, the reason being that – in spite of all its faults – it cannot annihilate the moral energies concentrated in the human being. In spite of the *"boring atmosphere and of decline, manifested as a paroxysm of ideological violence*", it is nevertheless capable of remaining in the space of culture, assuring the pre-eminence of the spiritual condition to the detriment of the instinctual one.

The very fact that the human being living in the end of the XXth century is still capable of remaining in the space of culture entitles F. Fukuyama to announce that the end of this age announces the beginning of a *victory*. *Victory* of what? The response of the American scientist is extremely prompt: *a calm and, at the same time, positive victory of liberalism.*

Why the victory of *liberalism* and not, for example, of *conservatorism*, *nationalism*, *reforming socialism*, *ecologism* and/or *feminism?*

Because, taking over the best ideas of these doctrines, and also of other, similar ones, *liberalism* displays a *style* and a *temper* which do induce/favour *the liberty of thought and of religious freedom*, *critic attitudes and an impressive diversity of relations*, *the possibility of seeing life in most varied colours and meanings*, *a diminished political expansionism*, *a considerable encouragement of the private interests*, in parallels with a *large-scale support given to the most important spheres of public life (a context within which economy, religion, moral and education hold a top position).* Defined as *courageous* [4], the concept of F. Fukuyama marks the beginning of a new historical cycle of humanity, an evolutive stage in which the ideology of liberal democracy triumphs over the others and in which – according to St. Sestanovich –: "*violence and restraint come to play a less and less important part both in the relations among people and in the sphere of world great politics*".

Obviously, the author of *The End of History and Last Man?* is not the only optimist convinced of the capacity of liberalism to grant to the world a new impulse, a new perspective, another direction. In this respect, mention should be made of the fact that, meanwhile, this position has been embraced by many other reputed analysts in sociology, philosophy and/or political sciences.

Which is the attitude of – let's say – R. Dahrendorf [5]? His analyses, included in *The modern social conflict* [6], a study focusing on the concept of *"social change without revolution*", states that, in the near future, people will benefit from new «*chances in life*». In the opinion of the above-cited author, more and more numerous actions and phenomena are indicative of a soon coming society which will value both the *differences* and the *profound links* («*ligatures*») occurring at the level of *cultural identity*, namely of a society within which *individualism* («*the options*») will harmoniously coexist together with the *collectivist spirit* («*rights*»). The manner in which the «*generations of tomorrow*» will live, affirms firmly the one considered as having thoroughly renewed the *London School of Economics* and *Oxford College St. Anthony,* will not aim at the «*communist society*» described by K. Marx or at the «*sta-*

tionary situation» of J. Mill, but at the «*policy of regularized conflict and at a social economy assuring optimum individual life opportunities*». When taxes will go down and the enterprising spirit "will flourish", people's options for the "*open selection possibilities*" will significantly increase, blocking any attempt of preventing private actions, the "*intention of breaking down privileges and of emancipating the non-privileged ones*" included.

When discussing the socio-economic and political changes registered in recent years, A. Toffler [7], another well-known contemporary thinker, observes that more and more numerous signs of *disintegration* occur within the complex structure of power – an entity assumed to maintain – as stated on numerous occasions – the world in an as assembled form as possible. Worth mentioning in this respect is the work entitled *Powershift: Knowledge, Wealth and violence at the Edge of the 21st century* [8], according to which, in the office, in the supermarket, in banking institutions, in administrative offices, in churches, hospitals, schools or at home, the old patterns of the social life appear as fractured, along some directions unknown up to now. The head of an office and the superviser in a factory discover, both of them, that the workers fail to accomplish their duties mechanically, as they once used to. They ask questions and they demand answers. The same holds true for the officers, when faced with their troops, the chief policemen with their agents, the teachers with their students, the doctors with their patients. Outlining the fact that such relational commutations may appear everywhere, A. Toffler puts forward the idea that *the human society is confronted with emancipation and secularization processes*. Making mention, in such a context, of the metamorphoses registered in the psychology of the groups of patients, the author insists upon the fact that, in the glorious period of physicians' domination, they had a strict monopoly over the medical knowledge they possessed. Recipes were written in Latin, which represented a sort of semi-secrete code of their profession, giving the patients no opportunity of being informed on their condition. The medical publications and texts were produced exclusively for professional readers, while the medical conferences were not accessible to outsiders. Doctors used to control the curricula and the admission files of the faculties of medicine. A. Toffler invites us to confront such situations with the present-day one, when patients have unbounded access to medical information as, with a *personal computer* and a *modem*, anyone can access directly, while staying comfortably at home, data bases such as *Index Medicus*, and have scientific documents about any topic, starting with the *disease of Addison* up to *Zygomicoza.* The American analyst also makes mention that, once or several times a week, any televiewer is offered programs providing medical information of highest scientific level. Many of such transmissions warn that «*part of these materials might not be recommended to the large public*». However, the one who decides is the *televiewer*. Briefly, the monopoly upon specialized medical information is wholly destroyed, so that the doctor is no longer a god.

The above examples are sufficient for asserting that an organic link does exist between what are we to live in the future and what we call liberalism. In relation with such a situation, we consider as truly

reliable the assertions according to which liberalism expresses *"either a primary syntax of political thinking"*, *"the only dimension of our social imaginary social*, or *the only structure of power promising to transform the whole world into a variant of California, under the mirage of the material and spiritual comfort"* [9].

Briefly, the conclusion to be drawn is that we are all evolving towards a future whose social «scene» will be dominated by *the game of alternatives*, *free thinking* and *diversity of interpretations*. It is absolutely certain that this future will impose a life style characterized essentially by *discontinuity, relativism* and *dynamism*. In spite of their limitations, *individualism, equalitarism*, *universalism* and *progressivism* will continue to be viewed as landmarks of all attitudes and lines of action.

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The author declare that they have no potential conflicts of interest to disclose

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4. *A. Bloom*, for example, professor at *Chicago University* and expert in the *Committee for social thinking*, mentions that «*the excellent and courageous book of F. Fukuyama represents a turning point in an extremely important discussion for all those who consider themselves faithful defenders of the democratic ideals*».

5. *Ralf Gustav Dahrendorf* (May 1, 1929 — June 17, 2009), a German-British sociologist and politician. During the Hitlerite regime in Germany, he was arrested, together with his father, and accused of anti-Nazi activities. He was the President of *Deutsche Gesellschaft für Soziologie*, member in the German *Bundestag*, parlamentary state secretary at the *German Ministry of Foreign Affairs,* member of the *European Commission* and director of the *London School of Economics and Political Science*, co-founder of the *University of Konstanz* and member of the *House of Lords* starting with July 15, 1993. According to the British tradition, in the *House of Lords* he was given the title of *Lord Dahrendorf*. In his works he criticized the Marxist concept of the struggle between social classes. In the English variant, its selective bibliography may be presented in the following manner:

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7. *Alvin Toffler* (born on October 4, 1928, in New York City) is a reputed American writer and futurologist. Along more than forty years, he was one of the most influential and well-known voices in both business and intellectual domains. With the issuing of his first work, *Future shock*, a new discipline – *futurology* – centered on the study of change and of its influence upon both business and culture, has been established. A. Toffler is especially endowed for defining the forces and tendencies on which our advance towards tomorrow are based. Apart from *Future shock*, Alvin Toffler wrote *The third wave*, *War and anti-war*, *Power shift* and, recently, *Creation of a new civilization* (some of them co-authored by his wife and long-life partner, the talented Heidi Toffler]. A.Toffler is an important consultant of several military and espionage communities of the world, laureate of the *McKinsey Foundation* for his contribution to literature and honorary co-president of *The American Committee for the Development of the UN Fund for Women*. The list of the most important works of A. Toffler includes:

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Case Reports

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Impaired neurocognitive functioning in acromegaly – Case Report

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ABSTRACT

Background: **Acromegaly is caused by a growth hormone (GH) excess generally due to a pituitary adenoma. Long term exposure to high levels of GH lead to structural brain alterations, especially in the temporal and prefrontal region. The consequence is the impairment of the neurocognitive functioning, and especially of the attention and the executive function.**

Case description: **We describe the case of a 66 year old woman diagnosed 33 years ago with acromegaly caused by a pituitary macroadenoma. She has received two cures of cobaltotherapy, and afterwards a treatment with bromocriptine and lanreotide for five years. In time, she developed an increased deterioration of her mood, being diagnosed with major depression and panic attacks. Tests applied showed below average scores concerning attention and executive function.**

Conclusion: **Long term acromegaly evolution induced in our patient impaired neurocognitive functions. The cognitive performance was damaged, particularly the attention, short and long term memory and executive function.**

KEYWORDS

acromegaly, cognitive dysfunction, memory, depression

INTRODUCTION

GH is an anabolic hormone and recently its involvement in the development of the central nervous system, in the process of myelination, differentiation of glial cells and cognitive functions have been proven. Research conducted on animal model highlights the role of GH / IGF-1 axis in regulating brain growth, development and myelination processes (1). IGF1 improves cerebral circulation, increases neuronal activity and inhibits neuronal apoptosis. (2, 3, 4, 5, 6).

Based on anatomical findings, it was postulated the GH and IGF 1 role concerning higher cognitive functions such as short term memory, long term memory and spatial orientation.

While normal GH- IGF1 axis has a neuroprotective role, on the contrary, the excess of those hormones may have negative effects. Cognitive dysfunctions associated with acromegaly may be justified by the fact that changes in structure and function occur in time and they are not fully reversible even if GH and IGF1 values normalize under treatment. Moreover, secondary complications of acromegaly triggered by the specific hormonal profile such as diabetes and arterial hypertension might be additional factors for cognitive impairment (7, 8, 9).

Acromegalic patients have a deficient activation of brain areas associated with memory, in this case, the temporal and prefrontal region. Both short-term memory and long-term memory are impaired. The severity of these dysfunctions is correlated probably directly with circulating levels of GH, IGF-1 and the duration of active disease (10).

Electroencephalography (EEG) and Low-Resolution Electromagnetic Tomography (LORETA) can provide a functional imaging of brain and were used in order to appreciate the neurophysiologic state of acromegalic patients. Decreased beta activity in left medial temporal cortex and a decreased alpha activity in the right prefrontal cortex was found in naïve acromegalic patients compared to healthy subjects (11). LORETA revealed a significant decreased activity in prefrontal and middle temporal cortex, which in healthy brain are proved to be areas that are responsible for cognitive functions, namely executive functions and memory (12).

We describe a case of acromegaly with a long history disease (33 years) that exhibits an attention deficit and an impaired executive function that might be the consequences of long term exposure to high levels of GH and IGF1 on prefrontal and temporal cortex.

CASE DISCUSSION

We present the case of a 66 year old woman known with acromegaly, since 1983 (pituitary GH macroadenoma).

At the moment of diagnosis, the patient showed acromegalic signs: enlargements of hands, feet and nasal pyramid. Investigations confirmed the presence of pituitary macroadenoma with excessive GH production. The patient refused surgery so she received two cycles of cobalt therapy (1984 and 1987) and subsequent treat-

ment with bromocriptine with a good control of the disease.

Symptoms like sadness, anhedonia, loss of appetite, insomnia, and fatigue have increased over the last 15 years. The patient was diagnosed with major depressive disorder accompanied by panic attacks. The diagnosis was confirmed by the Hamilton Depression Rating Scale as the patient obtained a score of 16 points.

On the basis of anterior studies that have already emphasized the deficit of activation of the prefrontal cortex, whose main role concerns the executive function of the brain, our case report focuses on investigation of this aspect in acromegalic patient.

We have decided to further investigate this patient because she complained of suffering from memory loss, decreased attention, physical and mental fatigue, tearfulness. In order to obtain a more specific self-estimated disease perception, we applied the-AcroQol (Acromegaly Quality of Live Questionnaire). Table number I reveals the scores the patient obtained.

Table I. *The scores obtained by patient in AcroQol*

	Physical scale	Appearance subscale	Personal relationships
The patience's score	18	26	25
The maximum score	40	35	35

On Trail Making Test well-known instrument to psychologists that can detect difficulties in attention and cognitive inflexibility (13, 14, 15) our patient scored 106 seconds in the first sample (Trail Making Test A) and 160 seconds on the Trail Making Test part B. These results are below average in comparison to age, sex and education level matches.

Verbal fluency tests were used to estimate the executive function. The patient obtained a total score of 17 which is below average.

For StroopTest (measuring the specific components of executive function, referring in particular to the prepotent response inhibition), the patient achieved the ratio inference score (I_R) of 0.417 which is also below average.

All test results are synthesised in table no. II.

Table no. II. *The scores the patient obtained to the performed tests.*

	Cognitive evaluation	The patient score	The median score
Trail Making Test Part A (time in seconds)	Attention	106 s	39 s
Trail Making Test Part B (time in seconds)	Executive functioning	160 s	86 s

	Cognitive evaluation	The patient score	The median score
Stroop Test-ratio inference score (I_R)	Executive functioning	0,417	0,64
Verbal Fluency	Executive functioning	17	26,13

DISCUSSION

Our case report shows an impaired attention and executive function in an acromegalic patient that has suffered from this disease for 33 years. Our patient had no other complications of the disease that might have an impact on cognitive function as diabetes or arterial hypertension.

The term of executive function covers a wide range of cognitive processes and behavioural skills such as mental flexibility, working memory, inhibitory control, cognition and emotion (16, 17).

Attention, cognitive flexibility, and impulse control are the attribute of executive function and can be tested using tests such as: Stroop Test, Trail Making Test A and B, Wisconsin Card Sorting Test, phonematic fluency test (18).

Trail Making Test is a very useful and easy to apply instrument that provides important information concerning attention and executive function. The fact that the patient needed 106 seconds for part A and 160 seconds for part B which are certainly below average and reveals cognitive deficits. According to Tombaugh for the 65 – 69 year age group with less than 12 years of study the normal average score is 39 for the first sample and 86 for the second (19). These below-average results of our patient obtained are in accordance with the results of Ashendorf (20). The number of seconds required to solve the part A task for her age and educational category (55 – 77) was on average between 25 – 42s, which means that the patient obtained aborderline result, as she is on 3 – 8 % percentile. As for Part B, the patient shows a significant decline in executive function. According to the authors, values higher than 154 seconds place the subject in this category, the average being 57 – 101 (20). Thus, we can conclude that during this test, the patient experienced a dramatic decrease in attention and executive function.

Verbal fluency test is also particularly important for predicting lesions in adults in the prefrontal brain area (21, 22, 23). Our patient scored 17, which is under the normal range according to the results obtained by Machado in 2009 on 345 healthy elderly persons (24). The average score for her age and education match control group was 26.13 , which revealed serious deficits.

Stroope Test is a wide spread instrument that can be used on healthy persons but also in the case of cognitive dysfunctions. It can investigate the selective attention, cognitive flexibility and processing speed. As our acromegalic patient achieved an IR of 0.417, that shows difficulties. Mean ratio interference scores across 19 studies were 0.64 for control (25).

Also, an interesting result was the lower score obtained at her personal relationships and a better result concerning her own appearance in comparison with other studies, where the result is opposite. This result might be explained by the fact that elderly people tend not to give so much importance to their physical appearance. The global score was of 65 which places the patient among the general results obtained by acromegalic patients.

Tiemensma *et al.* (26) studied 68 patients who underwent a long-term treatment for acromegaly and 60 control individuals, using a scale of apathy, a scale of irritability, depression and anxiety and a scale assessing cognitive function through 11 tests. The results testify that acromegalic patients had a worse score on all questionnaires, but not in cognitive tests.

On the other hand, Yedinak and Fleseriu evaluated the cognitive dysfunction of 10 patients with active acromegaly, 17 with controlled disease and 14 pituitary adenomas with no secretion. The results confirm that the patients with non secreting pituitary adenoma scored worse than the acromegalic patients and that there is no significant difference between patients with controlled and active acromegaly (30).

Martin-Rodriguez *et al.* highlights the fact that long-term exposure to high levels of GH / IGF1 may affect the brain function on long-term (11). The conclusion was that acromegalic patients have a neurocognitive impairment and the specific treatment cannot provide the complete recovery of neurocognitive function.

A connection between the anatomical changes and the neurocognitive disfunctions in acromegalic patients is possible, MRI showing an increased global grey matter and white matter (9).

Memory presents a negative correlation with GH and IGF-1 (12). Pathophysiological basis of such an effect would be that there are many GH and IGF1 receptors in choroid plexus, hypothalamus, hippocampus, neocortex and the grooved area.

CONCLUSION

The pathophysiological basis of cognitive dysfunction in acromegaly is not completely explained, and the studies are contradictory. Focusing not only on biochemical parameters but also on improving the cognitive functions we can increase the chances for a better quality of life. An early diagnosis of neurocognitive disorders can be the basis for pharmacologic and behavioural interventions with improvement of life quality in acromegalic patients.

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Particularities of a case of infective endocarditis with negative blood culture and renovascular hypertension

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ABSTRACT

Infective endocarditis is still a pathological entity of great interest, concerning the frequency and costs, involving lately more frequent the elderly. We present a 73 year old female patient, which was diagnosed with infective endocarditis, with negative blood cultures (because of previous antibiotic treatment), but Duke modified criteria were useful for the diagnostic, relying mainly on the major criteria of the echocardiogram. Some interesting features are underlined, such as coexisting pathologies that raised problems for the differential diagnosis. The therapy was started based on international criteria, according to the guides, and allowed a good evolution of the case, despite the age and comorbidities (gastric cancer), as well as side effects to the first medication used.

KEYWORDS

infective endocarditis, allergic reactions, gastric cancer, renovascular hypertension

INTRODUCTION

Infective endocarditis remains an important disease, considering the clinical consequences and the costs, with an estimated 25 % mortality rate, despite the treatment with antibiotics, that is becoming more efficient and the development of the cardiac surgery techniques (1). After 50 years where the incidence of infective endocarditis has remained approximately constant (an average of 6 in Europe) (2), the last ten years bring studies that emphasize a growth of the incidence of this disease not only in Europe (3), but also in USA, as much in patients with a higher risk, as in patients with a lower risk of disease (4, 5).

MATERIALS AND METHODS

We present the case of a 73 year old female patient, hospitalized in May 2015, in the Internal Medicine and Geriatrics-Gerontology Clinic for shivers, lack of appetite, with weight loss and dyspnea.

From the previous history, we mention an antral gastric cancer for which there was performed 2/3 gastrectomy with gastroduodenal anastomosis and a normochromic anemia. In January 2015, she saw her general practitioner-GP for persistant fever, shivers, loss of appetite, dyspnea on moderate effort, weight loss of 10 kg in the last five months, tiredness. After following a 10 day treatment with injected antibiotics, her condition improved, but in April she returns to the GP with the above mentioned complaints. The doctor prescribes the same treatment but the persistance of the symptoms leads to the hospitalization in the 5th Internal Medicine and Geriatrics-Gerontology Clinic.

In the moment of admission, the patient presented with an influenced general condition, pallor, gingival mucosa congestion, in the upper jaw (with a precarious condition of the patient's dentures worn for six years), back pain. She presented a systole-diastole murmur of V/VI grade in the aortic area, that radiated in Erb, a bilateral systolic murmur in the carotids and a systolic murmur of V/VI grade in the mitral area, radiating in the axillary area. The blood pressure: 170/90 mmHg.

The significant paraclinical investigations consisted of an inflammatory syndrome (ESR = 51 mm/h, fibrinogen = 600 mg %), normochromic anemia (RBC of 2.91 mil/ mcL, Hb = 8.80 g/dL, Hct = 26.30 %, MCV = 90.4μ^3, MCH = 30.3 pg), thrombocytopenia (97.000/ mL), hyperuricemia (6.15 mg/ dL) and macroscopic hematuria 5 RBC/µL. In the feverish spurt, three blood cultures were collected, which were negative (we have to take into consideration the fact that in the immediate history of the patient there were two treatments with injective antibiotics, within 4 and 2 months from hospitalization).

ECG highlights left ventricular hypertrophy with ST-segment depression in DII, DIII, avF, V2-V6, T+/- in V4-V6 (figure 1).

Transthoracic echocardiogram showed normal cavities and walls, with EF = 55 %, E/A>1, one vegetation with echodense inhomogenous limits on the aortic valve (vegetation of 11/6 mm on the intraaortic side, attached to the right coronary cusp), severe aortic regurgitation and severe mitral regurgitation (figures 2, 3, 4, 5).

The positive diagnosis was infective endocarditis of aortic valve (right aortic coronary leaflet), severe aortic regurgitation, severe mitral regurgitation, normochromic anemia (medium form, of inflammatory etiology), antral gastric operated cancer.

The entrance gate was the oral cavity and the negative blood cultures are due to the repeated antibiotics treatment, before admission.

Differential diagnosis is made with marantic endocarditis, associated with neoplastic processes, for which advocates the fever and the antral gastric cancer, but where the echocardiographic image is typical with numerous tiny vegetations, with frequent embolic complications and severe prognostic (unlike our case); endocarditis in collagenoses, specific for the female gender, that also associates fever, tiredness, weight loss, but with no systemic complications and no biological features of colagenosis in our case.

There was started administration of Penicillin G 12 million U i.v. bd and Gentamycin 3 mg/kc/24 h. After ten days, we observed a late allergic reaction manifested by bronchospasm (dyspnea, wheezing, wheezes). The treatment was replaced with Vancomycin 2 g /24 h i.v. for ten days and we've made recommendations for another ten days treatment with Vancomycin 2 g i.v., through GP. The treatment of the entrance gate consisted of local rigorous hygiene, the replacement of the dentures and the surveillance of the dentist. Calcium channel blockers were administered as antihypertensive medicines, because the patient was not eligible for renal revascularization of renal artery stenosis (resistivity index >0.8). Blood pressure was established at 140/70 mmHg.

After adding the antibiotics, a spectacular improvement in the general state, with the resumption of the appetite and a weight gain of 2 kg in 14 days was registered. The biological inflammatory syndrome released, and the clinical and echocardiographic surveillance revealed no complications. The patient will be re-examined, together with the cardiovascular surgeon, in order to establish the opportunity of heart valve replacement. The prevention and treatment of infectious outbreaks and the administration of Amoxicillin 2 g was advised; cardiological re-examination at 2, 3, 6 months and then annually.

The prognosis is maintained reserved due to the old age, the severe aortic regurgitation and comorbidities (gastric cancer).

A specific feature of the case is the association of neoplasia in immediate history (which also raised a high level of suspicion of marantic endocarditis, disproved by the therapeutical success of antibioticotherapy), and also the absence of clinical and echocardiographic elements of heart failure. The incrimination of the adverse reaction was very probable according to the French School criteria (6).

DISCUSSIONS

The case we are presenting has many common elements with the ones that were recently describe for IE. A few decades ago infective endocarditis was considered the disease of the young adult, with most frequent rheumatic valvular involvement. Nowadays, the disease has become more common among old patients, often as a consequence of the invasive medical procedures with patients without known valvulopathies or with heart valve replacement (8, 9, 10).

The described case also appears at an old patient, but with a classical cause: septic entrance gate within the oral cavity.

Very useful for diagnosis are the Duke criteria (11) and the modified Duke criteria (12). According to them our case has been confirmed as an infective endocarditis:a major criteria of positive – echocardiography, with a vegetation of 11/6 mm on the intraaortic side, attached to the right coronary cusp and with three minor criteria: mitral and aortic valvulopathies, fever and immunologic involvement (expressed by thrombocytopenia, hematuria). The association of a major criteria with three minor criteria confirms the IE diagnosis.

IE at older people is generally associated with a bad prognosis and a high rate of complications (13, 14), especially in cases of negative blood cultures (15), still the specific feature of our case is tied to a favourable evolution, without immediate complications, despite comorbidities.

In our case of IE with negative blood cultures, at an old female patient, with the oral cavity as the entrance gate, the modified Duke criteria were essential for diagnosis.

The beginning of antibiotic treatment, previous to hospitalization, explains the negative blood cultures, but the initiation of therapy based on firm criteria, according to the guides, has allowed a good evolution of the case, despite the age and comorbidities (gastric cancer).

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Book Review

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Book Review: Physical examination for surgeons

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Physical Examination for Surgeons – subtitled An Aid to the MRCS OSCE, written by Petruț Gogălniceanu, James Pegrum and William Lynn – was published in 2015 at Cambridge University Press, in a collection destined to medical literature. The three editors – surgeons with vast clinical experience – designed this manual as a synthetic instrument meant to help current practice for both professionals in various surgical areas and for ER doctors, medical students and, of course, for military healthcare practitioners.

This work is a guideline regarding the objective physical examination of patients from a surgical perspective, by maintaining correspondence with key references in objective structured clinical examination. At the same time, it associates anamnesis references, elements of optimizing communication with the patient, as well as fundamental aspects related to ER approach and the interpretation of imaging results.

The purpose of this book is to serve as a practical manual; it does not pretend to be exhaustive or specific, but it organizes synthetically and it pinpoints essential elements of physical examination from a surgical perspective, which may assist both surgeons and other medical specialists from related fields in their daily activities, and which serve as learning reference for medical students.

Physical Examination for Surgeons is divided into 67 chapters, organized on 12 main sections, covered in 512 pages. Each chapter is structured on certain key elements that remain constant in the text, such as checklists on how to perform any physical examination, examination notes, including focused questions and answers, differential diagnosis references that facili-

tate the formulation and determination of diagnoses, tips, mnemonics and examples.

The first section – called Principles of Surgery – describes the basic principles f general surgical practice and elements of surgical evolution and history. The second section – General Surgery – comprises several chapters, from a description of the particularities of examining stigma of general surgery conditions to the particularities of examining the abdomen, abdominal scars, the groin, a stoma; it also features renal access and transplant examination. The third section is dedicated to Breast Surgery and to the examination specific to this anatomical region, while the fourth section presents the Pelvis and perineum. The fifth section organizes the information related to orthopedic surgery on bone segments. The sixth section features Vascular Surgery and it focuses on the examination of the carotid artery, on the arterial and venous examination of upper and lower limbs and on the examination of ulcers. The seventh section covers the Heart and Thorax and it comprises two chapters: first, the thorax and the lungs; and second, the heart and great vessels. The eighth section is dedicated to Head and Neck Surgery and it discusses the particularities of clinical examination in ENT, oral and maxillofacial, neck and thyroid. The manual continues with a ninth section, focusing on neurosurgery particularities: it describes global neurological examination and focal neurological examination. The tenth section features Plastic Surgery and it includes the examination of skin lesions, scars, grafts and burns.

The eleventh section goes beyond the issue of examination per se and it depicts the surgical radiology particularities, such as the fundamental particularities of classic radiology and of CT; it provides specificities on thoracic, abdominal, spine, hip, pelvis, knee, leg X-ray, mammogram, etc, and on head CT, chest CT, CT abdominal, aortic, renal, etc. This section also includes a series of X-ray images that complete the written information, thus highlighting the importance of X-ray examination particularities, in its capacity of complementary exploration, not substitute of physical examination.

The twelfth section – Airway, Trauma, Critical Care – is a connecting point to ER medicine concerning the detection and management of surgical emergencies. It is divided into five chapters that describe the basic procedures within general examination of the trauma patient, within the examination of the critically ill surgical patient, the assessment of the airway for intubation, the assessment for the compromised airway and the examination of a tracheostomy.

The 12 sections are preceded by a list of abbreviations that add to the concision and operational character of the text; they are followed by an alphabetical index of specialized terms within the manual.

Besides the concise and well organized information, the book also contains certain plans and decision trees, which contribute to a clearer picture of physical examination from a surgical perspective, particularized on bodily systems and segments.

Objective clinical examination is a key orientation and diagnosis element in surgical practice; it is also a fundamental skill for all physicians who deal with patients.

This book is a salutary initiative and a very well structured tool, destined to both

learning and simply guiding readers regarding physical examination from a surgical perspective, including all its diagnostic implications and correlated with imaging and aspects that intersect with emergency medicine.

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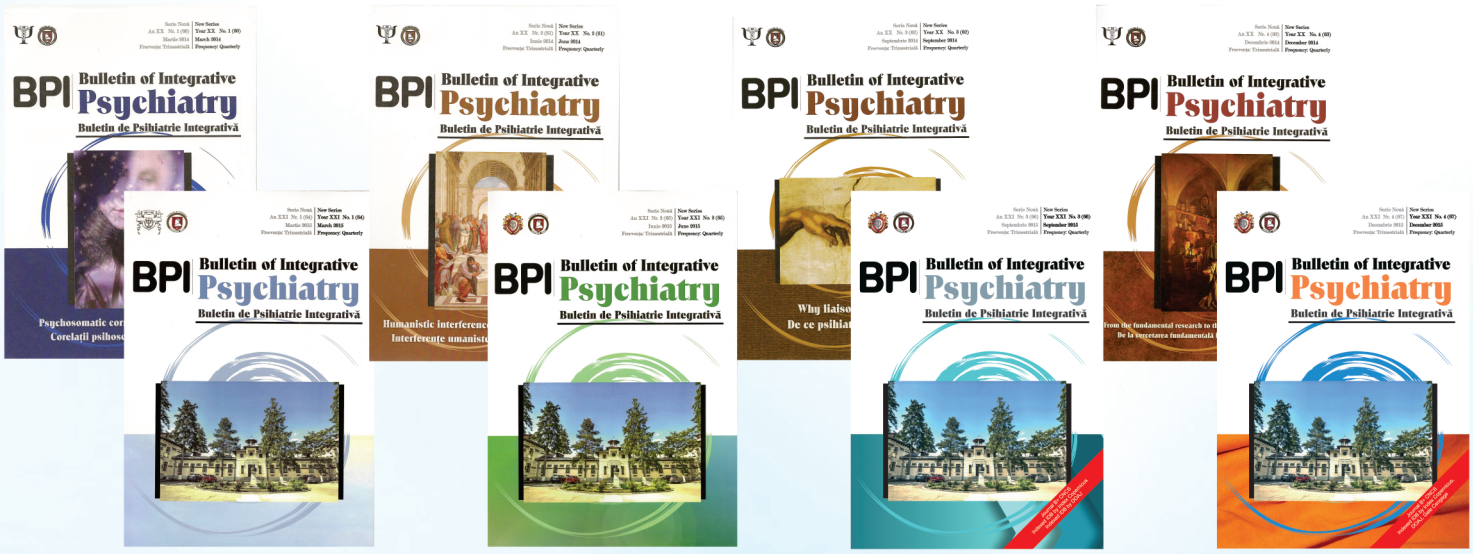
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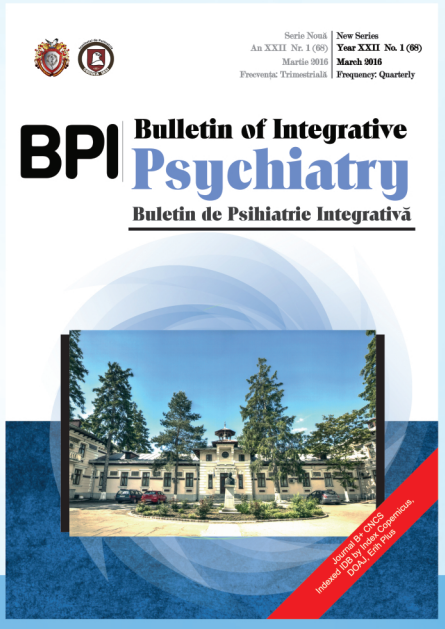
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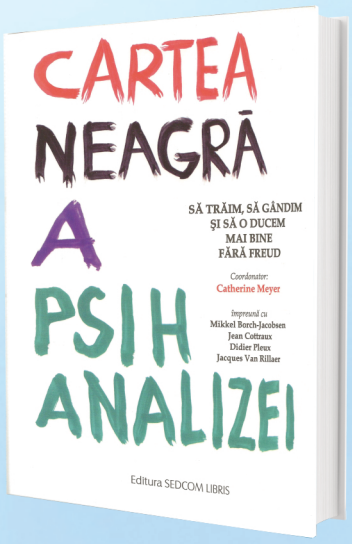
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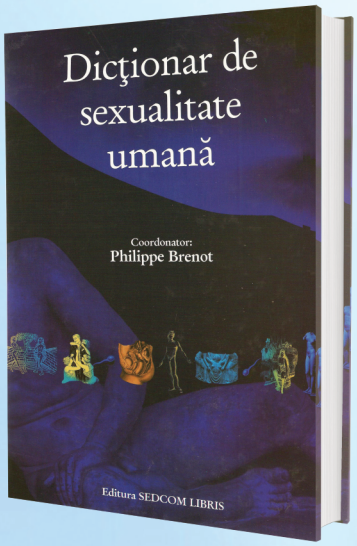


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