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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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"Aggression-a dimension of the human mind" *National Conference of Psychiatry 5-7 October 2023, Iași*

Roxana Chiriță, Eliza-Mihaela Cămănaru

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Aggression is a common phenomenon in today's society, both among the general population and in medical practice. It occurs in different forms - physical/verbal, direct/indirect, proactive/reactive, ranging from minor to severe, life-threatening acts. Aggressive behaviour has potentially harmful effects on physical and mental health and the consequences affect not only the individual committing the aggressive act, but also members of his/her social and family environment.

Taking into account the significant medical, social and legal implications linked to aggression, many researchers have tried over the years to discover and better understand the aetiopathogenesis of this phenomenon which is faced by specialists in various professional fields as well as the general population. Regarding aggression in the context of psychiatric services, studies have shown that there is an increased risk of aggressive behaviour in certain mental health patients compared to the general population. The causes and mechanisms leading to the development of aggression are complex and they are associated with a variety of predisposing factors, including biological, clinical, personal and social aspects.

Given these premises, the scientific event that marks *the Days of „Socola" Institute of Psychiatry* has aggression as the main theme and the title chosen for this year's edition is *Aggression-a dimension of the human mind.* The scientific event will include *Socola Summer School* held on 4-5 October 2023, followed by the *National Conference of Psychiatry* on 5-7 October 2023. Throughout this scientific event, we aim to review the state of the art on aggression and to better understand the nature of aggressive

behaviour, in order to improve prevention and treatment methods. For this purpose, the conference will include scientific lectures given by national and cross-border specialists, with the participation of guests from the Republic of Moldova, and both onsite and online presentations will be available. Psychiatrists, neurologists, forensic scientists, as well as psychologists, will present various aspects of aggressive behaviour, ensuring a complex, multidisciplinary approach on this subject which frequently represents a challenge for specialists in the medical field and beyond. The theme of aggression will be analysed from biological, clinical, social, cultural and legal perspectives. The implied mechanisms, causes and risk factors for the occurrence of aggressive behaviour will be discussed as well as various modern treatment options, including pharmacotherapy, psychotherapy and virtual reality-mediated therapeutic options. The particularities of aggression that occurs as a manifestation of certain mental disorders such as dementia, borderline personality disorder, bipolar affective disorder and substance use disorders will be presented. Different forms of manifestation will be analysed, including increasingly common types of aggressive behaviour in modern society, such as bullying and cyberbullying.

The scientific programme will also include presentations and workshops focused on the predictability of aggressive behaviour, as the early identification of risk factors and potentially aggressive subjects is essential for the prophylaxis of aggression in the hospital setting and, therefore, for increasing the safety of the working environment in psychiatric clinics and beyond, as well as for increasing the safety of the aggressive patients themselves. During the scientific event, there will also be a debate on the impact of aggression in Romanian society, in order to highlight the main challenges of specialists who are at significant risk of exposure to aggressive behaviour, as well as to find optimal solutions to prevent and manage these situations.

The scientific events that will take place in the context of this year's edition of *the Days of „Socola" Institute of Psychiatry* will bring together specialists in the field of mental health and not only, in order to to share professional experience related to aggression, in an attempt to better understand this concept and to improve prevention and treatment. This will contribute to the optimal management of the aggressive patient with a consequent reduction of the negative impact that aggression has on the safety of the patient himself, the healthcare providers and generally on today's society.

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Articles

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Psychopathological dimension of dissociation among people with psychotic disorder: meta-analysis

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ABSTRACT

The causal relationship between dissociation and psychosis remains insufficiently explored. This meta-analysis investigates this relationship, considering studies conducted on both clinical and non-clinical population. The systematic search was conducted according to the PRISMA-statement in the databases Medline, PsycInfo and Munich, and allows 8 records to be extracted. 499 studies were selected according to inclusion (e.g. articles on dissociation and psychosis; involving participants between the ages of 18 and 65; conducted on both clinical and non-clinical population) and exclusion (e.g. articles on dissociation and other medical conditions; qualitative studies; reviews, commentary, brief reports or book chapters) criteria detailed in the methods. The analyses showed a significant and positive association between forms of psychosis and dissociation, significant differences between the clinical and non-clinical groups, and a significant association between characteristics of schizophrenia and measured dissociation in the normal population. Because research in this field is difficult to undertake, we extracted a very small number of studies that could be included in our analysis. Even if the statistical results are limited, the process of reviewing the existing scientific literature in the field of dissociation and psychosis has been very useful for charting the direction of future research.

KEYWORDS:

Dissociation, psychosis, schizophrenia, clinical population and non-clinical population.

INTRODUCTION

There is no consensus on the meaning of the term dissociation (1). However, contemporary clinicians and researchers seem to adhere to the idea that dissociation involves the loss of the mental ability to integrate some of its higher functions (2). According to DSM-5 (3), dissociation represents the disturbance of

the normal integration function of consciousness, memory, identity, emotion, perception, bodily representation, motor control and behaviour, while ICD-10 (4) defines dissociation as the partial or total loss of normal integration between memory of the past, awareness of identity and control of body movements. It is mainly associated with psychopathological symptoms found in obsessive compulsive disorders (5), depressive and anxiety disorders (6), personality disorders (7), which include traumatic experiences as causal factors. As a result, dissociation is predominantly viewed from a maladaptive perspective (8).

Psychotic symptoms are non-specific and can have many causes. The DSM-5 definition of psychosis (3) includes pathological phenomena such as delusional ideation, hallucinations, disorganized language, or catatonic behaviour reflecting experiences typically associated with a diagnosis of schizophrenia.

The literature includes evidence of the link between dissociation and psychosis, particularly between dissociation and auditory hallucinations (9), but there are few studies that explore this link in the case of the other types of hallucinations.

The present study aims to identify and systematize the empirical studies published over a 10-year period on the relationship between dissociation and psychosis and to explore the following:

- To what extent dissociation is a characteristic of patients with schizophrenia and how strong is this link. We expect a meaningful and positive relationship between the two.
- To what extent dissociation is characteristic of different populations of participants with symptoms of schizophrenia and where the dissociation is greater, depending on the type of population. The same is done for participants described in the studies as a non-clinical population.
- To what extent dissociation is a characteristic of people who are not identified as being diagnosed with schizophrenia (e.g. normal population) and whether there is a significant link between characteristics of schizophrenia and measured dissociation in the normal population. We expect this relationship to be a significant one, but small in size.

2. METHODS

2.1 Research Strategies and Information Sources

We conducted a comprehensive search of indexed articles published between 2000 and April 2019 in the Medline, PsycInfo and Munich online databases using the following keywords: *Search strategy (("disociative disorder*" OR dissociat*).ti AND (Psychosis OR psychotic OR schizotyp* OR hallucinat* OR delusion* OR "negative symptom*" OR alexithymi* OR catatoni* OR disorganiz* OR schizophreni* OR depersonalization OR depersonalisation OR derealisation OR derealization OR compartmentalis* OR compartmentaliz* OR detach* OR amnesia OR absorption).ab) [DT 2000-2019] [Human age groups Adulthood 18 Yrs + Older] [Languages English]

2.3. Eligibility Criteria

Inclusion criteria:

1. Articles on dissociation and psychosis, including concepts suggesting psychotic symptoms such as hallucinations, or dissociative mechanisms such as: detachment, compartmentalization, dissociative amnesia, absorption, depersonalization, derealization;
2. Articles published in English;
3. Studies involving participants between the ages of 18 and 65;
4. Studies published between 2000 and 2019;
5. Studies conducted on both clinical and non-clinical population.

2.4. Identification and selection of studies included

Searching PsycInfo, Medline and the Munich online library, we identified 499 publications. After removing the duplicates, 242 items remained. The selection was then made on the basis of the titles, which led to the exclusion of 179 publications. Following selection on

the basis of abstracts, 35 more publications were excluded. The remaining 18 articles were read in full and as a result of this process 8 studies remained that met our pre-established criteria for inclusion and exclusion. Due to the small number of studies identified, we decided to extend the search time interval from 2009-2019 to 2000-2019. Thus, we introduced two more studies and finally included 12 studies in our analysis.

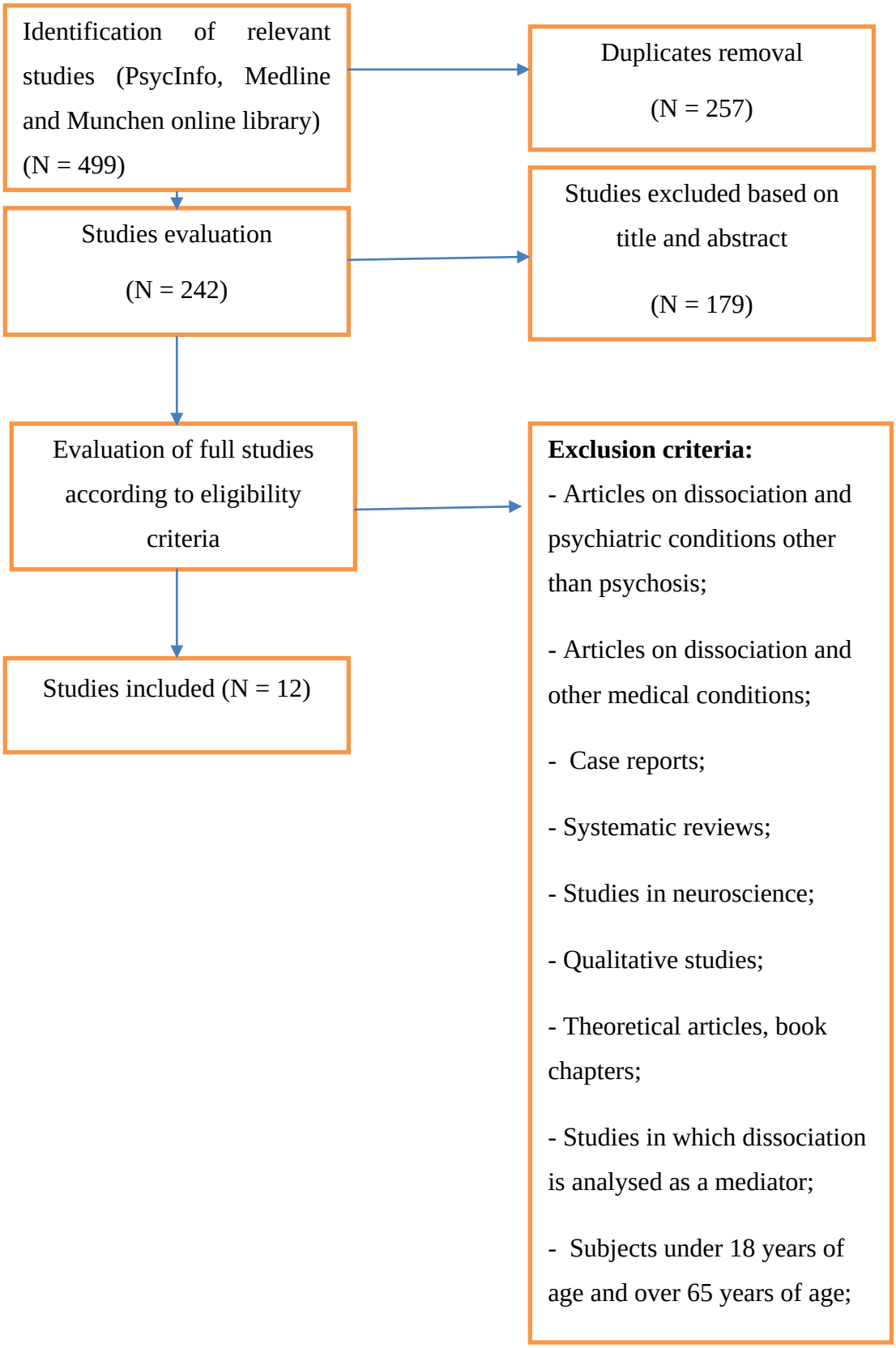

Figure 1. PRISMA flow chart

2.5. Quality assessment

The studies were reviewed by each author and the differences or questions arising in relation to the eligibility of the studies were resolved by seeking additional information and discussions between the authors. Only the studies (a) published in internationally recognized databases, which (b) explored dissociation in relation to psychosis and not to other psychiatric or medical conditions, were introduced.

2.6. Extracting data

From each study were extracted the following characteristics: the main author, the year of publication, the number of participants, the method of recruitment of participants, the tools used for evaluation.

2.7. Data analysis

The following information was extracted from each study: the mean age of each sample and the standard deviation, the total score for psychosis and standard deviation, the total score for dissociation and standard deviation, the subscale scores and the standard deviations, the correlations between the psychosis-specific subscales and dissociation.

3. RESULTS

3.1. Characteristics of the studies included

In the meta-analysis 12 studies were included, for which the main characteristics are summarized in Table 1. Five studies conceptualized dissociation as a disorder of the normal process of integration of identity, emotion, perception, body representation, motor control and behavior in the flow of consciousness and memory (9, 10, 11, 12, 13) while four fundamentally associated it with trauma, stating that dissociation results from the inability to integrate overwhelming traumatic experiences with experiences already included in other cognitive structures (13, 14, 15, 16). Varese et al. (9) are the only ones who describe dissociation as a continuum, including manifestations ranging from benign to severe dissociative disorders. Pec et al. (17) defines dissociation as a consciously lived conflict between opposing mental forces and associates it with stress. Perona-Garcelan et al. (18) does not give a definition of dissociation but conceptualizes it on the basis of phenomena of absorption and depersonalization.

Regarding the conceptualization of psychosis, three studies (11, 14, 15) give no definition, another refers to schizophrenia defining it succinctly as the splitting of the psyche (17), five studies conceptualize it by the presence of its main symptoms, namely hallucinations and delusional ideacy (9, 12, 13, 16, 18). A study (10) examines schizotipia and predisposition to schizophrenia rather than psychosis per se.

Table I Summary of characteristics of the included studies

Study and country	Study Design	Population	N	Mean Age/SD Age	Total Score (SD) Schizophrenia	Total Score (SD) Dissociation
Varese et al. (2011) UK		clinical & non-clinical	42 (21 hallucinating patients group & 21 non-hallucinating patients group); 23 controls	Hallucinating Group M = 40.09; SD = 13.56; Non-hallucinating Group M = 40.14; SD = 12.36; Controls M= 37.78, SD=15.21	Positive symptoms 19.20 (4.89) (hallucinating) and 12.35 (3.27) (non-hallucinating) and 7.41 (0.85) (controls); Negative symptoms 15.10 (5.43) (hallucinating) and 11.95 (4.96) (non-hallucinating) and 7.32 (0.48) (controls)	Hallucinating Group 3.59 (1.41); Non-hallucinating Group 2.00 (1.14); Controls 1.72 (0.98)

Zavattini et al. (2017) Italy, Portugal	cross-sectional	prisoners	320 Italian subjects (122 prisoners, 198 community participants/controls) and 67 Portuguese subjects	Italian prisoners: M= 39.97, SD= 11.76; Italian controls M=32.51, SD=10.30; Portuguese prisoners M=34.85, SD=8.98		Prisoners 17.74 (15.02); Controls 11.45 (13.10)
Chui et al. (2016) Taiwan	cross-sectional	clinical population	80	36+/-12	Positive symptoms 15.1 (6.1); Negative symptoms 11.3 (5.7)	23.4 (19.4)
Wearne et al. (2017) Australia	cross-sectional	clinical population	65	cluster 1 (high scores on hallucinations): 47.84; cluster 2 (low scores on hallucinations): 43.83		
Berry et al., (2017) UK	cross-sectional	non-clinical population	123	M=22, SD= 5.10	LSHS total scores 14.76 (7.85); PANAS 17.56 (7.09)	DES -II 46.63 (34.86)
Perona-Garcelán et al. (2012) Spain	cross-sectional	clinical population and non-clinical control group	124	5 groups: 1 - schizophrenic with hallucinations M =38.81, SD= 8.95; 2- schizophrenic with delusions M= 36.05, SD= 7.48; 3 - recovered schizophrenic M= 38.18, SD= 7.61; clinical control M= 39.32, SD= 12.80; 5 - non-clinical control M= 37.04, SD= 12.07		TAS: Group 1 = 52.67, Group 2 = 25.20, Group 3 = 30.32, Group 4 = 42.77, Group 5 = 30.22; CDS: Group 1 = 72.15; Group 2 = 28.90, Group 3 = 18.36, Group 4 = 30.59, Group 5 = 12.30

Irwin (2001) Australia	cross-sectional	non-clinical population	116	M= 22.7, SD = 7.36	SPQ-B cognitive-perceptual 3.41, SPQ - B Interpersonal 3.37, SPQ-B disorganized 2.47	DES absorption 22.77, DES pathological 7.36
Pec et al. (2014) Czech Republic	cross-sectional	clinical population	31 patients with schizophrenia, 36 patients with borderline personality disorder	Schizophrenia sample M 36.2+/-9.5; BPD sample M 31.0+/-8.7	HoNOS Schizophrenic 11.6, HoNOS BPD 15	DES Schizophrenic 13.7; DES BPD 18.54
Doğan et al. (2017) Turkey	cross-sectional	clinical	50	Males M = 38.2, SD = 11.2; Females M= 38.7, SD = 7.8		
Braehler et al. (2013) Canada	cross-sectional	clinical and non-clinical population	First-episode of psychosis group 62, chronic psychosis 43, community 66	First episode M = 23.2, SD = 3.3; Chronic M = 31.5, SD = 7.9; Community M = 27.9, SD = 7.4		DES community 6.6; DES first episode 13.01; DES chronic 21.56
Schroeder et al. (2016) Germany	cross-sectional	clinical	145	Males M =34, SD = 11.5	PANSS 66.1 (14.3)	DES 14.1 (12.0)
Vogel et al. (2006) Germany	cross-sectional	clinical and non-clinical population	87 clinical, 297 non-clinical	Clinical M= 34.3, SD = 12.7; Non-clinical M = 39.5, SD = 13.2	Paranoia Subscale schizophrenia without trauma self-rated M= 0.7 (1.0), Paranoia Subscale schizophrenia without trauma self-rated M= 1.0 (0.5), Paranoia Subscale schizophrenia with trauma self-rated M= 1.5 (0.7); Psychoticism Subscale schizophrenia without trauma self-rated M= 0.6 (0.5), Psychoticism Subscale schizophrenia with trauma not self-rated M= 10.7 (0.7), Psychoticism Subscale schizophrenia with trauma self-rated M= 1.1 (0.6)	DES schizophrenia without trauma self-rated M= 11.4 (11.2), DES schizophrenia with trauma not self-rated M= 15.0 (12.9), DES schizophrenia with trauma self-rated M= 21.0 (15.8)

3.2. Participants

The 12 studies included a total of 1.777 subjects of whom 758 had a diagnosis of mental illness, the most common in the psychosis group, 606 subjects from the general population/non-clinical population and 413 subjects in the constitution of control groups. They were recruited from the adult population aged between 18 and 65. Diagnostic in the studies included conditions from the following clusters: schizophrenia, dissociative disorders, affective disorders, anxiety disorders, personality disorders and post-traumatic stress disorder.

3.3. Measuring instruments

The 12 studies included in our analysis encompass a wide variety of tools. Out of them, only two appear in 50% of the studies, namely the Dissociative Experiences Scale (DES) and positive and Negative Syndrome Scale (PANSS). A total of 28 measuring instruments were used which we grouped into the following categories: scales for measuring psychotic symptoms, scales for measuring dissociative experiences, scales for measuring traumatic experiences, and other scales.

A. Scales for measuring psychotic symptoms

Among the 12 studies, four studies used the *Positive and Negative Syndrome Scale (PANSS)* (9, 12, 15, 18), two of the studies used the *The Symptom Check List-90-Revised (SCL-90-R)* (11, 12), while in the other six studies different instruments were used: *Schizotypal Personality Questionnaire – Brief (SPQ-B)* (10), *Psychotic Symptoms Rating Scale (PSYRATS*) (16), *The Health of the Nation Outcome Scales (HoNOS*) (17), *the Brown Assessment of Beliefs Scale (BABS)* (13), *Scale for the Assessment of Positive Symptoms* (13), *Scale for the Assessment of Negative Symptoms (SANS)* (13), *Clinical Global Inventory (CGI)* (19), *The Brief Symptom Inventory (BSI)* (20), *Launay-Slade Hallucination Scale (LSHS)* (21), *Positive and Negative Affect Schedule (PANAS)* (21). The most important information about these instruments, such as authors, type, number of items, scales and an example item, can be found in Table 2.

Table II Scales for measuring psychotic symptoms

Study	Instrument	Authors	Type	Items	Subscales	How evaluates	Example of items
Varese et al., 2011; Perona-Garcelan et al., 2012; Schroeder et al., 2016; Chiu et al., 2016	Positive and Negative Syndrome Scale (PANSS)	Kay et al., 1987	Semi-structured clinical interview	30	Positive psychotic symptoms, negative psychotic symptoms, general psychopathological symptoms, appearing in the week preceding the interview	Scale from 1 (the absence of symptom) to 7 (extreme severity of symptom).	Positive Scale: Delusions, Conceptual disorganization, Hallucinatory behavior, etc.
Wearne et al., 2017	Psychotic Symptoms Rating Scale (PSYRATS)	Haddock et al., 1999	Questionnaire	17	Hallucinations and delusional ideas	Scale from 0 (absent) to 4 (severe)	The items for delusions are: amount of preoccupation, duration of preoccupation, etc.
Chiu et al., 2016	Schizophrenia 11 items subscale from the Dissociative Disorders Interview Schedule (DDIS)	Ross, 1997	Highly structured interview	11	Somatic symptom disorder, borderline personality disorder and major depressive disorder, dissociative disorders	Yes=1, No=2, Unsure=3	Have you ever experienced voices arguing in your head
Vogel et al., 2006; Chiu et al., 2016	The Symptom Check List-90-Revised	Derogatis, 1983	Questionnaire	90	Somatization, obsessive-compulsive symptoms, interpersonal sensitivity, depression,	Scale from 0 (not at all) to 4 (extreme).	For the past week, how much were you bothered by: Headaches

					anxiety, anger hostility, phobic anxiety, paranoid ideation and psychoticism		
Pec et al. (2014)	The Health of the Nation Outcome Scales (HoNOS)	Wing et al., 1996	A set of 12 items	12	Behavioral problems, Impairment, Symptomatic problems and Social problems.	5-point scale ranging from 0 to 4.	Aggression/overactivity
Dogan et al. (2017)	Scale for the Assessment of Positive Symptoms (SAPS) Scale for the Assessment of Negative Symptoms (SANS) Brown Assessment of Beliefs Scale (BABS)	Andreasen, 1990 Eisen et al., 1998	Semi-structured interview	34 items 25 items 7 items	Positive symptoms scale: hallucinations, delusions/thought content disturbances, bizarre behavior and thought form disturbances Negative symptoms scale: flattening of affect, alogia, avolition, anhedonia and attention disorders	5-point scale from 0 (‘not at all’) to 5 (‘severe’) 5-point scale from 0 (‘not at all’) to 5 (‘severe’) Scale rated from 0 to 4 (from least to most severe)	The patient reports voices, noises, or other sounds that no one else hears. The patient's face appears wooden--changes less than expected as emotional content of discourse changes. Conviction
Busner & Targum, 2007	Clinical Global Inventory (CGI)	Busner & Targum, 2007	Inventory	2	CGI-Severity CGI-Improvement	Scale rated from 1=normal to 7=among the most extremely ill patients. Scale rated from 1= very much improved since the initiation of treatment to 7= very much worse	Considering your total clinical experience with this particular population, how mentally ill is the patient at this time? Compared to the patient's condition at admission to the project [prior to medication initiation], this patient's condition is:

						since the initiation of treatment.	
Irwin et al., 2001	Schizotypal Personality Questionnaire – Brief (SPQ-B)	Raine & Benishay, 1995	Questionnaire	22	Cognitive-perceptual scale, Interpersonal scale, Disorganization level scale	Yes= 1/ No=0	Have you ever had the sense that some person or force is around you, even though you cannot see anyone?

B. Scales for measuring dissociative experiences

Six studies used the *Dissociative Experiences Scale (DES)* to measure dissociative experiences (10, 11, 12, 14, 15, 17), the other instruments used being: *Traumatic Dissociation Scale (TDS*) (12), *Depersonalization -Depersonalization Scale (DDI)* (16), *Tellegen Absorption Scale (TAS*) (18), *Cambridge Depersonalization Scale (CDS)* (18), *Somatoform Dissociation Questionnaire (SDQ)* (13). The authors of the instruments, along with other information, are presented in Table 3.

Table III Scales for measuring dissociative experiences

Study	Instrument	Authors	Type	Items	Subscales	How evaluates	Examples of items
Irwin et al.,2001 Vogel et al., 2006 Braehler et al., 2013 Pec et al., 2014 Chiu et al., 2016 Schroeder et al., 2016	Dissociative Experiences Scale (DES)	Bernstein & Putnam (1986)	Questionnaire	28	Amnesia, depersonalization, derealization and absorption	0% = “never” 100% = “always”	Some people have the experience of driving a car and suddenly realizing that they don’t remember what has happened during all or part of the trip. Circle a number to show what percentage of the time this happens to you.
Chiu et al. (2016)	Traumatic Dissociation Scale (TDS)	Carlson & Waelde (2000)	Questionnaire	24	Depersonalization, derealization, gap in awareness, gap in awareness and intrusion, and amnesia	0 to 4, where 0 = „not at all” and 4 = „more than once a day”.	
Wearne et al. (2017)	Depersonalization -Derealization Scale (DDI-12	Cox & Swinson (2002)	Questionnaire	28	Symptoms of derealization and depersonalization	Yes= 1/ No=0	Surroundings seem strange and unreal

Perona-Garcelan et al.(2012)	Tellegen Absorption Scale (TAS)	Tellegen & Atkinson, 1974	Questionnaire	34	Focused attentional deployment	5-point scale (0 = „never" and 4 „always"	Some of my most intense memories are activated by smells
	Cambridge Depersonalization Scale (CDS)	Sierra & Berrios, 2000	Questionnaire	29	Depersonalization experiences	2 Likert scales: one measures the frequency of the experience (where 0 is "never" and 4 is "always"), and the other the duration of the experience (where 0 is "a few seconds" and 6 is "more than a week")	I feel like parts of my body don't belong.
Dogan et al. (2017)	Somatoform Dissociation Questionnaire (SDQ)	Nijenhuis et al., 1996	Questionnaire	20	Somatoform Dissociation	5-point Likert scale (1 „not at all" to 5 „extreme".	I hear sounds from nearby as if they were coming from far away

C. Scales for measuring traumatic experiences

Studies led by Irwin et al. (10) and Braehler et al. (14) measured the presence of traumatic childhood experiences using the *Childhood Trauma Questionnaire* (CTQ), Vogel et al. (11) used *Posttraumatic Diagnostic Scale* (PDS), Pec et al. (17) used *Trauma Sympttom Checklist-40* (TSC-40), Schroeder et al. (15) used *Structured Trauma Interview (STI)*, and Chiu et al. (12) used *The Brief Betrayal Trauma Survey* (BBTS), which will not be presented, as they do not serve the objective of the study.

D. *Other scales used in the analyzed studies were:*

Wechsler Adult Intelligence Scale (WAIS-III) (12), Experience Sampling Method (ESM) (9), The Relationship Scales Questionnaire (RSQ) (21) and Metacognitions Questionnaire (MCQ-30) (18), which, however, will not be presented, as they do not serve the objective of the study.

4. QUANTITATIVE ANALYSIS

4.1 Objective 1

The analyses (Table 4) indicate that there is a significant and positive association between forms of psychosis and dissociation (r = .314, CI 95% .190;. 428). Since the degree of diversity of studies is very high, as indicated by the variability index (Q = 12.85, df = 7, p = .0758, I2 = 45.54%), we chose to interpret the correlation coefficient calculated for fixed effects. These results can be interpreted on the basis that the majority of the studies explore

various topics and also based on the number of participants, which is roughly similar.

Table IV Meta-analysis – correlations

Study	Sample size	Correlation coefficient	95% CI	z	P
Chui-De Chiu et. al, 2016	80	0.270	0.0535 to 0.462		
Chui-De Chiu et. al, 2016	80	0.230	0.0108 to 0.428		
Dogan et al., 2017	50	0.150	-0.134 to 0.411		
Pec et al., 2014 (absorption)	31	0.470	0.139 to 0.707		
Pec et al., 2014 (amnesia)	31	0.170	-0.196 to 0.495		
Pec et al., 2014 (derealization)	31	0.650	0.384 to 0.816		
Pec et al., 2014 (total score)	31	0.530	0.216 to 0.745		
Schoeder et al., 2016	145	0.210	0.0487 to 0.361		
Total (fixed effects)	479	0.286	0.200 to 0.368	6.284	<0.001
Total (random effects)	479	0.314	0.190 to 0.428	4.809	<0.001

Below, we present a graph (Figure 2) showing which of the studies included in the analysis had the highest and lowest correlations. We notice that psychosis is most strongly associated with dissociation of a derealization and absorption type. These associations are also significant. The specific relationships in the Doğan et al. (13) study and in the case of the amnesia subscale in the study of Pec et al. (17) are not significant.

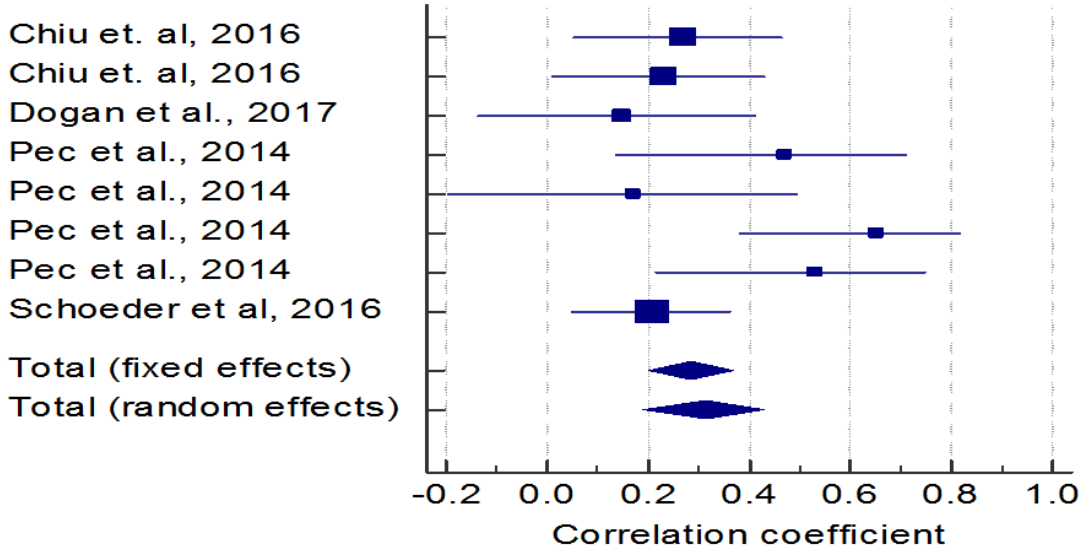

Figure 2. The correlation coefficients graph, specific to each study and subscale

Because there is a fairly wide variety of studies included in the analysis, we also investigated to what extent the results would actually be an error and not a real link. For this objective we inspected the error chart in publication, which indicates a symmetry of the studies, meaning that the results obtained are not an error. However, given that there are

very few studies included, we could not interpret the coefficients of this analysis. The chart is presented below (Figure 3).

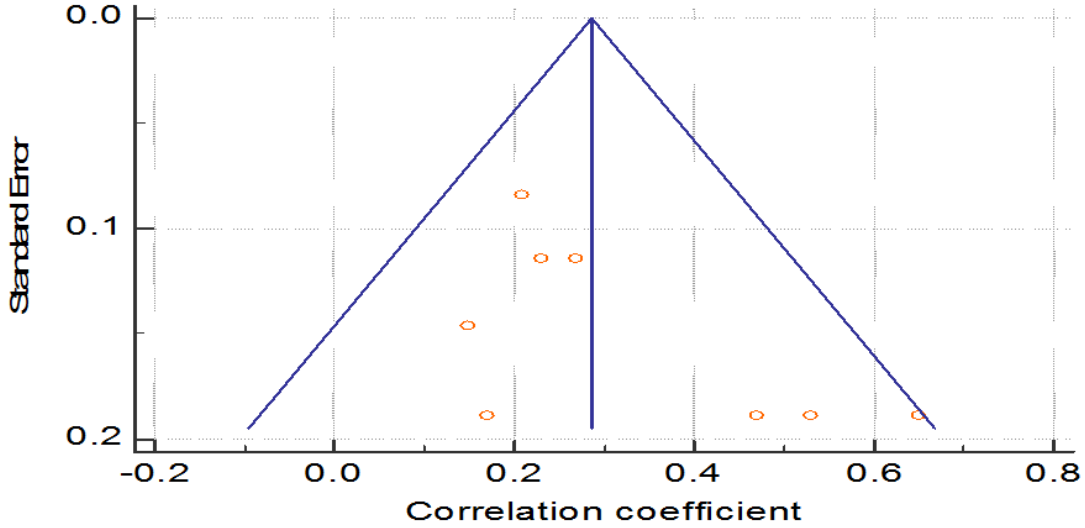

Figure 3. Funnel plot graph

Objective 2

Analyses indicate significant differences (t = 3.35, p = .001), but the indicators of study variability show an increased diversity, also significant, which could affect the interpretation of the results (Q = 1966.7173, df = 13, p < 0.0001, I2 = 99.34%) (Table 5).

Table V Meta-analysis: continuous measure

Study	N1	N2	Total	SMD	SE	95% CI	t	P
Braehler et al., 2013	62	66	128	0.631	0.180	0.274 to 0.988		
Braehler et al., 2013	43	66	109	1.172	0.210	0.755 to 1.588		
Varese et al., 2011	21	23	44	1.525	0.338	0.843 to 2.207		
Varese et al., 2011	21	23	44	0.260	0.298	-0.341 to 0.860		
Vogel et al., 2006	30	297	327	8.840	0.395	8.063 to 9.617		
Vogel et al., 2006	30	397	427	12.542	0.469	11.620 to 13.464		
Vogel et al., 2006	30	297	327	12.956	0.541	11.890 to 14.021		
Vogel et al., 2006	30	297	327	8.764	0.392	7.992 to 9.536		
Wearne et al., 2017	10	26	36	-3.768	0.574	-4.934 to -2.601		
Wearne et al., 2017	10	26	36	-2.684	0.482	-3.663 to -1.704		
Perona-Garcelan et al., 2012	20	27	47	-0.756	0.300	-1.361 to -0.151		
Perona-Garcelan et al., 2012	27	27	54	5.144	0.563	4.014 to 6.273		
Perona-Garcelan et al., 2012	27	27	54	6.789	0.706	5.372 to 8.206		
Perona-Garcelan et	20	27	47	1.807	0.345	1.113 to 2.502		

al., 2012								
Total (fixed effects)	381	1626	2007	2.301	0.089	2.127 to 2.476	25.865	<0.001
Total (random effects)	381	1626	2007	3.791	1.130	1.574 to 6.008	3.354	0.001

Below, we present a graph with the results of the studies included in the analysis (Figure 4). We observe increased means for the group including participants diagnosed with forms of psychosis, such as schizophrenia. The Mean differences between the groups are also high, thus indicating high mean differences between the two groups, with high dissociation Means recorded for clinic and non-clinic participants.

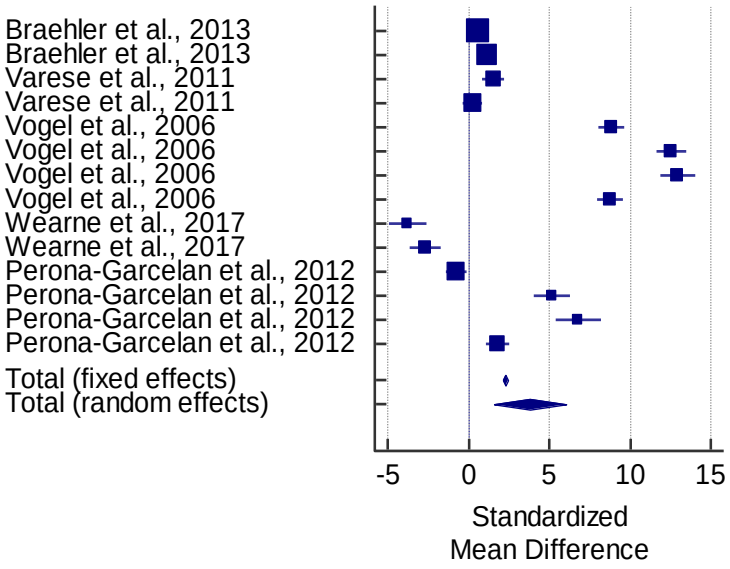

Figure 4. Mean Difference Graph

Finally, the analysis of the graph showing the error trend in publication indicates that the studies should be analysed according to new criteria, the graph being asymmetrical and the studies very different (Figure 5).

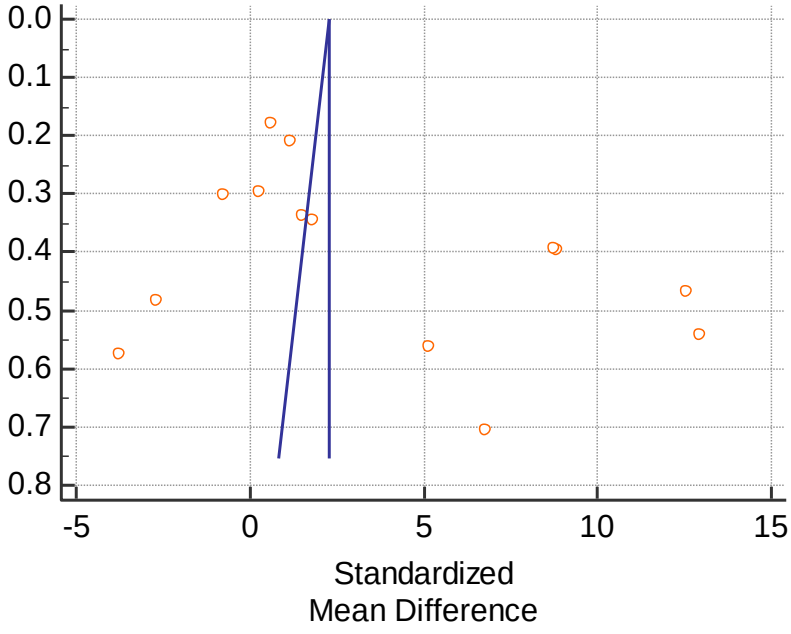

Figure 5. Funnel plot

Objective 3

Data analysis shoes a strong association between the main concepts of the study (r = .49, CI 95% [0.461; 0.529], and the indicators of study variability are insignificant and small (Q = 1966.7173, df = 13, p < 0.0001, I2 = 99.34%) (Table 6). However, the small number of studies analysed here and the fact that the analysis takes into account several types of dissociation, should be considered. As there are not many similar studies, analyses could not be carried out for each subscale of the study.

Table VI Correlational meta-analysis

Study	Sample size	Correlation coefficient	95% CI	z	P
Berry et al., 2017	123	0.540	0.401 to 0.654		
Berry et al., 2017	123	0.470	0.320 to 0.597		
Berry et al., 2017	123	0.570	0.437 to 0.679		
Berry et al., 2017	123	0.620	0.498 to 0.718		
Irwin, 2001	116	0.530	0.385 to 0.650		
Irwin, 2001	116	0.480	0.326 to 0.609		
Irwin, 2001	116	0.410	0.246 to 0.551		
Irwin, 2001	116	0.500	0.350 to 0.625		
Irwin, 2001	116	0.450	0.292 to 0.584		
Irwin, 2001	116	0.330	0.157 to 0.483		
Zavattini et al., 2017	114	0.330	0.156 to 0.485		
Zavattini et al., 2017	198	0.480	0.365 to 0.581		
Zavattini et al., 2017	114	0.490	0.336 to 0.618		
Zavattini et al., 2017	114	0.570	0.431 to 0.682		
Zavattini et al., 2017	114	0.520	0.372 to 0.642		
Zavattini et al., 2017	114	0.580	0.443 to 0.690		
Total (fixed effects)	1956	0.496	0.461 to 0.529	23.762	<0.001
Total (random effects)	1956	0.496	0.456 to 0.534	20.616	<0.001

The graph (Figure 6) shows high correlations between the two main variables of the study, but we believe that these analyses should be reorganized according to each dimension of dissociation in order to have a clearer picture of the types of links between the main variables of the study.

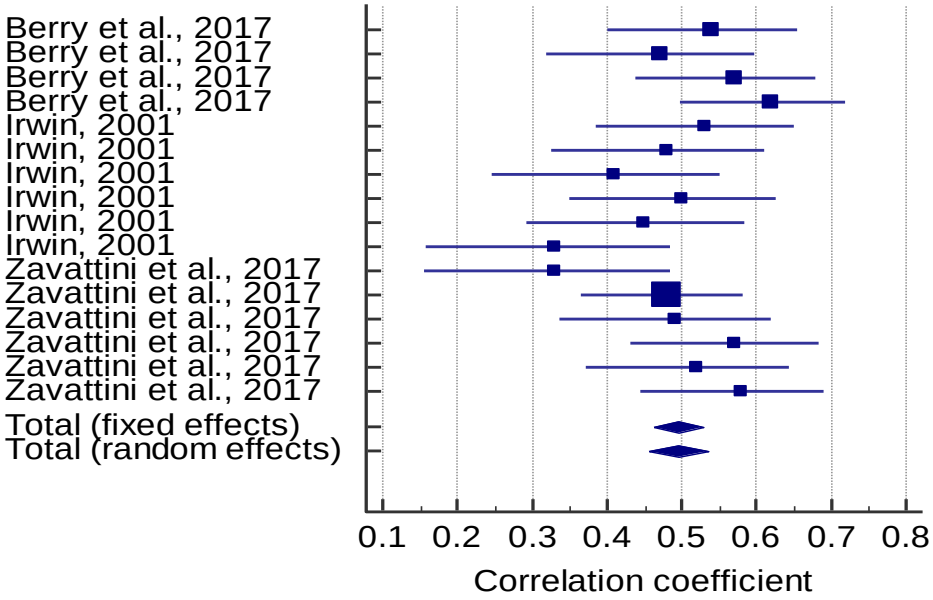

Figure 6. Correlations between the main

5. DISCUSSIONS

Through this meta-analysis, we aimed to identify the existence and intensity of the link between dissociation and psychosis, in people diagnosed with schizophrenia, people with symptoms of schizophrenia, but also those in the non-clinical population.

Of the 12 studies included in this meta-analysis, in only one study dissociation is seen as having manifestations that can be evaluated on a continuum (9), the general perspective being that dissociation is a disturbance of the normal process of identity integration, emotion, perception, body representation, motor control and behaviour, in the stream of consciousness and memory (9, 10, 11, 12, 13). Vogel et al. (11), for example, propose a bipartite model of dissociation. The authors demonstrate that dissociation was not placed on a continuum within the studied group but, on the contrary, was discontinuous, with aspects of detachment distinct from those of compartmentalization in relation to psychotic symptoms. Thus, dissociative detachment is related to the positive symptoms of schizophrenia and compartmentalization to the negative symptoms.

Regarding psychosis, it is mainly conceptualized by the presence of hallucinations and delusional ideation (9, 12, 13, 16, 18).

The link identified between psychosis and dissociation is a significant and positive one, despite the heterogeneity of the studies included in the meta-analysis, the strongest associations of psychosis being with derealization and absorption. One of the most recent studies that attempted an overview of the scientific literature exploring the relationship between dissociation and psychosis was published by Renard et al in 2017 (22). It included 75 studies published between 1980 and March 2016 and was limited to provide a systematic review without performing a meta-analysis. Renard et al. (22) showed that most studies demonstrate the presence of dissociative manifestations within schizophrenia spectrum disorders, and an important overlap of symptoms within the two diagnostic categories.

Dissociation is a feature of participants diagnosed with schizophrenia, but the results should be viewed with some caution. Another significant result of the present study is the one that signals a significant link between

characteristics of schizophrenia and measured dissociation in the normal population, which, again, we look at with caution. Humpston et al. (23) examined the contribution of dissociative processes to the emergence of psychotic-like phenomena in a nonclinical population. The results showed a significant correlation between detachment and absorption dissociation, but not compartmentalization, and pseudo-psychotic experiences in this population.

Such information can be extremely important for the formulation and implementation of psychotherapeutic intervention programs. For example, interventions focused on reducing dissociation could represent a potential treatment for auditory hallucinations (9).

Dissociation is a complex phenomenon involving different mechanisms that can modulate both the psychopathological processes underlying psychosis and recovery.

6. LIMITS

One of the major limitations is the small number of studies included in the analysis and their very diverse nature. Because research in this field is difficult to undertake due to the difficulty to conceptualize dissociation and the overlapping of the phenomenological manifestations of dissociation and psychosis (22), we identified a very small number of studies that could be included in our analysis.

Their diversity is determined by the theme, the number and type of population included, as well as the fact that the analysis takes into account several types of dissociation.

Another limit is that not all of the authors reported results on each dissociation subscale, and the small number of studies does not allow subscale analysis.

7. CONCLUSIONS AND RESEARCH DIRECTIONS

Analyses showed a significant and positive association between forms of psychosis and dissociation, significant differences between the clinical and non-clinical groups, and a significant association between characteristics of schizophrenia and measured dissociation in the normal population. Even if the statistical results of this study are limited, the process of reviewing the existing scientific literature in the field of dissociation and psychosis has been very useful.

The literature is extremely diverse and dissociation is a phenomenon with many facets, difficult to measure unitarily, but which can be conceptualized very specifically through its processes. Further research is needed to observe what happens to dissociative phenomena throughout the evolution of psychosis and not just in the acute phase of this illness.

CONFLICTS OF INTEREST: The authors declare no conflict of interest.

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Discernment or representation

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ABSTRACT

The field of forensic psychiatry involves the application of psychiatric expertise to legal cases involving individuals with mental illness. However, the use of this expertise raises questions about the rights of mentally ill patients, particularly regarding behaviour control and involuntary hospitalization. In order to avoid abuse of medical authority, it is important to uphold the principles of individual autonomy and the right to be informed about one's detention. Legal regulations must balance the protection of individual rights with the need for social protection, through the promotion of destigmatization of psychiatric patients and the elaboration of national studies to assess mental health and psychiatric-legal liability. Psychiatric forensic expertise must be conducted in accordance with scientific validity, avoiding diagnostic errors and expert iatrogenicity, and promoting only opinions based on proven truths. The expert's responsibility is to maintain scientific neutrality and independence while respecting the rights of the patient, avoiding any suspicion of abuse of medical authority and preserving the ability to explain, exonerate, or indict with truthful conclusions. This requires a balance between expert professionalism and the consciousness of one's own limits while prioritizing the rights and autonomy of the patient. Legal regulations and ethical-scientific requirements of psychiatric-legal exploration must be applied to ensure that the field of forensic psychiatry upholds the principles of justice and human rights.

KEYWORDS:

Forensic psychiatric expertise; involuntary hospitalization; patient rights; mental health laws.

INTRODUCTION

In the evolution of social life, the process of legislative adaptation imposed itself with the need for an act of social progress. Romanian legislation joins this process by ratifying some international legal norms and by conceiving laws consistent with European norms. Thus, for example, law 487/2002 on mental health defines mental illness as "*a state in which the person loses consciousness of the meaning and consequences of his acts*", a state expressed clinically and especially expertly through the non-existence of discernment. Thus, in clinical expertise and expert evaluations, lack of discernment becomes the essential criterion of the positive diagnosis of mental illness.

The criterion of discernment, as the basis of the relationship between mental pathology and behavioural acts of a person, presents risks of incorrect expert evaluation generated by several factors:

- failure to comply with the criteria of a positive diagnosis of mental illness in effect by superficial evaluation of the case;
- ambivalent, preferential evaluation, with risks of violation of the rights of the person or the community in their expert interpretation;
- preferential evaluation through abuse of medical "sentimentalism" in the desire to solve human problems related exclusively to the autonomy of the person;
- stigmatizing evaluation, based on patterns of behaviour specific to a community that inevitably lead to harmful behavioural reiteration;
- effects of overestimation or underestimation of the risk of behavioural harmfulness that is interpreted according to other factors (social, criminal) exceeding the exclusively medical criterion;
- effects of transforming the person's behaviour exclusively into a template behaviour through an anticipated interpretation of the antecedents, manner and circumstances of committing the deed;
- failure to respect the rights of the person or another expert opinion.

These risks can be primary, secondary or tertiary, and can result in either an abuse of " psychiatrisation" (of creating a mental illness when it does not exist) or a refusal to help a person at risk (fear of responsibility to formulate a diagnosis). These extremes can be corrected by professional competence, scientific neutrality (expert independence) and the awareness of own limits that oblige the expert to validate his conclusions only through scientific argumentation. Through these techniques it is possible to broaden the scientific content of the notion of discernment, being able to cover more effectively the "empty meshes of the sieve" of psychiatric forensic evaluation.

Classically, the criterion of discernment has become the cognitive psychological element of evaluating the behaviour towards a social deed, due to its position of differentiation between good and bad, which results from the correct perception of reality and the voluntary control of the behaviour in the effort to appease the self.

Considered, since ancient times, as a "right reckoning", discernment meets, especially, skills of analysis and synthesis, which, through permanent socialization, must be maintained in a vigilant state, "like a sword that must always be polished in order not to rust".

Piaget believes that the effects of discernment are:

- the correct measure of the consequences of one's own deeds;
- as a consequence, the manifestation of the autonomy of the will of the person.

For family sociology, discernment is the primitive form of intelligence that precedes language and for Patapievici it is "a natural sense over which the representation is superimposed"."

As a "primitive" form of intelligence, discernment is formed with the first germs of moral consciousness, which go through the stages from "heteronomy" (of accepting out of obligation the imposed norms) to those of "autonomy" (of conscious acceptance of the imposed norms). As the most primitive form

of intelligence (E. Pamfil), the distinction between good and evil predates language, at first, being unconscious (good being what is approved by parents and bad what is disapproved of by them). The lack of transition from the heteronomy of the discernment between good and evil to its autonomy made discernment be considered a criterion "of mental competence", a key quality of moral balance, determined by the rationality of human knowledge. Based on the innate distinction between good and evil, discernment is permanently built through the socialization of knowledge. As an inalienable human faculty and as an inevitable judgment of behaviour evaluation, discernment has become a criterion for the scientific evaluation of the ability to discriminate between right and wrong, lawful and illicit, legal and illegal, etc. thus evoking its pragmatic usefulness in the ability to judge good or bad deeds of behaviour.

However, the question arises whether this criterion also includes the affective-volitional states, which, in unity with the cognitive ones, offer an integral understanding of the attitude of behaviour towards a certain deed. It is known that in behaviour acts, affective states often have an influence that exceeds cognitive discrimination, because:

- the affective state is the main provider of energy for the cognitive world;
- affective states are those that give stability to the human attitude, like locks that close or open access to cognitive information, thus fulfilling the role of a binder for knowledge;
- Affective states are those that determine the hierarchy of thought stages by reducing its degree of complexity and by focusing on what is essential in a behavioural attitude.

In this respect, discernment brings into discussion the superior ability to assess and terminate a behavioural attitude in different life situations.

LEGAL PSYCHIATRIC REPRESENTATION AND EVALUATION

Representation, considered a natural law by the "light of intelligence placed in man," was even in Thomas D'Aquino's conception, a criterion for differentiating "what is to be done and what is to be avoided." Durkheim and, in our country A. Neculau, revealed the major role of representation in human behaviour, considered a more faithful guide of human relations with the existential environment.

As a fundamental and comprehensive element of the mental life, the representation evokes the connection of existence with its essence, as well as the ability to anticipate the consequences of behaviour (*one of the most specific features of representation*) that has detached the human from the animal world. Only the human who has representations can anticipate. Thus, the representation is also manifested in deviant conditions, because only humans act premeditated.

Representation is therefore the comprehensive way of organizing the knowledge of a social act, both upstream (through anticipation) and downstream (through justification), this structure having a primordial role:

- in giving meaning to lived reality;
- in integrating new notions and facts into behaviour;
- in providing common meanings to behaviour.

As innate behaviours with the role of anticipation and adaptation to the environment, the representations conditioned the evolution of man, the information received by the brain not being so much reflected as represented. For A. Neculau representations are therefore "superior and comprehensive forms of social consciousness through which man builds the reality of an event, interprets it and which, as an instrument of perception and orientation of life situations, elaborates adequate responses". Representations thus give a presence of spirit, have the ability to settle conflicts and organize a response to environmental

circumstances. They have a prescriptive role (influence behaviour) and control behavioural attitudes, their major role being manifested, especially, in situations of man-environment relational crises. The representation unites the internal response with the external one within behaviour and thus the individual integrates it into his own system of values (J. Cl. Abric), giving meaning to his acts of behaviour. Through all these, representation evokes its complex function of knowing the reality, of social communication, of behavioural guidance (of filtering the reality and by anticipation, of determining the type of behavioural action), of judging the behaviour, as well as a heuristic function, of behavioural progress. Indeed, representations are incorporated into mental schemes and patterns of adapted or deviant behaviour.

The response to any behavioural act is a reconstruction through the representation of reality, a response integrated into a social context and in the value system of the individual. By representation one can better understand a social reality, one perceives and orients more correctly his/her behaviour in a life situation, because, the central core of representation is the stable system of individual and group norms, around which representation is organized by anchoring the behaviour to the reality of the situation. The representations, therefore, have the role of regulating behaviour and adapting it to the concrete situations with which it is confronted. Representation connects the psychological state to the social situation, thus reflecting the quality of personal behaviour.

Representation is formed according to the stages of development of moral behaviour (Kohlberg). Characteristic for representations is therefore their ability to transform a concept into an action (its objectification) as well as the correct interpretation of the action. This phenomenon is modulated by the behavioural sensitivity to the situational context and its adaptability to concrete life situations. That is why, for S. Moscovici, "representations are born from life and impose on life a certain conduct, the human being nothing more but a mirror of his representations".

"The survival of the organism and its proper integration into the environment depends on the ability to anticipate the representation" (Dawkins), so representation becomes the key to adequate or inadequate adaptation to the environment.

Representations also include techniques of "masking" the violated norms by:

- their denial (and the motivation of action by accidental causes);
- denial of the harm produced (its minimization);
- denial of the victim (who deserves his fate);
- until the accusers are indicted.

In difficult situations of social orientation, representations allow us to assess the advantages and disadvantages by adopting appropriate behavioural solutions. In situations of deviance, the criminal norms become behavioural landmarks from which one can deduce the reason, the level of representation and the factors that direct the behaviour in a negative sense.

In conclusion, we consider that representations are elements of behaviour that regulate interpersonal relationships, and have a more elastic and optimal ability to reconstruct the real by mediating the cognitive sphere with the emotional one. In other words, everything in behaviour are social representations that include attitudes, opinions, the ability to discern and, in the end, orienting the behaviour and mastering or not a situation.

For example, paedophilia constitutes an alteration of representation about children (as victims of ill-treatment), autism and schizophrenia an alteration of representations about oneself and in relation to others. Representation reveals both physiological and pathological norms of the behaviour, in them being the neurobiological basis for behaviour. The representations are therefore categories of schemes, prior prototypes of behavioural response, which acquire precision in relation

to the amount of information received, allowing supple adaptation to environmental conditions for which the human organism has no innate solutions. Representations are fathomed as mental states through *intentionality*, through *the ability to adapt to situations, to anticipate the results* and through *the ability to evaluate the results of the behaviour*, thus overpowering discernment. By the fact that representation cumulates the judgement of an action with the adaptation of the behaviour to the circumstances, it becomes more justified to expertly state whether or not a person had the representation of the content and consequences of his acts of behaviour than whether or not he had the discernment of these facts. In other words, the ability to represent the content and consequences of a deed is a more complex criterion for evaluating behaviour and can replace discernment, with benefits for psychiatric forensic expertise.

FORENSIC PSYCHIATRIC EXPERTISE AND THE RIGHTS OF MENTALLY ILL PATIENTS

Through the prediction of mental harmfulness, the expertise raises the problem of behaviour control, the legitimacy of modifying the patient's ideas, permitted only for psychosis, as well as the involuntary hospitalization reserved only for situations in which the patient has lost contact with reality. In the absence of that loss, in accordance with the principle of individual autonomy, we cannot apply constraints. In practice, we have encountered situations generated by the lack of information provided to the family in order to prevent the risks related to the disease, the abuse of neuroleptics treatment and the non-follow-up of its effects, the failure to interrupt the treatment in case of extrapyramidal symptoms, the disclosure of confidentiality, premature discharge, escape from the hospital or the unjustified hospitalization.

The International Act on Civil and Political Rights ratified by Romania, the mental health law and the patient law stipulate that no one may be subjected to cruel, degrading or inhumane punishment and treatment and that anyone has the right to be informed of the reasons for his detention, including in hospital, and to request the verification of the validity of the detention.

As a consequence, it is necessary to promote more firmly by law the destigmatization of psychiatric patients as well as the elaboration of national studies to assess the mental health state or the conditions of psychiatric-legal liability. It should also be specified by its own regulations, the conditions for the application of safety measures, the regime of difficult patients, etc., in order to find a balance between the protection of individual rights and social protection. Through the process of legal adaptation, the legal regulations in Romania have enshrined the universal principles regarding the rights of the mentally ill, stipulated in the Resolutions of the Council and the Parliament of Europe no. 818/997 and 83/990. The expert is thus obliged to apply the provisions of the government ordinance 1/2000 and its amendments regarding forensic expertise, law 46/2003 on the rights of patients, the law on mental health and the protection of persons with mental disorders 487/2002 as well as law 17/2001 for the ratification of the European Convention for the protection of human rights and of the dignity of the human being towards the applications of biology and medicine elaborated in Oviedo in 1997.

Based on these regulations, psychiatric forensic expertise will adapt the analyzed behaviour to scientific realities to avoid the rigidity of the conclusions drawn up. Psychiatric forensic expertise is thus a science both by its object of activity and by the connections it has with the science of human behaviour. It is thus built on clear and rigorously defined fundamental concepts, on arguments tested by research and scientific validity.

The human and scientific structure of expert psychiatry thus acquires the ability to decipher the aberrant human behaviour that alters the human essence. Hence the working climate of the expert who is a doctor and not a representative of justice, although his

conclusions belong to justice. Excessive expert professionalism must be replaced by respecting the rights of the patient in order to avoid any suspicion of abuse of medical authority. The autonomy of the patient, together with the scientific neutrality and the independence of the doctor are the bases of the expert's responsibility. Only in this way will a psychiatric-legal expertise preserve the ability to explain, exonerate or indict, promoting only opinions based on scientifically proven truths. Neutrality and objectivity of the expert as well as the consciousness of his own limits will allow truthful expert conclusions and not with sanctioning facets. Avoiding the risk of psychiatric victimization through diagnostic errors, ambivalent conclusions or refuge of the patient in expert disease (expert iatrogenicity) must complete the ethical-scientific requirements of this kind of medical exploration.

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Emotional regulation and emotional processing among schizophrenia patients or patients at high risk for psychosis - a review

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ABSTRACT

Schizophrenia represents a serious mental disorder mainly characterized by psychotic symptoms (also called positive symptoms) such as hallucinations, delusions, disorganized thought and speech. People diagnosed with schizophrenia also experience symptoms like avolition, anhedonia, affective applatization and social withdrawal (which are known as negative symptoms). Studies show that schizophrenia patients or schizophrenia-prone patients have emotion regulation difficulties and impaired emotional processing involving experience, expression, and recognition of emotions, although they seem to be able to apply certain emotion regulation strategies (such as reappraisal or distraction) under experimental conditions. The aim of this narrative review is to gain an understanding of the existing research regarding emotion regulation and emotion processing deficits in patients with a schizophrenia spectrum disorder or at high risk for psychosis as well as highlighting what strategies work best for down-regulating negative affect or anxiety in psychosis. Both emotion regulation and processing are viable instruments in managing emotion, further studies are required to evaluate the impact of those strategies in schizophrenia patients.

KEYWORDS:

Schizophrenia; emotional regulation; emotion processing.

INTRODUCTION

Emotional regulation refers to a person's emotional response to a particular situation or event. It is an individual's conscious or automatic attempt to influence what emotions he has, when and how to have them and how to express them and can affect one or more points in the emotion-producing process (1). Among the most well-studied emotion regulation strategies are reappraisal, distraction, and expressive suppression (2-4). Reappraisal is defined as the attempt to reevaluate a situation in such a way that changes or reduces the generation of an emotional response (1). Distraction involves focusing on stimuli or aspects that are not related to the emotion-generating situation

(5). Expressive suppression represents the inhibition of expressive behavior (1). Reappraisal and distraction are antecedent-focused emotion regulation strategies (those strategies that are implemented prior to the completion of the emotion generation process). according to the process model (1, 6). Expressive suppression, on the other hand, is a strategy focused on response or in other words, a strategy used to modulate affect after an intense emotional experience (1, 6). Studies indicate that reappraisal is more effective than expressive suppresion in regulating negative affect (6-8).Distraction was also proven to be effective in reducing negative affect (3,9). It is known that patients with schizophrenia or at high risk for psychosis have emotion regulation difficulties (10-12) as well as difficulties regarding emotion processing (13-15). Emotional processing is the ability to perceive, use and understand emotions, including the ability use and understand non-verbal behavior, spoken language and facial expressions as well as the capacity to manage one's own emotions (16).
The systematic review conducted by Phillips and Seidman (2008) provided evidence that people at high risk for psychosis report emotion regulation and emotion processing difficulties. Another systematic review and meta-analysis conducted by Lawlor et. al (2020) confirmed that patients with schizophrenia spectrum disorders also have difficulties regarding emotion regulation and emotional processing (particularly in identifying, describing, accepting or understanding emotions) as well as unwillingness to experiment negative emotions as part of pursuing meaningful activities in life (14,17).

METHOD

We conducted a search for studies that analyzed the extent of emotion regulation and emotion processing deficits in schizophrenia patients and whether certain emotion regulation strategies are effective in down-regulating negative affect or anxiety.All the studies taken into consideration were published between 2014 and 2020 in Elsevier or PubMed, and contained either cross-sectional, longitudinal or experimental data.The searching strategy used was:"emotion regulation in schizophrenia", "emotion regulation difficulties in schizophrenia", "emotional processing in schizophrenia", "emotional regulation in psychosis", "emotion processing in psychosis", "emotion recognition in schizophrenia".

RESULTS

Emotion regulation and processing in schizophrenia patients or patients at high risk for psychosis

Regarding emotion regulation in patients diagnosed with schizophrenia, a cross-sectional study conducted by Tabak et. al (2015) which aimed to compare levels of perceived emotional intelligence (which includes abilities like perceiving emotions, understanding emotions and managing emotions), between schizophrenia, bipolar, and control participants and to examine the correlations between self-reported emotional intelligence and community function within each clinical group, found that individuals with schizophrenia report greater difficulties in managing their emotions compared to bipolar patients and healthy controls.It was also found that bipolar patients report similar difficulties, but not as much as schizophrenia patients (18).

Another cross-sectional study, conducted by Kimhy et. al (2016) compared patients at high risk for psychosis, schizophrenia patients and healthy individuals regarding emotional awareness and regulation; they also investigated the correlations between

emotional awareness, emotional regulation and social functioning in patients at high risk for psychosis. They hypothesed that individuals at high risk for psychosis will show emotional awareness and emotional regulation difficulties intermediate to the schizophrenia and healthy control groups and those difficulties will predict social functioning deficits. They found that, indeed, patients at high risk for psychosis display difficulties regarding emotional awareness and emotion regulation deficits, at severity comparable with those observed in schizophrenia individuals.They also found that those deficits predict a poor social functioning across all clinical groups (19).

Studies also show that, under experimental conditions, schizophrenia patients are able to apply successfully certain emotion regulation strategies. A study conducted by Grezellschak et. al. (2015) wanted to compare the efficacy of reappraisal and distraction in down-regulating anxiety across three groups: schizophrenia patients, patients with a history of cognitive-behavioral therapy and healthy non-clinical controls. They used pictures and sounds to induce anxiety, then they instructed participants to use either reevaluation or distraction in order to reduce anxiety. They demonstrated that schizophrenia patients are able to use both reappraisal and distraction for down-regulating anxiety. No differences were found between schizophrenia patients, patients with a history of therapy and healthy controls (20).Those results were similar to those obtained by van der Meer et. al (2014), who tested the efficacy of reappraisal and expressive suppression in down-regulating negative affect across three groups (schizophrenia patients, their healthy siblings and healthy controls) using the same experimental stimuli. All groups reported decreased negative affect after both regulation conditions (20, 21).

Recent studies show that emotion processing is also affected in schizophrenia patients. Cicero et. al (2016) conducted a research investigating whether those patients have emotion processing deficits and whether they are associated with anomalous self-experiences and positive symptoms. They compared schizophrenia patients with healthy controls and found that anomalous self-experiences, as well as positive symptoms are associated with emotion processing deficits in individuals diagnosed with schizophrenia (22).

Another study, conducted by Comparelli et. al. (2013) found evidence for the stability of deficits in emotion recognition (which is a component of emotional processing) throughout the course of schizophrenia. Their primary objective was to see whether those deficits are the similar between prodromal patients, patients with a single episode of psychosis, patients who experienced multiple episodes and healthy controls. They found that prodromal patients have difficulties recognizing emotions like sadness and disgust, while schizophrenia patients have issues recognizing all negative emotions (23).
Available longitudinal data shows that emotion processing deficits in schizophrenia are stable over time. An example is the study conducted by McCleery et. al (2016) examinated whether social perception and emotional processing deficits are stable over the course of 5 years. They evaluated recent-onset and chronic patients at baseline and five years later using pictures with actors that displayed different emotions and videos depicting interactions between men and women. The results show that indeed, social perception and emotional processing deficits are stable throughout the course of schizophrenia (24).Those results are similar to those obtained by Addington et. al (2012) which demonstrated that difficulties regarding

emotion recognition are stable over the course of two years. They measured emotion recognition across two groups (patients at high clinical risk for psychosis and controls seeking help for psychosis) using pictures with actors displaying different emotions as well as audio clips of 4 simple sentences (i.e. "he will come soon", "they must stay here", "she will drive fast" and "we must go there") spoken by three professional actors displaying following emotions: fear, sadness, anger, surprise and no emotion five times (at baseline, 6 months, 12 months, 18 months and 24 months) and found that both groups display pronounced emotion recognition deficits. They also observed that a quarter of the patients at high risk for psychosis converted to psychosis, but even so, there were no difference in terms of emotion recognition between them and those who haven't developed a psychotic disorder (24, 15).

DISCUSSION

It is worth mentioning that, as shown by the analyzed studies, schizophrenia patients or patients at high clinical risk for psychosis show emotion regulation deficits (18, 19). However, schizophrenia patients are able to apply certain emotion regulation strategies, such as reappraisal and distraction successfully under experimental conditions (20, 21). This aspect is confirmed by the study conducted by Visser et. al (2017) which demonstrated that certain emotion regulation strategies are effective but patients in the acute phase have difficulties identifying how they feel, what emotion regulation strategy they should use and how to implement it. Overall, those studies show that emotional regulation strategies are beneficial under certain circumstances and lesser use of adaptative strategies lead to poorer clinical outcomes (25, 26).

Regarding emotion processing in schizophrenia, analyzed studies demonstrated that schizophrenia patients or patients at high clinical risk show pronounced difficulties in this area (23, 24). However, the patients in those studies did not receive any treatment programs designed to address emotion processing deficits in schizophrenia.

It is worth mentioning that longitudinal studies show that difficulties in emotion processing and social perception remained constant even at a 2- and 5-year mark for prodromal as well as acute and chronic patients (Addington et. al 2012; McCleery et. al, 2016).

Future studies should consider controlling for different factors that may influence the results (such as context and emotion intensity) and examine whether emotion regulation deficits could be improved with specially-designed therapy programs or psychoeducational interventions (teaching patients how to use emotion regulation strategies). A study conducted by Perry et. al (2012) showed that schizophrenia patients could benefit from using acceptance as an emotion regulation strategy, in addition to reappraisal and distraction, which are demonstrated to be effective in reducing negative affect (27). Perhaps future studies are needed to see whether schizophrenia patients have difficulties inhibiting impulsive responses when facing a negative emotion and whether those responses could affect certain aspects of their life (such as social interactions and relationships, work performance or performance in regular everyday tasks).

CONCLUSIONS

Emotion regulation represents the way we respond to emotion-generating situations. Although some emotions or affective states (such as sadness or state anxiety) are easier to manage via reappraisal, distraction or acceptance, there are a series of emotions that are difficult to manage even for healthy individuals (such as anger, shame, frustration, disappointment and helplessness).Those emotions could be the target for future studies investigating the efficacy of the aforementioned emotion regulation strategies.

With regards to emotion processing (which involves the ability to perceive, use, understand and manage emotions from non-verbal behavior, spoken language and facial expressions) future studies should investigate whether individuals with a schizophrenia spectrum disorder or at high clinical risk are able to process more difficult emotions.

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Gender dysphoria and anorexia nervosa – a scoping literature review

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ABSTRACT

Gender dysphoria is a relatively new topic in psychopatology and even less studied among Romanian people. At the same time, until now, most studies related to another specific psychopatology, that is eating disorders, in particular anorexia nervosa, have been focusing on the cisgender population. Recent years have shown an increase in studies correlating eating disorders with gender nonconforming people and the ones suffering from gender dysphoria. Both anorexia nervosa and gender dysphoria are correlated with poor body image, although stemming from different causes. Gender dysphoria is also associated with other eating disorders, behavioural problems and minority stress. Anorexia nervosa may also represent a dysfunctional coping mechanism in order to alter the person`s appearance, so as to better suit their perception of their desired gender identity. We conducted a scoping review, focusing on the articles correlating gender dysphoria and eating disorders, especially anorexia nervosa, with the purpose of better acknowledging the extent of the phenomena and some of its correlations. Participants were people registered in studies which analysed interconnections among those psychopatological particularities, regardless of age. The main results were: eating disorders, in particular nervous anorexia are common to both cisgender people and people with gender dysphoria, eating disorders are greatly influenced by risk factors such as: negative body image driven mostly by media, general dissatisfaction regarding gender incongruence, social and minority stress. Gender affirming treatment (hormonal / surgical) can influence eating disorders, but researchers do not have a unitary viewpoint on the matter. Conclusions: more detailed studies are needed to understand how gender dysphoria influences nervous anorexia, and viceversa, and how this eating disorder evolves after gender affirming interventions. More specific information is also needed to educate medical caregivers in order to better assist people with gender dysphoria and eating disorders and offer them the best possible counselling for future treatment.

KEYWORDS:
Gender dysphoria, anorexia nervosa, eating disorders, body image.

INTRODUCTION

21st century society is constantly changing. This implies new perspectives and rewriting some of the established values of the past.

Changes on multiple layers of social, economic, political etc. life affect the daily existence of each individual. But the most serious problems of adaptation are faced by vulnerable people, as their physical health, occupational functioning, emotional and psychological balance may be affected. Individual maladaptive reactivity can be dominated by anxiety, disorientation, confusion, feelings of not belonging, fear, frustration, helplessness, rebellion. Eating disorders may also come from maladaptive reactivity to the stresses of life. These are of increasing interest to researchers today.

Anorexia nervosa has a multifactorial aetiology and is characterised by significantly low body mass, as a consequence of intense fear of gaining weight and persistent avoidance behaviour. The consequence is disruption of the person's perception of their own weight or body shape and a refusal to acknowledge the medical seriousness of this behaviour. The term 'anorexia' comes from the Greek language: *an* (”lack of”) and *órexis* (”craving, appetite”). Long- term effects can include organ failure, disability and, in extreme cases, death (1). In fact, among psychiatric disorders, anorexia nervosa has one of the highest mortality rates (2, 3). This type of eating disorder is also present in people with gender dysphoria, one of the most vulnerable categories of people, in terms of functionality in general, but especially social adaptation.

The phenomenon of gender dysphoria is increasingly visible worldwide and has specific behaviours associated with it, with both individual and social consequences. Gender dysphoria, a set of psychological traits and specific behaviours that is much studied and debated today, has at its core the profound mismatch between a person's biological sex, present at birth, and the gender they experience and express in society. There is marked discomfort and a desire to belong to the gender with which one identifies, which leads to nonconforming behaviour (wearing clothes considered appropriate to the desired gender, having a behaviour perceived as characteristic of that gender etc). The term ”dysphoria” also comes from Greek, from *dúsphoros* - ”painful” or *dus* – ”bad, difficult” and *phérō* – ”to bear”. The DSM V diagnostic criteria include manifestations that last for at least 6 months and consist of: an intense desire to escape from one's primary and/or secondary sexual characteristics, to have those of the desired gender, to belong to that gender, to be treated by society as if belonging to that gender, with the firm belief that one has the feelings and reactions typical of the gender with which one identifies. All of these manifestations cause clinically significant discomfort and deficits in social, occupational and other important areas of functioning (1).

The literature establishes correlations between eating disorders in general, especially anorexia nervosa, and gender dysphoria. These medical and social phenomena are increasingly being addressed by researchers and are attracting growing interest, both in terms of diagnosis, treatment and the possibilities for social integration and adaptation of those affected.

MATERIAL AND METHODS

We conducted a scoping review of the published literature in the field, in order to identify correlations between the two diagnostic entities: gender dysphoria and anorexia nervosa. We selected a number of 20 articles, which ranged from systematic reviews, case studies to original articles, published in English between 2015 and 2022, regarding gender dysphoria and anorexia nervosa and their possible interrelations.

RESULTS

The Google Scholar database provides, using the search terms ”gender dysphoria, eating disorders”, a number of 29600 results, which demonstrates the interest in this topic. In 2022 alone, 3940 studies were published, and in

2023, 1490 studies. The same database offers for the search terms ”gender dysphoria, anorexia nervosa”, a number of 15600 results, of which 1290 in 2022 and 480 during 2023.

For both cisgender people and those with other gender identities, body image is how they perceive themselves, and therefore how they perceive their gender identity. The literature shows that most people with gender dysphoria resort to habitual, basic means to adapt their appearance to what they want, for example gender - specific clothing. Others feel the urge to resort to dysfunctional eating patterns, such as anorexia nervosa behaviours, in order to drastically alter their appearance. They hide from others, distorting the dysfunctional reality they experience (4).

In the case of both cisgender and gender nonconforming individuals with gender dysphoria, a very important role is played by environmental factors in the development or worsening of anorexia nervosa, the most important of which are: social isolation, influence of the entourage, social pressure and cultural microenvironment (5). For any person, socio- economic status and profession can sometimes be risk factors for developing eating disorders, including anorexia nervosa. These factors have been found to be significantly more evident in gender minority individuals, especially those with gender dysphoria. Studies show that they most frequently face stigma, social, cultural, religious and workplace discrimination and also limitations in access to health services (6).

Dissatisfaction with the appearance of one's own body, which underlies the development of eating disorders, including anorexia, is also examined in a study published in 2015, in which the conclusion is that eating disorders serve the purpose of suppressing the physical features specific to one's biological sex and accentuating those of the desired gender (7). Similar conclusions can be drawn from the study published by Jones et al, who state that body dissatisfaction and negative self-appraisal are causes of distress for trans people and that this dissatisfaction may also put some at risk of developing eating disorders. Some authors find that treatment of gender dysphoria succeeds in increasing body satisfaction and improving self-image. Ålgars et al (2012), cited by Jones et al (2015), state that dietary restriction in trans women is a way to appear slimmer in order to suppress the characteristic features of their own gendered anatomy, thereby emphasising the features of their perceived desired gender. It is possible that trans women internalize the message presented by the Western media that feminine beauty also requires a slim figure. Internalising this type of message is thought to be a risk factor for the development of eating disorders in cisgender people as well, but may be particularly at risk for trans women (8).

Moreover, it is well known that social media plays a significant role in shaping self-image, with research showing a correlation between the use of social media platforms, especially those with rich visual content, and poor personal body image (9).

Thus, gender dysphoria, which is in fact a global negative perception of self-image, makes a person more susceptible to disordered eating behaviours.

In some cases, the correlation between gender dysphoria and eating disorders in general is noticeable even at young ages, as evidenced by a study published in 2019, according to which significantly increased rates of eating disorder symptoms have been documented in transgender youth compared to cisgender youth. One explanation is that they resort to such methods to prevent the onset or progression of puberty, and thus the development of unwanted gender-related sexual characteristics. This has been identified in people aged between 8 and 25 (10). The first case study of a child with gender dysphoria and eating disorders was published in 1997 (11), but since then the number of such cases has increased considerably, as has interest in the study of the field.

Hartman - Munick et al, in an article

published in 2021, reiterate the increased risk for transgender and gender-diverse youth of disordered eating, unhealthy body weight control behaviors, and eating disorders, respectively. It highlights three dominant themes that burden the study of the correlation between gender dysphoria and eating disorders: the barriers to screening and treatment of eating disorders, the complexity of the relationship between eating disorders and gender dysphoria, and the need for complex gender- affirming education within the healthcare provider system (12).

Of course, limiting calorie intake and physical exercise, even extreme ones, can be much more useful for young people in shaping their bodies to support gender affirmation than specific, radical, expensive treatments that require special conditions of accessibility. The prevalence of eating disorders has been found to be higher in those who transition female to male (FtM) than in those who transition male to female (MtF), suggesting that female biological sex would be an independent risk factor for the development of eating pathology.

At the same time, when discussing the psychopathology of eating disorders and gender dysphoria respectively, puberty should be seen as both a social and a biological risk factor (13). The importance of studying the psychopathological aspects involved is all the greater, since it has been shown that suicide rates are higher in transgender adolescents than in cisgender ones, partially attributed in this context to the development of secondary sex characteristics, which accentuate the discordance with their perceived gender identity (14).

In contrast to other studies, which attest to improvement in pathological eating behaviours following gender reassignment (hormonal/ surgical) treatments, a case study published in 2017 by Hiraide et al reaches an entirely different conclusion by illustrating the case of a patient whose anorexia nervosa began in the period following gender reassignment surgery (male to female). A particularity of the presented case was the person's origin in Japan, as it is known that there is a low tolerance towards sexual and gender minorities, with strong cultural values that promote the traditional family, because of which many people with other sexual orientations or gender identities choose to hide their belongingness by getting in cisgender marriages and having children. In this socio- cultural context, people suffering from gender dysphoria face significant stress, which can precipitate the onset or worsening of eating disorders, including anorexia. The major influence of socio- cultural environmental factors on the evolution of both diagnostic entities in question is thus confirmed (15).

In a paper published in 2021, Nowaskie et al evaluated the correlation between gender identity, gender- affirming interventions (hormone therapies, surgery) and the presence of eating disorders. It was concluded that there were differences depending on the intervention undergone. Thus, compared to those who had not undergone such therapies (”hormone and surgery naive”), or those who had undergone hormone therapies but not gender- affirming surgery (”hormone experienced but surgery naive”), those who had experience with both hormone therapies and surgery had lower rates of eating disorders, as well as less concern for physical appearance and body weight. According to the authors, the high prevalence of eating disorders in people with gender dysphoria would predominantly be the result of the combined negative impact of socio- cultural pressures and gender dysphoria. Both hormonal and especially gender- affirming surgical therapy could mitigate the severity of eating disorders as a consequence (16).

Multiple types of gender identities are currently being affirmed internationally, however, most of the reviewed literature does not differentiate between these (17). However, Watson et al's study, published in 2017, distinguishes between participants with binary and nonbinary gender identities, respectively, and concludes that stigma, manifested as harassment and discrimination, experienced by sexual and gender minority

individuals, is correlated with higher odds of self- reported past- year binge eating or, conversely, abstaining from food or inducing vomiting to lose weight. Protective factors such as healthy family relationships, school attendance, supportive entourage and social support were associated with reduced odds of eating disorders. According to this study, the prevalence of self- induced vomiting episodes in the past year was higher in nonbinary individuals than in those with binary FtM (female to male) identity, and prolonged food abstinence was more common in those with binary MtF (male to female) identity compared to nonbinary individuals. However, nonbinary individuals falling on the FtM gender identity spectrum may differ significantly behaviorally from nonbinary individuals falling on the MtF identity spectrum. Compartmentalizing gender identity subgroups into larger categories could mask potentially significant differences in the prevalence of eating disorders in transgender samples. This may lead to concrete implications for the design, development and implementation of subsequent interventions.

Regarding self- reported versus diagnosed eating disorders and risk/ protective factors, a 2016 study looked at differences between specific gender identity subgroups in transgender adults and found that these differences exist (18).

The literature also points out that with increased rates of pathological eating behaviours in people with gender dysphoria, there is an emerging need for standard screening to identify these manifestations and be applicable to both diagnostic categories, both at the time of initial assessment and during treatment. As such, the recommendations are that specialists in the field should always investigate gender identity issues in patients with eating disorders, for better prevention and therapeutic intervention strategies (19).

Currently, gender-affirming healthcare providers require certain body mass index (BMI) parameters for surgical eligibility, but there is no consensus on optimal values. However, these requirements can also have a negative impact on the health status of potential surgical candidates, even limiting their access to these services. It is believed that, in some cases, by requiring a certain BMI for gender- affirming surgery, pathological eating behavior (drastic weight loss) is encouraged (20).

According to Nagata et al, the theory of stress experienced by sexual and gender minorities has been used to explain the disproportionate rates of dysfunctional eating behaviors and body dissatisfaction among sexual and gender minorities compared to heterosexual individuals (21).

The same issue, with targeted reference to experiences of sexual orientation and gender identity in the context of a social atmosphere marked by heterosexism and ”sexual objectification” is incriminated in the generation of disordered eating behaviors and body dissatisfaction in Mason et al's study (22).

Minority stress theory, as it relates to people with gender nonconforming identities, explains why they more frequently exhibit mental health problems, including pathological eating behaviors. These may function as coping mechanisms to the stress they feel, rather than strictly as a response driven by gender dysphoria alone. Social stigma, violence and rejection stemming from gender nonconforming identity are emphasized (12, 23).

The objectification theory (a person internalizes an observer's negative perspective of his or her own self), might explain that the perception of an incongruence between one's own body and socio- cultural expectations of it can lead to dissatisfaction and dysphoria, especially in people with gender nonconforming identities, and can promote the onset of an eating pathology. Traditionally, the ideal masculine body needs to be muscular and the feminine one, slim (21).

As in cisgender individuals, high body dissatisfaction is a major risk factor for eating disorders (24). Perfectionism as a personality trait, anxiety, low self- esteem are also implicated (25).

Male - born persons identifying as females resorted to significant weight loss in order to appear slimmer, while the female – born identifying as males used it to reduce their chest and hips size and to seize their menstruation (15).

A case study published by Turan et al presents a gender dysphoric person, who also suffered for 20 years from anorexia nervosa with purging. The main goal of weight loss was getting rid of the secondary sexual characterstics (female biological sex, male gender identity) and stopping menstruation. In order to obtain this, the person kept on strictly monitoring their body mass for all those years. Once the gender affirming treatments were made, the pathological eating behaviour diminished, and the subject managed to reach a healthier weight and maintain it for a longer period of time (26).

Transgender people with eating disorders can also have various psychiatric comorbidities and a high risk of selfharm behaviour. In a case study published in 2022, a FtM patient with old psychiatric history (ADHD, bipolar affective disorder, borderline personality disorder and suicidal attempts) used self starvation, self induced vomiting and excessive physical exercise in order to anihilate the feminine secondary sexual characteristics. The psychostressing context also consisted of a lack of support on behalf of the family, which aggravated both the gender dysphoria as well as the self starvation severity (23).

CONCLUSIONS

Anorexia nervosa and other eating disorders affect vulnerable people with a negative, distorted self body image that is not concordant to their conceptual ”normality”.

Associating gender incongruence with gender dysphoria represents a risk factor for the development of eating behaviour disorders, especially anorexia nervosa. Both psychopathological entities are of ever growing interest for researchers in the field.

The common aspects identified during present research between anorexia nervosa and gender dysphoria are: a person`s marked discomfort within their own body, negative self image, the significant consequences that both diagnostic entities have on the general wellbeing, changing a person`s behaviour and the whole lifestyle, with self – harming behaviour.

Despite the common aspects between the discussed entities, the reasons underlying bodily dissatisfaction and impaired quality of life differ. Thus, in the case of anorexia nervosa, body dissatisfaction is rooted in the fear of weight gain and a distorted perception of one's own weight as exaggerated. In gender dysphoria, dissatisfaction with body image is often centred on secondary sexual characteristics that are at odds with the person's gender identity and that they want to get rid of. Importantly, people with gender dysphoria also express dissatisfaction with body parts that are not gender- specific, such as facial features and overall body shape.

Increased body dissatisfaction in people with gender dysphoria can become a risk factor for pathological eating behaviour. Depending on the developmental variants of gender incongruence, the eating disorders that can occur might manifest in different forms. Anorexia nervosa comorbid with gender dysphoria is one of them, and the precise evolution after hormonal or surgical gender reassignment treatments requires in- depth and long- term studies, as there is still no consensus on this matter.

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From classic to modern in the treatment of hidradenitis suppurativa and the impact on patient quality of life

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ABSTRACT

Hidradenitis suppurativa is a chronic, debilitating, progressive, recurrent inflammatory disease affecting the skin regions containing apocrine glands, characterized by the appearance of persistent, painful nodules, abscesses and fistulas, most commonly localized in the axilla, groin, buttock and genital. Due to the significant decrease in patients' quality of life and the delay in initiating treatment, the choice of appropriate therapy is extremely important in these patients. There are multiple treatment options for hidradenitis suppurativa, but no effective, curative therapy has been found. This article aims to list existing therapeutic methods and provide updates on current treatment options for inverse acne, in order to raise awareness of this condition and increase the quality of patient care.

KEYWORDS

Nodules, fistulas, pain, care.

INTRODUCTION

Hidradenitis suppurativa, also known as acne inversa or Verneuil's disease, is a chronic inflammatory condition characterized by the presence of painful nodules and abscesses with foul-smelling contents, which heal as fistulous tracts (1). Hidradenitis suppurativa has a devastating impact on quality of life, causing chronic pain (1, 2), emotional and psychiatric distress, association with increased substance abuse, impaired intimacy and increased suicide rates (3, 4).

Although there are several treatment guidelines for hidradenitis suppurativa, the lack of high-quality evidence limits the strength of their recommendations. This article reviews the classical to modern medical and surgical management of this disease by comparing international guidelines and aims to assess the impact on the quality of life of the hidradenitis suppurativa patient.

CLINICAL ASPECTS

Hidradenitis suppurativa is diagnosed clinically, histopathological confirmation is unnecessary. There are three criteria necessary for diagnosis: presence of characteristic lesions, predilection for flexural folds and recurrence of lesions. Characteristic lesions are deep nodules that expand to form abscesses, which subsequently ulcerate and drain contents to the surface of the integument, progressing to the formation of sinus, fibrous scars. Lesions favour the axillary and groin area, but also occur in the submammary folds, perineal folds, buttocks, pubic region, scalp, rectus arteriosus and back. There is often a significant delay between the onset of symptoms and diagnosis (on average 7.2 years), which underlines the need for familiarity with the above diagnostic criteria (2). Most patients present with more than one lesion at diagnosis. Lesions are usually accompanied by discomfort, itching and pain. Factors including heat, sweating, physical activity, shaving and rubbing can exacerbate symptoms. Acute exacerbations alternating with periods of rest are typical.

Hurley staging, introduced in 1989, involves classifying hidradenitis suppurativa into three stages of severity as follows (1):

- Stage I - formation of abscesses, single or multiple, without fistulous tracts and without scarring (mild disease).
- Stage II - recurrent abscesses with one or more fistulous tracts and scarring, separated from normal integument (moderate disease).

- Stage III - diffuse damage or multiple interconnected abscesses and fistulous tracts with no areas of normal integument (severe disease).

It is also useful to consider the degree of pain, number of eruptions and impact on daily life in hidradenitis suppurativa. *The Cardiff Dermatological Quality of Life Index or DLQI* questionnaire is often used (2,3).

PATHOGENY

The primary event in hidradenitis suppurativa is follicular hyperkeratosis, leading to hair follicle rupture and subsequent inflammation of the apocrine glands. IL-1, TNF-α and IL-17 are key cytokines in the pathogenesis of hidradenitis suppurativa, with TNF-α levels in lesional skin and serum IL-17 levels correlating with disease severity.

Initially, inflammation of the apocrine gland was proposed as the primary event in hidradenitis suppurativa. More recently, research suggests that follicular hyperkeratosis occurs first, causing obstruction and dilatation, leading to follicle rupture with subsequent inflammation, abscess and sinus tract formation. Apocrine gland involvement occurs secondary to dermal inflammation. Compared with healthy controls, in patients with hidradenitis suppurativa no differences in apocrine gland size, density or distribution have been noted, but the latter tend to have reduced sebaceous gland volume (2).

MEDICAL MANAGEMENT OF HIDRADENITIS SUPPURATIVA

Topical therapies

Clindamycin is the only topical antibiotic included in randomised trials with efficacy in mild stages of hidradenitis suppurativa. Its efficacy was demonstrated in a randomized clinical trial in 27 patients, in which a decrease in the number of pustules compared with placebo was shown; however, the number of abscesses and nodules remained unchanged (6, 7). Another randomized clinical trial involving 46 patients showed no significant difference between topical clindamycin versus oral tetracycline (6).

The addition of *antibacterials* may be considered with concomitant use of antibiotics. Because antimicrobial resistance is common among patients with hidradenitis suppurativa using topical or systemic antibiotics (9, 10), it is worth considering the addition of a local antiseptic to preserve antibiotic administration.

Resorcinol 15% cream can be used for acute and chronic lesions in mild to moderate hidradenitis. Observational studies involving the use of resorcinol cream 15% twice daily in mild to moderate disease have shown resolution of lesions in 66% of cases when used as maintenance treatment and relief of pain and decreased duration of pustules (10). Common side effects include desquamation, irritative contact dermatitis, and reversible hyperpigmentation (7, 10).

Systemic antibiotics

Systemic antibiotics are widely used and recommended in all published treatment guidelines (10). However, understanding of the mechanisms of action of antibiotics in treating hidradenitis suppurativa remains limited. Despite increased antibiotic resistance among bacteria cultured from hidradenitis suppurativa lesions (11), no link between antimicrobial resistance and treatment response has been established. Thus, microbiological examination and culture are not routinely recommended (12, 13). Tetracyclines are first-line therapy for mild to moderate forms of hidradenitis suppurativa, and clindamycin/rifampicin are

reserved for severe forms of the disease (13, 14).

Oral tetracyclines are the first line for mild to moderate hidradenitis suppurativa. The only clinical trial to study the efficacy of systemic antibiotics in hidradenitis suppurativa compared tetracycline 500 mg orally twice daily and clindamycin 1% topically, two applications daily. Both groups showed improvement in skin lesions, with no significant differences between the two groups (15). The duration of tetracycline antibiotic therapy can extend up to 4 months, but this may be extended depending on clinical response (14, 15).

Clindamycin/rifampicin may be a first-line treatment in patients with hidradenitis suppurativa moderate to severe form or second-line therapy for mild form. Patients who are ≥50 years old or who smoke are less compliant with this treatment (14, 16). Treatment duration is usually 10-12 weeks, longer courses of clindamycin/rifampicin treatment appear to confer similar risks (7, 9).

Metronidazole/Moxifloxacin/Rifampicin triple antibiotic therapy can be used as second- or third-line treatment in mild to moderate forms of hidradenitis suppurativa, with long-term benefits demonstrated by a reduced number of pushes 1 year after completion of treatment (6).

Intravenous *ertapenem* is reserved for severe, treatment-refractory hidradenitis suppurativa and may be initiated prior to surgery or as consolidation drug therapy. The optimal duration of treatment with ertapenem is 6 weeks. Common adverse reactions include oral/vaginal candidiasis, gastrointestinal discomfort and vaginitis (7, 12).

Corticosteroids

Intralesional triamcinolone acetonide can be used for nodules, abscesses, fistulous tracts in hidradenitis suppurativa, particularly in hidradenitis suppurativa pus for pain relief (11).

Systemic corticosteroids are recommended to be used with caution in patients with comorbidities such as hypertension, type 2 diabetes mellitus, osteopenia/osteoporosis and psychiatric disorders (13).

Hormonal therapies

Combined oral contraceptives are useful in pregnant women, when basic treatment of hidradenitis suppurativa is contraindicated and may reduce the side effects of spironolactone. Contraception with progesterone alone may aggravate the disease (16, 17). Finasteride may be an adjuvant treatment in those with mild to moderate disease in whom first- and second-line therapies fail. Significant improvement was observed in 13 of 14 participants in 4 case series (17).

Metformin is considered in diabetics, pregnant patients, women with polycystic ovary syndrome (13, 16). Clinical improvement was noted after 12 weeks of therapy and may continue up to 24 weeks of treatment (17).

Spironolactone can be used as adjuvant treatment in young, healthy women with mild to moderate hidradenitis suppurativa. Two case series totaling 66 women with mild to severe disease have shown improvement in pain, lesions and PGA (Physician's Global Assessment) score (16).

Systemic retinoids

Normal-weight women with acne and hidradenitis suppurativa mild form are more likely to respond to *isotretinoin* treatment (16,

17). Although isotretinoin is commonly prescribed for this disease, data supporting its efficacy are inconsistent, with isotretinoin not recommended as a routine treatment of hidradenitis suppurativa (16).

Acitretin can be used to treat severe hidradenitis in patients without fertile potential. Clinical improvement usually begins within 3 months and may continue for up to 6 months, and it is used as second- or third-line therapy in moderate disease (16, 17).

Biological therapies

Adalimumab is a human monoclonal antibody against tumor necrosis factor-α (TNF-α) and is the first-line biologic treatment in patients with moderate to severe hidradenitis suppurativa (17). Adalimumab is the only FDA-approved therapy for the treatment of hidradenitis suppurativa and is the first line of treatment in patients aged ≥12 years with moderate to severe disease.

Infliximab is a chimeric anti-TNF-α monoclonal antibody. It is a second-line therapy in patients with severe hidradenitis suppurativa. From published studies, infliximab is often useful for patients who do not respond to adalimumab, possibly due to greater dosing flexibility (13). Loss of clinical response associated with anti-infliximab antibodies can be prevented with the combination of methotrexate 7.5-10 mg weekly.

The interleukin 17 inhibitor, *secukinumab*, can be used to treat moderately-severe forms of hidradenitis suppurativa. Clinical response is achieved, on average, at 24 weeks in 70% of patients (11, 13).

Ustekinumab can be used in patients with moderate disease, with patients with lower expression of leukotriene A4 hydrolase having a more favorable response (11). Clinical response was achieved in half of the participants at 28 weeks and was maintained 12 weeks after cessation of therapy (8).

Lifestyle

Last but not least, lifestyle aimed at improving lesions in hidradenitis suppurativa are recommended, including: smoking cessation, weight loss, avoidance of dairy products, yeast-based products, avoidance of tight clothing and mechanical irritation, avoidance of hair removal.

PROCEDURAL MANAGEMENT OF HIDRADENITIS SUPPURATIVA

L*ong-pulsed Nd:YAG laser* (1,064 nm) causes selective photothermolysis of the follicular unit. A randomized clinical trial demonstrated a 65% reduction in disease severity after 3 monthly treatments, with better results in Hurley stage II and in inguinal and axillary locations (18, 19).

Deroofing technique or fist ulous tract debridement is a tissue "sparing" technique used to treat recurrent hidradenitis lesions. The surgical technique involves inserting a cannula through a fistulous tract and peeling back the tissue overlying it using a scalpel. The contents of the fistulous tract are debrided and the wound heals within 5 weeks (20, 21).

Unlike deroofing, *classic surgical excision* removes tissue deep into the subcutaneous tissue to completely remove the sinus tract. Excision is performed using scalpel, electrocautery or ablative CO2 laser (10,600 nm) (22).

THE IMPACT OF HIDRADENITIS SUPPURATIVA ON THE PATIENT'S QUALITY OF LIFE

This disease severely affects patients' quality of life due to its chronic, debilitating, painful nature, unpleasant purulent discharge and healed fibrotic bands leading to restricted mobility. The patient is often embarrassed because of malodorous secretions and staining of clothing (23). Patients have low self-esteem and depression has a higher incidence than in other dermatological conditions (1).

On an 11-point scale, where 0 represents no pain and 10 represents the worst pain imaginable, patients with hidradenitis suppurativa describe their pain in the range of 4-10, which is characterized by feeling hot, burning, pressure, stretching, cutting, stinging, gnawing, squeezing, or throbbing (1,26).

The mean visual analogue scale (VAS) pain score is 4.2, and the mean dermatological quality of life index (DLQI) ranges around 10, indicating substantial disease-specific quality of life impairment and is higher than other chronic dermatological disorders such as alopecia, acne, psoriasis and vascular malformations of the face (2, 23).

The father of communism, Karl Marx, is thought to have suffered from hidradenitis suppurativa. His thought process was largely influenced by the incapacitating pain that came with the disease. Not only did it contribute to his poverty, it also made him depressed and psychologically violent. Therefore, many believe that hidradenitis suppurativa shaped the theory of communism in the 20th century (23).

Classical therapies for hidradenitis suppurativa can help control symptoms and prevent secondary infections, but they do not specifically target the inflammatory pathways involved in the pathogenesis of hidradenitis suppurativa. They are aimed at managing acute symptoms such as secondary infections or pain and can be used short term or intermittently. Classical therapeutic options may have variable efficacy and may require frequent dose adjustments or changing antibiotics to treat infections. Side effects can include gastrointestinal problems, allergic reactions and, in the case of long-term antibiotics, bacterial resistance (8).

Biological therapies involve the use of drugs that specifically target certain molecules or biological processes involved in inflammation and the body's immune response. Typically, these drugs are biological proteins or monoclonal antibodies that are designed to block or modulate certain inflammatory pathways. The main aim of biological therapy is to reduce inflammation and, in addition to conventional therapies, to prevent recurrences of hidradenitis suppurativa. These drugs are often prescribed to patients with moderate or severe hidradenitis suppurativa and can be used long-term. Biological therapy has been shown in clinical trials to be effective in reducing the severity of hidradenitis suppurativa and recurrences. However, side effects such as site reactions, infections and other adverse effects may occur and should be closely monitored. Biologic therapy is often administered by subcutaneous or intravenous injections and may require regular administration, usually once a month or less frequently (18, 21).

CONCLUSIONS

Hidradenitis suppurativa is a chronic inflammatory disease with substantial impact on quality of life. Evidence-based guidelines provide insight into best management practices but remain limited by the limited quality of evidence. Understanding of hidradenitis suppurativa pathophysiology and therapeutic targets among the dermatology community is rapidly advancing, providing a rationale for many promising therapies in ongoing clinical trials.

Biologic therapy represents a significant step forward in the treatment of this condition, leading to a significant improvement in patients' quality of life by reducing pain, inflammation and purulent discharge. They contribute to decreased physical and emotional discomfort, partial recovery of mobility and increased self-confidence associated with hidradenitis suppurativa.

Hidradenitis suppurativa can have a significant impact on patients' emotional state, causing anxiety and depression. Biological therapy may reduce the frequency and severity of recurrences, which can help reduce the emotional distress and anxiety associated with the disease.

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The burden of patients with rosacea - psychosocial impact and psychiatric comorbidities

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ABSTRACT

Rosacea is a chronic skin condition with a global incidence ranging from 1% to 22%, affecting mainly women aged between 30 and 55 years. The etiopathogenesis of rosacea is complex, involving genetic factors, cutaneous or intestinal dysbiosis, neurovascular dysfunction, or immune disorders. Clinically, it is characterized by persistent or transient facial erythema, papules, pustules, phymatous changes, ocular manifestations, and associated symptoms such as burning sensation or local stinging.

Physical appearance and facial features significantly influence all social aspects a person experiences, from various interpersonal relationships to employment decisions. The disease can lead to social stigmatization and significantly reduce the quality of life. The chronic course of rosacea and its predominant facial localization, visible in the patient's social environment, justify the increased incidence of psychiatric comorbidities in these patients.

Rosacea is an easily observable condition, especially due to persistent redness, which often leads to the development of feelings of anxiety or social phobia, stigmatization, or comorbidities such as depression, generalized anxiety, or bipolar disorder.

Currently, the European Academy of Dermatology and Venereology (EADV) Task Force on Quality of Life in rosacea recommend the use of specific scores for inflammatory dermatological diseases, such as the Dermatology Life Quality Index (DLQI) and the Minimal Clinically Important Difference (MCID), as well as the specific rosacea score RosaQoL.

The current study aims to describe the psychosocial impact of rosacea on these patients. Due to the increased incidence of depression and anxiety in this patient group, great attention must be given to signs and symptoms of psychiatric comorbidities, and the therapeutic approach should target both dermatological treatment and associated treatment from the perspective of a psychiatrist or psychologist.

KEY WORDS:
Rosacea, psychosocial impact, quality of life, psychiatric comorbidities.

INTRODUCTION

Rosacea is a chronic inflammatory skin condition, frequently encountered in dermatological practice, whose etiology and pathophysiology remain partially understood.
Clinically, it is characterized by erythematotelangiectatic lesions in convex areas of the face (nose, cheeks, forehead, chin area). (1) Its global prevalence in the general population is 5.46%, but it varies between 1% and 22% depending on the geographical region. While most cases occur in the Caucasian population, other races can also be affected. Rosacea affects both men and women, but the majority of patients are women over the age of 30. However, men experience the burden of the disease much more profoundly than women. (2)

The etiopathogenesis of rosacea remains an incompletely elucidated subject. The condition occurs in genetically predisposed individuals, especially in those with fair skin types who are exposed to certain environmental factors (ultraviolet radiation, heat exposure, stress, microorganisms such as *Demodex folliculorum* or *Staphylococcus epidermidis*). The blood vessels of patients with rosacea have an increased diameter, tortuous shape, and increased permeability, factors that contribute to the development of facial erythema and edema. (3)

For thousands of years, facial erythema has been considered a shameful defect in terms of social relationships, mainly due to its association with alcohol abuse and psychiatric disorders. French novelists from the 19th century, such as Balzac or Proust, described with admiration the red or sanguine complexion, which denoted a difficult and violent temperament or simply symbolized the working class. The color red remains ambivalent today, signifying life on one hand and suffering, shame, and death on the other. Moreover, rosacea is a highly visible condition, significantly impacting the lives of patients (4), who are particularly affected by anxiety, depression, and social phobia. (5, 6)
There are increasingly more studies demonstrating the negative impact of rosacea on patients' quality of life. Patient-centered care, understanding how this condition is perceived and how it influences social

relationships, should be the foundation of all treatment programs. (7)

THE GUT-BRAIN-SKIN AXIS

The human microbiome represents a collection of bacteria and microorganisms that reside inside the human body and on the skin's surface. Homeostasis between the host's immune system and the microbiome allows for mutual and bidirectional benefits. Humans have up to 100 trillion bacteria and approximately 3.3 million microbial genes. From immunity to brain activity, nutrient synthesis, and toxin elimination, the balance of the intestinal flora plays a crucial role in the pathogenesis of many diseases. (8)

A plausible explanation for the increased incidence of psychiatric conditions among patients with rosacea could be represented by disruptions in the gut-brain-skin axis and common inflammatory pathways. Disruption of the intestinal microbiota balance has frequently been associated with the development of psychiatric conditions such as depression, anxiety, schizophrenia, bipolar disorders, or autism spectrum disorders. (9) It has been shown that psychological stress factors stimulate the synthesis of neurotransmitters or the release of neuropeptides from intestinal neuroendocrine cells. These molecules have the ability to increase intestinal mucosa permeability, resulting in local and systemic inflammation. The relationship between psychiatric disorders and rosacea may involve intestinal dysbiosis, but the pathogenic pathway requires further investigation. (10)

The role of dietary lifestyle emphasizes the importance of the gastrointestinal tract in the pathogenesis of rosacea. Specific changes in the intestinal microbiome contribute to the abnormal activation of Toll-like receptors in these patients. (11, 12) Recent studies have shown that patients with rosacea have an increased prevalence of *Helicobacter pylori* infection, small intestinal bacterial overgrowth (SIBO), as well as alterations in the local skin microbiota. (13) Therefore, there could be a connection between rosacea and psychiatric conditions through the brain-gut-skin axis. (14, 15) Interleukin 17 is a key cytokine involved in central nervous system inflammation and the pathophysiology of psychiatric disorders. It has been demonstrated that patients with depression have elevated serum levels of Th17, and in mice, it can induce depressive-like behavior. Similarly, IL-17 plays an important role in the onset and exacerbation of rosacea. (16)

CLINICAL ASPECTS

The clinical classification of rosacea was first published in 2002, aiming to standardize the diagnosis of the disease. The primary features of rosacea include transient or permanent flushing, telangiectasia, papules, and pustules with a centrofacial distribution. Secondary characteristics, which may occur independently or accompany the primary ones, include a sensation of burning or stinging, xerosis, edema, plaques, phymatous changes, and ocular manifestations. (17)

Based on this classification, there are four subtypes of rosacea. The first subtype (I), erythematotelangiectatic, is characterized by persistent erythema mainly on the face but can extend to the ears, neck, and posterior chest. The periocular and periorbital areas are usually spared. The second subtype (II), papulopustular, presents with inflammatory lesions such as papules and pustules. The third subtype (III), phymatous rosacea, involves skin thickening with the appearance of nodules, most commonly on the nose (rhinophyma). The last subtype (IV) refers to ocular involvement, being the most common extracutaneous manifestation, represented by

increased tearing, conjunctival redness, and a sensation of local burning. (17, 18)

In 2017, the ROSacea COnsensus (ROSCO) simplified the diagnostic approach by establishing a new classification that includes only two diagnostic features: persistent centrofacial erythema with transient intensifications in the presence of trigger factors and phymatous changes. (17)

MEASURING QUALITY OF LIFE IN PATIENTS WITH ROSACEA - QUESTIONNAIRES

Questionnaires regarding the quality of life (QoL) of patients represent a way to assess well-being and life satisfaction in all aspects for patients with dermatological diseases. Additionally, they allow disease monitoring, prognosis establishment, and treatment response evaluation. Currently, the most used is the Dermatology Life Quality Index (DLQI), a non-specific questionnaire used to evaluate over 40 dermatological conditions such as psoriasis, chronic urticaria, or vitiligo. Studies have shown that DLQI has high sensitivity and is directly proportional to the severity stages of the disease. The Minimal Clinically Important Difference (MCID) is a new tool for treatment response evaluation, calculated as the difference between two DLQI scores, representing the minimum clinically significant value for the patient. For inflammatory dermatological conditions, the minimum value of this score is considered to be 4. (19) A DLQI score of 0 or 1, indicating that the disease has no or minimal effect on the patient's quality of life, represents the gold standard of therapeutic management. (20)

In 2007, a group of researchers from the United States created a score specifically for rosacea, called RosaQol, consisting of 21 questions that assess the burden of disease in the daily life of these patients. Currently, it is approved in the US and some European countries, including France, Germany, Italy, and Spain. (20)

The European Academy of Dermatology and Venereology (EADV) Task Force on Quality of Life in Acne, Rosacea and Hidradenitis Suppurativa does not recommend the use of generic tools as the sole method of evaluating the quality of life of patients with rosacea, except in situations where comparison between rosacea patients and patients with other non-dermatological conditions or healthy subjects is desired. Instead, they recommend using the DLQI, DLQI MCDI, or RosaQoL scores for these patients. (20)

PSYCHOSOCIAL IMPACT

Physical appearance and facial features have a profound influence on all social aspects a person experiences, from various interpersonal relationships to employment decisions. Television, tabloids, or movies all emphasize attractive facial features characterized by symmetry, clean and healthy skin, and a normal complexion. However, permanent redness or flushing, papules, pustules, or phymatous changes negatively affect the paradigm of a pleasant appearance and thus have undesirable effects on the social life of these patients. (17)

Rosacea is an easily observable condition, especially due to persistent redness, which often leads patients to develop feelings of social anxiety, stigmatization, phobia, or other psychiatric comorbidities. Facial erythema, either transient or persistent and easily induced by physical or emotional factors, has a much stronger impact on patients' quality of life than inflammatory lesions such as papules or pustules. (18)

The association between rosacea and alcohol consumption is one of the main reasons for

stigmatization of these patients. An analysis conducted on 4,945 women with rosacea determined a direct proportional relationship between alcohol consumption and rosacea, with the highest risk associated with white wine and liquor. (18)

Quality of life (QoL) is determined by multiple factors that contribute to a person's well-being, both materially and emotionally. Factors influencing QoL in rosacea patients include (a) physical aspects like burning sensation, stinging, skin dryness, and ocular symptoms, (b) psychosocial aspects like frustration, anger, stigmatization, low self-esteem, shame, social phobia, or anxiety, and (c) occupational aspects like missed workdays due to rosacea, reduced job opportunities, or pharmacoeconomic considerations. (22)

Studies have shown that the severity of rosacea does not always correlate with the severity of psychosocial impairment; even very mild cases of the disease can have a more negative impact than more severe forms. A study conducted by the National Rosacea Society, which included over 400 subjects with rosacea, showed that 75% of them had low self-esteem, 70% were overwhelmed by feelings of shame, 69% experienced frustration, and 56% felt deprived of happiness or pleasure. (23) Another study conducted online in the United Kingdom, Germany, France, and the United States reported that approximately one-third of patients with rosacea associate feelings of stigmatization, with a higher prevalence among males. Stigmatization was associated with an increased incidence of depression and avoidance of social situations. (24)

In a questionnaire conducted online with more than 5000 healthy participants, who were shown images of both healthy individuals and individuals with facial erythema, it was observed that faces with redness were perceived as less relaxed or healthy. Flushing was strongly associated with a perceived influence on health status or personality disorders. (25)

The impact of rosacea extends to the workplace, with around 50% of patients reporting missing workdays due to their condition. (24) In another study, it was observed that 8.3% of 933 patients with moderate-to-severe forms of rosacea felt that their productivity at work was negatively affected by their disease. In the case of patients with severe forms of the disease, 47.8% of them reported that facial redness affects their professional activities. (26)

PREVALENCE OF PSYCHIATRIC COMORBIDITIES

Due to the chronic evolution of rosacea, with predominantly facial involvement visible in the patient's social environment, we can anticipate a higher prevalence of psychiatric comorbidities among these patients.

In 2021, Ru Dai et al. conducted the first meta-analysis to determine the prevalence of depression and anxiety in patients with rosacea. They concluded that 19.6% of these patients experienced depression, and 15.6% had anxiety. Individuals with rosacea are at least twice as likely to manifest symptoms of depression or anxiety compared to healthy individuals. The occurrence of psychiatric comorbidities was independent of age or sex, although in other studies, young (22) and male individuals (Heisig, Ru Dai) were more affected. This could be explained by the fact that young individuals are more concerned about their physical appearance, and males may develop more advanced forms of the disease. Egeberg et al. reported that the risk of depression in these patients is directly proportional to the severity of rosacea. (27)

In another study, it was demonstrated that patients with rosacea had multiple hospitalizations due to the association with psychiatric comorbidities. Among these, the highest prevalence was observed for phobic disorder (aHR: 7.84; 95% CI: 7.52–8.17), followed by obsessive-compulsive disorder (aHR: 6.38; 95% CI: 6.13–6.65), major depressive episodes (aHR: 3.78; 95% CI: 3.63–3.94), bipolar disorder (aHR: 3.06; 95% CI: 3.06–3.32), and anxiety (aHR: 2.91; 95% CI: 2.79–3.03). Women had a higher risk of developing generalized anxiety than men. (28)

Multiple studies have shown similar data regarding the increased risk of depression and anxiety in patients with rosacea. The association of these psychiatric pathologies with rosacea can be explained by the sharing of common inflammatory pathways and increased levels of metalloproteinases in the blood. (27,28)

THERAPEUTIC APPROACH

The multifactorial nature of this skin condition, along with the incomplete elucidation of its pathophysiology, makes the primary objective of therapeutic approach to prevent relapses and progression to severe forms. However, the therapeutic arsenal for rosacea has significantly improved in recent decades, with both topical and systemic therapies available, such as metronidazole, oxymetazoline, brimonidine, azelaic acid, or tetracyclines. (29) The choice of therapeutic strategy is often challenging for the physician, as treatment is complex, individualized, and of long duration, depending on the subtype of lesions present in each patient.

The first step in improving rosacea is identifying and removing triggering or aggravating factors. Avoiding sun exposure or using sunscreens, avoiding intense physical exertion, psychosocial stress, spicy or seasoned foods are some principles that rosacea patients should follow to reduce skin lesions. (30)

An important aspect of treatment is the choice of dermocosmetic products for skincare, as they play a crucial role in controlling the disease by directly repairing the skin barrier, reducing local inflammation, or inhibiting sebum secretion. A study conducted on 42 subjects demonstrated that a skincare routine consisting of cleansing foam, daytime sunscreen, and night cream improved hydration levels and strengthened the skin barrier function in over 90% of patients. (30)

A recent systematic review based on therapeutic strategies according to the phenotypic presentation recommends using topical brimonidine and oxymetazoline for patients with persistent erythema. For papules or pustules, this study suggests topical azelaic acid, ivermectin, or metronidazole. (17) In a retrospective study involving 50 patients that evaluated the efficacy and tolerability of 1% topical ivermectin, positive responses were observed not only in papulopustular forms but also in mild forms of rosacea. (31)

Systemic treatment or combined therapies can be recommended for patients with moderate to severe forms of rosacea. FDA-approved 40 mg doxycycline (in 2019) (32), isotretinoin, or minocycline are indicated therapies for papulopustular rosacea, as reported in a systematic review on therapeutic interventions in rosacea. (17) Systemic antibiotics are used in combination with topical therapies, as they are beneficial for their antibacterial and anti-inflammatory effects. Tetracycline, azithromycin, clarithromycin, or metronidazole can be used. (32)

Oral β-blockers can be used for persistent erythema or flushing, as they have the ability to antagonize the effects of the sympathetic nervous system and circulating catecholamines on β-receptors. A review study concluded that the use of propranolol or carvedilol may be a useful therapeutic option for patients with flushing or erythema. (33, 34, 35)

From an interventional therapy perspective, vascular laser, ablative or non-ablative lasers, and IPL can be used to target vascular lesions and hypertrophic lesions commonly seen in patients with rosacea.

Oral isotretinoin, topical azelaic acid, ivermectin, and specific skincare routines have shown an improvement in quality of life compared to placebo in clinical trials. (36, 37) Another recent study demonstrated the increased permeability of the altered skin barrier in papulopustular rosacea and the importance of skin integrity restoration. (38)

The new targeted therapies for rosacea require new quality of life measurement tools with increased sensitivity compared to current instruments. Currently, there is a lack of clinical trials with a sufficient number of patients and control groups to confirm the effectiveness and improvement in quality of life through the use of current treatment methods.

CONCLUSIONS

Rosacea is considered a chronic systemic inflammatory condition characterized by persistent or transient facial erythema, papulopustular lesions, phymatous changes, or ocular manifestations.

The negative impact of the physical appearance caused by rosacea affects the social life and self-esteem of these patients, leading to an increased incidence of psychiatric disorders such as depression or anxiety. An explanation for the association of rosacea with these comorbidities may be the sharing of common pathological pathways or cytokines. Metabolites synthesized by the microbiota can accumulate in the skin, leading to skin barrier injuries and local inflammation. Whether the microbiota acts as a causal agent or is an innocent factor in the development of the disease remains to be determined in future studies.

Currently, the European Academy of Dermatology and Venereology (EADV) Task Force on Quality of Life recommends using specific scores for inflammatory dermatological diseases, namely the Dermatology Life Quality Index (DLQI) and the Minimal Clinically Important Difference (MCID), as well as the specific rosacea quality of life score, RosaQoL.

Depression and anxiety are common comorbidities in patients with rosacea, so a multidisciplinary approach is necessary. The psychiatrist, through cognitive-behavioral therapy or medication, can break the vicious circle of rosacea patients and improve their quality of life. Healthcare professionals need to be aware of the frequent association of psychiatric and psychosocial disorders among rosacea patients and direct them to specialized help for appropriate therapeutic management.

More studies are needed to unravel the complexity of the relationship between rosacea and psychiatric comorbidities, hidden common pathophysiological mechanisms, and establish optimal strategies for managing these patients.

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Factitious disorders - a clinical and therapeutic challenge

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ABSTRACT

Factitious disorder represents a category of mental disorders still insufficiently known and diagnosed, which requires more studies and research for a better understanding of all its social and psychological characteristics and to discover a treatment that is as suitable for patients. Also, the positive diagnosis is often very difficult to be establish and not only psychiatrists are involved, but also other medical specialties or health professionals, with an impact on the general population by all the consequences and the costs. This is because patients can present only with physical symptoms or only with mental symptoms or with both. The association with other medical conditions or other mental disorders, which must be diagnosed and treated as early as possible, must also be taken into account. The prognosis is generally reserved, and the therapeutic options are still discussed among the specialists. That's why in this paper we present an overview, regarding the information provided by the specialized literature on this subject.

KEYWORDS:

Factitious disorder, therapy, diagnostic.

INTRODUCTION

The modern history of factitious disorder began in 1951, when Richard Asher described case reports of patients who habitually migrated from hospital to hospital, seeking admission through feigned symptoms while embellishing their personal history (1).

Factitious disorder (FD) imposed on self is one of the most challenging and controversial problems in medicine. It is characterized by falsified medical or psychiatric symptoms where patients misrepresent, simulate, or cause symptoms of an illness in the absence of obvious external gain or reward. FD can lead to diagnostic and therapeutic procedures that result in irreversible morbidity and iatrogenic harm, and even premature death (1, 2).

This combination of intentional falsification and lack of any obvious gain sets factitious disorder apart from similar conditions, such as somatic symptom disorder (where someone seeks excessive attention for genuine concerns) and malingering (where an individual falsifies symptoms for personal gain or secondary gain), and also makes the condition difficult both to diagnose and treat (2,3).

EPIDEMIOLOGY

Only 1% of in-patients present with criteria matching the disorder, but the prevalence of factitious disorder throughout the general population is unknown. Case studies suggest that the two main groups of people most commonly affected by factitious disorder are women between the ages of 20 and 40 with a healthcare background, and unmarried white men aged between 30 and 50 (4,5).

Etiology

Factitious disorder is still not very well understood, and only a low number of individuals are successfully diagnosed with the condition. It is difficult to identify causes of factitious disorder with any certainty, however, risk factors are believed to include childhood trauma, working in the healthcare profession and suffering from depression or a personality disorder. The origin of factitious disorder is believed to be of a psychopathological nature, most of the time, early emotional deprivation (in childhood) and abandonment. Later on, the patient discovers this "source of affectivity" from a direct or indirect experience with medical institutions and learn to see with time the advantages of the patient role (6, 7).

There are several mechanisms in relation to the behavior found in factitious disorder:

- the sick role, especially in those who sensed a lack of affection during childhood;
- seeking and maintaining relationships;
- enjoying being cared for by others;
- coping with stressful life events;
- coping with a distorted self-image or a lack of identity;
- a sense of accomplishment in obtaining medical consultations from various professionals (5,8).

Some experts have described factitious disorder as a type of behavioral addiction, due to the uncontrollable urge to maintain the sick role and, conversely, a desire to overcome their dependence (9).

Positive diagnosis

By its nature, factitious disorder can seem asymptomatic. In order to make a diagnosis of factitious disorder, it may be necessary for a health professional to look for clues and patterns in behavior that suggest an individual is being misleading. Some behaviors, however, do make factitious disorder easier to spot, including:

- Inconsistencies between patient history and medical observations.
- Vague details that seem plausible on the surface but that don’t hold up to scrutiny.

- Lengthy medical records with multiple admissions at different hospitals.
- Willingness to accept any discomfort and risk from many medical procedures, even surgery.
- Overdramatic or outlandish presentation of a factitious illness, or hostility when challenged (10, 11).

The individual may have unexplained injuries that present as being potentially self-inflicted, as well as significant surgical scarring from repeated unnecessary operations (the so-called 'gridiron abdomen'). The affected individuals may even resort to tampering with hospital charts or contaminating test samples. Whatever the symptoms, it is important that as many as possible are evidenced and preferably reviewed by a peer to rule out the possibility of a genuine rare or obscure illness, as many of these symptoms on their own can be purely circumstantial. Diagnosis of factitious disorder often requires a number of investigatory steps in order to accurately identify the condition without wrongful accusation, and treatment options can be both limited and difficult to administer if the individual refuses to admit the deception. The strain that factitious disorder causes not only on the relationship between patient and doctor, but also between the individual and their friends, family, work and daily life, can be immense (12, 13, 14).

Factitious disorders were recognized as a diagnostic category for the first time in DSM III, in 1980, later in DSM IV TR they were classified into three subtypes and in DSM V other changes were made to the diagnostic criteria and they were presented in the diagnosis category of somatic symptoms and related disorders. Thus, in table 1, the definition and the diagnostic criteria are presented comparatively, in the main diagnostic manuals DSM V versus ICD 10 and ICD 11 (12,15,16).

Tab. 1 Definition and diagnostic criteria, DSM V versus ICD 10 and ICD 11.

ICD 10 **Definition and diagnostic criteria**	**ICD 11** **Definition and diagnostic criteria**	**DSM 5** **Definition and diagnostic criteria**
F68.1 - Intentional production or feigning of symptoms or disabilities, either physical or psychological [factitious disorder]	*Factitious disorders*	Factitious disorder is diagnosis assigned to individuals who falsify illness in themselves or in another person, without any obvious gain. The diagnosis for an individual falsifying illness of another person is factitious disorder imposed on another.
The patient feigns symptoms repeatedly for no obvious reason and may even inflict self-harm in order to produce symptoms or signs. The motivation is obscure and presumably internal with the aim of adopting the sick role. The disorder is often combined with marked disorders of personality and relationships. Hospital hopper syndrome Münchhausen syndrome Peregrinating patient Excl.: person feigning illness (with obvious motivation) (Z76.5)	Factitious disorders are characterised by intentionally feigning, falsifying, inducing, or aggravating medical, psychological, or behavioural signs and symptoms or injury in oneself or in another person, most commonly a child dependent, associated with identified deception. A pre-existing disorder or disease may be present, but the individual intentionally aggravates existing symptoms or falsifies or induces additional symptoms. Individuals with factitious disorder seek treatment or otherwise present themselves or another person as ill, injured, or impaired based on	Diagnostic criteria: There are four primary criteria for diagnosing factitious disorder. These are: • Intentional induction or falsification of physical or psychological signs or symptoms • The individual presents themselves as ill, impaired or injured to others • The deceptive behavior persists even in the absence of external incentives or rewards • Another mental

	the feigned, falsified, or self-induced signs, symptoms, or injuries. The deceptive behaviour is not solely motivated by obvious external rewards or incentives (e.g., obtaining disability payments or evading criminal prosecution). This is in contrast to Malingering, in which obvious external rewards or incentives motivate the behaviour.	disorder does not better explain the behavior Factitious disorder may be diagnosed as either a single episode or as recurrent episodes (two or more instances of illness falsification and/or induction of injury).

Differential diagnosis

The differential diagnosis of factitious disorder remains a challenge and includes somatoform disorders, malingering, conversion disorder and anxiety disorders. Although these disorders may clinically resemble each other at first glance, they differ significantly in terms of motivation, potential for self-harm, benefit and willingness to change, the main difference being the unconscious desire to assume the role of the sick. (1, 3, 17)

- Somatization disorder: in which there is an emotional conflict responsible for triggering the somatization process, the patient's predisposition for prolonged hospitalizations or surgical interventions is missing, and the symptoms are produced unconsciously.
- Somatoform disorder: it is differentiated by the fact that the physical symptoms are not produced intentionally, but at an unconscious level, through a mechanism similar to somatization disorder, which leads to a high level of anxiety and suffering in their lives. They do not seek to assume the role of the sick or another secondary benefit.
- Hypochondria: patients are not so adhesive, willing to endure difficult interventions and investigations.
- Personality disorders: they are similar to factual disorders due to the manipulative behavior, demanding character, with the exception of those with antisocial personality disorders. In borderline personality disorder, self-harm can occur in the absence of suicidal intent, but in factual disorder, self-harm is associated with deception.
- Simulation: it differs from the factual disorder by the fact that the patient intentionally produces physical or somatic symptoms motivated by obtaining a secondary/external benefit (money, leave, medical retirement). In the factual disorder, the secondary benefit is missing, only the primary/internal benefit is present (to obtain attention, medical care and affection due to a sick person).
- Conversion disorder: Conversion disorder is characterized by one or more neurological symptoms that do not have an organic explanation, associated with a psychological trauma. The factual disorder differs from the conversion disorder in that the neurological symptom or deficit is intentionally produced.
- Early medical condition: when a factitious disorder is suspected, an early medical condition should always be excluded (3, 17).

Therapeutic approach

There is no known single treatment for factitious disorder. A key difficulty in creating treatments for the disorder is simply how few cases are reported, and how even fewer of those go on to receive continued

long-term treatment options. Of the few documented cases, it is noted that treating issues around the factitious disorder, such as any comorbid conditions, often brings an end to the factitious disorder itself or enables management of the condition. It is also theorized that treating potential underlying causes, such as historical childhood traumas, may produce similar results (1, 8, 9).

Similar to the diagnosis, the treatment of factitious disorder can be difficult and usually requires a multidisciplinary team consisting of a psychiatrist, general practitioner, psychotherapist, social worker and family members to help the patient. Patients are generally not receptive to psychiatric treatment and will frequently change doctors or clinics, having a high rate of giving up treatment (10).

Psychotherapy is considered to be the first line treatment. The main purpose of the treatment is to limit the risk of adverse reactions and self-harm of the patient and to reduce the costs related to investigations for diagnosis and treatment. Therapies that focus on helping the individual identify and address their own emotional need for attention or care may be suggested, although preference is given to supportive over insight-oriented therapies due to the increased recorded benefit. Medication may be used to treat symptoms and/or any co-occurring psychiatric disorders but not usually to treat factitious disorder itself. It should be noted, however, that few individuals with factitious disorder choose to receive psychiatric treatment (14, 18).

Prognosis and complications

The prognosis of factitious disorder is generally unfavorable, especially based on the fact that patients deny their behaviors and extremely few accept a therapeutic intervention. In addition, among those who accept the treatment, most give up in a short time, having an extremely low therapeutic adherence. However, the few patients who show a favorable compliance to the therapy obtain satisfactory results (13, 17).

Also, the category of patients with other associated psychiatric pathologies should not be ignored, the most common of which is depression. Patients who have psychiatric comorbidities such as affective, anxiety or addiction disorders have been shown to have a more favorable prognosis compared to those who have various personality disorders as comorbidities, especially borderline personality disorder (4).

Apparently paradoxical, factitious disorders are not benign pathologies, associating indicators of morbidity and mortality. Most frequently, these patients can self-harm or undergo risky procedures, increasing the economic burden on health services (especially emergency services) (7, 8).

CONCLUSIONS

Factitious disorder affects both the individual and those around them to a significant degree. The individual will have a need to receive attention and care, and will often undergo many unnecessary and potentially risky methods like surgery in order to obtain what they desire. They may induce illness in themselves in order to achieve this goal, potentially putting their need for affective nurture higher than their own safety.

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

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Case Reports

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Palace of illusions: a psychotic episode weighed by royal delusions

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ABSTRACT

This article describes the case of a 48-year-old female patient who was involuntary admitted by the authorities for a psychotic episode characterized by delusional ideas of grandeur, filiation and reference. The patient firmly believed that she was not only a member of the royal family of Monaco, but also had a special familial connection to the ruling dynasty. This case highlights the complexities of psychotic disorders and the presence of multiple delusional themes that can significantly impact an individual's perception of reality and functioning.

These delusions profoundly affected the patient's daily life and interpersonal relationships. Her strong conviction in her royal filiation led to strained interactions with family members, who were unable to validate her claims. The patient's preoccupation with her imagined connection to the royal family overshadowed her personal responsibilities, causing disruptions in her overall functioning.

This paper underscores the intricate nature of psychotic disorders and the multifaceted delusions that can arise within them. Understanding the interplay between these delusional themes is vital in guiding diagnosis and treatment strategies. By implementing a comprehensive approach that includes medication, psychotherapy, and a supportive environment, healthcare professionals can assist patients in regaining a more accurate perception of reality and improve overall functioning and well-being.

KEYWORDS:
Psychosis, delusions, grandiosity, insight, involuntary admission.

INTRODUCTION

Acute psychosis disorder represents a complex and multifaceted condition characterized by a transient but severe disturbance in an individual's perception, thinking, emotions, and behavior. It is a condition of great clinical significance, necessitating comprehensive understanding for effective diagnosis, treatment, and management. This paper aims to provide a comprehensive overview of acute psychosis disorder, including its definition, prevalence, incidence, symptoms, etiology, and relevant clinical considerations.

Acute psychosis disorder, also known as brief psychotic disorder or brief reactive psychosis, is a mental health condition that manifests as a sudden onset of psychotic symptoms lasting for a limited period, typically lasting less than one month (1). During this episode, individuals experience a significant disruption in their ability to interpret reality accurately, leading to distortions in their thoughts, perceptions, and overall functioning.

The prevalence and incidence of acute psychosis disorder vary across different populations and settings. While it is considered relatively rare compared to other psychiatric disorders, its occurrence is not uncommon. Estimates suggest that approximately 1-4% of individuals seeking mental health services may present with brief psychotic episodes at some point in their lives (2).

Acute psychosis disorder is characterized by a range of symptoms that significantly impact an individual's mental and emotional state. These symptoms typically include hallucinations, delusions, disorganized thinking and speech, disorganized or abnormal motor behavior, and affective disturbances such as heightened anxiety or emotional instability (3). The presence and severity of these symptoms may vary from person to person, contributing to the heterogeneity of the disorder.

The exact etiology of acute psychosis disorder remains elusive, and multiple factors are believed to contribute to its development. While the precise mechanisms are not fully understood, evidence suggests that a combination of genetic predisposition, environmental stressors, substance abuse, and alterations in brain chemistry and structure may play a role. Furthermore, acute psychosis disorder can be associated with medical conditions, such as infections, autoimmune disorders, or drug-induced reactions, which should be carefully evaluated during clinical assessment (4).

Given the unique and time-limited nature of acute psychosis disorder, accurate diagnosis and appropriate management are crucial. Differential diagnosis should consider other psychotic disorders, substance-induced psychosis, and mood disorders with psychotic features (5,6). Comprehensive psychiatric evaluation, including a thorough medical history, mental status examination, and laboratory investigations, is essential for ruling out underlying medical conditions and identifying contributing factors.

CASE PRESENTATION

The patient is a 48-year-old female who was referred to the clinic for the first time by the authorities due to presenting symptoms of acute psychosis disorder. These symptoms included psychomotor agitation, disorganized thinking, tangentiality, circumstantiality, disorganized motor behavior, affective inversion towards her family and men in general, emotional detachment, auditory hallucinations, delusional ideas of grandeur, reference and filiation, irritability, low

tolerance towards frustrations, impulsivity, verbal and physical hetero-aggressivity, as well as sleep disturbances.

The patient firmly asserted: "I am not like everyone else. I have an undeniable connection to royalty, you see. I am a member of the esteemed royal family of Monaco, destined for greatness. The world needs to recognize my true identity and treat me accordingly. I have an important role to play in shaping the destiny of this world." She continued, "I was brought here because I upset political leaders. I am the princess of Monaco. Please call the royal family and inform them of the horrible mistake the police made by bringing me here", “I am related to prince Albert of Monaco”, ” I also met king Mihai a couple of times” . She dives into her aversion towards men: “All men want something from me, because of my good looks, they all want to use me”. The family reports that these symptoms have been present for the past several years and have gradually worsened. Her mother mentions that she was diagnosed with depression 14 years ago (in 2009) after a stressful event in her life, specifically the break-up with her boyfriend, which had a significant impact on her. In 2010, she experienced her first psychotic episode and was prescribed medication, but she only took it for a limited amount of time. Despite that, she managed to maintain an acceptable level of daily functionality throughout the years, while displaying delusional ideas of grandeur and prejudice.

Family History: The patient's cousin has been diagnosed with paranoid schizophrenia. Apart from that, there is no other significant family history of mental health disorders.

Personal Physiological Background: Her mother declared that she had no medical issues during pregnancy and childbirth. The patient herself reported having a normal psychological and general development during her childhood, without any difficulties. She experienced menarche at the age of 9 and does not currently have any children.

Personal Medical History: She has been diagnosed with mild anemia and exhibited high cholesterol, but she is currently not taking any medication.

Social history: Regarding her work and living conditions, she has worked in a call-center company, as well as for a company in the field of economics, utilizing her Economics degree. She has also had brief periods of living abroad, working in both Germany and Canada. However, both of these experiences were cut short due to her psychotic decompensations. For the past 5 years, she has been unemployed and currently resides with her parents, who provide for her. She has a sibling, with whom she does not have a strong bond. The patient stated that she has no close friends.

Drugs and substance use: She denied smoking and consuming alcohol, and she had no prior history of substance use.

CLINICAL EXAM

Vital Signs: Blood pressure: 127/74 mmHg, Heart rate: 70 beats per minute, Respiratory rate: 16 breaths per minute, Temperature: 36.4°C, Oxygen saturation: 99% on room air

General Appearance: The patient appears well-nourished, alert, and oriented to person, place, and time. She is appropriately dressed for the weather and her age, and her grooming and hygiene are good. Pallor is observed in relation to her skin.

Head and Neck: The patient's head is normocephalic and atraumatic. Her neck is

supple, with no masses or tenderness. There is no jugular venous distention.

Eyes: The patient's pupils are equal, round, and reactive to light. There is no conjunctival injection, discharge, or edema. Visual acuity is normal.

Ears, Nose, and Throat: The patient's ears are without erythema, swelling, or discharge. There is no hearing loss. The patient's nose is patent, with no congestion or discharge. Her mucous membranes are pink and moist. The patient's throat is without erythema, swelling, or exudate. Tonsils are not enlarged.

Chest and Lungs: The patient's chest is symmetrical with normal respiratory effort. Lung fields are clear to auscultation bilaterally, with no wheezing, crackles, or rhonchi.

Cardiovascular: The patient's heart rate is regular with no murmurs or gallops. Peripheral pulses are strong and equal bilaterally. There is no edema.

Abdomen: The patient's abdomen is soft and non-tender. During deep palpation, she mentions discomfort in the epigastric area. There is no hepatosplenomegaly or masses. Bowel sounds are normal.

Musculoskeletal: The patient has full range of motion in all joints without pain or crepitus. There is no tenderness, swelling, or deformity.

Neurological: The patient is alert and oriented to person, place, and time. Cranial nerves II-XII are intact. Strength is 5/5 in all extremities, and sensation is intact.

Paraclinical assessment: Blood tests were also conducted, revealing a chronic mild anemia and high cholesterol levels. Additionally, an EEG was performed, which yielded normal results. Taking into account the clinical examination and the paraclinical tests, the patient appeared to be in good overall health with no immediate medical issues.

PSYCHOLOGICAL EXAMINATION REPORT

The patient was referred for a psychological examination due to presenting symptoms of acute psychosis disorder, including disorganized thinking, disorganized motor behavior, affective inversion towards her family, delusional ideas of grandeur, reference and filiation. The purpose of the assessment was to gather comprehensive information about the patient's current psychological functioning, assess the severity of symptoms, and contribute to a diagnostic formulation.

During the examination, the patient appeared to be cooperative, although their speech was tangential and disorganized. She exhibited minimal eye contact and displayed restlessness through constant fidgeting.

Psychological Test Results:

Wechsler Adult Intelligence Scale (WAIS): The patient's performance on the WAIS indicated average intellectual functioning, with a Full-Scale IQ score of 109 points. The patient demonstrated adequate verbal comprehension and perceptual reasoning abilities, suggesting intact cognitive functioning.

Brief Psychiatric Rating Scale (BPRS): The BPRS was administered to assess the severity of psychiatric symptoms. The patient's total score on the BPRS was 64, indicating marked symptom severity. Notable subscale scores included 7 points for “conceptual disorganization”, 7 points for “grandiosity”, 6

points for “suspiciousness”, 6 points for “unusual thought content”, 6 points for “uncooperativeness”, highlighting the presence of disorganized thinking, delusional ideas of grandeur, reference and filiation and lack of insight towards her disorder.

Positive and Negative Syndrome Scale (PANSS): The PANSS was utilized to assess the positive, negative, and general psychopathology symptoms associated with acute psychosis disorder. The patient's scores on the positive symptoms subscale were 37, negative symptoms subscale were 28, and general psychopathology symptoms subscale were 51. These scores suggest the presence of moderate positive symptoms, mild negative symptoms and moderate general psychopathology symptoms.

Based on the clinical presentation and assessment findings, a provisional diagnosis of acute psychosis disorder has been considered.

PSYCHIATRIC EXAM

Appearance and General Behavior

Attitude: minimum cooperativeness, wary of the surroundings and people around, suspicious

Gait: frequently pacing

Clothing: casual, neat

Appearance: uncombed hair, unkempt nails

Idiosyncrasies: idiosyncratic interpretation of life events

Voice: increased verbal flow, voice of medium tonality and high intensity, mood-congruent inflections

Look: doesn’t engage in visual contact at first, maintains intermittently visual contact with the examining physician, tends to look away

Facies: low expressiveness

Mimics and Pantomime: unusual gestural activity, relatively inconsistent with her story-telling

Cognitive functions

Sensation: hyperaesthesia, irritability, irascibility

Perception: subjectively denies the presence of hallucinatory phenomena, but reports receiving telepathic information from the governors of the USA and Monaco.

Attention: spontaneous and voluntary hypoprosexia, reduced ability to concentrate, selective hyperprosexia and hyperfixation towards preferred topics, low distributivity or dispersion

Memory: fixation and evocation hypomnesia

Thinking: accelerated, incoherent, disorganized thought pattern, delusional ideas of grandeur, filiation, reference, optimistic outlook, extremely interpretative, suspicious, tangential thought pattern, existential dilemmas

Imagination: increased, makes different creative scenarios in her mind, tends to catastrophize various situations

Affective and motivational functions

Mood: fluctuating dispositions, emotional instability, detachment, low tolerance towards frustration, increased anxiety, affective inversion towards men and her own family

Feelings: ambivalent, maladjustment, grandiosity, egotistic, high self-esteem

Passions: towards foreign languages, history, general knowledge

Motivation: selectively increased, delay in initiating activities, indecision

Instincts: eating-lowered (loss of appetite), preservation- increased, sexual-normal, social – lowered, social isolation, maternal- lowered

Executive functions

Volition: fluctuating, depending on purpose, dysbulia

Motor activity: exhibits restless and agitated behavior, purposeless movements
Verbal activity: reduced fluency in her speech, normal volume, a fast but pressured rate
Behavior: slight psychomotor agitation
Sleep: restless sleep, difficulty in initiating sleep and maintaining sleep (mixed insomnia)
Judgement and Insight
Conscience: orientated in time, space, person, situation
Insight over illness: absent
Intellect: high, in accordance with educational background
Personality type: schizoid
Character: inappropriate attitude towards society

Diagnosis: Based on the patient's symptoms and clinical assessment, she was diagnosed with acute psychotic disorder.

TREATMENT PLAN

Developing a treatment plan should be tailored to the individual's specific needs, involving medication, psychotherapy, family support and education, social support and rehabilitation, and also stress and lifestyle management.

Therefore, the patient was prescribed an antipsychotic medication (Risperidone), which was initiated at a low dose and gradually increased over time. In addition, she was given an anxiolytic drug (Lorazepam), a mood stabilizer (Valproic acid), and a sedative (Clonazepam). Due to her involuntary admission to the hospital, initially she adamantly refused the medication, as she believed it was unnecessary. She threatened the medical staff multiple times by suing them and reporting them to the authorities of Monaco. She stated:" I have no reason for being here. I am not ill. I can't wait to go to America and be done with all of this. I was caught in the cross-fire of political conspiracies". However, after a few days, she became less resistant to pharmacotherapy, as the medical team persuaded her that adhering to the treatment plan was crucial for regaining her previous level of functioning.

Besides the medical treatment, therapy plays an important role when dealing with an acute psychotic disorder. First of all, psychoeducation provided her with the necessary information regarding the nature of acute psychotic disorder, its symptoms, treatment options, and strategies for managing symptoms. It also helped her and her family to better understand and cope with the illness. During her admission, she began attending therapy sessions twice a week and actively participated in support groups. In her case, Cognitive Behavioral Therapy (CBT) aimed to assist her in challenging and modifying distorted thoughts and beliefs associated with her symptoms. Additionally, CBT focused on reducing distress, improving coping skills, and enhancing overall functioning. The medical team also involved the patient's family in therapy, facilitating their understanding of the illness, improving communication, reducing family conflicts, and providing enhanced support for the patient's recovery. Engaging in supportive therapy further provided her with emotional support, validation, and encouragement, while creating a safe and non-judgmental environment for her to express her feelings, concerns, and fears.

In addition to therapy and medication, individuals who have been diagnosed with acute psychotic disorder may benefit from developing adaptive coping skills to manage their emotions. This may include engaging in regular exercise, practicing relaxation techniques such as meditation or yoga, and

seeking social support from friends and family.

Therefore, our patient was also advised to engage in regular physical exercise and to improve her sleep hygiene. The patient was educated about the nature of her illness and the importance of adhering to treatment. She was encouraged to involve her family and friends in her recovery process and to reach out for support when needed. The patient's symptoms were closely monitored over the time she spent in hospital, and her treatment plan was adjusted as needed.

At discharge, she had a moderately favorable prognosis, as some of her general symptoms showed improvement with the help of the aforementioned interventions. During her stay on the ward, there was a noticeable improvement in her behavior, as she displayed less hostility, suspicion, and verbal aggression compared to when she was admitted. Her sleep significantly benefited from the treatment, as did her mood. However, only slight improvement was noted in her cognitive functions, as her delusional beliefs remained firmly entrenched. Objective measures, such as scores on psychological tests like BPRS and PANSS, showed slight improvement. Subjectively, based on interview evaluations, she appeared to be more open, calm and balanced. She was advised to maintain regular contact with her physician and attend periodic evaluations, as well as continue therapy sessions for an indefinite period of time.

When it comes to adherence to the prescribed treatment, the question arises: will she take the medication once she returns home? The matter of treatment adherence for a patient with acute psychotic disorder, who lacks insight into their illness and maintains a rigid delusional core, is indeed a challenging and complex issue. On one hand, treatment adherence is crucial for managing symptoms, reducing the risk of relapse, and promoting long-term recovery. Adherence to medication and therapy can help stabilize the patient's condition, alleviate distressing symptoms, and improve overall functioning.

However, when a patient lacks insight into their illness and firmly holds delusional beliefs, treatment adherence becomes more difficult. The rigid delusional core can create significant barriers to accepting and engaging in treatment interventions. The patient may resist taking medication or participating in therapy sessions, as they genuinely believe that their delusions reflect reality and that treatment is unnecessary or even harmful.

In such cases, it becomes important for healthcare professionals to approach the issue with empathy, patience, and a multidisciplinary approach. Building a therapeutic alliance, establishing trust, and providing education about the nature of the illness can be initial steps towards fostering treatment adherence. Involving family members or a support system can also play a crucial role in encouraging adherence and providing ongoing support.

In some instances, involuntary treatment or legal interventions may be necessary to ensure the patient's safety and well-being. However, it is important to strike a balance between respecting the patient's autonomy and protecting their best interests.

Ultimately, the matter of treatment adherence in patients with acute psychotic disorder and a lack of insight requires careful consideration of individual circumstances, a collaborative approach involving healthcare professionals, and a focus on balancing the patient's rights and well-being.

CONCLUSION

In summary, the presented case of a female patient with acute psychotic disorder, involuntarily admitted to the psychiatric unit, unveils the intricate complexities encountered when managing individuals who lack insight and display non-compliance to treatment.

The patient's involuntary admission serves as a poignant reminder of the severity of her condition and the urgent need for intervention. However, her limited awareness of her illness presents a formidable obstacle, impeding the recognition of the necessity for treatment. This, coupled with her refusal to comply with prescribed interventions, further complicates the therapeutic endeavor.

Despite concerted efforts by a multidisciplinary team to establish rapport, provide education, and involve the patient's family, the deeply entrenched nature of her delusions and distorted beliefs hampers engagement in treatment. Overcoming these barriers remains a significant endeavor, as progress towards desired treatment outcomes proves elusive.

This case underscores the pressing need for novel approaches and ongoing research to forge more effective strategies in addressing acute psychotic disorders in patients lacking insight and displaying non-compliance. It accentuates the significance of a holistic and empathetic approach that appreciates the unique circumstances and challenges faced by each individual.

Navigating the intricate interplay between symptoms, insight, and treatment adherence is paramount in optimizing the well-being and recovery of those grappling with acute psychotic disorders. Further collaborative research among healthcare professionals, researchers, and policymakers is essential to enhance treatment outcomes and augment the quality of life for both patients and their families.

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Psychiatric manifestations in patients with Creutzfeldt-Jacobs's disease. Challenges in neuroimaging and diagnostic concepts.

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ABSTRACT

Background: Rapid symptom progression is one of the most important clues that a person may have Creutzfeldt-Jakob's disease. There is no single test-or any combination of tests-that can conclusively diagnose sporadic Creutzfeldt-Jakob disease in a living person.

Objectives: The aim of this article is to study some distinct features of patients with Creutzfeldt-Jacobs's disease in order to make a differential diagnosis with other disorders.

Material and Methods. It is a review of publications from the last years, using medical sites such as PubMed, Medscape, NCBI, Med bullets. A clinical case is also presented.

Results. Creutzfeldt-Jakob's disease (CJD) is the most common human form of a group of rare, fatal brain disorders known as prion diseases. Prion diseases, such as Creutzfeldt-Jakob's disease, occur when prion protein, which is found throughout the body but whose normal function isn't yet known, begins folding into an abnormal three-dimensional shape. This shape change gradually triggers prion protein in the brain to fold into the same abnormal shape. Creutzfeldt-Jakob disease causes a type of dementia that gets worse

unusually fast. More common causes of dementia, such as Alzheimer's, Lewy body dementia and fronto-temporal dementia, typically progress more slowly. Generally, there are three types of Creutzfeldt-Jakob disease: sporadic, familial and acquired.

Conclusions. Creutzfeldt-Jakob's disease is a rare disease with psychiatric symptoms who include depression, agitation, apathy, disorientation, problems with memory, thinking, planning and judgment. The clinical presentation of variant Creutzfeldt-Jakobs disease usually begins with a psychiatric prodrome, often at least 6 months before the onset of traditional neurologic symptoms.

KEYWORDS:

Creutzfeldt-Jacobs's disease, prions, psychiatric symptoms, dementia.

INTRODUCTION

Creutzfeldt-Jacobs's disease is a rare, rapidly progressive neurodegenerative disease that belongs to a family of prion diseases. This disease can cause several fatal neurodegenerative disorders histologically described as spongiform encephalitis (1). It is a type of transmissible spongiform encephalopathy, which is caused by prions. Prions are misfolded proteins that occur in the neurons of the central nervous system (2). The pathology shows spongiform change that consists of the vacuolation of the neuropil of the grey matter. This is associated with astrocytosis and neuronal loss (3). CJD is a neurodegenerative disease with many controversial aspects. Speaking about pathology, morphology and physiology there are some objective criteria we can use in order to recognize it. When discussing psychiatric manifestations, this is difficult, because there are no distinct symptoms.

MATERIAL AND METHODS

This article is a review of publications from last years, using medical sites such as PubMed, Medscape, NCBI, Medbullets. For a better understanding of the topic, a clinical case is presented in this article.

RESULTS

The hallmark of CJD is rapidly progressive dementia of unknown origin. In addition, numerous atypical neurological examination findings are seen as myoclonus, visual changes leading to cortical blindness, ataxia and akinetic mutism in the last stages (6). Because no occupational exposure of patients with variant CJD to cattle on farms or in abattoirs has been identified, spread is likely to occur through consumption of BSE-contaminated meat producs (case reported in 2020) (4). A diagnosis of CJD should not be neglected in elderly patients presenting with recent onset and rapid progression of behavioral changes, anxiety, irritability, mood deflection, and insomnia with no psychopathological history (8).

There are several types: spontaneous one, familial CJD and aquired (iatrogenic transmission) (5). The most common type of the disease is the sporadic type-sCJD. It is thought that it results from a spontaneous neurodegenerative illness-a somatic mutation in the gene or a random structural change in the PrP protein causing formation of PrP (Sc) (6). Sporadic CJD is characterized by prominent neurological symptoms, periodic epileptiform discharges on EEG, a relatively short disease course, onset in old age, and the presence of 14-3-3 protein in the cerebrospinal fluid. The host codon 129 genotype and the molecular strain of the transmissible prion agent suggest this phenotype (19). Diagnostic criteria of probable sCJD include rapid cognitive

decline, at least 2 of the following six specific neurological manifestations as: myoclonus, pyramidal/extrapyramidal, visual, cerebellar, akinetic mutism, other higher cortical signs (neglect, aphasia, apraxia, acalculia), positive EEG or positive MRI (subcortical hyperintensity or cortical gyral hyperintensity) and the fourth one (routine investigations do not suggest an alternative diagnosis) (8). The classic clinical presentation of sCJD includes rapidly progressive dementia, myoclonus, pyramidal and extrapyramidal signs but it can begin with non-specific psychiatric symptoms such as: personality changes, behavioral changes, anxiety and even as a psychotic condition (9). Psychiatric symptoms in sCJD have a specific clinical evolution. In the prodromal phase patients present with depression and anhedonia (6 month outpatient care) (7). According to one clinical analysis made by University Hospital Center of Coimbra, Portugal - 26% of patients with sCJD have psychiatric symptoms at disease onset, increasing to 80% within the first 100 days (11).

This is a controversial theme, so in order to describe the first symptom/sign and first diagnosis in patients with sCJD, in Germany was made a clinical trial in order to reach some data on the first symptom/sign in 492 patient with probable sCJD and known M129V polymorphism. Unspecific prodromal symptoms such as headache, fatigue, sleep disturbances were found in about 10 % of the patients. Dementia was the most common first symptom (37%) followed by cerebellar (34%), visual (15 %), and psychiatric disturbances (14 %) (10).

Familial CJD results of known mutations of PRNP and is historically split into 3 pheonotypic categories of GSS syndrome, fatal familial insomnia (FFI) and fCJD (6). Iatrogenic form, for the first time reported in 1974 was in a patient who received a corneal transplant from an infected cadaver with incubation period lasting between 1-14 years. Pooled cadaveric growth hormone was used for injections and led to CJD after 30 years (6). Neurological signs of these patients, such as hyperkinetic movements and gait imbalance, can be interpreted as eventual adverse effects of the prescribed medication, in the literature, movement disorders induced by antipsychotics, such as sulpiride, and calcium channel blockers, such as cinnarizine (12).

There have been only a few case reports with little attention in the literature given to the psychiatric manifestations of CJD. Symptoms may be vague and can include weight loss, fatigue, dizziness, headache, disorders of sleep, impaired judgment and unusual behavior. An intense emotional response to the environment as well as delusions, hallucinations and agitation may be interpreted as a depressive or psychotic illness. In review of 232 experimentally transmitted cases of sporadic CJD, approximately one-third of the cases at the outset manifested only mental deterioration, with some form of emotional instability. Ten percent of patients with CJD are admitted to psychiatric wards (13). In early phase (3-4 weeks) patient, present with major depressive disorder, a propensity to cry, weight loss and insomnia. The third phase (intermediate one) which lasts for about 2 weeks we can distinguish mood disorder with psychotic symptoms: emotional lability, hypertalkativeness, referential delusions. It is important to note that in this period appear for the first time neurological symptoms as myoclonic jerks and urinary incontinence. The last phase lasts months and is characterized by dementia with psychotic symptoms (7).

These controversial stages of evolution are referred to phenotypic heterogenity in sCJD, which is well documented, but there is not yet a systematic classification of the disease variants. To define a full spectrum of variants, were examined a series of 300 sCJD patients. Seventy percent of subjects showed the classic CJD phenotype, PrP (Sc) type 1, and at least one methionine allele at codon 129. Twenty-five percent's of cases displayed the ataxic and kuru-plaque variants, associated to PrP (Sc) type 2 and methionine homozygosity. Finally, a rare phenotype characterized bu progressive dementia was linked to prP(Sc) type 1 and valine homozigosity (14, 15).

CASE PRESENTATION

A 67-year-old woman, diagnosed with rapidly progressive dementia was brought by her relatives at the emergency room in April 2022 with a 2-month history of progressive neurologic symptoms and was admitted to the inpatient neurology service. Her history included the following:

- a 2-month history of cognitive impairment: progressive memory disorders, difficulty maintaining focus and attention;
- a one-month history of gait impairment (gait apraxia), speech impairment (dysarthria);
- muscle limb rigidity;
- an unintentional weight loss of 4 kg since the onset of symptoms.

The patient lives in an urban area, in an apartment, with her husband. She is currently retired for medical reasons but has worked as an accountant for almost 30 years. Regarding her family, she is married and has one son, who is working abroad, the details regarding the other members of her family are unknown. She had been married happily for almost 45 years.

PHYSICAL EXAM

Mental status: Is alert and disoriented in herself, time and place.
Cranial-nerve function: Dysarthria.
Strength: Normal strength and extrapyramidal hypertonia.
Sensation: Difficult to examine.
Reflexes: Hyperreflexia.
Cerebellar function: Difficult to examine.
Gait: Gait apraxia.

PSYCHIATRIC EXAM

Appearance and General Behavior:
Attitude: partly cooperative, partially communicative, psychomotor restlessness
Clothing: adequate for the hospital environment, good hygiene status
Voice: diminished verbal flow, voice of medium tonality and decreased intensity, coherent speech
Look: doesn't maintain visual contact with the examining physician
Facies: hypomobile
Mimics and Pantomime: decreased gestural activity
Cognitive functions:
Sensation: irascibility
Perception: she denies the presence of psychoproductive phenomena
Attention: reduced ability to concentrate
Memory: fixation and evocation hypomnesia
Thinking: slightly incoherent
Affective and motivational functions: Mood: emotional lability, increased anxiety
Feelings: emotional blunting
Passions: loss of interest in general activities
Motivation: delay in initiating activities
Instincts: eating-loss of appetite, social-isolation.
Executive functions:
Volition: hypobulia
Motor activity: low energy, fatigability
Verbal activity: slow, tangential and circumstantial speech
Behavior: impulsivity, bizarre behavior

Sleep: mixed insomnia
Judgement and Insight:
Conscience: disorientation in herself, time and place.
Insight over illness: Hypertension. Hypothyroidism.
Intellect: Difficult to examine.
Character: inadequate attitude towards family and society
Psychological examination: emotional instability, delusional and hallucinatory manifestations.

During hospitalization, the patient's neurologic symptoms continued to progress. She eventually lost the ability to ambulate independently. She began to have sudden, jerky movements while lying down at night, and she was easily startled by sudden noises or people entering her room, a phenomenon known as startle myoclonus. She began to have visual hallucinations, became easily frustrated, and had increasing difficulty with the completion of daily tasks. Subsequently, she was no longer able to participate in conversation. She lost the ability to perform all activities involved in daily life and became both bedridden and mute. She received palliative care at home. The patient required complex medical assistance, which involved not only hospitalization but also the development of a doctor-patient relationship in order to achieve a better understanding of the disorder and how most symptoms are likely to improve with the right treatment.

Historically, neuroimaging were not a part of the diagnostic criteria for CJD, which was based more on clinical, neurohistopathological, EEG and CSF features. There is however growing support for MRI which can present with specific changes in order to include it as a neuroimaging in the diagnostic work-up for CJD. The specific features of sCJD on MRI are bilateral high signal in the caudate and putamen. The new publications highlighted the importance of cortical ribbon hyperintensity. Shiga and colleagues described 26 cases of sCJD and 45.8 % showed lesions in both the cortex and basal ganglia (19). Besides raised CSF 14-3-3 protein level, characteristic abnormalities on MR images in vCJD can be used in order to diagnose vCJD. This is about abnormal signal intensity in the posterior thalamus, called pulvinar sign and in dorso-medial thalamic nuclei (16). These organic changes are a reflection of an EEG pattern, called synchronous periodic epileptiform discharges, such as triphasic waves approximately 1-1.5 seconds apart. These changes are usually present during wakefulness and disappear during sleep (17). Psychiatric manifestations depend on the genetic polymorphism of genes implicated in the pathogenesis of this disease, in sporadic form the EEG exhibits characteristic changes depending on the stage of the disease, ranging from non-specific findings as diffuse slowing and frontal rhythmic delta activity to disease typical period sharp wave complexes in middle and late stages or even alpha coma in preterminal EEG recordings (18).

DISCUSSIONS

Creutzfeldt-Jacob's disease is rare, and is often a diagnostic challenge for physicians facing a rapidly progressing dementia. As of now, definitive diagnosis is provided with brain biopsy, but more often than not the results are inconclusive because not all areas of the brain will show the classic histological changes in CJD, even if the disease is present. Surgeons target areas that appear the most abnormal on imaging studies, but this is most often in deep-seated subcortical structures. The WHO criteria, as well as more updated suggested criteria, are outdated because they do not use newer tests that provide a less

invasive method for definitive diagnosis. Given these issues, a newer approach to diagnosis is needed. Creutzfeldt-Jakob's disease is classified as familial, sporadic, or acquired. Regardless of the type, the disease has a rapid clinical course that is uniformly fatal. There are some consistencies on physical examination, radiographic studies, and EEG, but the most common form is sporadic CJD (sCJD), and it follows a theme of heterogeneity. The infectious agent is the abnormal scrapie form (PrPSc) of the host-encoded cellular prion protein (PrPC) that causes a posttranslational modification of PrPC into the disease form, accumulating in the brain and causing neurodegeneration. Familial CJD (fCJD), or the genetic type, is due to a mutation in the gene encoding PrPC, whereas the sporadic form is thought to originate after a somatic mutation or a stochastic protein alteration. Creutzfeldt-Jakob's disease is also transmissible through iatrogenic causes or by ingesting beef with bovine spongiform encephalopathy (BSE or „mad cow disease"), leading to variant CJD (vCJD).

CONCLUSION

Creutzfeldt-Jakob's disease is a rare disease with psychiatric symptoms who include depression, agitation, apathy, disorientation, problems with memory, thinking, planning and judgment. Prion diseases are unique in that they can occur by three mechanisms: spontaneous (sporadic), genetic (familial), and acquired (infectious/transmitted). The sporadic Creutzfeldt-Jacob's disease is a rapidly progressive dementia with behavioral abnormalities, ataxia (usually gait), extrapyramidal features, and, eventually, myoclonus. The clinical presentation of variant Creutzfeldt-Jakob's disease usually begins with a psychiatric prodrome, often at least 6 months before the onset of traditional neurologic symptoms; cognitive dysfunction, cerebellar dysfunction, and involuntary movements (e. g, dystonia, myoclonus, or chorea) usually appear several months after psychiatric onset. Unfortuntelly, it is a missdiagnosed disease, because the only way to confirm de diagnosis is to examine the brain tissue by carrying out a brain biopsy, or more commonly after death in a post-mortem examination of the brain. Currently there are many possibilities, so they can be used in a smart way, that is, to make a connection between the EEG pattern, MRI scanning, genetic testing, CSF analysis and psychiatric manifestations – in order not to misdiagnose this disease. Some of the symptoms of human prion disease can be temporarily treated, but at present, no cures are available.

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

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

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

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Ashcroft FM.: Ion channels and disease, San Diego, London: Academic Press,
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ACKNOWLEDGMENTS AND DISCLOSURE

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