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Images on the first page represent: Inaugural board of "Socola" Hospital of Psychiatry Iaşi
The cover of the first number of "Bulletins et Mémoires de la Société de Neurologie, Psychiatrie et Psychologie de Iassy"
The image on the first cover represents the main building of "Socola" Institute of Psychiatry Iaşi

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

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

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

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

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

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

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

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# Summary

BPI Bulletin of Integrative Psychiatry
Buletin de Psihiatrie Integrativă

# Editorial

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# Professor C.I.Parhon – the founder of the Socola School

**Vasile Chiriţă, Dan Lupu**

**Vasile Chiriţă** - MD, PhD, Professor, Honorary Member of the Academy of Medical Sciences, Romania
**Dan Lupu** - MD, psychiatrist, Socola Institute of Psychiatry Iasi

*I laid the foundations of a "school" in this city [Iasi, Romania] known in the scientific world under the name "Școala de la Socola" (Socola School).*
*Professor C.I.Parhon*

The fate of the great scientist C.I.Parhon was closely intertwined with that of the Socola Psychiatric Hospital, whose director he was in the period 1918-1928, with that of the Faculty of Medicine in Iasi, where, as a university professor, he was the head of the Department of Neurology and Psychiatry in the period 1912-1933 and especially with that of the Socola School, a medical, scientific and social movement, perennial due to its depth and the selflessness of its illustrious collaborators, whose founder and mentor he was.

Born in the town of Campulung in the (now abolished) Muscel county, on October 15/28, 1874, C.I.Parhon came from a modest family, his father, Ion Parhon, being a teacher. Ever since his school years, he has stood out for his outstanding intelligence, meticulousness, critical spirit and desire for the best. Being passionate about the natural sciences, he attended the courses of the Faculty of Medicine in Bucharest in the period 1893-1900, where he obtained the title of Doctor of Medicine in 1900 with the thesis *Contributions to the study of vasomotor disorders in hemiplegia.*

Ever since 1897, a lasting collaboration with Prof. Gheorghe Marinescu (1863-1938), a Romanian neurologist, and founder of the Romanian School of Neurology, begins. It was also during this period that he began his collaboration with M.A.Goldstein (1872-1955), together with whom he published in Paris *Les secretions internes, pathologie et physiologie* (1909), considered to be the first treatise (in the full sense of the word) on endocrinology in the world. The research "on spinal locations and on internal secretions" are starting to make him known internationally.

Although between the years 1898-1912 C.I.Parhon published more than 160 works and studies, the topics covered being diverse, and participated in numerous congresses of neurology and psychiatry, the most prolific period of his entire activity, the period he declared brought him the greatest professional and spiritual satisfaction was the one in which

he carried out his activity in Iasi, respectively 1912-1933.

His coming to Iasi in 1912 happened as a result of the competitive occupation of the position of professor at the newly established Department of Neurology and Psychiatry within the Faculty of Medicine. In the course of 1913, Prof. C.I.Parhon also obtained a transfer from the position he held in Bucharest, that of primary psychiatrist of the Eforie Civil Hospitals, to the position of primary physician in Iasi, at the Socola Asylum for the Insane. Thus, he becomes the second primary physician of the hospice, the first position being held by Dr Alexandru Braescu.

If at the Faculty of Medicine Prof. C.I.Parhon was concerned with improving his courses and taking care of the students, at Socola he is mainly concerned with the establishment and proper equipment of the laboratory, with finding new therapeutic solutions for patients but also with the involvement of other researchers in the activity to.

During the years of Romania's participation in the first world war (1916-1918), years that brought the country and Iasi sufferings that are hard to describe, Prof. C.I.Parhon worked at Hospital no. 272 "Seminarul Veniamin Costachi", Lozonschi str. (500 beds) - here taking refuge the Brâncovenesc Hospital from Bucharest, and Hospital no. 321 nervous diseases, from "Girls' Primary School no. 8", Mitropolie str. (61 beds).

In 1918, following his insistence and the difficulties faced by the General Epitropia of the Hospitals and Hospices of St. Spiridon, the Socola hospital came under the administration of the Ministry of Health, which lead to its financial situation improving. The laboratories end up occupying an entire building, in which research on histology, pathological anatomy or biochemistry is carried out.

Regarding his own orientation in research, Prof. C.I.Parhon states the following:

"*At that time, in neurology, as understood by Charcot and Marinescu, the anatomic-clinical method generally ruled. Virchow said that we must think anatomically; Grasset, however, stated that we must think physiologically. In my lesson I said: we have to think physiologically or, if you want, better* ***biologically****. Indeed, biological thinking is broader than the so-called physiological one and allows us to analyze and see the phenomena that take place in our organism or outside it, under the widest horizon.*"

Biological orientation in research was, moreover, a constant that marked his entire activity. An intellectual emulation is created around Professor C.I.Parhon, in the research work involving the employees of the hospital, internal and secondary doctors or even students, the purpose of the research undertaken being the search for the material substrate of mental disorders. In the Socola laboratories, biochemistry research into mental illnesses was initiated, considered the first of its kind in the world.

On September 9, 1919, at the Socola Hospital, the foundations of an Association of Psychiatrists were laid, which would later debate neurology and endocrinology topics. Finally, after the inclusion of psychology, the name of the society will be that of the Romanian Society of Neurology, Psychiatry, Psychology and Endocrinology

Members of the first committee of the aforementioned society:

Prof. C.I.Parhon, Constantin Fedeles, Dr Gheorghe Preda, Petre Andrei, Dr Arnold Stocker, Dr Corneliu Popa-Radu and I.A.Scriban (professor at the University of Cluj).

The first meeting of the society took place on October 7, 1919, in Socola. Starting this year, the "Bulletin et memoire de la Societe de Neurologie, Psychiatrie et Psychologie" is published. In 1922, the bulletin appeared under the title "Buletinul asociației psihiatrilor din România" followed by "Bulletin et memoire de la Societe de Neurologie,

Psychiatrie, Psychologie et Endocrinologie de Jassy" published in French. The bulletin thus appeared, in French, until 1947. Congresses of neurology, psychiatry, psychology and endocrinology were held annually within the society, 18 in total, between 1921-1938. These congresses facilitated the establishment of links between specialists from all over the country and brought to the fore the current topics in research.

In 1928, he was elected as a corresponding member of the Romanian Academy, at the proposal of Professor Gheorghe Marinescu, and in 1929 he was permanently transferred as a primary psychiatrist to the Central Hospital for Mental and Nervous Diseases in Bucharest.

Although he actually lived in Bucharest, Prof. C.I.Parhon travelled to Iasi once or twice a week to hold classes and continue collaboration with his relatives at the Socola Hospital. This collaboration did not stop even after his appointment as a professor at the endocrinology department in Bucharest.
In the 20 years spent in Iasi, Prof. C.I.Parhon published over 400 papers and studies, addressing topics from psychiatry, neurology, endocrinology, genetics and therapeutics. The didactic and research activity of Professor C.I.Parhon from this period, the published works, and his organizational and social involvement, increased the prestige of the Socola School and contributed to his election in 1939 as a full member of the Romanian Academy. His reception speech, "Theoretical and practical importance of endocrinology. The need to organize the endocrinological scientific movement in our country" is said in the solemn public meeting of May 20, 1940.

Between December 30, 1947, and June 12, 1952, he held the highest position in the state, that of President of the Presidium of the Grand National Assembly of the Romanian People's Republic. After 1952, Prof. C.I.Parhon partially retired from political life, dedicating himself to scientific activity. He died on August 9, 1969.

Although far from Iasi, the connection with this city, with the Faculty of Medicine here, with the hospital where he worked, with the representatives of the Socola School - former collaborators who took his work further, was permanently maintained, being often tempted by the nostalgia of the years spent here. Through all his activities, medical, scientific and social, Prof. C.I.Parhon remains in the memory of the people of Iasi and especially of the collective of the Socola Institute of Psychiatry Iasi as a symbol of continuity, perseverance, selflessness and value.

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# Articles

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# The effects of mindfulness on critical thinking dispositions: implications for mindful learning

**Georgel Arhip**

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**ABSTRACT**

**This investigation explores the link between mindfulness factors (e.g., novelty-producing behaviour, novelty-seeking behaviour, and engagement with present activities) and critical thinking dispositions (e.g., mental focus and creative problem-solving). Data were gathered from one hundred forty-nine higher education students (*N* = 149). Participants aged 20 to 24 years (*M* = 21.85, *SD* = 0.86) were asked to fill out a questionnaire. This study employs hierarchical regression to investigate the link between mindfulness factors and critical thinking dispositions. The results emphasized the role of novelty-producing behaviour in mental focus as critical thinking disposition. Moreover, the results also show the importance of novelty-producing behaviour and engagement with present activities for creative problem-solving as critical thinking disposition. Further, the educational implications of mindful learning are discussed.**

**KEYWORDS:**

**Mindfulness, mindful learning, mindless learning, mental focus, creative problem-solving, critical thinking.**

## INTRODUCTION

Despite the general knowledge that the content of teaching should be more valuable, one prerequisite of effective teaching nowadays refers to how teaching is carried on. Individual attitudes toward learning may too often encourage mindless learning, while effective learning requires careful engagement with the material in question. The attitudes under scrutiny mindlessness, and mindfulness, are briefly defined to highlight the benefits of mindful learning (1). Mindfulness refers to a flexible state of mind characterized by context sensitivity and focus on the present. In contrast, the mindlessness state of mind implies robotic behaviour related to past individual behaviour. Therefore, mindfulness implies noticing new things in contrast to a mindless state of mind when the individual relies on decisions and attitudes drawn from the past. It can be considered a version of a tunnel-vision framework or rigid perspective. The rules and routines govern our behaviour in the mindlessness state, while in the mindfulness state, our behaviour is guided by rules and routines rather than predetermined by them (1).

## MINDLESS LEARNING AND MINDFUL LEARNING

Langer (2, 1) says that contemporary education imposes steadiness on a potentially varying environment. When students are encouraged to learn facts discounting their context, stability seeking is endorsed. This is referred to as premature cognitive commitment, which results from the mindlessness of learning and acceptance of information as valid without further information-seeking. Hence, alternative perspectives are discouraged promoting tunnel-vision of the target information. The result of this process is mindless learning. It happens that individuals can get locked into their predetermined versions of information, even though alternative information may be beneficial for their future needs. When we fail to acknowledge different perspectives, mindset stability can be confused with the stability of the phenomenon. In general, things are almost always changing, and they can be different from different perspectives, yet some information related to them is held constant in our minds (1). The challenge is for individuals to reconsider what they mindlessly accepted as being true (3). Usually, student teaching in the classrooms is done in rigid terms. They implicitly are delivered the message that the world functions in a certain way. In general, even students' assessment assumes that one specific answer is correct. By its nature, in the mindfulness process, the individual needs to distance himself from the perceived problem to grasp a new perspective on the situation (4).

## THE BENEFITS OF MINDFUL LEARNING

Recent studies have shown that mindful learning could improve creativity (5,6), mathematics performance in adolescents, pro-environmental behaviour (7) and even reducing stereotypes and stereotype related behaviour (8). Mindful learning mediated the link between self-determination and creativity in learning. The relationship between mindful learning and creativity is presumed a positive one, in this sense mindful learning can enhance creativity. Also, in specific educational contexts such as game-based learning, mindful learning supports the development of higher confidence in creativity competencies among elementary students (5). These results are significant in the context in which creative confidence stimulates creative potential (9). Moreover, research shows the benefits of mindful learning in terms of individual focus (10) while improving open-minded thinking (11). Several practices have been noted to support both, creative learning in the classroom and mindful learning such as allowing purposeful mind-wandering, time, and space for meditation in the curriculum, supporting creative thinking and reducing judgment or fear (6). Allowing purposeful mind-wandering represents one option for promoting creativity and mindful learning. Therefore, the heightened awareness over own cognitive process leads to ease of identifying creative ideas. Purposeful mind-wandering is guided by the teacher who encourages students to purposefully diverge from the topic at hand and directs them through intentional activities of mind-wandering (12). Regarding the time and space for meditation in the curriculum, the simple act of meditating has been shown to benefit creativity in learning settings (13). Practicing being more mindfully aware through meditation, even for a short amount of time each day, impacts learning holistically. Brief meditation breaks provide the downtime needed for creativity to be enhanced after returning to the task at hand. These breaks also may positively impact teachers who struggle to maintain their students' focus

during increasing curricular demands. Moreover, meditation even for short periods impacts learning. Short meditation breaks are needed for improving creativity by employing relaxation (6). Further, another research emphasizes the role of mindful learning in supporting pro-environmental behavioral intentions in positive ways (7). Also, research has shown that in experimental conditions, mindful learning can prevent automatic stereotype-activated behavior (8).

## CRITICAL THINKING AND MINDFULNESS

The developments in the technological field pushed educators to re-evaluate mandatory skills for individuals in the 21st century. Critical and creative thinking are the most frequently required 21st-century skills (14). Critical thinking is defined as a higher-order cognitive process that concerns several abilities such as analyzing and evaluating information and ideas without any bias from the prior background (15). Nowadays social contexts are characterized by an abundance of information, in this case, critical thinking becomes a valuable skill. This cognitive process supports individuals to evaluate the information they come across in various environments for truthfulness, validity, and bias (16). On the link between mindfulness and critical thinking, the scientific literature mentions two perspectives. The first one stipulates that mindfulness is not related to thinking processes (17). The second view suggests that if executive control is the result of mindfulness practice, it may facilitate the operation of reflective processes which are crucial to effective thinking (18). Shapiro's view emphasizes that mindfulness in educational environments facilitates critical thinking due to its connection with control and self-regulation (18). Therefore, mindfulness pedagogy may create the necessary context for learners to exercise the most required skills of the 21st century, creativity, communication, collaboration, and critical thinking (19). Yet, no consistent link between mindfulness and thinking skills has been established in the literature (20). Thus, the present study aims to investigate the effect of Langerian approach to mindfulness on critical thinking dispositions in a sample of higher education students. The research question focused on whether mindfulness predicts critical thinking dispositions, key factors of critical thinking. Such a hypothesis could provide directions for the benefits of mindful learning practices. Hence, it is hypothesized that mindfulness factors will predict critical thinking dispositions such as, creative problem solving and mental focus in the whole sample.

## METHOD

### PARTICIPANTS

The study participants were bachelor's students from a local University located in the northeast part of Romania. Participation in the research was voluntary. One hundred forty-nine ($N$ = 149) students agreed to participate to the study, 43.62% women ($N$ = 65) and 56.37% men ($N$ = 84) aged 20 to 24 years ($M$ = 21.85, $SD$ = 0.86). Students residing in rural areas comprised 37.58% of the sample, 62.41% residing in urban areas. The table below (Table 1) reports in details participants' characteristics.

Table I. Participants' characteristics

| Characteristics | *n* | % | M | SD |
|---|---|---|---|---|
| Age | | | 21.85 | 0.86 |
| Gender | | | | |
| Women | 65 | 43.62 | | |
| Men | 84 | 56.37 | | |
| Living area | | | | |
| Rural | 56 | 37.58 | | |
| Urban | 93 | 62.41 | | |
| Year of study | | | | |
| 1st year | 43 | 28.85 | | |
| 2nd year | 56 | 37.58 | | |
| 3rd year | 50 | 33.55 | | |

PROCEDURE

The information related to the scope and procedures of the research was announced in the classrooms of several courses. The information regarding the present research reached 300 students, almost half agreed to participate in the study. Before data collection, the researcher provided information regarding data privacy, voluntary participation, and the option to withdraw from the study at any time. All the participants signed written informed consent. The administration of the questionnaires was paper-and-pencil. The researcher participated in this process and offered support regarding the questions included in the form to avoid missing data on the measured variables. Filling out the questionnaire took approximately thirty minutes. This study was approved and followed the recommendations of the Code of Ethics of the University.

INSTRUMENTS

The assessment form included three sections. To assess mindfulness the Langer Scale of Mindfulness (LSM) was used (21). The scale includes 14 items divided in three factors which evaluate socio-cognitive mindfulness indicated by flexibility that manifests in novelty-seeking behaviours (e.g., curiosity, openness), novelty-producing behaviours (e.g., creativity, perspective taking) and engagement with present activities. All items were ranked on a 7-point Likert scale from 1 = strongly disagree to 7 = strongly agree. To verify the reliability of the items Cronbach's alpha was computed, hence for novelty-seeking behaviours $\alpha = 0.74$, novelty-producing behaviours $\alpha = 0.69$, and for engagement with present activities $\alpha = 0.73$.

Critical thinking dispositions, creative problem solving, and mental focus were assessed using the California Measure of Thinking Motivation (22). Creative problem-solving represents a disposition toward approaching problem-solving with an open and imaginative attitude that helps solve difficult problems. The mental focus disposition describes a task-oriented and organized individual. Overall, describes a focused and clearheaded individual. Both sub-scales include 7 items each, that need to be ranked on 4-point Likert scale from 1 = strongly disagree to 4 = strongly agree. For these sub-scales Cronbach's alpha resulted in satisfactory values ranging from $\alpha = 0.75$ for creative problem solving to $\alpha = 0.72$ for mental focus.

The third section refers to the demographic data of the participants.

## RESULTS

DESCRIPTIVE DATA ANALYSIS

Table 2 illustrates the means and standard deviations related to the studied variables, reliability coefficients for each measure and the Pearson correlation coefficients. Mental focus significantly and positively correlates with novelty-seeking behaviour (r = .39, p < .001), and novelty producing behaviour (r = .17, p < .05). Moreover, creative problem-solving positively and significantly correlates with novelty-seeking behaviour (r = .35, p < .001), and novelty producing behaviour (r = .42, p < .001), and engagement with present activities (r = .21, p < .05). The relationship between mindfulness components and the two critical thinking dispositions, mental focus and creative problem-solving was further investigated.

Table II. Descriptive Statistics, Cronbach's Alpha, and Pearson Correlations Coefficients

| Variables | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| **Mindfulness** | | | | | |
| Novelty- producing behaviour | ***.69*** | | | | |
| Novelty-seeking behaviour | .54** | ***.74*** | | | |
| Engagement | .48** | .34** | ***.73*** | | |
| **Critical thinking dispostions** | | | | | |
| Mental focus | .39** | .17* | .13 | ***.72*** | |
| Creative problem-solving | .35** | .42** | .21** | .21** | ***.75*** |
| Mean | 26.88 | 29.70 | 20.89 | 22.48 | 21.22 |
| SD | 4.73 | 3.75 | 4.66 | 3.49 | 3.74 |

Note: **p < .001; *p < .05

Alpha Cronbach's coefficients are shown on the diagonal

To test whether mindfulness factor predict critical thinking dispositions in higher education students, we conducted two hierarchical regression analysis. The three mindfulness factors were introduced in the model. Further, the results of the two hypothesized predictive models will be detailed.

The hierarchical regression investigated the predictive relationship between mindfulness factors and mental focus. In the first step of the analysis novelty-productive behaviours were found to positively influence mental focus (beta = .39, $p < .001$). The result of the regression shows that novelty-productive behaviours explained 14.9% of the variance (F (1, 147) = 26.90, p < .001, $R^2 = .14$). The next two steps of hierarchical regression that introduced novelty-seeking behaviours (beta = -0.11, $p = .211$), and engagement with present activities (beta = -0.008, $p = .925$), did not influence mental focus (Table 3).

Table III. Hierarchical regression of mental focus on mindfulness factors

| Predictor | *Beta* | *p*-value |
|---|---|---|
| Step 1 ($R^2$ = 0.15; $\Delta R^2$ = 0.14; $F$ (1, 147) = 26.90; p < .000) | | |
| Novelty- producing behaviour | .39 | .000 |
| Step 2 ($R^2$ = 0.16; $\Delta R^2$ = 0.15; $F$ (1, 146) = 1.57; p = .211) | | |
| Novelty- producing behaviour | .45 | .000 |
| Novelty-seeking behaviour | -.11 | .211 |
| Step 3 ($R^2$ = 0.16; $\Delta R^2$ = 0.14; $F$ (1, 145) = 0.009; p = .925) | | |
| Novelty- producing behaviour | .45 | .019 |
| Novelty-seeking behaviour | -.11 | .219 |
| Engagement with present activities | -.008 | .925 |

The second hierarchical regression investigated the predictive relationship between mindfulness factors and creative problem-solving. Novelty-productive behaviours were found to positively influence creative-problem solving (beta = .35, $p$ < .001). The result of the regression shows that novelty-productive behaviours explained 12.9% of the variance (F (1, 147) = 21.78, p < .001, $R^2$ = .12). The next step of hierarchical regression introduced novelty-seeking behaviours (beta = -0.03, $p$ = .723) which did not influence creative problem-solving. Yet, the third step that included three mindfulness factors showed that engagement with present activities positively influenced creative problem-solving (beta = .33, $p$ < .001). The result of the the third regression model explained 21.3% of the variance (F (1, 145) = 15.29, p < .001, $R^2$ = .19) (Table 4).

Table IV. Hierarchical regression of creative problem-solving on mindfulness factors

| Predictor | *Beta* | *p*-value |
|---|---|---|
| Step 1 ($R^2$ = 0.12; $\Delta R^2$ = 0.12; $F$ (1, 147) = 21.78; p < .001) | | |
| Novelty- producing behaviour | .35 | .000 |
| Step 2 ($R^2$ = 0.13; $\Delta R^2$ = 0.11; $F$ (1, 146) = 0.13; p = .713) | | |
| Novelty- producing behaviour | .34 | .000 |
| Novelty-seeking behaviour | .03 | .723 |
| Step 3 ($R^2$ = 0.21; $\Delta R^2$ = 0.19; $F$ (1, 145) = 15.29; p < .001) | | |
| Novelty- producing behaviour | .20 | .036 |
| Novelty-seeking behaviour | -.003 | .970 |
| Engagement with present activities | .33 | .000 |

## DISCUSSIONS

The gap between knowledge, and skills and employing them in real-life situations continues to expand (23). Knowledge acquired in school is rarely used to find solutions to everyday issues (24). Moreover, spontaneous transfer rarely happens even if the situation requires it (25). Research shows that individuals prefer, most of the time, to act based on the common sense impression rather

than relying on acquired knowledge (26), thus operating based on a least-effort principle. Langer (27) defined this type of action as mindless behaviour and concluded that is often encountered in real-life situations. The outcomes appear to be the results of how the learning process takes place, and not the result of the content of learning. The discussion on the learning process focuses on learners' choices associated with the mindfulness they exercise during this process. Unfortunately, in traditional educational contexts learners' manifest poor mindfulness leading to poorer learning and transfer of knowledge (23). Furthermore, critical thinking is considered one of the most important skills in the 21st-century skills (28). Critical thinking includes several processes that foster reasoning, questioning, and multiple perspectives with the main purpose of understanding the current reality (28). Hence, critical thinking symbolizes an empowering civic competence that is crucial for active and democratic participation in society and everyday life. Therefore, the present study aimed to explore the role of mindfulness in the development of critical thinking dispositions, mental focus, and creative problem solving with implications for mindfulness learning.

The results show that novelty-producing behaviour predicts mental focus, whereas novelty-producing behaviour and engagement with present activities predicts creative-problems solving. Therefore, there might be some benefits of employing mindfulness learning during classroom activities. Some suggested educational practices for mindfulness learning included allowing purposeful mind-wandering, time, and space for meditation in the curriculum, or supporting creative thinking and reducing judgment or fear (6).

This research presents a few limitations that should be considered. This study focused only on investigating two critical thinking dispositions, mental focus and creative problem-solving. Therefore, future studies should explore several facets of critical thinking. Moreover, other relevant variables related to the educational context, such as classroom climate, or personality traits should also be explored in future studies. The small number of participants included in the research could also represent a limitation of the present study. The sample size limits greatly generalization of the results. Therefore, future research could consider larger samples or even an interventional type of study. The nature of the research was exploratory which prevents us from illustrating any causal relationships. Nonetheless, our results emphasize the relationship between mindfulness factors and critical thinking dispositions with implications for educational contexts and mindful learning. The present investigation provides some insights regarding the relationship between mindfulness factors and critical thinking dispositions in higher education students.

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

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# The role of religion and spiritual approach in the management of patients with mental disorders

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**ABSTRACT**
**From ancient times, medical therapy was initially seen as the privilege of priests and has partly remained close to magic until today. The etymology of the word psychiatry makes us think that the treatment of the psychiatric patient should include a spiritual therapy closely related to the soul depending on the needs. Also, the etymology of the word psychotherapy refers to the healing of the soul, which has been discussed since ancient times, in a syncretic way, by the healers of all peoples. Thus, the need to open psychiatry to meditation, to prayer, and therefore to other therapeutic methods, can be taken into account. Any therapeutic process can also take into account the dialogue with the divinity, not necessarily in terms of the suffering person's communication with God, but especially taking into account the therapeutic attitude. It should not be forgotten that, as I have stated, since ancient times the art of healing was associated with the sacerdotal activity. Thus, in this article we aim to carry out an analysis of mental disorders, supported by the biblical foundation of religion and to highlight the symbolism of the concept of cleanliness (pure and impure – sacred and profane), as a necessary working condition in the medical service. The role of specialized medical personnel and the need for comprehensive care that looks at the person as a whole becomes an elementary necessity for the medical service everywhere.**

**KEYWORDS:**
**Mental disorder, ethics, social, responsibility, communication.**

## INTRODUCTION

In its complexity the human personality also includes a system of religious beliefs. As a type of social consciousness, religion is a phenomenon that accompanies the cultural development of mankind from the beginning until today. Mircea Eliade considered the sacred a key dimension of the human being, "it is an element in the structure of consciousness and not a stage in the history of

this consciousness". All religions are based on confession, which has as its main purpose the sacralization and, additionally, the catharsis, so that relief is achieved, a hope of healing through faith (1, 2). Spiritual-religious therapy is part of society's life and can be complementary to medical treatment methods by scientific evidence. But we must acknowledge the limits of science, beyond which a wide spectrum of suffering where religious faith can act still remains. That's why the vast majority of psychiatric hospitals have places for silence and prayer, and priests provide religious assistance (3, 4). Today, there is an extraordinary range of all types of therapy and especially those that apparently act only through the therapist's words and voice. The framework conditions expressed by Carl Rogers: *empathy*, *agreement* and *unconditional acceptance* can be found as the wisdom of the great religions of mankind. As preached by the Apostle Paul, Christian love requires to understand and communicate *completely* with the other, i.e. the elements of psychotherapy (5,6,7). Religious psychotherapy is part of the cathartic psychotherapies, which is based precisely on the therapeutic effect of confessing psycho-affective experiences. Thus, relying on another type of therapeutic relationship, a true emotional discharge is achieved, i.e. the catharsis. The religious service, through which the relationship with the divinity is mediated, is carried out by priests who play the role of the psychotherapist and who have the necessary means to mediate the relationship with the divinity (3).

**RELIGION AND MENTAL DISORDERS**

By using various and repeated names, the Bible refers to several particularly contagious diseases (8, 9). The Old Testament *law* mentioned the exclusion of the sick from the community until healing and the *purification* ritual, *accompanied by a sacrifice* (*Lev* 13-14). Leprosy was considered the plague par excellence with which God struck (*naga')* the sinners, and Israel was often threatened with it (*Dt* 28,27-35). The Egyptians were struck by it (*Ex* 9:9), as well as Miriam (*Num* 12:10-15) and Ozia (*2Cr* 26:19-23). Consequently, the category of diseases became a sign of sin. *Regarding the healing of illness*, the Bible quotes natural causes, but also miracles, such as that of Naaman in the waters of the Jordan: *Then went he down, and dipped himself seven times in Jordan, according to the saying of the man of God: and his flesh came again like unto the flesh of a little child, and he was clean* (*2Kg* 5,14), revealing the sign of divine goodwill and prophetic power. In the case of Jesus who heals, we read how He healed them and how He integrated people into the community: *And having seen them, He said to them, "Having gone, show yourselves to the priests."*, (*Lk* 17, 11-19), taking sickness and sin upon himself, to fulfill what was said through the prophet Isaiah, who says: *He took up our infirmities and bore our diseases,* (*Mt* 8, 17). Thus, through a miraculous gesture, He separates the disease from man, achieving that ontological break between **pure and impure - sacred and profane**, as we will see later (11, 12, 13). The introductory text (on which a lot has been written) and which raises a difficult question, is the one (*Lk* 8, 26-39) from which we reproduce the verses (38-39): *The man from whom the demons had gone out begged to go with him, but Jesus sent him away, saying, "Return home and tell how much God has done for you.",* and the question is: what kind of *demon-disease did* Jesus heal and why didn't he allow the man to follow him? A total mystery! Mental illness is one that affects a person's thoughts, behavior and social ability, so it is a dysfunction that affects feelings. Although few mental disorders can be prevented, almost all can be successfully addressed and treated. The causes of mental illness are complex and are influenced by hereditary factors, stressful life experiences, physical illnesses, difficulties in the family environment, etc. In order to properly manage the cases of patients with mental illness, the setting up of multidisciplinary teams made up of specialists is shown to determine together the best approach according to the particularities of each case, i.e.: psychiatrist, psychologist, cardiologist, social worker, spiritual assistant. The religious unit and its role must be in close connection and dialogue with the suffering family. This is the mere socio-human approach, a reality of life from which we find

that "the years pass quickly", and to live long and mentally healthy becomes the desire of the man who lives happily. Mental suffering knows no age, but it [mental illness] becomes a burden for the man who has been worn down by years, and who has reached the end of patience: *Why is light given to those in misery, and life to the bitter of soul* (*Job* 3,20). So, from the perspective of our research, mental illness acquires a different meaning, as it unfolds: as a path of decline towards death or as a path of growth towards happiness and eternal life. Life is a gift from God, even "threatened" by death; a long and healthy life is desirable and we will have been promised to the one who honors his parents: *Honor your father and your mother, that your days may be long in the land that the Lord your God is giving you*, (*Ex* 20, 12). A blessed and healthy life is a crown for the righteous: *The fear of the Lord prolongs days, But the years of the wicked will be shortened,* (*Prov* 10, 27), who will thus have the joy of seeing his children's offsprings: *Grandchildren are the crowning glory of the aged; parents are the pride of their children*, (*Prov* 17, 6). Like Abraham the "full of days" (*Gen* 25, 8) and the righteous, after a happy and flourishing old age: *They shall still bring forth fruit in old age; they shall be fat and flourishing,* (*Ps* 92,15), he can die in peace, aware that his life was blessed: *Then the Lord took Abram outside and said to him, "Look up into the sky and count the stars if you can. That's how many descendants you will have!"* (*Gen* 15, 15); *Thus the words of Tobit's thanks came to an end. He died in peace […] and was given an honorable burial*, (*Tob* 14, 1-2). We should not expect from the old man a metaphysical reflection on man, on nature, etc. Instead, we discover a deep sense of his existential presence and a careful scrutiny of destiny. Doctors take care of the person's life, they show themselves permanently sensitive to the greatness of man as well as to the misery of human psychic affections, to loneliness or fear in the face of pain (*Job* 7; 16) and death (*Qoh* 3); to personal anxiety in front of a God who seems incomprehensible (*Job* 10) or absent. We can analyse mental illness from a biological aspect, but we cannot understand it *naturally* because it contrasts with the deepest human instinct: life. Thus, the key *to solving* psychiatric problems is in our hands, because the person in a state of mental dependence does not only need medical care, but, above all, to be treated with love. And here is the key to Jesus' answer and the dilemma of solving the question: after healing go to the family and tell, and the family will surround you with the love you need (9, 10).

**PURITY (*PURE AND IMPURE – SACRED AND PROFANE*)**

Religions have developed a common concept of purity, as a commitment to be able to act in *the sacred area*, a necessary condition of the resemblance with God: "From the Paleolithic to the present day, the human being has manifested its fundamental structure of *being-in-the-sacred* through the *thirst* to live in a real world" (11, 12). This "thirst" involved, much later, the concept of moral virtue, as opposed to debauchery. In the beginning, the concept of *cleanliness* was ensured not through moral acts, but through rites and through the use of sexual symbols (marital or parental), precisely to express the pure relationship between man and Divinity. According to the biblical belief, according to which creation is considered entirely good, the notion of cleanliness (purity) began to change, gradually becoming *internal* and *moral*. So, in the end, Jesus Christ showed that its unique origin is found in the incarnate Word and in His sacrifice: "*Creation, defeats again the nothingness of our death, meaning an extinction of the biological life, one by one, of those who come to existence"* (13, 14). Within the concept of purity *physical cleanliness* first meant the removal of all that was dirty: garbage - (*Dt* 23,13ff); diseases - (*Lev* 13; *2Kg* 7,3); corpses - (*Num* 19,11; 2Kg *23,13s*). This being the case, the division of animals into clean and unclean: *You must not eat the meat from these animals or even touch their dead bodies; they are unclean for you* (*Lev* 11:8), often originating from primitive practices, could not be explained only by nutrition and hygiene reasons. The stain has been removed by *washing* clothes and the body: *Then the Lord told Moses, "Go down and prepare the people for my arrival.*

*Consecrate them today and tomorrow, and have them wash their clothing; But if he does not wash his clothes or bathe his body, he shall bear his guilt"* (*Ex* 19, 10; *Lev* 16,16); through the cleansing sacrifices: *He shall kill the lamb in the holy place where the animals for the sin offerings and the burnt offerings are killed* (*Lev* 13:13), and on the great day of Atonement, feast of purification; by sending a goat into the wilderness. He ***symbolically*** took over the impurities and even the sins of the entire people: *Then Aaron shall lay both of his hands on the head of the live goat, and confess over it all the iniquities of the sons of Israel and all their transgressions in regard to all their sins; and he shall lay them on the head of the goat and send it away into the wilderness* (*Lev* 15, 21). This acceptance somewhat empirical about purity lets glimpse the idea that a ***separation*** between body, spirit and soul still cannot be done. Thus the religious actions of man, no matter how spiritual they may be, still remain embodied in a community eager to overcome its natural state of existence and eternally consecrated to God. You didn't eat anything, you didn't touch anything, you didn't use life-giving forces randomly. In today's scientific medical discourse, we talk about *the integration of spirituality and religion* in therapy and about *the ethical aspects of therapy* of all kinds, referring to the Code of Ethics. We also talk about integrity, competence, responsibility, rights, consent, well-being, etc., acknowledging the reality that: "if the patient is ashamed to show the doctor his wound, medicine does not take care of what it does not know" (15). Only in this way we can understand the need for professional *cleanliness* as a working condition in the medical field, through the analogy made between the doctor who examines the wound before dressing it and God who, through his Word and his Spirit, sheds a living light on sin. The socio-professional effects of mental illnesses are intrinsic. These patients do not find or lose their job, they do not find their partner or they lose it, financial difficulties are added to their suffering and the vicious circle remains closed. For now, in these situations, we can only propose the solution of a comprehensive care that, in the spiritual field of refining creation, looks at the person as a whole, with body, spirit and immortal soul. It does not mean that suffering is easy to accept. Illness remains a trial and it is an act of love to help the sick bear it by visiting and comforting them (14, 15).

**THERAPY THROUGH RELIGION – THE COHERENCE OF UNITY**

We were surprised, quite astonished, to hear from the Papal throne, that after two thousand years of Christianity, *the polemics about the liturgy, to rediscover its beauty* might come to an end, because, you see, Lord, we just found out that it would be a moment of artistic emotion, of an aesthetic, cultural reality. If the *measuring unit of life* is *Jesus and His Gospel*, why after all this time are we still looking for the coherence of the unit? Why do we introduce concepts like *intellectual lucidity* to be able to justify the person's belief? Where is the apostolic credibility today, when we talk about: **the Latin tradition** with its *real, but hidden presence*; **the Orthodox tradition** with *the action of the Holy Spirit* and **the importance of faith in Protestant spirituality** with its *sense of presence*? What kind of religious therapy to do, when *the Christian religion has disappeared* and there have beentextbooks of the Orthodox religion and textbooks of the Catholic religion for a very long time? Likewise with the other acknowledged religions. What to tell the mentally ill person about a broken God, when the religions introduce themselves to society with shows similar to ancient Rome, where ***panem et circenses*** abound? More than a hundred years ago our grandparents read in the newspaper about what we want to exemplify regarding the concept of the *coherence of the unity of therapy through religion*. Here, in short, there are two journalistic references, because the editorial capacity does not allow us to publish the full texts, from the *Evenimentul* newspaper, Iași, June 1, 1901, series II, year IX: *Catholics and "Green Thursday"*: [...] *Today we sumptuously celebrated the end of the octave celebration that we call "Green Thursday". The pontifical liturgy began at 10:20 a.m. It was majestically celebrated by Monsignor Domenic Jacquet, surrounded by*

*several priests, excessively dressed in their rich sacerdotal robes, white flowers edged with gold flourishes* [...] and *Opinia Iași* newspaper, year VII, no. 1157, Thursday, November 11, 1910, entitled *Pastoral Conferences* where the priest P. Savin interprets for the people what should be understood about the "Eucharist": [...] *But if the argument is correct, then the innovators should be logical and give communion to the clergy only as bread, as according to them this type includes both elements. However they prefer to be lost in contradiction, rather than admit that they have deviated from the true and ancient faith and practice of the church. Moreover, we even find representatives of the western church, men who declare communion in the only form of bread as a superstition, as he says for example. In the 5th century Pope Gelasni commands: they are obliged to receive the sacrament either in full, or not to admit it at all, for the removal of one and the same sacrament cannot be done without a great profanation of the holy act.* Of course, there are countless examples and the people don't understand anything anymore. Naturally, the question arises: what should we do? And here we have the answer at hand in Jesus' parable about the *Good Samaritan*: ***Go and do the same!*** Nowhere in *the Gospels* do we find that they were urged to make statistics..., confessional [majority – minority]; diocesan pastoral plans: annual, three-year, five-year; to group ourselves in associations of all kinds citing the criterion of *availability*. That's what political parties do, and we see where we've ended up. On the contrary, we were taught that the so-called *spiritual capital* which gives meaning and significance to life on earth and that is especially useful to the mentally ill is acquired by mercy and by not being careless: *Go and do the same!*

## CONCLUSIONS

The possible integration of spirituality and religion within the psychiatric services must also take into account the cultural context of each country. The first step should be the inclusion of religious and spiritual norms in the diagnostic assessment (16). It is necessary to combine human, psychological, social and spiritual support for the family of the person with mental disorders by medical assistance. The medical act must also be viewed and understood through the moral action of each individual decision-maker who works to achieve the common good. While scientific research has increased the possibilities of prevention and healing, it is important to talk about *integral health*, which includes the vision of the human being created to "image and likeness" as a unity of body, spirit and immortal soul, harnessing the potential *coherence of the unity of faith*. These elements cannot be separated, because the person is one and at this point "the dialogue between the positivist and humanistic sciences, which facilitates the communication between medicine, bioethics and biotechnology in a way that makes it easier for both subjects to support and mutual reinforcement" must be found (17). When a human goes through suffering, this does not only affect the somatic, bodily dimension of the person, but the person as a whole, who must thus receive care in an integrated manner. If we started only from defining *public health*, as being: *a science of disease prevention, prolonging life and promoting physical and mental health through the community's effort to maintain a healthy environment, control infections, educate the population towards adequate personal hygiene, to organize the medical system for early diagnosis and treatment and the development of the social machinery, so that each member of the community has an adequate standard of living that allows him/her to keep his/her health*, by applying this definition in the case of "psychologically stigmatized" patients, we would avoid many errors. Fraternal sharing with the sick is the solution that opens us to the genuine beauty of human life, which includes even its fragility, so that we can ackowledge the dignity and value of every human being, whatever their condition, from birth to death (17, 18).

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# The consequences of the Covid 19 pandemic on eating disorders

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**ABSTRACT**

**The novel coronavirus has a great impact over mental health, individuals with eating disorders may be particularly affected by the distancing measures, quarantine thus to a difficult access to professional mental health services, this exacerbating phenomenology.**

**Eating behaviour disorders include anorexia nervosa, bulimia nervosa and binge-eating disorder in which individuals express abnormal eating behaviours, often resulting in either insufficient or excessive food intake.**

**Multiple implication factors such as genetic, biological, behavioural, and psycho-social have been incriminated. Multiple psychiatric comorbidities can be associated like anxiety, depression, obsessive-compulsive disorder, substance abuse, personality disorders, attention-deficit and an increased risk of suicide. Anaemia, hydro-electrolytic disturbances, cardiovascular diseases, gastrointestinal and endocrine dysfunctions may occur as medical complications.**

**The challenge regarding eating disorders is to understand their mechanism of occurrence, in an attempt to prevent them, as well as to treat them so that they do not put the individual's life in danger.**

**KEYWORDS:**
**Eating disorders, covid 19 pandemic, impact.**

## INTRODUCTION

Eating disorders are severe disturbances of eating behaviours, which are more frequent in adolescents and young adults, but it can appear also in other age groups. Predominantly, it manifests as a constant, even obsessive concern about body weight, body shape, with severe control over food intake. The most common eating disorders are: anorexia nervosa, bulimia nervosa and binge-eating disorder and their diagnoses are based on the DSM-V criteria and ICD-11 criteria (1, 2).

Numerous variables like genetic, biological, behavioural, social and psychological ones are involved in the risk of developing this disorder (3). Serotonin is involved in appetite regulation and many studies suggest that the alteration of 5HT-1A and 5HT-2A serotonin receptors, as well as the change in the levels of the serotonin transporter 5HTT and 5HIAA have an important role in the development of eating disorder (4). Psychological factors, certain personality traits and body image disturbance had a greater impact. Body image is associated with the exacerbation of the symptoms of eating disorders, and not necessarily with its development (5). Personality traits such as impulsivity, perfectionism, stress reactivity, harm avoidance and novelty seeking are common in people with eating disorders (6). Western cultural factors promote a slim body for women, having a major role in eating disorders development. In Singapore, Iran and Japan, the incidence of eating disorders is continuously increasing in women exposed to western cultural factors (7).

Multiple interpersonal maladaptive behaviors are implicated in eating disorders with an interpersonal deficit, being prone to rejection and avoidance of social reward. Key maladaptive interpersonal behavior include reassurance seeking, silencing the self, and co-ruminations, working as an emotions regulation strategy to handle difficult social situations, creating a feedback loop prone to aggravation.

Reassurance seeking, distress may occur when individuals do not receive the necessary assurance that they need from others to induce positive feelings about them.

Negative feedback-seeking, individual seek for negative feedback, which in turn, can lead to distress.

Self-silencing in order to avoid conflict with others individuals suppresses their thoughts and affects and internalizes them.

Co-rumination involves repeatedly discussing problems along with other people with little focus on problem-solving.

These maladaptive behaviors cause interpersonal conflict with others, particularly in one's close relationships.(8)

## ANOREXIA NERVOSA

Anorexia nervosa lifetime prevalence in women ranges from 0.5-2.2%, compared to men, where it is ten times lower. The onset of anorexia nervosa occurs frequently in adolescence, the average age being between 13-18 years. Studies have shown that anorexia nervosa with onset during adolescence tends to be associated with higher rates of remission, although the duration of treatment extends over a long period of time, and the risk of relapse is particularly high after the first 16 months after treatment and grows over time. Anorexia nervosa has a mortality rate of 5–6%, estimated to be amongst the highest of all psychiatric illnesses (9).

The symptoms of anorexia nervosa include restriction of food intake, extremely emaciation, the obsessive pursuit of methods to obtain a low and unhealthy weight, great fair of gaining weight, erroneous perception of size, weight and body shape, low self-image, not recognizing the severe weight loss. The main cause of death in anorexic patients are medical complications secondary to starvation, and suicide is the second cause.

Anorexia nervosa is associated with somatic complications in the reproductive, cardiovascular, gastroenterological, skeletal system, such as hypoestrogenism, decreased bone mass density, and consequent increased prevalence of osteopenia and osteoporosis, fertility problems, cardiac complications such as sinus bradycardia, prolonged QT interval on electrocardiography, arrhythmias, myocardial mass modification, and hypotension, refeeding syndrome. However, in addition to organic complications, anorexia nervosa is accompanied by multiple psychiatric comorbidities such as mood disorders, personality disorders, anxiety disorders, obsessive-compulsive disorders, and developmental disorders (e.g., autistic spectrum, attention-deficit hyperactivity disorder). Regarding the symptoms of this type of eating disorder, we can discuss the following: low body weight (generally below 85% of the ideal body weight), fixation on the prevention of excess weight, severe damage to body image, amenorrhea, cold intolerance, dry skin, lanugo (10).

Patients with anorexia nervosa require hospitalization in order to obtain a normal body weight with medical and psychological stabilization. Psychotherapy plays a major role in the treatment of these patients, because there are no studies that demonstrate the effectiveness of drug therapy (11).

Specialized treatment is recommended for anorexia nervosa, and through the prism of three decades of research and the most effective approach to eating disorders, it has been concluded that specific family-focused therapy for adolescents or family therapy for anorexia nervosa has the most satisfactory results (12). Other evidence-based psychological therapies for anorexia nervosa are the Maudsley Anorexia Nervosa Therapy for Adults (MANTRA), Specialist Supportive Clinical Management (SSCM) and Focal Psychodynamic Therapy (FPT). Remission rates at the end of treatment which usually lasts 40 weekly sessions vary from 23% to 33%, with only one third of patients with anorexia nervosa still in remission after 4 years of follow-up (13). Thus, there is a need for therapies aimed not only at somatic symptoms, but especially in the cognitive and behavioural sphere. Enhanced cognitive behavioural therapy is an individual-tailored treatment that targets the specific psychopathological mechanisms sustaining the eating disorder. Indeed, weight-based recovery does not necessarily reflect broader cognitive recovery, as the complex twist of cognitive and affective symptoms characteristic of anorexia nervosa, including the fear of weight gain, body dissatisfaction, emotional dysregulation, and fear of calorie-dense foods, frequently persist after weight restoration (9).

Anorexic patients have a prognostic that depends on the age of onset and treatment initiation, treatment duration and associated complications. About 30% of patients do not recover, and the rest of them recover in 5 to 6 years after the diagnosis (14).

**BULIMIA NERVOSA AND BINGE-EATING DISORDER**

Binge eating disorder can be defined as a disorder of eating behaviour in the sense of a

greater quantitative consumption of food accompanied by a feeling of losing control over eating (15). Binge eating was first described by Albert Stunkard in the 1950s, but was not integrated into clinical diagnoses until the publication of DSM-III in 1980 with the addition of "bulimia" which was later renamed bulimia nervosa. In subsequent DSM editions, the understanding of binge eating increased, leading to the inclusion of BED as a formal diagnosis in DSM-5 in 2013 (C., 2019). It is characterized by recurrent (≥1 per week for 3 months), brief (≤2 hours), psychologically distressing binge-eating episodes during which patients sense a lack of control and consume larger amounts of food than most people would under similar circumstances (14). This eating disorder, like anorexia nervosa, is more common in women (3.5%) than men (2.0%) and in obese individuals (5% to 30%) (6,7), especially those who are severely obese and those seeking obesity treatment (Brownley, 2016). It usually sets in in early adulthood, but it can also appear in adolescence and persist long after midlife.

A few decades ago, Bruch suggested that there is a connection between overeating and emotional state. Starting from this premise, more recent studies have shown that most people who suffer from binge eating disorder have at least one psychiatric comorbidity throughout their lives (67% to 79%), with mood and anxiety disorders amongst the most prevalent. In addition to mood being overall worse among individuals with binge eating disorder, it is especially poor directly prior to binge eating. Greeno et al. investigated binge antecedents in women with BED and concluded that poor mood directly preceded binge episodes. Depressive mood (i.e., sadness) has been the most frequently examined negative emotion in this disorder. Several cross-sectional, experimental and therapy outcome studies suggest an association between depressive symptoms, acute sad mood, and binge-eating behavior, and indicate that higher levels of depression are related to more severe binge eating. Besides the feeling of sadness, other emotions play a role in overeating. It should be noted that anxiety is less important than other emotions in the context of excessive eating, anger/frustration accounted for 95% of the moods preceding a binge-eating episode. Investigating a broad spectrum of emotions in binge eating disorder, Zeeck et al. found that the number of binges was best explained by anger, disappointment and feelings of being hurt or lonely. These authors also concluded that emotions that are related to interpersonal experiences seem to be particularly relevant in this disorder (15).

Regarding the treatment of this eating behavior disorder, specific psychological therapies like the trans-diagnostic Cognitive Behaviour Therapy – Enhanced (CBT-E) are the first-line treatment with the greatest impact on symptom reduction and other outcomes, which usually lasts 20 weekly sessions (17). In addition to psychotherapy, which has proven its usefulness in current practice, pharmacological treatment is also approved for binge eating disorder. Only one drug is currently approved by the US Food and Drug Administration for the treatment of binge eating disorder, which is the stimulant prodrug lisdexamfetamine . Numerous agents from several drug classes have been investigated in clinical trials or used as off-label treatments for this type of disorder, and many have shown positive results. However, each agent has distinct strengths and limitations, and patients should be matched with the treatment most likely to address their unique needs (18) .

## COVID-19 PANDEMIC AND EATING DISORDERS

The novel coronavirus has a great impact over mental health, individuals with eating disorders may be particularly affected by the distancing measures difficult access to mental health services, this exacerbating the problematic relationship with the food.

The lockdown has disrupted multiple routines increasing psychological distress, impeding the access to professional support and treatment disruption, changes in meals plans and routine. Food insecurity and harmful messages from social media have been associated with exacerbation of the disorder. Negative influence of mass media during COVID-19 have a negative impact on eating disorder by stigmatizing messages regarding quarantine weight gain and panicking sensational news about pandemics. (14)

A systematic review by Devoe. et al. have examine data from 53 studies reporting a tendency to symptom worsening, an increasing by 48% in hospital admissions compare to pre-pandemic time, increase in anxiety and depression symptoms. (20) Branley-Bellet. al(2020) evaluate the mental well-being during pandemic in a study effectuated in United Kingdom reporting from a group of 129 females that 87% have a worsened symptomatology concluding that social isolation, changes in living situation, lack on physical activity, and time spent online impacted symptoms.(21) Phillipou et al.(2020) conduct a Cross-sectional study on 5469 individuals from Australia, witch 96% are women reporting an increase in binge eating by 35.5%, a decrease by 43,4% in physical exercises, and high anxiety levels.(22)In United States Kim S. et al.(2021) reported from 7317 participants high levels of psychological destress compared to those without eating disorder, high perceiving of stress and loneliness.(23)

## CONCLUSIONS

Eating disorders have an increased incidence, numerous bio-psycho-social factors being involved. The COVID-19 have a profound impact over the mental health, various factors like weight stigmatizing messaging on media, disruptions of treatment, impeded access to personal/professional support, changes in routines, lack of physical activities, worsen the symptomatology during pandemic.

Public health must be involved in media messaging by encouraging nonstigmatizing weight-inclusive alternatives, specific and realistic achievable behaviour, concise, clear and understandable by everyone messages.

Multiple medical complication can appear in severe cases can be even life threatening. Psychotherapy represents the first line of treatment together with hospital care, favourable results can be obtained in most cases on the long term.

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# The psychosocial impact of labiaplasty on the lives of sexually active women

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**ABSTRACT**
**The number of labiaplasties has increased dramatically in the last decade due to the trend of seeking perfection in modern society. Genital aesthetic procedures have become important for the sexual, psychological and emotional life of women. The main reasons for performing labiaplasty surgery are: physical and emotional discomfort, aesthetic reasons and disorders caused by pain during sexual intercourse. An overview of the current data on the definition of labial hypertrophy, surgical indications, patient and surgeon motivations, and ethical considerations is needed to make the indication for labiaplasty. There are multiple optimal surgical techniques for labiaplasty, being classified into three main groups: margin resection, wedge resection, and central resection, the most appropriate technique being the one in which the surgeon feels most comfortable. Most women report high levels of satisfaction after labiaplasty, including improved sex life and psychological well-being. Overall, complication rates are low, most being minor ones. Sometimes revision surgery is necessary. Sexual problems after labiaplasty have rarely been reported, such as: difficulties with orgasm, decreased labial sensitivity and pain during sexual intercourse. Although in recent years, society's demands have evolved towards the concept of beauty and the social networks have affected women's awareness of their own bodies, there is enough data to support that labiaplasty improves the sexual and psychological well-being of patients, and a very careful understanding of the reason why women resort to this surgical treatment is needed.**

**KEYWORDS:**
**Labiaplasty, labia minora hypertrophy, psychological wellbeing, genital esthetic surgery.**

## GENERAL DATA

Labiaplasty represents the surgical reduction of the labia minora sizes as a result of their hypertrophy. The causes of labia minora hypertrophy are still incompletely elucidated, but are attributed to: congenital conditions,

sexual development disorders, treatment with estrogens or androgens during childhood, tissue expansion through repeated traction or infection, pregnancies, vaginal births, chronic irritation and increased elasticity of the labial skin due to age (1, 2).

According to Franco's classification (3), the labia minora hypertrophy can be divided into 4 grades: grade 1: <2 cm protrusion of the labia minora over the labia majora, grade 2: 2-4 cm protrusion, grade 3: 4-6 cm protrusion and grade 4: protrusion >6 cm. Taking into account the anatomical variations of the labia minora, only one study suggested an objective criterion for the indications of performing labiaplasty, namely width > 50 mm of the labia minora or asymmetry of the labia minora with a difference > 30 mm (4).

The number of labiaplasties has increased dramatically in the last 10 years due to the tendency to seek perfection in modern, economically developed societies (5). For example, in the United States, the number of labiaplasties performed had increased by 72% between 2013 and 2015 (6). Significant increases were also recorded in other Western countries such as Australia (7) and Great Britain (4). Although there is an increase in requests for labiaplasty, the total number of surgeries and the number of surgeons performing the procedure are unknown. Labiaplasty is performed in multiple hospitals, clinics, and private practices, making data collection difficult (8).

Genital aesthetic procedures have become important for the sexual, psychological and emotional life of women (9). The main reasons behind performing labiaplasty surgery are: discomfort caused by wearing tight clothes or performing physical exercises, such as riding a bicycle, aesthetic reasons, sexual disorders, discomfort and pain during sexual intercourse. An overview of the current data on the definition of labial hypertrophy, surgical indications, motivations of patients and surgeons, and ethical considerations is needed in order to make the indication for labiaplasty.

There is a multitude of natural biological variations in female genital anatomy (10, 11). Lloyd et al. (10) measured the labia minora in 50 premenopausal women and obtained values between 7 mm and 50 mm, but could make no correlation between labia size and age, parity, ethnicity, hormone use, or history of sexual activity. Basaran et al. (11) also performed measurements in 50 premenopausal and 50 postmenopausal women and observed that the size of the labia minora was significantly smaller in postmenopausal women. Taking these data into account, we can state that women who request labiaplasty generally fall within the range of natural anatomical variations (1, 8, 10, 11) and thus labiaplasty is performed in female patients who do not have a surgical indication according to current criteria. This behavior of female patients in economically developed countries is totally opposed to the requirements of Zambian women who resort to lengthening the labia minora by expanding the tissues with the help of weights, thus creating a specific ideal of beauty (1).

Another study conducted in Australia demonstrated that female patients' perception of vulvar appearance can be influenced by prior exposure to images of natural or surgically altered vulvas (12). Therefore, by exposure to altered images, there is a risk that surgically altered vulvas will be considered to have a natural and therefore ideal appearance. An analysis of images from Playboy magazine showed that only 2.7% of the images displayed in the 2007 and 2008 issues exhibited prominent labia minora, with labia majora visible in 82.2% of the magazine's genitalia images, while 15.1% of the images displayed the labia minora contained within the labia majora (13).

The need to expose the female patients who request a labiaplasty to photos with natural vulva, but also to photos showing the results obtained after the surgical intervention is very important in making decisions to perform a labiaplasty. The importance of using photographs was demonstrated in another study in the Netherlands, where the effect of exposure to images of natural vulvas on a

woman's genital self-image was analyzed using the Female Genital Self-Image Scale (FGSIS) (14). Schober et al. (15) analyzed in a study the fact that most women do not know what their vulva looks like, if there is an anatomical abnormality, or they are not able to self-assess their own vulva in relation to the sexual function.

## SURGICAL TECHNIQUES

The labiaplasty procedure was defined by Hodgkinson in 1983 (16). Many labiaplasty techniques have been described in the following years, such as those of Giraldo and Munhoz (17, 18). Nowadays there are different optimal surgical techniques for labiaplasty, to obtain an aesthetic and functional appearance with satisfactory results. They are classified into three main groups: margin resection, wedge resection, and central resection (1, 8, 9, 16, 17, 18). Most surgeries are performed under local anesthesia with lidocaine and adrenaline 1/100.00 to reduce the blood loss. To avoid the anesthetic side effects, it is preferable to avoid spinal anesthesia and general anesthesia.

The *resection of the* labia minora's *margin* can be performed by straight-line excision, by "Italic S"-shaped excision or by "W"-shaped excision (1, 8, 9, 19). It is also possible to opt for the use of a surgical scalpel, scissors, $CO_2$ laser, diathermy or a combination thereof. The laser has been used in gynecology for over 40 years (19). Many studies where $CO_2$ laser and radiofrequency were used for labiaplasty reported very few complications (19, 20). Pardo et al. described only a few complications of the laser, but also the great advantage of hemostasis (20). The advantages of radiofrequency are represented by limited thermal damage and accelerated wound healing. The marginal resection technique is easy to perform, does not require much time and has the advantage that the dark colored part of the labia minora is removed, thus the vulva acquires a rosy appearance, specific to puberty. The disadvantages are longitudinal scars and the creation of irregular labial shapes.

*Wedge resection* involves excision of tissue either from the most prominent area of the labia minora or from the central area, with or without identification and preservation of the labial artery (1, 19). The resection can also be placed posteriorly or inferiorly by creating a superior pedicle flap. It can be associated with a 90° Z-plasty to prevent scar contraction and can also be associated with clitoral hood reduction (1, 8, 19). Wedge resection is the most popular labiaplasty technique (19). It has the advantage of preserving the shape, color, function and sensitivity of the labia minora. The main complication of this technique is central or marginal dehiscence of the wound. Other disadvantages are: the laborious technique that requires a long time, the impossibility of excising a large amount of tissue and therefore, incomplete excision with unsatisfactory aesthetic results.

*Central resection* involves preserving the texture, contour and pigmentation of the labial margin by de-epithelialization (21) of the labia minora's central portion and its subsequent suturing.

From these three major categories, 12 surgical techniques have been developed, but despite this, there are no data to state which is the most suitable surgical technique according to the degree of labial hypertrophy (1, 8, 19, 21). The most appropriate technique is the one with which the surgeon feels most comfortable, given their own previous experience.

## RESULTS

An important issue in labiaplasty research is the examination of surgical outcomes' satisfaction predictors. Although most women report high levels of satisfaction after labiaplasty, a small percentage of women are not satisfied (3). Identifying the factors associated with poorer outcomes will help surgeons make a more rigorous selection of candidates for labiaplasty. Honigman et al. (22) conducted 14 studies analyzing predictors of poor psychosocial outcomes for cosmetic surgery and included demographic characteristics, psychological status, aesthetic appearance and previous surgical experiences.

However, according to Honigman et al (22), none of the 14 studies involved a rigorous statistical assessment of predictors and thus the results should be interpreted with caution.

According to current data from specialized literature, the satisfaction rates after labiaplasty are high. For example, 97% of 177 US women who underwent labiaplasty reported satisfactory results (22, 23). Rouzier et al. (24) stated that 89% of female patients were satisfied with the aesthetic outcome, 93% were satisfied with the functional outcome, and 96% were satisfied with the overall outcome.

In addition, some studies have also investigated the effects of labiaplasty on women's lives, including their sexual satisfaction and psychological well-being. To evaluate the sexual function, Kay et al used the FSFI questionnaire developed by Aygin and Aslan (25), which consists of nineteen questions grouped into six categories: desire, arousal, lubrication, orgasm, satisfaction and pain. The questions comprise four items for arousal and lubrication, three items for orgasm, satisfaction, pain, and two items for desire. To assess the severity of depression, the same group of researchers used the Turkish BDI Questionnaire developed by Ulusoy (26), composed of 21 questions with items scored between 0-3 points.

In a US study, 93% of the female patients involved in the study reported an increase in self-esteem after labiaplasty and 71% reported that their sex life also improved (4). In addition, a German study found that 90% of 812 patients reported a reduction in their psychological distress after surgery (5). These studies and others (1, 3, 4) suggest that women are very satisfied with the results of the labiaplasty, and this seems to extend to improvements in sexual aspects and their psychological function. However, despite the growing demand for labiaplasty in Australia, there have been no retrospective investigations of surgical and psychological outcomes in these women (1).

**COMPLICATIONS**

In general, low complication rates have been reported, most of which are minor such as bleeding, pain, hematoma, edema and wound dehiscence (1, 17, 19, 24, 27). Revision surgery is sometimes required, being reported rates of up to 7.9% of patients (8, 24). Alter et al. (8) reported sexual problems after labiaplasty such as: difficulty achieving orgasm, decreased labial sensitivity and increased pain during intercourse. Although complication rates are low and most complications are minor and they tend to resolve on their own, the most important complication is the amputation of the labia minora. Reconstruction in these cases is not possible and however, excess excision of the labia minora has not been reported as a complication. The rate of complications, even if they are minor, influences the level of postoperative satisfaction. Some women who experienced significant postoperative pain reported lower satisfaction rates, as well as the perception that their surgery was performed incompetently. Alter (8) recommended that the procedure be performed by experienced surgeons familiar with the potential complications for these surgical techniques to achieve optimal results.

**ETHICAL ASPECTS**

Some specialists dealing with vulvar surgery consider this procedure unnecessary, but there is sufficient evidence to support that labiaplasty improves the psychological well-being of female patients (1, 3, 4, 8). In recent years, society's demands have evolved towards the concept of beauty and social media has affected women's awareness of their own bodies. Minor labial hypertrophy can be associated with sexual problems, affectation of the couple's relationships and low self-esteem. Two studies (4, 28) stated that within a population, the natural biological variation does not necessarily correlate with the cultural beliefs of that population. Crouch et al. al (4) consider small labia with a thickness between 7 and 50 mm as normal anatomical variations. However, it was found in another study (28) that the female patients applying for labiaplasty have small labia ranging in size from 22 mm to 55 mm, most

of them falling within the normal anatomical variations. A study emphasized the beneficial effect of counseling sessions and psychosexual education on reducing the desire to undergo labiaplasty (29). There is also clear evidence to suggest that humans have an unconscious obsession with the sexual organs (30).

## CONCLUSIONS

Labiaplasty is a comfortable, safe method with a short recovery period, satisfactory aesthetic results and low complication rates. Current evidence emphasizes the importance of maintaining a positive genital self-image in optimizing women's emotional, sexual, and health care needs. The perception of "perfection" depends on the culture and the influence of the society which they live in. Women are often exposed to unrealistic, idealized images of the female genitalia and are not informed of the true extent of natural variations in the vulva. The main motivation to request an operation is dissatisfaction with genital aesthetic appearance and dissatisfaction with sexual relations (31), causing anxiety or inhibition of sexual relations.

The surgeon must fully evaluate the female patients seeking labiaplasty, including a complete physical exam and psychological testing to identify preoperative mental health issues and differentiate from the female patients who have true labial hypertrophy.

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# Treatment strategies in Alzheimer's disease: a mini-review of literature with focus on selenium supplementation

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**ABSTRACT**

**The term dementia derives from the Latin demens ("de": private, "mens": mind, intelligence, judgment — "without a mind"). The American Psychiatric Association (APA) describes it as "any mental impairment, or global cognitive decline in a previously unimpaired person" and is characterized by a deterioration of cognitive, intellectual, emotional, and behavioral skills, severe enough to interfere with the daily life of its sufferers. Alzheimer's disease (AD) is the major senile dementia, defined as a degenerative, progressive, and irreversible disorder, characterized by a gradual loss of cognitive function and by behavioral disturbances. No effective treatment exists. In recent years the main focus of AD research has been on the amyloid hypothesis, which postulates that extracellular precipitates of beta amyloid (Aβ) derived from amyloid precursor protein (APP) are responsible for the cognitive impairment seen in AD. Treatment strategies have been to reduce Aβ production through inhibition of enzymes responsible for its formation, or to promote resolution of existing cerebral Aβ plaques; these approaches have failed to demonstrate any significant cognitive improvements.**

**Intracellular rather than extracellular events may be fundamental in AD pathogenesis. Among the large number of chemical factors that have been implicated in the etiology of dementia, particularly its most common form, Alzheimer's dementia (AD), recent concern has focused on both increased and decreased exposure to the metalloid selenium (Se), an element of strong nutritional and toxicological interest. Selenate is a potent inhibitor of tau hyperphosphorylation, a critical step in the formation of neurofibrillary tangles. Some selenium (Se) compounds (selenoprotein P) also appear to protect APP against excessive copper and iron deposition. Selenoproteins show anti-inflammatory properties, and protect microtubules in the neuronal cytoskeleton. In the present paper, we review the role of Selenium in AD treatment, as presented in numerous studies in the last years, and suggests strategies for AD prevention by optimizing selenium intake; this includes in particular secondary prevention by selenium supplementation to elderly with mild cognitive impairment.**

**KEYWORDS**
**Alzheimer`s disease nutrition, Selenium central nervous system, Selenoproteins amyloid deposition, Selenium dementia, Selenium tau hyperphosphorylation.**

## INTRODUCTION

Alzheimer`s disease is characterized by the accumulation of amyloid plaques, the formation of neurofibrillary tangles and the loss of synapses followed by atrophy that manifests clinically as a progressive cognitive decline. The dementia stage of AD is preceded by mild cognitive impairment (MCI), a prodromal stage of AD, in which brain damage is not severe enough to compromise self-sufficiency (1). Oxidative stress is considered to be one of important pathogenic factors in the development and progression of AD. Nervous tissue is particularly vulnerable to the deleterious effects of free radicals for several reasons. The ATP used by neurons is produced primarily by oxidative phosphorylation, during which free radicals are generated. Moreover, the membranes of neurons are rich in polyunsaturated fatty acids, and the concentration of metal ions is high, which enables lipoperoxidation. In addition, the concentration of antioxidants in the brain is low in comparison to other tissues (2).

All aerobic organisms have a very complex and effective antioxidant system, which protects molecules against oxidative damage. Selenium plays a major role in antioxidant defense via the redox regulation of key enzymes. Selenium is incorporated into proteins such as selenocysteine, which is a part of important antioxidant enzymes, particularly glutathione peroxidase and thioredoxin reductase. Moreover, selenium attenuates amyloid beta production and amyloid beta-induced neuronal death by reducing the activities of beta and gamma secretases (3, 4).

## SELENIUM AND SELENOPROTEINS

Selenium is the most required micronutrient for human beings and animals. Inorganic selenium is mostly accumulated in plants via Sulphur assimilation pathway, whereas animals and humans consume these sources later as vegetables, meats and dietary supplements. Daily intake of selenium is highly recommended for maintaining the natural metabolism and homeostasis in the human body. The intake dosage of selenium is determined as 55 μg and 70 μg per day for adult males and females, respectively. Selenium consumption is mostly dependent on the food contents and dietary supplements

(5,6,7,8). Selenium is the integral compound of selenoproteins in the human body; the selenoprotein family consists of 25 eukaryotic genes where 25 are human genes and 24 are mouse genes. All these proteins have selenocysteine residue in their primary predefined structure. These selenoproteins are responsible for function and regulation of thyroid hormones, regulators of growth, development and differentiation, inhibitors of non-specific immune response, neutralizers of inflammatory, chemotactic and phagocytic responses like anti-male sterility, reproduction and oxidative stress influencer (9, 10, 11).

Selenomethionine is the principal chemical form of dietary selenium and its consumed widely. The initial metabolism starts by ingesting the Selenomethionine (SeMet) via food or supplements. The SeMet absorbed through intestinal transport channels, reaches the Methionine pool. The major function of Methionine pool is to store Selenomethionine and simultaneously incorporate them into proteins replacing the position of Methionine and forming Selenomethionine. The final step in the metabolism of selenium is the conversion of SeMet to selenocysteine (Sec) through Trans sulphuration pathway followed by biosynthesis of selenoproteins (12, 13).

Selenium is a trace element crucial to cerebral functions. During selenium depletion brain levels are maintained for a prolonged time at the expense of other tissues, whereas severe selenium deficiency causes irreversible brain damage (5). The circulating selenium transporter, selenoprotein P (SELENOP), appears to have a special role in the delivery of selenium to the brain by entering neurons via the apolipoprotein E receptor 2 (LRP8), a member of the lipoprotein-receptor family that is expressed exclusively in the brain (6). Interestingly, cholesterol and selenium are imported into neurons via this same receptor. While SELENOP is the important extracellular selenium transporter, the important intracellular antioxidants in neurons and glia are glutathione peroxidase 1 and 4 (GPX1 and GPX4). Strikingly, high extracellular levels of selenoprotein P (SELENOP) have been found in the brains of rodents. All regions of the mouse brain appear to be dependent on selenium for maintenance of proper functions (7).

**SELENIUM AS PROTECTIVE AGENT**

The central nervous system is appreciably dependent on an adequate selenium supply and, as mentioned above, diets that are slightly deficient in selenium do not elicit neurological deficits due to the preservation of selenium content in the central nervous tissue during dietary selenium restriction. On the other hand, a targeted reduction in brain selenium reduces SELENOP bioavailability and causes spontaneous neurological deficits, which are reversed by selenium supplementation (14). GPX1 was the first mammalian selenoprotein to be discovered and has been shown to protect the brain from oxidative insults. Like GPX1, GPX4 protects cortical neurons from exogenous oxidative stress-inducing agents.

Evidence from human studies suggests a role for Se and selenoproteins in protection against cognitive decline. In the InCHIANTI cohort study of 1012 Italian participants aged 65 years or older, 59 performance-based assessment scores of coordination as well as the MMSE-score were significantly reduced in participants with low plasma Se (<66.7 μg/L) compared to those with higher (>82.3 μg/L) concentrations (15). In the French EVA cohort of 1166 people aged 60–70 years a 58 % increased odds ratio of cognitive decline was recorded over four years in participants with a Se concentration <75.8 μg/L, as compared to a mean baseline

plasma Se level of 86.9 μg/L (16). Neurodegeneration was found to be present in all studied brain regions in the knock-out animals fed the Se-deficient diet. The neurodegeneration was predominantly axonal, however neuronal bodies in the somatosensory cortex and lateral striatum appeared also to be severely deteriorated. Morphological analysis of the hippocampus revealed decreased dendritic length, density and functionally. A defect in the long term potentiation of the hippocampus, essential for memory imprinting, was also noted. These findings are in line with the hypothesis that Se deficiency contributes to functional deficits seen in AD (17).

High extracellular selenoproteins (SEPP) levels of have been found in the brain. Knock-out of SEPP or ApoER2 in mice resulted in neurological dysfunction, particularly when fed a low Se diet, and it appears that under low Se supply these two proteins are necessary to maintain Se in the brain and prevent neuron degeneration. Regional progression of neurodegeneration in the brain of the SEPP knock-out mice has been studied in order to map neuronal cell death, and evaluate neuronal structural changes within the hippocampus (17).

The expression of SEPP in postmortem tissue from individuals with the hallmark lesions of AD and individuals without these lesions has been examined (29). SEPP immunoreactivity was co-localized with A$\beta$ plaques and neurofibrillary tangles. These observations suggest some form of interaction between SEPP and Aβ, leading to complex formation. Like SEPP, Aβ is also a strong metal chelator, binding for instance Cu and Fe (30, 31). Ternary complexes can be formed between metal cations, Aβ and SEPP and such complexes are presumably less toxic than Aβ-metal complexes alone. Since Cu is one of the metals abundant in A$\beta$ (32) and Cu binds very strongly to Se atoms, a ternary complex between Cu, Aβ and SEPP can explain the co-localization of SEPP with Aβ in AD (30). Thus, SEPP chelation blocks metal-mediated Aβ-aggregation and ROS generation, the trapping of SEPP by Aβ-plaques may reduce its availability for the synthesis of intracellular selenoproteins including thioredoxin reductase (TrxR) and GPx. Together with glutathione (GSH) these intra-neuronal selenoenzymes operate as intracellular antioxidants, thereby inhibiting tau aggregation.

## TAU HYPERPHOSPHORYLATION AND SELENOPROTEINS

Tau is a neuronal, microtubules-associated protein, which in healthy brains regulates microtubule dynamics. Intact microtubules are involved in transport of essential substances from neuronal bodies to synaptic structures. Phosphorylation regulates tau protein binding to microtubules. Under physiological conditions the tau protein remains soluble, but hyperphosphorylation compromises its normal functions, and leads to formation of insoluble neurofibrillary tangles, which are bundles of paired helical protein filaments (18, 19). Such excessive phosphorylation in AD must result from an imbalance between phosphorylating kinases and de-phosphorylating phosphatases. Increased expression of active kinases adjacent to neurofibrillary tangles has been described in AD (20). Sodium selenate reduces tau phosphorylation, both in cell cultures and in AD mouse models. Administration of selenate to rodents produces cognitive improvements and reduced neurodegeneration. In these models selenate is presumably converted to specific selenoproteins including glutathione peroxidases, which may attenuate the

intracellular burden of ROS and thereby protect microtubules in the cytoskeleton (21).

Sodium selenate supplementation has been found to deliver selenium to the brain and to reduce tau phosphorylation. In animal models, selenate appears to activate phosphatases and induce protective enzymes including glutathione peroxidases (GPXs), which may attenuate the intracellular burden of ROS (22). Early observations reporting selenate protection against cognitive decline may be related to its protection of microtubules in the cytoskeleton (23, 24). In healthy brains the microtubule-associated tau protein regulates microtubule dynamics. The exact role of GPx and its cofactor GSH for protection of microtubules has yet not been fully elucidated. It should be emphasized here that microtubules are essential parts of the cytoskeleton, thereby maintaining the three-dimensional structure of the neurons. Microtubules play crucial roles in a variety of cellular events, including axonal and dendritic transport and neuronal growth and differentiation (33).

Apparently, optimal function of GPx and SEPP is necessary for protection against the cognitive decline characterizing AD. Optimal function requires higher intakes of Se than officially recommended in Nordic and other European countries. Selenium intake in North-America and some other regions of the world are considerably higher than in Europe, which might contribute to inconsistencies in the clinical evidence as to the role of Se supplementation.

## SELENIUM AND THE NEUROINFLAMMATION HYPOTHESIS

As already known, the insoluble amyloid precursor protein (APP - a glycosylated protein that is uniformly found in cell membranes, most abundant in the brain) derivative A$\beta$ appears to be responsible for plaque formation, and A$\beta$ may induce oxidative stress and microinflammation (25). An early hypothesis was that suppressing of inflammation could arrest precipitation of A$\beta$ and cognitive decline. This therapeutic exploration began with the observation that several nonsteroidal anti-inflammatory drugs (NSAIDs) decreased A$\beta$ levels in animal models. Ibuprofen, sulindac and flurbiprofen were considered as promising drugs (26). Yet ibuprofen was ineffective for AD treatment in clinical trials, and independent research has failed to show positive results of treatment with NSAIDs in AD. Interestingly however, some NSAIDs possess copper-chelating properties and further research on possible therapeutic effects of selected NSAIDs in relation to the metal hypothesis of neuroinflammation is justified (27). Also the key role of microglia in neuroinflammatory processes deserves further attention; it has been reported that Se abrogates stress-induced microglial cell migration (28). Further research is necessary to explore if Se attenuates the inflammatory cascade associated with cognitive decline in AD.

## CONCLUSIONS

In conclusion, accumulated evidence proves that multiple biological pathways are involved in the neuropathology of Alzheimer`s disease and dementia. Various hypotheses, including the amyloid cascade, the decreased acetylcholine release, the metabolic theory, tau hyperphosphorylation and evidences of neuroinflammation, dominated the field for the last decades, resulting in a variety of pharmacotherapies, none of which succeeded to fully counter the pathogenesis of AD. Events

occurring intracellularly may prove to be more important for an understanding of the pathology of this disease. Thus, selenate proved to be a potent inhibitor of tau hyperphosphorylation (a critical step in the formation of neurofibrillary tangles), appears to protect amyloid precursor protein (APP) against excessive copper and iron deposition, shows anti-inflammatory properties, and protect microtubules in the neuronal cytoskeleton; primary prevention should aim at an adequate nutritional intake of Se securing optimal expression of selenoproteins.

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# Mini review on the current aspects regarding the possible interactions between anxiety, microflora and some metabolic dysfunctions

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**ABSTRACT**
**Anxiety is one of the most common neuropsychiatric disorders today, and its associated symptoms are mostly found among patients diagnosed with diabetes, compared to non-diabetic ones. There is a close correlation between the two diseases. The populations of microorganisms that colonize the digestive tract have many essential roles for the proper functioning of the human body. They communicate bidirectionally with the central nervous system and thus, dysbiosis installed at the digestive level can lead to both neuropsychiatric and metabolic disorders. This paper aims to present the correlation between the composition of the intestinal microflora and the appearance of metabolic and neuropsychiatric disorders (with special focus on anxiety).**

**KEY WORDS:**
**Anxiety, microflora, metabolics.**

## INTRODUCTION

Anxiety is one common neuropsychiatric disorder which symptoms are associated with diabetes symptoms. Thus, more symptoms are found in patients diagnosed with diabetes, compared with those who are non-diabetic. There is a close correlation between the two conditions, which generates a high risk of

medical complications and a decrease in the quality of life. The populations of microorganisms that colonize the digestive tract have many essential roles for the better functioning of the human body. They communicate bidirectionally with the central nervous system. Thus, dysbiosis installed at the digestive level can lead to both neuropsychiatric and metabolic disorders. This consideration encouraged scientific research to investigate the connection between the composition of gastrointestinal microflora and the degree of severity of symptoms of anxiety disorder associated with type 2 diabetes to obtain an alternative treatment for this comorbidity. The idea of correlation between the composition of the intestinal microflora and the appearance of metabolic and neuropsychiatric disorders is of great interest right now. Also, the analysis of the efficiency of probiotic consumption is also carried out to restore the balance of the digestive microflora, to improve the symptoms specific to the aforementioned pathologies (1).

**THE INTESTINAL MICROFLORA**

The term microflora (microbiota) represents the totality of the communities of microorganisms that inhabit a medium (2). The human body is covered by approximately 100 billion microorganisms (2), including protozoa, eukaryotes, viruses, fungi. All these microorganisms live in symbiosis on skin, in the oral cavity, in the genitals, respiratory tract and gastrointestinal tract (3).

The gut microbiota includes 300-500 species of bacteria that means a total of 10 times more than all the cells of the human body. Studies have shown that they fall into more than 50 branches (4), but most intestinal species belong to entrenches of the P*roteobacteria, Actinobacteria, Firmicutes and Bacteroidetes* (5), 90% of all being *Firmicutes* and *Bacteroidetes. Firmicutes* filum predominantly includes bacteria from the genera *Lactobacillus, Bacillus, Clostridium, Enterococcus* and *Ruminococcin*, *Bacteroidetes* are predominantly found in species of the genera Bacteroides and *Prevotella*, while *Actinobacteria* filum is represented by species of Bifidobacterium (6). Although it has been shown that there are 3 enterotypes, in which the genera *Prevotella, Ruminicoccus* and *Bacteroides* prevail, and this are influenced by age, sex and body mass index (5).

The name *Protebacterium* derives from the name of the Greek God Proteus, in the sense of highlighting the heterogeneity of this group of microorganisms. The Proteobacteria branch is the largest group in the field of bacteria and includes 6 classes: *Alpha-aproteobacteria, betaproteobacteria, Gammaproteobacteria, Deltaproteobacteria, Epsilonproteobacteria and Zetaproteobacteria* (4). All the bacteria in this filum are Gram-negative, but there are many differences between them.

Morphologically, proteobacteria can be cocci or bacilli with a spiral or filamentous form, mobile, peritracheal single-flagellates or biflagellate. There is also metabolic diversity, so these microorganisms can feed chemolithoautotrophy, chemoorganotroph, or autotroph (7).

Proteobacteria ranges from strictly anaerobic to strictly aerobic, optionally anaerobic and microaerophile. Analysis of this entangling from a taxonomic point of view led to the discovery that proteobacteria. These microorganisms can live free, symbiotic, endosymbiont or like intracellular parasites. Some parasites can have affinities for extreme temperatures: *Thiomonas sp*. (*Thermophilic species,* identified in thermal waters), *Polaromonas sp. (Psychrophilic species* that

lives in icebergs) (7). At the intestinal level, the most common microorganisms are from the filum *Proteobacteria*, which in increased numbers can cause disease. Numerous studies claim that the body's inability to maintain a balance in the composition of microflora can lead to the development of diseases (8).

Actinobacteria includes Gram-positive, immobile, non-sportive bacilli. There are least abundant in human intestinal microflora (6). Most of them are anaerobic and contain members of *Bifidobacteria*, *Propionibacterium* and *Corynebacterium* families and just the family *Streptomyces* family is aerobic (9).

At the intestinal level, the most common species of the *Bifidobacteria* family, genus Bifidobacterium are *B. asolescentis, B. animalis, B. brebe, B. bifidum, B. lonumg, B. angulatum* (9), that shows a great importance in boosting the immune system. Studies on the mentioned species have shown that the abundance of each depends on age - adults have a reduced number of actinobacteria and, in children, depends on the method of breastfeeding. For example, *B. longum* is generally identified in children receiving breast milk, while *B. teenentis*, common in adults, was found in the flora of children fed with powdered milk (10).

Along with the Bacteroidetes filum, Firmicutes is one of the two branches that predominate at the intestinal level. It contains Gram-positive bacteria with important functions for the health of the human body (11). The more than 250 identified genus are grouped into 3 main classes – *Clostridia*, *Bacilusi* and *Mollicutes* (12). The most important genres are represented by *Bacillus*, Clostridium, *Enterococcus, Lactobacillus* and *Ruminococcus* (13). They are involved in the fermentation process, where fibers are metabolized with the production of vitamins and short-chain fatty acids, such as butyrate, acetate, lactate with an essential role in preventing inflammation, or compounds with antimicrobial action (11).

Beside anaerobic–bound Gram-negative bacteria (14), Bacteroidetes filum comprises about 7000 species, predominantly identified in 4 genus – *Bacteroides, Alistes, Parabacteroides and Prevotella* (13). In addition to the positive roles, they have on the body, the species of the genus *Bacteroides* can also be pathogenic, as they leave from the intestinal level to other internal locations of the body (14).

Currently, it is well known that *Firmicutes* and *Bacteroidetes* branches predominate in the composition of the intestinal microflora, accounting for over 90% of the total microorganisms. Some diseases are also associated with an imbalance in the proportions of bacteria in the two groups (15).

Naturally and physiologically, there is variability in the composition of the intestinal microflora. The very diversity present at this level is considered an important marker of health of the digestive tract. It is difficult to identify the proportions of bacteria in a specific microbiota of an individual under normal physiological conditions, while the poor variability of microorganisms indicates the disturbance of homeostasis (16).

Intestinal dysbiosis is defined as disturbance of balance in the intestinal microflora, which means different proportions of the main groups of microorganisms in the gastrointestinal tract (15). There are many factors that can influence this aspect, including diet, age, birth method and antibiotic consumption (17).

**DIET**

It is believed that the diet affects microbial variability in the proportion of 50% in rodents and 20% in humans. It has been shown that short-lived changes in food style can greatly influence the composition of the digestive microflora, but for a short time. Although, even in the case of long-term changes, it may remain constant. Studies on several populations have led to results that suggest that diet is associated with microbial composition status (18).

The effects of protein consumption on intestinal microflora have been analyzed since 1977, when a low rate of *Bifidobacterium adolescentis* and an increased number of *Bacteroides* and *Clostridia* species were found in subjects consuming large amounts of beef compared to people who did not include meat in their diet (19).

Currently, studies of this kind continue and use the sequencing of the 16S subunit of RNA to analyze the composition of the digestive microflora. It has also been shown that high protein consumption from milk or peas causes an increase in the level of bacteria in the genera *Bifidobacterium* and *Lactobacillus* and a decrease in potentially pathogenic species such *as Bacteroides fragilis* or *Clostridium perfringens* (19).

As for the body of a newborn, the intestinal microbiota is mainly determined by the type of milk with which it is fed. Thus, in the case of children fed with breast milk, the composition of the microflora predominates the species Lactobacillus and Bifidobacterium. This fact greatly benefits the body in the sense of immunity because breast milk contains oligosaccharides broken down by commensal microorganisms into short-chain fatty acids that help to express immunoglobulin G. On the other hand, children fed with milk powder mainly have species of *Enterococcus, Enterbacteria, Bacteroides*, Clostridia and *Streptococcus* (17).

**THE AGE**

The aging process is genetically determined and regulated by environmental factors. Its effects include changes in the dynamics of biological processes, and researchers use sequencing technologies to establish the underlying mechanisms of this process and explain the connection between aging and some related diseases. More and more studies support the fact that, at the intestinal level, the composition of the microbiota is influenced by many changes that occur in the body with aging (20). For example, one study showed that with age, microaerophile bacteria predominate in the small intestine instead of aerobic bacteria (21).

The term immunosenescence is used to emphasize the alteration of the immune system over time. In the period of adulthood, the microbiota is relatively constant, aging affects the diversity in its composition and, implicitly, the defense function that these microorganisms perform (22).

**FUNCTIONS**

It is known that the intestinal microbiota is largely responsible for body health. This claim is supported by the many functions that the populations of microorganisms present in the gastrointestinal tract perform. These include nutrients digestion, metabolism of xenobiotics and drugs, antimicrobial protection, immunomodulation, but also maintenance of the structural integrity of the intestinal barrier (19).

One of the most important functions of intestinal microorganisms is the metabolism of some nutrients. The microbiota ferments

both exogenous and endogenous substrates, with the generation of compounds usable by the host organism. They can be directly beneficial, but they can also modulate immunological processes by positively impacting the general physiology of the body and especially the gene expression (23).

The fermentation process takes place in the colon. The reason for the presence and proliferation of bacteria in this place is given by environmental conditions that involve long transit period, high ph., low cellular renewal rate and limited redox potential. The source of nutrients for these microorganisms is macronutrients that have not been degraded during primary digestion due to their presence in excessive amounts or due to a very complex structure (23). As a result of this fermentation process, short-chain fatty acids such as acetate, propionate and butyrate are produced, as well as gases. Of these, acetate, essential for bacterial growth, is the most abundant and is very important in cholesterol metabolism and lipogenesis. Butyrate is the main source of energy needed by human colonocytes. Among its roles are induction of apoptosis of cancer cells, activation of intestinal gluconeogenesis, thus being important in glucose homeostasis. Propionate generated by microorganisms is also involved in the process of gluconeogenesis, but at the liver level and helps to generate satiety through interaction with fatty acid receptors (1).

Xenobiotics are defined as chemicals that are not naturally found in a living organism. These can be found in the external environment or as endotoxins, produced by some organisms (fungi, bacteria, plants) as a defense mechanism (24).

Xenobiotics that reach the digestive tract inevitably meet the populations of microorganisms present in the small intestine and colon. Studies to investigate the metabolism of xenobiotics have shown that enzymes in the cytochrome P450 group (about 3000) of bacteria are the key in the degradation of these foreign substances. Their neutralization can be achieved by inactivation or bioactivation, in the sense of turning them into an active metabolite (25).

Regarding the metabolism of drugs and the involvement of the intestinal microbiota in this process, specialists support the contribution of microorganisms. Also the fact that a better analysis of the complex relationship between the intestinal microflora and the host organism is needed to be well explained the mechanism behind the processing of drugs in the body. Studies conducted so far describe the existence of 2 main phases in the interaction of microorganisms with xenobiotics in general, including drugs, namely a first phase involving oxidation, reduction, hydroxylation reactions, mediated by the cytochrome P450 enzyme complex, and a second stage, in which conjugation reactions, such as glucuronidation and sulphuration, occur. At this stage, enzymes such as sulfotransferase, uridin-5-diphospho-glucuronosyltransferase, n-acetyltransferase, and glutathione-S-transferase conjugate the molecules resulting in the first stage, to promote their excretion through the urinary tract (26).

At the large intestine, the antimicrobial function is provided by its simple structure composed of double layer of mucus that prevents the penetration of pathogenic microorganisms at the epithelial level. The small intestine is protected by the microflora identified at its level. It has a discontinuous layer of mucus that does not provide good protection of the epithelium, and thus microorganisms are responsible, with the help

of the metabolites produced, to neutralize potential pathogens (19).

To obtain ecological advantages at the intestinal level, microorganisms develop different strategies that favor their survival and development at the expense of other microorganisms. These strategies can be categorized as non-peptide and peptide, depending on the mechanism of action or compound synthesized and released (27).

The non-peptide strategy involves removing some substrates from the environment, favoring the accumulation of D-amino acids, decreasing the redox potential, but also coaggregation. Bacteria can also produce reactive oxygen species, such as hydrogen peroxide, to limit the growth of other bacteria around, or contribute to acidification of the environment by producing short-chain fatty acids (27).

In the case of peptide strategy, microorganisms can produce or stimulate the synthesis of proteins with antimicrobial activity. Thus, they can stimulate the synthesis of catelicidins, type C lecithin and (pro)defensin by intestinal Paneth cells. This is due to pattern recognition receptors (PRR) that mediate this protein synthesis induction mechanism. Among the bacteria involved in this are Lactobacillus innocua and Bacteroides thetaiotaomicron (19). In the production of antimicrobial peptides, intestinal microorganisms can synthesize peptides of 10-50 amino acids that act against competing bacteria selectively, depending on the composition of the cell membrane and cell wall (19).

From the point of view of the location of synthesis, these peptides can be ribosomal or non-ribosomal. Non-ribosomal peptides are extensively studied secondary metabolites, from which antibiotics currently used such as penicillin, vancomycin and polymyxin derive. Ribosomal peptides are also called bacteriocins and have antiviral and antifungal potential. Many of these have been isolated from different strains of *Escherichia coli* but also from *Bacillus thuringiensis, Enterococcus fecalis* and *Bifidobacterium longum,* or different species of *Lactobacillus* (27).

Among the various mechanisms by which the intestinal microbiota manages to contribute to the organism's health is also the regulation of the homeostasis of the immune system. Numerous studies show that various signals from digestive tract populations are involved in the development of the immune system. They also manage to regulate both intestinal immunity and influence a systemic immune response (28).

In the first instance, the phases that are critical to the development of an individual's immune system take place in the first years of life, when the intestinal microflora has the greatest degree of variability. At 3 years old, the composition of the microbiota is very stable. The microflora interacts with both the innate and adaptive immune systems. Between microorganisms and innate immunity effectors, there is a two-way communication, in which the mucus-secreting Paneth cells, located at the intestinal level, produce antimicrobial peptides that interact with the microbiota and, consequently, determine its composition (29).

Most activated immune T cells are identified in some tissues colonized by commensal microorganisms, such as the skin and gastrointestinal tract. Most of these cells, producing interleukin molecules (30) IL-17 – cytokine with a role in mediating inflammatory processes (31) – and interferon

IFNγ (30)– cytokinin essential for activating macrophages and natural killer cells (32). They are found in the digestive tract and develop with signals from commensal bacteria (30).

Intestinal microbiota also plays a role in maintaining the structural integrity of the intestinal barrier. The term "intestinal integrity" is associated with the idea of continuity of mucus layer. The proliferation and controlled cell death of epithelial cells, and, not least, the good connection of these cells through intercellular junctions. Therefore, changes in these structures alter the integrity of the stable barrier which is important in separating the lumen content from the host organism (33). Some examples are: *Bacteroides thetaiotaomicron*, *Lactobacillus rhamnosus* and *Akkermansia muciniphilia*. *Bacteroides thetaiotaomicron* performs this function by inducing the expression of proline-rich 2A proteins, which are necessary to maintain the desmosomes of the intestinal villi (33). *Lactobacillus rhamnosus*, specifically the GG strain, synthesizes the proteins p40 and p75, which prevent apoptosis of epithelial cells, and *Akkermansia muciniphilia* is involved in reducing endotoxemia by stimulating the increase in endocannabinoid levels, which control the functions of the intestinal barrier (19).

## CONCLUSIONS AND DISCUSSIONS

Conditions such as diabetes and anxiety are commonly diagnosed worldwide, but the number of studies done to analyze a correlation between gut microbiota and these disorders is insufficient to generate generally valid conclusions. Demonstrating the influence of the composition of intestinal microflora in the conduct of physiological processes in the body can help implement a non-drug treatment alternative for metabolic and neuropsychiatric disorders.

Both disorders include high treatment costs, but also possible adverse reactions to the prescribed medication. In this context, restoring the composition of the intestinal microflora by taking probiotic supplements is an alternative treatment that can considerably reduce both costs and the possibility of unwanted reactions.

Numerous studies have been conducted to analyze the connection between taking probiotics and relieving anxiety or diabetes symptoms, but a very small number of investigations have been conducted in the context of the comorbidity of the two disorders. This certainly justifies the need to supplement the number of studies conducted with human subjects diagnosed with both diabetes and anxiety disorder.

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# Therapy management of treatment-resistant depression

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**ABSTRACT**

**Treatment resistant depression (TRD) is a subgroup of Major Depressive Disorder that does not respond to typical or first-line treatment approaches. Treatment-resistant depression is diagnosed when two appropriate antidepressant therapies fail. TRD may also be connected to lengthy stays in a hospital for medical attention. To distinguish authentic TRD, a number of definitions and standards have been presented, but no single definition or standard has yet gained acceptance. As a result, TRD poses unique difficulties for therapeutic strategies and efficient therapies. Recent meta-analyses, original studies of the PubMed literature were compiled. In this article, we'll try to give a comprehensive overview of TRD treatment options and discuss the difficulties that come with treating this condition.**

**KEYWORDS:**

**Treatment resistant depression, pharmacological treatment, therapy management.**

## INTRODUCTION

Among the most prevalent mental conditions in both specialized and general medical practice are major depressive disorder (MDD) and related mood syndromes. These disorders affect people at various phases of life and manifest in different ways. Although depressed symptoms occasionally occur as a natural component of human behavior, MDD can be crippling and, in the

worst cases, life threatening. There are variances in biological susceptibility, age of onset, risk factors, clinical presentation, and comorbidities among patients with the same diagnosis of MDD, and it can manifest at any stage of life. As a result, MDD is a very diverse illness, and around 30% of those who suffer from it are resistant to standard medical care (1).

The effectiveness of conventional therapy strategies for treating depression has been studied in a number of large-scale clinical studies. After four antidepressant treatment trials (within 14 months) in the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) research, the overall remission rate was 67% (2). 10% to 20% of MDD patients continued to experience substantial symptoms for at least 2 years after receiving successive therapies (3, 4).

Antidepressant medication fails to help a significant majority of depressed people. The psychopharmacology of mood disorders is facing a significant challenge in the form of treatment-resistant depression (TRD). Deep brain stimulation (DBS) and ketamine are two recent innovative therapies that offer immediate and occasionally sustained relief to a large percentage of TRD sufferers. The majority of diseases worldwide are neuropsychiatric illnesses. With an estimated 350 million sufferers globally, major depressive disorder (MDD) sufferers bear the heaviest single burden (5). Debilitating, recurring, and occasionally chronic in nature, MDD is now the second most common cause of disease burden in the world (5) and is expected to overtake it by the year 2030 (6). The large percentage of people who have co-occurring mental illnesses or other chronic health problems, as well as the duration and intensity of their symptoms, have a significant social and economic cost. The group with the greatest level of disability is those suffering from treatment-resistant depression (TRD).

The psychopharmacology of mood disorders is faced with a significant problem in the treatment of treatment-resistant depression (TRD) within major depressive disorder (MDD). Many people can see a reduction in depression symptoms attributed to existing pharmaceutical and behavioral therapies. However, the fact that some people's psychopathology is untreatable and that they haven't been able to achieve remission while receiving the present standard of therapy highlights the need for creative approaches. There are various ways to define treatment resistance (TRD), which is frequently defined as a poor response to at least two treatment trials. This includes switching between antidepressant classes, using pharmacological augmentation strategies, adding non-pharmacological interventions (such as psychotherapy, electroconvulsive therapy, vagus nerve stimulation, transcranial magnetic stimulation, etc.), and undergoing two to five antidepressant failures.

Treatment-resistant depression, also known as harder-to-treat depression, is a condition in which a patient's depressive illness does not improve sufficiently in response to adequate treatment (7). TRD is a complicated condition that takes into account a number of depressive subtypes, mental comorbidities, and associated medical conditions (8). It represents a frequent and challenging presentation to general physicians and psychiatric care (9).

Hospitalization is twice as common in those with TRD, and it costs more than six times as much as it does for depressive patients who are not treatment-resistant (10). Compared to costs for people whose MDD responds to therapy, TRD can almost quadruple both

direct and indirect medical expenses (11). Despite being most frequently linked to MDD, TRD episodes can also occur during the depressive phase of bipolar illness.

Among patients with bipolar illness who are undergoing therapy, more than 30% do not have a stable remission of depressive symptoms (12). There is no standardized operational definition of TRD (13).

Definitional conundrums restrict the capacity of guidelines authors or other specialists to integrate data and extrapolate TRD results to the variety of patient groups seen in routine practice. Furthermore, different conceptualizations of TRD have made it difficult and inconsistent to translate research outcomes or systematic reviews into clinical treatment guidelines.

Antidepressant therapy's goal is symptom remission or the restitution of euthymia, which is frequently indicated by a score of less than seven on the Hamilton Depression Rating Scale as a whole (HDRS) (14). The traditional definition of response—a score reduction of at least 50% from baseline on a depression rating scale (commonly the HDRS)—has been shown to be an inadequate objective because many patients who meet the requirements for response will still experience persistent symptoms and functional limitations (14,15). Additionally, unremitted patients have lower quality of life ratings and are more likely to experience relapses and recurrences of depression (16). In particular, 68% of respondents relapsed within the first year after therapy in the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial, the biggest randomized depression research to date, as opposed to 47% of remitters.

Additionally, lower acute remission rates and greater recurrence rates are to be anticipated when additional treatment stages are required. In fact, after undergoing four successive therapy trials, one-third of the STAR*D group never experienced remission (17,18). In addition, the citalopram Phase 1 therapy had a meager remission rate of 27.5% based on HDRS scores and 32.9% based on QIDS-SR (Quick Inventory of Depressive Symptomology, Self-Report) scores (19). These findings emphasize the significance of setting remission as the goal of treatment from the start for depression patients—and the requirement for better treatment approaches to achieve this goal.

Despite the shortcomings of existing antidepressant medications, progress has been achieved in treating resistant depression. As a result, this evaluation has three objectives: With an emphasis on ketamine and scopolamine, future approaches in the development of innovative treatments for TRD will be highlighted. These goals are to (i) define TRD, (ii) explain its causes, (iii) discuss existing methods for diagnosing and treating resistant depression, and (iv) describe the diagnosis and causes of TRD. In some studies (like STAR*D), treatment resistance has been identified prospectively through the use of a first antidepressant trial. In other studies, treatment resistance has been identified retrospectively through the examination of health records or patient recollection. Distinguishing treatment resistance from treatment failure or an early response followed by a recurrence has shown to be a major issue in research requiring retrospective evaluation.

Why do some depression patients respond to therapy with an one monoaminergic antidepressant whereas others take many treatments to achieve remission, assuming

remission is ever achieved? Major contributing variables are the variability of depression and the existing absence of accurate biological markers of responsiveness to specific treatments. Two distinct people can both meet the diagnostic criteria for major depressive disorder using the criteria from The Diagnostic and Statistical Manual of Mental Disorders (DSM), while having extremely different sets of symptoms (MDD)(20). In addition, there are differences in the comorbidity, course, and severity of depression (from moderate to incapacitating) (eg, anxiety disorders, substance misuse disorders).

TRD is thus a relative and somewhat deceptive phrase in of of itself. Patients with TRD aren't always "treatment-resistant," but rather, because depression is such a heterogeneous disorder, it is likely that patients don't receive healthcare that is tailored to their specific situation. More precisely, there is a requirement for therapy matching and innovative medicines that are especially geared toward "types" of depression that aren't currently covered by existing medications—thus, for individuals with TRD. TRD shows our incapacity as physicians to pair depressed patients with a treatment plan specifically for treating their individual psychopathology. It is not that individuals with TRD cannot react to antidepressant therapy. There are various clinical characteristics related with TRD, despite the fact that the neurobiology underlying depression and its subtypes has not yet been fully understood. Particularly, decreased function and quality of life, axis I and II comorbid illnesses, socioeconomic adversity, apprehensive and melancholy traits are linked to worse treatment results (21). Important clinical information: Anxious depression is a subtype of depression that affects 50% of individuals with depression, according to studies done between 2015 and 2017. Additionally, anxious depression, also known as MDD with concomitant anxiety disorder or MDD with anxiety symptoms, may have a distinct neurobiological profile (22). Individuals with anxious depression may benefit from antidepressant treatments, but they do not benefit for as long as patients without anxiety (23). Given the great frequency of depression, TRD is a condition that all psychiatrists who treat depression will undoubtedly run into. Before determining if a patient is indeed "treatment resistant," though, a comprehensive assessment is essential. When dealing with TRD, the maxim "diagnose before you treat" is applicable. Even if the patient has had the diagnosis for a long time, doctors should take their time to carefully assess it. The following stages in treatment, for instance, depend on determining if a patient has MDD with psychotic characteristics as opposed to melancholic sadness. Similar value can be gained from ruling out medical causes of depression, such as hypothyroidism or anemia. It is essential to evaluate adherence at every appointment since TRD can be brought on by failing to follow prescribed treatment plans. Patients often have mixed feelings regarding their diagnosis and course of therapy, as can their friends and family. Cost may also be a problem, although patients may find it awkward or difficult to discuss this with their doctor. As a result, the provider should establish a secure setting for these conversations. Treatment obstacles might also include cognitive impairments and trouble following instructions. It is extremely crucial in these situations for the provider to inform and support their patients, as well as to include family members and caregivers, if at all possible. When assessing individuals with TRD, it's critical to take into account their individual pharmacokinetics since some genetic variables may put them at higher risk

for developing treatment resistance and/or adverse effects. Fast metabolizers may experience more severe adverse events (especially in the early stages of treatment), which are thought to be connected to higher ratios of S-didesmethylcitalopram to S-desmethylcitalopram. For instance, several single nucleotide polymorphisms (SNPs) in the CYP1A2 gene, which codes for the hepatic enzyme CYP1A2, are indicators for rapid escitalopram metabolism (24). Smoking causes the CYP1A223 and CYP2B624 enzymes to become active, as well as the metabolism of the antipsychotic drugs clozapine and olanzapine (antipsychotic medications) (25). Smoking status may have a deleterious impact on the effective concentrations of numerous antidepressants (such as duloxetine, amitriptyline, bupropion, and fluvoxamine). On the other hand, quitting smoking might slow down the metabolism of antidepressants, which could result in higher levels and a heavier side-effect load. In addition, given the prevalence of polypharmacy, it is crucial to take into account drug-drug interactions since one medication's activation or inhibition of hepatic enzymes might have substantial adverse effects and/or affect how well other drugs work(26).

There are no simple formulas or diagrams for managing resistant depression. Instead, a variety of alternatives must be weighed and customized for each patient. Prior to making a referral to a higher level of treatment, optimization should be taken into account. For 6 to 12 weeks, optimization typically entails increasing the dosage of the medication as tolerated, at least to standard maximal doses, though it may also involve doses that are typically regarded as supratherapeutic (for example, sertraline 250 mg to 350 mg), especially for people who have previously required unusually high doses of the medication or have shown good tolerability and partial response (27,28). In addition to selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) for depression, atypical antipsychotics are the class of augmentation medicines that has received the most research (29). The FDA has specifically authorized olanzapine-fluoxetine combination therapy, as well as aripiprazole and quetiapine for augmentation (OFC). Risperidone and ziprasidone are two other atypical antidepressants that have been proven to be effective in randomized controlled studies (30). Numerous meta-analyses have shown that patients receiving atypical antipsychotics as augmentation drugs had almost two times the likelihood of going into remission as compared to placebo. (31). Target dose guidelines for antipsychotic augmentation are different from those for antipsychotic dosing and vary from 5 to 20 mg of aripiprazole, 150 to 300 mg of quetiapine, and 3 to 12 mg or 50 mg of OFC per day for aripiprazole. Because atypical antipsychotics have significant short- and long-term side effect consequences (e.g., drowsiness, metabolic syndrome and central obesity, extrapyramidal side effects), which raise the associated health hazards and risk of cessation, their use requires a comprehensive risk-benefit analysis (32).

## CONCLUSIONS

The very high percentage of individuals with MDD who may be categorized as having TRD poses one of several difficulties associated with treating TRD. Although a number of traditional and innovative techniques have been established, as previously discussed, more research is required to

fully comprehend the TRD as a disease in order to treat it effectively and, most importantly, to guarantee sustained response or continuing remission.

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# Pros and cons approach regarding the use of telemedicine in clinical practice

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**ABSTRACT**

**Telehealth and telemedicine cover similar services, including medical education, patient monitoring, patient consultation and transmission of medical images and reports. Improvements in health information technology, in addition to expanding access to health services, have spurred the advancement of telemedicine. The practice of telemedicine raises many questions regarding malpractice liability, including how to obtain informed consent, practice standards and protocols, oversight requirements for non-physician providers, and the implementation of professional indemnity insurance. Simply applying existing telemedicine malpractice liability principles is not sufficient, particularly when it is not clear what the appropriate "standard of care" is. That is why, through this paper, we aim to highlight the pros and cons issues related to the use of technology and telehealth services in clinical practice.**

**KEYWORDS:**

**Telemedicine, mental disorders, anxiety, technology.**

The use of technology in everyday life has become a necessity, so that 77.64% of the total population of Europe owns at least one smartphone, and among people with severe mental disorders, a percentage of about 70% has such a device.(1,2) The focus on the use of smartphones in the context of mental health insurance is supported by the high accessibility, on the one hand, as well as the unlimited possibility of creating applications

that offer therapeutic interventions for a wide range of mental disorders. (3) Smartphones devices have the ability to obtain multiple longitudinal data, which after an analysis could guide the diagnosis and monitor the treatment of the patient. (4)

This implementation of alternative care techniques of the patients required a particularly rapid development, especially in recent years, being also stimulated by the limitation of the capacity to refer to a specialized service, due to the COVID-19 pandemic. Thus, all of these have favored the development of telemedicine and mobile technologies for monitoring mental health. A recent study, which corroborated the data obtained from 17 countries, showed an important increase in the use of digital health technologies in institutions which take care of patients with mental disorders. Also, more effective support was ensured at home, for people with mental disorders, to overcome the pandemic period. (5)

The "digital health" covers a wide variety of technology areas, including wearable medical devices, telehealth (including telemedicine), mobile health (mHealth), and health information technology. Mobile applications (mHealth) are tools that can be used to encourage healthy behavior, to facilitate the access to useful medical information and, in some cases, to receive medical care or manage one's health. mHealth applications can contribute to the efforts to increase access to health, reduce the costs, improve quality of care and enable patients to receive personalized medicine. (6) A meta-analysis of 66 randomized controlled trials demonstrates the effectiveness of apps used for the management of depression, which far exceeded that of the placebo control group. In the case of anxiety disorders, the results of using specific apps were comparable to those of a face-to-face intervention, but professional support via telephone call or personalized therapist responses, in parallel with the use of the app, had longer-lasting and better effects, compared to the studies that focused only on the effectiveness of the software for the management of anxiety symptoms.(7) The major problem with the apps for depression and anxiety is the reduce number or even lack, in some cases, of evidence-based clinical trials. After analyzing 293 apps aimed to self-management of anxiety and depressive disorders, only 55.3% had credible references included in the description, and only 6.2% of them published some evidences related to the effectiveness of the app. (8) There are still many improvements which can be brought for these apps, but they already have some benefits, especially for people without severe symptoms or those who do not have access to traditional services, like easy accessibility, data scalability, and low cost of an effective self-management intervention for depression and anxiety symptoms. These improvements can be represented by(9):

- the involvement of people with psychological, psychiatric and medical skills in the development of applications;
-the implementation of a centralization system of the data collected by these applications at the national level;
- a more accurate evaluation of the effectiveness of these apps;
-optimizing the user experience;
-the use of validated treatment techniques;
- an evaluation of the possible long-term adverse effects related to the use of the applications.

Also, doctor-patient text messaging application is a new technology for managing the patients, but there is not much information about how often this technology is used by doctors and patients or how it affects patient outcomes. There can be benefits as well as

disadvantages to texting between doctors and patients, according to some experts. Although there is no exact substitute for in-person doctor visits, it can be beneficial for the patient to text the doctor with specific information, such as a question about using an over-the-counter medication. Thus, it is important to strike a balance between patient convenience and clinician availability so that the quality of care is not compromised. (10)
Digital therapeutic relationships, although not as effective as the therapist-patient relationship, can promote change without the need for human intervention. According to some researches, some patients prefer addressing a chatbot type service due to the increased comfort of anonymity and the detection of a pathology can be improved. (11) The development and implementation of more complex interactive systems is inevitable, as current chatbots are limited in their ability to provide appropriate contextual responses to complex language inputs, with important patient safety concerns.

The relationship between social media and mental health has been studied by both the medical literature and the media, which claim that there is an increased rate of mental health problems in people who use social media abusively. Subsequently, more and more studies began to support the idea that it is not social media time or exposure itself that is strongly associated with negative mental health outcomes, but the quality of time spent with a gadget and social media interactions seem to be much more important. (12)

In recent years, the issue of social media content has been an important topic for major social media companies as they try to remove content that may be related to self-harm or suicide. (13) The social networks can be utilized for the prediction of relapses or in the detection of the worsening of the symptoms of mental disorders, for example, in the case of patients with schizophrenia. Interpreting social media interaction through natural language processing provides a practical means of understanding the general trends of a population.(14) For example, Twitter had a significant increase in the number of posts in the period March-May 2020 compared to the previous year, and following an analysis of 60 million posts, an increase in a coping mechanisms was detected, in response to the COVID-19 pandemic. Also, the recognition of emotions based on the photo-video content of posts in the online is in continuous development.(15) Studies show a strong relationship between posting darker-colored photos and depressed mood, although the errors are considerable because of the lack of a broader context.

The different needs of young people can be achieved with the help of social networks, which represent a possible therapeutic tool.(16) There are applications, such as PRIME, which is designed for patients with schizophrenia and promotes recovery of function and reduction of negative symptoms, for example avolition, through a personalized support network. Another example would be the Moderated Online Social Therapy (MOST) platform that offers personalized therapy combined with social connections. However, we must take into account the risks of using social media as a therapeutic tool. Thus, misinformation and stigma cannot be ignored. Stigmatization on social networks is, unfortunately, a common reality, and ethical issues must be brought to the attention of the users. (17)

Among the most important advantages of telehealth are the reduction of health disparities in areas with limited access to medical services. About 20% of the United States population lives in rural areas, and only

9% of physicians serve these areas. Telehealth aims to eliminate transportation costs, which often burden patients of low socio-economic status. Through similar mechanisms, it can improve health literacy by providing patient education and prevent hospitalizations by ensuring medication adherence. (18, 19)

Online consultations have a number of limitations, being difficult to use due to socio-economic problems and the reluctance of some patients. Thus, there are people who do not have skills regarding the use of technology, show distrust regarding this type of consultation or the patients who want to keep the interaction "face to face" with the psychiatrist. Disadvantages of telehealth include limitations in performing complex physical examinations, technical difficulties, security breaches and ethical issues. Some critics argue that telehealth can negatively affect continuity of care, arguing that online interactions are impersonal and dangerous to the extent that the virtual doctor does not have a complete history and physical examination to aid in diagnosis and treatment. Although physical presence at the doctor is necessary in many cases, telehealth should be considered the best method to replace physical consultations. (20)

## CONCLUSIONS

In conclusion, there are some limitations of telemedicine and the use of tehnology and this procedure is not suitable for all patients. Therefore, further studies are needed to assess the correct needs of telepsychiatry.

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# Humanistic Contributions

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# A most actual topic: didactogeny as a source of a negative attitude towards learning

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**ABSTRACT**

**Teachers' inability to comply with the rules of the organization and conduct of the training process leads to a negative attitude of their students towards learning. The evidence that specialists from this field have been able to record to this day attests that, as a rule, the appearance of the targeted type of negativism is linked to cases where the inappropriate professional behavior of the teaching staff aims at disseminating *phobia-induced states in the classroom, classroom-induced anxiety, classroom-induced frustration, classroom-induced depression and/or classroom-induced neurosis*. As soon as they appear, the states in question impose themselves as factors affecting the working disposition and resistance to effort. In such a case, students will find it extremely difficult - or even impossible - to perform a rewarding, fast and high quality activity. Their attitude towards learning will degrade significantly, turning into a sort of position that will minimize - or even exclude - the idea that things aimed at acquiring knowledge, skills and abilities should be done with selflessness and pleasure, out of conviction and on one's own initiative, conscientiously and diligently.**

**KEYWORDS:**

**Didactogeny, negative attitude towards learning, classroom-induced phobia, classroom-induced anxiety, classroom-induced frustration, classroom-induced depression, classroom-induced neurosis, somato-physiological effects.**

A previous study of ours [1] showed that didactogeny, viewed as a concentrated

[1] See, in this respect, M. Șleahtițchi**.** Didactogeny, Between delay and fatigue, overwork and demotivation. in: *Bulletin of Integrative Psychiatry* , New Series, Year XXVIII, no.2(93), June 2022, pp. 115-127 [ISSN 2393-2694; ISSN-L 1453 - 7257] [Journal B+ CNCS and Indexed IDB by Index Copernicus International , DOAJ, Erih Plus, Gale Cengage, CEEOL, Crossref]. Available on: http://dev.buletindepsihiatrie.ro/bpi-nr-1-2022/ and/or M.Șleahtițchi. Didactogenia ca factor de patologizare a capacității de învățare (elemente pentru o meta-analiză a fenomenului de eșec școlar)/ Didactogeny as a factor pathologizing learning ability (elements for a meta-analysis of the phenomenon of school failure) . in: *Psihologie.* Revistă științifico-practică, volume 40, nr. 1, 2022, pp. 43-57 [Category B, ISSN E 2537-6276, ISSN P 1857-2502, http://key.upsc.md].

expression of the professional errors made – either voluntarily or involuntarily – by the representatives of the teaching staff, puts an unwanted pressure on their disciples, thus significantly eroding their learning capacity.

The topic will be developed in the following, for evidencing that, in parallels with alteration of the learning capacity, the incapacity of the teaching staff to comply with the organization norms of the education process also influences the manner in which their disciples manifest their position for what is generally defined as ”to study”, ”to know”, ”to acquire”. This time, the nature of the situation permits to mention, with no doubt, negativization of these disciples with respect to learning.

In the situations in which the errors made by teachers do not have significant negative effects – as shown by D. Popovici [1] –, the pupil has a positive attitude towards the process to which he takes part. He comes to school with pleasure, participating actively and with good results to the learning activities. If such errors persist and get extended, the teacher may provoke a change of this attitude, so that the pupil will either disregard the psychological and pedagogical norms, or he will not correctly fulfill his real obligations, the teacher becoming the source of hid negative attitude for learning.

Which are the conditions under which this type of negativization is to be manifested? Which signs do indicate its real presence?
A careful review of the specialized bibliographical sources [2] indicates the existence of at least five revealing signs to be necessarily considered and nuanced.

*The first sign* is related to the cases in which an unsuitable professional behaviour of the teaching staff results in *class-induced phobia*, manifested, in most of the cases, as an excessive and persistent concern for learning, as an unreasonable agitation firstly caused by the fear of not being humiliated or embarassed by the teacher. The unrest and fear are frequently accompanied by negative effects, such as unconcern for the study, manifestation of ”intellectual idleness”, and/or even as anger. As an expression of an authentic adaptation disorder, *class-induced phobia* results in the absence of such categories of pupils from all courses, of a dutiful preparation for each discipline of study, along with the disappearance of their openess, understanding and esteem for their teachers, of not using their mobile phones during test papers and exams or of not leaving the classrooms during the teaching process. Also, not rare are the cases in which, against the same background, *refusal reactions* may occur (the pupils openly giving up their studies) and/or *panic reactions* (when the attempts made at keeping them in the classroom by force produces a violent terror).

Inspired by the works of S.G. Hofmann – especially from *Cognitive factors that maintain social anxiety disorder: A comprehensive model and its treatment implications* [3], I can assert that all pupils forced to experience *class-induced phobia* will sooner or later come to think that:

- **(i)** their value is given by the manner in which their teachers evaluate them (which makes them fearful of a harsh judgement from their part);
- **(ii)** they lack the ability to communicate with both their teachers and colleagues (which makes them anxious that, soon in the near future, they will not be

capable to interact with them, any more);

**(iii)** they are not sufficiently good for learning activities (which makes them feel as ”unwelcome”, ”non-attractive”, ”inadequate”);

**(iv)** they cannot control their emotions, a situation they feel as impossible to be changed.

Obviously, *class-infuced phobia* causes considerable prejudices to the instruction process, limiting its energies and denaturating its effects. That is why, the persons who have to demonstrate involvement and responsibility in the process of acquiring knowledge, skills and practice will tend to consider it as ”a dangerous place” and finally of predicting the collapse of all hopes related to learning and to its probative role.

The *second sign* refers to the cases in which an inadequate professional behaviour of the teaching staff causes *class-induced anxiety*, a type of unrest representing, *en meso*, a deep restlessness derived from pupils’ fear of not being judged in too ruthless terms by their teachers. This condition is manifesting by an obsessive concern related to the possible installation of a conflictual climate and, respectively, by the tendency of resisting such a perspective. Also, as shown by the results of several empirical psychological investigations, *class-induced anxiety* may affect the manner in which pupils appreciate themselves, while inhibiting, at extremely high levels, their desire of showing off their expertise and the assimilated aptitudes. In certain cases, *selective mutism*, a psychic type disorder involving the inability to utter words/ to verbally communicate during the teaching-learning process (but not within the family or friends’ circle) gets installed. Looking ”dumbfounded”, with insipid facial expressions, in certain circumstances, pupils disclose one of the following features: avoidance of any visual contact with those surrounding them, excessive shyness, exaggerated sensivity to stimuli (especially to physical touch), negativism, oppositional conduct, tantrum.

Frequently, *class-induced anxiety* is manifested as *anxiety to testing* (exams, coloquia, test papers, etc.). Even if some pupil may have good or even very good theoretical knowledge or practical abilities, as well as a strong motivation to show them off, the anxiety induced by testing will prevent him to obtain the expected result. By virtue of the fact, this type of anxiety may affect both the concentration of attention and also the mnesic capacity, thus making difficult or even impossible recalling of the previously assimilated material. Consequently, the marks obtained will not reflect pupil’s real level, while not fully characterizing the efforts he made for preparing the evaluation. A vicious circle is finally created or, in other terms – a diabolic chain, leading, as asserted by the specialists in the field, to the fact that ”anxiety induced by testing leads to poor results which, in their turn, increase the two dimensions of the anxiety caused by testing, more exactly the convinctions and the negative emotional states manifested when faced to situations of evaluation”.

Nothing gratifying, obviously. One may observe, with real concern, how the learning process loses part of its role and vigour, being affected by an extremely hostile attitudinal-emotional condition which, putting in a bad light the psychomoral condition of those ”expected to study diligently”, transforms the learning activities into sources of increased agitation and obscure panic.

*The third sign* is related to the circumstances in which the professional errors made by

teachers contribute to the installation of *class-induced frustation*. Acting with indifference, intolerance, lack of tact and/or empathy, those entrusted with the high mission of teaching succeed only in provoking in their disciples uncertitudes and inhibition, insecurity and pesimism, feelings of inferiority and helplessness, discontent and unconcern. What should have appeared as ”a progressive, methodical and intensive activity permitting full access to knowledge and action, under the supervision of the teaching staff and based on pupils' personal effort”, or ”a complex, systematic activity organized by both disciples and teachers, aimed at providing the former ones a system of expertise, skills, capacities and competences” is a wholly different thing. Some essential elements disappear, such as: the personal interest of the pupils, their effort and their responsible involvement. The best and most beautiful part of the learning process gets dark, goes out, ceases to exist. Pupils are facing an accomplished negative situation: they are considered unimportant. Consequently, in their mind, the idea of learning is manifested as ”a breakdown of hope” or – in other terms – a ”deprivation of things” (for which, in the beginning, full interest and opening did exist).

*The fourth sign* is manifested each time when *class-induced depression* gets installed. When – either designedly or not – teachers treat their disciples with indifference, arrogance and/or triviality, the latter ones lose their temper, coming to be dominated, to a more or less extent, by a deep affective restlessness, characterized by irritability, discontent and sadness. One may observe their tediousness, their lack of interest for the discipline they are taught, their disengagemnet, objection, rejection. Feelings of uselenessness, unhappiness and failure act as intimate obstacles which, in such a moment, alter considerably their ability of sensing, knowing and acting.

The specialized sources already mentioned put forward the idea according to which the depressive disorder induced in the classroom may be, as in many other situations, of three distinct types – *major*, *distimic* and *double*.

*The major depressive disorder* is characterized by the presence of one or several episodes. Depending on their number, it may be classified into *major depressive disorder with a single episode* and *reccurent major depressive disorder.*

*The major depressive disorder with a single episode* characterizes the type of whirling of the learning process, occurring when, almost on a regular basis, the following symptoms are observed along about a fortnight:

- A bad mood (the pupil manifests deep prostration and an intense despair);
- Lack of interest for the current didactic activities (the pupil is not capable of being pleased by the discipline that used to draw his attention, any more);
- Decreased energy and fatigue (the pupil feels he is no longer capable of achieving his learning tasks, he feels tired and exhausted);
- Installation of feelings of guilt, futility and inaptitude (the pupil is continuously blaming himself of an non-existent guilt, he feels he disturbs his teacher, considering useless his presence in the classroom);
- Difficult concentration and thinking (the pupil shows retardation of his reasoning capacity, which may be explained by the attempt at reducing

the disconfort induced by learning activities).

In the opinion of several specialists, not all such symptoms have necessarily to be manifested for ascertaining the existence of major depressive disorders, only two of them – namely, a bad mood and the loss of interest for study – being sufficient. They also consider that, in cases of major depressive disturbances, actually representing ”a change compared to the previous level of work”, interventions of medical nature are not to be justified, in any way.

When *depressive disorders of recurrent nature* are manifesting, some depressive episodes with multiple/ varied intensity occur, interrupted by calm intervals, characterized by chronic evolution over a large time period. Usually, the pupils susceptible to recurrent depression evidence the following defining traits:

- They have suffered more than three major depressive episodes;
- They suffered two episodes of mood disorder in the last three years;
- They manifested one episode of depressive disorder a year ago;
- They constantly show residual symptoms of a depressive episode (for example, the absence of any interest for learning and/or avoidance of participating to the activities organized in the classroom/ academic circle);
- Severity of the depressive episode (including traits with a pronunced psychotic character).

In its turn, *distimic depressive disorder* is characterized by a long duration (approximately two years), as well as by symptoms whose severity is not sufficient for defining them as ”signs of a major depressive episode”. Along the two year-duration of this type of disorder, symptomsm may not appear for a maximum of two months. In cases related to the occurrence and maintenance of depressive disorders of distimic nature, the pupil has a reduced energy, facing difficulties in concentration or decision making situations, a low self-esteem, unconcern for study and despair. Once again, according to specialists, not all symptoms may be necessarily manifested, but only two (whichever) of them.

As to the *double depressive disorder*, it is manifested when pupils affected with it show simultaneously a major depressive disease.

Contributing significantly to the instauration of a low tonus of the psychic activity, accompanied by an asthenic mood, excessive sadness, deep melancholy and an over-amplified fatigue, *class-induced depression* expresses the type of malefic energy which can easily deform the meaning of the learning process (= ”selective and permanent change of knowledge and conduct centered upon pupil’s whole personality, on his genetic endowment, on his intellect and motivation”). Obliged to face such depression, many – if not all – of those expected to register performances involving ”a selective and permanent change in their expertise and conduct” will not be able to resist difficulties of cognitive type and will lack the initiative necessary for the assimilation of new ideas and aptitudes. From one day to another, and more and more frequently, they will suffer, as expressed by N. Sillamy [4], by this helplessness, feeling that their intellectual capacity, especially their atention and memory, are degraded.

Finally, the *third sign* shows that the professional errors willy-nilly made by the representatives of the didactic staff provoke to

their disciples a *class-induced nevrosis* or – as a considerable number of specialists prefer to call – a *didactic neurosis*. Expressing a specific manner of defense against the fear, hate and aggressivity generated by the professional incompetence of their teachers, this nevrosis may be manifested in a variety of ways. Along the time, at least eight types have been established, as follows: *alarming, obsessive, depressive, hysterical, asthenic, hypochondric, logoneurotical* and *anorexic*.

*Didactic neurosis of alarming type* may be associated with the installation of deep unrest and disorder, a condition generated by the defying/ aggressive conduct of the teacher and/or by the possibility of obtaining bad marks at different tests (exams, coloquia, etc.).

*Didactic neurosis of obsessive type* is characterized by the manifestation of some nervous tics, capable, as ”mild” defense mechanisms, to protect the pupils, at least to some extent, against the psychoemotional stress induced by such unadequate behaviours from the part of the didactic staff (grimace, frown, raising eyebrows, blink of the eyes, wrinkling of the nose, movements of the head in various directions, fist clenching, yawning, sighs, voice correction, jerky exhalation, use of obscene words in public (coprolalia), repeating of one’s own words (palilalia), imitation of the movements and gestures of those around him/ her (ecokinesis), etc.). The observation to be here made is that such tics tend to become more and more frequent, if the teachers will insist mentioning them or if they will ironize them.

*Didactic neurosis of depressive type* characterizes a depressive condition and a low self-esteem of the pupil, his estrangement from colleagues or even a suicidal tendency.

*Didactic neurosis of hysterical type* is accompanied by disproportionate emotional discharges (laughter or crying accesses, asphyxia, clenched teeth, unnatural bodily positions, etc.) manifested by a pupil when faced with an impulsive, intolerant and defying teacher.

*Didactic neurosis of asthenic type* occurs when, because of the hostile behaviour of the teacher, his disciples are affected by intellectual fatigue (diminished attention, difficult concentration, memory loss, slow thinking), diminution of vitality (lack of initiative, inhibition, loss of interest for school activities, loneliness) and/or even altered personality (irritability, loss of emotional control).

*Didactic neurosis of hypohondric type* occurs when the pupil, strongly influenced by the behavioural attitude expressing hate, disdain and antipathy manifested by the teacher, concentrates his attention on his own health condition, fearing of not getting ill.

*Didactic neurosis of logoneurotic type* is installed when the pupils, confronted with the psychotraumatizing attitudes of their teachers start, from some moment on, to stammer, their speech being affected by hesitations, abrupt repetitions, embarassing pauses or imposibility to articulate certain words.

*Didactic neurosis of anorexic type* reveals the connection existing between an excessively brutal behaviour of the teachers and the alimentary alterations observed among his pupils (reduced apetite, refusal to eat, strange alimentary habits, etc.).

As a natural consequence of the communication errors done, either voluntarily or not, by the representatives of the teaching staff, *class-induced neurosis* or – in other

words – *didactic neurosis* – expresses, in its turn, the type of psychomental disorder through which the interest for learning is relatively easily lost. Or, one cannot ask pupils to have a positive attitude for what actually is ”a change in knowledge and conduct”, if they are not ready to make the necessary efforts, manifesting a low self-esteem, being fearful and showing, from one day to another, disproportionate emotional states, intellectual fatigue, lack of initiative, inhibition, loneliness, irritability and an increased concern for one’s own health condition. Against such a background, as stated by the same N. Sillamy [5], one does not feel comfortable, losing confidence in his own forces, denying his own actions, becoming aggressive towards others and towards himself.

When speaking of the maleficent conditions caused by the behavioural errors made – either voluntarily or involuntarily – by the didactic staff representatives, one should necessarily mention that each of these states – be it *class-induced phobia* or *class-induced anxiety*, *class-induced frustation* or *class-induced depression*, *didactic neurosis of alarming type* or *didactic neurosis of asthenic type* - is characterized by the capacity of producing various effects of somato-physiological nature.

However, manifestation of such effects is quite natural. When something bothers us, affecting our daily activities, our brain produces, as frequently observed, a *negative emotion with an intense impact upon our body*. The frequency of nervous impulses increases, so that the brain has to rapidly produce neurotransmitters, such as *adrenaline* (a hormon secreted in the blood, in situations of stress, by the meduloadrenal gland, whose function is to prepare the organism for ”fear, run and fight”) and *cortisol* (a steroid hormone produced by the adrenal for supressing the answers coming from the immunitary system). ”Combining their efforts”, these two neurotransmitters are eventually responsible for various bodily disfunctions.

According to the specialists – some new names [6] besides the already mentioned ones –, depending on the hurtful condition induced by an inadequate professional behaviour in the classroom, the mentioned effects may appears as:

- *class-induced phobia*: difficult breathing, muscle tension and trembling, tachycardia, flushing of the face, abundant perspiration, palpitations, nausea and other manifestations of digestive discomfort;
- *class-induced anxiety*: cold and sweat hands, palpitation, dry throat and mouth, flushing, abdominal pain, excessive perspiration, feeling faint, rapid respiration, muscle tension, difficult walking;
- *class-induced frustration*: circulating disorders (hypertension), respiratory disorders, bruxism (gritted teeth), migraine, muscle tension, colitis, insomnia, acne (blak or white spots or pimples present on the surface of the skin), ulcer, anemia, pancreatitis;
- *class-induced depression*: vertigo, too long or too short sleep along several nights, involuntary loss or increase in bodily weight, altered apetite, low energy, insomnia, agitation or slow psychomotor movements, headaches, chest aches, digestive didorders (diarrhea, constipation);

- *class-induced nevrosis*: anorexia or bulimia, sleep disorders, headaches, dispnea (sensation of insufficient air), cardiac palpitations (the feeling that the heart ”wants to come out from the chest”), suffocation (laboured breathing), the sensation of a lump in the throat, abdominal discomfort (nausea), transpiration, shiver (tremor).

Obviously, the effects of somato-physiological nature do not affect equally all pupils facing the professional incompetemce of their teachers. The impact of emotions upon physical health vary, once again, from one individual to another, in closest relation with one’s personality, character and temper, with one’s manner of feeling and thinking.

It is beyond any doubt that, once installed, such somato-physiological disorders amplify the negativization attitude manifested by pupils *vs* learning. The physical condition, the health state and the physiological equilibrium impose themselves – according to the specialists in the field [7] – as factors leaving their mark on the inclination towards work, and also on the resistance to effort. Accordingly, for a pupil affected by dificult breathing, muscle tension, tachicardia, abundant perspiration, palpitations, abdominal pain, circulation disorders (hypertension), migraine, anemia, feeling faint, insomnia, head and chest aches, dispnea, cardiac palpitations or shiver, it will be extremely difficult – or even impossible – to perform a satisfactory, rapid and high-quality activity. The anomalies and disorders of somato-physiological nature will favor installation of a huge insatisfaction, a condition which, sooner or later, will drastically reduce the interest/ opening towards learning.

A study developed in the first half of the '70s by M. Gilly showed that somato-physiological weakness, that may be manifested as sensorial disorders, affections of the nervous system, nasopharingeal diseases, metabolic or endocrine disfunctions, perturbation of sleep, breathing or blood circulation, will considerably influence the learning process, in general, as well as the attitude for this type of activity, in particular. Counting on the obtained results, the well-known French researcher draws the attention on the fact that the somato-physiological disorders, even if not severe, may alter school activity and, respectively, the attitude towards learning. In his opinion, it is sufficient that such disorders should be chronic for compromising the presence in school.

The same researcher asserts that the dfificulties of somato-physiological nature may have an either *direct* or *indirect* influence on the attitude of pupils *vs* learning. The direct influence is expressed by an increased degree of dissatisfaction and, respectively, by a reduced mobilization and concentration capacity. The indirect influence assumes the intervention of certain attitudinal factors from the part of the teaching staff, of the parents and of the child, as a reaction to such difficulties. In many situations, the teachers and/or parents involved are not sufficiently aware of the fact that the difficulties of somato-physiological nature may considerably deform the attitude towards learning. Usually, such positioning involves either their understatement and their substitution with other elements (laziness, malevolence, carelessness, lack of attention and energy, insufficient maturation, etc.), or an interpretative supra-protection optics. While the former type of approach deepens the intraschool and/or intrafamily conflicts, the latter perpetuates the ”infant” condition, maintaining a passive attitude from the part of

the child, perpetually dependent on adults. By pampering a pupil she sees as ”clumsy and frail”, his mother will offer to him, in too many cases and without realizing what is she doing, ”an affective compensation to his school disappointments”, which will finally lead to child’s indulging in this position of avoiding to face any obstacle [8].

The difficulties of somato-physiological nature, correlated with a negative attitude towards learning, trigger mechanisms which actually suppress the labour force, the resistance to effort, the rhythm and efficiency of school activities. A considerable number of pupils, even endowed with a normally developed intellect, experience the impact of the difficulties of somato-physiological type, manifest passivity, get hardly mobilized, are excessively slow, needing a double or triple time period – compared with their colleagues – for accomplishing their school tasks. Contrary to the relatively good intellectual level and to the desire to be successful, they are not capable, as observed by several specialists – D. Sălăvăstru [9] or T. Kulcsár, for example [10] - of working more rapidly, of registering a satisfactory quality and precision. Any attempt from the part of the school or of the family to render their pupils more concentrated, more rapid, more efficient leads to dissensions, confusions and failure.

To conclude with, the incapacity of the teaching staff of observing the organizational and developmental norms of the schooling process leads to negativization of their disciples attitude *vs* learning. The proofs recorded, up to now, by the specialists of the field demonstrate that, usually, the manifestation of such a negativization attitude is related to the cases in which an inadequate professional conduct of the teaching staff leads to the installation of *class-induced phobia,class-induced anxiety*, *class-induced frustration*, *class-induced depression* and/or *class-induced nevrosis.* Once installed, such conditions represent factors which equally affect the desire to work and the resistance to effort. In such cases, it will be extremely difficult – or even impossible – for pupils to perform a fully satisfactory, rapid and high quality activity. Their attitude towards learning will significantly degrade, being transformed into a position which will minimize – or even exclude – the idea according to which the acquisition of knowledge, competences and aptitudes should involve abnegation and enjoyment, one’s full conviction and initiative, dutifully and diligently.

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# Digitization of medical practice through telemedicine

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**ABSTRACT**
**The present study proposes an interdisciplinary approach correlating the new research devoted to the concept of telemedicine and the practice of telehealth services with the legislative norms and recommendations for telehealth services as part of a more complex process of digitization and democratization of medicine. Evidencing of the relations manifested between the results of recent analyses and the legal norms and recommendations may throw light on the possibilities of a performant medicine, developed in a digital environment, for the benefit of patients. Marking the areas characterized by inconsistencies, shortages, and overlays, along with their rightful elimination might improve and adapt the medical practices of today into such a new milieu, under conditions of safety and confidentiality, while increasing the quality of the medical services and their targeting upon patient's needs.**

**KEYWORDS:**
**Telehealth, telecare, eHealth, digital literacy, digital exclusion.**

## INTRODUCTION

Nowadays, medical practice faces an ample transformation process. If traditionally, medicine has been mainly practised as an affront meeting of those involved in the process, in a pre-established physical setting, today it gets extended in the virtual/online background, as well. In time, the care health services performed in hospitals and clinics will occur at patients' homes, by means of mobile devices (1). The fitting of the procedural paradigm is supported by unprecedented communication technologies. At the same time, such change is accelerated by the necessity of granting access to patients from isolated areas to high-quality medical services, as well as a safe, efficient, and low-cost interaction.

The complex situation created by the COVID-19 pandemic (2,3), the quarantine, the restrictions, the isolation, and the physical distances called for the development of a digitalized medical system capable of assuring and supporting the patients living at either short or long distances from a sanitary unit. In this context, some authors (4) view the telemedicine practised during the pandemic as doctors' first line of defence to slow the spread of coronavirus, maintaining social distancing and providing services by phone or videoconferences for mild to focus personal care and limited supplies to the most urgent cases.

If in high-income economies there exist traditions, procedures, and professional standards for practising telemedicine even prior to the COVID-19 pandemic, in lower-middle-income economies, telemedicine was either hardly regulated in general terms or no legislative regulations were in force in this respect. The process of medicine's translation in the digital framework has been accelerated in the last two years, at an unprecedented pace. The manner in which the new paradigm of medical practice develops requires interdisciplinary research, cooperation between disciplines, the collaboration of medical specialists with researchers from disciplines such as philosophy, ethics, communication sciences and communication technologies, and collaboration with policy-makers.

The present study attempts at correlating, by an interdisciplinary approach, and in the first stage, the new investigations developed in the field of telemedicine, with the legislative regulations regarding the practice of telemedicine, the recommendations of the international forums, professional associations, and policy-makers. Evidencing of the relational connections between the results of recent investigations and the actual legal norms and recommendations throw light on the possibilities of performing medicine in a digital framework, so that both the recipients of medical services and the service providers become aware of the benefits and limits of such a new practice, coming to know their rights and obligations and to find the most efficient solutions for its adaptation to the new conditions. At a second level, the study will provide a qualitative interpretation, from the perspective of the ethics and philosophy of communication, of the pros and cons characterizing the idea of telemedicine.
Besides the articles approaching topics such as telemedicine, telehealth, medicine digitization, medicine democratization, and grey literature, the present study has also considered the legislative regulations issued at a national level and the recommendation of international or European institutions.

Critical analysis of this data was based on the principles laying at the basis of medicine democratization, on the principles and ethical values capable of assuring a safe physician-patient relation, relying on their confidence in the digital environment.

## THE CONCEPT OF TELEMEDICINE: STANDARDS AND GUIDES

The concept of telemedicine *(tele* = distance in Greek) is not a new one. It is based on an old practice, researchers (5,6) establishing that, with the development of remote communication means, delivery of some rudimental telemedicine services began. Among the most elaborated means, mention should be made of telephony, photos, and radiology, followed, by the advance of the new technologies, of closed circuit television systems, up to, nowadays, remote-control operations based on online connections.

Nowadays, even if the progress recorded in telemedicine has considerably increased, no generally accepted definition of the concept of telemedicine does exist. The specialists have written down, with special precision, more than one hundred definitions (7,8). Without aiming at providing an integrative definition, or at reviewing the numerous attempts of better catching and rendering the whole sphere of the concept, a mention should be made – as to some essential aspects – of certain resemblances, superpositions, as well as of different aspects of understanding the concept of telemedicine, with direct repercussions upon its practice. To simplify and improve the utilization of all important aspects of the concept, the present study connects the elements known as stabilizing the term of telemedicine, following the classical interrogative communication pattern: who, what, when, how, by which means, to what ends and with what effects will be the communication performed. According to this classical structure, WHO in 2021 (9) considers as an important factor the distance at which delivery of telemedicine services is assured through ”information and communications technologies for the exchange of valid information for the diagnosis, treatment, and prevention of disease and injuries, research and evaluation, and the continuing education of healthcare workers, to advance the health of individuals and communities”.

For a better understanding and application of the concept of telemedicine and for connecting the information that stems from various sources, different authorities, and organisms, a clear-cut distinction between standards and guidelines becomes necessary. In the opinion of Antoniotti (10), the standards are established through the consensus of an authorized organism, based on the proof available about a certain therapy, intervention, approach, surgical procedure, etc. A standard is viewed as the highest level of care provided, expressing the best practices supporting the decision-making processes. On the other hand, guides synthesize the general rules, principles, orientations, and recommendations which indicate or outline the policies or conduct to be followed. Also, they recommend the method through which the best practices, aimed at being followed and applied individually as a function of the patient’s condition, can be attained.

## TELEMEDICINE: NORMS AND METHODOLOGIES APPLIED IN ROMANIA

In Romania, telemedicine services are regulated from a legislative point of view starting in 2020. Although the legislature issued the ordinance with the intention of initiating the digitalization process of the public health system, one should also consider the emergency induced by the COVID-19 crisis, which drastically restricted access to hospitals during the entire quarantine period. The Romanian legislature issued in the last two years two documents that substantiate the delivery of telemedicine services briefly outlined in Table 1 (11). The former one, issued as an emergency order (OUG no. 196/2020)(12) aims at modifying and completing Law no. 25/2006 referring to the reformation of the health domain. The latter, (Decision no. 1.113 ), issued in September 2022, broadly establishes the methodological norms for implementing the provisions of OUG no. 196/2020.

The implementation of these regulations in Romania is favoured by at least two different aspects. First of all, it is about the internet infrastructure and the enthusiasm of the Romanian population to access telemedicine services. The technology that ensures Internet connections in the territory of Romania (13) is

relatively new and the country is currently ranked 3rd worldwide for fixed broadband according to SpeedTest.net review of October 2020 (Download 188.55 Mbps; Upload 128.74 Mbps; Latency 12 m/s).

Although telemedicine services in most European countries began to be accessed by patients mainly starting in 2020 (14), especially due to the COVID-19 quarantine, they have a certain tradition. According to Observatoire Centelem (2021) (15), 6 out of 7 Europeans have used telemedicine services or are interested. Regarding the degree of satisfaction, according to the aforementioned study, patients from Eastern European countries declared themselves dissatisfied with the quality of telemedicine services. Only 28% of Romanian patients who used telemedicine services declared themselves satisfied. The same percentage was recorded in Hungary. While in Bulgaria the lowest level was recorded, of only 17%. At the other pole is Sweden with a degree of satisfaction of 64%, followed by the United Kingdom with 55% and France with a percentage of 53%. Regarding the intention to use telemedicine services in the future, 69% of Romanians declared their interest, standing alongside the Portuguese 68%, Italians 67%, Poles 66% and Spaniards 66%, among the most interested in Europe of digitized medical services. Among the most reluctant towards digitized medicine are the Belgians 62%, the French 54%, the Slovaks 54% and the Austrians 53%.

Table 1: Telemedicine in Romania. Norms and methodologies

| | | |
|---|---|---|
| Principles | Priority granted to the development of health systems to the benefit of people in an ethical, reliable, safe, and sustainable manner | |
| | Transparency<br>Accessibility<br>Scalability<br>Replicability<br>Interoperability<br>Security<br>Confidentiality<br>Protection and observance of intimacy | |
| Normative aspects | Remote medical services, through information and communication technologies | |
| | Without the simultaneous physical presence of the medical staff and the patient | |
| | Establishment of the diagnosis, treatment, monitorization of the disease, and prevention | |
| | Teleconsult | Doctor-patient meetings performed through remote communication technologies for the establishment of the diagnosis, treatment, or prevention measures |

| | | |
|---|---|---|
| Services | Tele-valuation | Exchange of medical opinions among several doctors through remote communication means, on the basis of the patient's medical records, without his physical presence |
| | Teleassistency | The doctor assists another practitioner, placed in a different place, who performs a medical or surgical action either in previously scheduled situations or in cases of a medical emergency |
| | Teleradiology | Electronic transmission of radiological images by means of digital technologies capable of catching images, for their interpretation by specialists |
| | Telepathology | Remote transmission of microscopic images for their interpretation by anatomopathologists |
| | Telemonitorization | A medical specialist is able to remotely monitor and interpret the medical situation through approved devices that measure and transmit information about the health condition of the patient |
| Normative implemen-tation | ● Patient's information about the right of the doctor to decide on the opportunity of the telemedicine service<br>● Provision of the infrastructure, procedures, and mechanisms for the safe utilization of platforms<br>● Schooling of professionals for the utilization of the communication platforms<br>● Filing and securing the information and records about the patient | |

**THE POTENTIAL OF TELEMEDICINE**

In certain countries, telemedicine services have been successfully delivered long before 2020. Their benefits, risks, challenges, limitations, and effects are known to some extent and continue to be researched to ensure the best effects for patients. Among the benefits and risks that researchers (16) have attributed to telemedicine, the following should be mentioned: the high quality of services, reduced costs, extended access to medical services, easy access to the opinion of another specialist regarding the same medical situation, as well as the simple storage of patients data (radiology reports, images or video records) in a digital file. In a more extended conceptual approach, Haleem et al. (2021)(17) add to the benefits of telemedicine the fact that it facilitates access to services for patients with disabilities, elderly people or for culturally isolated groups and the incarcerated. The same authors have already mentioned the capacity of telemedicine to improve medication management, and patient quality of life, and of providing reduced healthcare costs. Another defining feature of telemedicine takes into account, according to its legislation, the increased cooperation among doctors from different regions, countries or specialized medical fields. It also facilitates the electronic transmission of patients' medical files to other specialists, at either national or international levels.

On the other hand, among the negative characteristics, the instability of the doctor-patient relationship was mentioned (16), an aspect that can turn telemedicine into an unsafe practice. In the digital environment, the quality of the doctor-patient interaction may be affected by contextual factors, which cannot be adjusted even with the support of health specialists. For example, the space in which the patient is placed during the access and delivery of the telemedicine service is considered a clinical space, and maintaining an appropriate climate for the meeting belongs to the patient or people close to the patient. If the patient's location does not offer the necessary security, privacy/intimacy or quiet, the doctor-patient communication process will be affected. One of the most important aspects which substantiate, maintain and develop the doctor-patient relationship in a positive direction is represented by communication (18, 19). In cases of synchronous telemedicine services, of the videoconference type, the doctor-patient relationship may be affected by the physical distance between the two and, besides the possible problems that may be caused by technical difficulties, the patient experiences feelings of alienation and fragmentation (16). The practice of medicine in a digital environment should not register differences, comparatively with the classical environment. From this perspective, investigations aimed at identifying the problems that might occur, along with tracing possible solutions for meliorating or solving difficult situations are necessary. Also, one should not forget that the ethical principles and the legal norms usually applied in conventional medicine are equally valid for doctor-patient interactions in the digital environment (20). Accordingly, the quality of telemedicine services should be at least equal and comparable, in their essential aspects, with the traditionally delivered services, despite the considerable differences between the two methods, while telemedicine should not be viewed as a substitute for the conventional healthcare system, its role being of improving it in its minimal functions (17). Some specialists (21, 22) have evidenced the limitations of performing comprehensive physical examinations, possibilities for technical difficulties, security breaches, and regulatory barriers. Among such limitations, Haleem et al. (2021)(17) included the danger of delays in drug administration, especially in emergency cases, once the doctors cannot perform laboratory tests, due to the distance between them and the patient. Another danger, that might easily lead to an incorrect diagnosis and inadequate treatment, in the absence of direct examination and biological analysis, is that the patient can involuntarily forget to describe a symptom. Haleem et al. (2021) (17) consider that, in such situations, the doctor is obliged to ask more questions than in the case of a face-to-face session with his patient. Another problem mentioned by the same authors is of legislative type, namely of recognizing the right of the physician of practising medicine outside the borders, as long as a patient living in another country can contact him. In the European context, if considering the present migration phenomenon, such an aspect may have consequences that should be taken into account. It is highly probable that a patient will contact a doctor who speaks his native language than address one from the country in which he works and speaks its language/dialect, for fear of not being understood or of not understanding the medical recommendations he receives. That is why, licensing of the right to telemedicine and telehealth practice needs regulations outside the national borders, as well, at the federal or union level.

**CHALLENGES OF TELEMEDICINE IMPLEMENTATION: DIGITAL LITERACY AND DIGITAL EXCLUSION**

Despite the different logical relations established between them, telemedicine and telehealth are considered interchangeable terms. Logically, telemedicine is considered to be under the umbrella of telehealth, referring specifically to clinical services which also include other similar services, such as medical education, remote patient monitoring, patient consultation via videoconferencing, wireless health applications, and transmission of imaging and medical reports (21, 23). On the other hand, Raposo (2016) (24) considers that the terms of telehealth, telecare and telemedicine are all aspects of eHealth. From this perspective, eHealth includes services or devices which make use of informational technologies, attempting at assisting, preventing, diagnosing, treating, monitoring a patient's health condition. He explains the tele-health/care/medicine inclusion in eHealth by the manner in which the technologies of health services delivery are applied. Among them, Raposo (24) makes mention of telephony, television, webcams, video links and fixed or wireless telecommunication, computing devices, environmental controllers and apps. Timmermans and Kaufman (2020) (25) include in eHealth or digital health the following: health information systems, electronic patient records, wireless mobile digital devices, wearable biosensors, telemedicine, social media sites, and electronic support groups.

Under such circumstances, the patient resorting to telemedicine services should be able to attain them and be capable of utilizing them. The absence of technology and digital literacy (26), of the capacity to use such technologies, represent a serious obstacle in the delivery of telemedicine and access to such types of services. Some specialists (27,28) define health literacy as the degree to which individuals have the capacity to obtain, process, and understand the basic health information and services needed to make appropriate health decisions. At the European Union level (29), it was observed that insufficient levels of digital skills hamper the prospects of future growth, deepen the digital divide and increase risks of digital exclusion. Even if 87% of the people (aged 16-74) used the internet regularly in 2021, only 54% of them possessed at least basic digital skills. According to DESI (2022) (29), the Netherlands and Finland are the frontrunners in the EU, while Romania and Bulgaria are lagging behind. Educated and wealthy persons have more chances to use technologies in their early stages, and have access to healthcare providers more familiar with technological innovations (25). To facilitate the access of the population having no technological resources and digital literacy to telemedicine services, GPs/community assistants, the connection with the specialists should be first created, with the patient's consent and at his solicitation, even if, in poorer countries, the GPs from localities far away from hospital centres and facilities do not have the necessary funds for implementing such technologies and for obtaining the right of delivering medical services according to the legislation in force. Instead, the private health centres and hospitals, especially the clinics of dermato-aesthetic/aesthetic surgery, stomatology, and the centres and laboratories for medical analysis will improve their telemedicine services. The absence of funds necessary for the implementation of the new technologies will increase digital exclusion.

In schools and private kindergartens, where parents financially support telemedicine services, their delivery will increase

children's safety and will prevent the spreading of contagious diseases in such environments. If a child complains of pain in class during the lessons, the nurse may, based on a subscription with a telemedicine centre, ask for an emergency teleconsultation. Such a problem may be solved rapidly, with no intervention from the parent, if the case is not an emergency. In special situations, the medical centre could deliver a specialist able to consult and promptly intervene. The same type of monitoring may be implemented in all health centres for seniors, who will not be obliged to go personally to a doctor, anymore.

## CONCLUSIONS

Digitalization of medical practice should be accompanied by adequate support for services to be truly accessible and inclusive. Apart from the development of the digital competence of medical specialists, as well as of the population, the values and ethical principles of the process of societal digitization and, implicitly, of medicine, should be promoted. The unprecedented progress of information technology should not forget that behind each screen or digital file there is a human, who represents the main concern for us all, needing protection adequate to the environment in which the interaction is on.

The digitization of society is accelerated and follows a series of principles (30) capable of ensuring universal access to internet services; a safe and reliable online environment; education and universal digital competencies, granting the active participation of citizens to the democratic processes of their society; access to eco-friendly digital systems and devices; accessible public digital services and administration centred on the human factor; ethical principles for the human-centred algorithms; protection and accountability of children in the online environment; access to digital health services.

Efficient, effective telemedicine services at low costs, promised to be a click away, need clear legislation, methodologies and protocols that promote the patient's autonomy and his right to be treated to become a reality.

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