Journal of
PSYCHOPATHOLOGY

Editor-in-chief: Alessandro Rossi

Special Issue

VOL. 25 - 2019

3

NUMBER

Further exploration of suicidal behavior

Guest Editor: M. Pompili, A. Rossi

SOPSI
SOCIETÀ ITALIANA DI PSICOPATOLOGIA

PACINI
EDITORE
MEDICINA

www.jpsychopathol.it

Journal of
PSYCHOPATHOLOGY

Editor-in-chief: *Alessandro Rossi*

www.jpsychopathol.it

Contents

M. Pompili[1], A. Rossi[2]

[1] Department of Neurosciences, Mental Health and Sensory Organs, Suicide Prevention Center, Sant'Andrea Hospital, Sapienza University of Rome, Italy; [2] Department of Biotechnological and Applied Clinical Sciences (DISCAB), University of L'Aquila, Italy

Further exploration of suicidal behavior: from mental to psychopathological perspectives

Suicide is a major public health problem on a global scale, with large regional variations. According to the World Health Organization, about 880,000 suicides are reported each year [1]. This estimate represents the tip of an iceberg that hides self-injurious behavior, hospitalization for self-inflicted injuries, suicide ideation and attempts. In fact, it is estimated that suicide attempts represent 30 times the estimate of suicide deaths [2]. Although, mental disorders are important contributing factors to suicide risk, new trends in neuroscience, psychiatry, and suicidology suggest that neurodevelopmental factors are of crucial importance. Of course, among mental disorders, mood disorders, substance use disorders, and psychoses as well as some personality disorders heighten the risk for suicide.

Knowledge of these aspects is important in order to address and prevent suicide through comprehensive assessment and management strategies.

In this issue, Pompili suggests that a phenomenological approach is of crucial importance for a proper understanding of the human experience of mental pain. Although an empathic understanding of the pain of the suicidal individual is not sufficient, it is the first step of a process that may eventually prevent suicide in unique individuals.

Following the multiaxial organization of current diagnostic systems, the features and main innovations that can guide clinicians in their assessment and clinical management of suicide risk are examined by Lingiardi et al.

Recent systematic reviews and meta-analyses confirmed that Obsessive-Compulsive Disorder (OCD), historically considered to be associated with a relatively low risk of suicide, is actually in itself associated with considerable risk for lifetime suicide attempts and suicidal ideation (Albert et al.).

Maina et al. reported on the high rate of suicide attempts and deaths in bipolar disorder patients and the social impact of this behaviour, suggesting the need for the early recognition and treatment of such patients. Among medical disorders, Ciuffini et al. reported that epilepsy represents a challenge for life expectancy and quality of life either for social and relational consequences due to stigma than for the consequences of the disorder itself. Suicidal behaviors are more frequent among individuals with epilepsy than in the general population.

Rossi et al. systematically reviewed evidence on the mediating role of dissociation between trauma and non-suicidal self-injury that has not been addressed in the literature and needs further exploration/examination/investigation (one of these words would be better)

This special issue dedicated by the Journal of Psychopathology to 'suicide' addresses peculiar topics that advance our understanding of the complex problem of suicide, providing further support to clinicians in the management of this multifaced human phenomenon.

Correspondence

Alessandro Rossi
Department of Biotechnological and Applied Clinical Sciences (DISCAB), University of L'Aquila, via G. di Vincenzo 16/B, 67100 L'Aquila, Italy • E-mail: alessandro.rossi@cc.univaq.it

References

1 World Health Organization. *Preventing suicide: a global imperative.* World Health Organization, 2014 (https://apps.who.int/iris/handle/10665/131056).

2 Bachmann S. *Epidemiology of suicide and the psychiatric perspective*. Int J Environ Res Public Health 2018;15:1425.

A plea for the understanding of the suicidal mind

M. Pompili

Department of Neurosciences, Mental Health and Sensory Organs, Suicide Prevention Center, Sant'Andrea Hospital, Sapienza University of Rome, Italy

Summary

Although suicide is a major public health issue worldwide, both mental health professionals and lay-people struggle to cope with suicide. Part of the problem comes from the myths, obsolete paradigms, and stigma associated with suicide that results in anxiety and fear. However, most suicidal individuals want to live even when facing serious suicidal stress. Clinicians are, therefore, called upon to unlock the suicidal mind, relieve the suffering, and pay attention to the unmet needs of these individuals.

There are so many unmet needs in individuals at risk of suicide. Too often, the medical model is imposed as a treatment plan. Therapists are more likely to treat the psychiatric disorder and, therefore, assume that this treatment also reduces suicide risk. In this way, the "one fits for all" model precludes understanding the suicidal mind, with its unique characteristics for each subject.

Furthermore, there are still no agreed-upon models for managing patients accessing the emergency room and, besides, there is still no data on patient adherence to prevention programs at follow-up.

One of the central elements of caring for people at risk of suicide lies in the ability to formulate the question, "What is like to be suicidal?". To answer this question, the therapist must necessarily leave his formal position and try to identify himself with the subject in crisis. It is an exercise that is not necessarily easy but for which you can train. Throughout this chapter, the reader is helped to understand the suicidal mind to facilitate this action.

This essay focuses on some of the unmet needs of suicidal patients and points to some key elements for clinicians in the management of suicidal individuals. The concept of mental pain as the main ingredient of suicide is used to explore some of the most prominent features of the suicidal mind.

Key words

Suicidal mind • Mental pain • Prevention

Despite massive research on the topic of suicide, the mystery of such a peculiarly human phenomenon remains generally unsolved. Results from studies from different disciplines, however, emphasize the complexity and multifactorial nature of suicide. Often, unfortunately, such complexity is restricted by the use of an obsolete paradigm and dismissed with single diagnostic labels.

Psychiatrists and mental health professionals often feel responsible for the lives of their patients. Suicide is, without doubt, the event that is most daunting in clinical practice. According to Simon [1], the law tends to assume that suicide is preventable if it is foreseeable. Some scholars oppose such a view by supporting the notion that suicide is never foreseeable, assuming that such a notion has the same meaning of predictability. While psychiatrists can never predict suicide because they are not prophets, we need to assume that they can foresee a suicide because they are clinicians. Delivering a message that a clinician has no tools to master, at least in part, the complexity of a given phenomenon, is equal to exposing that clinician to a lawsuit. Having the opportunity to assess suicide risk and provide whatever means necessary to clinicians in order to prevent

Correspondence

Maurizio Pompili
Department of Neurosciences, Mental Health and Sensory Organs, Suicide Prevention Center, Sant'Andrea Hospital, Sapienza University of Rome, via di Grottarossa 1035, 00189 Rome, Italy
• E-mail: maurizio.pompili@uniroma1.it

suicide is the major goal when dealing with suicidal individuals.

Suicidologists have now switched from risk assessment (such as collecting data regarding the presence *vs* absence of risk factors and protective factors as well as warning signs) to risk formulation (such as understanding of how risk factors combine, interact and fuel suicidal behavior, and are buffered by protective factors, and knowing which warning signs place individuals at increased short-term risk). Prediction is, therefore, something that should not worry about mental health professionals. Rather, they should focus on the interventions necessary to reduce suicide risk. Scholars now point to the need of comparing current risk state to the patient's "baseline" state and worst-point state which may shed light on effective interventions and foreseeable changes that could increase or decrease risk [2]. Foreseeable here means having collected as much information as possible and being able to make the best decision for a given individual. It should be clear that adverse events (suicide or suicide attempt) after such a meticulous documented assessment should not constitute a source for accusing mental health professionals of malpractice.

In support of the need to broaden our view on how to deal with suicide risk are the recent results for nationwide data. These findings point to the fact that the narrow vision encrypted in past models of suicide is challenged by the urgent need to reconceptualize suicide risk in an individual in crisis, regardless of the psychiatric diagnosis or other nosological labels.

The Italian National Institute of Statistics [3] conducted a study of the Italian population on suicide in the three years 2011-2013, evaluating the presence of any physical or mental disorders. In the period considered, there were 12,877 suicides (of which 10,065 were men), and about one case of suicide out of 5 had significantly associated morbidities [3]. In particular, in 737 suicides, the presence of relevant physical diseases was documented, of which 288 had a comorbid mental disorder. In 1,664 cases, the study reported the presence of mental disorders without comorbidity from relevant organic diseases. However, in more than 80% of the cases, there were neither mental disorders nor relevant physical illnesses.

Similarly, the Centers for Disease Control and Prevention in the United States found, between 1999 and 2016, a 30% increase in the suicide rate, indicating that about 54% of cases were not associated with any mental disorder [4].

We are now in need to open a new discussion on suicide prevention by providing a paradigm shift that takes into consideration how more precise approaches should substitute obsolete models. In the era of precision in medicine and mental health, there should be precision in suicide prevention. This is achieved with the fight against stigma and the surrounding taboo of suicide. While centuries of condemnation still influence our present view of suicide, we can catch up with new and positive perspectives with help for those with suicidal risk.

Understanding the suicidal mind

Campaigns have been launched to make sense of what makes a specific individual suicidal. However, encountering a suicidal individual remains for the majority of professionals and common people, a challenging task. We know that suicidal individuals give definite warning signs, mostly derived from their ambivalence about ending their own lives. Among the constructs used to describe the wish to die, a simple but extraordinary model has proved, at least for its straightforwardness, to be useful in describing the suicidal mind. Edwin Shneidman [5] first posited that the suicidal individual experiences unbearable psychological pain (*psychache*) or suffering and that suicide might be, at least in part, an attempt to escape from this suffering. Shneidman [5] considered psychache to be the main ingredient of suicide. According to this model, suicide is an escape from intolerable suffering, emphasizing that suicide is not as a movement toward death but rather as an escape from intolerable emotion, unendurable or unacceptable anguish. Experiencing negative emotions, with an internal dialogue making the flow of consciousness painful and leading the individual to the ultimate conclusion, may be related to the fact that, if tormented individuals could somehow stop consciousness and still live, they would opt for that solution. Suicide occurs when the psychache is deemed by that individual to be unbearable [6].

For Shneidman [7], suicide is the result of an explosive mixture consisting of four basic ingredients. He listed such ingredients as follows: heightened inimicality (acting against the individual's best interest); exacerbation of perturbation (refers to how disturbed the individual is); increased constriction of intellectual focus; tunneling or narrowing of the mind's content (dichotomous thinking); and the idea of cessation: the insight that it is possible to stop consciousness and put an end to suffering.

The concept of inimicality in this instance refers to those attitudes of the individual that lead him to act in a way that is not at all friendly to himself, to the point of becoming his perverse enemy. In suicidal individuals, this state is present, and the individual is struggling with pressures of various kinds such as physical health, refusals, feelings of failure, pain and other negative emotions. The individual fails to manage these issues with the resources he has available.

Shneidman believed that in suicide, "death" is not the keyword. The key word is "psychological pain" and, if the pain were relieved, then the individual would be willing to continue to live.

Two main concepts are relevant to this discussion: perturbation and lethality. Perturbation refers to how upset (disturbed, agitated, discomposed) the individual is; while lethality refers to the likelihood of an individual dying by suicide in the future.

The understanding of the suicidal mind requires knowledge of the perturbed state of the individual in crisis since this provides the motivations for the individual to contemplate suicide. Therefore, asking where the suffering comes from and how it has changed and become more acute is a method of intervention which, although simple and intuitive, is often forgotten by those, who are responsible for managing the person in crisis. In the internal debate, essentially involving ambivalence, being able to tune into the suffering of the person makes it possible to stem such ruminations and bring the discussion back to a position of vitality and hope.

Perturbation supplies the motivation for suicide; lethality is the fatal trigger. Everyone who dies by suicide feel driven to it and feels that suicide is the only option left [8]. The concept of "constriction" is defined as tunnel vision or rather finding oneself with a reduced number of options to cope with the suffering. Suicidal individuals experience dichotomous thinking, that is, wishing either some specific (almost magical) total solution for their perturbation or for cessation, in other words, suicide It seems that, although there may be effective supports from family and friends, the individual is unable to benefit from them. The pleasant memories and their history in relation to others are not helpful, and the individual focuses on intolerable emotions and how to escape from them.

The concept of cessation comes into play when the individual develops the idea that one can put an end to the drama that takes place in his mind through dying. The individual then realizes that with death he will bring a solution to his experience by eliminating all the elements that torment him in life.

Suicide is the result of an interior dialogue during which the mind scans its options [8]. During the early phases of this process, suicide is considered as an option, but it may be rejected a number of times. Shneidman [9] reported an emblematic process referring to the word 'therefore' "*almost every decision that a person makes (based on some unspoken reasoning in the mind): it is the logical bridge between almost every thought and every action (or deliberated inaction). Among all the ... therefore, I ...*" sequences that are possible in the mind, one of the most important ones is contained in the words: I' ... therefore, I must kill myself".

Suicide planning is often a long and complex process. The person begins to think of a propitious moment; he must have time to prepare. During the weeks and days preceding the actual planning until the act is implement-

ed, the individual continues to dialogue with himself or herself with a large number of thoughts. They can refer to the fact of not being worth anything for themselves let alone for others, of not having been a success, of being a burden for oneself and one's loved ones, that no one will ever love them, or to be a coward so much that one cannot even die by suicide. After debating, to overcome the survival instinct the person must have, at least just before the act, such impulsiveness, and aggression as to make a gesture against nature. Thus begins an increasingly tight challenge in which a moment of excitement in the mood may also occur during which the person sees salvation in suicide, begins to glorify the act and configures it as a plan to put into practice, avoiding any interference on the part of the others. One must think of an act that appears to the subject as something forbidden but which feels necessary to improve his state. Suicide is an act that, in many cases, is premeditated for a longer time than is believed. Only after this time does the act become an impulsive gesture. The individual has repeatedly thought about taking his own life but this option, every time it occurred, although it was discarded, took on a greater value. It is at this juncture that the subject at risk of suicide begins to give signals in which he conveys the message of being tired of living, of thinking about death and of wanting to die. It is a problem of human life for which "emotional storms" occur, great movements of ambivalence, and at the same time changes in sleep habits, appetite, personal hygiene, and social relations. In this period of premeditation of the lethal act, the subject at risk also thinks of his loved ones, feeling regret and guilt for considering such a tragic solution. In some cases, there are also complex dynamics within the family, with the partner, or with friends, such that the suicidal individual almost reproaches them for not receiving adequate help from them.

Moreover, the subject at risk feels hopeless, and his mental pain feels unique, and he reaches this conclusion after experiencing the fact of not being able to communicate his suffering to the people assigned to help. The desire to die happens in each person with substantially unique motivations and thoughts, which makes him different from all other people at risk of suicide.

Shneidman [5] also considers that the main sources of psychological pain are shame, guilt, anger, loneliness, and despair originating in the frustrated and denied psychological needs. In the suicidal individual, it is the frustration of these needs and the pain that results from it, that is considered by him to be an unacceptable condition for which suicide is seen as the most appropriate remedy. There are psychological needs with which the individual lives and which define his personality and psychological needs which, when frustrated, induce the

individual to choose to die. We could say that this is the frustration of vital needs. These psychological needs include the need to achieve some goal such as joining a friend or a group of people, gaining autonomy, opposing something, imposing on someone, and the needs to be accepted and understood and receive comfort.

It is essential to monitor suicide risk at all time by taking into consideration warning signs for suicide, such as any change in habits, especially if insomnia is presented and any reference to the wish to die. People may feel trapped and may engage in maladaptive behavior, such as drinking alcohol and using psychoactive substances. Suicidal individuals also often put their affairs in order and give away symbolic items, as if they wish another person will take care of a prized possession, regardless of their economic value.

Studying the content analysis of the pain narratives of suicidal patients, Orbach [10] refers to specific features of the suicidal mind: These include; change in the self, experiences of self-estrangement accompanied by dissociative characteristics; a sense of worthlessness, emotional impoverishment, and loss of self-esteem. Furthermore, the mind is often characterized by the experience of loss, such as events of loss that lead to an interruption in one's sense of self-continuity together with loss in one's meaning of life. There are also oxymoronic experiences, extreme contradictions in feelings, thoughts, and desires – to live and die at the same time or grandiosity *vs* humiliation. Besides, the language of pain points to the fact that ordinary words do not suffice to describe these idiosyncratic experiences.

Critical appraisal of psychiatric disorders in the context of the suicidal scenario

Unlike the decision to confine suicide risk to the realm of symptomatology of psychiatric disorders, nowadays new insights into the phenomenon of suicide have led to considering that psychiatric disorders do play a contributing role, but a more profound understanding of the suicidal mind is needed [11]. Rather than categorizing the suicidal individual under the diagnosis of psychiatric entities, clinicians need to be able to recognize the drama occurring in the mind of a unique individual who may also be depressed, bipolar or suffering from other disorders. Most psychiatric patients do not die by suicide. Psychiatric patients are suicidal only when negative emotions are so painful that suicide is the only option left, and when the suicidal mind is hosted in an individual's mentally disturbed brain. Suicide is not, therefore, a specific and narrow symptom of depression. Instead, it is a behavior "combining features of a declaration of war with a petition for bankruptcy" [12] as well as having profound social implications [13].

Considering suicide risk to be merely a symptom impairs the opportunity to fully investigate and understand suicide. Attempts to explain, predict, and control suicide requires an understanding of what suicidal thoughts and feelings mean to those who live it. Other than collecting a huge amount of data for research activities, efforts should also be directed to understanding first-person data of the subjective, lived experience. Such an approach is an essential complement to the objective, third-person data, and methods of traditional science. Understanding the unbearable mental pain means thinking phenomenologically and, therefore the development of suicidal tendencies can be traced back to a state with similar characteristics as falling in love but flipped for affective valences. It is a pervasive condition with both psychological and somatic roots which incorporate the individual as a whole. An unpleasant sensation is often localized in the chest and hypochondrium. The mind tries each option to release the tension but never finds a safe haven and ends up convinced that nothing will bring relief.

To distinguish suicidal contents from psychiatric diagnosis it is necessary to think that the elements that support the desire to dying constitute a process in its own right, with a logic typical of the mind that suffers and that tries to devise a solution to reduce and resolve this suffering. Since the nature of suffering that results in suicide is due to the personality of the individual, to his frustrated psychological needs, and to the wounds of the ego (defeats, humiliation, shame, etc.), one can, therefore, differentiate that suffering from the typical suffering of depressive symptoms. Subjects at risk of suicide develop a thinking process called dichotomous thinking because they reason with only two options when confronting the suffering that has become unbearable: continue to suffer or obtaining immediate relief from pain by suicide [8].

This process derives from an inner dialogue that the individual has with himself to seek a solution to his drama in the mind. Independent of psychiatric disorder, clinicians are required to understand this complexity, without which the risk of suicide cannot be decoded. If this process is not interrupted by a change through, for example, help from someone, the individual approaches the final decision and, to quote Shneidman, *"The spark that ignites this potentially explosive mixture is the idea that one can put a stop to the pain. The idea of cessation provides the solution for the desperate person"* [7].

Communication of suicidal intentions

Among the myths often cited to describe idiosyncrasies in the phenomenon of suicidal behavior, current popular opinion state that people who talk about killing themselves rarely die by suicide; whereas, most peo-

ple who die by suicide have given some verbal clue or warning of their intentions. Some studies show that as many as 2/3 rds of suicide deaths share their intentions before dying by suicide. The study by Robins and colleagues [14] was probably the first attempt to address this issue through collecting data for a sample of suicides, and the study remains as one of the few contributions to the literature in this area. Despite the understanding of the communication of suicidal intent, no previous work has examined this fact through a meta-analytic investigation. A recent meta-analysis has shown how suicidal communications are key elements preceding suicides, confirming for the first time with clear figures how suicidal individuals express their intentions before the final act [15].

Unlocking the suicidal mind by a proper understanding of the subjective experience

Unlocking the suicidal mind is the most challenging of all tasks. Many models describing suicide fail to provide a proper understanding of this multifaceted human condition. Stigmatization and fear often provide reasons for empathic disconnection. Furthermore, even when dedicated clinicians are willing to consider all of the patient's needs, we cannot imagine how much these patients suffer. In fact, in order for empathy to occur it is necessary that we should have, in our own experience and in our own minds, some points of reference that correspond to those of the patients' experience of states of intense suicidal arousal or excitement [16][17].

I agree with Zoe Boden [18] in her view of the experience of suicidal individuals, *"Acknowledging the felt aspect of the experience is, I will argue, necessary for developing a fuller understanding. Recognizing that feelings do not exist solely within a person, but between people, intersubjectively, is also necessary to understand the experience of suicidality more deeply. However, because feelings are immediate and sensory, I will suggest that there are times when understanding is difficult, not because the experience or meaning is hard to discern, but because the visceral power of understanding can feel too much. Feeling overwhelmed is one of the ways that we respond at the edges of our understanding. In our suicide research, there were times when understanding, really understanding, was more problematic than I initially wanted to admit. Sitting, listening to what follows from the partial quote at the start of this chapter was one of those times"*. To understand suicidality, the individual must be understood holistically and met in his or her experience as it is, rather than broken down into risk factors and behaviors.

I also support what suicidologist David Jobes [19], recently stated. *"First, the goal of the clinician is to develop a mutual understanding of an individual's suicidality with the respective patient. This goal differs from the medical model emphasis, which tends to emphasize immediate and overriding emphasis on clinical diagnosis. Second, clinicians must be cognizant of a suicidal person's potential anguish and total loss of self-respect. Many patients are likely to withdraw and express vulnerability when discussing their own suicidal thoughts and behaviors. Third, the clinician should express a nonjudgmental and supportive attitude toward the patient. Empathy is significant in strengthening the therapeutic alliance, and the patient should be validated as the expert of their own experiences. Fourth, suicidal crises are not simply about the present but also often about the past. In the exploration of the crisis/crises, the clinician should encourage the patient to tell their story in a narrative fashion. Fifth, new models are necessary to conceptualize suicidal behavior so that the clinician and patient share an understanding of the patient's suicidality. An objective of this guideline is to not view the patient just as someone with psychopathology, but as someone with logical reasons for being suicidal. Sixth, the ultimate goal in clinical work is to garner a therapeutic relationship with the patient, right from the initial assessment".*

Conclusions

There are still many unmet needs for suicidal individuals, and too often such needs are disregarded as unimportant or of secondary importance. Clinical experience and recent data point to the need for a broader understanding of the suicidal mind. Although many scholars emphasize the importance of risk factors for suicide, such factors are usually static and derived from studies of people not necessarily representative of suicidal individuals in the general population. Such cohorts are sometimes small and belonging to narrow subpopulations which impair proper generalization.

Each individual is unique, with a unique presentation of suicidal wishes. However, most individuals can refer their suffering to specific unmet needs, allowing categorization according to the nature of what is lacking in their lives.

Modern psychiatry now witnesses is conveyed in a paragraph of the introduction of DSM-5 [20], that is *"Diagnosis of a mental disorder should have clinical utility"* but *"the diagnosis of a mental disorder is not equivalent to a need for treatment. Need for treatment is a complex clinical decision that takes into consideration symptom severity, symptom salience (e.g., the presence of suicidal ideation), the patient's distress (mental pain)"* and *"Clinicians may thus encounter individuals whose symptoms do not meet full criteria for a mental disorder but who demonstrate a clear need for treatment or care.*

The fact that some individuals do not show all symptoms indicative of a diagnosis should not be used to justify limiting their access to appropriate care" (p. 20). Far from being an unexpected phenomenon, suicidal behavior is characterized by many warning signs that often allow key clinical decisions that save the lives of individuals in crisis. The challenge of suicide prevention is to painstakingly develop a culture both in clinical populations and the general population to take care of suicidal individuals starting from their basic frustrated psychological needs. The task is to adopt a phenomenological approach that directs the attention of helpers inside the human experience of mental pain.

Conflict of interest

The Authors have no conflict of interest to declare.

References

1. Simon RI. *Suicide risk assessment: what is the standard of care?* J Am Acad Psychiatry Law 2002;30:340-4.

2. Pisani A, Murrie D, Silverman M. *Reformulating suicide risk formulation: from prediction to prevention.* Acad Psychiatry 2016;40:623-9.

3. ISTAT. *Malattie fisiche e mentali associate al suicidio: un'analisi sulle cause multiple di morte.* Nota informativa 15 febbraio 2017.

4. Stone DM, Simon TR, Fowler KA, et al. *Vital signs: trends in state suicide rates — United States, 1999-2016 and circumstances contributing to suicide — 27 States*, 2015. MMWR Morb Mortal Wkly Rep 2018;67:617-24,

5. Shneidman ES.; *Suicide as psychache.* J Nerv Ment Dis 1993;181:145-7.

6. Pompili M. *La prevenzione del suicidio.* Bologna: il Mulino 2013.

7. Shneidman ES. *A psychologic theory of suicide.* Psychiatr Ann 1976;6:51-66.

8. Shneidman ES. *The suicidal mind.* New York: Oxford University Press 1996.

9. Shneidman ES. *On "therefore I must kill myself".* Suicide Life Threat Behav 1982;12:52-5.

10. Orbach I. *Taking an inside view: stories of pain.* In: Michel K, Jobes DA, Eds. *Building a therapeutic alliance with the suicidal patient.* Washington, DC: American Psychological Association 2011, pp. 111-28.

11. Pompili M. *The increase of suicide rates: the need for a paradigm shift.* Lancet 2018;392:474-5.

12. Weisman AD. *Is suicide a disease?* Life Threatening Behav 1971;1:219-31.

13. Pompili M. *Social network theory and rising suicide rates in the USA*. Lancet 2019;393:1801-2.

14. Robins E, Gassner S, Kayes J, et al. *The communication of suicidal intent: a study of 134 consecutive cases of successful (completed) suicide.* Am J Psychiatry 1959;115:724-33.

15. Pompili M, Belvederi Murri M, Patti S, et al. *The communication of suicidal intentions: a meta-analysis.* Psychol Med 2016;46:2239-53.

16. Pompili M. *Our empathic brain and suicidal individuals.* Crisis 2015;36:227-30.

17. Pompili M. *Critical appraisal of major depression with suicidal ideation.* Ann Gen Psychiatry 2019;18:7.

18. Boden Z. *Terror and horror: feelings, intersubjectivity and 'understanding at the edges' in an interview on a suicide attempt.* In: Pompili M, Ed. *Phenomenology of suicide: unlocking the suicidal mind.* Berlin: Springer 2017, pp. 51-71.

19. Jobes DA, Piehl BM, Chalker SA. *A collaborative approach to working with the suicidal mind.* In: Pompili M, Ed. *Phenomenology of suicide: unlocking the suicidal mind.* Berlin: Springer 2017, pp. 187-201.

20. *Diagnostic and statistical manual of mental disorders: DSM-5.* Arlington, VA: American Psychiatric Publishing 2013.

Personality, mental functioning, and symptoms: assessing suicidal risk with the Psychodynamic Diagnostic Manual, 2nd ed. (PDM-2)

V. Lingiardi[1], G. Di Cicilia[1], T. Boldrini[1,2]

[1] Department of Dynamic and Clinical Psychology, Faculty of Medicine and Psychology, Sapienza University of Rome, Italy; [2] Department of Developmental Psychology and Socialization, University of Padua, Italy

Summary

Comprehensive and careful diagnostic assessment is a crucial aspect of the clinical management of suicidal patients. The new edition of the Psychodynamic Diagnostic Manual (PDM-2; Lingiardi & McWilliams, 2017) adds a needed perspective on symptom patterns depicted in existing taxonomies, enabling clinicians to describe and categorize personality patterns, related social and emotional capacities, unique profiles of mental functioning, and subjective experiences of symptoms. This paper provides an overview of the PDM-2, focusing on its diagnostic approach to evaluating patients presenting suicidal intention and behaviors. First, the basic premises of the PDM-2, including its rationale and structure, are briefly discussed. Second, following the multiaxial organization of this diagnostic system, the features and main innovations that can guide clinicians in their assessment and clinical management of suicidal risk are examined.

Key words

Suicide • Psychodynamic Diagnostic Manual • Diagnosis • Assessment

Introduction

Clinicians routinely investigate the presence of suicidal ideation, suicidal intention, a history of such ideation and intention, and the nature and severity of any suicide attempts in all patients they encounter in their practice. Suicide is the second leading cause of death among persons aged 15 to 29, and almost 800,000 people die by suicide worldwide, each year [1]. Therefore, for many patients, the clinician's highest priority when determining the therapeutic intervention is to assess the risk of suicidal behavior. As suicidality is widely considered a transdiagnostic dimension [2][3], it can assume different meanings, functions, and clinical priorities according to the presence of other psychiatric comorbidities, as well as the cognitive, affective, and interpersonal patterns demonstrated by the patient [4][5]. Accordingly, a comprehensive, careful, and wide-ranging diagnostic assessment is a crucial aspect of the clinical management of suicidal patients [6][7].

Notwithstanding the advantages of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) and the *International Classification of Diseases* (ICD) systems, their classifications often fail to meet the needs of clinicians. In particular, several scholars have questioned the usefulness of such diagnostic categories in guiding clinicians to formulate a management plan and predict outcomes [8-10]. A recent global survey reported that a large sample of mental health professionals rated the ICD-10 and some editions of the DSM as having the lowest utility in "selecting a treatment" and "assessing probable prognosis"; the frameworks were deemed primarily useful for administrative purposes [11]. The limitations of these official diagnostic systems are significantly problematic in the context of the

Correspondence

Vittorio Lingiardi
Department of Dynamic and Clinical Psychology, Faculty of Medicine and Psychology, Sapienza University of Rome, via dei Marsi 78, 00185 Rome, Italy
• E-mail: vittorio.lingiardi@uniroma1.it

routine management of suicidal risk, due to the urgent requirement for the careful and accurate evaluation and assessment of patients.

The recently published 2nd edition of the *Psychodynamic Diagnostic Manual* (PDM-2) [12] [13] adds a much needed new perspective on the symptom patterns depicted in existing taxonomies, enabling clinicians to describe and categorize personality patterns, related social and emotional capacities, unique profiles of mental functioning, and subjective experiences of symptoms. Specifically, the PDM-2 highlights patients' *internal experiences*, adopting a multidimensional approach to describe the intricacy and depth of patients' overall functioning in various areas (e.g., interpersonal, cognitive, emotional). This comprehensive diagnostic framework can guide clinicians in formulating individual cases and planning treatments, and hence improve the *clinical utility* of psychiatric diagnoses [14].

In this article, we provide an overview of the PDM-2, focusing on its diagnostic approach to evaluating patients presenting suicidal intention and behavior. First, we briefly describe the basic premises of the PDM-2, including its rationale, structure, and organization. Second, we review, following the multiaxial organization, its features and primary innovations that can guide clinicians in their assessment and clinical management of suicidal risk.

Rationale of the PDM-2 classification system

The PDM-2 [15] reflects an effort to articulate a diagnostic system that bridges the gap between clinical complexity and empirical and methodological validity. Taking a "prototypic" approach to diagnosis, the manual rejects the idea that a diagnostic category can be merely described as a collection of symptoms (e.g., [16] [17]). Specifically, the PDM-2 diagnostic categories emphasize both individual variation (i.e., an individual's unique experience and personal history) and commonalities (i.e., patterns of intercorrelated reported experiences [symptoms] and observed behaviors [signs]), integrating nomothetic understanding and idiographic knowledge of clinical presentations.

Although the PDM-2 differs in its diagnostic approach to the DSM and ICD, it also aspires to complement these manuals in their efforts to catalogue symptoms and syndromes. Therefore, the manual is not intended to replace the official diagnostic systems, but aims at improving the diagnostic process with the richness and complexity of psychoanalytic constructs, infant research, developmental psychopathology, attachment theory, and neuroscience.

The PDM-2 framework attempts to systematically describe *personality functioning*; individual profiles of *mental functioning* (including, e.g., patterns of relating to others, comprehending and expressing feelings,

coping with stress and anxiety, regulating impulses, observing one's own emotions and behaviors, and forming moral judgments); and *symptom patterns*, including patients' personal, subjective experiences of symptoms.

The PDM-2 devotes specific sections to discrete age groups and developmental stages (adults, adolescents, children; infancy and early childhood, later life), and it structures and operationalizes diagnoses around three axes: the P Axis ("Personality Syndromes"), the M Axis ("Profile of Mental Functioning"), and the S Axis ("Symptom Patterns: The Subjective Experience"). The P Axis comprehensively describes a range of healthy to disordered personality functioning. Its major organizing principles relate to levels of personality organization (i.e., on a spectrum of personality functioning ranging from healthy to neurotic, borderline, and psychotic levels [18]) and personality styles (i.e., clinically familiar personality styles/types that intersect with levels of personality organization). The M Axis provides an assessment of overall mental functioning based on 12 specific capacities (i.e., the capacities involved in overall psychological health or pathology) grouped into four main domains: cognitive and affective processes; identity and relationships; defense and coping; and self-awareness and self-direction. Finally, the S Axis, while retaining a high degree of overlap with DSM and ICD diagnostic categories, provides a more specific description of individual experience of the patient related to any symptom pattern, and any non-pathological conditions that may require clinical assessment (relating to, e.g., demographic minorities, LGB populations, and gender incongruence). Moreover, it thoroughly emphasizes the critical role of transference and countertransference patterns relative to distinct clinical syndromes (e.g., [19-23]).

PDM-2 S Axis: the subjective experience of suicidal patients

In all S Axes of the PDM-2, the clinical importance of the proper assessment of suicidal risk is emphasized. According to most psychodynamic and neurobiological literature (e.g., [4] [24]), *suicidal ideations*, *behaviors*, and *attempts* are typical "cross-sectional" symptoms, attitudes, and behaviors that may be present in many disorders at different times. From this standpoint, suicidality does not have diagnostic specificity; rather, it is a transdiagnostic dimension. According to the PDM-2, "suicidal risk should be carefully assessed for any patient, regardless of the 'primary diagnosis' or the patient's primary treatment request" ([3], p. 137). Thus, subjective experiences of suicidal thoughts and behaviors may vary widely within a single patient, over the course of life or treatment, and they should always be considered one of the main risk factors for suicide attempts. In addition, to support the assessment of the clinical complexities of suicide risk, the PDM-2 provides guidelines that can

be applied in various clinical conditions. Specifically, it is fundamental for clinicians to assess the following variables: presence of suicidal or homicidal ideation, intent, or plans; ready access to means for suicide, and the lethality of those means; presence of psychotic symptoms, especially command hallucinations; presence of suicidal or homicidal alters in dissociative identity disorder; distinction between suicidal intent and parasuicidal intent (especially regarding self-injury); presence of serious alcohol or other substance misuse; history and seriousness of previous self-harm attempts; family history of, or recent exposure to, suicide; and absence of a significant network of supportive relationships and social services.

Another key issue highlighted by the PDM-2 is the distinction between suicidal and parasuicidal behavior (e.g., SA28 Non-Suicidal Self-Injury). Most commonly, the aim of parasuicidal action is to reduce negative emotions, such as tension, anxiety, and self-reproach, and/or to resolve an interpersonal difficulty. Though these self-harming behaviors are not intended to destroy one's life, they represent a maladaptive way of expressing distress and seeking help, and their seriousness should not be minimized. Since impulsive self-harm generally stems from emotional pain, in therapeutic work it is essential to help patients improve their affective language and other communication skills in order to reduce these behaviors.

Given that the highest suicide rate is recorded in youth populations [25] [26], the PDM-2 devotes a specific section to suicidality in both of the sections on diagnosis in childhood and adolescence, including specific diagnoses of suicidality (SC27, SA27) that are classified among those included within mood disorders. These diagnostic categories overlap that of "Suicidal Behavior Disorder," as illustrated in Section III of the DSM-5. Nevertheless, for all S Axes (as applied in adulthood to old age), the PDM-2 highlights patients' subjective experiences within cognitive, affective, somatic, and relational patterns. The essential manifestation of suicidal behavior disorder is a suicide attempt, which is defined as a behavior that the individual has undertaken with at least some intent to die. According to the DSM-5 [2], the behavior may or may not lead to injury or serious medical consequences, because several factors can influence the outcome of the attempt (e.g., poor planning, lack of knowledge about the lethality of the chosen method, low intentionality or ambivalence, or the chance intervention by others after the behavior is initiated). In addition, it can be challenging to determine the degree of intent, as this may not be clearly acknowledged by the individual involved, also because of the common presence of dissociative symptoms that may be difficult both to recognize and to express [27-29].

According to the PDM-2, suicide attempts frequently occur in adolescents and young adults with various mental disorders; but they are also observed in youth with no specific pathology, particularly in certain cultural contexts (e.g., India, China [30-32]). Consequently, particular attention should be paid to young patients reporting suicidal ideations, behaviors, or attempts of any clinical manifestation, even though these may be difficult to correctly identify. The PDM-2 can guide clinicians in this crucial evaluation, for example by listing and illustrating the main affective states and cognitive patterns described by suicidal adolescents and young adults. Specifically, in addition to feeling sadness, sorrow, despair, detachment, and anger, suicidal patients may experience negative emotions about themselves, such as a devalued sense of self or reduced self-esteem, with feelings of failure, uselessness, incompetence, and unworthiness. Their inner experience may be one of a loss of life meaning and a feeling of being trapped in a suffering present, with no possibility of a better future. The suicidal act may seem to offer them an escape from an overwhelming, unmanageable life situation and to give devastated adolescents a feeling of mastery over their bodies and the lives they feel they have lost. Likewise, self-injury, which is frequently associated with suicidal attempts, may express a similar effort to regain control. Moreover, a failed suicide attempt may be experienced as yet another demonstration of ineptitude and thus may reinforce an adolescent's negative perception of the self. The somatic states of suicidal adolescents are mainly characterized by high levels of anxiety. Anxiety can be a proximal risk factor for the suicidal act and should be monitored attentively in at-risk adolescents. The PDM-2 describes the main relational patterns of suicidal adolescents, illustrating how relational dynamics characterized by rigidity, conflict, separation, lack of trust and acceptance, and incommunicability, as well as feelings of being different or rejected, can all explain the decision to act. In essence, suicidal behavior can be considered predominantly interpersonal, concerning not only oneself, but also significant others. It can thus be interpreted as a last option when all other attempts at communication have failed.

In addition to its section on adolescents, the PDM-2 also contains a dedicated section on childhood. Many clinicians tend to underestimate suicidal risk in childhood, because the idea that a child might choose suicide to escape unbearable pain is generally considered overwhelmingly tragic and unimaginable. In addition, there is widespread belief that children lack a sufficient cognitive understanding of the biological/scientific concept of death to contemplate suicide. Although this assumption is not empirically justified, it has led to a clinical and epidemiological underestimation of suicidal behavior

in this age group. By contrast, suicide is currently the fourth leading cause of death among young persons aged 10 to 14; for even younger children, it is likely to be underreported [33]. In fact, more than 12% of children aged 6 to 12, across both genders, report having had suicidal thoughts [26]. The PDM-2 notes, however, that there is a developmental sequence in the manner in which children think about and discuss death. In particular, four stages of the biological/scientific concept of death have been identified [34]: *universality* (the understanding that death must happen to all living things), *irreversibility* (the recognition that the dead cannot come back to life), *non-functionality* (the understanding that death is characterized by bodily processes ceasing to function), and *causality* (the understanding that death is ultimately caused by a breakdown of bodily function). Children under the age 5 do not recognize death as final, but instead think of it as reversible. Likewise, children between the ages of 5 and 9 tend to consider death temporary, although by age 7 they are thought to be cognitively able to understand death as irreversible and permanent. These stages of cognitive development may play a pivotal role in the assessment of suicidal risk in children. Consequently, the PDM-2 provides the clinically useful suggestion to consider developmental norms in the assessment of suicidality in childhood.

The manual also describes the affective states of suicidal children, which are characterized by hopelessness, anhedonia, impulsiveness, and high emotional reactivity. In addition, suicidal children may express feelings of omnipotence, manifested in a need for power and control over others, as well as the opposite – profound feelings of hopelessness and helplessness. Their thoughts and fantasies may include obsessive ruminations about painful relationships with family members and peers, desire for retaliation and revenge, and curiosity about the death of people and/or animals; they may also ask questions about what happens after death. The somatic states of suicidal children may also relate to mood and physiological responses to trauma and abuse (if present). Finally, the PDM-2 points out the importance of the relationship context in understanding children's suicidal behavior, with particular regard to attachment style, familiarity, abuse, lack of parental warmth, bullying, and rejection by peers.

Suicidal risk and psychological experiences that may require clinical attention

The PDM-2 pays particular attention to psychological experiences that may derive from ethnic, cultural, linguistic, religious, and political factors, as well as from issues of sexual orientation and gender incongruence. All of these experiences, in themselves, are "non-patholog-

ical". Nevertheless, living in stigmatizing environments may undermine one's psychological and relational well-being by routinely subjecting them to experiences of social oppression, stereotyping, "minority stress" (i.e., psychological stress derived from belonging to a minority [35]), and internalized homophobia (i.e., the mental condition of believing same-sex sexual orientation to be wrong, sick, or inferior, while simultaneously experiencing oneself as having that orientation). It is not uncommon for patients living in minority conditions to resort to suicide as a last tragic solution to escape the overwhelming experience of minority stress [36-39]. Consequently, in the diagnostic assessment of such patients, suicidal risk should be constantly monitored. By describing minority conditions along standardized subjective experience areas (i.e., affective states, cognitive patterns, somatic states, relationship patterns, and the subjective experiences of the therapist), the PDM-2 provides a guide for clinicians to assess and manage suicidal risk in such at-risk populations.

The role of personality organization and patterns

Another innovation provided by the PDM-2 is its emphasis on the importance of personality constellations in the assessment of an individual's symptoms [40]. Such constellations are particularly important in assessments of suicide risk, which, as already mentioned, represents a cross-sectional diagnostic entity. The long-term prediction of suicide according to personality disorders represents an important challenge for clinicians [4,41], and some studies have indicated that specific personality traits can be important predictors of suicide [6,42]. Moreover, contextualizing suicidal behaviors in a personality diagnosis can promote clinical case formulation by helping clinicians understand an individual's difficulties in the broader context of his/her personality functioning. Such an understanding can inform treatment planning to better prevent suicide.

In the P Axis of the PDM-2, suicidal ideation, behaviors, and attempts represent possible symptoms of both borderline and psychotic personality organization at all ages [a]. In fact, in patients with borderline personality organization, suicidality may be explained by their typical identity diffusion, their prevalence of primitive defensive operations, and their difficulties with affect and impulse regulation. Such individuals may engage in suicidal or parasuicidal behaviors when they become unable to tol-

---

[a] With regard to adolescence and childhood, the PDM-2 refers to *emerging personality patterns* because the personality is still under development in these age ranges.

erate the emotional burden that arises from significant relationships. Furthermore, individuals with psychotic organization may be at risk of suicide due to significant deficits in their capacity for reality testing and forming a coherent sense of self, manifested in their consistently maladaptive ways of dealing with feelings about themselves and others.

In the context of personality patterns, the meaning of suicidal intent can be understood along the *anaclitic–introjective* (or *relatedness vs self-definition*) polarity proposed by Blatt and colleagues [43-45]. According to this model, personality evolves through dialectic interaction between two fundamental psychological coordinates: *anaclitic* (or *relatedness*) and *introjective* (or *self-definition*). More specifically, relatedness and self-definition are involved in the development of the capacity to establish and maintain (respectively): reciprocal, meaningful, and satisfying relationships; and a coherent, realistic, differentiated, and positive sense of self. These two developmental processes influence each other. High-level personality organization is characterized by feelings of satisfaction and well-being on both poles of the spectrum; on the contrary, personality pathology is characterized by excessive and defensive emphasis in one of the two dimensions, at the expense of the other. Consequently, among personality syndromes that fall mainly on the anaclitic pole (e.g., dependent, borderline, or histrionic personalities), suicidal intent may have greater relational significance and may emerge in reaction to loss or rejection, accompanied by feelings of emptiness, inadequacy, and shame. On the other hand, in patients with personality syndromes that fall mainly on the introjective pole (e.g., narcissistic, antisocial, or obsessive-compulsive personalities), feelings of guilt, self-criticism, and perfectionism may increase the risk of suicidal intent through the tendency to isolate oneself and not ask for help.

Suicidality and mental functioning domains

The assessment of mental functioning (M Axis) represents an additional PDM-2 diagnostic tool to evaluate suicide risk. An understanding of patients' basic mental functioning can provide therapists with useful insight into the development of symptoms and help them capture the complexity and individuality of each patient, especially when dealing with the intricacies of suicidal behavior. By systematizing and operationalizing numerous dimensions of mental functioning, the M Axis helps clinicians flesh out – at a granular level – the mechanisms that contribute to and shape suicidal ideation, behav-

iors, and attempts in each patient. While the evaluation of suicidality may benefit from a complete assessment of all mental capacities, some mental functions are more directly involved in this assessment. Specifically, suicidality may be explained by dysfunctions in the following mental capacities: (2) *capacity for affective range, communication, and understanding*; (7) *capacity for impulse control and regulation;* (9) *capacity for adaptation, resiliency, and strength*; and (12) *capacity for meaning and purpose*. Thus, suicidal persons may be unable to symbolize affectively meaningful experiences (i.e., to represent such experiences mentally rather than in somatic or behavioral form) and to appropriately verbalize affective states – all difficulties that should be carefully considered by clinicians in choosing the proper treatment [46 47]. They may show unmodulated expressions of impulses (impulsivity) with a concomitant inability to tolerate frustration. This may lead to a loss of ability to adjust to unexpected events and changing circumstances and to cope effectively and creatively when confronted with uncertainty, loss, stress, and challenge. In addition, individuals with suicidal intent may have lost the ability to construct a personal narrative that gives coherence and meaning to personal choices, a sense of directedness and purpose, and a concern for succeeding generations that imbues one's life with meaning.

Conclusions

Suicidal risk is a central concern and serious challenge for clinicians assessing patients with a wide variety of psychopathological profiles. Suicidal ideation and behaviors may be predictable or unpredictable, according to several variables that require careful assessment. The PDM-2 provides a valid cross-sectional prospective on suicidality, focusing on personality patterns, related social and emotional capacities, unique mental profiles, and personal experiences of symptoms. When assessing a complex phenomenon such as suicidality, it can be more important for clinicians to consider *who one is* rather than *what one has* [12]. Accordingly, the comprehensive approach to diagnosis provided by the PDM-2 can enable clinicians to capture the subjective experiences of suicidal patients, allowing for more effective strategies to be developed for the early assessment of suicidal behavior and the preventive treatment of suicide attempts.

Conflict of interest

The Authors have no conflict of interest to declare.

References

1. World Health Organization. *International statistical classification of diseases and related health problems (11th Revision),* 2018.

2. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders, 5th ed.* Washington, DC: APA 2013.

3. Mundo E, O'Neil JA. *Symptoms patterns: the subjective experience-S Axis.* In: Lingiardi V, McWilliams N, Eds. *Psychodynamic diagnostic manual.* 2nd ed. New York, NY: Guilford Press 2017, pp. 134-259.

4. Kernberg OF. *The suicidal risk in severe personality disorders: differential diagnosis and treatment.* J Pers Disord 2001;15:195-208.

5. Kernberg OF. *Suicide prevention for psychoanalytic institutes and societies.* J Am Psychoanal Assoc 2012;60:707-19.

6. Pompili M, Rihmer Z, Akiskal HS, et al. *Temperament and personality dimensions in suicidal and nonsuicidal psychiatric inpatients.* Psychopathology 2008;41:313-21.

7. Van Meter AR, Algorta GP, Youngstrom EA, et al. *Assessing for suicidal behavior in youth using the Achenbach system of empirically based assessment.* Eur Child Adolesc Psychiatry 2018;27:159-69.

8. Hyman SE. *The diagnosis of mental disorders: the problem of reification.* Annu Rev Clin Psychol 2010;6:155-79.

9. Lingiardi V, Boldrini T. *The diagnostic dilemma of psychosis: reviewing the historical case of pseudoneurotic schizophrenia.* J Nerv Ment Dis 2019;207:577-84.

10. Maj M. *Why the clinical utility of diagnostic categories in psychiatry is intrinsically limited and how we can use new approaches to complement them.* World Psychiatry 2018;17:121-2.

11. Reed GM, Keeley JW, Rebello TJ, et al. *Clinical utility of ICD-11 diagnostic guidelines for high-burden mental disorders: results from mental health settings in 13 countries.* World Psychiatry 2018;17:306-15.

12. Lingiardi V, McWilliams N. *The psychodynamic diagnostic manual, 2nd ed. (PDM-2).* World Psychiatry 2015;14:237-9.

13. Lingiardi V, McWilliams N, Eds. *The psychodynamic diagnostic manual (PDM-2),* 2nd ed. New York, NY: Guilford Press 2017 (Tr. it. Milano: Raffaello Cortina 2018).

14. Jablensky A. *Psychiatric classifications: validity and utility.* World Psychiatry 2016;15:26-31.

15. Lingiardi V, McWilliams N, Bornstein RF, et al. *The psychodynamic diagnostic manual version 2 (PDM-2): assessing patients for improved clinical practice and research.* Psychoanal Psychol 2015;32:94-115.

16. Borsboom D. *Psychometric perspectives on diagnostic systems.* J Clin Psychol 2008;64:1089-108.

17. Westen D, Shedler J, Bradley R. *A prototype approach to personality disorder diagnosis.* Am J Psychiatry 2006;163:846-56.

18. Kernberg OF. *Severe personality disorders: psychotherapeutic strategies.* New Haven, CT: Yale University Press 1984.

19. Betan E, Heim AK, Zittel Conklin C, et al. *Countertransference phenomena and personality pathology in clinical practice: an empirical investigation.* Am J Psychiatry 2005;162:890-8.

20. Colli A, Tanzilli A, Dimaggio G, et al. *Patient personality and therapist response: an empirical investigation.* Am J Psychiatry 2014;171:102-8.

21. Tanzilli A, Colli A, Del Corno F, et al. *Factor structure, reliability, and validity of the Therapist Response questionnaire.* Personal Disord 2016;7:147-58.

22. Tanzilli A, Muzi, L, Ronningstam E, et al. *Countertransference when working with narcissistic personality disorder: an empirical investigation.* Psychotherapy 2017;54:184-94.

23. Tanzilli A, Colli A, Gualco I, et al. *Patient personality and relational patterns in psychotherapy: factor structure, reliability, and validity of the Psychotherapy Relationship questionnaire.* J Personality Assess 2018;100:96-106.

24. Roy B, Dwivedi Y. *Understanding epigenetic architecture of suicide neurobiology: a critical perspective.* Neurosci Biobehav Rev 2017;72:10-27.

25. Centers for Disease Control. *Youth suicide,* 2015 (www.cdc.gov/injury/ wisqars/pdf/leading_causes_of_ death_by_age_ group_2015-a.pdf).

26. Nock M, Green J, Hwang I, et al. *Prevalence, correlates, and treatment of lifetime suicidal behavior among adolescents: results from the national comorbidity survey replication adolescent supplement.* JAMA Psychiatry, 2013;70:300-10.

27. Patel V, Ramasundarahettige C, Vijayakumar L, et al. *Suicide mortality in India: a nationally representative survey.* Lancet 2012;379:2343-51.

28. Calati R, Bensassi I, Courtet P. *The link between dissociation and both suicide attempts and non-suicidal self-injury: meta-analyses.* Psychiatry Res 2017;251:103-14.

29. Fagioli F, Telesforo L, Dell'Erba A, et al. *Depersonalization: an exploratory factor analysis of the Italian version of the Cambridge Depersonalization Scale.* Comprehensive Psychiatry 2015;60:161-7.

30. Levinger S, Somer E, Holden RR. *The importance of mental pain and physical dissociation in youth suicidality.* J Trauma Dissoc 2015;16:322-39.

31. Phillips MR, Yang G, Zhang Y, et al. *Risk factors for suicide in China: a national case-control psychological autopsy study.* Lancet 2002;360:172836.

32. Radhakrishnan R, Andrade C. *Suicide: an Indian perspective.* Indian J Psychiatry 2012;54:304-19.

33. World Health Organization. *Fact sheets: suicide,* 2018.

34. Speece MK. *Children's concept of death.* Michigan Family Review 1995;1:57-69.

35. Comas-Diaz L. *Ethnopolical psychology: healing and transformation.* In: Aldarondo E, Ed. *Advancing social justice through clinical practice.* New York, NY: Routledge 2007.

36. Baams L, Grossman AH, Russell ST. *Minority stress and mechanisms of risk for depression and suicidal ideation among lesbian, gay, and bisexual youth.* Dev Psychol 2015;51:688-96.

37. Baiocco R, Ioverno S, Cerutti R, et al. *Suicidal ideation in spanish and italian lesbian and gay young adults: the role of internalized sexual stigma.* Psicothema 2014;26:490-6.

38. Lea T, de Wit J, Reynolds R. *Minority*

stress in lesbian, gay, and bisexual young adults in Australia: associations with psychological distress, suicidality, and substance use. Arch Sex Behav 2014;43:1571-8.

39 Mereish EH, Peters JR, Yen S. Minority stress and relational mechanisms of suicide among sexual minorities: subgroup differences in the associations between heterosexist victimization, shame, rejection sensitivity, and suicide risk. Suicide Life Threat Behav 2019;49:547-60.

40 Hilsenroth MJ, Katz M, Tanzilli A. Psychotherapy research and the psychodynamic diagnostic manual (PDM-2). Psychoanal Psychol 2018;35:320-7.

41 Stelmachers ZT. Assessing suicidal clients. In: Butcher JN, Ed. Clinical personality assessment. New York, NY: Oxford University Press 1995, pp. 367-9.

42 Heisel MJ, Duberstein PR, Conner KR, et al. Personality and reports of suicide ideation among depressed adults 50 years of age or older. J Affect Disord 2006;90:175-80.

43 Blatt SJ. Polarities of experience: Relatedness and self-definition in personality development, psychopathology, and the therapeutic process. Washington, DC: American Psychological Association 2008.

44 Blatt SJ, Blass RB. Attachment and separateness: a dialectic model of the products and processes of psychological development. Psychoanal Study Child 1990;45:107-27.

45 Blatt SJ, Luyten P. Reactivating the psychodynamic approach to classify psychopathology. In: Millon T, Krueger RF, Simonsen E, Eds. Contemporary directions in psychopathology. Scientific foundations of the DSM-V and ICD-11. New York, NY: Guilford 2010, pp. 483-514.

46 Boldrini T, Nazzaro MP, Damiani R, et al. Mentalization as a predictor of psychoanalytic outcome: an empirical study of transcribed psychoanalytic sessions through the lenses of a computerized text analysis measure of reflective functioning. Psychoanalytic Psychology 2018;35:196-204.

47 Ogrodniczuk JS, Piper WE, Joyce A. S. Effect of alexithymia on the process and outcome of psychotherapy: a programmatic review. Psychiatry Res 2011;190:43-8.

U. Albert[1], L. Pellegrini[1], G. Maina[2],
A.-R. Atti[1], D. De Ronchi[1], Z. Rhimer[3]

[1] Department of Medicine, Surgery, and Health Sciences, University of Trieste, Italy; [2] Rita Levi Montalcini Department of Neuroscience, University of Torino, Italy; [3] Department of Clinical and Theoretical Mental Health, Kútvölgyi Clinical Center, Semmelweis University, Budapest, Hungary

Suicide in obsessive-compulsive related disorders: prevalence rates and psychopathological risk factors

Summary

Objectives
To estimate prevalence rates of suicide attempts and suicidal ideation in individuals with a principal diagnosis of obsessive-compulsive related disorders (OCRDs); 2. to identify predictors of suicide risk among subjects with OCRDs (where available).

Methods
The systematic review was conducted by searching PubMed from the date of the first available article to December 31, 2018. The search terms [suicide] OR [suicidality] OR [suicide attempts] OR [suicidal ideation] OR [suicidal thoughts] were combined with the following: [BDD] OR [body dysmorphic disorder]; [HD] OR [hoarding disorder]; [trichotillomania] OR [hair pulling disorder]; [excoriation disorder] OR [skin picking disorder].

Results
In BDD, data concerning lifetime suicide attempts are consistent across studies: mean rate is 21.5% (range 9-30.3%). Mean rate of current suicidal ideation is 37.4% (range 26.5-49.7%) and mean rate of lifetime suicidal ideation is 74.5% (range 53.5-85%). BDD-specific factors such as early onset, severity, poor insight and muscle dysmorphia and comorbid disorders increase the risk of suicide attempts or suicidal ideation. Only 2 studies recruited individuals with DSM-5 HD: suicidality appears to be low, with rates of current suicidal ideation comprised between 5% and 10%, although 19% of individuals attempted suicide during their lifetime. Concerning the grooming disorders, lifetime rates of suicide attempts are low as compared to rates in other OCRDs; approximately 40% of individuals, however, reported lifetime suicidal ideation.

Conclusions
OCRDs taken together may be at risk for suicide attempts and suicidal ideation independently from comorbid disorders (and specifically independently from comorbid OCD); BDD remains the disorder more strongly associated with an increased risk for suicide, followed by HD and then the grooming disorders.

Key words
Suicide attempts • Suicidal ideation • BDD • HD • Trichotillomania • Skin Picking Disorder

Correspondence
Umberto Albert
Department of Medicine, Surgery, and Health Sciences, University of Trieste, via G. de Pastrovich 3, 34128 Trieste, Italy
• Tel. +39 040 3997327 • E-mail: ualbert@units.it

Introduction

Recent systematic reviews and meta-analyses confirmed that Obsessive-Compulsive Disorder (OCD), historically considered to be associated with a relatively low risk of suicide, is actually in itself associated with considerable risk for lifetime suicide attempts and suicidal ideation [1 2]. Data from recent large epidemiological studies performed on National Registers, providing data on the longitudinal association between OCD and death by suicide and lifetime suicide attempts over a follow-up of several years [3 4], confirmed that individuals with OCD are at greater risk for committing suicide as compared to the general population.

Less is known about suicidality and other DSM-5 Obsessive-Compulsive Related Disorders (OCRDs); in the *new* chapter, *new* disorders such as Hoarding Disorder (HD) and Skin Picking Disorder (SPD) and disorders once classified elsewhere (Body Dysmorphic Disorder – BDD – previously in the chapter of Somatoform Disorder, and Trichotillomania – TTM – previously classed among the Impulse Control Disorders) have been grouped together with the *nosological organizer* OCD [5]. All disorders included in this chapter share similarities with OCD, although some appear to have a stronger cognitive component – and thus are closer to OCD – while others mainly consist of body-focused repetitive behaviors.

While several issues concerning phenomenological characteristics of these disorders have been studied, less attention has been devoted to suicidality. A recent systematic review and meta-analysis examined the strength and patterns of the association between suicidality and BDD, concluding that BDD is actually associated with increased odds for both suicide attempts and suicidal ideation [6]. No similar studies are available for the other disorders of the OCRDs chapter.

Given the prevalence of these disorders in the general population and the impact in terms of psychosocial impairment associated with these disorders, the investigation of suicidality and the identification of potential socio-demographic and clinical factors that could increase the risk for suicide is, to our opinion, of particular clinical relevance.

The aims of the present systematic review were: 1) to estimate prevalence rates of suicide attempts and suicidal ideation in individuals with a principal diagnosis of obsessive-compulsive related disorders; 2) to identify predictors of suicide risk among subjects with OCRDs (where available).

Methods

Search strategy

The systematic review was conducted using the PRISMA guidelines by searching PubMed from the date of the first available article to December 31, 2018. The search terms [suicide] OR [suicidality] OR [suicide attempts] OR [suicidal ideation] OR [suicidal thoughts] were combined with the following: [BDD] OR [body dysmorphic disorder]; [HD] OR [hoarding disorder]; [trichotillomania] OR [hair pulling disorder]; [excoriation disorder] OR [skin picking disorder].

Article selection and review strategy

Articles were identified and assessed for eligibility by two independent reviewers (UA and LP), who independently decided which identified articles to include according to clinical importance and eligibility criteria. In case of disagreement, a third author (GM) was consulted to mediate consensual decisions. Duplicate studies were excluded. Cross-references from the articles identified were also examined. Unpublished studies, conference abstracts or poster presentations were not included. The database search was restricted to English language papers.

Eligibility criteria

The inclusion criteria for the studies were the following: 1) studies with appropriate definition of the obsessive-compulsive related disorder (diagnosis made through specific structured interviews and/or established international criteria); 2) adolescents and/or adults; 3) cross-sectional or prospective designs; 4) performed in clinical samples or in the general population (epidemiological studies); 5) employed a quantitative measure of suicidality in order to derive prevalence rates of current/lifetime suicide attempts, suicidal ideation and/or family history of suicide attempts/completed suicide; and/or 6) reported an outcome measure of the association between suicidality and OCD (e.g. odds ratios) or examined factors associated with suicidality.

Results

Search results

The flowchart of studies selected and included in the systematic review for BDD is provided in Figure 1. In total, 24 studies were included in the qualitative synthesis (providing data on prevalence rates of suicide attempts, suicidal ideation). Additional 17 studies were retrieved from PubMed search and manual search providing data on suicidality and HD (N = 8), TTM (N = 4) and SPD (N = 5).

Body dysmorphic disorder

Table I reports prevalence rates of suicide attempts and suicidal ideation in individuals with BDD as from clinical studies; 17 studies provided information, although some of the studies included partially overlapping samples. Additional studies included exactly the same sample of Phillips et al. 2005 [7] and thus were excluded from the table (see Appendix 1).

Concerning lifetime suicide attempts, data are consistent across studies: mean rate is 21.5% (range 9-30.3%; median value: 22.4%). Higher rates are reported in individuals with comorbid OCD (OCD+BDD: 40%) [8], in Veterans with comorbid MDD (92% of the sample) (58.3%) [9] and among inpatients (75% had comorbid Substance Use Disorder) (93.8%) [10]. Mean rate of current suicidal ideation is 37.4% (range 26.5-49.7%; median value: 36.9%) and mean rate of lifetime suicidal ideation is 74.5% (range 53.5-85%; median value: 77.9%).

Studies performed in the general population confirmed that BDD is associated with a significantly higher risk of suicide attempts and suicidal ideation as compared to individuals without that diagnosis (Tab. II), although reported prevalence rates somewhat lower than those in clinical settings. When suicide risk was estimated in the general population using specific instruments, such as the

```
┌──────────────────────────────────────┐
│  Records identified through database  │
│              searching:               │
│               N = 290                 │
│          Duplicates removed           │
│               N = 77                  │
└──────────────────────────────────────┘
                  │
                  ▼
┌──────────────────────────────────────┐        ┌──────────────────────────────────────┐
│    Records screened for eligibility   │ ─────▶ │ Records excluded following reading    │
│               N = 213                 │        │        title or abstract              │
└──────────────────────────────────────┘        │               N = 145                 │
                  │                              └──────────────────────────────────────┘
                  ▼
┌──────────────────────────────────────┐        ┌──────────────────────────────────────┐
│  Records eligible for full-text       │        │         Records excluded N = 28       │
│             screening                 │ ─────▶ │ N = 23 non structured diagnosis,      │
│               N = 68                  │        │ prevalence rates not given or no      │
└──────────────────────────────────────┘        │ relevant data on suicidality and BDD  │
                  │                              │      N = 5 review/meta-analyses        │
                  ▼                              └──────────────────────────────────────┘
┌──────────────────────────────────────┐        ┌──────────────────────────────────────┐
│  Studies that met criteria for        │ ─────▶ │ N = 16 studies with overlapping       │
│       qualitative synthesis           │        │            samples                    │
│               N = 40                  │        └──────────────────────────────────────┘
└──────────────────────────────────────┘
                  │
                  ▼
┌──────────────────────────────────────┐
│ N = 24 studies with independent       │
│   samples included in qualitative     │
│             synthesis                 │
└──────────────────────────────────────┘
```

FIGURE 1. *Flow chart showing the selection of BDD studies.*

SBQ-R (Suicide Behaviors Questionnaire Revised) or the ACSS (Acquired Capability Suicide Scale), it was found elevated [11-13].

Twenty-six studies provided information on predictors of suicidality. Table III presents results of the analysis of socio-demographic and clinical factors potentially associated with increased risk for suicide.

Hoarding disorder

We could find only two studies that recruited individuals with DSM-5 criteria HD [14 15]. All the other studies shown in Table IV investigated suicidality in individuals with a diagnosis of OCD and hoarding symptoms (in one study only subjects with hoarding as the primary problem were included, thus suggesting that these individuals could have been diagnosed with HD provided that DSM-5 criteria were available at that moment). Interpretation of data concerning suicidality in HD is then compromised by these limits.

Suicidality in individuals with HD appears to be low, with rates of current suicidal ideation comprised between 5% and 10%, although 19% of individuals attempted suicide during their lifetime [14 15]. Suicidality appears to be higher in samples composed of individuals with OCD and hoarding symptoms (Table IV).

Only one recent study [14] specifically examined factors associated with increased suicide risk in individuals diagnosed with HD according to DSM-5 criteria: severity of HD (as measured by the SI-R total score), hoarding-related impairment (as measured by the ADL-H total score), higher number of psychiatric comorbidities, and specifically MDD and BD, all predicted suicidality [14].

Trichotillomania (hair pulling disorder) and skin picking disorder

Only four studies provided information concerning suicidality in individuals with TTM. These studies, moreover, suffered from the inclusion of few subjects whose diagnosis was made without structured interviews. In one study [16], data concerning suicidality in individuals with OCD and grooming disorders were provided without specifying whether it was TTM or SPD. Table V presents results of our review: lifetime rates of suicide attempts are low (3.7-12%) as compared to rates in other OCRDs; approximately 40% of individuals, however, reported lifetime suicidal ideation. Concerning SPD, five studies provided prevalence rates of suicide attempts and suicidal ideation; however, only two studies included samples made of non-comorbid SPD (Tab. VI). The only study that investigated lifetime suicide attempts rate in individuals with SPD without comorbid disorders found a low prevalence (5.7%) [17]. Approximately 40% of individuals reported lifetime suicidal ideation.

Discussion

Obsessive-compulsive disorder (OCD) has long been considered a disorder which did not carry a notable risk for suicide. Recent meta-analyses and systematized reviews, however, challenged this opinion and found that OCD may actually be considered at risk for suicidal ideation, suicide attempts and committed suicide. A recent systematic review from our research group [2] found a mean prevalence of current suicidal ideation in OCD of 25.9% (median: 15.6%); lifetime suicidal ideation of 44.1% (median: 36.4%) and lifetime suicide attempts of 14.2% (median

TABLE I. *Suicidality in BDD: studies in clinical samples.*

Author	Country	Design	BDD diagnosis	Screening for suicidality	Mode of suicidality	Sample N / Mean age / % males	Suicidality (%) Suicide attempts	Suicidality (%) Suicidal ideation
Veale et al., 1996 [20]	UK	Cross-sectional	BDDE BDD-YBOCS	n/r	Lifetime suicide attempts	50 / 32.6 (range 19-58) / 24	24 (1 completed suicide)	-
Perugi et al., 1997 [21]	Italy	Cross-sectional	DID DSS HSCL-90	BDSS for suicidal ideation	Current suicidal ideation	58 / 25 (SD 5.9) / 59	-	45
Zimmerman & Mattia, 1998 [22]	USA	Cross-sectional	SCID-I	n/r	Lifetime suicide attempts	16 / 31.6 (SD 10.8) / 25	18.8	-
Albertini & Phillips, 1999 [23]	USA	Cross-sectional	SCID-I BDD Form BDD-YBOCS	BDD data form	Lifetime suicidal ideation & lifetime suicide attempts	33 (adolescents) / 14.9 (SD 2.2) / 9	21	67
Altamura et al., 2001 [24]	Italy	Cross-sectional	SCID-I BDD-YBOCS	SCID-I	Current suicidal ideation	30 / 28.5 (SD 2.3) / 13	-	49.7
Grant et al., 2002 [25]	USA	Cross-sectional	BDD-Q Self-report screening measure for BDD SCID-I	SCID-I	Lifetime suicide attempts	AN+BDD: 16 / 27.4 (SD 9.7) / 0	62.5	-
Frare et al., 2004 [26]	Italy	Cross-sectional	SCID-I	ADPI	Current suicidal ideation	BDD: 34 / 24.7 (SD 5.6) / 55.9	-	26.5
						BDD + OCD: 24 / 16.4 (SD 2.3) / 62.5	-	29.1
Phillips et al., 2005 [7]	USA	Cross-sectional	SCID-I BDD-YBOCS	BDD Form	Lifetime suicidal ideation & lifetime suicide attempts	200 / 32.6 (SD 12.1) / 31.5	27.5 (2 completed suicide)	78
Fontanelle et al., 2006 [27]	Brazil	Cross-sectional	SCID-I	Specific questionnaire	Current suicidal ideation & lifetime suicide attempts	20 / 29.2 (SD 8.6) / 45	15	35
Phillips et al., 2007* [8]	USA	Cross-sectional	SCID-I BDD-YBOCS	SCID-I HAM-D	Lifetime suicidal ideation & lifetime suicide attempts	BDD: 45 / 36.5 (SD 12.7) / 62.3	13.3	77.8
						BDD + OCD: 40 / 36.5 (SD 11.7) / 55	40	85
Conroy et al., 2008 [10]	USA	Cross-sectional	BDD-Q SCID-I/P	A brief version of the BDD data form	Lifetime suicidal ideation & lifetime suicidal attempts	16 / 31.9 (SD 11) / 31.2	93.8	100
Philipps & Kelly, 2009 [28]	USA	Prospective	BDD-YBOCS	HAM-D	Current suicidal ideation	67 / 32.1 (SD: 10.5) / 32.3%	-	38.8
Costa et al., 2012 [29]	Brazil	Cross-sectional	SCID-I	Questionnaire assessing suicidality	Lifetime suicidal ideation & lifetime suicide attempts	OCD + BDD: 109 / 31.3 (SD 10.2) / 44	23.8	53.5 (suicidal plans 36.6)
Bjornsson et al., 2013* [30]	Iceland	Cross-sectional	BDD-YBOCS BDD-PSR BDDE	Suicidality items from the HAM-D	Lifetime suicidal ideation & lifetime suicide attempts	Sample 1: 184 / 16.7 (SD 7.3) / 33.15	30.3-14.5#	81-69.4#
						Sample 2: 244 / 16.7 (7.2) / 46.7	29.9-16.7#	83.9-79.7#

(continues)

TABLE I (*follows*). *Suicidality in BDD: studies in clinical samples.*

Author	Country	Design	BDD diagnosis	Screening for suicidality	Mode of suicidality	Sample N Mean age % males	Suicidality (%) Suicide attempts	Suicidal ideation
Hart et al., 2013* [31]	USA	Cross-sectional	SCID-I BDD-YBOCS BDD form	SCID-I	Lifetime suicidal ideation & lifetime suicide attempts	Sample 1: 160 28.80 (SD 11.04) 41	29.4	78.0
						Sample 2: 115 32.93 (SD 11.83) 30	28.2	74.1
De Brito et al., 2015 [32]	Brazil	Cross-sectional	BDDE Clinical assessment	n/r	Lifetime suicidal ideation & lifetime suicide attempts	300 n/r 14.6	9	18.4
Kelly et al., 2015 [9]	USA	Cross-sectional	BDD-Q SCID-P	n/r	Lifetime suicidal ideation & lifetime suicide attempts	12 49.6 (SD 13.7) 83.3	58.3	66.7

n/r: not reported; *: partially overlap with Phillips 2005. The additional studies which used exactly the same cohort of participants are included in Appendix (not shown in the table); #: age of onset before 18 – age of onset after 18; BDDE: Body Dysmorphic Disorder Examination; BDD-YBOCS: Yale-Brown Obsessive-Compulsive Scale adapted for BDD; DID: Diagnostic Interview for Body Dysmorphobia; DSS: Body Dysmorphic Symptom Scale; HSCL 90: Hopkins Symptom Checklist 90; SCID-I: Structured Clinical Interview for DSM-IV Axis-I Disorders; BDD-Q: The Body Dysmorphic Disorder Questionnaire; BDD-PSR: Psychiatric Status Rating Scale for Body Dysmorphic Disorder; SCID/P: Structured Clinical Interview for DSM-IV Patient Edition; ADPI: Adult Demographic and Personal Inventory; HAM-D: Hamilton Rating Scale for Depression.

TABLE II. *Suicidality in BDD: epidemiological studies.*

Authors	Country	Design	BDD diagnosis	Screening for suicidality	Mode of suicidality	N BDD-sample§ Mean age % males	Suicidality Suicide attempts	Suicidal ideation
Rief et al., 2006 [33]	Germany	Cross-sectional	DSM criteria Clinical assessment SOMS-7	n/r	Current suicidal ideation & lifetime suicide attempts	42 44.3 (SD 17.2) 40	7.2 (1.0 in no-BDD, p < .001)	19.1 (3.4 in no-BDD, p <. 001)
Buhlmann et al., 2010 [34]	Germany	Cross-sectional	DSM criteria	Specific questionnaire	Lifetime suicidal ideation & lifetime suicide attempts	45 48.9 (SD: 17.1) 37.7	22.2 (3.5 in no-BDD, p = 0.02)	31.0 (2.1 in no-BDD, p = 0.02)
Schieber et al., 2015 [35]	Germany	Cross-sectional	DSM-IV and DSM-5 criteria	PHQ-9	Current suicidal ideation	62 42.1 (SD 13.6) 21	-	31.1 (7.3 in no-BDD)
Moolman et al., 2017 [36]	Germany	Cross-sectional	DSM-5 criteria BDSI	Items 10, 16, 17, and 18 from the FKS	Current suicidal ideation	11* n/r 18.2	-	36.4 (8.8 in no-BDD, p < .001)
Shaw et al., 2016 [12]	USA	Cross-sectional	BDD-SS	BDD-SS ACSS	Current suicide risk	235 32.1 (SD 9.9) 43	INQ-burd: 2.71 (SD 1.50) INQ-belong: 3.37 (SD 1.62) ACSS: 8.01 (SD 4.67)	
Weingarden et al., 2016 [13]	USA	Cross-sectional	BDD-Q BDD-YBOCS	SBQ-R	Current suicide risk	114 30.2 (SD 10.9) 8%	SBQ-R: 8.18 (SD 3.70)	
Weingarden et al., 2017 [11]	USA	Cross-sectional	BDD-Q BDD-YBOCS	SBQR BDD-SS	Current suicide risk	184 29.7 (SD 10.1) 7.6	SBQ-R: 9.69 (SD 4.25)	

§: N of BDD patients from the general population; *: adolescent population; SOMS-7: Somatoform Disorders Screening Symptoms-7; BDSI: Body Dysmorphic Symptoms Inventory; BDD-SS: Body Dysmorphic Disorder Symptoms Scale; BDD-Q: The Body Dysmorphic Disorder Questionnaire; BDD-YBOCS: Yale-Brown Obsessive-Compulsive Scale adapted for BDD; PHQ-9: Patient Health Questionnaire-9; FKL: Fragebogen körperdysmorpher Symptoms; ACSS: Acquired Capability Suicide Scale; SBQ-R: Suicide Behaviors Questionnaire Revised; INQ: Interpersonal Needs Questionnaire - INQ-burd: INQ perceived burdensomeness subscale; INQ-belong: INQ thwarted belongingness subscale.

TABLE III. *Studies with data on associated factors or predictors of suicidality in body dysmorphic disorder.*

Predictors		Current/lifetime suicidal ideation	Lifetime suicide attempts	Deaths by suicide
Socio-demographic or personal factors	Lifetime academic/occupational/role impairment	Didie et al., 2008 [49] Witte et al., 2012 [50]	Didie et al., 2008 [49] Witte et al., 2012 [50]	Philipps et al. 2005 [7]
	Lifetime/current social and functional impairment	Witte et al., 2012 (lifetime) [50] Philipps et al., 2005 (lifetime and current) [7]	Philipps et al., 2005 (lifetime and current) [7]	-
	Age 20 or younger	Philipps et al., 2006 [51]	-	-
	Being single or divorced	Philipps et al., 2005 [7]	-	-
Disorder-specific (BDD-related) variables	Early onset (< 18 yrs)	Bjornsson et al., 2013 [30]	Bjornsson et al., 2013 [30]	-
	Appearance related symmetry concerns	Hart & Philipps, 2013 [31]	-	-
	BDD-SS Severity	Philipps et al., 2005 [7] Philipps & Menard, 2006 [52] Shaw et al., 2016 [12]	-	Philipps et al. 2005 [7]
	Delusional form of BDD	-	Philipps et al., 2005 [7] Philipps & Menard, 2006 [52]	-
	Muscle dysmorphia	-	Pope et al., 2005 [53]	-
	BDD-related restrictive food intake	-	Witte et al., 2012 [50]	-
	BDD-related excessive exercise (protective)	-	Witte et al., 2012 [50]	-
	Type of plastic surgery performed for correction of apparent defects: rhytidectomy[1]	De Brito et al., 2016 [32]	De Brito et al., 2016 [32]	-
Comorbidities	Comorbid OCD	Frare et al., 2004 [26] Philipps al., 2007 [8]	Philipps et al., 2007 [8]	-
	Comorbid social phobia	Coles et al., 2006 [54]	-	Philipps et al. 2005 [7]
	Comorbid panic attacks	Philipps et al., 2013 [55]	-	-
	Lifetime history of PTSD	-	Phillips et al., 2005 [7] Witte et al., 2012 [50]	-
	History of psychiatric hospitalization	-	Philipps et al., 2005 [7]	-
	Substance/alcohol use disorders	Grant et al., 2005 [56] Witte et al., 2012 [50]	Philipps et al., 2005 [7]	Philipps et al. 2005 [7]
	MDD (current and lifetime)	Philipps et al., 2005 [7] Philipps et al., 2007 [8] Witte et al., 2012 [50] Shaw et al., 2016 [12]	-	Philipps et al. 2005 [7]
	Lifetime bipolar disorder	Philipps et al., 2005 [7]	Philipps et al., 2005 [7]	-
	Comorbid eating disorder	-	Philipps et al., 2005 [7]	-
	Any personality disorder	Philipps et al., 2005 [7]	Philipps et al., 2005 [7]	-
	Borderline personality disorder	Philipps et al., 2005 [7]	Philipps et al., 2005 [7]	-
Emotion-cognitive factors	Childhood trauma (emotional, physical and sexual abuse)[2]	-	Didie et al., 2006 [57]	-
	Shame/defectiveness beliefs	Weingarten et al., 2016 [13]	-	-
	Anxiety (considered as emotion)	Weingarten et al., 2016 [13]	-	-
	Weight concerns	-	Kittler, 2007 [58]	-
	High levels of impulsivity	Phillips & Menard, 2006 [59]	Phillips & Menard, 2006 [59]	-

1) Compared to other types of surgery: abdominoplasty and rhinoplasty; 2) Measured by Childhood Trauma Questionnaire (CTQ).

10.8%). Specific factors are more strongly associated with suicide in OCD patients; the severity of OCD, the unacceptable thoughts symptom dimension (aggressive, sexual, religious obsessions), comorbid Axis I disorder (bipolar disorder or major depressive disorder but also substance use disorder), the severity of comorbid depressive and anxiety symptoms, a previous history of suicide attempts, and some emotion-cognitive factors, such as alexithymia and hopelessness, all increase the risk of having suicidal ideation or attempting suicide [18]. Our systematic review clearly showed that OCD is at a greater suicide risk, compared to the general population. Hence, clinicians should actively inquire about suicidal thoughts and attempts when interviewing a patient with OCD, keeping in mind that risk identification remains a crucial factor for establishing preventive strategies. The recognition that specific risk factors

TABLE IV. *Suicidality in HD (or in OCD subjects with hoarding symptoms).*

Author	Country	Design	Hoarding disorder symptoms diagnosis	Screening for suicidality	Mode of suicidality	Sample N Mean age % males	Suicidality (%)	
							Suicidal attempts	Suicidal ideation
Balci &Sevincok, 2010 [37]	Turkey	Cross-sectional	YBOCS	SSI	Current suicidal ideation	11* n/r n/r	-	36.4
Matsunaga et al., 2010 [38]	Japan	Cross-sectional	YBOCS	Self-report questionnaire	Lifetime impulsive behaviors (including suicide attempts)	54* 30.8 (SD 8.9) 44.4	41 (*vs* 18 non-hoarders, p < 0.01)	
Alonso et al., 2010 [39]	Spain	Prospective	YBOCS	Beck suicide intent scale	Lifetime suicide attempts	62* n/r n/r	6.45 (*vs* 5.91 in total OCD population)	-
Torres et al., 2011 [40]	Brazil	Cross-sectional	DYBOCS	Specifically created questionnaire	Lifetime and current suicidal ideation, lifetime suicidal plans & lifetime suicide attempts	297* n/r n/r	13.1	11.5 (current) 39.4 (lifetime) 24.2 lifetime suicidal plans
Chakraborty et al., 2012 [41]	UK	Cross-sectional	SI-R	Clinical interview	Current suicidal ideation & lifetime suicide attempts	20# 31.5 (SD 9.98) 50	40	20
Torres et al., 2012 [42]	Brazil	Cross-sectional	DYBOCS	Specific questions	Current and lifetime suicidal ideation, lifetime suicidal plans & lifetime suicide attempts	528 (4 of them only HD)* 35.9 (SD 13.2) 40.2	12.7	12.3 (current) 38.9 (lifetime) 23.7 lifetime suicidal plans
Ayers et al., 2015 [15]	USA	Cross-sectional	DSM-5 criteria UHSS SI-R CIR	n/r	Current suicidal ideation	71 67 (SD 5.8) 31	-	4.69
Archer et al., 2018 [14]	USA	Cross-sectional	SIHD	MINI	Current suicidal ideation & lifetime suicide attempts	313 59 (SD 11.8) 25.9	19	10

*: patients with OCD and hoarding symptoms as measured by the Dimensional YBOCS; #: patients with OCD and hoarding symptoms. In all cases, hoarding was a primary problem, that is, not secondary to other OCD symptoms. YBOCS: Yale Brown Obsessive Compulsive Scale; DYBOCS: Dimensional Yale Brown Obsessive Compulsive Scale; SI-R: Saving Inventory Revised; UHSS: UCLA Hoarding Severity Scale; CIR: Clutter Image Rating Scale; SIHD: The Structured Interview for Hoarding Disorder; SSI: Scale for Suicidal Ideation; MINI: Mini International Neuropsychiatric Interview.

are associated with suicidal ideation and attempts among individuals with OCD could potentially lead to saving lives in the future.

Less research has been devoted to understanding suicidality among individuals with obsessive-compulsive related disorders; this group of disorders may share with OCD the high risk for suicide attempts and suicidal ideation. However, only for BDD systematic reviews and a meta-analysis are available on the topic [6] [19]. This lead us to perform the present systematic review including all papers on suicidality among individuals with OCRDs.

Concerning suicidality among individuals with BDD, our results are consistent with those of a previous systematic review and meta-analysis which, however, included only seventeen studies [6]: a positive and statistically significant association was found between BDD and suicidality (attempts and ideation together, without differentiating between current and lifetime rates): OR = 3.63 (CI 2.62-4.63).

Our systematic review found that approximately 20% of individuals with a primary diagnosis of BDD attempted suicide during their lifetime and 75% had suicidal ideation. Studies performed in the general population confirmed that BDD is in itself at greater risk for suicide as compared to the general population. Suicidality in BDD appears, then, even higher than among patients with OCD. Clinicians, then, should not overlook BDD as being not at risk for suicide and should actively inquire about past suicide attempts and current suicidal ideation in each patient with a diagnosis of BDD, independently from other comorbid disorders eventually present.

However, we found that BDD-specific factors such as early onset, severity, poor insight and muscle dysmorphia and comorbid disorders (mainly MDD, anxiety disorders or OCD) increase the risk of suicide attempts or suicidal ideation, and thus may constitute specific predictors of suicidality to be actively inquired and that clinicians could

TABLE V. *Suicidality in trichotillomania.*

Author	Country	Design	TTM diagnosis	Screening for suicidality	Mode of suicidality	Sample N Mean age % males	Suicidality (%)	
							Suicide attempts	Suicidal ideation
Streichenwein et al., 1995 [43]	USA	Clinical trial	DSM-IV criteria	n/r	Lifetime suicide attempts	16 39 (SD 12) 12.5	6.3	-
Seedat & Stein, 1998 [44]	South Africa	Cross-sectional	Specific questionnaire DSM-IV criteria YBOCS	Specific questionnaire	Current suicidal ideation & lifetime suicide attempts	27 29.8 (SD 10.7) 37	3.7	44.4
Lejoyeux et al., 2002 [45]	France	Cross-sectional	MIDI	Specific questionnaire	Lifetime suicide attempts	3* 30 (SD 5) 0	66.6	-
Lovato et al., 2012 [16]	Brazil	Cross-sectional	SCID-I DYBOCS	n/r	Current suicidal ideation & lifetime suicide attempts	121** 31.0 (SD 11.8) 27.3	12.0	39.3

YBOCS: Yale Brown Obsessive Compulsive Scale; MIDI: Minnesota Impulsive Disorders Interview; SCID-I=Structured Clinical Interview for DSM-IV Axis-I Disorders; DYBOCS: Dimensional Yale Brown Obsessive Compulsive Scale; *: patients diagnosed with TTM taken from a sample of depressed patients; **: population with OCD and GD (grooming disorders, either skin-picking disorder or trichotillomania).

consider when planning treatment and visit schedules. Results of our systematic review are in accordance to those of previous reviews on the same topic [6][19]. It has to be stated, however, that few studies specifically examined potential predictors of suicidality in BDD, and many of those studies are flawed by methodological biases, suggesting caution in the interpretation of these findings.

It has to be noted, moreover, that some of the factors found to increase suicidality among subjects with BDD do also increase suicide risk in individuals with OCD [2]. Risk identification and stratification of risk remain essential components of suicide prevention and should guide the clinical approach to subjects with OCD. Whether and how these risk factors for suicide work together, and whether the spe-

cific factors act as moderators or mediators, remains to be fully elucidated.

The evaluation of suicide risk in individuals with HD, Trichotillomania and SPD is hampered by the very low number of studies investigating suicidality specifically in samples of individuals with these DSM-5 disorders. The revision of the classification made by DSM-5 (with the creation of the OCD and related disorders new category and with the new disorders – HD and SPD) surely represented an advance for clinicians and researchers, but unfortunately very few studies at yet investigated whether individuals with these new disorders are at risk for committing suicide. When examining suicide risk and hoarding, moreover, we have still to rely on data gathered from samples of subjects

TABLE VI. *Suicidality in skin picking disorder.*

Author	Country	Design	SPD diagnosis	Screening for suicidality	Mode of suicidality	Sample N Mean age % males	Suicidality (%)	
							Suicide attempts	Suicidal ideation
Philipps et al., 1995 [46]	USA	Cross-sectional	n/r	n/r	Lifetime suicide attempts	33* - 42.4	33	-
Grant et al., 2006 [47]	USA	Cross-sectional	SCID-I YBOCS	n/r	Lifetime suicide attempts	79* 30.5 (SD 11.3) 17.7	25.3	-
Grant et al., 2010 [17]	USA	Cross-sectional	proposed DSM criteria	n/r	Lifetime suicide attempts	53 34.2 (SD 13.11) 13.2	5.7 (*vs* 13.7 in OCD)	-
Lovato et al., 2012 [16]	Brazil	Cross-sectional	SCID-I DYBOCS	n/r	Current suicidal ideation & lifetime attempts	121** 31.0 (SD 11.8) 27.3	12.0	39.3
Machado et al., 2018 [48]	Brazil	Cross-sectional Epidemiological	SPSQ	PHQ-9	Current suicidal ideation	259 27.8 (8.4) 17.8	-	41.3

*: individuals with BDD and SPD; **: population with OCD and GD (grooming disorders, either skin-picking disorder or trichotillomania); SCID-I: Structured Clinical Interview for DSM-IV Axis-I Disorders; YBOCS: Yale Brown Obsessive Compulsive Scale; DYBOCS: Dimensional Yale Brown Obsessive Compulsive Scale OCD: Obsessive Compulsive Disorder; SPSQ: Skin Picking Stanford Questionnaire; PHQ-9: Patient Health Questionnaire-9.

with OCD as the primary diagnosis and prominent hoarding symptoms; it is not clear, then, whether suicidality is associated with HD in itself or whether it is associated with the specific subtype of OCD with hoarding symptoms. It is possible that HD, being usually associated with poor insight and then with a long delay from onset to help-seeking, is not at risk for suicide at the beginning of its history, and subsequently becomes associated with a higher risk when comorbid with OCD or MDD, or when the impairment associated with HD is huge. However, this is only a hypothesis that needs to be confirmed.

Concerning the grooming disorders (TTM and SPD), too few studies are available to draw some conclusions; very preliminary data seem to suggest that suicide attempts are low in TTM and SPD as compared to other OCRDs. The inclusion of these disorders among the chapter of OCD and related disorders will for sure draw attention on such neglected disorders, and we will expect that more reliable data on suicidality will appear in the next future.

In conclusion, our present systematic review showed that like in the case of pure OCD [2], 3 OCRDs taken together may be at risk for suicide attempts and suicidal ideation independently from comorbid disorders (and specifically independently from comorbid OCD); BDD remains the disorder more strongly associated with an increased risk for suicide, followed by HD and then the grooming disorders. A greater awareness of such suicide risk should prompt clinicians to actively inquire about past suicide attempts and current suicidal ideation whenever a patient with one of the obsessive-compulsive related disorders presents for a visit.

Conflict of interest

The Authors have no conflict of interest to declare.

References

[1] Angelakis I, Gooding P, Tarrier N, et al. *Suicidality in obsessive compulsive disorder (OCD): a systematic review and meta-analysis*. Clin Psychol Rev 2015;39:1-15.

[2] Albert U, De Ronchi D, Maina G, et al. *Suicide risk in obsessive-compulsive disorder and exploration of risk factors: a systematic review.* Curr Neuropharmacol 2018 Jun 20.

[3] Fernández de la Cruz L, Rydell M, Runeson B, et al. *Suicide in obsessive-compulsive disorder: a population-based study of 36 788 Swedish patients*. Mol Psychiatry 2017;22:1626-32.

[4] Meier SM, Mattheisen M, Mors O, et al. *Mortality among persons with obsessive-compulsive disorder in Denmark.* JAMA Psychiatry 2016;73:268-74.

[5] Albert U, De Cori D, Barbaro F, et al. *Hoarding disorder: a new obsessive-compulsive related disorder in DSM-5.* Off J Ital Soc Psychopathol 2015;21:354-64.

[6] Angelakis I, Gooding PA, Panagioti M. *Suicidality in body dysmorphic disorder (BDD): a systematic review with meta-analysis*. Clin Psychol Rev 2016;49:55-66.

[7] Phillips KA, Coles ME, Menard W, et al. *Suicidal ideation and suicide attempts in body dysmorphic disorder*. J Clin Psychiatry 2005;66:717-25.

[8] Phillips KA, Pinto A, Menard W, et al. *Obsessive-compulsive disorder versus body dysmorphic disorder: a comparison study of two possibly related disorders.* Depress Anxiety 2007;24:399-409.

[9] Kelly MM, Zhang J, Phillips KA. *The prevalence of body dysmorphic disorder and its clinical correlates in a VA primary care behavioral health clinic.* Psychiatry Res 2015;228:162-5.

[10] Conroy M, Menard W, Fleming-Ives K, et al. *Prevalence and clinical characteristics of body dysmorphic disorder in an adult inpatient setting.* Gen Hosp Psychiatry 2008;30:67-72.

[11] Weingarden H, Renshaw KD, Davidson E, et al. *Relative relationships of general shame and body shame with body dysmorphic phenomenology and psychosocial outcomes.* J Obsessive Compuls Relat Disord 2017;14:1-6.

[12] Shaw AM, Arditte Hall KA, Rosenfield E, et al. *Body dysmorphic disorder symptoms and risk for suicide: the role of depression.* Body Image 2016;19:169-74.

[13] Weingarden H, Renshaw KD, Wilhelm S, et al. *Anxiety and shame as risk factors for depression, suicidality, and functional impairment in body dysmorphic disorder and obsessive compulsive disorder.* J Nerv Ment Dis 2016;204:832-9.

[14] Archer CA, Moran K, Garza K, et al. *Relationship between symptom severity, psychiatric comorbidity, social/occupational impairment, and suicidality in hoarding disorder.* J Obsessive Compuls Relat Disord. 2018; Nov. [Epub ahead of print]

[15] Ayers CR, Dozier ME. *Predictors of hoarding severity in older adults with hoarding disorder.* Int Psychogeriatr 2015;27:1147-56.

[16] Lovato L, Ferrão YA, Stein DJ, et al. *Skin picking and trichotillomania in adults with obsessive-compulsive disorder.* Compr Psychiatry 2012;53:562-8.

[17] Grant JE, Odlaug BL, Kim SW. *A clinical comparison of pathologic skin picking and obsessive-compulsive disorder.* Compr Psychiatry 2010;51:347-52.

[18] Albert U, Speciani M, De Ronchi D, et al. *Factors associated with increased suicide risk in obsessive-compulsive disorder.* Off J Ital Soc Psychopathol 2018;24:154-63.

[19] De La Vega D, Giner L, Courtet P. *Suicidality in subjects with anxiety or obsessive-compulsive and related disorders: recent advances.* Curr Psychiatry Rep 2018;20:26.

[20] Veale D, Boocock A, Gournay K, et al. *Body dysmorphic disorder. A survey of fifty cases.* Br J Psychiatry J Ment Sci 1996;169:196-201.

[21] Perugi G, Giannotti D, Frare F, et al. *Prevalence, phenomenology and comorbidity of body dysmorphic disorder (dysmorphophobia) in a clinical population.* Int J Psychiatry Clin Pract 1997;1:77-82.

[22] Zimmerman M, Mattia JI. *Body dysmorphic disorder in psychiatric outpatients: recognition, prevalence, comorbidity, demographic, and clinical correlates.* Compr Psychiatry 1998;39:265-70.

[23] Albertini RS, Phillips KA. *Thirty-three cases of body dysmorphic disorder in children and adolescents.* J Am Acad Child Adolesc Psychiatry 1999;38:453-9.

[24] Altamura C, Paluello MM, Mundo E, et al. *Clinical and subclinical body dysmorphic disorder.* Eur Arch Psychiatry Clin Neurosci 2001;251:105-8.

[25] Grant JE, Kim SW, Eckert ED. *Body dysmorphic disorder in patients with anorexia nervosa: prevalence, clinical features, and delusionality of body image.* Int J Eat Disord 2002;32:291-300.

[26] Frare F, Perugi G, Ruffolo G, et al. *Obsessive-compulsive disorder and body dysmorphic disorder: a comparison of clinical features.* Eur Psychiatry 2004;19:292-8.

[27] Fontenelle LF, Telles LL, Nazar BP, et al. *A*

sociodemographic, phenomenological, and long-term follow-up study of patients with body dysmorphic disorder in Brazil. Int J Psychiatry Med 2006;36:243-59.

28 Phillips KA, Kelly MM. Suicidality in a place-bo-controlled fluoxetine study of body dysmorphic disorder. Int Clin Psychopharmacol 2009;24:26-8.

29 Conceição Costa DL, Chagas Assunção M, Arzeno Ferrão Y, et al. Body dysmorphic disorder in patients with obsessive-compulsive disorder: prevalence and clinical correlates. Depress Anxiety 2012;29:966-75.

30 Bjornsson AS, Didie ER, Grant JE, et al. Age at onset and clinical correlates in body dysmorphic disorder. Compr Psychiatry 2013;54:893-903.

31 Hart AS, Phillips KA. Symmetry concerns as a symptom of body dysmorphic disorder. J Obsessive Compuls Relat Disord 2013;2:292-8.

32 De Brito MJA, Nahas FX, Cordás TA, et al. Body dysmorphic disorder in patients seeking abdominoplasty, rhinoplasty, and rhytidectomy. Plast Reconstr Surg 2016;137:462-71.

33 Rief W, Buhlmann U, Wilhelm S, et al. The prevalence of body dysmorphic disorder: a population-based survey. Psychol Med 2006;36:877-85.

34 Buhlmann U, Glaesmer H, Mewes R, et al. Updates on the prevalence of body dysmorphic disorder: a population-based survey. Psychiatry Res 2010;178:171-5.

35 Schieber K, Kollei I, de Zwaan M, et al. Classification of body dysmorphic disorder – what is the advantage of the new DSM-5 criteria? J Psychosom Res 2015;78:223-7.

36 Möllmann A, Dietel FA, Hunger A, et al. Prevalence of body dysmorphic disorder and associated features in German adolescents: a self-report survey. Psychiatry Res 2017;254:263-7.

37 Balci V, Sevincok L. Suicidal ideation in patients with obsessive-compulsive disorder. Psychiatry Res 2010;175:104-8.

38 Matsunaga H, Hayashida K, Kiriike N, et al. Clinical features and treatment characteristics of compulsive hoarding in japanese patients with obsessive-compulsive disorder. CNS Spectr 2010;15:258-66.

39 Alonso P, Segalàs C, Real E, et al. Suicide in patients treated for obsessive-compulsive disorder: a prospective follow-up study. J Affect Disord 2010;124:300-8.

40 Torres AR, Ramos-Cerqueira ATA, Ferrão YA, et al. Suicidality in obsessive-compulsive disorder: prevalence and relation to symptom dimensions and comorbid conditions. J Clin Psychiatry 2011;72:17-26.

41 Chakraborty V, Cherian AV, Math SB, et al. Clinically significant hoarding in obsessive-compulsive disorder: results from an Indian study. Compr Psychiatry 2012;53:1153-60.

42 Torres AR, Fontenelle LF, Ferrão YA, et al. Clinical features of obsessive-compulsive disorder with hoarding symptoms: a multicenter study. J Psychiatr Res 2012;46:724-32.

43 Streichenwein SM, Thornby JI. A long-term, double-blind, placebo-controlled crossover trial of the efficacy of fluoxetine for trichotillomania. Am J Psychiatry 1995;152:1192-6.

44 Seedat S, Stein DJ. Psychosocial and economic implications of Trichotillomania: a pilot study in a South African sample. CNS Spectr 1998;3:40-3.

45 Lejoyeux M, Arbaretaz M, McLoughlin M, et al. Impulse control disorders and depression. J Nerv Ment Dis 2002;190:310-4.

46 Phillips KA, Taub SL. Skin picking as a symptom of body dysmorphic disorder. Psychopharmacol Bull 1995;31:279-88.

47 Grant JE, Menard W, Phillips KA. Pathological skin picking in individuals with body dysmorphic disorder. Gen Hosp Psychiatry 2006;28:487-93.

48 Machado MO, Köhler CA, Stubbs B, et al. Skin picking disorder: prevalence, correlates, and associations with quality of life in a large sample. CNS Spectr 2018;23:311-20.

Appendix 1

16 studies referring to the same sample of patients of Phillips 2005.

49 Didie ER, Menard W, Stern AP, et al. Occupational functioning and impairment in adults with body dysmorphic disorder. Compr Psychiatry 2008;49:561-9.

50 Witte TK, Didie ER, Menard W, et al. The relationship between body dysmorphic disorder behaviors and the acquired capability for suicide: BDD and the acquired capability for suicide. Suicide Life Threat Behav 2012;42:318-31.

51 Phillips KA, Didie ER, Menard W, et al. Clinical features of body dysmorphic disorder in adolescents and adults. Psychiatry Res 2006;141:305-14.

52 Phillips K, Menard W, Pagano M, et al. Delusional versus nondelusional body dysmorphic disorder: clinical features and course of illness. J Psychiatr Res 2006;40:95-104.

53 Pope CG, Pope HG, Menard W, et al. Clinical features of muscle dysmorphia among males with body dysmorphic disorder. Body Image 2005;2:395-400.

54 Coles ME, Phillips KA, Menard W, et al. Body dysmorphic disorder and social phobia: cross-sectional and prospective data. Depress Anxiety 2006;23:26-33.

55 Phillips KA, Menard W, Bjornsson AS. Cued panic attacks in body dysmorphic disorder. J Psychiatr Pract 2013;19:194-203.

56 Grant JE, Menard W, Pagano ME, et al. Substance use disorders in individuals with body dysmorphic disorder. J Clin Psychiatry 2005;66:309-16.

57 Didie ER, Tortolani CC, Pope CG, et al. Childhood abuse and neglect in body dysmorphic disorder. Child Abuse Negl 2006;30:1105-15.

58 Kittler JE, Menard W, Phillips KA. Weight concerns in individuals with body dysmorphic disorder. Eat Behav 2007;8:115-20.

59 Phillips KA, Menard W. Suicidality in body dysmorphic disorder: a prospective study. Am J Psychiatry 2006;163:1280-2.

60 Phillips KA, Didie ER, Menard W. Clinical features and correlates of major depressive disorder in individuals with body dysmorphic disorder. J Affect Disord 2007;97:129-35.

61 S. Ruffolo J, Phillips KA, Menard W, et al. Comorbidity of body dysmorphic disorder and eating disorders: severity of psychopathology and body image disturbance. Int J Eat Disord 2006;39:11-9.

62 Phillips KA, Menard W, Fay C, et al. Demographic characteristics, phenomenology, comorbidity, and family history in 200 individuals with body dysmorphic disorder. Psychosomatics 2005;46:317-25.

63 Phillips KA, Menard W, Fay C. Gender similarities and differences in 200 individuals with body dysmorphic disorder. Compr Psychiatry 2006;47:77-87.

64 Phillips KA. Suicidality in body dysmorphic disorder. Prim Psychiatry 2007;14: 58-66.

G. Maina, F. Quarato, S. Bramante

* SCDU Psichiatria, AOU "S. Luigi Gonzaga;"
Dipartimento di Neuroscienze,
Università di Torino.

Risk factors for suicide in bipolar disorder

Summary

Objectives

Aim of this review is to analyse, update and categorize data coming from literature about risk factors for suicide in Bipolar Disorder (BD). Suicide represents the most fearsome complication of BD. The epidemiological rates of suicide attempts and deaths in BD are extremely high compared to the general population and other psychiatric conditions, underlining the need for a specific assessment of risk factors for suicide in BD patients.

Methods

The authors performed a systematic literature search in order to give a detailed overview of risk factors for suicide in bipolar disorder.

Results

Suicide risk factors have been classified into three categories: sociodemographic, biological and clinical factors. In each group, there are several disease-specific risk factors which should be considered in the evaluation of suicide risk of a patient.

Conclusions

Considering the high rate of suicide attempts and deaths in bipolar subjects and the social impact of this behaviour, it is important to early recognise such patients, thus allowing for better prediction and prevention of suicidal behaviours.

Key words

Bipolar disorder • Suicide • Risk factors • Suicide attempt • Suicide death.

Correspondence

Stefano Bramante
SCDU Psichiatria, AOU "S. Luigi Gonzaga;
Dipartimento di Neuroscienze,
Università di Torino, Italy
Tel. +39 0119026517
• E-mail: stefano.bramante@unito.it

According to the World Health Organization, the global burden of suicide accounts for around one million deaths per year. More than 90% of people who die from suicide are affected by a psychiatric disorder and, among those, Bipolar Disorder (BD) is one of the most common diseases: about half the people with BD have suicidal thoughts, 21% a plan, and 16% report a suicide attempt within the past year [1][2]. Furthermore, lethality of suicide attempts is higher in bipolar population than in the general population [3]. Concerning suicide attempts method, some studies evaluated the frequency of violent *vs* non-violent methods: non-violent methods, in particular self-poisoning, are the most frequently used [3]. Considering the high rate of suicide attempts and deaths in bipolar subjects and the social impact of this behaviour, it is important to early recognise such patients and identify specific suicidal risk factors, in order to timely implement therapeutic interventions. There is an extensive literature about risk factors for suicide in BD, pointing out the importance of this issue. Aim of this review is to analyse, update and categorize data coming from literature and regarding risk factors for suicide attempts and deaths in BD.

Methods

We performed a systematic review of articles regarding risk factors for suicide in Bipolar Disorder. A PubMed research of studies published from 1980 to 2018 has been conducted, using search terms as "bipolar disorder", "sui-

cide", "risk factors". In addition, we evaluated data from recently published reviews and international guidelines. All papers were analysed. In the event that a study was mentioned in a subsequent review or guideline, we decided to reference the latest published paper.

Risk factors for suicide attempt and suicide death

Suicide risk factors mentioned by literature data may be systematically analysed and divided in three categories: sociodemographic, genetic-biological and clinical factors (Table I).

Sociodemographic factors
Gender
Most of the studies available in literature highlight an association between female gender and suicide attempts: women appear to have an increased risk of suicide attempts compared to men and this association seems to be stronger in BD than in other psychiatric conditions [4]. However, lethality of suicide attempts seems to be higher in men [5].

Race
There is a paucity of data regarding the relationship between suicidality and ethnicity. Only one study showed that bipolar non-Hispanic whites had a higher risk of suicide behaviours, compared to other races. No such difference was found by other authors [4].

Age
Among subjects who committed suicide, those who were affected by BD appear to be significantly younger than others[4]. Regarding the relationship between age and suicide in BD, there are findings which showed that attempters are significantly younger compared to non-attempters: the age group 20-29 reported the highest lifetime suicide attempt rate (42.9%), followed by the 30-39 age group (25%) [4 6]. Moreover, young people with BD are more vulnerable to develop suicidal ideation [7]. That is associated with some clinical conditions: in particular, onset of the disorder after the age of 12, mixed and psychotic symptoms, greater severity of depressive symptoms, psychiatric comorbidities, such as attention deficit hyperactivity disorder (ADHD), panic disorder and substance use, history of physical and/or sexual abuse and family history of suicide and mood disorder are related to an increased likelihood of suicide attempt [4 7]. Some authors suggest that children with decreased familial support, increased conflict, greater family rigidity and lower self-esteem may run a higher suicidal risk [5 8]. No age difference has been found when analysing the methods of suicide attempt (violent vs non-violent) [4 9].

Family status
Data from literature show that suicide attempts are strongly associated with a condition of psychosocial isolation [4 5].

Indeed, patients with BD who are single or divorced and without children present an increased risk of suicide [4 5]. This is evident for both mothers and fathers [4].

Religious affiliation
The correlation between religious affiliation and suicide is controversial. Suicidal behaviour seems to be correlated to the moral and religious objection to this conduct. However, in a mixed sample of patients affected by mood disorders (unipolar and bipolar disorder), high religious belief was associated with greater likelihood of suicide attempts [4].

Biological factors
Genetic factors
The assumption according to which certain genes may play a role in suicide in bipolar patients is supported by twin, family and adoption studies [10]. There is an extensive literature about the association between suicidal behaviour in BD and family history of suicide or mood disorders in first-degree relatives [10 11]. That appears to be the most important risk factor for suicide in BD and it is still significant even after controlling for the effect of familial aggregation of psychiatric disorders, suggesting an independent genetic predisposition for suicide, which is different from the familial predisposition for bipolar disorder. Many genes have been studied and appear to be possible predictors of completed suicide and suicide attempt. Among those, some findings show a possible association between the brain-derived neuro-trophic factor (BDNF) gene and suicidal behaviours; this correlation seems also to apply to the modality of suicide (violent vs non-violent). Other candidate genes under study are the polymorphisms of the tryptophan hydroxylase 1 and 2, who seem to be correlated with a higher lethality of suicide attempts and with completed suicides. Moreover, some authors showed that the serotonin transporter polymorphism 5-HTTLPR is significantly associated with violent suicidal behaviour in BD individuals [5 12]. Nonetheless, other researches are needed to discuss this issue in more detail [4].

Biomarkers
Some biological elements could be considered as possible predictors of suicide in patients affected by BD. Nevertheless, there were no significant findings among studies about non-genetic central and peripheral markers. Neuroimaging researches have focused on white matter, cerebral cortex (dorsolateral prefrontal cortex, orbitofrontal cortex, anterior cingulate, superior temporal cortex, parieto-occipital cortex) and basal ganglia, but results require replications [3]. Living at higher altitude seems to be correlated to a major risk of death by suicide in bipolar samples, compared to other psychiatric illnesses [4 5]. A possible explanation is that higher altitude, which has a reduced oxygen partial pressure, may result in a different concentration of cerebral neurotransmitters: due to hypox-

TABLE I. *Risk factors for suicide in bipolar disorder.*

Risk factors for suicide	Strong evidence	Weak evidence
Sociodemographic factors	• Female gender • Young age • Psycho-social isolation	• Race • Religious affiliation
Biological factors		
Genes		• BDNF • TPHL 1 and TPHL 2 • 5-HTTLPR • Other genes
Biomarkers		• Living at higher altitude • HPA axis alterations • Neurobiological alterations
Clinical factors		
Disorder features	• Early age of onset • Family history of suicide • Family history of mood disorder • Prior suicide attempt • Rapid-cycling course • Depressive polarity of the first affective episode • Depressive predominant polarity • Longer DUI • N. of previous depressive episodes • Psychiatric comorbidities (substance use, anxiety and cluster B personality disorder)	• Bipolar disorder subtype • Medical comorbidities (metabolic syndrome) • Psychiatric comorbidities (eating disorders)
Current episode features	• Depressive episode polarity • Mixed features • Suicidal ideation	• Psychotic features • Atypical features
Treatment features	• AD as monotherapy • Treatment discontinuation	

BDNF: Brain-Derived Neurotrophic Factor; TPHL 1: Tryptophan Hydroxylase 1; TPHL 2: Tryptophan Hydroxylase 2; 5-HTTLPR: 5-Hydroxy Tryptamine Transporter Gene-Linked Polymorphic Region; HPA: Hypothalamic-Pituitary-Adrenal; DUI: Duration of Untreated Illness; AD: Anti-Depressant.

ia, lower levels of serotonin and higher levels of dopamine and norepinephrine could increase irritability, depression, instability of mood and suicide rates [5]. The hypothalamic-pituitary-adrenal axis may be related to suicidal attempts in BD as well: more elevated bedtime salivary cortisol has been found in subjects who have a lifetime history of suicidal behaviour, compared to those who have not [3 13].

Clinical factors
There is an extensive literature concerning clinical risk factors for suicide in BD. By using a systematic approach, they could be divided into three categories: factors related to disorder features, those related to current episode characteristics and those associated with pharmacological treatment.

Disorder features
Age of onset. Data from literature underline that earlier age of onset of BD is related to a higher rate of suicidal behav-

iours [4]. Nevertheless, it is unclear if this is an independent risk factor or it is associated to other variables linked to a greater risk of suicide (for example, psychiatric comorbidities, rapid cycling, severity of illness and increased childhood physical abuse) [10].

Family history of suicide and mood disorder. This topic has been discussed within the genetic risk factors of suicide.

Prior suicide attempts. A lifetime history of suicidal behaviours is thought to be one of the most important predictors of suicide attempt and death in the general population. This appears to be particularly significant in BD: up to 56% of suicide deaths have a history of suicide attempts [3 10]. Preliminary data suggest that the presence of previous suicide attempts can be associated with lower social skills (conversational skills, social self-confidence, social openness to new people and situations, self-control of ag-

gressiveness and individual reactions to aversive stimuli), which may be related to the risk of suicidal behaviours [14].

Rapid-cycling course. There is a consistent evidence underlining that rapid-cycling patients show a higher risk of suicide attempt. Furthermore, rapid-cycling course is associated to a higher intent and lethality [10].

Polarity of the first affective episode. Individuals with a first mood episode of depressive polarity present an increased suicide risk [10]. Moreover, despite depressive polarity of the onset of the disorder is associated with a lifetime history of suicidal behaviours, a first episode of mania has been correlated with a greater likelihood of suicide by a violent method [4].

Predominant polarity. Data from literature suggest that depressive predominant polarity is strongly associated to lifetime suicide attempts, compared to manic predominant polarity [4].

Bipolar disorder subtype. Several studies analysed the correlation between the subtype of the disorder (BD I *vs* BD II) and suicidal behaviours. Costa and colleagues underlined that BD II patients have a greater risk of suicide than BD I [5]; however other authors did not find clear differences [4].

Duration of untreated illness (DUI). A longer DUI has been associated to a higher risk of suicide [4]. In individuals with more than two years of DUI, suicide attempt rates were significantly higher compared to patients with a DUI ≤ 2 years [10].

Number of previous episodes. Data from literature show that subjects with a lifetime history of suicidal behaviours were found to have twice as many previous depressive episodes, compared to non-attempters [10].

Comorbidities. <u>Medical comorbidities</u>: patients affected by BD present high rates of metabolic syndrome, which has been associated to a more severe course: lower response to treatment, increased illness burden and suicide [15]. Individuals who had a lifetime history of suicidal behaviour showed higher mean Body-Mass-Index values, compared to those who have not (30.2 *vs* 27.9) [16]. To date, only one study specifically analysed the correlation between metabolic syndrome, lipid profile and methods of suicide, without finding a significant association [17]. However, considering the paucity of data, more researches are needed.
<u>Psychiatric comorbidities</u>: substance use disorder, anxiety disorder and personality disorder have been constantly associated to an increased risk of suicide. International guidelines underline that substance use disorder in BD patients is related to a poorer course of illness and to an increased risk of suicide [11][15]. Even

analysing alcohol and other substances separately, authors found out that both categories were associated with suicide [4]. Furthermore, cigarette smoking (currently or lifetime) has been strongly correlated with suicidal behaviours [4]. Comorbidity with anxiety disorder is one of the most studied risk factors for suicide in BD patients. Considering different subtypes of anxiety disorders, generalized anxiety disorder, panic disorder and post-traumatic stress disorder turn out to be more common among suicide attempters. There are no such clear findings about agoraphobia and social phobia [4]. It is well known that a cluster B comorbid personality disorder is correlated with higher risk of suicide attempts, but there is a paucity of data concerning the relationship between other personality disorders and suicide [4]. Focusing on personality traits, levels of aggression and hostility were found to be significantly correlated with suicidal behaviours; findings about the effect of impulsivity are less clear and conducted to contradictory results. Other personality features associated with a history of suicide attempts in BD were: extreme attributional style, lower social skills or self-directedness, hopelessness and affect lability [2][4][5]. Hopelessness appears to be a multi-faceted construct, in which lack of positive future thinking would seem more relevant than the presence of negative future thinking. However, hopelessness could be also a consequence of a more severe BD and could predispose to suicide from that perspective [5]. Subjects with high affect lability present a greater risk of suicidal ideation. This may be linked to suicide by the perception of a lack of control on the mood and a greater fear of relapse [2]. Available data as regards temperaments show that cyclothymic, irritable, depressive and anxious affective temperaments are more frequent in attempters than in non-attempters, in contrast to hyperthymic temperament [4][10]. Moreover, some findings suggest a correlation between eating disorders and suicidal behaviours [4].

Current episode features
Episode polarity. Suicidal behaviours seem to be strongly correlated to major depressive episodes and mixed episodes (as classified in DSM-IV), compared to pure mania and euthymia. Less than 3% of all suicide attempts in individuals with BD occur during manic episodes [4].

Mixed features. The presence of mixed features during major depressive episode is another important suicide risk factor. Considering that mixed features are more likely to happen in BD than in unipolar depression, this may contribute to increase suicide rates in bipolar patients compared to unipolar [18]. Moreover, mixed depressive episodes are associated not only to a greater amount of suicide attempts, but also to an increase of suicide deaths [1][11][19] which could be explained by the phenomenon of antidepressant-induced suicidal behaviour [10].

Psychotic features. Data regarding a possible association between psychotic symptoms and suicidal behaviour are not clear. Some authors found that suicide attempters showed fewer psychotic symptoms, compared to non-attempters [18]. A possible explanation is that psychotic features might hinder the capacity to plan and perform suicide. Other studies found an association between history of psychosis during depression and an increased number of suicidal behaviours [10]; instead, others reported no differences [20]. Moreover, psychotic features seem not to be correlated to the lethality of suicide [4].

Atypical features. Atypical symptoms are more common in bipolar-II depression, compared to unipolar depression, ranging from 12% up to 60%. In some studies, individuals with atypical depression, both bipolar and unipolar, showed higher risk of suicidal behaviours [4,10].

Peripartum episodes. Even if women affected by BD present high rates of affective recurrences in the peripartum and particularly in post-partum period [21], there is no evidence that such period exposes BD patients to an increased risk of suicide.

Suicidal ideation. It has been highly correlated with suicide attempts and deaths [5,10]. Suicidal ideation presents a high prevalence in subjects with BD (up to 79% of major depressive episodes) and is itself a risk factor associated with suicide [10].

Treatment features

Some aspects related to the pharmacological treatment of BD should be considered when risk factors for suicide are analysed. Several studies underline that the risk of suicidal behaviour is higher in individuals treated with antidepressants (AD) as monotherapy and lower in those treated with mood-stabilizers as monotherapy [18]. It is well known that AD may induce manic switch; thus, McElroy and colleagues suggested that AD could be correlated with suicide by manic conversion in a subset of depressive presentations [5,22]. International guidelines indicate that treatment discontinuation exposes to high risk of relapse, recurrence and suicide [15].

Protective factors of suicide

There is a paucity of data regarding factors that could protect patients from suicidal behaviours in BD. International guidelines indicate that the use of lithium or anticonvulsants reduces the risk of suicide in BD [1,11,15,19]. Nonetheless data regarding the anti-suicidal effect of lithium mostly come from retrospective researches, thus more prospective studies are needed [4]. Despite the large use of others treatment in BD (atypical antipsychotics, psychotherapeutic approaches and electroconvulsive therapy), there is a lack of research about the relationship between these therapies and suicide [4]. The European Association guidance on suicide treatment and prevention underlines that some elements could be recognized as protective factors in the general population, such as cognitive flexibility, active coping strategies and healthy lifestyles (diet, sleeping schedule and physical exercise) [23]. Focusing on BD, only one study with a small sample found that having a good social network could be protective against suicide [24]. More research is needed to study this issue.

Conclusions

Aim of this review was to analyse, update and categorize data coming from literature and regarding risk factors for suicide in Bipolar Disorder. BD is a mood disorder characterised by periods of low mood (depressive episodes) and periods of elevated mood (ipo/manic episodes), with a prevalence of 2.4% in the general population[1]. Suicide represents the most fearsome complication of BD. The epidemiological rates of suicide attempts and deaths in BD are extremely high compared to the general population and other psychiatric conditions, underlining the need for a specific assessment of risk factors for suicide in BD patients. Many studies evaluate risk factors for suicide attempt and death in BD [3,4]; by using a systematic approach, we classified them into three categories: sociodemographic, biological and clinical factors.

Regarding sociodemographic elements, there is a strong evidence that female gender, younger age and psychosocial isolation (single, divorced and widowed individuals) are associated with a higher risk of suicide behaviours. However, despite women have a higher rate of suicide attempts, man frequently commit suicide by violent methods, resulting in a greater lethality of suicidal acts. There is a paucity of data about the role of religious affiliation and ethnicity in the contest of suicidal behaviours: more research is needed to explore these issues.

Data concerning biological factors are preliminary. At this time, it is not possible to highlight a specific correlation between genes or biomarkers and suicide attempts/deaths. Few genetic polymorphisms, neurobiological alterations and peripheral biomarkers abnormalities have been found to be correlated to suicide in preliminary studies; however, results require replications. In order to timely implement therapeutic interventions, the use of specific biological markers could help clinicians to promptly recognize individuals with a higher risk of suicide, even in the early stages of BD.

A lot of studies underline the importance of clinical factors in the assessment of suicide risk in BD. Among those, disorder features strongly related to suicidal behaviours are: early age of onset, family history of suicide/mood disorder, previous suicide attempts, rapid-cycling course, depressive polarity of the first affective episode and depressive predominant polarity, longer DUI, number of previous

episodes and some psychiatric comorbidities (substance use, anxiety and cluster B personality disorder). Further analysis is needed to clarify if specific bipolar disorder subtype, metabolic syndrome and comorbid eating disorder are associated to suicide. Current episode characteristics consistently linked to suicidal behaviours are: depressive episode polarity, mixed features and suicidal ideation, as well as can be expected. Even if the presence of psychotic and atypical features seems to be a possible risk factors for suicide, more research is necessary. Finally, using AD as monotherapy and interrupting the assumption of mood stabilizers are established risk factors for suicide in BD.

To date, the only verified protective factor for suicide that is consistently mentioned by literature is lithium therapy, due to the anti-suicidal effect that this treatment has proved to have.

Acknowledgements

References

1. Yatham LN, Kennedy SH, Parikh SV, et al. *Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) 2018 guidelines for the management of patients with bipolar disorder*. Bipolar Disord 2018;20:393-4.

2. Ducasse D, Jaussent I, Guillaume S, et al. *Affect lability predicts occurrence of suicidal ideation in bipolar patients: a two-year prospective study*. Acta Psychiatr Scand 2017;135:460-9.

3. Schaffer A, Isometsa ET, Tondo L, et al. *Epidemiology, neurobiology and pharmacological interventions related to suicide deaths and suicide attempts in bipolar disorder: part I of a report of the International Society for Bipolar Disorders Task Force on Suicide in Bipolar Disorder*. Aust N Z J Psychiatry 2015;49:785-802.

4. Schaffer A, Isometsa ET, Azorin JM, et al. *A review of factors associated with greater likelihood of suicide attempts and suicide deaths in bipolar disorder: part II of a report of the International Society for Bipolar Disorders Task Force on Suicide in Bipolar Disorder*. Aust N Z J Psychiatry 2015;491006-20.

5. Costa LDS, Alencar AP, Nascimento Neto PJ, et al. *Risk factors for suicide in bipolar disorder: a systematic review*. J Affect Disord 2014;237-54.

6. Ryu V, Jon DI, Cho HS, et al. *Initial depressive episodes affect the risk of suicide attempts in Korean patients with bipolar disorder*. Yonsei Med J 2010;51:641-7.

7. Das Neves Peixoto FS, de Sousa DF, Rodrigues Pereira Luz DC, et al. *Bipolarity and suicidal ideation in children and adolescents: a systematic review with metaanalysis*. Ann Gen Psychiatry 2017;16:22.

8. Weinstein SM, Van Meter A, Katz AC, et al. *Cognitive and family correlates of current suicidal ideation in children with bipolar disorder*. J Affect Disord 2015;173:15-21.

9. Neves FS, Malloy-Diniz LF, Correa H. *Suicidal behavior in bipolar disorder: what is the influence of psychiatric comorbidities?* J Clin Psychiatry 2009;70:13-8.

10. Gonda X, Pompili M, Serafini G, et al. *Suicidal behavior in bipolar disorder: epidemiology, characteristics and major risk factors*. J Affect Disord 2012;143:16-26.

11. *American Psychiatric Association: practice guideline for the treatment of patients with bipolar disorder (revision)*. Am J Psychiatry 2002;159:1-50.

12. Neves FS, Malloy-Diniz LF, Ma, et al. *Is the serotonin transporter polymorphism (5-HTTL-PR) a potential marker for suicidal behaviour in bipolar disorder patients?* J Affect Disord 2010;125:98-102.

13. Kamali M, Saunders EF, Prossin AR, et al. *Associations between suicide attempts and elevated bedtime salivary cortisol levels in bipolar disorder*. J Affect Disord 2012;136:350-8.

14. Rocca CC, Gerchmann L, Abreu LN, et al. *Lifetime history of suicide is associated with poorer social skills in patients with bipolar dosorder type I*. Braz J Psychiatry 2011;32:200-1.

15. Malhi GS, Bassett D, Boyce P, et al. *Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for mood disorders*. Aust N Z J Psychiatry 2015;49:1087-206.

16. Fagiolini A, Kupfer DJ, Rucci P, et al. *Suicide attempts and ideation in patients with bipolar I disorder*. J Clin Psychiatry 2004;65:509-14.

17. D'Ambrosio V, Salvi V, Bogetto F, et al. *Serum lipids, metabolic syndrome and lifetime suicide attempts in patients with bipolar disorder*. Prog Neuropsychopharmacol Biol Psychiatry 2012;37:136-40.

18. Seo HJ, Wang HR, Jun TY, et al. *Factors related to suicidal behavior in patients with bipolar disorder: the effect of mixed features on suicidality*. Gen Hosp Psychiatry 2016;39:91-6.

19. Grunze H, Vieta E, Goodwin GM, et al. *The World Federation of Societies of Biological Psychiatry (WFSBP) Guidelines for the Biological treatment of bipolar disorders: acute and longterm treatment of mixed states in bipolar disorder*. World J Biol Psychiatry 2018;19:2-58.

20. Johnson SL, McMurrich SL, Yates M. *Suicidality in bipolar I disorder*. Suicide Life Threat Behav 2005;35:681-9.

21. Maina G, Rosso G, Aguglia A, et al. *Recurrence rates of bipolar disorder during the postpartum period: a study on 276 medication-free Italian women*. Arch Women Ment Health 2014;17:367-72.

22. McElroy SL, Kotwal R, Kaneria R, et al. *Antidepressant and suicidal behavior in bipolar disorder*. Bipolar Disord 2006;8:596-617.

23. Wassermann D, Rihmer Z, Rujescu D, et al. *The European Association (EPA) guidance on suicide treatment and prevention*. Eur Psychiatry 2012;27:129-41.

24. Owen R, Gooding P, Dempsey R, et al. *A qualitative investigation into the relationships between social factors and suicidal thoughts and acts experienced by people with a bipolar disorder diagnosis*. J Affect Disord 2015;176:133-40.

R. Ciuffini[1,2], A. Marrelli[2], E. Perilli[1],
P. Stratta[3]

[1] Department of Life, Health and Environmental Sciences, University of L'Aquila, Italy;
[2] Clinical Neurophysiology Unit, Epilepsy Centre, San Salvatore Hospital, L'Aquila, Italy;
[3] Department of Mental Health, ASL1, L'Aquila, Italy

Epilepsy and suicide: a narrative review

Summary

The epilepsy represents a challenge for life expectancy and quality of life either for social and relational consequences due to stigma and for the consequences of the disorder itself. Suicidal behaviors are more frequent in the persons with epilepsy than in the general population. In addition to those shared with other chronic diseases, the condition of a person with epilepsy recognizes particular risk factors related to the clinical characteristics, demographic, socioeconomic and relational conditions. The frequent comorbidity with psychiatric disorders, first of all depression, complicates the clinical picture both because of neurobiological underpinnings underlying the two disorders and the negative interaction on the quality of life. The hopelessness is strongly correlated to suicidal ideation and its evaluation can be considered a relevant and reliable tool for measuring suicidal ideation. A careful evaluation of suicidal ideation, taking into account demographic and psychological conditions of patients, as well as clinical, social, economic situations, is warranted. The diagnosis and treatment of the disease has to take into account a bio-psycho-social approach that allows the integration of medical, psychological and social aspects.

Correspondence

Roberta Ciuffini
UO Neurofisiopatologia,
Ospedale "San Salvatore",
67010 Coppito (L'Aquila), Italy
• Tel./Fax + 39 0862 368777
• E-mail: roberta.ciuffini@univaq.it

The epilepsy burden

The epilepsy affects the quality and expectations of life, with existential repercussions, both for the clinical characteristics and for the social consequences of the disease [1]. The impact of epilepsy is multiform. The unpredictability and the danger of seizures increase the risk of trauma, hospitalization and mortality and frequently alter the mental health of the person resulting in anxiety, depression, cognitive disorders. Seizures also involve stigma, marginalization and social exclusion with negative effects on self-confidence and self-esteem. However, the weight of epilepsy extends beyond the effects of seizures [2]: as a matter of facts epilepsy is more than just seizures. All multiple and interacting medical, psychological, economic and social repercussions must be considered to fully understand the impact of the disease. The psychosocial impact and stigma surrounding epilepsy can contribute to the increased risk of unnatural death. In addition, treatment with anti-epileptic drugs is often associated with side effects that further impairs quality of life.

The epilepsy and the suicide

In comparison with people without epilepsy, those with epilepsy present a 2 to 3 times greater risk of unnatural death and should be adequately warned about the prevention of trauma and monitored for suicidal thoughts and behaviors. Numerous epidemiological data point to a link between epilepsy and suicide. Andrijc et al. [3] report the presence of suicidal ideation and thoughts of death in 38% of epileptic patients. Tellez-Zenteno et al. [4] showed a twice higher prevalence of suicidal ideation in persons with epilepsy than controls. Christensen et al. [5] found a suicide risk three times higher than controls.

Suicide is a global health problem and includes a wide range of self-aggressive behaviors including complete suicides, suicide attempts and suicidal ideation. In addition to suicides and suicide attempts, ignored, disguised, hidden, sub intentional suicides and suicidal equivalents have also to be taken into account. Suicidal ideation is a medical term that indicates thoughts, desires and plans to commit suicide and can range from passive ideas to ideas with detailed plans and intent to commit suicide.

We report a narrative review of literature on studies on suicidal behaviors in persons with epilepsy.

Suicidal risks factors

In the general population, suicide risk is higher in the presence of certain demographic, psychopathological and socioeconomic factors [6]. The older males, the singles, immigrants, the unemployed, the Protestants, middle-upper classes, residents in urban areas, the socially and emotionally isolated, chronic pain sufferers seem to be more predisposed [7]. Seasonal variables (spring, summer) the presence of severe frustrations (sentimental disappointments, death of relatives, economic losses, changes in social role and working activity) may be triggering factors [8]. Many psychopathological, psychodynamic, socio-economic and cultural factors contribute to the ethology of suicide. In terms of psychopathological substrate, psychiatric symptoms (especially depressive symptoms, less psychotic or otherwise) are frequent [9].

The diagnosis of "suicide risk" or rather the risk assessment of self-aggressive behavior is based on: history (suicide familiarity, previous attempts, childhood affective deficiencies or neglect, family problems), general and biological data (age, chronic painful and/or incurable diseases, puberty, puerperium, involution and climate), psychopathological data (depressive syndromes, personality traits, anxiety symptoms, guilt feelings, self-accusation, alcoholism and drug addiction), subjective statements (general or explicit boredom for life, statements, projects or structured resolutions, preparations), socio-economic, interpersonal and family conditions (loss of emotional, economic, social balances). Efforts to identify the so-called "suicidal syndrome" have failed and, as a result, the recognition of suicidal potential is based on the empathic abilities and diagnostic insights of the physician. In view of the lack of "tests based on evidence" many risk factors have been considered, especially in aggregation between them, but the translation from studies on groups to the individual may hesitate in a high percentage of false positives and false negatives. Poor validity and reliability in the prediction of suicide may also depend on the rarity of suicidal events as well as the complexity of clinical,

psychological, cultural and environmental variables. The history of previous suicide attempts seems to be the strongest predictor of a successful future suicide [10]. Psychosocial factors include stigma [11], fear of crises, discrimination, job loss, lack of support. Psychopathological factors such as mood disorders, cognitive flexibility, inhibitory control, personality traits, alterations in problem solving abilities may increase the suicidal risk. Most of these risk factors are relevant for persons with epilepsy too [12]. The suicidal risk was found higher at the onset of the disease, in the first six months immediately after diagnosis and more frequently in adolescents [13]. The location of the epileptogenic focus in the temporal lobe, the rate of seizures, surgical therapy, psychiatric comorbidity and personality disorders [14], the history of suicide attempts, depression and substance abuse in family members [15] appear to play a significant role in increasing the risk of suicide. Anti-epileptic drugs, especially those with a GABAergic mechanism of action, appear to increase the presence of suicidal ideation at the beginning of treatment. Based on analysis of randomized controlled studies of 11 anti-epileptic drugs [16], the Food and Drugs Administration issued an alert regarding a double risk of suicidal events (behavior and ideation) in patients treated with anti-epileptic drugs compared to placebo. The risk appears to be more relevant right after the start of treatment, for about two weeks and appears to be independent of the type of medication used. However, meta-analysis studies suffer from the lack of a standardized definition of suicidal behavior and ideation. The real impact on suicide of anti-epileptic drugs as an independent factor remains uncertain [17].

The psychiatric comorbidity in persons with epilepsy

Individuals with epilepsy are more likely to develop psychiatric comorbidity and this comorbidity is strongly related to the negative impact on the subjective state of health and quality of life. The greater tendency to suicide during epilepsy was often justified by the fact that it is the impaired quality of life of the person with epilepsy that makes him more prone to depressive disorders and, therefore to suicidal ideation and behaviors. As a matter of fact, 6% of the people with epilepsy also suffers from a psychiatric disorder [18]. The percentage rises to 10-20% in the case of temporal epilepsy and drug resistant epilepsy. The most common disorders are mood disorders (24-74%), especially depression (30%), followed by anxiety disorders (10-25%), psychosis (2-7%) and personality disorders (1-2%). This comorbidity is linked to endogenous and exogenous factors (including iatrogenic ones) and to the severity and chronicity of epilepsy. Psychiatric disorders comorbidity may precede,

be concomitant or follow the diagnosis of epilepsy. With respect to the seizures can be inter-ictal, ictal, postictal. Epilepsy is a chronic disease that alters social function, so that one could conclude that depression in epileptics is simply reactive or situational but the association may underlie the sharing or contribution of genetic and environmental common pathogenic mechanisms. However, the prevalence of depression in epilepsy is higher than in other chronic diseases of similar severity. For example, a population-based study of 181,000 individuals [19] found a prevalence of depression in epilepsy of 29%, compared to 17% in diabetes, 16% in asthma, 8.7% in other chronic diseases. Furthermore, not only is epilepsy a risk factor for depression, but depression can be a risk factor for epilepsy. In a case/control study in patients with new diagnosis of epilepsy a history of depression prior to seizures was found in epileptics, seven times greater than controls [20]. Neurological factors, including the site and lateralization of the epileptogenic focus may be important for the development of depression [21]. They include features of epilepsy that involve limbic structures and produce mood changes. Forced normalization [22] may be a paradoxical factor in the development of depression in those persons in whom seizures become abruptly well controlled by therapy. Based on these data, the role of "auto convulsive therapy" against depression or an excess of post-critical electrophysiological inhibition involving dopaminergic neurotransmitter systems have been hypothesized. Chronic subclinical limbic and para limbic seizures were believed to contribute to the genesis of affective disorders [23]. Also lowering the level of folic acid due to anti-epileptic drugs can influence the expression of depression in persons with epilepsy.

Inter-ictal depression is more common in focal and especially temporal lobe epilepsy. The association is based on the structural and functional relationships between the temporal regions that mediate the emotions and the frontal areas. Results of neuropsychological studies [24] and SPECT findings of reduced metabolism in bilateral lower frontal areas in persons with temporal lobe epilepsy and depression suggest that the development of frontal dysfunction is a necessary component in the genesis of depression in temporal lobe epileptic patients [25]. In the temporal lobe epilepsy, the limbic epileptogenic areas, such as amygdala, are involved in social behavior, including impulse control, anxiety, emotional memory [26]. Subjects with suicidal behavior often have problems with cognitive inhibition [27] and serotonin projection abnormalities to the prefrontal cortex.

A possible link between epilepsy, impulsivity, suicide and depression is possible. It has been proposed [28] that the neurophysiological substratum of seizures may predispose to a state of neuronal hyper excitability respon-sible for the impulsiveness in epilepsy. Persons with epilepsy are four times more likely to have attempted suicide before having seizures [29].

The tendency to suicide and depression cannot simply be a consequence of the poor quality of life of the persons with epilepsy and seem to indicate the role of common mechanisms underlying suicidal and epilepsy behavior. Conversely depression and suicide could be related to different mechanisms.

Hopelessness as risk factor for suicidal ideation

The hopelessness, defined as a set of cognitive patterns leading to negative life expectancy, is an aspect of demoralization and this is a relevant risk factor for self-injurious and suicidal behavior, especially at a young age. Beck's Hopelessness Scale (BHS) [30] consisting of twenty items, self-administered, multidimensional, originally developed and validated in 294 patients who attempted suicide has proven to be a valuable and reliable tool for measuring suicidal risk. It measures the predisposition of persons with various mental disorders to suicidal behavior. Studies on the structure of BHS have identified three main factors of evaluation: 1) feelings towards the future, 2) loss of motivation, 3) future expectations. The long-term predictive sensitivity of BHS suggests that hopelessness is a relatively stable trait in patients who are developing a suicide risk. Further evidence indicates that hopelessness is a useful variable in determining the possibility of long-term suicide by adding credibility to the hypothesis that it is helpful in predicting suicidal risk regardless from the measures of depression [31]. In this case the role of emotional dysregulation must also be considered. Studies on the relationship between negative emotions and suicide, considering hopelessness as a risk factor for both ideation and suicidal behavior [32] are needed. Although the correlation between hopelessness and suicide is relatively high, it is not always related to actual suicidal behavior, but it may be present in people who will never attempt suicide in their lives as well as be absent in those who do.

Hopelessness as a link between epilepsy and suicidal behaviors

Suicide and epilepsy have been hypothesized to share common neuro-physio-pathological mechanisms [33] that may explain the increased risk of suicide. The relationship between suicidality and epilepsy is complex, multifactorial and bi-directional. Not only do people with epilepsy present a higher risk of suicide, but, conversely, population-based studies show a five-fold greater risk of developing epilepsy among persons who experienced suicidal behavior prior to the onset of epilepsy [34].

The risk seems independent from the history of depressive disorder. Population-based studies [35] found that people with a history of depression are four to seven times more likely to develop epilepsy. These data were explained by a common abnormal brain serotonin activity [36]. Epilepsy and depression may both be symptoms of superimposable neuronal network dysfunction (limbic regions). Christensen et al. [5] show that the risk of suicide in epileptics is 14 times higher in the presence of psychiatric comorbidity, particularly depressive disorders (32 times) and anxiety disorders (14 times). Kanner et al. [37] reported the frequency of post-critical suicidal ideation also in relation to post-stroke psychotic episodes. Increased risk 6 to 25-fold was reported to be associated with temporal lobe epilepsy [38].

Evaluation of Hopelessness by BHS may complement the clinical approach to the epileptic patient [39]. The level of hopelessness may have predictive value for significant suicidal ideation in epileptic patients. Andrjic et al. [3] found that suicidal ideation in persons with epilepsy is independently and significantly related to the level of hopelessness and unemployment as an important psychosocial factor.

In a recent study our research group investigated the association of hopelessness with demographic, social and clinical variables, in people with epilepsy without comorbidity with psychiatric disorders (Tab. I) [40].

Four of the variables studied, such as temporal lobe localization, more frequent seizures rate, higher intellectual level, low socio-economical level, significantly predicted the Hopelessness evaluation. These results can be considered in agreement with the recent observation of the dissociation between function and cognitive performance, showing people with suicidal ideation worse functioning but with higher cognitive performance. It may suggest that high intelligence cannot be seen by physicians as a protective factor from

suicidal ideation [41]. High intellectual level could be related to higher insight of having a severe illness, above all if the seizures are very frequent and polypharmacy is needed. So, a better insight can paradoxically not lead to an advantage but can be related to depression and hopelessness eventually. This is also the case of a severe mental illness, such as schizophrenia, where the so-called 'insight paradox' is related to depression, including demoralization, decreased self-esteem, hopelessness and suicidal ideation [42]. Although several studies indicate that hopelessness is well conceptualized as a risk factor for suicide ideation, this does not mean that it is able to distinguish attempters from ideators, i.e. the progression from ideation to attempt [43]. As a matter of fact, suicidal ideation is not directly linked to the real suicidal behavior. It can be present in people that will never attempt to their life and lack in those who really commit suicides; hopelessness has not been found as a strong predictor of suicide risk, as previously imagined [44]. Furthermore, recent systematic literature researches on suicide prediction models have shown a very limited accuracy of prediction and practical utility [45].

Although speculatively, if hopelessness, along Beck's formulation can be considered as a link between depression and suicide [46], it can at least be hypothesized as link between epilepsy and suicidal ideation. These warning flags for suicidal ideation need to be coped with a complex bio-psycho-social approach [47].

Suicidal behaviors in persons with epilepsy: which interventions?

The management of the person with epilepsy, even more if suicidal ideation has been shown, is complex. The pharmacological treatment itself could become a possible risk factor for the suicide, both in relation to the timing (at the beginning or when changes in therapy are done) and related to pharmacodynamics. Possible cognitive adverse effects that may affect the socio-relational status and quality of life of the patient, should be carefully assessed. The drug resistance decreases the patient's compliance and leads to a worsening of the psychic state with accentuation of the tendency to self-injurious behaviors. Alternative treatments, such as ketogenic diet, also lead to less motivation and adherence to prescription. Surgical treatment, although directed to the etiological causes of epilepsy, is conditioned by the motivation and collaboration of the patient. In addition, the phenomenon of forced normalization with depressive reactions, even of a severe degree, is described for both pharmacological and surgical therapy. Psychiatric comorbidity, mostly with anxiety and depression, but not infrequently with personality disorders and with psychosis, requires attention especially with regard to

TABLE I. *Risk factors for suicide behavior found associated with higher Beck Hopelessness Scale score in persons with epilepsy without psychiatric comorbidity* [40].

Demographic	Clinical	Socio-cultural
Female gender	Right side	High intellectual level
Young age	Temporal focus	Low socio-economic level
	Higher seizure frequency	
	Disease at onset	
	Higher number of drugs	

drug combinations so as to avoid negative interference on the effectiveness of both the treatment of seizures and of the psychopathological symptoms. Alternative techniques to drug therapy such as neuromodulation can be considered as useful therapeutic tools in people with epilepsy, even more so if with depressive psychiatric comorbidity. PET studies in people with epilepsy undergoing vagus nerve stimulation (VNS) have shown a relative activation of areas associated with depression (prefrontal dorsolateral cortex, insula, orbitofrontal cortex, cingulated gyrus) [48]. The proposed mechanisms for the effectiveness of the VNS are the induction of neuron plasticity at the level of the hippocampus [49] and the stimulation of serotonin and noradrenergic systems [50]. The results of an observational study of 4.5 years in depressed patients resistant to drug therapy treated with VNS confirmed its effectiveness [51]. Likewise, in patients with epilepsy the treatment can be considered.

The diagnosis and treatment of epilepsy are difficult to accept. Once the therapeutic process is started, psychosocial problems, which are the cause of mainly anxious and depressive disorders, often become relevant. Seizures have an extremely traumatic impact due to their sudden character. Anxious symptoms can sometimes become so overwhelming that they require psychotherapeutic intervention. It is necessary to share the patient will into the decision-making process for each stage of disease management through appropriate empowerment, or an interactive process between subject and environment suitable for improving health and well-being. A good level of empowerment allows the person with epilepsy to develop tools, safety and knowledge to interact functionally with the environment and improve the health by moving from a passive to active condition. Cognitive impairment should be evaluated in order to monitor the patient's ability to understand his condition and to implement appropriate tools both for the individual wellness and for his or her family and social context. Epilepsy punctuates everyday life and requires adaptation to the new condition. So it is necessary to remodel habits and expectations about the future, reformulate its own identity and the social role.

For many years, research has shown how in people suffering from chronic diseases, the incidence of psychopathological conditions is frequent. This not only leads to a significant deterioration in the quality of life of the patient, but also affects adherence to care. The emotional, cognitive and behavioral responses to the marked existential changes imposed by a chronic illness could be relevant. These can be expressed in various forms of psychic suffering, some of which assume the characteristics of true psychopathological pictures. Often, those who experience a disease such as epilepsy manifest depression, anxiety, high stress that make it more difficult to cope with the new condition of life and the course of illness. The psychological management in epilepsy consists in a first phase of assessment of the subject's difficulties and resources and in planning appropriate strategies [52]. The psychological approach must necessarily consider the patient and its family as well as the environmental context. It is not easy to consider the perception that the patient has of his clinical condition, of his experience, of the whole family, of the possible stigma [53]. The epilepsy cannot only involve a risk in terms of cognitive functions but also emotional and behavioral. Both overprotection and the tendency to hide the diagnosis in the family and in the social environment could worsen the burden of epilepsy. The seizures restrict the autonomy and the chance of social integration. The social discriminations born from the fear not to know whether to do during a seizure. The psychological support is recommended at the onset of the disease. The so-called baseline from which to take the movements to check during time the functions such as attention, memory and language is needed. Difficulty of adaptation and the emotional impairment can be present at the diagnosis. It is opportune to repeat the psychological evaluation in the time, particularly during the evolutionary passages with the purpose to foresee the therapies and the necessary supports.

The psychological support is always suitable: it promotes the mechanisms of reinforcement and adaptation, it favors the adherence to the therapies and the indications of the referent neurologist, it reduces the fears and the imaginations of death tied to the seizures. It protects from the isolation and from emotional troubles. A qualitative observation and a detailed interview about cognitive and behavioral changes can result useful during the modifications of the rate of the seizures or during the variations of the therapy with the purpose to contribute to future decisions on the pharmacological and psychological treatments. From a first evaluation suitable psychological interventions will can emerge, such as support or cognitive-behavioral therapies. Focus groups and the empowerment projects could improve the management of the illness. The comparison with the group promotes personal strategies of psychological adaptation, coping and resilience, the ability to react to difficulties. The crucial problem for persons with epilepsy is to live with a chronic disease that damages autonomy, implies the fear of being alone, about the future and acceptance by others. Talking about it transforms the group into an instrument of protection, awareness and information and makes person's life more reassuring.

Conclusions

The link between epilepsy and increased risk of suicide is evident. Either neurobiological factors related to the

site of the epileptogenic outbreak and neurotransmitters alterations as well as psychiatric comorbidity, social consequences of the illness, its unpredictable course, the incapacity resulting from the seizures and the stigma, play an important role in the patient's quality of life and in possible self-harm and suicide drifts.

This is a narrative review on the relationship between epilepsy and suicide. This kind of review presents limitations due to a lack of systematic methods in literature selections. Being the number of sources employed incomplete, a possible risk is that of having a limited knowledge base from which to draw conclusions. Although taking into account this non-negligible pitfall, this narrative review summarizes primary studies from which conclusions can be drawn into a holistic interpretation contributed by relevant existing theories and models.

On the basis of the observations we report, the need of development of collaborations between physicians treating patients with epilepsy with mental health professionals is warranted in order to provide comprehensive treatment for persons at suicide risk. This partnership between neurologists, epilepsy specialists, psychiatrists, as well as other mental health professionals can allow for the development of suicide prevention programs, preventing the loss of life and improving the quality of life.

Disclosure of conflicts of interest

None of the authors has any conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

References

1. Kerr MP. *The impact of epilepsy on patients' lives*. Acta Neurol Scand Suppl 2012;194:1-9.

2. Forsgren L, Nystrom L. *An incident case-referent study of epileptic seizures in adults.* Epilepsy Res 1990;6:66-81.

3. Andrijić NL, Alajbegović A, Zec SL, et al. *Suicidal ideation and thoughts of death in epilepsy patients.* Psychiatr Danub 2014:26:52-5.

4. Téllez-zenteno JF, Dhar R, Hernandez-Ronquillo, et al. *Long-term outcomes in epilepsy surgery: antiepileptic drugs, mortality, cognitive and psychosocial aspects.* Brain 2007;130:334-45.

5. Christensen J, Vestergaard M, Mortensen, et al. *Epilepsy and risk of suicide: a population-based case-control study.* Lancet Neurol 2007;6:693-8.

6. Moscicki EK. *Identification of suicide risk using epidemiologic studies.* Psychiat Clin North Am 1997;20:499-517.

7. Large MM. *The role of prediction in suicide prevention.* Dialogues Clin Neurosci 2018;20:197-205.

8. GBD 2016 Epilepsy Collaborators. *Global, regional, and national burden of epilepsy, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016*. Lancet Neurol 2019;18:357-75.

9. Nilsson L, Ahlbom A, Farahmand BY, et al. *Risk factors for suicide in epilepsy: a case control study.* Epilepsia 2002;43:644-51.

10. Posner K, Melvin GA, Stanley B, et al. *Factors in the assessment of suicidality in youth.* CNS Spectr 2007;12:156-62.

11. Boling W, Means M, Fletcher A. *Quality of life and stigma in epilepsy, perspectives from selected Regions of Asia and Sub-Saharan Africa*. Brain Sci.2018;8. pii: E59.

12. Hecimovc H, Popovic Z. *Risk factors for suicide in epilepsy patients.* Future Neurol 2014;9-5:553-61.

13. Verrotti A, Cicconetti A, Scorrano B, et al. *Epilepsy and suicide: pathogenesis, risk factors and prevention*. Neuropsychiatr DisTreat 2008;4:365-70.

14. O'Connor RC, Portzky G. *Looking to the future: a synthesis of new developments in suicide research and prevention.* Front Psychol 2018;9:2139.

15. Liu RT. *The psychological scars of suicide: accounting for how risk for suicidal behavior is heightened by its past occurrence*. Neurosci Biobehav Rev 2019;99:42-8.

16. Hesdorffer DC, Kanner AM. *The FDA alert on suicidality and anti-epileptic drugs: fire or false alarm.* Epilepsia 2009;50:978-86.

17. Machado RA, Espinosa AG, Melendrez D, et al. *Suicidal risk and suicide attempts in people treated with antiepileptic drugs for epilepsy.* Seizure 2011;20:280-4.

18. Gaitatzis A, Trimble MR, Sander JW. *The Psychiatric comorbidity of epilepsy.* Acta Neurol Scand 2004;110:207-20.

19. Blum D, Reed M, Metz A. *Prevalence of major affective disorders and manic/hypomanic symptoms in persons with epilepsy: a community survey.* Neurology 2002;(Suppl 3):A-175.

20. Harden CL, Goldstein MA. *mood disorders in patients with epilepsy.* CNS drugs 2002;16:291-302.

21. De Oliveira GMN, Kummer A, Salgado JV, et al. *Suicidality in temporal lobe epilepsy: measuring the weight of impulsivity and depression.* Epilepsy Behav 2011;22:745-9.

22. Landolt H. *Some clinical electroencephalographical correlations in epileptic psychoses (twilight status).* Electroencephalogr Clin Neurophysiol 1953;5:121.

23. Raust A, Slama F, Mathieu F, et al. *Prefrontal cortex dysfunction in patients with suicidal behavior.* Psychol Med 2007;37:411-9.

24. Oquendo MA, Placidi GP, Malone KM, et al. *Positron emission tomography of regional brain metabolic responses to serotoninergic challenge and lethality of suicide attempts in major depression.* Arch Gen Psychiatry 2003;60:14-22.

25. Steiger BK, Jokeit H. *Why epilepsy challenges social life.* Seizure 2017;44:194-8.

26. Hesdorffer DC, Hauser WA, Ludvigsson P, et al. *Depression and suicide attempt as risk factor for incident unprovoked seizures*. Ann Neurol 2006;59:35-41.

27. Herman BP, Seidenberg M, Haltiner A, et al. *Mood state in unilateral temporal lobe epilepsy.* Biol Psychiatry 1990,30:1205-18.

28. Bromfield EB, Alshuler I, Leiderman DB, et al. *Cerebral metabolism and depression in patients with complex partial seizures.* Arch Neurol 1992;49:617-23.

29. Barrat ES, Stanford MS, Felthous AR, et al. *The effect of phenytoin on impulsive and premeditated arression: a controlled study.* J Clin Psychopharmacol 1997;17:341-9.

30. Beck AT, Steer RA, Kovacs M, et al. *Hopelessness and eventual suicide: a 10-year prospective study of patients hospitalized with suicidal ideation*. Am J Psychiatry 1985;142:559-63.

31. Innamorati M, Lester D, Balsamo M, et al. *Factor validity of the Beck Hopelessness Scale in Italian medical patients.* J Psychopathol Behav Ass 2014;36:300-7.

32   Kanner AM. *Suicidality and epilepsy: a complex relationship that remains misunderstood and underestimated.* Epilepsy Cure 2009;9:63-6.

33   Ribeiro JD, Huang X, Fox KR, et al. *Depression and hopelessness as risk factors for suicide ideation, attempts and death: meta-analysis of longitudinal studies.* Br J Psychiatry 2018;212:279-86.

34   Kanner AM *Epilepsy, suicidal behavior and depression: do they share common Pathogenic mechanisms.* Lancet Neurol 2006;5:107-8.

35   Jones JE, Hermann BP, Barry JJ, et al. *Rates and risk factors for suicide, suicidal ideation, and suicide attempts in chronic epilepsy.* Epilepsy 2003;4:S31-8.

36   Goddard GV, McIntyre DC, Leech CK. *A permanent change in brain function resulting from electrical stimulation.* Exp Neurol 1969;25:296-30.

37   Kanner AM, Sotp A, Gross-Kanner H. *Prevalence and clinical characteristics of post-ictal psychiatric symptoms in partial epilepsy.* Neurology 2004;62:708-13.

38   Currie S, Heathfield KW, Henson RA, Scott DF. *Clinical course and prognosis of temporal lobe epilepsy: a survey of 666 patients.* Brain 1971;94:173-90.

39   Kao YC, Liu YP, Lu CW. *Beck Hopelessness Scale: exploring its dimensionality in patients with schizophrenia.* Psichiatr Q 2012;83:241-55.

40   Ciuffini R, Stratta P, Perilli E. et al. *Hopelessness in persons with epilepsy: relationship with demographic, clinical and social variables.* Epilepsy Behav 2019 (in press).

41   Barzilay R, Calkins ME, Moore TM, et al. *Neurocognitive functioning in community youth with suicidal ideation: gender and pubertal effects.* Br J Psychiatry 2019;28:1-7.

42   Lysaker PH, Pattison ML, Leonhardt BL, et al. *Insight in schizophrenia spectrum disorders: relationship with behavior, mood and perceived quality of life, underlying causes and emerging treatments.* World Psychiatry 2018;17:12-23.

43   Qiu T, Klonsky ED, Klein DN. *Hopelessness predicts suicide ideation but not attempts: a 10-year longitudinal study.* Suicide Life Threat Behav 2017;47:718-22.

44   Beck AT, Ward CH, Mendelson M, et al. *An inventory for measuring depression.* Arch Gen Psychiatry 1961;4:561-71.

45   Bradley E Belsher, Derek J et al. *Prediction models for suicide attempts and deaths: a systematic review and simulation.* JAMA Psychiatry 2019; Mar 13. [Epub ahead of print]

46   Miller JM, Kustra RP, Voong A, et al. *Depression symptoms in epilepsy: prevalence, impact, etiology, biological correlates and effect of treatment with antiepileptic drugs.* Drugs 2008;68:1493-509.

47   Engel GL. *The need for a new medical model: a challenge for biomedicine.* Science 1977;196:129-36.

48   Henry TR1, Bakay RA, Pennell PB, et Al. *Brain blood-flow alterations induced by therapeutic vagus nerve stimulation in partial epilepsy: II. Prolonged effects at high and low levels of stimulation.* Epilepsia, 2004;45:1064-70.

49   Biggio F1, Gorini G, Utzeri C, et al. *Chronic vagus nerve stimulation induces neuronal plasticity in the rat hippocampus.* Int J Neuropsychopharmacol 2009;12:1209-21.

50   Manta S, Dong J, Debonnel G, et al. *Enhancement of the function of rat serotonin and norepinephrine neurons by sustained vagus nerve stimulation.* J Psychiatry Neurosci 2009;34:272-80.

51   Aaronson ST, Sears P, Ruvuna F, et al. A 5-Year *Observational study of patients with treatment-resistant depression treated with vagus nerve stimulation or treatment as usual: comparison of response, remission, and suicidality.* Am J Psychiatry 2017;174:640-8.

52   Cull C, Goldstein LH, ed. *The clinical Psychologist's handbook of epilepsy: assessment and management.* 1st ed. New York, NY: Routledge 1997.

53   Ramaratnam S, Baker GA, Goldstein LH, Ed. *Psychological treatments for epilepsy.* Cochrane Database Syst Rev 2008:CD002029.

Dissociation in stress-related disorders and self-harm: a review of the literature and a systematic review of mediation models

R. Rossi[1], L. Longo[1,2], D. Fiore[3],
A. Carcione[3], C. Niolu[1,2],
A. Siracusano[1,2], G. Di Lorenzo[1,2]

[1] Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy; [2] Psychiatry and Clinical Psychology Unit, Fondazione Policlinico Tor Vergata, Rome, Italy; [3] Third Centre of Cognitive Psychotherapy. Italian School of Cognitive Psychotherapy (SITCC), Rome, Italy

Summary

Traumatic experiences are a risk factor for suicide and non-suicide self-injury. However, it has been hypothesized that the relation between trauma and self-harm is not a direct one, rather it is mediated by dissociation. The scope of this work is to review advances in psychopathology and pathophysiology of dissociation and its role in the context of stress-related disorders. Furthermore, a systematic review on the mediating role of dissociation between trauma and self-harm has been carried out. The systematic review confirms robust evidence of a mediating role of dissociation between trauma and non-suicidal self-injury; suicidal ideation and complete suicide as outcomes have not been addressed in the literature and need further assessment.

Introduction

Traumatic experiences (TE), especially those occurring in childhood, are a major risk factor for poor general and mental health [1], involving a vast array of psychological adverse outcomes ranging from sub-threshold post-traumatic symptoms to impaired global functioning, severe persistent psychiatric and physical morbidity [2] and increased risk of self-harm [3]. Furthermore, TE represent a serious concern for global health not only because of its direct consequences on mental health, but also because TE are an established risk factor for further violent behaviors [4], creating an epidemic-like spread of violence known as "violence cycle".

Among the long-term adverse outcomes of TE, self-harm is the most concerning one. A broad definition of self-harm includes on the one hand suicidality, that is an act (complete suicide), an attempt (suicide attempt) or the thought of (suicidal ideation) intentionally causing the death of the person, and on the other hand non-suicidal self-injury (NSSI) which is instead an intentional act pointed either at regulating emotional states or at serving interpersonal communication functions. NSSI may include self-destructive and reckless behaviors as well, such as reckless driving, risky behaviors, sexual promiscuity, gambling and substance abuse [5].

The psychopathological pathways leading from TE to self-harm are complex and depend on a number of pre-existing moderating factors, including personality trait, resiliency [6], the age of the victim, duration of victimization, and on a number of different intermediate psychological constructs that mediate the effect of the traumatic experience on the outcome.

Among such intermediate psychological factors, dissociation is currently considered one of the most important mediating variables between TE and self-harm. The present review summarizes the most recent evidence on dissociation as a mediator between TE and self-harm. Firstly, the most

Correspondence

Giorgio Di Lorenzo
Department of Systems Medicine,
University of Rome Tor Vergata
via Montpellier 1, 00133 Rome, Italy
• E-mail: di.lorenzo@med.uniroma2.it.

recent advances in psychopathology and pathophysiology of dissociation will be examined, secondly the role of dissociation in the context of stress-related disorders will be reviewed, finally we will systematically review evidence of dissociation mediating the effects of trauma on self-harm.

Dissociation

DSM-5 defines dissociation as "disruption of and/or discontinuity in the normal integration of consciousness, memory, identity, emotion, perception, body representation, motor control, and behavior"[7].

Dalemberg[8] have further defined dissociation as:

"(a) a loss of continuity in subjective experience with accompanying involuntary and unwanted intrusions into aware-ness and behavior (so-called positive dissociation); and/or (b) an inability to access information or control mental functions, manifested as symptoms such as gaps in awareness, memory, or self-identification, that are normally amenable to such access/control (so-called negative dissociation); and/or (c) a sense of experiential dis-connectedness that may include perceptual distortions about the self or the environment."

The first studies on dissociation date back to the early work of Pierre Janet at the beginning of the XX century. Janet[9] proposed that dissociation regarded a lack of integration among "systems of ideas and functions that constitute personality", suggesting that dissociative symptoms were the expression of an impaired integrative capacity of the consciousness, that would eventually lead to an inability to integrate experiences and to develop a coherent representation of the self and reality as is, hindering adaptive and self-regulating behaviors. Dissociation is more commonly associated with the integrative function, dissociative symptoms are more frequently regarded of as disorders of consciousness. However since its first descriptions in Janet's work it was clear that dissociation concerned different instances of personality, thus affecting the psychic life of an individual in a rather radical way beyond discrete mental states (see below).

The strong presence of dissociation in contemporary psychopathology is mainly due to its transdiagnostic aspects: dissociative symptoms can be conceptualized along a continuum that goes from normal dissociative phenomena, for example while driving, daydreaming, or while being absorbed in an intellectual activity, to dissociative disorders, i.e. depersonalization/derealization disorder, dissociative amnesia and dissociative identity disorder. Between the two extremes of the dissociative spectrum, dissociative symptoms occur in several mental disorders: first and foremost in stress-related disorders[10][11] and personality disorders[12], but dissociative symptoms may also occur in schizophrenia, affective disorders, obsessive-compulsive disorders and somatoform disorders[13].

Classification

Dissociation is generally considered to be a multidimensional phenomenon with different phenotypes, including disengagement, emotional constriction, amnesia, depersonalization, derealization and identity dissociation[14]. However, current research on dissociative symptoms divides them into two main groups: compartmentalization and detachment symptoms[15].

Compartmentalization[16] refers to lack of integration between psychological processes with a partial inability to control or monitor mental processes that normally would be under one own's will control. It is assumed that such mental processes, while not being under one's voluntary control, still continue to operate relatively normally and influence implicitly one's psychic life. Compartmentalization symptoms include dissociative amnesia and conversion disorders.

Detachment refers to an altered state of consciousness experienced as "alienation" of oneself or the external world. During a detached state, an absence or flattening of emotions can be experienced. Detachment is the basis of derealization/depersonalization and numbing, as well as other unusual phenomena such as out-of-body experiences[16]. Subjects experience detachment as an altered state of consciousness characterized by a sense of *separation* from certain aspects of everyday experience, including their body (as in out-of-body experiences), their self (as in depersonalization), or the external world (as in derealization).

Pathophysiology

(for an extensive review see Lanius et al.[17])

The pathophysiology of dissociative symptoms is largely derived from studies on stress-related disorders and, to a lesser extent on personality disorders. Theories explaining the pathophysiology of dissociation are based on the assumption that dissociation is the expression of a complex of neural mechanisms activated by fearful stimuli. One interesting model is the undermodulation/overmodulation one[17][18]. This model derives from the evidence of the coexistence in the dissociative subtype of PTSD of detachment states and emotional dysregulation states. Overmodulation implies states of detachment and derealization, while undermodulation would disinhibit emotional responses leading to emotional dysregulation. Individuals with dissociative PTSD cycle between these two states. Centromedial amygdala (CMA) and basolateral amygdala (BLA) complexes have been involved in these mechanisms, as central modulators of fear processing receiving top-down inhibitory control from the mPFC and starting fear reaction via projections to different mid-brain structures. In the mid-brain, the

periaqueductal gray (PAG) is in turn responsible for the autonomic responses that characterize both overmodulated and undermodulated dissociative fear reactions. Traumatic experiences are core elements of dissociative symptoms. Trauma and dissociation determine, however, structural abnormalities that may have different clinical correlates in under or overmodulated phenotypes, with predominant PTSD or dissociative symptoms [19]. It has been proposed that such alterations may be due to alterations in neurotrophic factors [20].

Structural dissociation of personality

Although dissociation is more commonly expressed as a symptomatologic dimension, it has to be considered that trauma, especially complex trauma (CT), may have a deeper destructuring effect on adult personality and profoundly interfere with personality development in children. The process by which personality development is affected by CT is known as *structural dissociation of personality* (for a review, see Van Der Hart et al. [11]). In brief, personality can be conceptualized as a balanced and integrated constellation of finalized psychobiological functions, known as *action systems*, that need to be orchestrally coordinated in order to adapt to different life situations. Action systems include, among others, sexual, competitive, cooperative systems and so forth[21]. Defensive systems are or particular importance to dissociation, as they comprise several subsystems: hypervigilance, freeze, flight, fight and submission. After exposure to CT, defensive subsystems appear to function in a non-integrated fashion respect to other action systems, causing dissociative phenomena (depersonalization) as well as inappropriate activation of agonistic/aggressive systems (rage attacks). Attachment system disruption that occur in childhood trauma contribute to this personality aspects by introducing distorted appraisal on the self as worthy of care and on the other as potentially available as a source of care or danger [22] [23]. Over time, dissociated components of personality continue to separate from each other progressively losing mutual cohesion, introducing aspects of ambivalence and incoherence, to the extreme point in which some personality systems are completely unaware of what other systems do, as in Dissociative Identity Disorder.

Dissociation in stress-related disorders

After reviewing the neurobiological underpinnings of dissociation, the role of dissociation in two prototypical stress related disorders characterized by dissociative symptoms will be reviewed.

To many authors, the primary response to TE, and therefore the shared underpinning of all stress-related disorders, is dissociation[11]. The trauma/avoidance model of dissociation is the prominent psychological model of dissociation in the literature: according to this model, dissociation would be an escape response to overwhelming trauma-related emotional contents.

Although evidence of a traumatic basis of dissociation is robust, an alternative model focusing on fantasy proneness has been proposed [24] [25]. According to this model, dissociation would make individuals more prone to fantasy, thereby generating confabulated traumatic memories [26]. Nevertheless, the hypothesis that the dissociation-trauma relationship is due to fantasy proneness or confabulated memories of trauma is generally weakly supported by empirical evidence [8].

For the purpose of the following review, a distinction between at least two different types of TE is required, given their different psychopathological consequences. On the one hand single TE, i.e. a car accident or a natural disaster, more often imply vivid memories of the TE, alongside with cognitive reappraisals and misperceptions. On the other hand, longstanding repeated TE, generally occurring on an intentional interpersonal basis, are more frequently associated with emotional numbing, dissociative symptoms and emotional dysregulation [27]. Enduring repetitive interpersonal TE are often referred to as "complex trauma" (CT).

D-PTSD

The relevance of dissociation to stress related disorders has been recognized by the introduction of a novel diagnostic category in DSM 5: PTSD – dissociative subtype (D-PTSD) (Tab. I). In the DSM-5 several changes regarding stress-related disorders were introduced, including a subtype of PTSD presenting prominent depersonalization or derealization symptoms [7] [28]. Dissociative symptoms are not new to PTSD diagnostic criteria, as in the DSM IV edition re-experiencing symptoms and partial lack of recall were actually included as diagnostic criteria [29]. Flashbacks are accounted as dissociative symptoms in the DSM, and intrusive memories and flashbacks have been related to peri-traumatic detachment, with dissociation interfering with the encoding and consolidation of traumatic memories, resulting in poorly integrated representations of the trauma which are considered central in the development of intrusions [15]. Under a certain dissociation-centered perspective, several if not all of PTSD symptoms point back to, or are mediated by dissociation. According to the 4-D model of post-traumatic dissociation [30], dissociative symptoms may be classified according to four dimensions of consciousness: body, time, though and emotion [31]. Re-experiencing and intrusions would depend on a lack of continuity in the subjective experience of time; voice-hearing would derive from dissociative aspects of thought; depersonalization would be determined by impaired and dissociated first-person

perspective of body and, finally, emotional numbing is related to dissociative aspects of emotion regulation. From this standpoint, PTSD symptomatology as a whole is essentially mediated by dissociation. However, research have supported different connections between PTSD and dissociative symptoms, including a "comorbidity model" of PTSD and dissociation, in which both dissociation and PTSD symptoms are parallelly caused by TE, and a "component model" in which dissociation is considered a discrete component of PTSD [32]. Epidemiological evidence produced by latent class and latent profile analysis however suggest that D-PTSD is a distinct subtype of PTSD that accounts for about 15% and 30% of the cases in males and females respectively and it is more often associated with early and repetitive life trauma than adult non-cumulative TE [33], shows more severe substance use and reported [34] and more frequent comorbid depression and hostility [35].

The clinical presentation of D-PTSD is different from non-dissociative PTSD beyond the absence/presence of dissociative symptoms. Differences between the two disorders reflect the dichotomy of the emotional modulation hypothesis, according to which PTSD may present with under/over corticolimbic modulation of affective states [18]. D-PTSD is roughly characterized by overmodulation of affect, putatively due to an excess of top-down inhibitory control on limbic structures, in response to exposure to traumatic memories or trauma reminders. On the other hand, a failure of corticolimbic inhibition would be at the basis of a hyperaroused/re-experiencing PTSD, or undermodulated type, that involves the prevalence of re-experiencing and hyperarousal symptoms, and may be referred to as [18]. However, the boundary between D-PTSD and hyperaroused PTSD is not clear-cut as individual patients may display features of both presentations at the same time.

Evidence about suicidality in D-PTSD is overall scarce. To the best of our knowledge, one single study reports specifically on D-PTSD. In a cohort of 459 individuals with substance abuse disorder, patients with D-PTSD compared to PTSD reported more severe suicidal ideation and previous suicide attempts [34].

cPTSD

In the ICD-11 two main reforms of stress-related disorders have been introduced: firstly, PTSD has been modified, with more strict criteria, in an attempt to minimize comorbidity with other non-stress-related disorders. In ICD-11 a diagnosis of PTSD requires at least one symptom from each of three dimensions, i.e. re-experiencing, hyperarousal and avoidance, while symptoms that could be shared with an affective disorder such as sleep disorders, irritable mood or difficult in concentrating have been removed from the diagnostic criteria. Secondly, and most important to this review, a sibling disorder of

PTSD has been introduced, "complex" PTSD (cPTSD), a disorder characterized by enduring personality changes including a wide range of alterations in regulation of affect and impulses, attention, consciousness, self-perception, perception of the perpetrator, interpersonal relationships and systems of meaning. cPTSD is an evolution of the preceding disorder in ICD "Enduring personality change after catastrophic experience" (EP-CACE), and largely derived from Disorder of Extreme Stress Not Otherwise Specified (DESNOS) in the Appendix of DSM-IV-TR [36] [37]. cPTSD diagnosis serves to acknowledge the major self-organization and personality disturbances that occur as a response to enduring interpersonal trauma, otherwise referred to as "complex trauma" (CT). CT exposure involves enduring and repetitive interpersonal traumas, more frequently occurring during childhood and adolescence with repeated childhood sexual or physical abuse, but it may also affect adults as in the case of torture, slavery, genocide campaigns, prolonged domestic violence. CT disrupts early attachment relationships and brain development, with severe outcomes involving significant difficulties with emotional, behavioral, somatic, and cognitive dysregulation [38].

How central dissociation is in cPTSD is unclear as a consensus on what constitutes the construct is still lacking [11]. cPTSD criteria include standard post-traumatic re-experiencing, avoidance and hyperarousal symptoms in addition to disturbance in self-organization (DSO) symptoms, a cluster that includes Affective Dysregulation, Negative Self-Concept and Interpersonal Problems.

While the latter two clusters derive from disruption in the attachment system [23] [39], affective dysregulation has been proposed to be more closely related to dissociative phenomena. In fact, affective dysregulation has been conceptualized according to a model that closely resembles the emotional modulation hypothesis of dissociation, with a hyperactivation sub-cluster that comprises heightened emotional reactivity and emotional vulnerability together with reckless behavior, and a deactivation sub-cluster that comprises depersonalization, derealization and numbing [40].

Restructuring of diagnostic criteria from DSM IV to DSM 5 and from ICD-10 to ICD-11 may yield to some confusion regarding differential diagnosis between DSM 5 PTSD and ICD-11 cPTSD, because some of the new criteria in DSM 5 share some dissociative aspects of the DSO [41] [42]. In Table I we compare diagnostic criteria across 4 different systems for PTSD and cPTSD. cPTSD items were derived from Cloitre et al. [43] (Tab. I).

Dissociative symptoms are crucial to cPTSD and for the differential diagnosis between cPTSD, although this evidence is more often referred to DESNOS. For exam-

TABLE I. *Comparison of the diagnostic criteria for PTSD and sibling disorders across different diagnostic manuals.*

DSM-IV-TR PTSD Re-experiencing 1/5	DSM 5 PTSD Intrusion 1/5	ICD 10 PTSD Remembering - reliving	ICD 11 PTSD Remembering – reliving (1/3)	cPTSD Remembering - reliving
Recurrent and intrusive distressing recollections of the event, including images, Thoughts, or perceptions	✓	✓	✓	✓
Recurrent distressing dreams of the event	✓	✓	✓	✓
Acting or feeling as if the traumatic event were recurring (reliving the experience, illusions, hallucinations, and dissociative flashback episodes)	✓ Modified – dissociative flashbacks	✓	✓	✓
Psychological distress at exposure to internal or external reminders of trauma	✓	✓		
Physiological reactivity at exposure to internal or external reminders of trauma	✓	✓		
Avoidance and numbing 3/7	Avoidance 1/5		Avoidance (1/3)	Avoidance
Efforts to avoid internal reminders	✓		✓	✓
Effort to avoid external reminders	✓		✓	✓
	Negative alterations in cognitions and mood 2/5			Disturbance is self-organization
Dissociative amnesia	✓	✓		
Markedly diminished interest or participation in significant activities	✓			
Feeling of detachment or estrangement from others	✓			✓ (DSO Interpersonal)
Restricted range of affect	*Modified* – persistent inability to experience positive emotions			✓ (DSO)
Foreshortened future	*Modified* – negative beliefs or expectations about oneself, others, or the world			✓ (DSO negative self-concept)
	New – persistent distorted blame of self or others for causing the traumatic event or for resulting consequences			✓ (DSO negative self-concept)
	New – persistent negative emotional state			
Hyperarousal 2/5	Hyperarousal 2/5	Hyperarousal	Hyperarousal 1/3)	Hyperarousal
Difficulty falling or staying asleep	✓	✓		
Irritability or outbursts of anger	✓	✓		✓ DSO affect dysregulation
Difficulty concentrating	✓	✓		
Hypervigilance	✓	✓	✓	✓
Exaggerated startle response	✓	✓	✓	✓
	Self-destructive or reckless behavior			
	Specifier: w/dissociative symptoms			

ple, two works [44] [45] have addressed dissociation in individuals with cPTSD. Both studies have found a higher prevalence of depersonalization and derealization, however cPTSD cases were selected using diagnostic instruments designed for DESNOS, that has different diagnostic criteria compared to cPTSD and includes dissociation in its diagnostic criteria, hence making such conclusion spurious. However, in two studies comparing DSM 5 and ICD 11 of PTSD and cPTSD assessed with dedicated instruments, dissociative symptoms levels effectively separated ICD 11 PTSD from cPTSD [42] [46]. In another study, Elklit and colleagues [47] found higher levels of dissociation in cPTSD compared to PTSD patients, although the finding of other unspecific symptoms dimensions being heightened in cPTSD could be explained by a general clinical severity.

Contrasting positions are present in research whether dissociation should be considered as a part of cPTSD or a closely related, but separated, cluster of symptoms. Some authors have questioned dissociation as being a part of emotional dysregulation, having successfully tested the hypothesis that dissociation is indeed a mediator between CT and cPTSD [48]. However, the authors have addressed cPTSD using a structured interview for DESNOS that originally included symptoms of dissociation, removing those items and testing dissociative symptoms from the outside on cPTSD, making their conclusions questionable. A recent network analysis on a sample of 219 traumatized individuals assessed the network structure of symptoms of PTSD, cPTSD and Borderline Personality Disorder (BPD) [40]: in this work dissociative symptoms were central to both cPTSD and PTSD, with dysregulation symptoms, namely anger, reckless behavior, feelings of being distant from others, and identity disturbances, clustering together with BPD symptoms. The evidence of BPD and cPTSD symptoms clustering away from each other supports that BPD and cPTSD are indeed two separate disorders, a thing that has been questioned in the literature [49]: BPD is typically associated with instability in the sense of self that cycles between positive or negative self-evaluation and by emotionally intense and unstable relationships with idealizing and denigrating cycles and paranoid ideation. CPTSD in contrast is a stable condition. Moreover, a history of CT is not a diagnostic criterion for BPD.

Dissociation and self-harm

Dissociation and dissociative disorders have been associated with increase rates of self-harm. Meta-analytical summary of findings on the relation between self-harm and suicidality may be found in Calati et al. [50]. In this meta-analysis rates of suicide attempts and NSSI were compared in psychiatric patients with and without dissociative disorders, finding a 6-fold increase in

suicide risk and 7-fold increase in NSSI risk for patient with dissociation disorders. Dimensional rather than categorical dissociation, assessed using the Dissociative experience Scale, was associated with a significant increase in suicide attempts and NSSI. In the following section, we will review the main theoretical implications linking dissociation with NSSI and suicide.

NSSI

(for an extensive review see Cipriano et al. [51])
NSSI has often an interpersonal function and is more frequent in adolescents. NSSI is the deliberate damage of one's own body in the absence of lethal intent, including, among others, cutting, head-banging, burning, slashing behaviors. NSSI is such a concerning issue that has been introduced in the DSM 5 as a separate disorder [52]. NSSI is highly prevalent among general and clinical populations: Briere and Gil [53] reported a 21% of prevalence in a clinical sample, with a particular focus of PTSD and dissociative symptoms, while others have estimated a prevalence of 6.7% in the general adolescents' population [54] and up to 50% in an adolescents' inpatient sample. NSSI is prevalent across several disorders beyond BPD, of which it is a diagnostic criteria, including PTSD and dissociative disorders above all [51]. In particular, in an Italian study a strong association of NSSI and dissociation was found, with individuals with a history of NSSI having higher levels of dissociation [55]. Early TE such as parental neglect, abuse, or deprivation are among the major risk factors for NSSI. In particular, child emotional abuse, compared to other types of adverse childhood experiences has the largest effect [56]. Research suggests that NSSI has two major "functions": an *intrapersonal* and an *interpersonal* or *compensatory* one. Both intrapersonal and interpersonal functions can positively and negatively reinforce NSSI. For example, NSSI could help regulating negative mental states including dissociation or anger, experiencing positive feelings or thoughts during or after engaging in NSSI (i.e., feeling alive), reinforcing social interaction (i.e., getting attention or communicating), or escaping unpleasant social interactions (i.e., ending an argument, not attending sports class) [57] [58]. Compensatory NSSI seems to be the most frequent type, enacted as a strategy for compensating stressful emotional states and dissociation, and is the most relevant in individuals experiencing dissociation after TE [54] [59].

Suicidality

While an extensive literature addresses the association of dissociation and NSSI, the relation between suicide and dissociation has received less attention, and to date no autonomous model of suicidality in dissociative disorders has been proposed. In fact, the issue of suicidality is often addressed in continuity with NSSI. A

review [60] has addressed extensively the association between NSSI and suicidal behavior. Three main models address the relation between NSSI and suicidality: in a first model, the Gateway model, NSSI and suicide are conceptualized along a continuum of severity, with NSSI being an extreme of the spectrum and complete suicide the other and NSSI preceding the onset of suicide. This model is supported by a number of both cross-sectional and longitudinal evidence of NSSI predicting suicide. Under a "third variable" theory, an unspecific factor would be responsible for both NSSI and suicide, with their mutual association being spurious. According to the "Theory of Acquired Capability for Suicide"[61], NSSI is one way among many others individuals may increase their acquired capability for suicide with, as NSSI may habituate an individual to the fear and pain associated with suicidal self-harming behaviors.

Systematic review of mediation models

The most commonly proposed model that unifies TE, dissociation and self-harm is a mediational model: in statistical terms, a mediation occurs when an independent variable, TE in this case, does not exert a direct effect on an outcome variable, i.e self-harm, but act *indirectly* via a third variable, dissociation. Mediation implies a number of assumptions and consideration when assessing relationships among more than two variables: firstly, in order to ascertain mediation, the independent variable has to be related to the outcome variable when not controlling for the mediator; secondly the independent variable has to be related with the mediator variable; thirdly the mediator has to be related to the outcome. Mediation occurs when the effect of the independent variable on the outcome is significantly reduced or abolished when controlling for the mediator. Translating statistics to psychopathology, mediation occurs when it is demonstrated that TE cause both dissociation and self-harm, when dissociation causes self-harm and when TE no longer have an effect on self-harm when taking into account dissociation.

For the following section, a systematic search was performed on Pubmed and Scopus with the following keywords: mediation AND (dissociation OR dissociative) AND (suicide OR self harm OR nssi OR self-harm OR self-injury OR "suicide attempt" OR self-injurious behavior OR mutilation). The search returned the same 17 articles on both databases. Articles were inserted in the following section only if meeting the criteria of addressing the mediating role of mediation between TE and self-harm.

Evidence for dissociation as a mediator between TE and NSSI is robust: Briere and Eadie [58] have addressed mediation in a large sample from the general population using a robust path analytical model. In their sample dissociation fully mediated the effect of adverse events, posttraumatic stress and depression on NSSI. They propose that rather than resulting directly from stress-related or depressive symptoms, NSSI occurs in response to dissociation, as a compensatory strategy to interrupt unwanted hypoarousal and numbing.

In their work Zetterqvist et al. [59] have addressed differentially if dissociation and depression would mediate the effect of TE on NSSI with a compensatory or interpersonal function, finding that NSSI serves as a relief for painful or dissociative mental states rather than as a dysfunctional communication channel in the case of traumatized individuals.

Another work by Chaplo et al. [62] confirmed a similar model in a sample of over 500 youths recruited from the US juvenile justice system, hence inherently displaying externalizing behaviors. In their sample childhood sexual abuse (CSA) was the TE with the largest effect on post-traumatic symptoms and NSSI. Mediation analysis confirmed dissociation and emotional dysregulation as intermediate variables between sexual abuse and NSSI. Howard and colleagues [63] failed to replicate the mediation, probably due to small sample size, in an otherwise interesting study in which different mediators were tested, including separated PTSD dimensions, emotional dysregulation and dissociation. In this work only hyperarousal and emotional dysregulation partially mediated the TE-NSSI relationship. The authors hypothesize that dissociation failed to mediate the TE-NSSI relationship in their sample because TE were assessed in an excessively broad way, while previous report that the effect of CSA in particular is mediated in the TE-NSSI relationship. This interpretation is interesting, as it warrants further systematic studies to assess the differential role of different types of TE on NSSI and on dissociation. In a sample of over 400 female college students [64] different self-destructive outcomes have been investigated. This study has extended the CSA-dissociation relationship on self-destructive behaviors other than NSSI, finding an effect on drug and alcohol use. A mediating role for dissociation was replicated in this study.

In an interesting work the established mediation model TE-dissociation-NSSI introducing narcissism as a moderator [65]. In statistical terms, a moderation occurs when the relation between two or more variables, TE-dissociation-NSSI in our example, occurs differently at different levels of a moderator variable, narcissism in this case. Both vulnerable narcissism and grandiose narcissism were found to moderate the relation between dissociation and self-harm. In this study the relation between dissociation and NSSI was stronger in individuals with high levels of vulnerable narcissism, while it was weaker in individuals with high levels of grandiose narcissism, suggesting that vulnerable narcissism could be a factor

of risk-enhancement for NSSI in traumatized and dissociating individuals. This is somewhat coherent with the concept that vulnerable narcissists tend to engage into grandiose fantasies in a dissociative like-state.

PTSD and dissociation were explored as mediators of polyvictimization on a number of outcomes, including suicide ideation, in another sample of youths involved in the juvenile justice system [66]. In this study dissociation was found to mediate the effects of TE on internalizing symptoms and suicidal ideation, while PTSD symptoms mediated the effect on externalizing symptoms. In this study dissociative symptoms were derived from a PTSD assessment instrument, which could confuse the results, highlighting the importance of assessing PTSD symptoms separately from dissociative symptoms, although belonging to parent constructs. However, this study is of great importance as it provides the first evidence of a mediation of TE-Dissociation of suicidal ideation rather than on NSSI, and secondly because it addresses externalizing and internalizing behaviors together, providing different pathways from TE to the one or the other. An externalizing/internalizing mixed clinical presentation may occur more often than what expected, and externalizing behaviors should be taken into account for future studies, given the importance they have in perpetuating the interpersonal violence cycle. Externalizing behaviors have been taken into account

under a different conceptual model [67]: in this study both dissociation and hostility were entered in the model as mediators between sexual assault and suicidal ideation, finding that both mediators had a partial mediating effect. This finding is in line with the above reported TE-PTSD-suicidality, suggesting that both under and over modulated response to TE could lead to risk of suicide, through different pathways.

Conclusions

In the present paper we systematically reviewed the evidence of dissociation being the principal mediator of the effects of TE on self-harm. We found a robust evidence of the mediating role of dissociation on NSSI, confirmed by different studies in different populations. Evidence for suicidal ideation was nevertheless weak, and we couldn't find any evidence on suicide attempts. Such a lack of evidence on suicidal ideation and suicide attempts should be addressed in the future. NSSI is a major risk factor for suicide attempts and complete suicide, however a number of mechanisms may differentiate the pathways that terminate at NSSI from those that progress to complete suicide.

Conflict of interest

The Authors have no conflict of interest to declare.

References

1. Sumner SA, Mercy JA, Dahlberg LL, et al. *Violence in the United States: status, challenges, and opportunities*. JAMA 2015;314:478-88.

2. Herzog JI, Schmahl C. *Adverse childhood experiences and the consequences on neurobiological, psychosocial, and somatic conditions across the lifespan.* Front Psychiatry 2018;9:420.

3. Dube SR, Anda RF, Felitti VJ, et al. *Childhood abuse, household dysfunction, and the risk of attempted suicide throughout the life Span.* JAMA 2001;286:3089-96.

4. Talevi D, Imburgia L, Luperini C, et al. *Interpersonal violence: identification of associated features in a clinical sample*. Child Abuse Negl 2018;86:349-57.

5. Wolff JC, Thompson E, Thomas SA, et al. *Emotion dysregulation and non-suicidal self-injury: a systematic review and meta-analysis*. Eur Psychiatry 2019;59:25-36.

6. Rossetti MC, Tosone A, Stratta P, et al. *Different roles of resilience in depressive patients with history of suicide attempt and no history of suicide attempt*. Braz J Psychiatry 2017;39:216-19.

7. American Psychiatric Association. *Diagnostic and Statistical manual of mental disorders, 5th ed*. Washington, DC: American Psychiatric Association Publishing 2013.

8. Dalenberg CJ, Brand BL, Gleaves DH, et al. *Evaluation of the evidence for the trauma and fantasy models of dissociation*. Psychol Bull 2012;138:550-88.

9. Janet P. *L'automatisme psychologique: Essai de psychologie expérimentale sur les formes inférieures de l'activité humaine.* Paris, France: Alcan 1889.

10. Lanius RA, Brand B, Vermetten E, et al. *The dissociative subtype of posttraumatic stress disorder: rationale, clinical and neurobiological evidence, and implications.* Depress Anxiety 2012;29:701-8.

11. Van Der Hart O, Nijenhuis ERS, Steele K. *Dissociation: an insufficiently recognized major feature of complex posttraumatic stress disorder.* J Trauma Stress 2005;18:413-23.

12. Scalabrini A, Cavicchioli M, Fossati A, et al. *The extent of dissociation in borderline personality disorder: a meta-analytic review.* J Trauma Dissociation 2017;18:522-43.

13. Lyssenko L, Schmahl C, Bockhacker L, et al. *Dissociation in psychiatric disorders: A meta-analysis of studies using the dissociative experiences scale*. Am J Psychiatry 2018;175:37-46.

14. Briere J, Weathers FW, Runtz M. *Is dissociation a multidimensional construct? Data from the Multiscale Dissociation Inventory*. J Trauma Stress 2005;18:221-31.

15. Spitzer C, Barnow S, Freyberger HJ, et al. *Recent developments in the theory of dissociation*. World Psychiatry 2006;5:82-6.

16. Holmes EA, Brown RJ, Mansell W, et al. *Are there two qualitatively distinct forms of dissociation? A review and some clinical implications*. Clin Psychol Rev 2005;25:1-23.

17. Lanius RA, Boyd JE, McKinnon MC, et al. *A Review of the neurobiological basis of trauma-related dissociation and its relation to cannabinoid and opioid-mediated stress response: a transdiagnostic, translational approach*. Curr Psychiatry Rep 2018;20:118.

18. Lanius RA, Vermetten E, Loewenstein RJ, et al. *Emotion modulation in PTSD: clinical and neurobiological evidence for a dissociative subtype*. Am J Psychiatry 2010;167:640-7.

19 Sierk A, Daniels JK, Manthey A, et al. *White matter network alterations in patients with depersonalization/derealization disorder*. J Psychiatry Neurosci 2018;43:347-57.

20 Stratta P, Sanità P, Bonanni RL, et al. *Clinical correlates of plasma brain-derived neurotrophic factor in post-traumatic stress disorder spectrum after a natural disaster.* Psychiatry Res 2016;244:165-70.

21 Panksepp J. *Affective neuroscience: the foundations of human and animal emotions*. New York, NY: Oxford University Press 2005.

22 Bowlby J. *Attachment and loss – Vol. 1 – attachment.* New York, NY: Basic Books 1969.

23 Liotti G. *Trauma, dissociation, and disorganized attachment: three strands of a single braid.* Psychotherapy 2004;41:472-86.

24 Loewenstein RJ. *Dissociation debates: everything you know is wrong.* Dialogues Clin Neurosci 2018;20:229-42.

25 Merckelbach H, Boskovic I, Pesy D, et al. *Symptom overreporting and dissociative experiences: a qualitative review*. Conscious Cogn 2017;49:132-44.

26 Giesbrecht T, Lynn SJ, Lilienfeld SO, et al. *Cognitive processes in dissociation: an analysis of core theoretical assumptions*. Psychol Bull 2008;134:617-47.

27 Terr LC. *Childhood traumas: an outline and overview.* Am J Psychiatry 1991;148:10-20.

28 Nemeroff CB, Weinberger D, Rutter M, et al. *DSM-5: a collection of psychiatrist views on the changes, controversies, and future directions.* BMC Med 2013;11:202.

29 American Psychiatric Association. *Diagnostic and statistical manual of mental disorders, 4th ed., Text revision.* Washington, DC: American Psychiatric Association Publishing 2000.

30 Lanius RA. *Trauma-related dissociation and altered states of consciousness: a call for clinical, treatment, and neuroscience research.* Eur J Psychotraumatol 2015;6:27905.

31 Zelazo PD, Moscovitch M, Thompson E. *The Cambridge handbook of consciousness.* New York, NY: Cambridge University Press 2007.

32 Dalenberg C, Carlson EB. *Dissociation in posttraumatic stress disorder part II: how theoretical models fit the empirical evidence and recommendations for modifying the diagnostic criteria for PTSD.* Psychol Trauma 2012;4:551-9.

33 Hansen M, Ross J, Armour C. *Evidence of the dissociative PTSD subtype: a systematic literature review of latent class and profile analytic studies of PTSD.* J Affect Disord 2017;213:59-69.

34 Mergler M, Driessen M, Lüdecke C, et al. *Relationships between a dissociative subtype of PTSD and clinical characteristics in patients with substance use disorders.* J Psychoactive Drugs 2017;49:225-32.

35 Tsai J, Armour C, Southwick SM, et al. *Dissociative subtype of DSM-5 posttraumatic stress disorder in U.S. veterans.* J Psychiatr Res 2015;66-67:67-74.

36 van der Kolk BA, Roth S, Pelcovitz D, et al. *Disorders of extreme stress: the empirical foundation of a complex adaptation to trauma.* J Trauma Stress 2005;18:389-99.

37 van der Kolk BA, Pelcovitz D, Roth S, et al. *Dissociation, somatization, and affect dysregulation.* Am J Psychiatry 1996;153:83-93.

38 Kliethermes M, Schacht M, Drewry K. *Complex trauma.* Child Adolesc Psychiatr Clin N Am 2014;23:339-61.

39 Farina B, Liotti M, Imperatori C. *The role of attachment trauma and disintegrative pathogenic processes in the traumatic-dissociative dimension.* Front Psychol 2019;10:933.

40 Knefel M, Tran US, Lueger-Schuster B. *The association of posttraumatic stress disorder, complex posttraumatic stress disorder, and borderline personality disorder from a network analytical perspective.* J Anxiety Disord 2016;43:70-8.

41 Brewin CR, Cloitre M, Hyland P, et al. *A review of current evidence regarding the ICD-11 proposals for diagnosing PTSD and complex PTSD*. Clin Psychol Rev 2017;58:1-15.

42 Hyland P, Shevlin M, Fyvie C, et al. *Posttraumatic stress disorder and complex posttraumatic stress disorder in DSM-5 and ICD-11: clinical and behavioral correlates*. J Trauma Stress 2018;31:174-80.

43 Cloitre M, Garvert DW, Brewin CR, et al. *Evidence for proposed ICD-11 PTSD and complex PTSD: a latent profile analysis.* Eur J Psychotraumatol 2013 May 15;4.

44 Zucker M, Spinazzola J, Blaustein M, et al. *Dissociative symptomatology in posttraumatic stress disorder and disorders of extreme stress*. J Trauma Dissociation 2006;7:19-31.

45 Dorahy MJ, Corry M, Shannon M, et al. *Complex trauma and intimate relationships: the impact of shame, guilt and dissociation.* J Affect Disord 2013;147:72-9.

46 Powers A, Fani N, Carter S, et al. *Differential predictors of DSM-5 PTSD and ICD-11 complex PTSD among African American women*. Eur J Psychotraumatol 2017;8:1338914.

47 Elklit A, Hyland P, Shevlin M. *Evidence of symptom profiles consistent with posttraumatic stress disorder and complex posttraumatic stress disorder in different trauma samples*. Eur J Psychotraumatol 2014 May 19;5.

48 van Dijke A, Ford JD, Frank LE, et al. *Association of childhood complex trauma and dissociation with complex posttraumatic stress disorder symptoms in adulthood.* J Trauma Dissociation 2015;16:428-41.

49 Cloitre M, Garvert DW, Weiss B, et al. *Distinguishing PTSD, complex PTSD, and borderline personality disorder: a latent class analysis*. Eur J Psychotraumatol 2014 Sep 15;5.

50 Calati R, Bensassi I, Courtet P. *The link between dissociation and both suicide attempts and non-suicidal self-injury: meta-analyses.* Psychiatry Res 2017;251:103-14.

51 Cipriano A, Cella S, Cotrufo P. *Nonsuicidal self-injury: a systematic review*. Front Psychol 2017;8:1946.

52 Washburn JJ, Potthoff LM, Juzwin KR, et al. *Assessing DSM-5 nonsuicidal self-injury disorder in a clinical sample*. Psychol Assess 2015;27:31-41.

53 Briere J, Gil E. *Self-mutilation in clinical and general population samples: prevalence, correlates, and functions.* Am J Orthopsychiatry 1998;68:609-20.

54 Zetterqvist M, Lundh LG, Dahlström Ö, et al. *Prevalence and function of non-suicidal self-injury (NSSI) in a community sample of adolescents, using suggested DSM-5 criteria for a potential NSSI disorder.* J Abnorm Child Psychol 2013;41:759-73.

55 Cerutti R, Presaghi F, Manca M, et al. *Deliberate self-harm behavior among italian young adults: correlations with clinical and nonclinical dimensions of personality*. Am J Orthopsychiatry 2012;82:298-308.

56 Brown RC, Plener PL. *Non-suicidal self-Injury in adolescence.* Curr Psychiatry Rep 2017;19:20.

57 Nock MK, Prinstein MJ. *A functional approach to the assessment of self-mutilative behavior.* J Consult Clin Psychol 2004;72:885-90.

58 Briere J, Eadie EM. *Compensatory self-injury: posttraumatic stress, depression, and the role of dissociation.* Psychol Trauma 2016;8:618-25.

59 Zetterqvist M, Lundh L-G, Svedin CG. *A cross-sectional study of adolescent non-suicidal self-injury: support for a specific distress-function relationship.* Child Adolesc Psychiatry Ment Health 2014;8:23.

60 Hamza CA, Stewart SL, Willoughby T. *Examining the link between nonsuicidal self-injury and suicidal behavior: a review of the literature and an integrated model.* Clin Psychol Rev 2012;32:482-95.

61 Joiner TE, Van Orden KA, Witte TK, et al. *Main Predictions of the interpersonal-psychological theory of suicidal behavior: empirical tests in two samples of young adults.* J Abnorm Psychol 2009;118:634-46.

62 Chaplo SD, Kerig PK, Bennett DC, et al. *The roles of emotion dysregulation and dissociation in the association between sexual abuse and self-injury among juvenile justice-involved youth*. J Trauma Dissociation 2015;16:272-85.

63 Howard R, Karatzias T, Power K, et al. *From childhood trauma to self-harm: an investigation of theoretical pathways among female prisoners*. Clin Psychol Psychother 2017;24:942-51.

64 Rodriguez-Srednicki O. *Childhood sexual abuse, dissociation, and adult self-destructive behavior*. J Child Sex Abus 2001;10:75-90.

65 Talmon A, Ginzburg K. *The differential role of narcissism in the relations between childhood sexual abuse, dissociation, and self-harm*. J Interpers Violence 2018:0886260518799450.

66 Ford JD, Charak R, Modrowski CA, et al. *PTSD and dissociation symptoms as mediators of the relationship between polyvictimization and psychosocial and behavioral problems among justice-involved adolescents.* J Trauma Dissociation 2018;19:325-46.

67 Keefe KM, Hetzel-Riggin MD, Sunami N. *The mediating roles of hostility and dissociation in the relationship between sexual assault and suicidal thinking in college students.* J Interpers Violence 2017:0886260517698282.

How to cite this article: Rossi R, Longo L, Fiore D, et al. *Dissociation in stress-related disorders and self-harm: a review of the literature and a systematic review of mediation models.* Journal of Psychopathology 2019;25:162-71.

A complex phenotype of suicidal behavior: a case of post brain injury dissociative disorder

L. Longo[1,2], R. Rossi[1], C. Niolu[1,2],
A. Siracusano[1,2], G. Di Lorenzo[1,2]

[1] Department of Systems Medicine,
University of Rome Tor Vergata, Rome, Italy;
[2] Psychiatry and Clinical Psychology Unit,
Fondazione Policlinico Tor Vergata, Rome, Italy

Summary

We describe a case of a 54-year-old Caucasian woman with a complex phenotype for suicidal behavior after traumatic brain injury. At the admission patient had Bipolar Disorder, Post Traumatic Stress Disorder, Dissociative Identity Disorder, Conversion Disorder (with Psychogenic Non Epileptic Seizures) and a drug treatment for a post-traumatic epilepsy. During a follow up period of 30 months, despite the symptomatological improvements due to psychopharmachological treatments (including also lithium) and psychoeducation treatment, the patient showed yet high risk of suicide and high levels of dissociation.

Key words

Suicide risk • Dissociation • Dissociative Identity Disorder • Traumatic Brain Injury • Psychogenic Non Epileptic Seizures • Epileptic Seizures • Post Traumatic Stress Disorder • Bipolar Disorder

Introduction

Annually, up to 50 million people experience a traumatic brain injury (TBI) in worldwide [1]. Individuals with a history of TBI have higher rates suicidal ideation and behaviours than general population [2]. People with a history of TBI experience the development of several mental disorders increasing the suicide risk. TBI has been associated with a risk of Bipolar Disorder (BD) [3][4], a mental illness in which a high risk of suicide attempts is well estabilished [5]. Post-Traumatic Stress Disorder (PTSD) is frequently associated with suicidal ideation and suicide attempts [6]. A recent systematic review and meta-analysis of prevalence rates of PTSD after civilian traumatic brain injury reports that PTSD was present in 13.5% of patients with mild TBI and in 11.8% of those patients with a moderate or severe TBI [7]. Considering those studies including only motor vehicle accidents PTSD prevalence was higher ranging from 19.6 to 36% [7]. Dissociative Identity Disorder (DID) is a chronic post-traumatic condition [8] characterized by "disruption of identity characterized by two or more distinct personality states" [9]. Rates of attempted suicide range from 61 to 72%, with 1 to 2.1% completing suicide among patients with DID [10]. Moreover, dissociation is a major mediator between early traumatic experiences and suicidal behavior [11]. Different studies show the co-occurrence of TBI and Psychogenic Non Epileptic Seizures (PNES) varying between 16 and 83% [12]. PNES can occur in isolation as a form of dissociative disorder, or in association with various neurological and psychiatric conditions such as epilepsy or PTSD [12]. Suicide risk is higher in epileptic patients [13] and in PNES patients [14] with no significant difference between two groups [14][15].

But what happens when all these clinical conditions are together?

We describe a complex case of woman that, after TBI, had a post-traumatic epilepsy and developed a complex phenotype for suicidal behaviour characterized by BD, PTSD, DID, PNES.
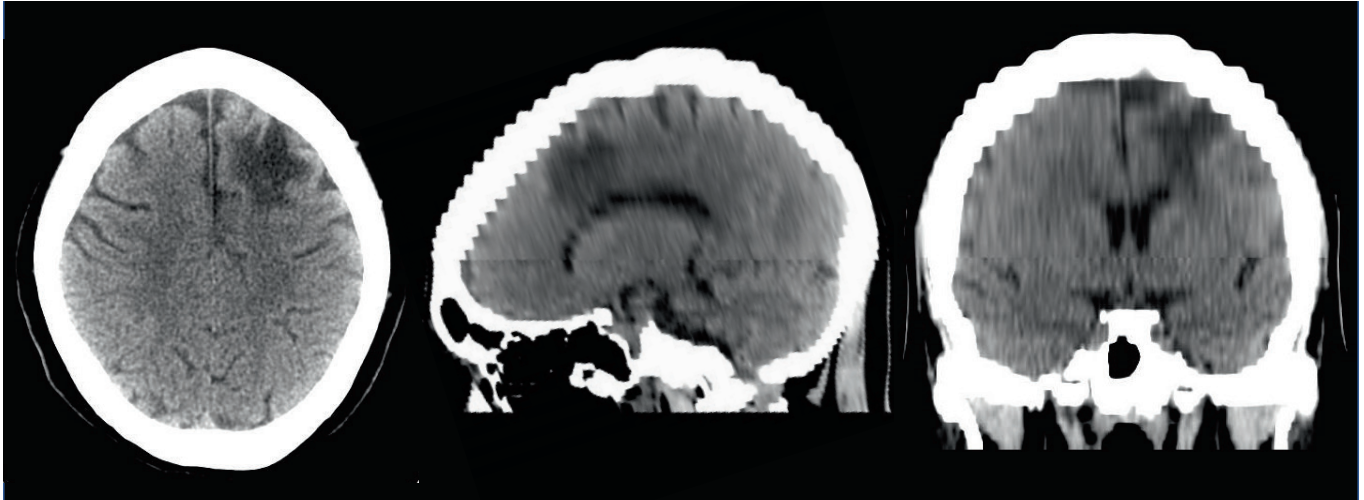
Correspondence

Giorgio Di Lorenzo,
Department of Systems Medicine,
University of Rome Tor Vergata,
via Montpellier 1, 00133 Rome, Italy
• E-mail: di.lorenzo@med.uniroma2.it

FIGURE 1. *Computed Tomography (CT) imaging scan of head. It is clearly evident a large lesion in right frontal area.*

Case report

A.T. is a 54-year-old Caucasian right-handed woman, married, with no children. A.T. sets the onset of her symptoms in 2011 (47 years old) after a road accident (the patient had a collision with a car while was driving on her motorcycle). From her clinical documentation, we learned that the patient reported: right clavicle fracture, left ankle fracture, cervical verticalization, displaced fracture of the right peroneal malleolus, and cerebral hemorrhage in the frontal right lobe with perilesional edema. For this reason, she was hospitalized for 20 days. A metal plate was used for displaced fracture of the right peroneal malleolus and for this reason the patient could not perform a Magnetic Resonance Imaging (MRI) scan. During the hospitalization, the patient reported several episodes of depersonalization ("I was on the ceiling and I looked my body on the bed"). After the road accident, she presented a "treatment-resistant" epilepsy, accompanied by Psychogenic Non Epileptic Seizures (PNES), with a multiple frequency of these crises during the day (about 4/day).

From January 2012 to December 2016, A.T. had 8 accesses to the emergency room (ER) of different hospitals for PNES characterized by: average duration of about 20 minutes, situational onset, presentation of crises with discontinuous and asynchronous shocks, pelvic thrust movements, absence of loss of urine and feces.

In January 2017, A.T. was conducted to the ER of our University Hospital for a suicidal attempt with cuts to the wrists. At her arrival in the hospital, she presented a subcontinuous state of epileptic-type crises characterized by alterations of the state of consciousness along with repetitive, stereotyped motor behaviors. Due to the prolongation of this epileptic-type state, she was hospitalized. After seven days of clinical observation and execution of instrumental investigations (resting EEG, video-EEG dur-

ing seizures; Computed Tomography (CT) imaging scan of head, see Figure 1), neurologists discharged the patient with a diagnosis of "Psychogenic Non Epileptic Seizures in post-traumatic epilepsy", with a therapy consisting of lacosamide 400 mg, fenobarbital 50 mg, zonisamide 300 mg, citalopram 20 mg, clobazam 10 mg, quetiapine 50 mg, and levotiroxine 50 mcg; during hospitalization, the attempt to use valproic acid as an anti-epileptic drug was interrupted because it caused the patient's hair loss.

At discharge, the patient was referred to Day Hospital Service of our Psychiatry and Clinical Psychology Unit, where she performed, in addition to the standard clinical interview, a complete psychopathological and diagnostic assessment, composed by structured and semi-structured interviews as well as psychometric battery.

During the clinical interview (including also Dissociative Disorders Interview Schedule, DDSI), we evaluated the specific characteristics of the PNES and we recollected the traumatic history. PNES characteristics were: average duration of about 20 minutes, gradual onset and extinction, situational onset, presentation of crises with discontinuous and asynchronous shocks, pelvic thrust movements, absence of loss of urine and feces, possibility of external agents to modulate the crisis, fast post critical recovery. On several occasions during the clinical evaluations, A.T. presented PNES crises. After crises, we observed the presence of two other identities in the patient: one identity was a woman of 31 years old (before the road accident), who state that "I am single, I live with my mother ... I'm well, I'm happy, why I'm in the hospital?"; and another identity was a woman of 47 years old (age of road trauma), that was constantly crying, that reported things like "I'm sick, I'm so sick. My husband prefers to go to his dying mother rather than staying with me. I feel like I could die, I feel very bad". When the dominant identity (host) returned, the pa-

tient reported severe headaches and she had no memory of the other identities. The host denied to suffer because her husband wasn't going to visit her in the hospital saying "I was out of danger; his mother was dying".

The psychometric battery included: Hamilton Depression Scale (HAM-D), Mania Rating Scale (MRS), Beck Depression Inventory (BDI), Beck Hopelessness Scale (BHS), Clinician-Administered PTSD Scale (CAPS), Dissociative Experiences Scale (DES), Clinician-Administered Dissociative State Scale (CADSS). This psychometric assessment was administered at baseline and after 6, 12, 18, 24 and 30 months of follow-up. (see Table I for the scores).

In the medical history, before the motor vehicle accident, the patient reported periods of sub-threshold depressive and hypomanic symptomatology; no psychotropic drug therapy or psychiatric hospitalization was described. A history of migraine was also reported. At baseline observation, the patient had the criteria for the following DSM-5 diagnoses: Bipolar Disorder subtype I (with actual Mixed State), Post Traumatic Stress Disorder, Dissociative Identity Disorder (DID) and Conversion Disorder (with Psychogenic Non Epileptic Seizures).

A.T. refused psychotherapy treatment, so she was offered psychotropic medications (quetiapine 300 mg, lorazepam 2 mg; citalopram 20 mg and clobazam 10 mg were discontinued) and psychoeducation treatment. In March 2017, the patient attempted suicide by self-defenestration: she was stopped by her husband that unexpectedly returned home. Consequently, the patient was admitted in an acute psychiatric unit for 11 days. After the discharge, she did return in our Day Hospital Service: lithium treatment was gradually introduced (until 900 mg/die) and quetiapine was increased to 400 mg/die as well. Additionally, due to her continuous refusal to the psychotherapy, the patient continued psychoeducation treatment, with a gradual improvement on insight of her clinical condition. In November of the same year, A.T. reported suicidal ideation and planning, so she was recovered again in an acute psychiatric unit for 10 days. A.T. returned again in our service: lithium was titrated up to 1200 mg/die and quetiapine until 500 mg/die; she also continued psychoeducation treatment, with gradual reduction of intensity and frequency of PNES crises, that were gradually replaced by episodes of trance. These episodes were characterized by: initial stereotyped hands movements, acute loss of consciousness and insensitivity to environmental stimuli, with a duration about 2-3 minutes. No other identities were observed or were referred by the husband throughout 2018 until the last follow-up assessment in July 2019. During the entire follow-up period, the patient continued refusing any type of psychotherapy treatment. In January 2019, based on neurologists' indication, the patient suspended therapy with fenobarbital 50 mg, continuing taking lacosamide 400 mg and zonisamide 300 mg. The last pharmacotherapy

TABLE I. *Psychometric assessment at the baseline (T)) and during the follow-up period (T6 to T30).*

|	T0	T6	T12	T18	T24	T30
HAM-D	27	16	9	12	6	10
MRS	18	12	8	4	2	4
BDI	52	46	36	35	26	24
STICSA-S	81	54	47	26	29	30
BHS	18	18	16	14	14	14
DES	90.35	59.85	66.07	71.42	74.07	59.5
CADSS	82	57	55	47	49	52
CAPS	99	92	76	65	63	59

HAM-D: Hamilton Depression Scale; MRS: Mania Rating Scale; BDI: Beck Depression Inventory; BHS: Beck Hopelessness Scale; CAPS: Clinician-Administered PTSD Scale; DES: Dissociative Experiences Scale; CADSS: Clinician-Administered Dissociative State Scale.

(July 2019) was: lacosamide 400 mg; zonisamide 300 mg; carbolithium 1200 mg, quetiapine 400 mg, lorazepam 1.5 mg, levotiroxine 50 mcg.

At the follow-up of 30 months, the patient satisfied the criteria for the following DSM-5 diagnoses: Bipolar Disorder subtype I (with actual Eutimic State), Post Traumatic Stress Disorder and Other Type of Dissociative Disorder with Dissociative Trance. No criteria for Dissociative Identity Disorder (DID) and Conversion Disorder (with Psychogenic Non Epileptic Seizures) were satisfied. At that time, A.T. reported a general improvement of her clinical conditions; moreover, her husband also confirmed a general, positive advancement in his wife's functioning. Psychometric assessment confirmed symptomatologic improvements (Tab. I). As depicted in Figure 2, during the follow-up period of 30 months it was observed a decrease of mean duration (in minutes) of dissociative crisis despite their monthly number remained high. Unfortunately, despite the reported and observed symptomatologic improvements, A.T. showed yet a high risk of suicide (see BHS score in Tab. I), as well as the patient showed high levels of dissociation (see DES and CADSS score in Tab. I). Consequently, we hypothesize that the patient's high risk of suicide is associated with dissociation levels that remain high in follow-up.

Discussion

The present case illustrates a complex interaction between environmental, biological and psychological factors in the pathogenesis of suicidal behaviour. Following exposure to a motor vehicle accident, our patient developed a complex psychiatric symptomatology such as mood disorder (Bipolar Disorder), trauma-related
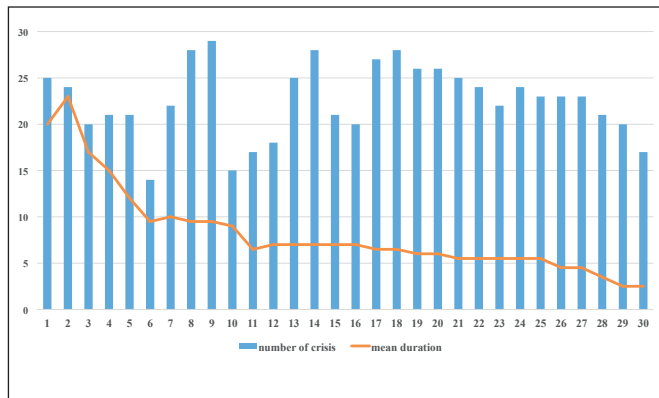
FIGURE 2. *Monthly number of mean duration (in minutes) of dissiociative crisis during the follow-up period of 30 months.*

disorder (PTSD), dissociative disorder (Dissociative Identity Disorder), conversion disorder (Psychogenic Non Epileptic Seizures) and organic disorder (Epileptic Seizures). Each of these disorders is associated with a greater risk of suicide than the general population [5 6 10 13 14], such as for the TBI2. In particular AT's psychopathological picture at the beginning of our clinical observation was consistent with recent literature that shows crisis states in DID include self-mutilation, flashbacks, non-epileptic seizures and suicide attempts [16].

After two months of observation, the patient attempted suicide and lithium was gradually inserted in pharmacotherapy (until 1200 mg/die). During the follow up period (T6-T30) the patient reported symptomatological improvements of all domains, except for dissociation and suicidal risk (see Table I). Consequently, we suppose that these two clinical features could be strongly related to each other.

In follow up period, the DES score declined from 90.35 to 59.5 and the CADSS score from 82 to 52. We hypothesized that this reduction could be caused by the transition from Dissociative Identity Disorder and Other Type of Dissociative Disorder with Dissociative Trance. This transition can be understood by integrating Porges' theory [17] with the theory of structural dissociation of the personality, a trauma model that presents a unitary framework to understand diverse trauma-related responses [18]. According to this theory, different parts of personality (called dissociative emotional parts) are based on diverse defensive subsystems (fight/flight responses) that remain rigidly blocked in traumatic experiences and can appear when the subject is facing traumatic issues [19]. In complex dissociative disorders, these responses are rooting dissociative parts with different levels of mental structure and autonomy and the activation of dissociative parts may be clinically expressed in the more extreme dissociative cases, overt personal-

ity switching [19]. Furthermore, a dorsal-vagal activation ('system shutdown') is characteristic of life-threatening situations with no chance to escape and the presence of a structured dissociative part is not so frequent. Consequently, we can hypothesize that at beginning our patient had dissociative emotional parts and a sympathetic activation and later she presented a dorso-vagal activation without structured dissociative parts.

Furthermore, dissociative behaviour may simply reflect behavioral disinhibition secondary to right frontal damage. Moreover, we also hypothesize that TBI and subsequent hospitalization might have been sufficient to trigger a complex behavioral response.

In the literature relatively few cases of DID after TBI are reported. For example, a dissociative behavior after right frontal TBI was found in a Vietnam Veteran [20]. The study hypothesized that the structural focal lesion in the right superior prefrontal cortex (Brodmann area 6), causing a selective amnesia of the details of the TBI, acted together with the bilateral dysfunction of anterior paralimbic regions (orbitofrontal, anterior temporal, and cingulate cortices) not only to favor the intrusion of memories related to previous traumatic experiences, but also to trigger dissociative flashbacks. The authors conclude that dysfunction of certain regions of the prefrontal cortex and anterior temporal cortex involved with old episodic memories may play a role in the occurrence of dissociative flashbacks [20].

Similarly, a recent case report shows a transiently dissociation of identity in a 67 years old right-handed man with a left parietal lobe hematoma with mass effect and an old lacunar infarct in the right frontal lobe [21]. The alterations of personality gradually subsided after six to eight weeks and coincided with the resolution of the hematoma. The authors hypothesized that a neurological insult to the left parietal brain can lead to a compensatory uninhibited activity of contralateral right parietal lobe. This can lead to retrieval of repressed traumatic, implicit episodic memory, streaming in to the consciousness leading to the onset of Dissociative Identity Disorder [21]. It should be noted that suicidality has not been reported in the two clinical cases mentioned above.

ECT studies show two contrasting case report. In fact, a study shows a new onset of Dissociative Disorder Not Otherwise Specified (only one other identity) after 7 temporal right-sides Electroconvulsive Therapy [22] in 51 years old woman with bipolar disorder, hypothyroidism, migraine and history of anorexia nervosa admitted for depression and suicidal ideation. The study hypothesized that the fact that the ECT treatments were unilateral right-hemisphere may have contributed to the patient's presentation [22]. In contrast, a recent case report show treatment with ECT weekly for 2 years for a 39-years-old woman with DID, complex PTSD and Ma-

jor Depressive Disorder-Congruent Psychotic Features and chronically suicidal behaviour contributed in some capacity to this patient's personality integration [23].

Dissociative experiences are common across different psychiatric disorders [24]. A recent meta-analysis [25] showed that in comparison to non DD psychiatric patients, DD patients were more likely to report a lifetime history of both suicide attempts (SA) and nonsuicidal self-injury (NSSI). SA and NSSI could represent an attempt to cope with dissociative symptoms or an ultimate attempt to reach a dissociative state [25].

A.T. presented a PTSD. In 1 to 12% of people experiencing major psychological trauma [26], PTSD could be presented as a complex and symptomatologically heterogenous clinical picture [27], dysregulating, from molecular level (including neuroplasticity mechanisms [28]) to large brain networks [29], several biological functions. Despite a decrease in posttraumatic symptoms over time, at the follow-up of 30 months A.T. showed yet a moderate PTSD symptomatology (see CAPS score in Table I). Unfortunately, she refused, repeatedly, psychotherapy. The first line of PTSD treatment is a trauma focused psychotherapy such as Trauma-Focused Cognitive Behavioral Therapy (TF-CBT) or Eye Movement Desensitization and Reprocessing (EMDR) [30]. Several studies demonstrated EMDR clinical efficacy is determined by large and complex brain modifications of people affected by PTSD [31-34], including also those affected by TBI [35]. Unfortunately, she refused, repeatedly, psychotherapy.

We cannot exclude that A.T.'s clinical condition could have benefited from EMDR treatment, both for dissociative symptoms both for suicidality, particularly for EMDR effect on limbic and associative cortex.

Despite the improvement of depressive symptoms over time, A.T. suicidality persisted (see BDI and BHS scores in Table I). This may be interpreted as a reduction of somatic depressive symptoms in spite of persistence of depressive ideation, associated to low personal resources and coping strategies [36]. We believe that in A.T.'s clinical case a psychotherapy approach might determine a clinical improvement also through an improvement of personal coping resources.

Another clinical issue arises from our clinical case: the presence of multiple diagnoses. Both at the beginning and after 30 follow-up months A.T. presented several DSM diagnoses with several psychopathological overlapping areas. If this situation is a diagnostic distortion of our current diagnostic classification systems in Psychiatry is debating [37].

Results from this our clinical observation suggests that more structured researchers with accurate clinical assessment are needed in order to better understand the complex relation between dissociative experiences and suicidal behaviors, particularly in those patients with TBI.

Conflict of interest

The Authors declare to have no conflict of interest.

References

1. Maas AIR, Menon DK, Adelson PD, et al. *Traumatic brain injury: integrated approaches to improve prevention, clinical care, and research*. Lancet Neurol 2017;16:987-1048.

2. Bahraini NH, Simpson GK, Brenner LA, et al. *Suicidal ideation and behaviours after traumatic brain injury: a systematic review*. Brain Impair 2013;14:92-112.

3. Drange OK, Vaaler AE, Morken G, et al. *Clinical characteristics of patients with bipolar disorder and premorbid traumatic brain injury: a cross-sectional study*. Int J Bipolar Disord 2018;6:19.

4. Perry DC, Sturm VE, Peterson MJ, et al. *Association of traumatic brain injury with subsequent neurological and psychiatric disease: a meta-analysis*. J Neurosurg 2016;124:511-26.

5. Tondo L, Pompili M, Forte A, et al. *Suicide attempts in bipolar disorders: comprehensive review of 101 reports.* Acta Psychiat Scand 2016;133:174-86.

6. Pompili M, Sher L, Serafini G, et al. *Posttraumatic stress disorder and suicide risk among Veterans: a literature review*. J Nerv Ment Dis 2013;201:802-12.

7. Van Praag DLG, Cnossen M, Polinder S, et al. *Posttraumatic stress disorder after civilian traumatic brain injury: a systematic review and meta-analysis of prevalence rates*. J Neurotrauma 2019; Aug 2. [Epub ahead of print]

8. Dell PF. *The long struggle to diagnose Multiple Personality Disorder (MPD): MPD*. In: Dell PF, O'Neil AJ, Eds. *Dissociation and the dissociative disorders: DSM-V and beyond.* New York, NY: Routledge, Taylor & Francis Group 2009, pp. 383-402.

9. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders, 5th ed.* Washington, DC: American Psychiatric Association Publishing 2013.

10. Brand B. *Establishing safety with patients with dissociative identity disorder*. J Trauma Dissociation 2001;2:133-55.

11. Rossi R, Longo L, Fiore D, et al. *Dissociation in stress-related disorders and self-harm: a review of the literature and a systematic review of mediation models.* Journal of Psychopathology 2019;25:162-71.

12. Popkirov S, Carson AJ, Stone J. *Scared or scarred: could 'dissociogenic' lesions predispose to nonepileptic seizures after head trauma?* Seizure 2018;58:127-32.

13. Christensen J, Vestergaard M, Mortensen PB, et al. *Epilepsy and risk of suicide: a population-based case-control study*. Lancet Neurol 2007;6:693-8.

14. Guillen A, Curot J, Birmes PJ, et al. *Suicidal ideation and traumatic exposure should not be neglected in epileptic patients: a multidimensional comparison of the psychiatric profile of patients suffering from epilepsy and patients suffering from psychogenic nonepileptic seizures*. Front Psychiatry 2019;10:303.

15. D'Alessio L, Giagante B, Oddo S, et al. *Psychiatric disorders in patients with psychogenic non-epileptic seizures, with and without comorbid epilepsy.* Seizure 2006;15:333-9.

16. Dorahy MJ, Huntjens R *Memory and attentional processes in dissociative identity disorder: a review of the empirical literature*. In: Vermetten E, Dorahy MJ, Spiegel D, Eds. *Traumatic dissociation: neurobiology and treatment.* Arlington, VA: Ameri-

can Psychiatric Publishing, Inc., 2007, pp. 55-75.

17   Porges SW. *The polyvagal theory: new insights into adaptive reactions of the autonomic nervous system*. Cleve Clin J Med 2009;76:S86-90.

18   Van der Hart O, Nijenhuis E, Steele K. *The hauted self: structural dissociation and the treatment of chornic traumatization*. New York, NY: W.W. Norton & Company, 2006.

19   González A, Del Río-Casanova L, Justo-Alonso A. *Integrating neurobiology of emotion regulation and trauma therapy: Reflections on EMDR therapy*. Rev Neurosi 2017;28:431-40.

20   Berthier ML, Posada A, Puentes C. *Dissociative flashbacks after right frontal injury in a vietnam veteran with combat-related posttraumatic stress disorder*. J Neuropsychiatry Clin Neurosci 2001;13:101-5.

21   Sreenivasa V, Mayur P. *Dissociation of identity following left parietal haematoma – a single case report*. Australas Psychiatry 2019; Apr 16. [Epub ahead of print]

22   Zaidner E, Sewell RA, Murray E, et al. *New-onset dissociative disorder after electroconvulsive therapy*. J ECT 2010;26:238-41.

23   Webster KD, Michalowski S, Hranilovich TE. *Multimodal treatment with ECT for identity integration in a patient with dissociative identity disorder, complex post-traumatic stress disorder, and major depressive disorder: a rare case report*. Front Psychiatry 2018;9:275.

24   Lyssenko L, Schmahl C, Bockhacker L, et al. *Dissociation in psychiatric disorders: a meta-analysis of studies using the dissociative experiences scale*. Am J Psychiatry 2018;175:37-46.

25   Calati R, Bensassi I, Courtet P. *The link between dissociation and both suicide attempts and non-suicidal self-injury: meta-analyses.* Psychiatry Res 2017;251:103-14.

26   Shalev A, Liberzon I, Marmar C. *Post-traumatic stress disorder.* N Engl J Med 2017;376:2459-69.

27   Yehuda R, Hoge CW, McFarlane AC, et al. *Post-traumatic stress disorder*. Nat Rev Dis Primers 2015;1:15057.

28   Stratta P, Sanità P, Bonanni RL, et al. *Clinical correlates of plasma brain-derived neurotrophic factor in post-traumatic stress disorder spectrum after a natural disaster.* Psychiatry Res 2016;244:165-70.

29   Fenster RJ, Lebois LAM, Ressler KJ, et al. *Brain circuit dysfunction in post-traumatic stress disorder: from mouse to man.* Nat Rev Neurosci 2018;19:535-51.

30   NICE guideline [NG116]. *Post-traumatic stress disorder. National Institute for Health and Care Excellence 2018* (https://www.nice.org.uk/guidance/ng116/chapter/Rationale-and-impact).

31   Pagani M, Di Lorenzo G, Verardo A, et al. *Neurobiological correlates of EMDR therapy.* Riv Psichiatr 2012;47:16-8.

32   Pagani M, Di Lorenzo G, Verardo AR, et al. *Neurobiological correlates of EMDR monitoring – An EEG study*. PLoS One 2012;7:e45753.

33   Pagani M, Di Lorenzo G, Monaco L, et al. *Neurobiological response to EMDR therapy in clients with different psychological traumas*. Front Psychol 2015;6:1614.

34   Santarnecchi E, Bossini L, Vatti G, et al. *Psychological and brain connectivity changes following trauma-focused CBT and EMDR treatment in single-episode PTSD patients*. Front Psychol 2019;10:129.

35   Pagani M, Castelnuovo G, Daverio A, et al. *Metabolic and electrophysiological changes associated to clinical improvement in two severely traumatized subjects treated with EMDR-A pilot study*. Front Psychol 2018;9:475.

36   Rossetti MC, Tosone A, Stratta P, et al. *Different roles of resilience in depressive patients with history of suicide attempt and no history of suicide attempt*. Braz J Psychiatry 2017;39:216-9.

37   Luciano M, Sampogna G, Del Vecchio V, et al. *Critical evaluation of current diagnostic classification systems in psychiatry: the case of DSM-5*. Riv Psichiatr 2016;51:116-21.

The Journal of Psychopathology publishes contributions in the form of monographic articles, news, update articles in clinical psychopharmacology, forums in the field of psychiatry. The material submitted should not have been previously published, and should not be under consideration (in whole or in part) elsewhere; it must conform with the regulations currently in force regarding research ethics. If an experiment on humans is described, a statement must be included that the work was performed in accordance with the principles of the 1983 Declaration of Helsinki. The Authors are solely responsible for the statements made in their paper, and must specify that consent has been obtained from patients taking part in the investigations and for the reproduction of any photographs. For studies performed on laboratory animals, the authors must state that the relevant national laws or institutional guidelines have been adhered to. Only papers that have been prepared in strict conformity with the editorial norms outlined herein will be considered for publication. Eventual acceptance is conditional upon a critical assessment by experts in the field, the implementation of any changes requested, and the final decision of the Editor.

Conflict of Interests. In the letter accompanying the article, Authors must declare whether they obtained funds, or other forms of personal or institutional financing – or if they are under contract – from Companies whose products are mentioned in the article. This declaration will be treated by the Editor as confidential, and will not be sent to the referees. Accepted articles will be published accompanied by a suitable declaration, stating the source and nature of the financing.

SOPSI - Società Italiana di Psicopatologia and Pacini Editore Srl inform readers and users of the Journal of Psychopathology, that the published articles reflect only the research and the opinion of the authors signing the contents. These articles therefore do not represent and do not in any way constitute indications or guidelines of the SOPSI itself. This differs from the texts and contents that are explicitly declared as official institutional matrix and published in the appropriate sections of the Journal, which are dedicated to the Guidelines of SOPSI.

The Journal of Psychopathology is sent to SOPSI members, subscribers, doctors, health professionals, exclusively for professional training and improvement and to inform and promote activities and products / services, strictly related to the professional activities of users, always ensuring a strong affinity between the message and the user's interest. Please read the Privacy Policy at the following link: http://www.pacinimedicina.it/privacy-policy-informativa-privacy/. For communications / information: info@pacinieditore.it

General instructions
– *Online submission*: authors are requested to submit their manuscripts to: **submission.jpsychopathol.it**
Manuscripts should be accompanied by the "Permission form" downloadable from the website, signed by all authors to transfer the copyright.
– *Software and text*: please saving files in.DOC or in.RTF format.
– *Illustrations*: a) send pictures in separate files from text and tables; b) software and format: preferably send images in.TIFF or.JPEG or.PDF format, resolution at least 300 dpi (100 x 150 mm).

The text must be written in English. The paper must include:
1. **title**;
2. **summary** (Summary should be about 3000 typewritten characters (including spaces). It should be divided into 4 sections: Objectives, Methods, Results, Conclusions);
3. **a set of key words**;
4. **legends for tables and figures** (each figure and/or each table on separate pages);
5. **authors are invited to suggest 3 national or international** referees for their article.

The *first page* of the manuscript must also contain the names of the Authors and the Institute or organisation to which each Author is affiliated; the category under which the Authors wish the work to be published (although the final decision rests with the Editor); the name, mailing address, and telephone and fax numbers of the Author to whom correspondence and the galley proofs should be sent.

Tables (in 3 copies) must be limited in number (the same data should not be presented twice, in both the text and tables), typewritten one to a page, and numbered consecutively with Roman numerals. In the text and legend to the tables, Authors must use, in the exact order, the following symbols:, †, ‡, ¶,, ††, ‡‡ …

Figures, please strictly follow the above-mentioned instructions.

The *references* must be limited to the most essential and relevant references, identified in the text by Arabic numbers in upper script and listed at the end of the manuscript in the order of mention. The first 3 Authors must be indicated, followed by et al. Journals should be cited according to the abbreviations set out by *Index Medicus*.
DOI NUMBER MUST BE INCLUDED WITH EACH REFERENCE (when available).
Examples of the correct format for citation of references:
Journal article
Berretti G, Colletti G, Parrinello G, et al. *Pilot study on microvascular anastomosis: performance and future educational prospects*. Acta Otorhinolaryngol Ital 2018;38:304-9. https://doi.org/10.14639/0392-100X-1583.
Books:
Kaplan HI, Sadock BJ. *Comprehensive textbook of Psychiatry*. Baltimore: Williams & Wilkins 1985.
Chapters from books or material from conference proceedings:
Cloninger CR. *Establishment of diagnostic validity in psychiatric illness: Robins and Guze's method revisited.* In: Robins LN, Barret JE, editors. *The validity of psychiatric diagnosis.* New York: Raven Press 1989, pp. 74-85.

Acknowledgements and the citation of any grants or other forms of financial support should be provided at the end of the paper, after the list of references.

Notes to the text, indicated by asterisks or similar symbols, should appear at the bottom of the relevant page.

Mathematical terms and formulae, abbreviations, and units of measure should conform to the standards set out in *Science* 1954;120:1078.

Drugs should be referred to by their chemical name; the com-

mercial name should be used only when absolutely unavoidable (capitalizing the first letter of the product name and giving the name of the pharmaceutical firm manufacturing the drug, town and country).

Authors are required to correct and return galley proofs of their paper within 2 days of receipt.

Specific instructions for the various categories of papers:

1. Editorials: only upon invitation by the Editor-in-chief or the Editorial Board are brief discussions on general and practical aspects of topics of current interest. The text must not exceed 10 typewritten pages (2000 typewritten characters).

2. Original articles (which may also include invited articles). The text should be subdivided into the following sections: Introduction, Materials and methods, Results, and Discussion and Conclusions. The manuscript should not exceed 40.000 typewritten characters, including the summary, tables, figures and references (max 35). Summary should be no more than 3000/3500 typewritten characters (please strictly follow the above-mentioned instructions). In the Objective(s) section, the aim (or the aims) of the work must be clearly summarised (i.e., the hypothesis the Authors aim to verify); in the Method(s) section, the Authors must report the context of the study (i.e., general paediatrics, Hospital, Specialist Centre …), the number and the kind of subjects under analysis, the kind of treatment and of statistical analysis used. The Results section should refer to the results of the study and of the statistical analysis. In the Conclusion(s) section should report the significance of the results as related to clinical implications.

3. Brief articles: this space is dedicated to brief communications of clinical and experimental data and to preliminary data of ongoing research of particular interest. The manuscript should not exceed 20.000 typewritten characters, including the summary, tables, figures and references (max 10).

4. Case reports: brief articles (maximum 4000/4500 typewritten characters) in which clinical original experiences from medical practice are described.

5. Assessment and instruments in psychopathology. This section hosts articles on psychological and psychopathological assessment instruments aiming at improving knowledge of psychological functioning of those subjects with mental and behavior disorders in different reference models. The use of such instruments is not limited to clinical population but also includes non-clinical and general population. This section also accepts studies on validation and translation into Italian of instruments, new assessment instruments and competing studies of new assessment instruments with other procedures of assessment than psychopathological constructs. The manuscript should not exceed 40.000 typewritten characters, including the summary, tables, figures and references (max 35).

6. Clinical psychopharmacotherapy: articles reporting the latest developments in the area of drug therapy should be subdivided into the following sections: Introduction, Materials and Methods, Results, and Discussion and Conclusions. The text must not exceed 30.000 typewritten characters including the references, tables, figures, and summary (3000/3500 typewritten characters, excluding figure legends and table captions).

Subscriptions

The Journal of Psychopathology is published quarterly. Annual subscription: € 70,00 for Italy; € 85,00 for all other countries; € 30,00 for single issues (when available). All correspondence concerning subscriptions (including payments) should be addressed to: Journal of Psychopathology, Pacini Editore Srl, Via Gherardesca 1, 56121 Pisa (Italy) – Tel. + 39 050 313011 – Fax + 39 050 3130300

abbonamenti@pacinieditore.it - www.pacinieditore.it

Articles in open access, information for authors including editorial standards for the preparation of manuscripts and submission and Publisher's note also available on-line: www.jpsychopathol.it

---