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# The impact on psychiatric rehabilitation of personal recovery-oriented approach

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## SUMMARY

### Objectives

Psychiatric rehabilitation focuses on the main disabling consequence of mental disorder and has the ultimate aim of helping the person to heal, meant as to control the symptoms, to remove the interpersonal and environmental barriers caused from disability, to recover the abilities to live independently, to socialize, and to effectively manage daily life and accept one-self limits. In recent years, rehabilitation services have been closely associated with the 'recovery' approach. Thus, the purpose of this article is to highlight the contribution in psychiatric rehabilitation of a virtuous contamination with a recovery-oriented framework.

### Methods

In this narrative review paper, we focus on a review of conceptual papers and empirical studies that proposed new methods or concepts or engendered important debate in the field of psychiatric rehabilitation. We used three online databases: PubMed, GoogleScholar, SCOPUS, and the following keywords: 'mental health rehabilitation' or 'psychiatric rehabilitation', 'mental health recovery' and 'mental health recovery-oriented practices' or 'mental health recovery-oriented interventions'.

### Results

Since its development, psychiatric rehabilitation has undergone continuous evolutions in vision, mission, and principles. Born in the mid-eighteenth century, during the moral treatment era, and developed after the deinstitutionalization in the 1960s and 1970s, in the beginning, the task of the psychiatric rehabilitation was considered completed with the discharged of thousands of chronic patients from hospitals. It was soon clear that, for the discharged patients, there were not enough interventions, therapeutic programs or opportunities to spend time and socialize. In the 80s and 90s, the effort of traditional rehabilitation to achieve the goal to prevent or reduce social disadvantages and functional limitations and increase role performances was insufficiently achieved with a predominance of non-specific interventions. Later, non specific psychiatric rehabilitation interventions were reduced, and recovery values and principles were embodied in their vision. The concept that individuals with a psychiatric disability can live as normally as possible in society became an important goal of treatment. Nowadays, evidence shows that recovery-oriented approach and recovery-oriented interventions have positive health and social outcomes in people with severe mental illness.

### Conclusions

The overall review of the interplay between rehabilitation and recovery-oriented practices highlights that the mission now is to further implement patients and their caregivers' engagement to collaborate in a treatment process that favors empowerment and provides support to disease management, psychosocial functioning, and personal satisfaction. However, recovery-oriented rehabilitation practices are still a matter of further development, and the concrete declination of these principles into everyday life seems to be still inhomogeneous and conditioned by local factors.

**Key words:** mental health services, personal mental health recovery, psychiatric rehabilitation, review

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### Conflict of interest

The Authors declare no conflict of interest

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## Introduction

Psychiatric rehabilitation focuses on the main disabling consequence of mental health disorder and has the ultimate aim to help the person to heal, meant as to control the symptoms, to remove the interpersonal and environmental barriers caused by disability, to recover the abilities to live independently, to socialize, and to effectively manage daily life and accept one-self limits<sup>1-3</sup>.

In the last 30 years, mental health recovery has constituted a major theoretical and practical framework in mental health care<sup>4</sup>. However, there is still no general consensus on a single definition of the concept of recovery, that is a reason of debate among the main stakeholders. Generally, recovery is distinguished in personal/subjective and clinical/objective. The guiding principles of personal recovery emphasize hope and a strong belief that it is possible for people with mental illness to regain a meaningful life, despite persistent symptoms. Thus, the approach does not focus on full symptoms resolution but promotes resilience and control over problems and life<sup>5</sup>.

The purpose of this article is to highlight the contribution in psychiatric rehabilitation of a virtuous contamination with personal recovery-oriented framework. The review retraces the history of psychiatric rehabilitation since its very beginning, describes the main principles and processes of the psychiatric rehabilitation, highlights the interplay between psychiatric rehabilitation and personal recovery, and reports evidence of personal recovery-oriented approach.

## Methods

Three methods for article identification were used: electronic database searching, web-based searching, and hand searching as a cross-check.

Electronic literature searches used three online databases: PubMed, GoogleScholar, SCOPUS.

The following keywords were selected: 'mental health rehabilitation' or 'psychiatric rehabilitation', 'mental health recovery' and 'mental health recovery-oriented practices' or 'mental health recovery-oriented interventions'.

The result was a pool of scientific articles, guidance documents, and books both in Italian and in English from 1980 to 2019. The selection resulted in 35 references: 20 articles, 10 books, and 5 guidance and procedures documents for mental health organizations.

## Results

### The historical evolution of psychiatric rehabilitation

The first vision of psychiatric rehabilitation was closely connected with the philosophical ideas of Humanism, civil liberties, individualism, freedom of choice and per-

sonal responsibility born in the mid-eighteenth century. The rehabilitative principles were inspired by a combination of liberal democracy, the search for happiness, the diffusion of public health interventions, and the rebellion to the horrible condition of the confinement of the mentally ill in prisons and hospices for the poor<sup>1</sup>. In the era of the "moral treatment", reformers such as Samuel Tuke of the Quarter York Retreat in England and Dorothea Dix in the United States believed that moving the mentally ill from overcrowded urban areas to rural settings would improve the patient's abilities and mood. The proponents of the moral treatment took in the importance of compassion, cleanliness, work, and activities planned to improve thoughts, feelings, and behaviors. The founders of psychiatric hospitals believed that patients could recover if the institutions had given them the opportunity to behave normally<sup>1,2,6</sup>.

Unfortunately, as the population grew rapidly in the second half of the nineteenth century, hospitals became crowded, custodial and therapeutic nihilism increased, and – in the meanwhile – the living conditions of psychiatric hospitals worsened. In the mid-90s the introduction of psychotropic drugs raised optimism on the possibility to discharge the patients from large psychiatric hospitals into their communities<sup>2</sup>.

Thus, in the 1960s and 1970s, the deinstitutionalization process, supported by experts all over the world (e.g. Basaglia, 1968; Cooper, 1979; Foucault, 1961; Goffman, 1961; Szasz, 1984) has been developed, leading to the discharge of thousands of chronic patients from large psychiatric hospitals<sup>1</sup>. In the beginning, when the large mental hospitals closed, there was the growth of the idealistic belief that the task of psychiatric rehabilitation was completed<sup>3</sup>. However, this belief was not in line with the real state of mental health services, as for ex-patients there were a few services or therapeutic programs that offered opportunities to spend time, socialize or have fun.

In the 80s and 90s the model of Ciompi and collaborators, who planned rehabilitative programs and the evaluation of their outcomes considering housing and work activity, became a reference for mental health services<sup>7</sup>. However, the model did not produce sufficient effective professionals' capacity building in terms of providing to the patients skills generalizable to everyday life<sup>8</sup>.

Thus, the traditional approach to psychiatric disability usually consisted of a dynamic combination of pharmacotherapeutic, psychotherapeutic and containment interventions (hospitalization), not enough personalized, specific and structured to appropriately achieve the goal to prevent or reduce social disadvantages and functional limitations or increase role performance<sup>2</sup>.

However, in the last few years, psychiatric rehabilitation has undergone profound changes, that have led to a

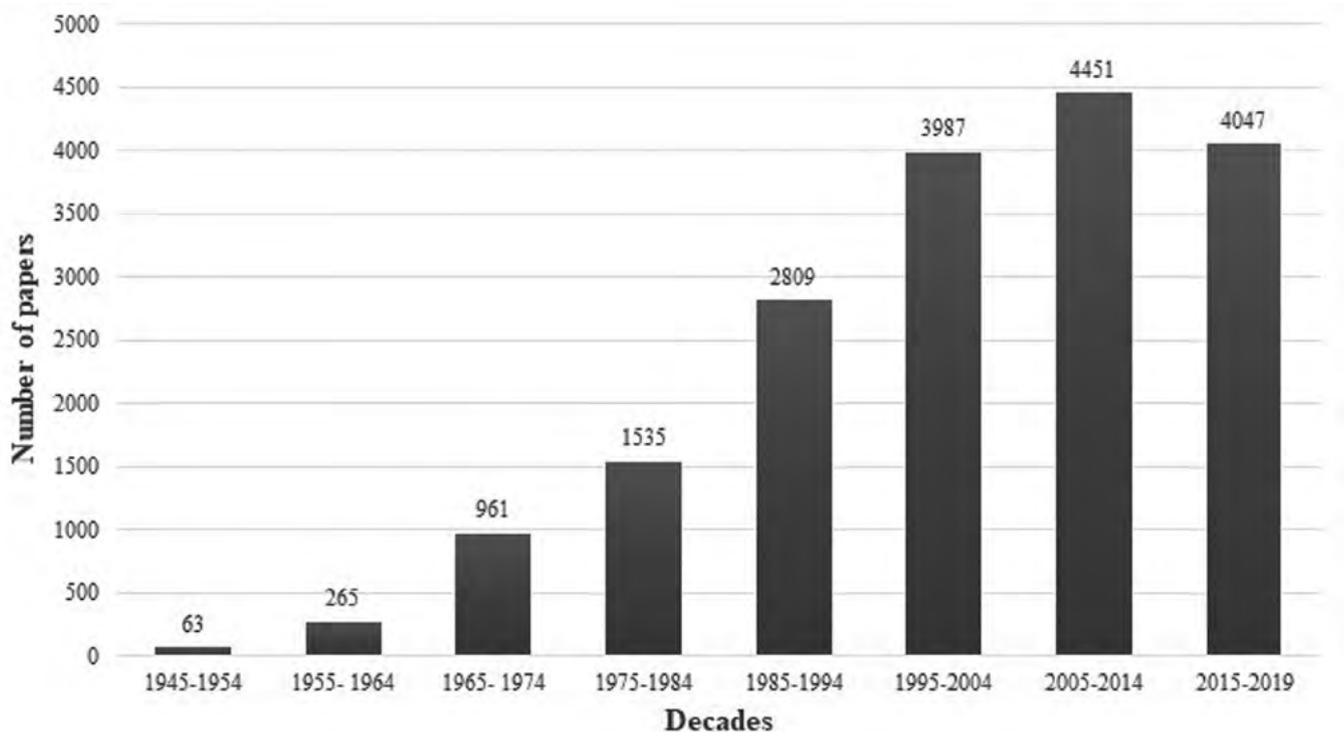
progressive reduction of non-specific interventions, and of local experiences not supported by evidence of efficacy<sup>9</sup>.

Nowadays, clinicians and researchers in the field of psychiatric rehabilitation have structured a fairly consolidated theoretical-practical corpus, decreeing with a certain delay *the end of the entertainment* desired by Saraceno already in 1996<sup>10</sup>.

There are numerous synergic factors that have determined these changes<sup>2,9</sup>. We enlist 5 main contributors due to the remodeling of rehabilitation in mental health following the deinstitutionalization process. 1) The psychiatric rehabilitation has gained more and more respect in the academic field, with an increased inclusion in scientific production<sup>1</sup>. From 1945 to 2019 19.465 papers focused on psychiatric rehabilitation have been published (data obtained using the keyword “Psychiatric Rehabilitation” in the online database *Pubmed*) see Figure 1. 2) New epidemiological and clinical evidence regarding the heterogeneity of the schizophrenic and severe mental illnesses course have set specific and personalized standards for rehabilitative interventions<sup>9,11</sup>. 3) Rehabilitative activities become evidence-based, including the evaluation of the outcomes of the disease, an aspect that has not always been adequately

considered in clinical practice in the past<sup>12</sup>. 4) The dissemination of accredited rehabilitation methods and the results achieved by them<sup>2</sup>. Several authors have shown that, when a rehabilitation treatment was added, appreciable outcomes were achieved even in the presence of undercurrent admissions<sup>13</sup>, in the work functioning<sup>14</sup>, autonomy in living and resumption of studies<sup>15</sup>. 5) The results of studies that involved users and family members proved the added value provided by subjects not involved in professional and institutional care showing that they can more sharply identify the most needed kinds of rehabilitation treatment<sup>2</sup>.

Other factors are linked to new discoveries and developments in disciplines that indirectly have an impact on mental health rehabilitation, such as 1) The contamination of psychosocial intervention techniques with specific psychotherapeutic approaches, such as the cognitive-behavioral approach<sup>16</sup> whose efficacy has been demonstrated<sup>9</sup>. 2) The introduction of atypical antipsychotics that had less extrapyramidal adverse effects, an aspect that has contributed to stigmatizing patients, and decreased the negative symptoms, major obstacles to involvement in social networks<sup>17</sup>. 3) The delivery by the community of more support and resources that can help the users to achieve their goals and increased



**FIGURE 1.** The trend of number of papers published on “psychiatric rehabilitation” from 1945 to 2019 for decades (source *Pub-Med*).

awareness that a change is required not only in the individual but also in the community<sup>2</sup>. 4) The switch from the 'Deficit Model' to the 'Strengths Model'. The founding assumption of the 'Strengths Model' is the identification of the users' strengths and of the environment rather than of the deficits. Several studies highlight positive outcomes deriving from the adoption of the 'Strengths Model' in mental health practice<sup>1,8,9</sup>. 5) The implementation of 'client-centered therapy' techniques<sup>18</sup> based on respect and partnership as a primary aim<sup>2</sup>. 6) The inclusion of social and work functioning deficits among the criteria used in the DSM-IV that highlights how mental disorders and their clinical symptoms also cause 'significant distress or impairment in social, occupational, or other important areas of functioning'<sup>2,19</sup>.

**Vision, mission, and goals of psychiatric rehabilitation**

In the historical context previously described, psychiatric rehabilitation has been defined in many ways, in most cases characterized by general statements and paucity of well-defined procedures<sup>2</sup>. However, psychiatric rehabilitation might be considered a systematic synthesis of theoretical contributions from various fields of human sciences, based on a set of specific values having as a common denominator the 'concept of person rights', which should be the primary reference for anyone involved in the sector<sup>20</sup>.

Psychiatric rehabilitation is one of the main approaches that act on disability, dysfunction, and handicaps<sup>2</sup>, focusing on the main disabling consequences of a mental disorder such as the impairment of the ability to perform social roles<sup>21</sup>; its mission is to increase social and work functioning, to make people with disabilities able to play a valid successful and satisfactory role in the environ-

ment they choose (work, housing, school, social and recreational environments), requiring as little as possible continuous professional interventions<sup>2,20</sup>.

According to the Royal College of Psychiatrists, psychiatric rehabilitation '*...at the present time, with the advent of new regulations in the field of mental health, has the task of assisting people with severe psychiatric disabilities who already live in the community to reach a life as autonomous and satisfying as possible*'<sup>22</sup>.

Thus, the ultimate goal of psychiatric rehabilitation is to help the person to heal<sup>21</sup> with a series of actions such as 1) to remove interpersonal and environmental barriers caused by disability<sup>2</sup>, 2) to facilitate the increase of social articulation through learning and use the social skills (instrumental, interpersonal, intrapersonal) that enable the individual to respond appropriately, and to adapt to the demands and needs, implicit and explicit, of oneself or of those with whom he lives<sup>23</sup>, 3) to modify the environment in order to reduce stress factors as much as possible<sup>2</sup>, 4) to ensure access to the responsibilities and social, professional and leisure opportunities as a citizen who participate in the community life<sup>1</sup>, 5) to control symptoms, 6) to increase skills to live independently, 7) to effectively manage daily life and to accept one-self limits because, despite these, it is possible to live most experiences of other human beings<sup>2</sup>.

**Principles and process of psychiatric rehabilitation**

Psychiatric rehabilitation based its own vision and mission on principles, that regulate the delivery of rehabilitative interventions, form the basic assumptions and the key concepts, and the ethics of the professionals<sup>1,2</sup>. They are also fundamental for the design, development, and implementation of rehabilitation treatments<sup>1</sup>.

**TABLE I.** *The seven principles of psychiatric rehabilitation.*

Carozza, 2006 <sup>2</sup>	Liberman, 2009 <sup>1</sup>
The functioning	The recovery of a normal life is possible for many people with psychiatric disabilities if the best rehabilitative practices are provided
The delivery of support	Impairments, disabilities, and handicaps can be reduced or overcome by integrating pharmacological, and psychosocial treatments with advocacy interventions in order to improve the clinical, professional, and scholastic and government policies
The environmental specificity	The individualization of treatment is the fundamental pillar of rehabilitation
The involvement	Rehabilitation is more effective when patients and families are actively involved
The choice	Building on the strengths, interests, and abilities of the patient is a cornerstone of rehabilitation
The outcome orientation	The integration and coordination of the interventions are essential in promoting rehabilitative progress
The confidence in people's growth potential	Rehabilitation takes time, progresses gradually, and requires perseverance, patience, and resilience by patients, families, and therapists

The principles derive both from conceptual bases and awareness of practical needs for interventions<sup>1,2</sup>. Thus, the fundamental concepts of psychiatric rehabilitation stimulate the development of practices, that are tested by research, and, in turn, provide empirical results<sup>1</sup>.

The principles were elevated to a system by Anthony<sup>20</sup> and accepted, with general consent, by main thinkers of psychiatric rehabilitation<sup>2</sup>. Table I shows the 7 main principles that characterize psychiatric rehabilitation today.

To achieve the goals of psychiatric rehabilitation, a systematic work of inclusion and definition of a set of values has to be translated into a structured process constituted by different activities, all essential to achieving outcomes.

The first step is the rehabilitative diagnosis, which includes the evaluation of availability for rehabilitation, functioning and resources, and the definition of the global rehabilitative aim.

The second phase is the planning of the interventions that are focused on the development of skills and resources<sup>2</sup>.

The last phase is the implementation of a range of interventions that make it possible for people with disabilities to use cognitive, emotional, social, intellectual and physical skills necessary to live, learn, work and function as normally and independently as possible in the community with minimal interference from symptoms.

The methods by which these goals are achieved are: medications, cognitive rehabilitation, and disease management interventions to eliminate or reduce symptoms; functional evaluation of all dimensions; to teach people specific skills; to organize and plan supporting environments and programs; to involve families; work rehabilitation; to provide accessible treatments and interventions; to provide special interventions for special people (for example for people with substance misuse); to provide professional and natural supports.

Rehabilitation interventions varies in shape, intensity, and duration depending on the type of psychiatric disorder and the degree of disability. Thus, the type and extent of treatment is modified according to a series of variables such as severity, chronicity, and co-morbidities of various disorders; response to drug treatment; intelligence, learning ability, social competence, cognitive functioning, growth and development process, level of education, cultural and ethnic background, social class and economic resources, family support and satisfaction with the current quality of life; changes in the availability of mental health services and community resources<sup>1</sup>.

### Recovery-oriented psychiatric rehabilitation

In recent years, psychiatric rehabilitation has been closely associated with recovery<sup>6</sup>. A recent definition

of recovery-oriented psychiatric rehabilitation is *'...a whole systems approach to recovery from mental illness that maximizes an individual's quality of life and social inclusion by encouraging his skills, promoting independence and autonomy in order to give him hope for the future and leads to successful community living through appropriate support'*<sup>3</sup>.

In a recovery framework, the vision of psychiatric rehabilitation is to make individuals with a psychiatric disability able to achieve recovery and live as normally as possible in society<sup>1</sup>. This implies to activate care pathways oriented towards personal recovery even when disabilities and difficulties of various kinds are present<sup>6</sup>, and engage patients and their family members or caregivers to actively collaborate in a treatment process that promotes empowerment, disease management, psychosocial functioning, and personal satisfaction<sup>1,2</sup>. Valuing hope and optimism becomes fundamental, and the importance of good physical and mental health, the respect for individuals of all ages and cultures, and the right to live a life not defined by illness or diagnosis are values that should underlie all effective rehabilitation practices<sup>4,6</sup>.

The recovery approach, as claimed by Slade and collaborators<sup>24</sup>, offers an opportunity to use rehabilitation to encourage users to get involved in defining their care goals<sup>25</sup>. Rehabilitation interventions have to embrace measures that capture the direct experience of the service user, and mental health professionals have to address problems and difficulties in a manner that includes and recognizes the user's wishes and ambitions. Mental health organizations should also consider how users can take benefit of the role of peer experts, and service users should be consulted about the need for service developments, management, and design in a co-production perspective<sup>6</sup>.

Moreover, psychiatric rehabilitation should be activated on one hand at the onset of a disorder to preserve the skills for everyday life and goals<sup>26</sup>, and on the other hand for people with disabilities with longer-term mental health problems, to address the disabilities of users who have not made a rapid recovery and may experience difficulties in global functioning<sup>6</sup>.

Rehabilitation interventions should be both evidence-based and based on the best rehabilitative practices; the combination favors significant improvements in attitudes and initiatives that promote empowerment, self-responsibility, hope, and user satisfaction, and quality life<sup>1</sup>.

Recently, recovery-oriented approach and, particularly the shared decision-making process, has shown evidence in improving self-management, autonomy, and health outcomes of service users with mental health disabilities<sup>27-31</sup>. Moreover, it correlates positively with a re-

duction of the costs for the health systems<sup>32</sup> and overall makes mental health practices fit for the 21<sup>o</sup> century<sup>28</sup>. Thus, individualized and user-centered projects are indicated as quality objectives for mental health services in general<sup>29,32,33</sup>, and in particular for mental health rehabilitation.

Research proves positive outcomes for people with mental health disorders adopting personal recovery-oriented interventions with a bulk of evidence such as 1) *peer support workers*, who are experts by experience who offer to users and families members a model of successful care path in a range of more or less formal approaches within mental health organizations; 2) *Advanced treatment directive*, a document that specifies a person's future preferences for treatment if the person loses the mental ability to make treatment decisions; 3) *refocus*, a program of research aimed to find ways of making community-based adult mental health services in England more recovery-oriented; 4) *the strengths model*; 5) *the individual placement and support (IPS) model*, a psychosocial intervention of supported employment, with a considerable body of evidence for effectiveness in helping people with severe mental illness to obtain and maintain competitive employment according to their preferences; 6) *the recovery colleges*, that offer educational courses about mental health and recovery designed to increase students' knowledge and skills to feel more confident in self-management; 7) *supported housing*, a rapid re-housing in independent accommodation for people with severe mental illness, according to their preferences; 8) *mental health trialogues*, community forums where service users, carers, friends, mental health workers, and others with an interest in mental health participate in an open dialogue<sup>24</sup>.

## Conclusions and future directions

The main limitation of the current paper is the chosen methodology for achieving the purpose, that was based

on a series of key words. Subjectivity in the study selection might have lead to selection bias.

However, this methodology enabled to explore a large number of papers, selecting the most relevant conceptual papers and empirical studies in the field that introduced new methods or concepts or engendered important debate in psychiatric rehabilitation.

The findings of this review report that evidence shows how recovery-oriented rehabilitation, users' involvement, individualized and user-centered projects, and shared choices, have a positive impact on health outcomes. Current international guidelines and policy papers consider the recovery-oriented approach as the quality objective for psychiatric rehabilitation services<sup>28,29,33</sup>. These approaches have an increasingly powerful influence on everyday professional practice<sup>6</sup> and have been experimenting in different contexts<sup>32</sup>.

However, recovery-oriented practices have not well spread and implemented yet in psychiatric rehabilitation<sup>34</sup>. Recovery-oriented practices and user involvement in the co-production of health interventions are still a matter of debate in numerous documents by qualified agencies and bodies<sup>35</sup>, and the concrete declination of these principles in the daily practices of mental health services, even in Italy, seems to be still inhomogeneous and conditioned by local factors<sup>27</sup>, such as different historical contexts and different organizational structures, and considerable uncertainty about the precise meaning of these concepts and their effective application in the practice of services<sup>8</sup>. However, optimism about recovery can be easily found in policy documents or guidelines for good clinical practice.

In conclusion, finding a way to adequately implement the recovery-oriented approach in psychiatric rehabilitation without dismantling but instead integrating the traditional rehabilitative approach is a difficult but important struggle for all the stakeholders involved in the process<sup>1,6,8</sup>.

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# The contribution of autobiography and literature to the understanding of Tourette syndrome

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## SUMMARY

### Objective

*Tourette syndrome (TS) is a neurodevelopmental condition characterised by the presence of multiple tics and often associated with co-morbid behavioural problems, such as obsessive-compulsive symptoms, attentional problems and affective dysregulation. First-person accounts of TS are particularly important to understand key features of subjective experiences related to tic expression and other aspects at the interface between neurology and psychiatry. We therefore set out to explore the role of modern literature and autobiography in portraying TS to the general public.*

### Methods

*We reviewed the full-text of a representative sample of modern literary texts and autobiographies and critically appraised their contributions to the understanding of Tourette syndrome.*

### Results

*The reviewed texts explored the experience of TS from a variety of literary perspectives and demonstrated the contribution of autobiographical accounts to understanding tics and the rich inner world of patients with TS.*

### Conclusions

*Our findings highlight the importance of literary accounts (particularly if written from a first-person perspective) in providing education about potentially stigmatising conditions, such as TS.*

**Key words:** Tourette syndrome, tics, autobiography, subjective experiences, behaviour

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### Conflict of interest

The Authors declare no conflict of interest

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## Introduction: Tourette syndrome and the purpose of patient narrative

Tourette syndrome (TS) is a neurodevelopmental condition characterised by multiple motor tics and at least one phonic tic<sup>1</sup>. Tics are defined as repetitive, non-rhythmic and a-finalistic movements (e.g. blinking, grimacing, shoulder shrugging) or vocalisations (e.g. grunting, throat clearing, shouting) perceived as involuntary and associated with characteristic subjective experiences of urges to tic, also called sensory tics<sup>2</sup>. TS is a chronic disorder with onset around the age of 6 and chronic course with waxing and waning severity across the lifespan<sup>3</sup>. Once thought to be a rare and somewhat bizarre medical curiosity, TS has been re-conceptualised by recent epidemiological studies as a relatively common neurological condition, affecting up to 1% of the general population, with different degrees of severity<sup>3</sup>. Co-morbid behavioural problems are present in about 90% of patients, with obsessive-compulsive symptoms and attention-deficit

and hyperactivity being most commonly reported and playing a significant role in the impact of TS on health-related quality of life<sup>4,6</sup>. The aetiopathological models of TS have undergone a paradigm shift between the beginning and the end of the last century, from Ferenczi's psychoanalytic observations on tics to modern biological models in which genetic factors play a central role<sup>3</sup>. Historically, TS has often been viewed in literature as "shorthand for concealed insanity or malevolence"<sup>7</sup>, but the place of this condition in non-medical literature reaffirms the value of the patient's own story<sup>8</sup> and the importance of the patient as an individual<sup>9</sup>.

The meaning of patient narratives or autobiographical accounts has been thought to lie in providing the unique opportunity for patients to consider and approach their illness differently, and for the clinician, the means by which to treat the patient as a whole<sup>10</sup>. Making the 'whole' person matter more in modern clinical encounters is an important asset of these patient autobiographies or 'pathographies'<sup>11</sup>. Such pathographies have had considerable historical importance at times when patients chose to communicate with their physicians via personal correspondence, a practice which characterised 18<sup>th</sup> century medicine<sup>12</sup>. While doctors cannot experience the patient's illness with them, they can learn to look for those personal reactions which are an important part of patient narratives<sup>12</sup>. Others have suggested that the benefits of these accounts can permeate right through to the very mind-set which doctors use in their communication, and that bringing mindfulness into their interactions can benefit themselves as well as their patients<sup>13</sup>. Using this kind of awareness and sense of empathy are skills which are in high demand in psychiatry given the emotional weight of the situations which psychiatrist and patient are part of<sup>8</sup>.

The benefits of these narratives are valuable in the understanding of TS, firstly in the description of the motor and phonic tics which characterise this condition. This paper will explore the experience of TS from a variety of perspectives and demonstrate the contribution of these accounts to understanding this condition and the rich inner world which we may be privileged to observe. The authors will then consider how comparisons can be made and the lessons which can be learned from published academic accounts, which are derived from a different part of the spectrum of style, form, and language.

### Physical symptoms

In the first of these accounts, *Passing for Normal* by Amy Wilensky, the author inevitably provides some description of her tics<sup>14</sup>. However, the value to the reader lies in the language used to describe them and what they mean to Wilensky and others like her. She recalls:

*I could feel the tension building in the joints and muscles of my shoulders, neck, torso, and arms, the half of my body that bears the brunt of most of my tics* (p. 20). Here the physical symptoms are described almost like an assault on the body, which becomes a notable style of writing in this account<sup>15</sup>. Again, there is the reminder that symptoms such as motor tics do not just happen to the patient, but that they also have personal consequences and significance for them which should not be overlooked<sup>16</sup>. This added quality to the experience of tics is described by Wilensky:

*Wrong movements are tics, motions with no point, black sheep cousins of the hand that reaches over the shoulder to scratch the back* (p. 35).

This is reflected in the second account, *Twitch and Shout* by Lowell Handler<sup>17</sup>. Handler provides this added quality to his tics, describing how "*my Tourette was expressing itself*" (p. 31) and the variability in his symptoms by explaining that "*I never knew what form it would take, and when*" (p. 45). Here the tics are a wholly separate entity, and this relationship of the patient to their TS is an important second theme of these accounts.

### A personal relationship

Doctors have been criticised for distancing themselves from their patients too easily<sup>16</sup>, and being primarily concerned with treatment<sup>18</sup>. The need to rediscover the importance of personal reactions to illness<sup>8</sup> may benefit much from these autobiographical accounts<sup>19</sup>. The nature of a patient's personal relationship with their tics is described in Handler's account using rich visual imagery, which helps to promote understanding in those who are unfamiliar with the condition<sup>20</sup>:

*If I could come to grips with some elusive inner demon that was strangling me, I thought, I would be able to imagine myself miraculously "cured". If I could solve my problems, then my calmer, more "normal" self would emerge as if from a cocoon* (p. 33).

Thus, while Handler gives a visual representation to his tics, Wilensky puts a personal distance between herself and her TS, viewing her tics as "*characteristics of somebody else: a casual acquaintance, a friend of a friend*" (p. 14). Literature therefore demonstrates to the reader that there can be a complex relationship between individuals and their TS, *cautioning against oversimplifying this dynamic relationship and preventing to the creation of false assumptions*.

### False assumptions

Wilensky wrestles with the idea that her tics may define her as much as any other unique physical characteristic:

*Eliminating them with the pop of a pill was an eradication of my very soul, a self-inflicted stab wound to the*

*integrity of my character, the very make-up of my molecules* (p. 161).

Through this powerful description, Wilensky demonstrates one of the key values of such autobiographies – their ability to bring the condition to the very centre of one's personal identity and underline its importance to the experience of life<sup>11</sup>.

The second assumption is that patients will necessarily find support groups beneficial, something which is contradicted in the accounts discussed here. When being confronted with a spectrum of severity within support groups, both authors find it an uncomfortable experience to contemplate a worse future for themselves and their relationship with their TS. Handler recalls:

*I was afraid that I might see how much worse the disorder could be, or that I would in fact become worse through this contact, as if Tourette were contagious, even to a Touretter* (p. 46).

While Wilensky describes seeing another member of the group:

*[It] was like stumbling upon a funhouse-mirror version of myself, like covering my eyes with my hands at the gruesome parts of a movie* (p. 49).

Literature can be an important tool for clinicians simply through guarding against making assumptions about patients and preventing a paternalistic approach to managing conditions such as TS. While literature can help illustrating a patient-centred description of symptoms, how patients relate to them, and the assumptions which may be made, it can also make clinicians more aware of the consequences of formally diagnosing patients.

### The formal diagnosis

The diagnosis for Wilensky is a pivotal part of her story, especially because of a difficult and misunderstood relationship with her father<sup>9</sup>. In a direct address to her father, she describes:

*"I have a neurological disorder," I enunciated carefully. "You were wrong. I was right. I can't make myself stop"* (p. 144).

Here the diagnosis empowers Wilensky to prove the assumptions of her father wrong with conviction, and therefore once again literature reminds the clinician that the diagnosis carries great significance. These accounts can be equally helpful as coping tools, using them to aid understanding from others' perspectives, a process termed 'contextualisation'<sup>18</sup>. Moreover, it could be argued that from a philosophical perspective certain literary accounts can save the patient's own moral identity<sup>21</sup>. While the diagnosis was equally cathartic for Handler, giving sense to an oftentimes bewildering past, his cautionary note was that "I began to see things in terms of 'them' and 'us' (p. 47). Handler's account could be beneficial for clinicians as an example of how

labels can force patients into expected categories and ultimately lead them to lead less fulfilled lives<sup>20</sup>. In addition to the value the diagnosis holds for the patient, both authors also demonstrate how the diagnosis leads to a sense of ownership over the condition (and empowerment), to the point that they are presenting the facts and the experience of having TS to the reader. Wilensky achieves this and shows a desire to educate the reader themselves. Again, like Handler, she resorts to visual imagery to communicate the experiences familiar to her:

*Picture your skin as comprised of only nerve endings with no neutral ground; in this case, the barely discernible pat of a fingertip would send sensations vibrating through every atom in your body. Welcome to Tourette's* (p. 26).

This type of autobiography, termed "didactic" where the main purpose is to inform<sup>11</sup>, is a consistent model across these accounts, possibly due to the relatively poor public understanding of conditions like TS. However, the ways in which these narratives inform the reader are not always complementary to a straightforward clinician-patient relationship.

### Self-medication

Handler describes his long-term reliance on a "self-prescribed regimen of pot and Prozac" (p. 127), a routine which contributed to the end of his marriage but which provided him "a sense of inebriation and wellbeing" (p. 120). Wilensky is much more experimental in her use of cannabis, leading her to a realisation which clinicians may find difficult to respond to. She recalls:

*The pot, I knew, had rendered me me again, but it was a version of me I only faintly recognised now* (p. 123).

The realisation that conditions such as TS can be managed – to some extent – by self-medication with substances of abuse leads to the creation of a complex relationship with the condition and therefore an important lesson for clinicians. The benefits both authors found from cannabis is important for clinical training, as it emphasises that patients *will not always make the same carefully regulated and informed decisions as those of the clinician, and that actions such as these should be anticipated rather than ignored. Having described the ways in which these literary autobiographies of TS can help in better understanding the condition, the reader and clinician must bear in mind some key criticisms of this narrative form which should not be overlooked.*

### Limitations of autobiography

Firstly, it should be anticipated that some level of publication bias exists in the same way in non-medical literature as it does in evidence-based medicine. Facts on their own are insufficient to attract an audience, and

in the process of their transformation to become more appealing, we can lose the sense of intimacy and personal encounter with the author<sup>22</sup>. Secondly, there is an expectation in the nature of these accounts that the author undergoes a personal transformation and sense of resolution with the world<sup>22</sup>, both of which could be said of Wilensky and Handler's accounts. Moreover, neither of these criticisms could be said to be resolved by biographical over autobiographical accounts<sup>23</sup>. Shapiro recently argued that the reader can come to a resolution, and since "the story of the thing is never the thing itself", being aware of the way that the narrative may have been affected is not necessarily an excessive compromise<sup>23</sup>.

Secondly, these accounts can perhaps mislead individuals with conditions such as TS, into the belief that they too can have the same freedom as the author to express their experience and most exposed feelings to their clinician, when this is unlike the true nature of clinical consultations<sup>13</sup>. Given then that the reader may be being misled into the realism of these accounts, the use of fictional narratives could offer a helpful compromise.

### *Motherless Brooklyn*, by Jonathan Lethem

Lethem's character, Lionel Essrog, finds himself at the centre of a murder mystery which forms a chaotic side-line to his experience of TS<sup>24</sup>. Lethem, like Handler, uses rich visual imagery to communicate Lionel's internal struggle, as reflected in the use of "cultural and physical metaphors and similes"<sup>25</sup>. Here Lionel provides a way for the reader to access the experience of palilalia (self-repetition), a complex vocal tic associated with TS since its very first description by Georges Gilles de la Tourette in 1885<sup>2</sup>:

*My own name was the original verbal taffy, by now stretched to filament-thin threads that lay all over the floor of my echo-chamber skull. Slack, the flavour chewed out of it.* (p. 7)

While there is a rather complex use of language to be found in this account, Kravitz points out the plain and colloquial language used to describe Lionel and his appearance to the world. When he describes those people who have labelled him as 'crazy', he is demonstrating the cultural influences on his identity<sup>25</sup>. However, Lethem's character also toys with cultural references, asking the reader: "*If a Touretter curses in the woods and there's nobody to hear does he make a sound?*" (p. 10). Through this observation and others, Lionel challenges the culture around him and indeed he is able to observe life in a way that others are not able to: *Tourette's teaches you what people will ignore and forget, teaches you to see the reality-knitting mechanism people employ to tuck away the intolerable, the incongruous, the disruptive- it teaches you this because you're the one lobbing the intolerable, the incongruous, the disruptive their way* (p. 43).

In fact, Lionel achieves this by assimilating the identity of a "freak", rather than ignoring it, feeling that to be otherwise would be to "dodge your destiny": this attitude inevitably leads to Lionel becoming "Overt Freak Supreme" (p. 68). Awarding himself this accolade is a powerful representation of his constant clashing with culture.

However, despite Lethem's inventiveness with language, Lionel's character is ultimately not supported by the story which surrounds it, calling into question any added benefit from writing a non fictional account in this style<sup>20</sup>. Indeed there are occasions where Lethem's use of language distances the readers rather than bringing them closer to a genuine understanding of TS. Through his constant vocal tics, Lionel informs the reader:

*I collected words, treasured them like a drooling sadistic captor, bending them, melting them down, filing off their edges, stacking them into teetering piles, before release I translated them into physical performance, manic choreography* (p. 47).

If this style, in contrast to Wilensky and Handler, is to be used, then a balance must be found between engaging the readers and excluding them, something which Lethem may not have achieved consistently. Having therefore considered what patient autobiographies and fictional accounts have to offer, a balanced exploration can be achieved by considering the contribution of academics who have documented their own experiences of TS.

### Two contrasting academic accounts

Compared to literary accounts, academic accounts are less likely to be accessed by the general population, despite being often written in an adequately thought out and engaging style. The first of these accounts is provided by Dr Lance Turtle and demonstrates a far more formal style in writing about personal experiences of TS<sup>26</sup>. This account sees the clash between formal and attempted informal elements, which means that it is more challenging to determine the intended audience. Turtle begins his account with the sub-heading "In the Beginning", providing the author with a quasi-Biblical reference which is at odds with the overall presentation of his experiences.

In contrast to the patient autobiographical narratives presented in this article, Turtle switches between the technical style of a medical history and linguistic registries which provide more of a personal insight into his subjective experiences. Perhaps the reason for this struggle is found in the words of the author: "*It is very hard for anyone who has never had a tic to know what it is like to tic*"<sup>26</sup>. Again, it is more convincing that without being able to use colourful language, narratives published in this domain encounter greater difficulty in educating the lay audience.

However, there are consistent themes which are found also in the other narratives presented, such as the sensory urges to tic. Liking the feeling preceding the tic to an itch is described by Turtle: “*The relief is temporary, however, and, much like scratching a mosquito bite, having executed the tic the relief is very transient*”<sup>26</sup>. Likewise, Lionel in Lethem’s account describes his urge to tic:

*It’s an itch at first. Inconsequential. But that itch is soon a torrent behind a straining dam. Noah’s flood. That itch is my whole life* (p. 2).

Similarly, just as Wilensky observed that her tics define her as much as any other physical characteristic, so Turtle also recognises the contribution that tics have made to himself. He challenges the reader:

*This is how I am, tics and all, and if you don’t like it, tough.*

Similarly, as was noted in Handler and Wilensky’s narratives, the diagnosis of TS is an important moment, particularly for Wilensky in challenging her father. For Turtle, the diagnosis ultimately endows a sense of belonging. He concludes his own narrative with the conclusion:

*Everything has its place. Now I have my label of “TS”; I too have my place.*

The second academic account, by Peter J. Hollenbeck, chooses to address the audience more directly and finds the difficult line between making the reader interested and alienated<sup>28</sup>. Here the identity of the audience is much clearer: Hollenbeck is directing the narrative towards society in its broadest terms. He describes TS as “*largely a disease of the onlooker. When I tic, I am usually not the problem. You are*”<sup>27</sup>.

Again, there is similarity in this context to its patient narrative counterpart. Hollenbeck echoes the same observation made by Lionel in Lethem’s narrative:

*If I have a tic and there is no one there to mock me, is it a tic?*

Hollenbeck even questions the existence of his TS if it is without an observer, and part of his challenge to the society around him lies in the fact that his tics go against the rules of order which society depends on. This is something which has been described as lying at the heart of how this condition is perceived, the patient as an unstoppable and frightening person<sup>8</sup>. Hollenbeck describes others’ reactions to his tics:

*I was a disordered body in their field of view, and they could not resist the urge to establish order.*

These influences lead to a second theme shared by Hollenbeck and Wilensky: given the way that TS is considered part of the self, in both accounts there is a strong sense of ownership over the condition in which the individuals are exhibitors, presenting the condition for the world. Hollenbeck observes:

*Like all people afflicted with chronic disease, we Tourette sufferers become experts on our own condition.*

Wilensky communicates the same principle through the style of language that has been noted previously:

*Picture your skin as comprised of only nerve endings with no neutral ground; in this case, the barely discernible pat of a fingertip would send sensations vibrating through every atom in your body. Welcome to Tourette’s* (p. 26).

Since there are these macroscopic differences and similarities between patient/fictional narratives and academic work, deciding on their contribution to the understanding of TS is not simple, and perhaps meaningless. The two latter authors are in the position of publishing among their peers and as such, the lay readers only benefit from as much as the author is prepared to give away of themselves. Hollenbeck provides a rather humble perception of the impact of his narrative:

*Tourette is frustrating, annoying, occasionally humiliating, but it is hard to imagine others finding inspiration in my paltry battles.*

If Hollenbeck describes the potential for inspiration from his published narrative as limited, it could be argued that this is a contribution which is mainly achieved in patient narratives<sup>11</sup> and therefore that the limitations described earlier are an acceptable cost for providing this inspiration.

## Conclusions

Literature and autobiographical accounts have a great deal to offer to patients and clinicians, providing a unique platform from which to approach illness. The autobiographical accounts of TS described in this paper have demonstrated how literature can teach clinicians and lay readers valuable lessons in how patients relate to their symptoms and their complex interaction with the tic symptoms and the external observers. Within the narratives of TS presented here, readers are privileged to witness an interlinking and intricate world of language which is used to communicate several important key themes. Descriptions of the tics themselves, patient’s personal relationships to them, the meaning of the diagnosis, and the assumptions that may be made by clinicians, are all beneficial in helping to understand the narrative context of TS. However, the realism of these accounts can be called into question, meaning that the contributions of other forms of narrative must be considered. Unfortunately both fictional and published academic accounts seem to convey their own limitations, in addition to unique insights. Lethem’s account could be in danger of alienating its audience, while the stories of Turtle and Hollenbeck differ considerably in style and only provide as much benefit to the understanding of TS as the authors can afford to provide of themselves. TS as “largely a disease of the onlooker” will always have a

place within both patient autobiography and literature, but the ways in which they assist the reader in understanding the condition vary considerably and carry their own limitations. The role of education should not be underestimated, as the following semiserious lines epitomize: "I've just invented a new drug for Tourette syndrome!" "Will it stop people with Tourette syndrome having tics?" "No, it's an acceptance pill for everyone else". In the future, the contribution of other forms of

narrative can be fruitfully explored, including - perhaps surprisingly - the use of comics by patients, calling for an even more active participation from the reader<sup>28</sup>. Finally, the novel *Motherless Brooklyn* has recently been adapted as a neo-noir crime film directed by Edward Norton. Cinema and television can usefully complement the role of novels, plays, and poems dealing with movement disorders in providing education about potentially stigmatising conditions<sup>29,30</sup>.

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# Melancholy and the function of forgetting A psychopathological note about depression and memory

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## SUMMARY

*A long lasting psychopathologic tradition concerns the alteration of time perception and of the structure of lived-time in severely depressed (melancholic) patients. This literature can be reappraised in light of the more recent study on the functioning of memory and especially of emotional autobiographical memory. In depressive episodes, the memory of past events overrides the present, preventing the individual from synchronizing with the environment and planning the future. Forgetting the events would be a major strategy for recovery; however, most of the patients are not able to disengage themselves emotionally from the past. This is true not only for melancholic depression, but for complicated bereavement too. From this point of view, melancholy can be considered an illness in which the balance between recalling and forgetting is altered. Based on a phenomenological method, the use of neurocognitive assessment instruments on melancholic patients could shed light on the pathogenesis of depressive episodes with melancholic features.*

**Key words:** melancholy, mood disorders, time, temporality, memory, recalling, re-actualization, persistent bereavement, forgetting

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## Introduction: the classic phenomenology of time experiences in melancholic states

The earliest description of depressive states in modern psychiatry is that of Nostalgia (*Heimweh*), the affective pain of soldiers far from home, that is to say an illness of autobiograph memory <sup>1</sup>. Since the beginning of the nineteenth century however, Melancholy has been considered, from a medical-psychopathological point of view, the result of a cognitive <sup>2</sup> or mainly an affective <sup>3</sup> disorder. Since the half of the nineteenth century, classifying depression as a mood disorder has become the most popular approach, even though cognitivist paradigms have never disappeared and recently have been reappraised because of the focus on neurocognitive symptoms of depression in view of their pharmacological treatment. Only since the early decades of the twentieth century, the classical essays of Freud <sup>4</sup>, Straus <sup>5</sup>, von Gebattel <sup>6</sup>, Minkowski <sup>7</sup>, Binswanger <sup>8</sup>, and, later, Tellenbach <sup>9</sup> and others <sup>10-14</sup> have paid attention to the existential stasis, and the subjective standstill of time as the fundamental dimensions of Melancholy. The main feature of this condition is the *presentification* of the past, that places in second order actuality, relationships and obligations, so that the present cannot be lived and the future cannot be planned. Freud<sup>4</sup> studied Mourning as a clinical model for Major Depression (*Melancholie*). Both Mourning and Major Depression follow the loss of a love object in the recent or far past, but in the former the lost object is external, in the latter internalized, consequently the patient experiences a loss of a part of himself. Following Freud's studies, "depressive states" have been considered in psychoanalysis the "pathological equivalent of hopeless mourning" <sup>15</sup>.

Straus<sup>5</sup> distinguished “ego-time” from “world time; he observed that the inhibition of inner time in melancholy does not allow the patient to progress toward the future nor to close up and leave behind his/her past experiences. Minkowski<sup>7</sup> described the subjective depersonalization state of the melancholic patients who does not perceive anymore the flow of time in the usual sense (*le temps veçu*) and concluded that “the melancholic patient feels he is running towards the past as if he was captured by it”. Binswanger<sup>8</sup> observed and emphasized the alteration of the “temporality texture” in the melancholic patient, according to which memories of the past (*retentio*) overwhelm the present (*praesentatio*) preventing the patients to project themselves in the future (*protensio*). Binswanger’s patients complaints are in past tense form in sentences such as: “*if I hadn’t done it!*”, “*If this hadn’t happened!*” and so they are fatally coloured by guilty feelings. Similarly, Tellenbach<sup>9</sup> focused on the fact that the melancholic patient always believes that they never complete their tasks and aims (so called “remainder constellation”). Finally, Ballerini<sup>12</sup> defined the peculiar experiences on which the melancholic patient is compelled to ruminate on the past as “irremediable, incorrigible”; analogously, Kuiper<sup>16</sup> confirms in a personal report of a depressive state: “*What has happened can never be undone again. Not only the things go by, but also possibilities pass by unused*”. If everything has already happened and cannot be changed, nor viewed from different perspectives and interpreted with different meanings (worked through), then the future time cannot be anything other than an extension of the past. Because of this dominance of the “absolute past”, “memories become regrets, the events of life faults”<sup>11</sup>.

These psychopathologic observations mirror some earlier philosophical intuitions, such as the well-known Friedrich Nietzsche’s quotation “Blessed are the forgetful; for they get the better even of their blunders”<sup>17</sup>. Nietzsche’s quotation was allegedly/anectotically inspired by a subjective melancholic state. In the nineteenth century, the great Italian poet and philosopher Giacomo Leopardi had already described his own “stubborn, black, ugly, barbarous melancholia” as the “turnover of the future in the past, of hope in recalling, because of the absence of life that wastes reality and depletes the desire of objects”<sup>18</sup>. Finally, the rumanian-french aphorisms-writer Emil Cioran describes his own melancholic experience: “To live means undergoing the appeal of the possible: but when we perceive in the possible in itself only a becoming past, everything is virtually past, and there is no present nor future”<sup>19</sup>.

Patients frequently verbalize similar realizations: “*I felt a void full of past time conjugated in the present time; the present is the past and the past is the present. It’s the same thing. It’s a blank and still oscillation of the time without future*” (C.T); “*I felt my heart squeezed by a*

*painful constriction, memories came back without rest, it is not the future to kill you but the past, when it returns, harasses you, hollow you until it kills you*” (M.H.); “*if what happened in my adolescence hadn’t happened, I wouldn’t be here looking for psychological help*” (E.B.) In his almost completely forgotten psychopathological research on endogenous psychoses, Janzarik<sup>20</sup> has been the first to discuss not only the altered perception of time, but also the alteration of memory during manic-depressive episodes: past events are “re-actualized” in the acute manic-depressive episodes so that old facts are retrieved and updated as if they were present. Following Leopardi and Cioran’s psycho-philosophical argumentations, we should is past event rumination ask it is a sequela or the cause of the plenty of present objects? Each psychiatrist well knows how much the depressed patients, prisoners of the past, are not able to find new activating aims and objects, lack of “teleological time”, even if “conative drive” is preserved<sup>14</sup>. Even in course of treatment, this position increases the feelings of hopelessness both in them and in the therapist. Effective remission of the phase of illness can be observed only when the patient begins to get rid of the past memories; however relapses are frequent and, with them, the return of the painful ruminations on events believed or perceived as irremediable.

The aim of this psychopathological note is to rise some questions from a clinical and neurocognitive (not psychoanalytical, not philosophical) point of view about the relationship between depressive states (melancholy), disturbances of lived-time and memory, and to underline the fundamental, complex, bi-univocal, ambivalent link between mood disorders, remembering and forgetting, in view of further clinical observations and researches.

### The DSM-5 and the complicated mourning

Perhaps because of the academic crisis of the psychopathological European tradition, the current diagnostic criteria<sup>21</sup> of Depressive Disorders show almost no traces of the phenomenological contributions of the early twentieth century. The term “melancholic feature” exclusively refers in modern manuals to the lack of reactivity, anhedonia, vital symptoms, and to an “excessive or inappropriate guilt”<sup>22</sup>. However, references to time experience are explicit in the criteria of Post-traumatic Stress Disorder (“recurrent, involuntary, and intrusive distressing memories of the traumatic event(s)”) and in those proposed for the Persistent Complex Bereavement Disorder, in the section “Conditions for further study”. This category recalls Freud’s study on mourning as a model for melancholy; the first criteria B1 is “Persistent yearning/longing for the deceased”. This criterion refers to persistent suffering because of the loss of a love object prolonged for at least 12 months.

This condition may be complicated by “traumatic” features of the linked experiences, such as a violent or dramatic type of death (traumatic bereavement). Complicated bereavement overlaps with both Depressive Disorders, Post-traumatic Stress Disorder, and Separation Anxiety Disorder (i.e. a condition defined by anxiety feelings referring to hypothetical, future events of loss). This is the only observable link between the current nosography and the classic concepts of “Reactive Depression”<sup>23</sup> or “Endoreactive depressions” of the Heidelberg school<sup>23,24</sup>. From a psychopathological point of view Fuchs<sup>13</sup> underlines that during emotive, acute, interpersonal experiences (e.g. trauma, guilt, loss, or separation) “the person temporarily loses the lived synchrony with others”. Prolonged desynchronization becomes the marker of a characteristic melancholic depressive state. The depressive patients do not share the “temporal orientation that we ordinarily take for granted”<sup>14</sup>. Implicit time, in the terminology of Fuchs<sup>13</sup>, replace the explicit, chronological, shared time.

Current nosography appears to have “thrown away the baby with the dirty water” with the aim of excluding not empirically definable diagnostic criteria. DSM-5<sup>21</sup> admits that “adverse childhood experiences and stressful life events” may be considered “precipitants of major depressive episodes”, however it maintains that “the presence or the absence of adverse life events near the onset of episodes does not appear to provide a useful guide to prognosis or treatment”.

This point of view rules out memory as an important pathogenetic factor in Persistent or Complicated Bereavement as well as in Major Depression. If the past is present, if the events are re-actualized, and if melancholic patients are compelled to ruminate exclusively on past “irremediable” events, then the *function of forgetting* is necessarily impaired, suspended, or overwhelmed by remembering. In complicated mourning processes, the course of time halts, while the dead person is ever-still-present, as it appears in this short poem<sup>25</sup>: “*Mourning: What bores me/abrasive blade inside my brain/is not your dead/in a bed, a spring,/but that you still die/every day, in every season*”.

In the Persistent Bereavement Disorder, the recovery cannot occur until the feelings of the yearning/longing or post-traumatic dysregulation associated with the death vanish. Only then the accompanying backwards ruminations and interrogations that for months completely absorb the mind of the survived, negatively colouring and depleting of sense their life<sup>26</sup> regress: “*I still think about him [the dead father], but no more with the deep anxiety and the ruminations I suffered for two years; I used to feel bad, now not anymore*”. (MB)

Current literature on memory failures and depression is very heterogeneous and not conclusive; there is a gen-

eral assumption that memory is concerned, biased and, in some cases, impaired in depressive episodes<sup>27,28</sup>, such as the effect of a dysregulation of emotions by way of inhibitory processes and deficit in working memory. These would support ruminative responses to negative mood states and negative life events, as well as difficulties in disengaging from negative material<sup>29</sup>.

### A short reference to a movie

*Eternal sunshine of the spotless mind*, written by the Oscar winner screenwriter Charlie Kaufmann<sup>30-31</sup> provides a witty representation of the functioning of autobiographical memory in its narrative, emotive e imaginative (imaginery) elements<sup>29</sup>. The movie talks about the story of two young ex partners who, following their separation, singly ask for help to a physician (Dr. Merzwyack), in the fictional medical-psychological institute “Lacuna Inc.”, with the aim of relieving their depressive pervasive feelings. The physician can identify the memories linked to their love affair by mean of a sort of functional RMN and delete them while the protagonists are asleep, so removing the psychical pain linked to the memories. The therapy is doomed to fail not because of its inefficacy, but especially because of the resistance of the patients who are not completely asleep and resist the feeling of losing parts of their personal story and identity.

The idea of this science-fictional plot is not so bizarre and its “scientific principle”, explained by Dr. Merzwyack, could have even some real scientific value: “*There is an emotional nucleus in our memories; when we delete it, the downgrade process starts*”. In clinical practice, it is obvious that some bereavement processes as well as some depressions unleashed by stressful events (loss or death or separation) remit only when the emotional nucleus of the memories begins to fade away.

But what do the current scientific data of experimental neuropsychology say about the process of *emotional forgetting*?

### The neuropsychology of forgetting

Memory is a very complex function that encompasses different short-term and long-term neuropsychological processes, from working memory to conditioning acts and all sort of learning, declarative memory, including the autobiographical memory<sup>32,33</sup>. A plethora of studies on memory disturbances in depression concern the impairment of attention and working memory<sup>34,35</sup>. However, the processes of remembering (or forgetting) personal experiences (autobiographical memories) seem to be more relevant for psychopathology, especially when such experiences are charged with emotions<sup>33,37</sup>. The autobiographical memory is the result of a complex integration of memories, thoughts, representations, affects, needs, and

aims of the individual, and it has a well-defined role in establishing the identity of the Self and the organisation of personality (Self-schema<sup>38</sup>; autobiographical Self<sup>39</sup>); it includes the simple recalling of the event, which seems to involve hippocampal circuits, and the emotional components of the remembering, which implicate the role of amygdala<sup>40</sup>. Some vivid images ineffaceably linked to specific events are called “flashbulb memories”<sup>40</sup>.

Earlier researches in the field of psychology of recall processes established that memory traces are better fixed if connected to a reinforcing stimulus<sup>42,43</sup>. More recently, it has been demonstrated that emotions themselves are reinforcing stimuli. Hence, the memories concerning negative personal events are more strongly fixed and more vividly remembered<sup>44</sup>. However emotional memories exhibit a lower number of details and a higher number of mistakes because the high emotional arousal causes a narrowing of the attention field at the time of the event<sup>45</sup>. On the one hand, state or mood-congruence enhances the recall of the event<sup>40</sup>, while, on the other hand, different mood states repress it. The emotional memories, in comparison with the neutral ones, are resistant to forgetting (so called “slow forgetting”)<sup>46,47</sup>, even if the time of recalling may be delayed for many years<sup>47,48</sup>. This case reminds the involuntary memories triggered by sensorial stimuli, well described at the beginning of the nineteenth century by the novel-writer Proust<sup>48,49</sup>.

The literature on sexual abuses has widely shown the complexity of recalling traumatic or almost-traumatic memories, that can be repressed or removed from awareness for years and even decades, until some mood-congruent situations or other conditions, for example a manic-depressive episode, triggers their recalling<sup>50</sup>. The recalling of traumatic life episodes often partially overlaps with the reality of facts, because of the well-known process of continuous rebuilding of memories and their interplay with more or less consolidated beliefs. Sometimes, only single “now print” images are remembered and recalled<sup>51-53</sup>.

In summary, many data support the persistence or retrieval of emotionally charged memories of life events, whose presentification unleashes mood alteration or, conversely, is accomplished because of the mood congruence. It is time to open a new field of clinical research on neurocognition of memory in depressive states, especially melancholic, that explores the inhibition and enhancement processes of remembering.

### Can Melancholy be considered an illness of memory?

If in the melancholic conditions the time is still (the temporality is halted or desynchronized from the environment<sup>13</sup>) and the patient cannot enjoy at all the usual

activities in the present nor project himself in the future because of the persistence of the past, of ideas of guilt, ruminations on events that seem to be irreparable and beyond every remedy. Thus Melancholy is not only an illness of lived-time and temporality, but overall of forgetting or recalling.

*Something* must have happened before the uprising of a melancholic state; one or more facts that, by coming back in mind as it was present, interfere with the normal dynamic and evolution of existence. The question is whether events unleash melancholy or conversely, the melancholic episode keeps or recalls the events and associated secondary set of guilt ideas, ruminations, regrets in the mind. The typical conditional sentences (e.g. “*If it hadn't happened...*”) of the melancholic patient demonstrate that there is no melancholy without some key-unleashing-event, or without a key-event that has frozen the subjective course of life in time. A melancholic patient can be considered a survivor who tries to cope with their past life to overcome it, without finding a concrete solution: life passes by on the surface, but not really in his/her inner world. He/she sometimes feels as “a disconnected witness to a life that is over”<sup>14</sup>.

But different nosographic categories beside melancholy, and probably different types of depression<sup>14</sup>, imply the function of memory and forgetting. Criteria for Post-traumatic Stress Disorder recognize the specific role of an event as a pathogenetic factor, and DSM-5 shows significant overlaps between PTSD and major depression. If we focus on time and memory interplay, we can argue that the overlap is greater than usually admitted.

The memory of a Panic Attack causes clinical sequelae such as anticipatory anxiety and hypochondriac ideas or agoraphobia. Even the dysfunctional patterns in the different Personality Disorders imply fixated and consolidated ways of coping with early childhood experiences (i.e. not declarative memory). Finally, episodes in Bipolar disorder independently from the quality of mood (depressive, mixed, dysphoric and so on – any sort of Mood could ease mood-congruent memories) can reactualize past life-events.

What is specific to Melancholy, then? The *duration of the time-period before the emotional component of the memory of a negative event* (for example a death, a loss etc.) *fades*. Such interval of time depends on the interaction between the event and the personality, and, also, on some features or details of the event (e.g. faulty or traumatic aspects). There is a sort of *biological time* needed to isolate narrative and autobiographical memories from their emotional component. In this sense we can understand why some traditional cultures prescribe standard periods of time after the death of a strict rela-

tive before the individual can begin to live without the psychological interference of the bereavement. However, not all events can be completely emotionally forgotten and worked-through; mood-congruent situations can reactivate old, appeased emotions linked to specific, ineffaceable events, signalling a problem, a risk, a threat, a challenge for ego-identity, and the vulnerability areas of the personality, already struck by the event many years earlier. Several melancholic patients have been dramatically affected by early childhood events, such as the death of a parent, as incurable wounds always bleeding.

### The different kinds of time in subjective experience: learning from clinical conditions

The clinical-phenomenological analysis of time experience in depressed (melancholic) patients raises the question of the different kinds of time experienced and conceived by human mind. The first kind of time is, obviously, the *chronological or astronomical or watch- or objective (objectualized), scientific time*, that is needed to measure a period of time consensually.

The second is *the subjective experience of the flow of time, the duration*; it has been largely studied by psychologists and philosophers until the end of nineteenth century<sup>54,55</sup>. This includes different perceptions of time in boredom<sup>56</sup>, depression, mania, during the usual routine or in extraordinary circumstances of life and at different life stages. A form of subjective time is also the autobiographic one: in the twentieth century, psychoanalysis and psychoanalytic experiences, as well as many literary autobiographic (psychoanalytic) narratives point out the anarchic stream of subjective, un-linear, or multivectorial memories and autobiographical writing could be a way to work-through painful memories and events (for an example<sup>57</sup>).

The third kind of time is the *biological time*: it is the time needed for the fading of the emotional, painful component of memories of autobiographical events, so that they cannot intrude anymore in disturbing the present. It reflects the duration of biological processes needed for the transition from short- and long-term memories, the encoding processes, the reshaping work and so on. The final form of the memory of an event is mainly cognitive and the emotional component of the memory itself is a narrative memory with ever more feeble emotional components. The biological time is fundamental for the clinical course of some depressive or post-traumatic experiences: until the memories are not emotively neutralized, the subject suffers from the emotional correlation of memories.

The fourth kind of time is even more subjective: it is *the time that makes some events ever present*, outside the normal process of working through. We might call it

*psychopathological inability to forget*; it concerns specifically the events associated with melancholic chronic experiences (clinically called chronic, complicated, or resistant depressions) but also recurrent episodes and relapses of the illness and chronic course of Post-Traumatic Stress Disorder. These events seem to escape the processes of forgetting and to strictly connect with mood alterations.

### Conclusions: melancholy, time, memory, forgetting

We can argue that two types of retrieval memories are involved in the subjective melancholic experience:

- a) memories of recent events affectively charged as in recent traumas or in bereavement or losses and so on;
- b) memories of far events or traumas that are repressed or removed but never really forgotten because of their emotional impact, and that can arise many years after their occurrence because of occasional circumstances, sensorial stimuli or mood-state congruence.

In case a), the subject is a sort of hostage of the *biological time* needed to overcome the painful effect of an event. Until this time, that varies depending on the event and on the individual, has passed by, the melancholic mood cannot change.

In case b), the relationship between events and the process of forgetting or recalling is much more complex, because it is mediated by manic-depressive episodes (mood-congruent memories), life circumstances (associative paths), or sensorial stimuli (involuntary memory). But whatever the way, the common result is that a past event is perceived as present again, with its emotional charge, and the awareness of its ineffaceability.

*Being able to forget or to forget quickly negative events is perhaps a good trait marker of melancholy-invulnerability.*

Because of the autobiographical memory implications, a wide number of melancholic episodes are full of subjective, personal meanings for the patients. The subtle and dynamic equilibrium between remembering (recalling and reconstructing events) and forgetting (letting autobiographical memories become affectless codes) could be perhaps the main system neurobiologically and psychopathologically involved in Melancholy, although it is scarcely taken into account both by patients and clinicians. It could be a cause of treatment-resistance, because we actually have not any drug to delete the emotion still linked to past events. It is a very simple and trivial finding, but it seems to be quite true.

The aim of this psychopathological note is to rise some questions from a clinical and neurocognitive (not psy-

choanalytical, not philosophical) point of view about the relationship between depressive states (melancholy), disturbances of lived-time, and memory, and to underline the fundamental, complex, bi-univocal, ambivalent link between mood disorders and remembering and forgetting, in view of further clinical observations and research.

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# The “Personal Health Budget” intervention model in early psychosis: preliminary findings from the Parma experience

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## SUMMARY

### Objectives

Personal Health Budget (PHB) has recently been provided to people with severe mental illness, reflecting a policy shift towards a personalized mental health care based on individual unmet needs. However, evidence on effectiveness of PHB initiatives is still limited. Aim of this research was to provide preliminary data about the beneficial effects of adding PHB to a multicomponent EIP intervention in patients with First-Episode Psychosis (FEP) along a 2-year follow-up period.

### Methods

Participants (n = 49) were FEP patients, aged 18-50 years, entered the “Parma Early Psychosis” program and completing the Health of Nation Outcome Scale (HoNOS), the Brief Psychiatric Rating Scale (BPRS) and the Global Assessment of Functioning (GAF). Friedman test for repeated measure (with Wilcoxon test as post-hoc procedure) was performed to evaluate the longitudinal stability of functioning and clinical parameters. A linear regression analysis was also carried out.

### Results

A significant effect of time on all HoNOS, BPRS and GAF scores along the 2 years of follow-up was found. Regression analysis results specifically showed a relevant association between a PHB multiaxial intervention and the longitudinal decrease in BPRS “Negative Symptoms” subscores, as well as in HoNOS “Behavioral Problems” and “Social Problems” scores.

### Conclusions

Our results support the general applicability of a PHB approach within an “Early Intervention in Psychosis” program for help-seeking adults with FEP.

**Key words:** personal health budget, early intervention in psychosis, first episode psychosis, early psychosis, mental health services, rehabilitation

## Introduction

Welfare systems of modern Western societies have recently implemented new forms of organization and social/health integration increasingly centered on patients and their unmet needs, and structured on a local community basis<sup>1</sup>. This paradigm shift was a consequence of providing a better service to the users, as well as more tailored interventions aimed at leading to innovative, network-based practices that integrated public

health services, patients' and their families' resources and local communities ones (such as those of social agencies, third sector and voluntary associations) <sup>2</sup>. This also translated into a reduction of intensive or residential treatments in favor of long-term care interventions at home, within the belonging community <sup>3</sup>. In this context, *Personal Health Budget* (PHB) has been proposed as an innovative rehabilitation model that consists of funds and/or indirect resources addressing users, aimed to specifically support their individual health, social and personal needs <sup>4</sup>. It is a contract following an agreed plan between the person, his family and the social/healthcare services involving in taking care, within an individualized ("person-centered") rehabilitation program implemented thanks to the all interested part cooperation <sup>5</sup>.

### PHB in Italy

In Italy, the welfare system has in recent years undergone radical changes, moving from an institution-based healthcare model to a community-based service model, aimed at enhancing the person's point of view, his strengths and needs to be implemented within his life context <sup>6</sup>. Given these premises, some Italian public mental health departments introduced the PHB as part of the patient's "Individual Rehabilitation Plan" (IRP), in order to promote his social inclusion, in spite of the severe and chronic mental health disorder he was suffering from <sup>7</sup>. Indeed, it was specifically addressed to people with Severe Mental Illness (SMI), requiring rehabilitation processes made of both social and healthcare interventions <sup>1</sup>. The PHB is inclusive of individual, familiar, social and healthcare resources, all gathered to prevent mental health disorders from becoming chronic and to prevent patients' isolation. It is intended to connect social and healthcare systems and was developed either to allow patients' discharge from psychiatric residential facilities or to avoid/delay patients' new residential admissions <sup>8</sup>. However, over time, the PHB model has expanded its purposes and has focused specific interventions on citizens' global health rather than on patients' disease, preventing the most fragile subjects from being isolated from their native community. Indeed, PHB is intended to merge social interventions with healthcare system ones, but also with individual, familiar and environmental resources, in order to create tailor-made pathways to care, promoting and maintaining patients' social inclusion within their belonging communities <sup>9</sup>. In this context, the 2015 Emilia-Romagna Regional Council Deliberation Act n.1554 ("Guidelines for the implementation of individual pathway to care through the PHB methodology application) has officially given start to the PHB model implementation in all the regional mental health departments, with specific attention to adult psychiatric services <sup>7</sup>.

Starting from this background, the *aim* of this research was to provide preliminary data about the beneficial effects of adding PHB to a multicomponent EIP ("Early Intervention in Psychosis") intervention in adults with First-Episode Psychosis (FEP). Specifically, we wanted to compare clinical and functional outcome indicators across a 2-year follow-up period. Main hypothesis of the current study was that positive outcomes could be obtained – in terms of clinical recovery and socio-occupational functioning – thanks to the PHB approach application (i.e. an integrated rehabilitation treatment on the axis "housing-work-sociality") within a specific EIP protocol for FEP patients provided in all adult psychiatric services of the Parma Department of Mental Health (i.e. the "Parma Early Psychosis" [Pr-EP] program) <sup>10</sup>, already compounding psychoeducational, pharmacological and psychotherapy interventions in patients' native environment. To the best of our knowledge, no study on PHB model in early psychosis has been published in the literature to date.

## Materials and methods

### Participants

Data were retrospectively collected at the baseline and at the follow-up routine assessments of help-seeking adults recruited through the Pr-EP program between January 2015 and December 2018. All participants (n = 49) agreed to participate to the study and gave their written informed consent prior to their inclusion in the research. Local ethical approval for the study was obtained (AVEN Ethics Committee: protocol n. 36102/09.09.2019). The present research has been also carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments including humans.

For the purpose of this study, inclusion criteria were: (a) specialist help-seeking; (b) age between 18 and 50 years; (c) presence of FEP criteria within one of the following psychiatric diagnoses as defined in accordance with the Diagnostic and Statistical Manual of mental disorders, IV edition, Text Revised (DSM-IV-TR) <sup>11</sup>: schizophrenia, bipolar disorder with psychotic symptoms, major depressive disorder with psychotic symptoms, delusional disorder, brief psychotic disorder, schizophreniform disorder and psychotic disorder not otherwise specified; and (d) a Duration of Untreated Psychosis (DUP, defined as the period of treatment delay [in months] between the onset of psychotic symptoms and the first pharmacotherapy administration) <sup>12</sup> < 2 years. According to the FEP criteria defined by the Italian version of the "Comprehensive Assessment of At-Risk Mental States" (CAARMS-ITA) <sup>13</sup>, the threshold of a full-blown psychotic episode is defined by operationalized

clear-cut levels of overt positive symptoms occurring for > 1 week, either daily or > 3 times a week with each symptom lasting for > 1 hour on each occasion. Furthermore, we opted for a DUP cut-off of < 2 years because it is considered the limit to start a specific care protocol according to the EIP paradigm<sup>14</sup>.

Exclusion criteria were: (a) history of previous affective and non-affective psychosis, in accordance with the DSM-IV-TR criteria (DSM-IV-TR)<sup>11</sup> (b) past exposure to antipsychotics or ongoing antipsychotic treatment started more than three months before the baseline assessment (c) current substance abuse/dependence, according to the DSM-IV-TR<sup>11</sup>; (d) known intellectual disability (Intelligence Quotient < 70); and (e) neurological disorders, head injury, or any other medical condition associated with psychiatric symptoms. In the Pr-EP program, we specifically considered previous exposure to antipsychotics (i.e. before the Pr-EP enrollment) as an equivalent of a past psychotic episode. Indeed, according to the FEP criteria proposed by Yung and co-workers (2005)<sup>15</sup> in the original version of the CAARMS, the threshold of a full-blown psychotic episode is the clinical condition requiring an antipsychotic medication to be started in the common clinical practice. Furthermore, we opted for an antipsychotic treatment interval shorter than three months because of our attempt to select FEP patients at the very beginning of their pharmacological treatment.

### Instruments

The psychopathological assessment for this study included the Brief Psychiatric Rating Scale (BPRS) – version 4.0<sup>16</sup>, the Global Assessment of Functioning (GAF) scale<sup>11</sup> and the Health of Nation Outcome Scale (HoNOS)<sup>17</sup>.

The BPRS – version 4.0<sup>16</sup> – is an instrument enabling the clinician to quickly collect information about the presence/absence and the severity of 24 main psychiatric symptoms, rated on a Likert scale ranging from 1 (“not present”) to 7 (“extremely severe”). In the present study, we used the BPRS 5-factor model proposed by Dazzi and colleagues (2016)<sup>18</sup> and including “Positive”, “Negative”, “Affect”, “Activation” and “Disorganization” dimensions. In the current research, we used the authorized Italian translation of the BPRS – version 4.0, which showed good psychometric properties in Italian clinical populations<sup>19</sup>.

The GAF is a scale used to rate patient’s social, occupational and psychological functioning. Scores range from 100 (“extremely high functioning”) to 1 (“severely impaired functioning”). In the present study, we used the Italian version of the GAF scale included in the DSM-IV-TR<sup>20</sup>, already previously administered in Italian clinical populations of adolescents and adults with FEP<sup>21,22</sup>.

The HoNOS was developed to measure improvements in health and social functioning of people with endur-

ing mental health problems<sup>17</sup>. Structurally, the HoNOS includes 12 items, each one rated on a 4-point Likert scale (from 0 = “no problem” to 4 = “severe to very severe problems”). A total score is obtained and subscale scores can also be calculated by combining groups of items as follows: (a) “Behavioral Problems” (items 1-3), (b) “Impairment” (items 4 and 5), (c) “Psychiatric Symptoms” (items 6-8) and (d) “Social Problems” (items 9-12)<sup>23</sup>.

### Procedures

The axis-I diagnosis was made accordingly with the DSM-IV-TR diagnostic criteria<sup>11</sup> through the Structured Clinical Interview for DSM-IV-TR axis I disorders (SCID-I)<sup>24</sup> administered by two trained Pr-EP team members<sup>10,25</sup>. After the SCID-I evaluation, all the help-seekers meeting the CAARMS-defined FEP criteria<sup>15</sup> were included in the Pr-EP program and were assigned to a multi-professional team, generally within 3 weeks from the referral. Based on severity of their symptoms, FEP patients were provided with a comprehensive 2-year intervention program including pharmacological treatment and a multi-component psychosocial intervention (combining individual cognitive-behavioral-oriented psychotherapy, psychoeducational sessions for family members and a recovery-oriented case management), according to the most recent guidelines<sup>26,27</sup>. Low-dose atypical antipsychotics were prescribed as first-line treatment.

The PHB methodology was proposed as an integration of the standard Pr-EP interventions to all FEP patients with a relevant complexity on the following areas of functioning: housing, employment and/or social participation. Individuals who accepted the PHB proposal were included in the study. The PHB model is an integrated (social and healthcare) approach supporting the IRP of people with SMI and consisting in a mixture of social, health, personal and family resources. It is aimed to improve their clinical and functional recovery, as well as their social inclusion and active participation in the native community through the activation of rehabilitation programs<sup>8</sup>. Specifically, it may be activated to sustain home care programs, to support family care through specific interventions of supported accommodation and social/occupational empowerment, and to prevent social isolation<sup>7</sup>.

The qualifying elements of the PHB model were: (a) a Multidimensional Evaluation Unit (MEU), including mental health and social services, defining the IRP and the PHB resources according to the principles of appropriateness and equity; and (b) an IRP, recovery-oriented, person-tailored and based on a careful evaluation of the patient’s needs and abilities (rather than depending on the services’ offer), developed together with the user, his family members and (if appropriate) with other local

community agencies (such as social cooperatives) <sup>8</sup>. In the current study, the PHB integrated the standard PR-EP protocol by providing specific interventions within the social areas most affecting people's health (i.e. housing, employment and social relationships), in order to create and maintain virtuous connections between community healthcare and social systems through an appropriate use of their resources <sup>27</sup>.

Within the "Housing" axis, interventions could include actions aimed at supporting life at home or at gaining a new home/accommodation, either individually or in co-housing groups. Depending on personal needs, different forms of support were provided, ranging from temporary, active home support (in order to strengthen the autonomy in everyday life) to more prolonged interventions for the maintenance of a good family and environmental conditions. Within the "Sociality" axis, rehabilitation treatments aimed at promoting friendship, family relationships and social networks, enhancing the patient's empowerment and/or the development of social skills. Specifically, interventions had to stimulate the participation in cultural, relational, recreational, and sport activities into the individual's living environment. Finally, the "Training/Work" intervention axis included all actions aimed at promoting social inclusion and active participation in the community through training activities and supported employment, also within the Italian legislative framework regarding apprenticeships and job placements <sup>4</sup>.

PHB resources could include: (a) healthcare ones, provided by community adult mental health services, often relying on social cooperatives; (b) social resources, provided by the local social agencies for integration and social inclusion (e.g. social service professionals, educators, public housing, meals at home, financial aids); (c) patient's resources including both economic and relational ones (i.e. family members, friends); and (d) resources coming from local voluntary associations. The IRP was signed by all the involved subjects (i.e. patient, family, mental health case manager, social service professional, etc.), therefore making the individual PHB official.

### Statistical analysis

Data were analyzed using the Statistical Package for Social Science (SPSS) for Windows, version 15.0 <sup>28</sup>. All tests were two-tailed. Threshold of significance was set at  $p = 0.05$ . Frequencies and percentages were used to describe categorical parameters, whereas mean values  $\pm$  standard deviation were used to represent continuous parameters. Due to non-normality in all explorations (i.e. Kolmogorov-Smirnov test with Lilliefors correction:  $p < 0.05$ ) <sup>29</sup>, non-parametric statistics were used. Specifically, Friedman test for repeated measures (and Wilcoxon test with Bonferroni correction as post-hoc pro-

cedure for multiple comparisons) <sup>30</sup> was performed to evaluate the longitudinal stability of BPRS, HoNOS and GAF scores in the FEP group across the 2-year follow-up period. Finally, linear regression analysis (with functioning and psychopathological scores as dependent variables, and PHB intervention [multi-axial vs uniaxial] as independent variable) was also performed.

## Results

Over the course of the study, 49 FEP patients (36 [73.5%] males, 42 [85.7%] white Caucasians, mean age =  $26.08 \pm 6.29$  years) were retrospectively enrolled in the research (see Table I for details on sociodemographic and clinical characteristics of the FEP total group). The sample included individuals with DSM-IV-TR schizophreniform disorder ( $n = 16$ ; 32.6%), schizophrenia ( $n = 14$ ; 28.6%), affective (bipolar or major depressive) psychosis ( $n = 7$ ; 14.3%), brief psychotic disorder ( $n = 6$ ; 12.2%), psychotic disorder not otherwise specified ( $n = 4$ ; 8.3%), delusional disorder ( $n = 1$ ; 2.0%) and schizoaffective disorder ( $n = 1$ ; 2.0%). As regard the PHB intervention typology, 18 (36.7%) FEP participants received a PHB multi-axis approach. Moreover, 44 (89.8%) of FEP individuals were provided with a PHB intervention on the "Training/Work" axis, 21 (42.9%) on the "Sociality" axis and 4 (8.2%) on the "Housing" axis. All FEP patients concluded the 2-year follow-up period, with the exception of 3 (6.1%) individuals who dropped out during the second year of the study.

### Follow-up data

Across the 2-year follow-up period, a statistically significant decrease in the severity of all BPRS and HoNOS scores was found (Tab. II). A relevant longitudinal improvement in GAF score was also observed. However, in the time period between T1 and T2 (i.e. between 1-year and 2-year assessment times), no further decrease in BPRS "Negative" and "Disorganization" factor subscores was reported.

Finally, linear regression analysis results showed a statistically significant negative association between multi-axial PHB intervention (as independent variable) and the difference (delta [ $\Delta$ ]) between T2 and T0 (baseline) BPRS "Negative" factor subscores (as dependent variable) (Tab. III). A multi-axial PHB approach also had a relevant negative association with the deltas between T2 and T0 HoNOS "Behavioral Problems" and "Social Problems" subscale scores.

## Discussion

In the past two decades, empirical evidence showed that psychopharmacological treatment alone, despite clinical improvement, is not enough to prevent relapses

**TABLE I.** Sociodemographic and clinical characteristics of the FEP total sample (n = 49).

Variable	
Gender (males)	36 (73.5%)
Age at entry	26.08 ± 6.29
Education (in years)	11.71 ± 3.96
Ethnic group (white Caucasian)	42 (85.7%)
Mother tongue (Italian)	36 (76.5%)
DUP (in month)	9.21 ± 7.56
DSM-IV-TR diagnosis	
<i>Schizophreniform disorder</i>	16 (32.6%)
<i>Schizophrenia</i>	14 (28.6%)
<i>Brief psychotic disorder</i>	6 (12.2%)
<i>Affective psychosis</i>	7 (14.3%)
<i>Psychosis not otherwise specified</i>	4 (8.3%)
<i>Delusional disorder</i>	1 (2.0%)
<i>Schizoaffective disorder</i>	1 (2.0%)
Participants who dropped out during the 2-year follow-up period	3 (6.1%)

Legend – FEP: first episode psychosis; DUP: duration of untreated psychosis; DSM-IV-TR: Diagnostic and statistical manual of mental disorders, 4<sup>th</sup> Ed., Text Revised. Frequencies (percentages) and mean ± standard deviation are reported.

**TABLE II.** Functioning and psychopathological characteristics across the 2-year follow-up period in the FEP total sample (n = 49).

Variable	T0	T1	T2	F <sub>[2]</sub>	Post-hoc <sup>†</sup>
BPRS scores					
<i>BPRS “affective”</i>	14.53 ± 5.22	10.81 ± 3.80	9.09 ± 2.59	55.04 <sup>*</sup>	T0 > T1 > T2
<i>BPRS “positive”</i>	16.85 ± 5.64	11.02 ± 4.46	9.50 ± 3.57	55.11 <sup>*</sup>	T0 > T1 > T2
<i>BPRS “activation”</i>	12.56 ± 6.25	8.58 ± 3.50	7.52 ± 2.32	52.92 <sup>*</sup>	T0 > T1 > T2
<i>BPRS “negative”</i>	8.67 ± 3.32	6.46 ± 2.51	7.31 ± 2.07	31.49 <sup>*</sup>	T0 > T1 = T2
<i>BPRS “disorganization”</i>	9.19 ± 3.84	6.49 ± 2.62	7.04 ± 2.51	45.42 <sup>*</sup>	T0 > T1 = T2
<i>BPRS total score</i>	66.38 ± 17.98	47.47 ± 12.43	43.83 ± 10.13	55.96 <sup>*</sup>	T0 > T1 > T2
HoNOS scores					
<i>“Behavioral problems”</i>	3.49 ± 2.74	1.77 ± 2.01	0.83 ± 0.96	55.77 <sup>*</sup>	T0 > T1 > T2
<i>“Impairment”</i>	2.83 ± 2.01	1.98 ± 1.58	1.60 ± 1.36	29.44 <sup>*</sup>	T0 > T1 > T2
<i>“Psychiatric symptoms”</i>	10.04 ± 3.37	5.85 ± 2.81	4.06 ± 2.34	83.37 <sup>*</sup>	T0 > T1 > T2
<i>“Social problems”</i>	8.00 ± 2.83	5.85 ± 2.79	4.50 ± 2.51	66.94 <sup>*</sup>	T0 > T1 > T2
<i>HoNOS total score</i>	29.87 ± 11.26	18.29 ± 9.15	11.16 ± 5.05	54.05 <sup>*</sup>	T0 > T1 > T2
GAF score	44.02 ± 13.14	58.39 ± 11.81	64.48 ± 11.96	90.04	T0 < T1 < T2

Legend – FEP: first episode psychosis, BPRS: Brief Psychiatric Rating Scale; HoNOS: Health of Nation Outcome Scale; GAF: global assessment of functioning; T0: baseline assessment; T1: 1-year assessment time; T2: 2-year assessment time; [df]: [degrees of freedom]. Mean ± standard deviation and Friedman test ( $\chi^2$ ) value are reported. Wilcoxon test with Bonferroni correction was used as post-hoc procedure for multiple comparisons. <sup>\*</sup>p < 0.001; <sup>†</sup>Bonferroni corrected p value < 0.0167.

or to ensure a stable functional recovery in people with FEP both in the medium and the long term<sup>31-33</sup>. With reference to this, recent systematic reviews suggested that integrated psychosocial interventions (together with pharmacological therapy) in FEP patients are more effective in reducing inpatient care, treatment drop-out, morbidity and related disability, as well as in improving

long-term clinical and functional outcomes, and in combining a symptom reduction/remission with a relevant improvement in terms of quality of life, social and cognitive functioning and less frequent self-injurious behaviors<sup>34-38</sup>.

In the EIP paradigm context, the PHB model may therefore represent an innovative, integrated psychosocial

**TABLE III.** Linear regression analysis results by multi-axis PHB intervention (independent variable) on functioning and psychopathological scores along the 2-year follow-up period (dependent variables) in the FEP total group (n = 49).

T2-T0 Delta BPRS “affective” factor subscore	B	SE	$\beta$	p	95% CI for B	
					Lower	Upper
Constant	-3.137	2.087	-	0.140	-7.342	1.067
Multi-axis PHB intervention	-1.696	1.446	-0.172	0.247	-4.608	1.215
Model summary: R <sup>2</sup> = 0.030; F = 1.377; p = 0.247						
T2-T0 Delta BPRS “positive” factor subscore	B	SE	$\beta$	p	95% CI for B	
					Lower	Upper
Constant	-5.013	2.553	-	0.056	-10.152	0.126
Multi-axis PHB intervention	-1.729	1.778	-0.142	0.336	-5.307	1.850
Model summary: R <sup>2</sup> = 0.020; F = 0.946; p = 0.336						
T2-T0 Delta BPRS “activation” factor subscore	B	SE	$\beta$	p	95% CI for B	
					Lower	Upper
Constant	-3.279	2.688	-	0.229	-8.690	2.132
Multi-axis PHB intervention	-1.302	1.872	-0.102	0.490	-5.069	2.466
Model summary: R <sup>2</sup> = 0.010; F = 0.484; p = 0.490						
T2-T0 Delta BPRS “negative” factor subscore	B	SE	$\beta$	p	95% CI for B	
					Lower	Upper
Constant	1.480	1.180	-	0.216	-0.895	3.855
Multi-axis PHB intervention	-2.093	0.822	-0.352	<b>0.014</b>	-3.747	-0.439
Model summary: R <sup>2</sup> = 0.124; F = 6.490; p = 0.014						
T2-T0 Delta BPRS “disorganization” factor subscore	B	SE	$\beta$	p	95% CI for B	
					Lower	Upper
Constant	0.102	0.628	-	0.872	-1.163	1.367
Multi-axis PHB intervention	0.331	0.435	0.113	0.450	-0.545	1.208
Model summary: R <sup>2</sup> = 0.013; F = 0.580; p = 0.450						
T2-T0 Delta HoNOS “behavioral problems” subscale subscore	B	SE	$\beta$	p	95% CI for B	
					Lower	Upper
Constant	-0.444	1.043	-	0.673	-2.545	1.658
Multi-axis PHB intervention	-1.653	0.734	-0.318	<b>0.029</b>	-3.131	-0.175
Model summary: R <sup>2</sup> = 0.101; F = 5.076; p = 0.029						
T2-T0 Delta HoNOS “impairment” subscale subscore	B	SE	$\beta$	p	95% CI for B	
					Lower	Upper
Constant	-1.340	0.773	-	0.090	-2.896	0.217
Multi-axis PHB intervention	0.082	0.538	0.022	0.880	-1.002	1.165
Model summary: R <sup>2</sup> = 0.022; F = 0.023; p = 0.880						
T2-T0 Delta HoNOS “psychiatric symptoms” subscale subscore	B	SE	$\beta$	p	95% CI for B	
					Lower	Upper
Constant	-4.332	1.210	-	0.001	-6.768	-1.896
Multi-axis PHB intervention	-1.216	0.843	-0.208	0.156	-2.913	0.480
Model summary: R <sup>2</sup> = 0.043; F = 2.083; p = 0.156						
T2-T0 Delta HoNOS “social problems” subscale subscore	B	SE	$\beta$	p	95% CI for B	
					Lower	Upper
Constant	-0.552	0.968	-	0.571	-2.501	1.396
Multi-axis PHB intervention	-2.286	0.681	-0.448	<b>0.002</b>	-3.657	-0.916
Model summary: R <sup>2</sup> = 0.201; F = 11.286; p = 0.002						
T2-T0 Delta GAF score	B	SE	$\beta$	p	95% CI for B	
					Lower	Upper
Constant	18.953	6.254	-	0.004	6.363	31.542
Multi-axis PHB intervention	1.112	4.355	0.038	0.800	-7.654	9.878
Model summary: R <sup>2</sup> = 0.001; F = 0.065; p = 0.800						

Legend – PHB: personal health budget; FEP: first episode psychosis; T2: 2-year assessment time; T0: baseline assessment; T2-T0 Delta: difference between T2 and T0 scores; BPRS: Brief Psychiatric Rating Scale; HoNOS: Health of Nation Outcome Scale; GAF: Global Assessment of Functioning; B: unstandardized regression coefficient; SE: Standard Error;  $\beta$ : standardized regression coefficient; p: statistical significance; 95% CI: 95% confidence intervals; R<sup>2</sup>: R square; F: F test value. Statistically significant p values are in bold.

approach aimed at an effective social and healthcare integration, placing the person in his life environment and giving him an active role in the co-planning of his life project<sup>4</sup>. Indeed, PHB has been proposed as a new design of assistance resulting in a promotion of individuals instead of certain services or service institutions<sup>39</sup>, as a way for personalizing care based around what matters to people and their personal strengths and needs<sup>7,40</sup>. Thus, the PHB model becomes feasible only within an effective *social-health integration*, aimed at creating a continuity of care for patients whose health is compromised and rebuilt in the daily life of their existence<sup>4</sup>. Within this conceptual framework, the main aim of the present research was to provide preliminary data about the beneficial effects of adding PHB to a specialized EIP multicomponent intervention (i.e. the Pr-EP program)<sup>10,25</sup>.

### Follow-up data

The results of the current study showed a significant improvement on functioning and on all the examined psychopathological and outcome variables (i.e. BPRS and HoNOS scores) in the FEP total group across the 2 years of follow-up. This confirms an overall effectiveness of a specialized EIP program (i.e. the Pr-EP protocol) in improving clinical and functional recovery of FEP patients, and supports promising add-on benefits of PHB interventions on “Sociality”, “Training/Work” and “Housing” axes, also within the Italian public mental health network<sup>22,25,41</sup>. However, within a continuous and progressive reduction in psychopathology severity, the improvement in negative symptoms and disorganization appears to be more relevant during the first year of intervention. These findings support the great therapeutic effort required by negative and disorganized dimensions of psychosis<sup>42,43</sup>, already at the onset of illness<sup>14,21</sup>.

Linear regression analysis results also showed that a PHB multi-axial approach significantly predicted a specific improvement in negative symptoms and in behavioral and social problems of FEP patients after 2 years of follow-up. This supports findings reported in other studies on PHB approach conducted in the UK and in the Netherlands<sup>40,44-46</sup>, suggesting a positive impact of PHB interventions on psychological well-being in patients with SMI. Specifically, in these studies outcomes mainly included decreased severity in psychopathology, a better daily functioning, improved relationships and reduced drug misuse. The success of PHB model has been attributed to both a “flexibility through partnership” (creating a policy framework to enable decisions about how many resources each person should get within a cash-limited budget) and a “self-directed support” (based on the individual being given a budget with which to plan his own care)<sup>45</sup>. In this context, it is

crucial for the individuals (particularly those with problems that already restrict their ability to live the life they want) to have autonomy in choosing their own care. Indeed, PHB should not be considered as new money, but as a different way of spending social/health funds in order to meet specific personal needs<sup>46</sup>.

### Limitations

Some limitations of the study should be acknowledged. First, this research was a descriptive, retrospective cohort study with no control group. Thus, a longitudinal case-control research is needed in order to better examine the PHB effectiveness.

Second, FEP participants provided with PHB intervention voluntarily accepted the PHB proposal. Thus, randomized controlled trials on effects and outcomes of PHB model are needed.

Third, in the present retrospective research the follow-up duration was limited to 24 months. Therefore, our findings should be replicated in longer-term perspective studies.

Another weakness was also the relatively limited sample size of the FEP group. This probably reduces the generalizability of our findings, which should be replicated in larger clinical samples.

Finally, in the current study we considered a wide age range (18-50 years) as an inclusion criterion. Thus, our findings should be replicated in more uniform age groups, such as in clinical populations of FEP adolescent and young adult help-seekers.

### Conclusions

The results of the current research overall support the general effectiveness of a specialized EIP intervention and the add-on benefits of PHB to a specialized EIP protocol in terms of improving functioning and decreasing psychopathology severity in help-seekers with FEP across a 2-year follow-up period. Indeed, this improvement (especially in negative symptoms and in behavioral and social problems) appears to be further enhanced by a PHB approach, based on the integration of professional knowledge and technical skills in order to provide person-tailored social/healthcare pathways within a community care system<sup>4</sup>. In other words, the implementation of PHB in Italian public mental health services has no detrimental effect to people in treatment, does not seem to be in conflict with a multicomponent EIP program and suggests that it may be effective in addressing the hot issue of social retirement and unmet social needs<sup>46</sup>.

In this regard, the England National Health Service (NHS) suggested that subjects who are eligible for a PHB, are individuals “having a medical illness that requires a highly specialized healthcare support”<sup>42</sup>. Since

2009, the England NHS implemented PHBs for patients with SMI and for children and adolescents in residential care, aiming at encouraging innovative rehabilitation approaches to effectively improve well-being outcomes<sup>38</sup>.

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# Mental fatigue and emotional states following high altitude hypoxia exposure

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## SUMMARY

Altitude is a hypoxic environment known to induce several psychophysiological changes. Previous studies found an increase of the negative emotions and a decrease of positive emotions at high altitude. In addition, hypoxia modifies the normal physiological parameters observed at sea level. In the present study we firstly hypothesized, that high altitude may affect the somatization status and mental fatigue; secondly, that altitude is not a sufficient condition to generate psychiatric disturbances. Moreover, the third hypothesized is an increase of the negative emotions and a decrease of the positive emotions.

Seven volunteers climbed a mountain and underwent psychophysiological assessment during three distinct times: before ascendance (at sea level), at Ararat Base Camp (hypoxic natural environment 4150 m a. s. l.) and after ascendance (at sea level). Volunteers underwent psychological tests assessing somatic symptoms, perceived exertion and positive/negative emotions. At Base Camp, a significant increase of somatic symptomatology was observed in respect to sea-level scores. We found a significant increase in mental fatigue at Base Camp in respect to sea-level scores. An increase of positive emotional states and a reduction of negative states at Base Camp in respect to sea level values was found. The physiological measurements showed a significant decrease in saturation of peripheral oxygen and a significant increase for heart rate scores at Base Camp in respect to sea-level scores, as well as significant correlation with psychological tests.

This preliminary research shows that high altitude impairs the psychophysiological functions and it could be considered an important parameter to predict the climbers adaptation to hypoxia.

**Key words:** mental fatigue, emotional states, mountain altitude, environmental hypoxia, psychophysiology

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## Conflict of interest

The Authors declare no conflict of interest

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## Introduction

Altitude is a natural environment characterized by a hypoxic condition. Hypoxia is a reduction of partial pressure of the oxygen, causing a lack of oxygen in the blood. The human brain suffers a long time without oxygen, and at an extreme altitude condition, it may be irreversibly damaged<sup>1</sup>. Hypoxia causes an imbalance of the physiological homeostasis<sup>2-4</sup> with dramatic impairment of the psychophysiological functioning, such as fatigue<sup>5-7</sup>.

The first distinction between physical and mental fatigue is that of Angelo Mosso in 1891<sup>8</sup>. Physical fatigue can be defined as the result of neurochemical and muscular activity, whereas mental fatigue is the result of defensive strategies intended to preserve the 'mental health' of a person in extreme conditions, including the mood state of tiredness or exhaustion induced by the prolonged time of stressful cognitive activity<sup>9</sup>. It can be considered as a temporary impairment of cognitive functions and it is one of the major reasons of accidents at mountain level. When mental fatigue occurs, frequently anxiety and panic attack, and, in some extreme cases,

also depersonalization, fear and loss of control<sup>10</sup>, accompanied it. Above all, hypoxia induces psychophysiological changes in mood states, in cognitive functions and in the sensory perceptions<sup>5,6,11</sup>. Abnormal visual, auditory and somatosensory- perceptions, that can be defined hallucinatory experiences, are very common at extreme altitude (above 5000 m a.s.l.)<sup>12</sup>. These alterations are the result of a lack of serotonin caused by hypoxia, as pointed out by Young<sup>13</sup>, who investigated the relationship between low levels of serotonin and low mood and high impulsivity in people living at a high altitude, that may induce climbers' death for suicide. It has been stated that the critical altitude threshold for psychological changes is at around 4000-5000 m a.s.l.<sup>14,15</sup>, and when this threshold is overpassed, depression, anger<sup>7</sup>, paranoid ideation and obsessive-compulsive symptoms are observed<sup>14</sup>, with also, in extreme cases, a loss of consciousness and orientation<sup>16</sup>. However, several physiological parameters, such as blood pressure, heart rate, breath rate and ventilatory response, that signal an imbalance of the body homeostasis, are predicting of psychophysiological impairment<sup>6,17,18</sup>. Despite numerous investigations about effects of high altitude hypoxia exposure, data about the role played by the high altitude environment on the perception of emotions are lacking. Present study aims to fill this gap. In particular we hypothesized that high altitude may affect the somatization status and mental fatigue, but it is not a sufficient condition to generate psychiatric disturbances. We hypothesized an increase of the negative emotions and a decrease of the positive emotions. In order to verify this hypothesis, we investigated the correlation between the physiological parameters (collected during the expedition) and the variation of the emotional states.

## Materials and methods

### Subjects

Seven (7) healthy volunteers, (5 males and 2 females, age  $56.86 \pm 9.19$  years old), climbed Mount Ararat (Eastern Turkey) for three days. Before the expedition, volunteers were selected after appropriate cognitive assessment and a psychiatric interview. The exclusionary criteria was the inappropriate cognitive level and the general medical, neurological and psychiatric disorders in the present as well as in the history of the subject. All volunteers usually lived at 250 m a.s.l. and were not expert climbers. The numerosity of sample is in line with the mean participants in mountain expedition.

### Instruments

#### *Psychometric tests*

We administered three questionnaire: the Self-Report

Symptom Inventory-Revised<sup>19</sup>, the Rated Perceived Exertion Scale<sup>20</sup>, the Positive and Negative Affect Schedule Questionnaire<sup>21</sup>.

The Self-Report Symptom Inventory-Revised (SCL-90 R) is a five-point Likert self-reported scale allowing to measure specific aspects of the personality. The SCL-90 was very fast and it is usually used like general measure of psychiatric symptomatology in both clinical and research context. It consists of 90 Items divided into 11 scales:

- Somatization (SOM) subscale assesses the uncomfortable body perception: subjective somatic state. The symptoms are focused with cardiovascular, gastrointestinal and respiratory apparatus. Muscular pain and the other body anxiety symptoms are other components of this scale;
- Obsessive-Compulsive (O-C) includes the typical symptoms of obsessive-compulsive syndrome. The items focused on persistent thoughts and irrepresible actions;
- Hypersensitivity-Interpersonal (I-S): includes the uncomfortable and the inadequacy feelings of yourself. The typical feeling manifestations are low self-efficacy and awkward interpersonal relationships;
- Depression (DEP) includes the items related to the typical clinical manifestations of the depression syndrome. The DEP scale assesses the social retire, lack of motivation, loss of energy, feeling of desperation and kill oneself through;
- Anxiety (ANX): includes the items that evaluate the general anxiety symptoms: irritability, tension, panic attacks, feeling of fear, trepidations;
- Hostility (HOS) includes the items that evaluate the typical negative through, feeling and behaviour. In particular, HOS detects clinical manifestation of anger, aggression and irritability;
- Phobic Anxiety (PHOB). The items detect a persistent fear reaction for a specific person, place or situation. This reaction is irrational and excessive than the stimulus;
- Paranoid Ideation (PAR) describes the typical manifestation of the paranoid thought: projective thought, hostility, suspiciousness, grandeur, reference to oneself, fear of autonomy loss;
- Psychoticism (PSY) includes items of primary symptoms of schizophrenia as well as the social retire;
- Sleep Disorders (SLEEP) assesses the sleep disorders;
- Global Severity Index (GSI): it is a global indicator of psychological distress level.
- The Rated Perceived Exertion Scale (RPE) assesses the rate of the perceived exertion in sport athletes. It consists of a Likert-like scale ranged from 0 ("nothing") to 11 ("maximum possibility"). Volunteers an-

swered three statements and the mean values were used for statistical analysis.

The Positive and Negative Affect Schedule Questionnaire (PANAS) is considered a reliable instrument used and validated in sport science, also in clinical and research contexts. It consists of 20 items of which, 10 items assess the Positive Affect (PA) and 10 assess the Negative Affect (NA). Volunteers answered a five-point likert-scale ranging from 1 (“very little or nothing”) to 5 (“most”).

### *Psychophysiological measures*

Since the described imbalance of the human cardiovascular system during exposure to the hypoxic environments<sup>4-6,9</sup>, measuring the cardiovascular parameters is necessary in order to establish the physiological trend of the body condition and, then, to correlate this with the psychological status. The electronic portable pulse oximeter 503 OXY-5 GIMA® (Oximeter) has been used to collect the Saturation of Peripheral Oxygen (SpO<sub>2</sub>). This represents index of the blood oxygen saturation measured in percent variation (%) with normal values identified with 99%.

Moreover, we used the M2 Basic Omron® (Sphygmomanometer) to measure the pressure as a blood strength intensity on vasal artery. BPmax and BPmin represent the maximum and minimum blood pressure values, respectively, measured in mmHg and (normal range values between 120 and 80 mmHg). Moreover, with the same instrument we measured the Heart Rate (HR), representing the number of the heart pulses in one minute (normal range values: 60-90 beats per minutes) and Breath Rate (BR), that is the number of the breath rate in one minute (normal range values: 12-20 cycles per minutes).

### **Procedures**

All the evaluations were conducted in different times and at two different altitudes as follow: before ascendance and at sea level (Pre-Exp), at 4150 m a.s.l. (Base Camp) and after descent at sea level (Post-Exp). The volunteers underwent a psychophysiological evaluation and psychometric assessment in a standardized condition (the same hour of the morning, before food and drink consumption). At Pre-Exp and Post-Exp (i.e., at sea level) the assessment was carried out in the same quiet and ventilated room, whereas at Base Camp the assessment was performed in a quiet and large tent. Volunteers were asked to rest before the psychophysiological and psychometric assessment; they were free to interrupt the testing sessions at any time. Before the test assessment, they read and signed an informed consent to participate in the study. At sea level and during climbing, the volunteers were free of drugs, and women were not in the ovulatory phase.

The Base Camp assessment was conducted on August 14<sup>th</sup>, in ideal weather conditions and the air temperature was 15°C. All experimental procedures were not inva-

sive and in line with ethical principles of the Helsinki Declaration 2008.

### **Data analysis**

To quantify the effects of altitude on psychological functioning assessed by SCL-90 R, RPE, two different repeated-measures of Analyses of Variance (rmANOVA) were computed with one repeated-measure factor “Time” considering Pre-Exp, Base Camp and Post-Exp, for each subscale of the SCL-90 and the RPE scores.

Moreover, in order to quantify the effect of altitude on positive and negative emotions, a mixed-model ANOVA, with one repeated-measure factor “Time” and one within-group factor the PA-NA scores) was carried out with PANAS scores. To assess the relationship between the scores of the three different questionnaires, a rank Spearman’s correlation coefficient was calculated and, where possible, a Bonferroni’s multiple comparison correction was also applied.

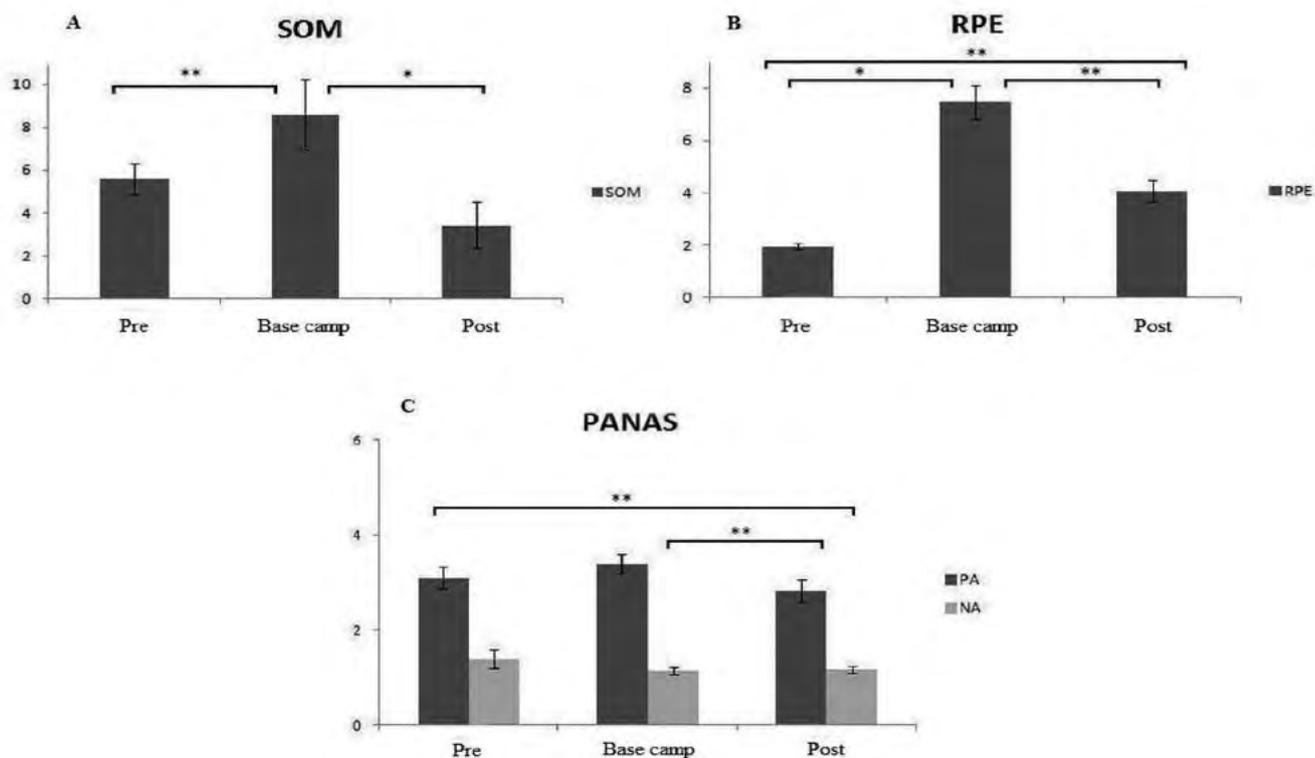
To assess the effects of moderate altitude on physiological parameters during the expedition, we calculate the differences between the maximum and minimum values as  $\Delta = (\max - \min)$  for the SpO<sub>2</sub>, the BPmax, the BPmin, the HR and the BR, for each time; (Pre-Exp, Base Camp and Post-Exp). The obtained  $\Delta$  values were considered as dependent variables. To assess the effect of “Time” on the psychophysiological results, we tested the normal distribution with the Kolmogorov-Smirnoff Test, and the homogeneity of variances with the Levene’s Test. If these criteria were violated, non-parametric tests were applied. The descriptive statistics, ANOVAs and Spearman’s rank coefficient correlation were performed by means of STATISICA (STATSoft 8.0). Data were expressed as a mean  $\pm$  standard deviation.

### **Results**

For the SCL-90 R, the rmANOVA showed significant effect of “Time” on SOM ( $F(2,12) = 12.76$ ;  $p < 0.05$ ). The Base Camp period showed higher significant values ( $0.71 \pm 0.36$ ) in respect on the Pre-Exp ( $0.46 \pm 0.16$ ;  $p < 0.05$ ) and the Post-Exp ( $0.29 \pm 0.23$ ;  $p < 0.00$ ), (Fig. 1A). No significant results were observed for other SCL-90 R subscales.

Similarly, the rmANOVA showed significant effect of “Time” on the RPE Scale scores at Pre-Exp, at Base Camp and at Post-Exp ( $F(2,12) = 75.24$ ;  $p < 0.0001$ ). The Post-Hoc comparison showed significantly higher RPE Scale scores for the Base Camp condition ( $7.47 \pm 1.66$ ) respect on the Pre-Exp ( $1.93 \pm 0.31$ ;  $p < 0.00001$ ) and the Post-Exp ( $4.04 \pm 1.07$ ;  $p < 0.001$ ), (Fig. 1B). Whereas, the Post-Exp period showed higher RPE Scale values than the Pre-Exp period ( $p < 0.001$ ).

The PANAS Questionnaire showed a significant effect of “Time” ( $F(2,24) = 6.24$ ;  $p < 0.01$ ) and a significant



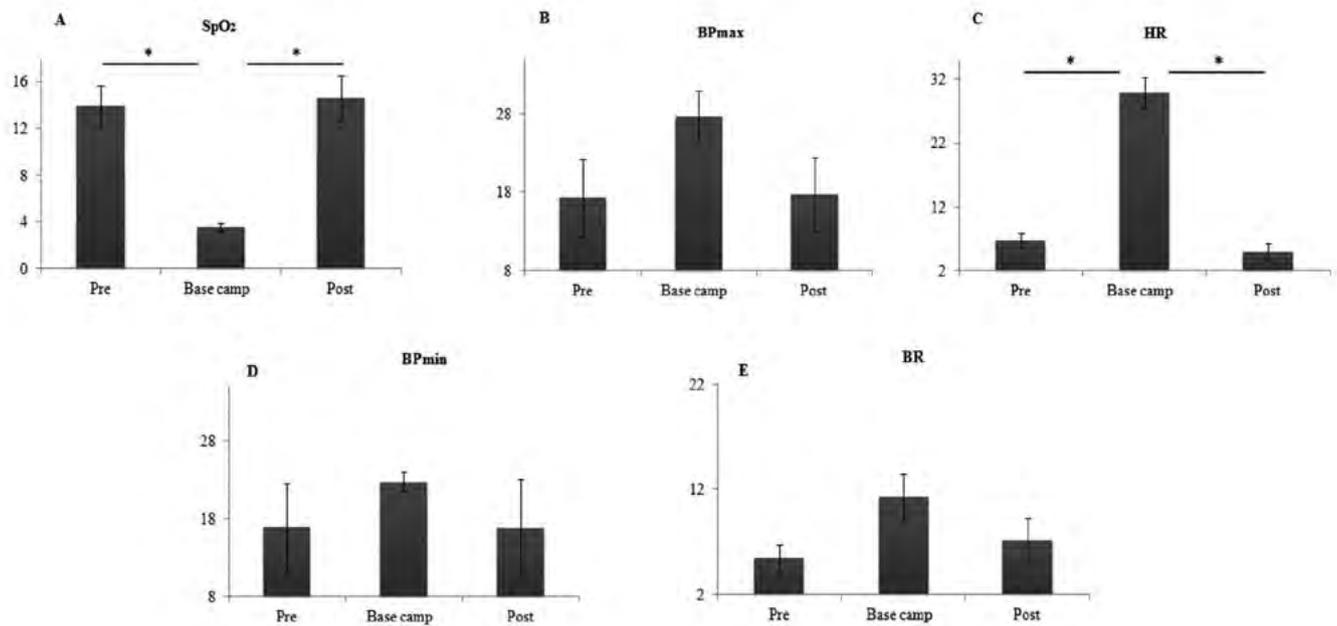
**FIGURE 1.** The histograms show as hypoxic natural environment induces progressive and significantly increments of the somatic symptoms at hypoxic station,  $p < 0.05$  (A); a significant increment of the perceived exertion at hypoxic station,  $p < 0.05$  (B); a significant increment of the positive affective and significant decrement of the negative affective state,  $p < 0.05$  (C). Vertical bars denote the standard errors of mean (SEM).

interaction “Time x PA-NA” ( $F(2,24) = 7.55$ ,  $p < 0.005$ ). At Base Camp (PA:  $3.38 \pm 0.51$ ) the values were higher compared to the Post-Exp period ( $2.82 \pm 0.61$ ). The values of the Pre-Exp period (NA:  $1.38 \pm 0.52$ ) were higher compared to the Post-Exp period ( $1.17 \pm 0.21$ ), ( $p < 0.01$ ), (Fig. 1C). The Duncan’s post-hoc for interaction “Time x PA-NA” highlighted a significant difference for PA compared to Time, but not for the NA.

The physiological measurements showed significant results for the  $SpO_2$  and the HR. The  $SpO_2$  showed a significant difference for Time ( $F(2,12) = 31.73$ ,  $p < 0.01$ ). Duncan’s post-hoc test revealed significant difference between the Pre-Exp ( $95.23 \pm 1.42$ ) and the Base Camp period ( $84.09 \pm 4.14$ ;  $p < 0.001$ ) and between the Base Camp ( $84.09 \pm 4.14$ ) and the Post-Exp period ( $96.23 \pm 1.03$ ;  $p < 0.001$ ) (Fig. 2A). The rmANOVA on HR showed significant main effect of “Time” ( $F(2,12) = 55.75$ ,  $p < 0.0001$ ). Duncan’s post-hoc test revealed a significant difference between the Pre-Exp ( $60.52 \pm 7.30$ ) and the Base Camp period ( $83.71 \pm 5.09$ ;  $p < 0.0005$ ); as well between the Base Camp ( $83.71 \pm 5.09$ ) and the Post-Exp period ( $58.52 \pm 4.85$ ;  $p < 0.0001$ ) (Fig. 2C).

No significant results were obtained for the BPmin, the BPmax and the BR (Fig. 2B,D,E).

To assess the relationship between the SOM, the RPE and the PANAS (sub-scale PA and NA) values, Spearman’s rank correlation was calculated. We observed a significant positive correlation between the RPE Post-Exp values and the SOM Post-Exp values ( $\rho(7) = 0.77$ ,  $p < 0.05$  uncorrected). Significant relationship was observed between sub-scale PA and RPE for the Post-Exp values ( $\rho(7) = 0.80$ ,  $p = 0.03$ ) and the SOM values for the Post-Exp period ( $\rho(7) = 0.81$ ,  $p < 0.03$ ). To assess the relationship between the SCL90-SOM, the RPE and the PANAS values and the psychophysiological parameters, Spearman’s rank correlation was calculated. We observed a significant positive correlation between the Base Camp values of the SOM and the BPmax ( $\rho(7) = 0.84$ ,  $p < 0.05$ ) as well as the values recorded at the Pre-Exp period for the SOM and the HR ( $\rho(7) = 0.88$ ,  $p < 0.05$ ). Significant negative correlation was observed between the Pre-Exp values of the SOM and the BR ( $\rho(7) = -0.79$ ,  $p < 0.05$ ) (Fig. 3).



**FIGURE 2.** The histograms show as hypoxic natural environment induces a significant decrement of the saturation of peripheral oxygen at hypoxic station,  $p < 0.05$  (A); a significant increment of the heart rate at hypoxic station,  $p < 0.05$  (C), no significant results were obtained for the maximum blood pressure (B), for the minimum blood pressure (D) and the breath rate (E). Vertical bars denote a standard errors of mean (SEM).

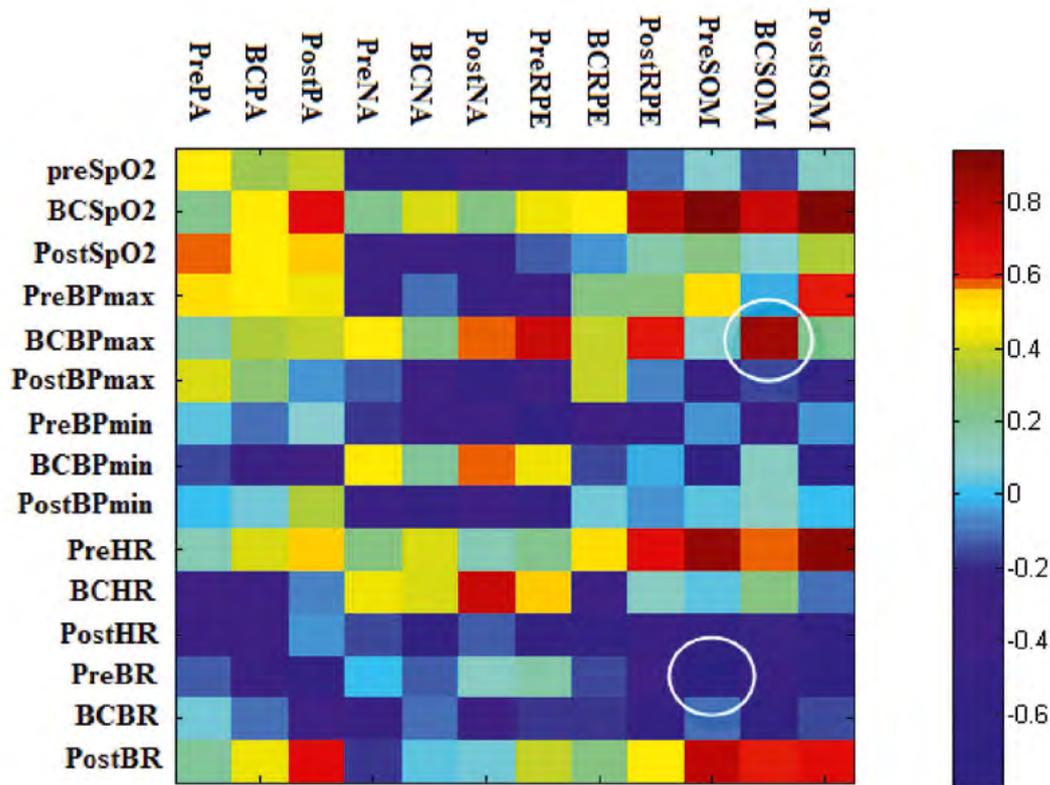
## Discussion

The present study represents one of the few reports about the effect of moderate altitude, i.e., less than 5000 m a.s.l., on the psychological and physiological status.

Our results showed a significant effect of altitude-hypoxia on the subjective somatic state of climbers, as given by the significant results of somatization subscale. Although the altitude-hypoxia affects the subjective somatic state of climbers, it is not a sufficient condition to generate psychiatric transitory status, confirming our initial hypothesis. Numerous reports suggest the negative effects of altitude on the mood. Indeed, after experiencing euphoria, climbers may also become irritable, anxious and apathetic<sup>22</sup>. In our study, we observed an increase in the positive emotions. This effect may be due to the initial euphoric stage after arriving at the Base Camp, given that we did not observe significant effects on the NA. This result, can be explained at light of the relationship between physical activity and the mood. Several studies Pasco and<sup>23</sup> found a positive correlation between the Positive Affect and the physical activity. It is possible that the physical effort perceived during the climb could have influenced the experience of well-being and the positive emotions in general.

Although the physical effort perceived during climbing,

our study showed an increase of mental fatigue in a hypoxic environment, in agreement with our assumption. Previous studies have investigated the physiological effects of fatigue in a controlled condition<sup>7,24</sup> but there are no studies describing the time-course of mental fatigue in a natural altitude setting. Mental fatigue is an unusual parameter investigated, due to the difficulty in quantification. Several physiological aspects seem to condition mental fatigue. Hunger and dehydration are the principal aspects that may induce tiredness. For this reason, we tested the volunteers after food and water consumption. Volunteers underwent psychological and psychophysiological tests after adequate rest at Base Camp. The RPE scores display the principal effects of hypoxia on mental fatigue at Base Camp and persistent tiredness after returning to sea-level. The correlation between the SOM and the RPE scores prove the close relationship between two common aspects of tiredness. The higher scores of the SOM at Base Camp were the indirect evidence of the imbalance of physiological parameters. We found a significant correlation between the SOM and the BP<sub>max</sub> at Base Camp. Furthermore, we found increased PA scores at Base Camp, with a dramatic decrease after returning to sea-level. These findings are unexpected and in contrast with our assumptions and with previous studies. The nega-



**FIGURE 3.** The coloured map depict the Spearman's rank correlation results. Spearman's rank correlation showed a significant positive correlation between the SOM and the BPmax at hypoxic station ( $p < 0.05$ ), a significant negative correlation between the SOM and the BR at hypoxic station ( $p < 0.05$ ).

tive mood states are very common at mountain altitude and previous studies have shown an higher incidence of AMS (Acute Mountain Sickness) with typical negative symptoms of headache, dizziness, nausea, loss of appetite and insomnia<sup>15,25,26</sup>. It is important to note that climbers were exposed at sub-acute hypoxia (3 days of trekking and 1 day at 4150 m a.s.l.).

Sub-acute hypoxia exposure provokes a temporary neurotransmitter imbalance. The hypoxic environment can cause the alteration in the neurotransmitters utilization and concentrations<sup>27</sup>. The cholinergic system appears to be the most vulnerable to hypoxia, but it is possible that the rate of synthesis of neurotransmitters, like, dopamine, serotonin and amino acids, are affected by acute hypoxia<sup>28</sup>.

In future studies emotional processing will be important to investigate the psychological adaptation at altitude exposure, especially in an emergency context. In conclusion, our findings suggest that exposure to high altitude could put a strain on the physical endurance of mountaineers, without affecting the emotional state.

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# Clinical differences between people with borderline personality disorder with and without romantic relationships: a case-control study

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## SUMMARY

### Background

The aim of this study was to determine the clinical differences (e.g., psychopathology, attachment style, self-esteem) between people with BPD with and without a romantic relationship.

### Methods

The sample consisted of 49 BPD outpatients. Clinical variables were measured through the Borderline Symptom List, the Aggression Questionnaire, the BDI the Experience Close in Relationship, The Childhood Trauma Questionnaire, the Conflict Tactics Scale, the Interpersonal Reactivity Index, the Communication Patterns Questionnaire, the Dyadic Adjustment Scale the Index Sexual Satisfaction and the Interpersonal Reactivity Index. Stepwise MANOVA, multiple binary logistic regression analysis and Pearson correlates were performed.

### Results

BPD with RR scored significantly higher than BPD without RR in aggression, childhood trauma and Psychological Health. Physical aggression was the most significant predictor of being engaged in a romantic relationship in BPD.

### Conclusions

People with BPD and RR have a higher-level symptomatology in comparison to BPD without RR sample. In addition, it was found that physical aggression was the most predictive marital variable of the presence/non-presence of a RR.

**Key words:** borderline personality disorder, romantic relationships, partner, aggression, intimacy, cross-sectional

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### Conflict of interest

The Authors declare no conflict of interest

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Borderline personality disorder (BPD) is a severe mental disorder observed in 2 and 5.9% of community samples, 10% of psychiatric outpatients, and 15% and 20% of psychiatric inpatients<sup>1-3</sup>. Different factorial studies indicate that BPD is characterized by four core clusters of symptoms: identity alterations, emotional dysregulation, severe impulsivity, and interpersonal problems<sup>4-8</sup>. Several studies indicate that these symptoms affect the general functioning of people with BPD, in particular, their relationships<sup>3</sup>. This finding is relevant considering that people with BPD have more difficulty in maintaining positive and stable social relationships than people with other psychiatric disorders (*i.e.*, major depression or obsessive-compulsive disorder)<sup>3,9,10</sup>. Regarding this issue, different authors suggest that the duration of an RR for people with BPD is shorter compared with people with other personality disorders<sup>11,12</sup>. Specifically, a prospective 27-year follow-up study suggested that the prevalence of an emotional break-up in people with BPD is 40-60% higher than people without BPD<sup>14</sup>. Similarly, differ-

ent cross-sectional studies indicate that the presence of emotional dysregulation (*i.e.*, emotional hyperactivity) and impulsivity in people with BPD is associated with an increased risk of break-ups<sup>14-18</sup>.

Besides the stability of these RRs, different studies have found that people with BPD, have a higher number of sexual partners throughout the course of their life, which even affects their commitment (fidelity) during the establishment of the RR in comparison to people without BPD<sup>19-26</sup>. Regarding the quality of RRs, different longitudinal and cross-sectional studies suggest that people with BPD have less emotional satisfaction in their RRs in comparison with their partners throughout the course of their relationships<sup>15,16,19,20</sup>. In addition, a cross-sectional study showed that some symptoms of BPD (*i.e.*, impulsivity, depression, interpersonal distrust) predicted a lower emotional satisfaction in RRs for people with BPD<sup>18</sup>. Conversely, different cross-sectional and longitudinal studies suggest that this lower emotional satisfaction at baseline predicted the presence of pathological behaviors by people with BPD at follow-up (*i.e.*, ambivalent attachment, passive-aggressive communication, continued affection demand towards the partner)<sup>15,18,19,27</sup>. In particular, an 18-month longitudinal study found that women with BPD showed anxious attachment in their RR at the end of the follow-up period<sup>19</sup>. With regard to predictors, several cross-sectional studies have reported that the presence of childhood trauma is positively associated with the development of insecure attachment in adults with BPD who are involved in RRs<sup>28</sup>. Moreover, some longitudinal studies over 18 months have found that a lower emotional satisfaction of the member with BPD predicted poorer clinical features of the partner without BPD (*e.g.*, presence of personality disorders [antisocial, obsessive-compulsive, and avoidant] anxious attachment, passive-aggressive communication style)<sup>19,20</sup>.

Despite the growing literature cited above on RRs in people with BPD, the evidence is still far from clarifying relevant aspects. This is more remarkable taking into account the solid research on RRs in other types of clinical samples such as major depression obsessive-compulsive disorder<sup>3,9,10</sup>. For instance, research on the functioning of RRs in people with BPD is scarce. In fact, previous studies have focused on the evaluation of general clinical variables of RRs (*i.e.*, satisfaction and quality of the RR); however, the incidence of BPD people psychopathology has not been evaluated (*i.e.*, impulsivity, emotional emptiness, hostility emitted) in their RRs. On the other hand, the influence between traumatic episodes in childhood in the BPD patient and their RRs has not been evaluated.

In particular, the exposed findings have focused on the study of the variables of sentimental relationships (*i.e.*,

emotional and sexual satisfaction and the quality of the RR) of healthy people or people with other personality disorders. However, these results do not clarify that some people with BPD maintain a stable RR despite their psychopathology. Overall, the interest in addressing the RR of people with BPD with more clinical accuracy is also importantly due to healthcare parameters<sup>3</sup>. In fact, a large proportion of the emotional relapses treated in psychiatric emergencies and/or psychiatric hospitalization have their cause in the emotional problems that these patients present<sup>28</sup>. Ultimately, these emotional crises result in a direct economic cost of up to 13,000 euros per year<sup>28</sup>.

In this context, the general objective of the current comparative study was to determine the clinical profile of a sample of people diagnosed with BPD who maintained an RR and compare it with a sample of people with the same diagnosis who did not have an RR at the time of the assessment. In addition, the specific objectives were the following: (1) to determine whether there were significant differences between the two samples of people with BPD (*i.e.*, in the general and specific psychopathology of BPD (depression, hostility, impulsivity)), type of adult attachment, self-esteem, quality of life, and type of traumatic episodes in childhood; (2) to determine whether some of the differential clinical variables between the two groups can predict romantic status (with or without a RR) in people diagnosed with BPD; and (3) to observe the correlation between the clinical variables of the person with BPD and the clinical variables of their partner (*i.e.*, personality type, communication style, attachment style, self-esteem, quality of life, emotional and sexual satisfaction, and hostility).

## Method

### Participants

Potentially eligible patients for the current study were initially referred to us by their clinicians as they consecutively attended the Adult Outpatient Mental Health Center of Mataró (Barcelona, Spain) from December 2016 to May 2018. Inclusion criteria for both groups were a lifetime diagnostic criteria for BPD according to the DSM-5 (APA, 2013) and being aged 18-65 years. Following other similar studies, inclusion criteria for people with BPD in an RR were twelve months in an RR or living together for four months<sup>19,20</sup>. Exclusion criteria for both groups were the following: (1) lifetime comorbidity with a psychotic disorder and/or pervasive developmental disorder according to DSM-5; (2) diagnostic of intellectual disability (IQ < 70) as recorded by the clinical charts; and (3) idiomatic barriers for reading/speaking Spanish or Catalan languages. Because of the great prevalence of current substance misuse among BPD patients, only

those who manifested symptoms of intoxication or substance withdrawal at the time of the assessment were excluded. Of the 55 potentially suitable outpatients, three declined to participate, mainly because they did not want to respond to sensitive issues in the questionnaires. Another three patients did not meet lifetime criteria for BPD, but had borderline traits. Hence, the final sample comprised a total of 49 BPD women: 23 patients with an RR (BPD patients and their partners) and other 26 BPD women without an RR at the time of assessment (see Figure 1). Regarding marital status of the total sample, 43.50% had married or were living with a partner at the time of the study, 18.80% with an RR not living together, and 37.70% single.

Participants attended individually, on average, one session of two hours in order to complete the administered questionnaires and the semi-structured interviews. All participants (people with BPD and partners) were interviewed directly by the authors of the manuscript, who are doctoral-level clinicians or clinical psychologists widely experienced in personality disorders and trained specifically for the assessment. The degree of agreement between interviewers for the diagnosis of BPD was high (*Cohen's Kappa* = .87). One week later, self-administered questionnaires were completed by the participants in a second session, in which any doubt regarding the items was resolved by the interviewers. The study was approved by the hospital's Institutional Review Board, and informed consent was obtained from all patients after a full explanation of the nature of the study.

### Instruments

Demographic information was collected by ad hoc questionnaires, as well as via interviews with participants when data were either no longer available or contradictorily registered in clinical records.

*Personality disorder diagnosis and clinical psychopathology: SCID 5-PD, Personality Disorders*<sup>29</sup>. For patients with BPD, diagnoses of personality disorders were determined by the Spanish version of the Structured Clinical Interview for DSM-5 (SCID 5 PD). The Spanish validation presented adequate internal consistency (*Cronbach's alpha* = .81).

BSL 23, Borderline Symptom List (Short version)<sup>30,31</sup>. Psychopathology of BPD was measured by the Spanish validation that presented adequate internal consistency (*Cronbach's alpha* = .97).

*NEO-PI-R, Personality Inventory NEO*<sup>32,33</sup>. For patients with BPD and their partners the Spanish validation presented adequate internal consistency (*Cronbach's alpha* = .60 to .90).

*Depressive mood: BDI, Beck's Depression Inventory*<sup>34,35</sup>. The Spanish validation proved to be a reliable instrument for assessing the severity of depressed mood.

The Spanish validation presented adequate internal consistency (*Cronbach's alpha* = .90).

*Aggression symptomatology: AQ, Buss and Perry Aggression Questionnaire*<sup>36,37</sup>. For patients with BPD and partners, the Spanish validation of the (AQ) was used to assess aggression. The Spanish validation presented adequate internal consistency (*Cronbach's alpha* = .72-.88).

*Quality of life and self-esteem: the Spanish validation of the World Health Organization Quality of Life, Short-Form (WHOQOL-BREF) was used to assess quality of life*<sup>38,39</sup>. For patients with BPD and partners. The Spanish validation presented adequate internal consistency (*Cronbach's alpha* > .80). RSE, Rosenberg Self-esteem<sup>40,41</sup>. It was measured by the Spanish validation of the Rosenberg Self-esteem Scale. The Spanish validation of the RSE presented adequate internal consistency (*Cronbach's alpha* = .87).

*Type of attachment: ECR-R, Experience Close in Relationship*<sup>42,43</sup>. For patients with BPD and partners, The ECR-R has two dimensions: anxiety and avoidance. The Spanish validation presented adequate internal consistency (*Cronbach's alpha* > .65).

*History of childhood trauma: CTQ, Childhood Trauma Questionnaire*<sup>44,45</sup>. The CTQ is a standardized, retrospective 25-item self-report inventory that measures the severity of different types of childhood trauma, producing five clinical subscales, each composed of five items: emotional abuse, physical abuse, sexual abuse, emotional neglect, and physical neglect. The Spanish validation presented adequate internal consistency (*Cronbach's alpha* = .66 to .94).

*Communication patterns: CPQ, Communication Patterns Questionnaire*<sup>46,47</sup>. It has three scales: the scale of mutual constructive communication, mutual avoidance communication, and the demand/withdraw communication scale. The English validation presented adequate internal consistency (*Cronbach's alpha* > .75).

*Emotional satisfaction: DAS, Dyadic Adjustment Scale*<sup>48,49</sup>. The DAS was used to assess level of relationship quality and satisfaction. The Spanish validation presented adequate internal consistency (*Cronbach's alpha* > .80).

*Social cognition: IRI, Interpersonal Reactivity Index*<sup>50,51</sup>. For patients with BPD and partners. The measure has four subscales: Perspective Taking, Fantasy Empathic, Concern, and Personal Distress. The Spanish validation presented adequate internal consistency (*Cronbach's alpha* > .70).

### Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS for Windows, Version 23.0). The Chi-square test, Mann-Whitney U test, and t-test were first used to analyze the sociode-

mographic data, depending on the nature of the variables. Then the Shapiro-Wilk test was used to confirm the normal distribution of quantitative clinical data for both clinical groups.

A multivariate analysis of variance (MANOVA) was performed with the resolution of reducing the risk of type I error for univariate contrasts of the dependent variables that could differentiate the BPD group with RR and without RR. The partial eta square was chosen as the measure of effect size. Those variables that vary between-group significant differences ( $p < .05$ ) are included as predictors of the sentimental status of people with BPD using a subsequent multiple binary logistic regression analysis (*Cox & Snell R-square and Nagelkerke R-square*) in order to predict the presence (= 0) or (= 1) absence in people with BPD, depending on the variables used in the analyses. All  $p$ -values are based on 2-tailed tests with  $\alpha = .05$ . Most values were presented in terms of means and standard deviation (SDs).

## Results

### Sociodemographic comparison between people with BPD with and without RR

No significant differences were obtained between the groups ( $p > .05$ ), except in the criterion of marital status linked to the methodological condition of the study and gender (Tab. I).

### Clinical comparison of people with BPD with and without RR

The psychopathological variables of people with BPD with and without RR are shown in Table II. The MANOVA did not yield significant differences in psychopathological variables ( $F = .18$ ,  $p = .18$ , *Wilks  $\lambda = .81$* ).

The univariate analysis did not report significant differences in the severity of BPD symptomatology ( $p > .05$ ). Regarding aggression (AQ scale), the BPD group with RR obtained significantly higher scores than the BPD group without RR for various types of aggression (physical aggression, verbal aggression, rage and hostility)

**TABLE I.** Sociodemographic comparison between BPD women with and without RR.

	BPD with RR (n = 23) n (%)	BPD without RR (n = 26) n (%)	Statistics $\chi^2/t$	$p$
Gender			$\chi^2 = 13.93$	.00**
Male	1 (4.50)	1 (3.80)		
Female	22 (95.50)	25 (96.20)		
Age (mean/SD)	38.65 (6.46)	38.88 (9.38)	$t = -.10$	.92
Education level			$\chi^2 = 2.28$	.50
No Studies	4 (18.20)	3 (11.50)	-	-
Primary	4 (18.20)	9 (34.60)	-	-
Secondary	8 (31.80)	9 (34.60)	-	-
University	7 (31.80)	5(19.20)	-	-
Marital Status			$\chi^2 = 49.00$	.00**
Married or living with a partner	17 (72.70)	0 (.00)	-	-
RR NLT	6 (27.30)	0 (.00)	-	-
No-stable RR	0 (.00)	26 (100)	-	-
Occupation			$\chi^2 = 1.97$	.74
Student	3 (13.60)	5 (19.20)	-	-
Employee	6 (27.30)	10 (38.50)	-	-
Unemployed	5 (22.70)	5 (19.20)	-	-
Retired due to disability	4(22.71)	3 (11.50)	-	-
Medical leave	3 (13.60)	3 (11.50)	-	-
Childs (mean/SD)	.87 (.81)	.38 (.49)	$t = 2.54$	.13
RR previous			$\chi^2 = 1.60$	.20
Yes	18 (77.30)	16 (61.50)	-	-
No	5 (22.70)	10 (38.50)	-	-

BPD: Borderline Personality Disorder; NLT: Not Living Together; RR: Romantic Relationship; SD: Standard Deviation

\*\* $p < .01$  in BPD with RR vs BPD without RR

\* $p < .05$  in BPD with RR vs BPD without RR

( $p < .05$ ). The effect size was low for these variables, and the moderate-high powers.

As regards depressed mood, no significant differences were evidenced ( $p > .05$ ).

The multivariate analysis did not report significant differences between the attachment variables ( $F = 2.39$ ,  $p = .10$ , *Wilks*  $\lambda = .90$ ). Similarly, these differences were also not observed in the univariate analysis ( $p > .05$ ).

The MANOVA test reported significant differences in the variables of quality of life and self-esteem ( $F = 3.93$ ,  $p = .00$ , *Wilks*  $\lambda = .65$ ).

Regarding the quality of life, the BPD group with RR showed significantly higher scores in psychological health and lower scores in physical health compared to the BPD group without RR ( $p < .05$ ). The effect sizes were mild and the powers moderate-high.

Regarding self-esteem, the BPD group with RR showed significantly lower scores compared to the BPD group without RR ( $p < .05$ ). The effect size was small and the power was high.

The MANOVA analysis reported significant differences between childhood traumatic episodes variables ( $F = 2.79$ ,  $p = .02$ , *Wilks*  $\lambda = .74$ ).

The univariate analysis showed significantly higher scores in the BPD group with RR than in the BPD group without RR for various types of traumatic episodes in childhood (emotional abuse, sexual abuse and emotional abandonment) ( $p < .05$ ). The effect sizes were slight and the potencies were moderate-high.

The multivariate analysis did not report significant differences between the variables of social cognition ( $F = .17$ ,  $p = .94$ , *Wilks*  $\lambda = .97$ ). Similarly, these differences

**TABLE II.** Psychopathological comparison among clinical variables between BPD patients with and without RR.

Variables	BPD with RR (n = 23) M (SD)	BPD without RR (n = 26) M (SD)	Statistics F	P	<i>h</i> <sup>2</sup>	P
BSL 23	61.68 (22.64)	48.52 (32.40)	2.53	.11	.05	.34
AQ						
Physical aggression	47.14 (12.49)	37.08 (12.94)	7.29	.01*	.14	.75
Verbal aggression	49.32 (7.64)	41.96 (10.76)	7.11	.01*	.13	.74
Rage	26.50 (4.16)	23.68 (5.32)	4.01	.05*	.08	.50
Hostility	18.55 (4.09)	14.60 (5.92)	6.86	.01*	.13	.72
BDI	22.64 (5.90)	18.40 (8.80)	3.64	.06	.07	.46
ECR						
Anxious attachment	36.39 (6.73)	39.54 (5.34)	3.17	.08	.06	.41
Avoidant attachment	38.13 (4.22)	36.46 (5.88)	1.24	.27	.02	.19
WHOQOL						
Physical health	16.45 (4.76)	19.35 (4.75)	3.96	.05*	.08	.49
Psychological health	13.30 (3.35)	10.43 (2.76)	9.43	.00**	.18	.85
Social relationships	8.60 (4.53)	7.65 (3.63)	.57	.45	.01	.11
Environment	17.80 (5.43)	17.96 (6.23)	.00	.93	.00	.05
Self-esteem	16.40 (3.99)	20.54 (4.87)	8.35	.00**	.16	.80
CTQ						
Emotional abuse	13.87 (3.79)	10.63 (2.63)	11.68	.00**	.21	.91
Sexual abuse	14.04 (5.20)	10.25 (3.87)	8.06	.00**	.19	.79
Physical abuse	7.52 (3.23)	7.29 (3.36)	.05	.81	.01	.05
Emotional abandonment	11.61 (2.79)	9.25 (2.48)	9.36	.00**	.20	.85
Physical neglect	11.57 (5.09)	9.96 (4.56)	1.30	.26	.05	.20
IRI						
Perspective taking	11.82 (4.65)	12.35 (4.97)	.33	.56	.00	.08
Fantasy	10.76 (6.36)	11.04 (5.41)	.19	.66	.00	.07
Empathic preoccupation	9.80 (4.45)	10.01 (4.45)	.01	.89	.00	.05
Personal distress	9.06 (4.91)	10.52 (5.50)	.44	.51	.00	.09

AQ: Aggression Questionnaire; BDI: Beck Depression Inventory; BPD: Borderline Personality Disorder; BSL 23: Borderline Symptom List; CTQ: Childhood Trauma Questionnaire; IRI: Interpersonal Reactivity Index; RR: Romantic Relationship; SD: Standard Deviation; WHOQOL: World Health Organization Quality of Life.

\*\* $p < .00$  in BPD people with RR vs BPD people without RR

\* $p < .05$  in BPD people with RR vs BPD people without RR

were also not observed in the univariate analysis ( $p > .05$ )

### Clinical predictors of romantic status in people with BPD

The clinical predictors among romantic status in people with BPD with and without RR is shown in Table III. The multiple binary logistic regression analysis was found to be statistically significant and the model explained roughly half of the variance of the marital status in BPD ( $\chi^2 = 21.83$ ,  $p = .00$ , *Cox and Snell* = .40, *Nagelkerke* = .54). Specifically, the results showed that the most significant predictor of RR status was physical aggression and self-esteem. Specifically, greater self-esteem predicted the absence of sentimental attachment, while greater physical aggression was associated with the presence of a sentimental attachment.

### Association between clinical and relational variables in BPD patients and their partner

The correlation analysis reported significant positive associations between the dimension of agreeableness of the group of couples and the demanding communication of the TLP group ( $r = .47$ ,  $p = .03$ ). Likewise, the satisfaction of the BPD group was positively associated with the conscience dimension of the group of couples ( $r = .53$ ,  $p = .01$ ).

## Discussion

The main objective of this study was to address the clinical differences between people with BPD with an RR and those and without an RR. The main findings of this study were: (1) the BPD patient sample with an RR presented a higher level of aggression emitted, a higher incidence of childhood traumatic episodes, poorer physical health, higher levels of psychological health and lower self-esteem; (2) physical aggression was the most relevant clinical predictor to the marital status of patients with BPD; and (3) positive associations be-

tween the dimension of agreeableness of the group of couples and the demanding communication of the BPD group.

First, as in other similar studies, the present investigation showed that people with BPD and an RR exhibited high scores in aggression and presence of childhood traumatic episodes<sup>6,19,20,52</sup>. These results support theoretical lines of other correlative studies regarding the severity of the psychopathology of BPD (*i.e.*, impulsivity, hostility emitted, avoidant attachment style) and the presence of childhood traumatic episodes<sup>53-56</sup>. As in other longitudinal and cross-sectional studies, the present investigation found that people with BPD who maintain an RR have greater avoidant attachment and childhood trauma than those without an RR<sup>19,46,57</sup>. In addition, following the line of these authors, it is possible that people with BPD with presence of trauma in childhood have a greater search for stable RR due to patterns of emotional dependence generated by the "false stability" in their RR<sup>46,57</sup>. However, unlike these studies, this research establishes a more specific clinical and methodological framework by delimiting the differences between groups of patients with the same diagnosis (inter-BPD), which makes it possible to clarify that aggression is not merely a psychopathology, primarily more observable in people with BPD, but RRs are erected in a psychosocial context of high risk for the risk, either as an eliciting, triggering and/ or exacerbating external variable of its manifestation.

Another finding of this study was that people with BPD with a RR had a significantly higher self-esteem deficit than people with BPD without a RR. In turn, they presented significantly greater psychological well-being (WHOQOL scale). This apparent contradiction suggests that patients with RS could "use" the sentimental attachment as a compensatory mechanism for a minor "self-love", so that relationship would acquire a very relevant meaning for their identity or self-concept.

Second, the most predictive marital status variable was "physical aggression". This result supports a prospec-

**TABLE III.** Clinical predictors of romantic status in people with BPD.

Predictive variables	B	Standar error	Wald	p	Odds ratio Exp[β]
<b>CTQ</b>					
Emotional abuse	-.25	.24	1.02	.31	.77
Sexual abuse	-.02	.13	.03	.84	.97
Emotional abandonment	-.13	.27	.22	.63	.97
Self-esteem	.20	.10	3.5	.05*	1.22
<b>AQ</b>					
Physical aggression	-.07	.03	4.90	.02*	.92

AQ: Aggression Questionnaire; BPD: Borderline Personality Disorder; CTQ: Childhood Trauma Questionnaire; SD: Standard Deviation

\*\* $p < .01$

\* $p < .05$

tive four-month follow-up study about BPD and RR, which suggests that 37% of couples of people with BPD were victims of physical and psychological violence<sup>26</sup>. In the same line, other correlative studies on aggression in people with BPD and RRs indicate that approximately 20 to 60% of couples presented physical aggression and 80% verbal aggression in their RR<sup>19,27</sup>. In addition, different studies indicate that the determining variable of the cyclic pattern of ruptures-reconciliations in the RRs of people with BPD was domestic violence<sup>19,20,57,58</sup>. On the other hand, the results of the present study follow the line of various correlative studies on emotional hyperactivity and aggression in the BPD, which suggest that people with BPD have more reactive response to their partners due to marital conflicts<sup>19,59-61</sup>.

Another relevant result for this research was that positive correlations were found between the pleasantness of couples and the demanding communication of people with BPD. This result makes us tentatively hypothesize that RR is consolidated in a pathogenic and insanely persistent relational dynamic. These findings are consistent with a longitudinal study on a BPD sample<sup>19</sup>. Along the same lines, significant positive correlations were also found between conscience of the partner and emotional satisfaction of people with BPD. Taken together, this suggests that relational dynamics are exercised on the basis of clearly established roles within an interdependence, with a more emotionally demanding tendency (hyper-demand) on the part of the patient with BPD and a more restraining predis-

position at the level emotional on the other side of the relationship.

In summary, the findings of the present research tentatively support the approach of systemic partner interventions in patients with BPD (e.g., TICP)<sup>62,63</sup>. Likewise, the implementation of cognitive-behavioral techniques to work codependency in the partner of the patient with BPD would be justified<sup>63</sup>.

This study has several limitations that must be considered. First, it is a cross-sectional study in which casual relationships cannot be established between the variables of the RR and the psychopathology of the people with BPD. Second, because this study is cross-sectional, we do not know the evolution of the RRs of the participants and their current marital status. Similarly, some data were collected retrospectively (*i.e.*, childhood traumatic episodes), which increases the risk of bias. Third, the sample size makes it difficult to generalize the results. Also, research has been limited to heterosexual associations and the participants with BPD were generally female. This limitation reduces the generality of the conclusions shown above.

Finally, different longitudinal and cross-sectional studies are needed on RR in people with BPD. Specifically, it would be decisive to know the incidence of Axis I and Axis II psychiatric disorders, childhood trauma and early maladaptive schemes in BPD samples and their couples. These results could provide relevant clinical information to elucidate more clearly a relational pattern between people with BPD and their partners.

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# The choice and the change of the allocated primary mental health professional in community-based mental health services: a focus-group qualitative study

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## SUMMARY

### Objectives

It is generally agreed that it is important to take into consideration users' preferences in the choice of their allocated primary mental health professional (PMHP). Our aim was to explore experiences of users, care givers and psychiatrists on users' initial choice and request of change the PMHP in Community Mental Health Services (CMHSs).

### Methods

Three focus groups were conducted in March-May 2017 in two CMHSs in Modena, Northern Italy. Transcripts were analyzed using MaxQda 11.

### Results

Six users, 7 psychiatrists and 5 care givers were enrolled. Casual or fixed allocation is commonly performed (so-called "fixed rota"). Lack of empathy and a bad therapeutic relationship seem to be the most important reasons to change the PMHP.

### Conclusions

Neither users nor professionals are generally involved in the initial choice of the PMHP. The availability of evidence-based guidelines for managing users' request to choose/change the PHMP may improve quality of care.

**Key words:** recovery, choice; primary mental health professional, community mental health, quality of care

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## Conflict of interest

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## Introduction

In recent times, healthcare has shifted from a paternalistic to a collaborative model<sup>1</sup>, giving more importance to patients' Autonomy, one of the main principles of biomedical ethics<sup>2</sup>.

In mental health care, the recovery model embodies this dramatic change of attitude, promoting service users' involvement in the co-construction of their pathways of care<sup>3</sup>. In line with such innovative principles, it is generally agreed that it would be important to take into account users' opinions about the relationship with their primary mental health professional (PMHP) in Community mental health services (CMHSs).

The UK National Health Service affirmed the right for users to choose their mental healthcare provider for out-patient treatment<sup>4</sup>. Similarly, this topic

has acquired an important role in the agenda of mental health care providers in Australia <sup>5</sup>, New Zealand, USA and Canada <sup>6</sup>. In Sweden, recent reforms have encouraged the exercise of patient choice in outpatient settings not only in General Medicine, but also in other specialties, including mental health <sup>7</sup>. Users' organizations are vocal on the choice issue as part of their efforts to achieve parity between mental health and physical health <sup>8</sup>.

Nevertheless, users' choice of mental health professional appears problematic and only partially applied in real practice <sup>9</sup>. In Italy, despite the presence of a long tradition of community-centred provision of mental health <sup>10</sup>, users cannot generally choose their PMHP <sup>11</sup>. Only anecdotal reports exist that some Italian community mental health centres (i.e. the Department of Mental Health of Bologna) have locally implemented operative instructions guiding how to manage users' request to choose and/or change their PMHP.

Little research on this topic is available. Hill & Laugharne confirmed that patients would like to express their preference about their own PMHP in the NHS <sup>12</sup>. Similarly, a study investigating the opinions of 368 subjects with chronic depression found that the majority of them rated the free choice of their PMHP as important <sup>13</sup>. Matching in age, gender, ethnic and linguistic background seem to influence user preferences, but studies are few, small in size and far from being conclusive.

To our knowledge, no study explored users', caregivers and psychiatrists view on this topic by means of focus groups and grounded theory qualitative analysis.

Therefore, the aim of this study was to explore users, care givers, and psychiatrists' attitudes, opinions and personal experiences towards the topic of the choice and the change of the allocated PMHP in CBMHSs.

## Material and methods

### Study design

This is a qualitative research, conducted according to the grounded theory methodology <sup>14</sup>. Three focus groups were implemented in order to explore, respectively, users, caregivers and psychiatrists' attitudes and opinions on the research topic. The study was reported according to COnsolidated criteria for REporting Qualitative research (COREQ) principles for qualitative research <sup>15</sup>.

### Research team and reflexivity

The first focus group was conducted by GR and BG, the second by CA, AM and RV, the last one by NG and GG; researchers were residents in Psychiatry at the University of Modena and Reggio Emilia respectively at their second (GR, AM, NG) and third (CA, GG) year of training, at the time of the study. RV and BG were final year medical students. GMG, Associate Professor in Psy-

chiatry at the University of Modena and Reggio Emilia, supervised the general research methodology.

### Participant selection

All users, care givers and psychiatrists of the two community mental health centres in the town of Modena, North of Italy, were invited to the focus groups, without limitation of sex, age or disorder.

On January 2017, an e-mail describing the study was sent to the directors of the centres, including a flyer invitation to the focus groups to be forwarded to all users, care givers and psychiatrists. Flyer invitations were also posted to the walls of the out-patient clinics. The flyer invitation illustrated the project and reported date, location, time and duration of the focus groups; a phone contact was also provided. Participation in the focus group was voluntary. No interactions or personal contacts were established prior to the study between researchers and participants.

### Setting

The three focus groups were held in the meeting room of one of the mental health centers. Each group had an expected duration of 90 minutes. At the beginning of each focus group, researchers briefly introduced themselves, and provided information on how to proceed with the group activity.

### Data collection

During the meetings, field notes were taken by a co-facilitator and used later in the coding phase. Meetings were audio-recorded. After the focus group, each participant was asked to fill in a research questionnaire collecting socio-demographic and clinical (when applicable) variables; the questionnaire also explored previous experiences and opinions on the investigated topics and prompted further feedbacks, in order to reach theoretical data saturation. A second questionnaire was subsequently sent by e-mail to each psychiatrist who participated in the study, as respondent validation. Transcripts were not returned to participants for comment and/or correction.

### Data analysis

Rough, anonymized transcripts of the focus groups' audio-recordings were analysed independently by two researchers (BG, GR) by means of MaxQda 11 software (VERBI GmbH) so as to develop a hierarchical code system *a posteriori* (derived from the data), with the independent supervision of a third researcher (RV), according to the principles of grounded theory.

### Data reporting

Data were reported according to the COREQ. The COREQ checklist for this study is available for readers as supplementary material.

## Ethics

This research work was part of the wider research project "The choice and change of Mental Health Care provider in Community Mental Health services", approved by Modena Ethics Committee (EC 270/16-Protocol number 204/CE) on 24/1/2017. Written and signed informed consent was obtained from each participant; the study was performed according to the principles of the Declaration of Helsinki and to the Clinical Good Practice rules for medical research.

## Results

The three focus groups were conducted on March, 17<sup>th</sup> 2017 (users), May, 8<sup>th</sup> 2017 (care givers) and May, 23<sup>rd</sup>, 2017 (psychiatrists). Six users (4 males, 2 females; mean age  $34 \pm 13.37$  years) attended the first focus group; 5 care-givers (1 male, 4 females; mean age  $59.2 \pm 16.78$  years) attended the second; 7 psychiatrist (2

females, 5 males; mean age  $54.29 \pm 10.49$  years) attended the third and final.

All participants completed the research questionnaire at the end of each focus group. Five of the 7 (71.43%) psychiatrists also completed the respondent validation questionnaire.

At the MaxQda analysis, the first focus group provided 85 coded segments, the second 57 and the third 57. Coded segments were grouped *a posteriori* in 2 thematic macro-areas: 1) the initial choice of the PMHP (71 segments from the first focus group, 23 from the second and 13 from the third); 2) the request to change the allocated PMHP (4 segments from the first focus group, 10 from the second and 44 from the third). Table I provides the retrospective hierarchical code system and results of the qualitative analysis of each focus group.

Figure 1 provides a coding tree of the major and minor explored themes.

**TABLE I.** Retrospective hierarchical code system and results of the qualitative analysis.

USERS' FOCUS GROUP		
Macro area	Sub-codes	Number of coded segments
Choice of the PMHP	Possible	0
	Not possible	4
Request to change the PMHP	Modality	7
	Motivation	
	Empathy	6
	Perceived care	1
	Logistic reasons	1
	Ethnicity	0
	Religious/cultural background	5
	Gender	6
	Age	6
	Unwanted change	10
	Subjective difficulties	4
	Desire to follow the psychiatrist in another service	6
PSYCHIATRISTS' FOCUS GROUP		
Macro area	Sub-codes	Number of coded segments
Choice of the PMHP	Possible	5
	Not possible	2
	Modality	3
Request to change the PMHP	Modality	3
	Motivation	

TABLE I. *continue*

Macro area	Sub-codes	Number of coded segments
	Outcome	1
	Specific competence	2
	Duration of the relationship	4
	Gender	1
	Age	1
	Possible	3
	Not Possible	1
CARE GIVERS' FOCUS GROUP		
Macro area	Sub-codes	Number of coded segments
Choice of the PMHP	Possible	1
	Not possible	8
	Modality	1
Request to change the PMHP	Modality	2
	Motivations	6
	Privacy	2
	Previous involuntary Admission	4
	Empathy	10
	Ethnicity	1
	Religious/cultural background	1
	Gender	4
	Age	0
	Unwanted change	5
	Subjective difficulties	4
	Desire to follow the PMHP	1

A brief summary of the main findings of the study is displayed in Table II.

#### *The choice of the PMHP*

According to all participants and to users' personal experience in community-based mental health settings, the usual method of initial allocation of a service user to a PMHP is via a "fixed rota" and it usually takes place usually during team meetings, so that generally users, as well as professionals, can not have a say in the initial choice of their PMHP.

Psychiatrists confirmed that, to the best of their knowledge, no guidelines regulating users' involvement in the choice of their PMHP are currently available.

Users also said that, especially at the very first contact with services, people generally have neither full awareness of their right to choose, nor sufficient information on the nature of mental disorders and their possible

treatments to properly guide an informed choice of the PMHP.

The group of psychiatrists alone highlighted the organizational and practical issues supporting the system as it is (the rota system described above), which serves the aim to evenly distribute across professionals the often very high caseload. A smaller caseload (that is, an increase in the number of mental health providers) could allow to take into consideration users' requests. Most users and care givers expressed their disappointment at being denied choosing their own PMHP.

*"What I regret is that I would also have preferred to take part in the doctor's decision" (a care giver).*

*"In the same way that patients can choose their own GP, it would be appropriate for psychiatric patients to have the opportunity at least to exhibit their own personal choice regarding the PMHP" (a psychiatrist).*

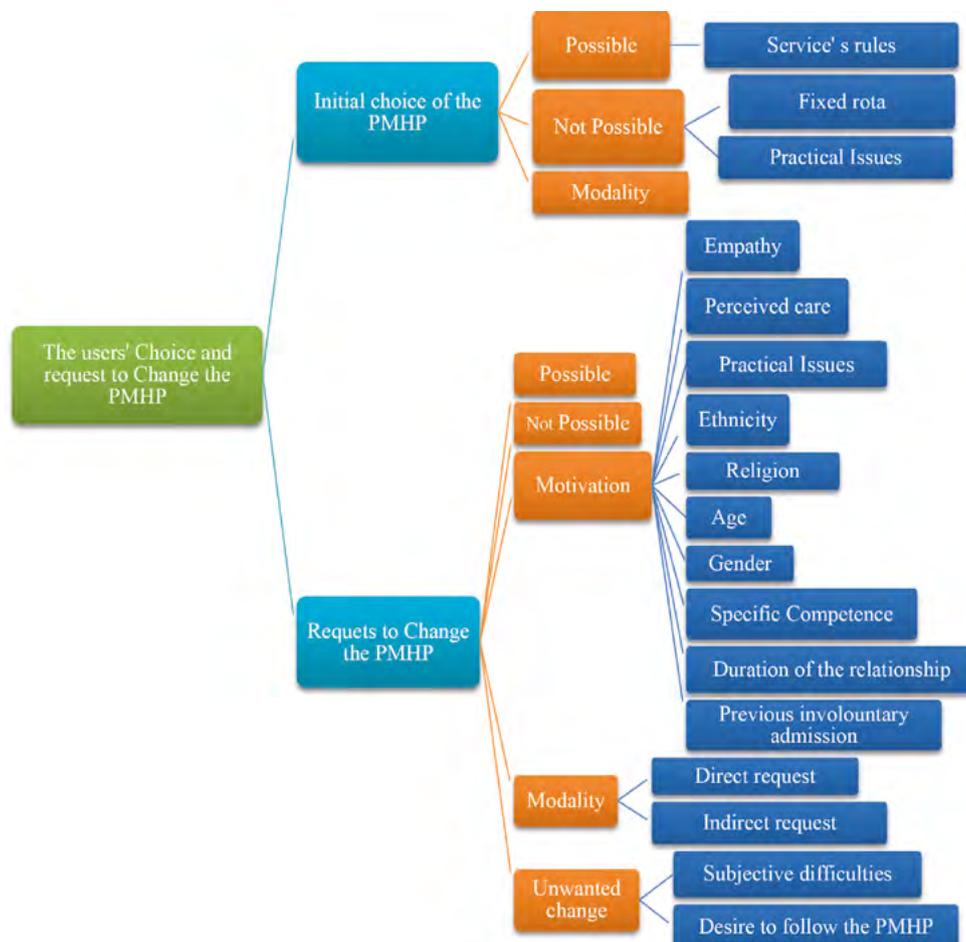


FIGURE 1. Coding tree of the major and minor themes explored in the focus groups.

TABLE II. Summary box of the main findings of the study.

Main OVERLAPPING THEMES
The feeling and empathy between the PMHP and the user is considered essential for a good therapeutic relationship
The management of drug therapy is a very sensitive topic for both patients and caregivers, and can influence the need to choose/change the allocated PMHP
The management of the request to choose/change the allocated PMHP is highly regarded as relevant. There is the need for well-defined policies to deal with these requests in Community Mental Health Centres.
Allocation via a fixed rota is the usual sytem to allocate PMHP to service users: users and professionals are not generally involved in the initial choice.
The lack of empathy and a bad therapeutic relationship seem to be the most important reasons behind the request to change the PMHP
The topic was considered “relevant” or “very relevant”
SPECIFIC THEMES FROM THE FOCUS GROUP OF PSYCHIATRISTS
Caseload size influence the way requests for choosing/changing the PMHP are dealt with: a smaller workload would allow a more accurate management and a higher rate of acceptance
PMHPs may also be given the possibility to request to change patients, especially after long-term relationships or when the therapeutic relationship is felt to be “at a deadlock”

According to users and most of care givers, the free initial choice of the PMHP would in fact be considered as an opportunity for active involvement of the user in his care process.

*“An advantage of being able to choose your own doctor would be to make the patient more involved in the therapeutic process” (a user).*

#### *The request to change the allocated PMHP*

Most of participants acknowledged that a user's request to change the allocated PMHP is generally at least discussed, and a change granted more often than it used to be years ago.

*“Usually today if one proposes a change they change it, it is not like it used to be” (a user).*

Empathy in the therapeutic relationship is the most important reason prompting a request to choose or change the PMHP, according to users. Therapeutic relationships described as “good” feature reciprocal trust, the PMHP accessibility and the user's experience of being actively listened during sessions. Requests of changing therapist usually come up when such features are felt to be lacking.

*“Empathy is felt differently from person to person and it may be that a psychiatrist is good for one person but is not good for another; this is not a failure, it is a change” (a user).*

Care givers as well emphasized the importance of empathy in the users/PMHP therapeutic dyad, and the role of poor empathy as a reason to ask for a different doctor. Furthermore, care givers outlined that especially in long-lasting therapeutic interactions which are frequent in mental health care, it may be that a change of the PMHP every now and then could result in improved recovery. The psychiatrists added that it may be not only the user wanting to change the PMHP, but also the other way round, the PMHP wanting to change users: after a certain amount of time, the therapeutic relationship may reach a stagnation point and a change could improve satisfaction and other outcomes.

Care givers also suggested that having experienced an involuntary admission may be a reason for users' wanting to change the PMHP who took such decision. Psychiatrists strongly expressed their disagreement on such motivation to be considered valid.

*“If a person who has ‘been at the service’ for ten years undergoes an involuntary admission, perhaps it is a sign that there is something that is not going well in the care pathway” (a care giver).*

Participants in all the three focus groups expressed conflicting opinions about the topic of age, gender, ethnicity or religion concordance between the PMHP and the user as an appropriate reason to ask for a change. A request to change the PMHP motivated by the desire to achieve age and gender matching was considered appropriate by care givers and users, but of little or no importance according to psychiatrists. One user also expressed the fear that a younger age of the PMHP may be a sign of less clinical experience. Users did not express the need for ethnic concordance, only one care giver suggested that ethnic matching could be a good reason to request the change of the PMHP.

Finally, according to both psychiatrists and care givers, the PMHP expertise in managing the specific disorder affecting the user may be a valid criterion for allocation or re-allocation.

Psychiatrists informed that no official service or department policy was available to help dealing with users' requests to change PMHP. One of the two mental health centers implemented a list of operative instructions in case of such requests, which essentially consists in submitting them to the senior Consultant of the community mental health centre and discussing them with users', relatives and the CBMHS team.

Users felt that specific information and options on how to change PMHP should be given to them. They agreed that requests of change which happen after a considerable duration of the therapeutic relationship, should be given a priority.

The opposite scenario of unwantedly having to change the allocated PMHP, for example because of the user relocating to a different catchment area, or because of a temporary absence or definitive retirement of the psychiatrist, was also discussed. Four users and one care giver expressed the desire to keep on with the same PMHP anyway. It was a shared opinion that to suffer an unwanted change may cause of serious discomfort for users, especially if a substitute is not immediately available. Users asked to be informed and psychologically prepared about the possible change of their allocated PMHP.

All participants agreed that discussing the topics of the choice and change of the PMHP is relevant and that it would be helpful if specific policies were developed and implemented in CMHSs.

## **Discussion and conclusions**

There was agreement among participants on considering the topic of the choice and change of PMHP as a very relevant one to discuss. This finding is in line with previous studies<sup>12,13</sup>.

Problems in establishing a good empathic therapeutic relationship was commonly recognized as the main mo-

tivation prompting a request to change the PMHP. This finding is also in line with previous studies, showing that mental health service users, not surprisingly, express their preference for a supportive, flexible, respectful and professional relationship<sup>16</sup>, based on trust<sup>17</sup>.

Age, gender and ethnicity matching were generally not considered sufficient motivations for requesting a specific PMHP or to change PMHP if users had a specific preference in regard to these characteristics in the PMHP. With respect to gender, this finding is consistent with previous studies investigating users' gender preferences<sup>18,19</sup>. As to ethnicity, this results is in contrasts with some studies<sup>20-25</sup> that showed that users tend to prefer therapists of their ethnicity. It must be noticed that several of these previous studies were implemented across ethnic minorities; also, Italy has been a multi-ethnic society for much less time than other countries, and to a much less extent, possibly limiting the development on the discourse on the issue of ethnic concordance in the dyad PMHP-users.

In the user and care giver groups, the opposite issue, that is the desire of maintaining the relationship with the allocated, PMHP provided results similar to those outlined by previous studies, showing that sudden changes of PMHP were experienced as setbacks in treatment<sup>26</sup>. Psychiatrists described the lack of policies to support mental health workers in dealing with these requests. Request of change may come not only from users or caregivers, but also mental health professionals may need a change at times.

Finally, while care givers suggested that having experienced an involuntary admission may be a reason for users' request to change the PMHP who took such decision, psychiatrists did not consider such motivation as valid. This result from the focus group of psychiatrists is quite surprisingly, because it is well known that several previous studies on users' perceptions of coercion showed that compulsory admissions may be related to anxious, depressive and even traumatic symptoms. Therefore, these users' experiences could reasonably

justify their request to change the PMHP who ordered their previous involuntary treatment<sup>27,28</sup>.

A few limitations in the present research should be acknowledged, especially as a consequence of the qualitative methodology adopted. Firstly, as in every focus group occurs, participants were self-selected and study results are therefore harder to generalize to the larger population. Secondly, the respondent validation analysis was not possible for all the participants, because of the majority of users and care givers did not share their personal e-mail contacts to researchers. On the contrary, all psychiatrists received and completed the respondent validation questionnaire via their institutional e-mail. Finally, transcripts were not returned to participants for comments or corrections because the audio-records of the whole focus groups were literally transcribed, thus limiting the risk of transcription error; as several papers on member checks in qualitative research underlines, this limitation is unlikely to significantly affect research findings<sup>29,30</sup>.

In conclusion, improvement of users' involvement in decision-making is a relevant topic according to the recovery model of care, and more research is warranted on effective methods to achieve it. Users, care givers and psychiatrists' views should be better explored, in order to discuss ethical and practical issues and to elaborate policies to appropriately manage users' requests of a change of PMHP. Discussion and sharing experiences at a regional and national level should be promoted, as well as relevance and feasibility in different clinical settings.

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# Psychopathological excursus on anti-social personality disorder, psychopathy and the dark triad: a review of international literature

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## SUMMARY

### Aim

*This work is made up of two parts. The first part aims to give a general overview of psychopathy and anti-social personality disorder. The second part goes into more depth on the conceptual and empirical studies of the three correlated personality constructs, until now defined as the Dark Triade, but considering them independently.*

### Methods

*We consulted information available in literature through the PubMed site and Google Scholar without filtering by year. Searches were made using the keywords “psychopathy”, “psychopathy and anti-social personality disorder” and “dark triad”.*

### Results and discussion

*We highlight not only the specific peculiarities, but also similarities and differences that help the reader better understand that the two terms, psychopathy and anti-sociality, are not synonyms although often used as such. We also offer a definition of the concept of Dark Triad, outlining both its “undesirable” and functional aspects.*

**Key words:** psychopathy, psychopathy and anti-social personality disorder, dark triad

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## Conflict of interest

*The Authors declare no conflict of interest*

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## Introduction

Very often the terms anti-sociality and psychopathy are mistakenly used as synonyms. Hare believes the distinction between psychopathy and anti-social personality disorder is very important, both for clinicians and for the rest of society<sup>1,2</sup>. Anti-social behaviour disorder and psychopathy are two separate disorders<sup>3</sup>. According to the DSM-5, the basic characteristics of anti-social personality disorder are negligence and infringement on the rights of others, expressed in irresponsibility, absence of self-accusation, lack of compassion and aggressiveness<sup>2,4,5</sup>. Psychopathy (or “Primary psychopathy”) is a personality disorder characterised by the lack of social norms, and a deficit of empathy and remorse. It usually manifests itself as impulsiveness with a lack of anxiety or sense of guilt, through manipulation and persistent violation of social norms<sup>1,2</sup>. Both disorders are characterised by a lasting pattern of anti-social behaviour beginning in childhood, however psychopathy also includes a number of specific emotional and interpersonal deficits.

The other concept dealt with in this article is that of the Dark Triad, which has aspects interrelated with the disorders described above. The dark triad is a personality construct developed by Paulhus and Williams (2002). It includes three personality traits that lead to maladjusted, socially undesirable behaviour, namely Machiavellianism, psychopathy and narcissism. The adjective “dark” attributed to the combination of these personality traits is indeed used to underscore the malevolent and at

times criminal characteristics of persons who present these peculiarities to a high degree<sup>6</sup>. Psychopathy, narcissism and Machiavellianism are independent of each other, but positively associated<sup>7</sup> and distinguished by common elements such as manipulative behaviour, inflated ego and the tendency to exploit others to achieve their goals<sup>8</sup>. The dark triad is thus constituted by personality traits not of immediate clinical interest, but that exercise a strong influence on the relational models of the individuals affect, their way of understanding their own emotions and those of others, and even on their behavioural and mating strategies<sup>9</sup>.

### **Psychopathy versus anti-social personality disorder: differences and similarities**

DSM-IV-TR (2000) only defines the diagnosis criteria for anti-social personality disorder, but not those of psychopathy. However, Section III of DSM 5 mentions psychopathy in an area of the manual that includes an 'alternative model for diagnosing personality disorders'. The criteria for psychopathy are specified and assessed through the revised Psychopathy Checklist (PCL-R)<sup>10</sup>. The current conception of psychopathy was introduced by Cleckley in his celebrated didactic work entitled the *Mask of Sanity* (1941)<sup>11</sup>, and refined by Hare through the construction of the PCL<sup>12,13</sup>, which is still the gold standard for assessing the disorder.

Psychopathy is a personality disorder characterised by a constellation of interpersonal, affective and behavioural traits. These characteristics correspond to the 20 items in the PCL-R (Psychopathy Checklist – Revised), a semi-structured interview with the purpose of investigating the disorder. The items on the list, and so the aspects characteristic of the disorder are: glibness/superficial charm, grandiose sense of self, need for stimulation/propensity for boredom, pathological lying, cunning and manipulative behaviour, lack of remorse or guilt, shallow emotional response, callousness and lack of empathy, parasitic lifestyle, poor behavioural control, sexual promiscuity, early behavioural problems, lack of realistic long-term goals, impulsivity, irresponsibility, failure to accept responsibility, short-term relationships, juvenile delinquency, revocation of conditional release, criminal versatility<sup>14</sup>.

Neurobiological models of psychopathy tend to concentrate on the limbic and paralimbic systems<sup>15</sup> involved in regulating emotions and social behaviour, in particular the amygdala and ventromedial prefrontal cortex<sup>16</sup>. Neuroimaging studies have confirmed the association between dysfunction of the amygdala and psychopathy<sup>17</sup>. The studies showed that high PCL scores are associated with a smaller amygdala. The importance of the dysfunction in the ventromedial prefrontal cortex

in psychopathy depends mainly on the interaction between this zone and other cortical and subcortical regions of the brain involved in the affective process, in social cognition and decision making. Two areas are of particular interest: the amygdala and the medial parietal region, including the precuneus and the posterior cingulate cortex. Both the precuneus and posterior cingulate cortex are densely and reciprocally connected with the ventromedial prefrontal cortex, and are both regions characterised by reduced activity in psychopathy<sup>17,18</sup>. In psychopaths reduced differentiation, with respect to non-psychopaths, in heart rate in response to neutral vs. threatening stimuli has been observed. In the same way, psycho-physiological studies have shown a reduced electro-dermal response to aversive stimuli in psychopaths, just as a reduced potentiation of the startle blink reflex<sup>19</sup>. This could suggest that psychopaths have a reduced defensive fear capacity when exposed to threatening situations<sup>20</sup>.

The cognitive characteristics of psychopathy include somewhat rigid and inflexible schemata of self, others and the world. Psychopaths see themselves as strong and autonomous, while seeing others as exploiters or to be exploited, or weak, vulnerable and to be preyed upon. Another fairly common characteristic is a marked cognitive bias in perceiving malicious intent in others<sup>21</sup>. The emotional characteristics of psychopathy manifest themselves in difficulty processing emotional information and responding empathically to others. Deficit in processing emotions is one of characteristic aspects Cleckley identified in psychopaths<sup>11</sup>.

If on one hand it is true that anti-social personality disorder and psychopathy have many common traits, it is also true that they have a great many differences. The principal characteristics able to distinguish psychopathy from any other personality disorder – including anti-social personality disorder – is the incapacity to form ties; while at lower levels than normal, an anti-social person has the capacity for form bonds with others, the psychopath does not. For the psychopaths there is only themselves, and their own needs. Likewise there is a clear distinction in the motivations that drive these people: the psychopath aims for a precise goal, while the anti-social acts on impulse without a specific goal. The latter lacks emotional control (inhibitory functional deficit), reacts with violence and aggression to a threat perceived as imminent (defensive attack); the cause of the psychopath's behaviour is instead traceable to a deficit in aversive conditioning assimilation: he is a predator fully aware of exploiting others to achieve his deviant goals (predatory attack). The final consideration regards the sociological aspect. Most of the individuals affected by anti-social personality disorder come from the most disadvantaged social classes, and their illicit

behaviour is very much aimed at assuring personal survival; the anti-social acts on impulse and makes no effort to disguise their nature. Psychopaths usually come from the middle-upper social classes, are well integrated in society and their crime serves to satisfy their desire for control and power; they hide behind a mask, plot in the shadows and act with calculation and prudence to achieve their devious aims <sup>22</sup>.

### The concept of empathy

Empathy is the capacity to understand the state of mind of other people, and is compromised in all of the personality traits described above. Empathy is fundamental for social interaction, it allows us to understand the suffering of others, and attenuate maladjustment in terms of aggressive behaviour <sup>23,24</sup>. Reduced empathy, together with other traits, is proposed as the “core” that interconnects three constructs of maladjusted personality – Machiavellianism, narcissism and psychopathy – which together are conceptualised in the Dark Triade <sup>25,26</sup> and associated with aggressiveness <sup>27</sup>.

Empathy is a multi-dimensional construct <sup>28,29</sup>, comprising cognitive and affective components. Cognitive empathy has been defined as the capacity to understand the mind of another person, recognising what the other thinks. This kind of awareness is essential for predicting the behaviour of others and manipulating it <sup>30</sup>. Affective empathy implies an indirect response to the emotions of others, feeling what they feel. It's the kind of empathy involved in the model of violence inhibition mechanisms <sup>31</sup>, and it is thought that the selective deterioration of this capacity is the underlying cause of aggressiveness, at least in psychopathy <sup>32,33</sup>. Over and above deficits in affective empathy, compromised cognitive empathy (defined as the capacity to know rather than feel the emotions of another) has been found in institutionalised criminals with psychopathic tendencies <sup>34</sup>. These mechanisms are also found in the other traits of the dark triad. Indeed, deficits in affective empathy have been linked with all three of the dark traits, indicating a reciprocal incapacity to share the emotional experience of others. In other cases, cognitive empathy seems to be spared, or even augmented as in the case of narcissism, which would suggest a normal or perhaps better comprehension of the thoughts and intentions of others <sup>35</sup>, allowing the narcissist to create a more favourable image of themselves through understanding and predicting the reactions of others.

In the case of Machiavellianism, a partial cognitive deficit has been observed. In effect, the conserved part of cognitive empathy allows the person to predict the intentions of others, facilitating them in their manipulative strategies <sup>30</sup>. Lastly, in psychopathy empathy is compromised at all levels, both cognitive and affective,

and is associated with aggressive behaviour. Thus, in line with previous research into direct aggression <sup>36,37</sup>, psychopathy present a more serious overall model of maladjusted traits.

### The dark triad

The dark triad has three underlying structures – narcissism, psychopathy and Machiavellianism <sup>6</sup>, it is a predominantly malevolent type of mentality, manifest in self-interest, aggressiveness and ruthlessness <sup>38</sup>.

Each trait of the DT has its own unique characteristics: Machiavellianism describes a cynical, parasitic, manipulative nature <sup>39,40</sup>. Narcissism is characterised by an exaggerated sense of personal entitlement, superiority and grandeur <sup>5</sup>. Psychopathy includes a constellation of interpersonal-affective deficits (superficial charm, insensitivity) and behavioural deficits (irregular lifestyle, anti-social behaviour) <sup>41,42</sup>.

The traits of DT share a propensity for an insensitive, manipulative type of interpersonal lifestyle, and previous research has examined the empirical superimposition of these subclinical personality traits in order to identify the underlying core of the malevolent personality. The so-called “dark core” thus identified offers a better understanding of the series of emotive traits and empathic deficits that combine to promote an egotistical type of lifestyle <sup>27</sup>. In effect, the dark core is constituted by all three of the dark traits<sup>7</sup>, such as a sense of grandeur <sup>25</sup>, low honesty-humility <sup>30,43,44</sup> and interpersonal exploitation <sup>45</sup>.

### Psychopathy

The etymological root of the word psychopathy comes from the Greek *psych* (soul or mind) and *pathy* (suffering or disease). Psychopathy refers to the incapacity to perceive, comprehend or confront emotions due to a lack of emotive intelligence and empathy. Its principal traits are manipulation, deception, ruthlessness and the need of high levels of excitement and stimulation. Psychopaths are insensitive to loss or risk, and have no fear of failure <sup>46</sup>, allowing them to risk far more. They despise social norms and are fully prepared to oppose the status quo <sup>47</sup>. Psychopathy is characterised principally by deceit, ruthlessness and the search for stimuli <sup>48</sup>. Psychopathic people show indifference toward others and low sensitivity to risk, but often achieve high level social standing and are considered intelligent, attractive and efficient <sup>49</sup>.

### Narcissism

The characteristic traits of narcissism are domination, exhibitionism and an augmented sense of entitlement

and superiority<sup>50</sup>. Narcissists not only feel good about themselves, but also feel more worthy of respect from others<sup>51-52</sup>. They tend to be egocentric and in constant search of admiration and attention from others<sup>53</sup>, and gain self-esteem, power and status through the effective utilisation of social relations<sup>54</sup>. At the same time, they lack human values and have a strong desire to control others<sup>55</sup>, they are good at using their charisma to their advantage, inducing others to follow their plans<sup>56</sup>, and expect others to accept their vision of the world. The principal characteristics of narcissism are an inflated sense of self-importance, expansive perception of self and self-love<sup>57</sup>. Individuals with high-level narcissist traits tend to have a high degree of self-acknowledgement and are very good at creating and grasping opportunities<sup>49</sup>. Moreover, they are highly motivated in the pursuit of personal objectives<sup>58</sup> and fully aware of their abilities<sup>59</sup>; even in aversive conditions, it seems that persons affected by high-level narcissist traits believe they are more capable than others<sup>60</sup>. This quality gives them greater self-confidence in doing things in their own interests. Brookes<sup>61</sup> indicates that people with high levels of narcissism tend to have greater confidence in their capacity to achieve their own objectives, which significantly increases self-effectiveness.

## Machiavellianism

Machiavellianism describes an egotistical, deceitful, scheming and manipulative personality trait<sup>62,63</sup>. Individuals of this kind are usually self-serving, driven by their own interests and have a strong desire to control others<sup>64</sup>. They lack affinity and responsibility, and tend to be highly persuasive<sup>65</sup>. In general terms, their persuasive abilities helps them facilitate and motivate others toward any given objective<sup>49</sup>. This particular capac-

ity feeds their desire to control and achieve status<sup>66</sup>, by manipulating and using others to realise their own personal interests<sup>61</sup>. Hence the fundamental traits of Machiavellianism include the pursuit of personal interests, deception, strategy and manoeuvrability<sup>63</sup>. They often resort to unsavoury methods to achieve their goals or maximise their interests<sup>49</sup>. Perhaps as a result of these characteristics they are more inclined to be enterprising. These people believe that the end justifies the means and have a strong disposition toward wealth, power and competition<sup>67</sup>, often choosing short-term strategies that demand immediate satisfaction, and that are closely correlated with a propensity for life 'in the fast lane'<sup>68</sup>.

## Conclusions

This article is made up of two sections forming part of a psychopathological continuum.

The first analyses anti-social personality disorder and psychopathy, two disorders often confused, to shed light on the differences between them and make a distinction.

The second part analyses DT, highlighting both the negative aspects: criminal tendency, insensitivity, interpersonal exploitation and the potentially destructive effects that these individuals have on their environment and interpersonal relations, and the functional-adaptive prospects that these personality traits present, at least in certain limited contexts. In effect, DT shows positive correlations with factors capable facilitating them in achieving their goals, with strong points ranging from creativity to courage, leadership, assertiveness and a predisposition for power, achievement and self-valorisation.

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## Vortioxetine for the treatment of depressive episodes associated with Parkinson's disease: a case series of six patients

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### Conflict of interest

Gennaro Barbato, Pietro Marano, Bruno Passarella, Giulio Riboldazzi, Francesca Spagnolo, and Paola Vanni declare that they have no conflict of interest. Andrea Pilotto received speaker honoraria from BioMarin Pharmaceutical, Chiesi Pharmaceuticals, Nutricia Pharmaceuticals, UCB Pharma and Zambon Pharmaceuticals. He has also received travel grants from AbbVie Pharmaceuticals, BioMarin Pharmaceutical, Nutricia Pharmaceuticals, Zambon Pharmaceuticals and the Italian movement disorder society, and has received research support from Vitaflo Germany and Zambon Italy

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## SUMMARY

### Objectives

We present six case reports of patients with Parkinson's disease (PD) at various stages, who experienced major depressive episodes that were successfully treated with vortioxetine.

### Methods

The patients whose cases are reported in this manuscript were treated in the setting of daily clinical practice.

### Results

Of the six cases presented (2 females and 4 males, aged between 56 and 80 years) three had long-standing PD. The remaining three cases were diagnosed with PD at presentation. Most patients had a history of depressive episodes preceding the onset of the motor symptoms typical of PD, or experienced depressive symptoms concomitantly with the onset of the movement disorder. Most patients had therefore been previously exposed to conventional antidepressant medications. Vortioxetine proved consistently effective on depression and related aspects and was generally well tolerated. Symptoms of depression commonly shown by patients with PD, including apathy, cognitive function and sleep disturbances, responded particularly well to vortioxetine.

### Conclusions

These observations suggest that vortioxetine has a potential for the management of depressive episodes occurring in the complex and heterogeneous population of patients with PD. Vortioxetine also appears to be well tolerated when taken concomitantly with antiparkinsonian medications. This potential is worth investigating in adequately designed, prospective studies.

**Key words:** cognitive function, major depressive, multimodal antidepressant, Parkinson, vortioxetine

## Introduction

Depression is one of the most frequently reported neuropsychiatric disturbances in patients with Parkinson's disease (PD) <sup>1</sup>, with a prevalence ranging from 20 to 35% <sup>2</sup>. The 1-year incidence of minor depression is 18% <sup>3</sup>, and annual rates of newly diagnosed major depression disorder, following the diagnosis of PD, range from 1.9 to 10% <sup>1</sup>. Besides causing distress and affecting quality of life, depressive episodes can negatively impact other disease aspects including motor and cognitive impairments, functional disability, and psychiatric comorbidities <sup>1</sup>.

The mechanism behind depression in PD remains poorly understood. Psychological factors and disability are relevant determinants, but neu-

rological factors related to neurodegenerative disease are also involved<sup>1</sup>. Supporting this view is the fact that the neurodegenerative process associated with PD affects not only the dopaminergic system, but also results in the loss of noradrenergic and serotonergic neurons<sup>1</sup>. According to the prevailing hypothesis, changes in all these neuronal systems play a key role in the pathophysiology of depression in PD<sup>2</sup>.

Treatment of depression in PD is indicated when depressive symptoms are persistent and contribute to distress or dysfunction<sup>1</sup>. Evidence suggests that multiple antidepressant classes are potentially efficacious in the treatment of depression in PD<sup>4,5</sup>. For example, according to a recent network meta-analysis including 45 publications (8,890 patients), selective serotonin reuptake inhibitors (SSRIs) were highly effective for the treatment of depression in PD patients and improved activities of daily living and motor function, albeit with a relevant profile of adverse events<sup>6</sup>. Serotonin noradrenalin reuptake inhibitors (SNRIs) emerged as the safest medications with high efficacy for depression, while their effectiveness on activities of daily living and motor function was limited<sup>6</sup>.

Vortioxetine is a newer-generation antidepressant that combines two separate modes of action: inhibition of the serotonin (5-HT) transporter and a strong affinity for several 5-HT receptors, potentially leading to enhanced antidepressant activity<sup>7-9</sup>. More specifically, vortioxetine acts as an antagonist at 5-HT<sub>3</sub>, 5HT<sub>1D</sub> and 5-HT<sub>7</sub> receptors, as a partial agonist at 5-HT<sub>1B</sub> receptors, and as a full agonist at 5-HT<sub>1A</sub> receptors<sup>7</sup>. The net effect of this pharmacological profile is the enhancement of serotonin, noradrenalin, dopamine, acetylcholine, and histamine levels in specific areas of the brain<sup>10</sup>. A new classification system for psychotropic drugs proposed by a Task Force of the European College for Neuropsychopharmacology classifies vortioxetine as an antidepressant with a multimodal mechanism of action that combines modulation of 5-HT receptor activity with inhibition of the serotonin transporter<sup>7</sup>. Vortioxetine was approved by the US Food and Drugs Administration and by the European Medicines Agency in 2013 for the treatment of major depressive episodes in adults<sup>11,12</sup>. The recommended dose ranges from 5 to 20 mg/day; in patients aged < 65 years and ≥ 65 years the recommended starting dose is 10 mg/day and 5 mg/day, respectively<sup>11</sup>.

The efficacy and safety of vortioxetine have been investigated in a comprehensive program of large randomized, double-blind, placebo-controlled, and active-referenced trials<sup>13</sup>, including one study conducted in elderly patients (≥ 65 years)<sup>14</sup> and one study investigating vortioxetine for maintenance therapy<sup>15</sup>. These studies have mostly demonstrated statistically significant improvements in overall symptoms of depression

in adults with major depressive disorder based on the Montgomery-Åsberg Depression Rating Scale (MADRS) or Hamilton Depression Rating Scale scores.

A series of trials have specifically investigated the effects of vortioxetine on cognitive symptoms of depression<sup>14,16,17</sup>. An improvement in cognitive function in patients with major depressive disorder was observed in patients aged ≥ 65 years<sup>14</sup>. In this study, patients treated with vortioxetine performed better than the placebo group in cognitive tests (Digit Symbol Substitution Test [DSST]; Rey Auditory Verbal Learning Test scores) measuring processing speed, verbal learning, and memory<sup>14</sup>. These findings were confirmed in successive studies in adult patients<sup>16-18</sup>, and in a meta-analysis that compared the cognitive effects of various classes of antidepressants<sup>19</sup>.

Overall, clinical trials with vortioxetine (5-20 mg/day) have revealed a favorable safety and tolerability profile. According to an analysis of data pooled from 11 randomized placebo-controlled acute treatment studies (3,018 patients treated with vortioxetine; six studies included venlafaxine as active reference) and five open-label long-term extension studies (2,457 patients treated for up to 52 weeks with vortioxetine), the most common treatment-emergent adverse events associated with vortioxetine were nausea (20.9-31.2%) and vomiting (2.9-6.5%), the incidence of which reached a plateau at 15 mg/day<sup>20</sup>. For vortioxetine, the incidence of treatment-emergent adverse events associated with insomnia and sexual dysfunction was 2.0-5.1% and 1.6-1.8 *versus* 4.0 and 1.0% for placebo, respectively. Vortioxetine had no effect compared with placebo on clinical laboratory parameters, body weight, heart rate or blood pressure. It did not show any clinically relevant effect on electrocardiogram parameters, including the QTcF interval. Long-term treatment with vortioxetine was not associated with new or unexpected adverse events.

As vortioxetine is approved for the treatment of major depressive episodes in adults it was of interest to investigate its potential as a valid treatment option for the management of depression in patients with PD. In this report, we present six cases of patients with PD at various stages, who experienced major depressive episodes that were successfully treated with vortioxetine. All patients described in this case series gave informed consent.

## Case reports

### Case 1

A 56-year-old man presented to our out-patient clinic because of persistent low mood, anxiety, and insomnia, which he had experienced over the past few months. He had been absent from work for 1 month, had low ap-

petite, and had lost interest in all his usual activities. He was very concerned about his condition, but was unable to react. According to the patient's wife, substantial sleep disturbances, with agitation and screaming, had started well before the onset of low mood. The patient had been prescribed paroxetine for the depressive episode by his physician, which had however been discontinued after 10 days because of nausea, vomiting, and strong agitation. In addition, the patient reported to be feeling physically unwell, with slowness of movements, a slight tremor of the left hand, and a sense of agitation and instability when standing. Another matter of concern to the patient was the fact that his brother had been diagnosed with PD.

The physical exam revealed the typical motor symptoms of PD, including tremor at rest, rigidity and limited mobility of the left upper extremity, as well as a mask-like face expression. A question about his sense of smell revealed that the patient had hyposmia. He had no cognitive impairment related to dementia, as assessed using the Mini-Mental State Examination (MMSE). The diagnosis of PD was confirmed by brain magnetic resonance imaging (MRI), <sup>18</sup>F-DOPA positron emission tomography, and laboratory tests. PD was assessed using the Unified Parkinson's Disease Rating Scale (UPDRS). Main depressive symptoms shown by the patient were low mood, anxiety, apathy, and sleep disturbances. These symptoms were severe.

The patient initiated dopaminergic therapy with low-dose levodopa (up to 300 mg/day) combined with rasagiline (1 mg/day). Combined therapy was selected to achieve a rapid and substantial improvement of motor symptoms. The patient was also encouraged to start physical activity. Motor symptoms improved rapidly and substantially. Antidepressant treatment with vortioxetine was initiated after 1 month from presentation. Vortioxetine (10 mg tablets) was selected because of its favorable safety profile in terms of body weight, sexual function, and cognitive function. The initial dose was 5 mg/day (for 7 days), successively increased by 5 mg per week to reach a final dose of 20 mg/day. Alprazolam (0.5 mg tablets) was prescribed to treat anxiety (1/2 of the recommended dose in the morning and 1/2 in the afternoon; full dose in the evening to improve sleep). After 1 month of treatment with the prescribed therapy, the patient had a marked improvement both in motor function and mood. After 3 months, PD assessment showed a substantial improvement across all items of the UPDRS questionnaire, with the best results being achieved for non-motor symptoms, and for apathy in particular. The patient resumed his normal life and discontinued alprazolam during the day. At the last visit (6 months after presentation), the patient continued to be well, with no changes needed in his treatment.

## Case 2

A 61-year-old female teacher was referred by her physician to our clinic with a diagnosis of suspected PD. The patient had reported problems with her handwriting, which had become smaller and irregular. She had also noticed slowness and awkwardness in her fine movements, especially with regard to the right extremities. The patient was affected by hyposmia and constipation and had suffered from depression for 4 years. She was in treatment for depression with sertraline (50 mg/day). Over the past year, depressive symptoms had reappeared, despite antidepressant therapy, along with sleep disturbances and anxiety. The medical history of the patient included an intervention of hysterectomy at the age of 48, an intervention of breast lump resection, and thyroid nodules with normal thyroid function. The patient had hypertension and was also in treatment with ACE-inhibitors because of a nephritis event that had occurred when she was 45 years old. The patient's father, who had been affected by PD, had died at the age of 92.

The neurologic assessment revealed mild hypomimia and clumsiness in fine motor skills involving the right upper extremity; gait and arm swings were normal. Brain MRI and thyroid examination did not reveal any abnormality. Six months after presentation, the patient again underwent a physical examination that revealed a worsening of the motor symptoms affecting the right upper extremities. Based on these findings, PD was diagnosed. Neuropsychological assessment did not reveal any abnormality, while assessment of depression using the Beck Depression Inventory (BDI)-II provided a score of 21. Due to the family history of PD, genetic testing for Gaucher's disease was proposed. The patient underwent testing and was found to be a heterozygous carrier of a pathologic mutation in the glucocerebrosidase (GBA) gene (A>G substitution at position 1216 in exon 9 resulting in the substitution Asn409Ser in the enzyme). Given the limited extent of motor symptoms, antiparkinsonian treatment was not initiated. It was decided to discontinue treatment with sertraline due to the lack of efficacy of this SSRI antidepressant. After a few weeks, the patient started treatment with low-dose vortioxetine. Titration to the final dose of 10 mg/day was gradual due to nausea, which resolved rapidly. After a few weeks of treatment with vortioxetine, anxiety, mood, and sleep quality improved. Acceptance of the disease was also improved. As motor symptoms had begun to interfere with the patient's professional activity, it was decided to start a therapy with an inhibitor of monoamine oxidase B (rasagiline 1 mg/day). The therapy was well tolerated and moderately effective on motor symptoms. The patient continued treatment with vortioxetine (10 mg/day) and rasagiline (1 mg/day) with a relatively good control of depressive and motor symptoms.

### Case 3

A 60-year-old man was referred to our center for motor symptoms (rigidity and akinesia) affecting his right body side. The patient had been affected by these symptoms for 3 years. Furthermore, 4 years before presentation the patient had also suddenly experienced depressive episodes with symptoms including apathy, lack of initiative, loss of appetite with substantial loss of weight, crying for no reason, and general loss of interest. The onset of depression had been accompanied by the onset of back pain and forward falling while walking. The patient had been diagnosed with asthenia by his physician and had been prescribed S-adenosyl methionine 400 mg/day for 15 days, folic acid 5 mg/day, and Griffonia-based food integrators, without any improvement. He had then been referred to a psychiatrist who diagnosed major depressive disorder and prescribed a treatment with escitalopram (10 mg/day). At the control visit after 30 days, the patient had reported no improvement. He had therefore consulted another psychiatrist who had confirmed the diagnosis of major depressive disorder and prescribed paroxetine (20 mg/day). This treatment had been associated with a modest improvement, mainly of asthenia. Family history was negative for severe neuropsychiatric diseases. The patient's father had died at 70 years of lung cancer.

At presentation, the patient scored 2 on the 5-point Hoehn and Yahr scale for PD staging. The patient also underwent brain MRI that did not reveal any abnormalities. Brain scintigraphy with dopamine transporter (DaT) scan, on the contrary, showed a marked deficiency in receptor tracer uptake at the right striatum, which confirmed the diagnosis of idiopathic PD. The patient started a therapy with transdermal rotigotine (6 mg/day) and levodopa/carbidopa (100 mg/25 mg, three times a day). Paroxetine was replaced by the SNRI venlafaxine (75 mg/day). This treatment was associated with an improvement of depression, but the patient continued to show low acceptance of his condition. He then had an accident at work that caused a relapse of asthenia and depression. Venlafaxine was replaced by vortioxetine (10 mg/day initially, followed by 15 mg/day). In 20 days the patient resumed all his activities and his acceptance of PD improved. The choice of vortioxetine was determined by the multimodal mechanism of action of this molecule and by its favorable profile of adverse events with, possibly, a lack of negative effects on movement. At 9 months from presentation at our clinic, the patient continued to be in treatment with vortioxetine with a beneficial effect on his mood, while motor and cognitive functions were not affected. Depression, assessed using the BDI score, had improved from 22/39 at presentation to 11/39 at the last visit.

### Case 4

An 80-year-old male patient, who had been in treatment for 4 years for PD, presented with symptoms of depression. These included marked social withdrawal, anxiety, lack of interests in activities that he used to like (stamp collection and traveling with his wife), and a negative view of the future. The patient was also irritable and verbally aggressive, two traits that he had never shown before. He was not entirely aware of these behavioral changes, which were pointed out by his wife. Depression assessment using the BDI provided a score of 18. PD stage was 2 according to the Hoehn and Yahr scale, while the UPDRS-III score was 28.

The first manifestations of PD, 4 years before when the patient was 76 years old, had been characterized by the typical motor symptoms, including bradykinesia, hypokinesia, rigidity, and asymmetrical rest tremor. These symptoms had been accompanied by severe asthenia and orthostatic hypotension. PD diagnosis had been confirmed by brain MRI and  $^{123}\text{I}$ -FP-CIT (DaTscan). The medical history of the patient included hypertension, elevated blood cholesterol, valve replacement surgery, and prostatectomy 10 years before due to prostate cancer. For PD the patient had been in treatment with rotigotine (2 mg/day) and selegiline (5 mg/day) with good control of motor symptoms and fatigue. After 2 years, due to the worsening of motor symptoms, antiparkinsonian therapy had been intensified with the addition of low-dose levodopa (100 mg, three times a day), with beneficial effects on motor symptoms. With the intensified therapy the patient was able to resume his normal life and was completely independent in all basic and instrumental activities of everyday life.

For the treatment of depression and irritability, it was decided to use vortioxetine (5 mg/day) after discontinuation of selegiline. At the control visit after 3 months, the patient showed a slight behavioral improvement; according to the patient's wife, irritability and verbal aggressions had decreased. Also reduced was the anxiety towards new activities. The patient confirmed to be feeling better. With regard to motor symptoms, the patient reported a slight but marked improvement especially in the gait that appeared to be more fluid than before, with no differences for fine motor skills alterations. The UPDRS-III score was 19 and was markedly improved compared with the score at presentation. The patient did not report any falls or any other relevant event. Sleep had also improved with a lower frequency of REM sleep behavior disorder. Depressive symptoms improved substantially and only few, minor symptoms were persistent (BDI score, 8). Because of the good response and the good tolerability, the dose of vortioxetine was increased to 10 mg/day, while antiparkinsonian therapy remained unchanged. At the following visit at 6 months from vor-

tioxetine introduction, the patient was stable in terms of motor symptoms (UPDRS-III score, 15). The patient still presented mild left hypokinesia and bradykinesia, with mildly awkward alternate movements, though slightly improved compared with the previous visit. Depressive symptoms were absent according to the Patients' wife (BDI score, 5 at the assessment). Apathy, which had been reported by the patient as well as by his wife, was also substantially improved. Treatment with vortioxetine 10 mg/day was well tolerated with no adverse events, despite the advanced age of the patient and his comorbidities.

### Case 5

A 73-year-old female patient, who had been diagnosed with PD 10 years before, presented to our clinic to undergo a planned neurological examination. The patient had a history of mild hypertension and depression. Depression had been successfully treated with venlafaxine (15 mg/day). At presentation the patient was in treatment with levodopa/carbidopa/entacapone (125 mg, 1 tablet 4 times a day) plus pramipexole (2.1 mg/day, extended-release). Other concomitant treatments included the ACE-inhibitor ramipril (2.5 mg/day). Extrapyramidal symptoms were well controlled. Off-time was about 1.5 hours/day. During the day, no dyskinesias were reported. The UPDRS-III was 16, and the PD stage according to the Hoehn and Yahr scale was 2.5. The patient's mood appeared good. The diagnosis of PD was confirmed and the patient continued with her current therapy. The next neurological examination was planned within 5 months.

The planned visit had to be anticipated because of the occurrence of a depressive episode characterized by social withdrawal, anhedonia, negative thoughts, as well as subjective worsening of motor symptoms. The patient's husband confirmed that the patient appeared inattentive, apathetic and less focused. Motor symptoms had only slightly worsened from the previous visit (UPDRS-III, 19; Hoehn and Yahr scale score, 2.5; off-time, 2 hours/day; MMSE 29/30). The neuropsychological exam revealed moderate depression, with normal cognitive function and mildly impaired executive function. It was therefore decided to intensify dopaminergic therapy (levodopa/carbidopa/entacapone (125 mg, 1 tablet 5 times/day) plus pramipexole (same dose as before) and to add antidepressant medication (venlafaxine, up to 150 mg/day). The patient also underwent brain MRI that showed small areas of nonspecific gliosis of the periventricular white matter. At the control after 60 days, no improvement in depression was reported, while motor symptoms had decreased (UPDRS-III score, 11). Body weight had increased by 3 kg, due to greater food intake not directly related to antidepressant therapy. The patient did not perceive any improvement

of motor symptoms and had negative feelings about her life expectancy. Neuropsychological findings were similar to those of the previous visit and confirmed the patient's difficulties in concentrating and problem solving. It was therefore decided to discontinue venlafaxine and to introduce vortioxetine (up to 10 mg/day). At the planned visit 3 months after vortioxetine introduction, both the patient and her husband described a substantial improvement with increased attention and ability in daily activities. The patient appeared more focused and motivated. Motor symptoms were stable, with no relevant off-periods. No changes in current antiparkinsonian treatment were therefore made. At the next visit after 3 months, mood improvement and motivation persisted. Neuropsychological assessment revealed a significant improvement in executive function, divided attention and working memory. The patient had lost weight (2.5 kg). Stable motor symptoms, mood control and normal cognitive function were also reported in the following visits.

### Case 6

A 73-year-old male patient, diagnosed with PD at the age of 64 years and referred to our center, had developed sleeping disturbances, characterized by difficulties in falling asleep and short sleep duration, loss of appetite, and loss of interest in his daily activities. The patient had a university degree and had occupied until recently an executive position. At presentation, he was taking the antidepressant escitalopram (10 mg/day) added to antiparkinsonian therapy. The addition of antidepressant medication had been suggested by a friend psychiatrist to treat the depressive episode. However, escitalopram had proven ineffective and depression had worsened over the past year.

The patient had hypertension for which he had been prescribed calcium antagonists and angiotensin II receptor antagonists. With regard to his medical history, at 45 he had experienced an episode of major depression that had been successfully treated. At 66, he had undergone prostatectomy. The UPDRS score at PD diagnosis was 8. The patient had started antiparkinsonian therapy with rasagiline followed, after about 2 years, by the addition of levodopa/carbidopa (100 mg, twice daily). This treatment had proven overall effective and had been maintained over the past 9 years, with only minor adjustments. A dopamine agonist (pramipexole) could not be added because it was associated with increased agitation.

At presentation, the patient was in treatment with levodopa/carbidopa (250/25 3/4 tablets, 4 times a day plus 1/2), melevodopa (100 mg, twice daily), rasagiline (1 mg/day), and alprazolam (5 drops 3 times a day). The UPDRS-III score was 23. The patient had a negative view of life, thought his death was imminent,

and expressed the wish to sleep for extended periods during the day. The levodopa/carbidopa dosage was increased to 250/25 mg, 1 tablet 4 times/day; he was also prescribed pramipexole (0.26 extended-release, 1 tablet/day). At the next visit no improvement was reported and the patient's wife requested a new neurological visit. Based on the findings of this visit [UPDRS, 20; MMSE, 24; Columbia University Scale for the evaluation of suicide risk, 9 (no immediate risk of suicide)] the patient was prescribed vortioxetine (10 mg in drop-formulation; 10 drops/day) added to delorazepan (15-20 drops/day) with progressive down-titration and discontinuation of escitalopram. At the next visit after about 20 days, the patient did not report any improvement and said to be feeling slow and foggy; his wife added that the patient was napping for extended periods in the morning and seemed very apathetic. By contrast, nausea and appetite had improved. Blood tests and head CT examination did not reveal any abnormalities. The vortioxetine dose was increased (15 drops/day), while the delorazepan treatment was maintained unchanged. After about 1 month, the patient showed a marked improvement in mood and sleep duration in the night; also improved were daytime somnolence, motor performance (UPDRS, 17), and cognitive function (MMSE, 29). The patient was no longer thinking about death and had resumed his daily activities. At the last visit, after about 1 month, motor UPDRS score was 19, and MMSE score was 29. No dyskinesias were reported.

## Discussion

Patients affected by PD frequently experience depressive episodes as comorbidity, which can negatively influence the course of motor disease and the occurrence of other neuropsychiatric disturbances. Currently, there are no guidelines for the treatment of PD-associated depression, and no optimal therapy has been identified to date. Treatment for depression should therefore be chosen based on the patient's medical status, severity of depression, patient's preference, and neurologist's expertise in using antidepressants<sup>3</sup>. To our knowledge, this is the first time the use of vortioxetine has been described for the treatment of major depressive episodes in patients with PD. Overall, the present case series highlights the relevance of this non-motor comorbidity in the management of patients with PD. PD-related depression needs to be promptly recognized and assessed by appropriate tools. The effective treatment of depressive episodes may have a positive impact on motor and non-motor manifestations of the disease, including cognitive changes (cases 5 and 6), sleep disturbances (cases 2 and 5), and apathy (cases 1 and 4). Of the six cases presented (2 females, 4 males, age ranging from 56 to 80 years) three had long-standing

PD (cases 4, 5, and 6). In the remaining three cases, PD was diagnosed conclusively at presentation. With the exception of case 4, all patients had a history of depressive disorder with the onset of motor symptoms, or experienced depressive episodes concomitantly with the onset of PD motor symptoms. All patients with a history of depression had already been treated with antidepressant medications (mostly SSRIs and SNRIs). In the six cases described, the choice of vortioxetine was motivated primarily by its relatively favorable safety and tolerability profile compared with that of other antidepressant medications<sup>20</sup>. The favorable safety and tolerability profile of vortioxetine was confirmed in our case series with no reports of unexpected or unacceptable adverse events. This was true also for an 80-year-old patient (case 4) who had never been previously exposed to antidepressant medication.

Although the case series described here was heterogeneous, especially in terms of medical history and PD characteristics, among neuropsychiatric disease manifestations there was a remarkable prevalence of apathy. Apathy responded well to treatment with vortioxetine. Thanks to a rapid and substantial response, patients were able to resume their daily activities, with a positive impact on other depression- and PD-related outcomes. Apathy, defined as a substantial loss of motivation not caused by emotional distress, cognitive impairment, or diminished level of consciousness, is common in neurocognitive disorders<sup>2</sup>. In PD, apathy can manifest early and its prevalence ranges between 16.5 and 40%<sup>2</sup>. Risk factors are severe motor symptoms and cognitive decline<sup>2</sup>. A recent prospective randomized trial compared, for the first time, the efficacy of SSRIs (paroxetine, escitalopram) and an SNRI (duloxetine) in improving depressive symptoms and apathy, as well as gait instability, in patients with PD (n = 55)<sup>5</sup>. The study found that both depressive and motor symptoms were significantly improved from baseline to 10 weeks by the two antidepressant classes, with no statistically significant differences between treatment groups. A tendency for reduced apathy was observed at 10 weeks with both SSRIs and the SNRI, but the changes from baseline to 10 weeks did not reach statistical significance. Therefore, the effectiveness of the SSRI and SNRI classes on PD-related apathy is currently unclear.

Case 2 describes the effective treatment of depression with vortioxetine in a patient affected by PD with a GBA mutation. Gaucher's disease is a lysosomal storage disorder caused by a mutation in the gene encoding for the enzyme GBA. Heterozygous carriers do not present the disease, but have a 20- to 30-fold increased risk of developing PD compared with wild-type individuals<sup>21</sup>. At the same time, at least 7% of people affected by PD have mutations in the *GBA* gene<sup>22</sup>, with a pattern of protein accumulation similar to that of idiopathic PD and

parkinsonism caused by storage of alpha-synuclein<sup>23</sup>. Patients with PD and mutations of the *GBA* gene are not clinically distinct from patients with idiopathic disease (identical neuroimaging findings, including functional studies related to the dopaminergic system)<sup>24</sup>. In case 2, the antidepressant therapy was changed before discovering that the patient carried a *GBA* mutation. The ineffective SSRI was replaced by the newer-generation antidepressant, vortioxetine.

The patient in case 5 was treated in a center for movement disorders because of the prevalence of motor symptoms over other PD-related comorbidities. Over time, the patient also developed mood and cognitive disturbances. The patient had a history of major depression that had been successfully treated with venlafaxine. Her current treatment with venlafaxine, however, failed to alleviate the depressive symptoms. At the current stage of PD, depressive symptoms were associated with executive dysfunction and were distinct from those experienced several years before. This may explain why venlafaxine, which has no demonstrated effect specifically on executive function, was no longer effective. By contrast, multimodal vortioxetine was presumably able to improve mood symptoms via its action on cognitive and executive functions. The effects of vortioxetine on cognitive performance are well documented. The early findings by Katona and coworkers in patients aged  $\geq 65$  years, who underwent a series of cognitive tests addressing processing speed, verbal learning, and memory<sup>14</sup>, were confirmed in a large adult population<sup>17</sup>. In this study, the effect of vortioxetine on cognitive performance was shown to be a direct effect of vortioxetine on cognition and not the consequence of the antidepressant response<sup>17</sup>. A more recent study in patients with acute recurrent major depressive disorder, who self-reported cognitive dysfunction, compared the effect of vortioxetine with placebo on cognitive functioning, including specific measures of attention, executive functioning, and psychomotor speed<sup>16</sup>. The study was active-referenced (duloxetine). Vortioxetine produced significant improvements compared with placebo on cognitive function as measured by the DSST (primary endpoint), a sensitive and widely used test that targets multiple domains of cognition. Vortioxetine was also statistically superior to placebo on other cognitive outcomes tested (perceived deficits questionnaire [PDQ], physician-assessed clinical global impression [CGI-I], University of San Diego performance-based skills assessment [UPSA]) and on depression (MADRS). Path analysis indicated that the cognitive benefit was a direct treatment effect rather than due to alleviation of depressive symptoms. Duloxetine was not significantly different from placebo in terms of DSST or UPSA scores,

but was superior to placebo on the PDQ, CGI-I and MADRS assessments. A recent network meta-analysis assessing the relative effect of antidepressants on cognitive dysfunction in major depressive disorder focused on 12 randomized controlled studies using the DSST<sup>19</sup>. The analysis found that vortioxetine was the only antidepressant that improved cognitive dysfunction as assessed with the DSST versus placebo. In addition, vortioxetine was statistically more efficacious than escitalopram, nortriptyline, SSRI and tricyclic antidepressants on the DSST.

Case 6 documents the importance of sleep disturbance and its proper management. Insomnia (which is frequent in PD patients)<sup>25</sup> has also been associated with depression. Sleep disturbance can manifest as difficulty in falling asleep or maintaining sleep. In this case, vortioxetine improved night sleep and reduced daytime sleepiness, in addition to exerting the expected antidepressant effects.

It must be highlighted, however, that there are a number of limitations associated with case series. As results are reported retrospectively, there may be gaps in the availability of data records. The observations described may also be subject to selection bias, which, along with the lack of a control arm, prevent the generalization of treatment outcomes to larger patient populations. Nonetheless, the present case series contains useful information, not only in a research perspective, but also in clinical practice. Indeed, the preliminary data reported here provide support for future undertaking of adequately designed, prospective, double-blind, randomized controlled trials to better assess the role of vortioxetine in PD-associated major depressive disorder.

## Conclusions

The observations presented in our case series suggest that vortioxetine may be a valid option for the management of depression in the complex and heterogeneous population of patients with PD. Consistent with evidence from clinical trials, treatment was easy to implement, safe, and well tolerated in these patients, who were all receiving polytherapy for PD and other comorbidities. Further support for the favorable safety and tolerability profile of vortioxetine is the fact that three of the patients were aged  $> 70$  years while one patient was naïve to antidepressant medications. The role of vortioxetine in PD-associated major depressive disorder needs to be further investigated in adequately designed, prospective studies.

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## Compliance with Ethics Guidelines

The patients whose cases are reported in this manuscript have been treated in the setting of daily clinical practice, and not as part of a clinical study of any kind. They represent a retrospective analysis and, according to Italian law, no approval from an Ethics Committee or institutional review board is required.

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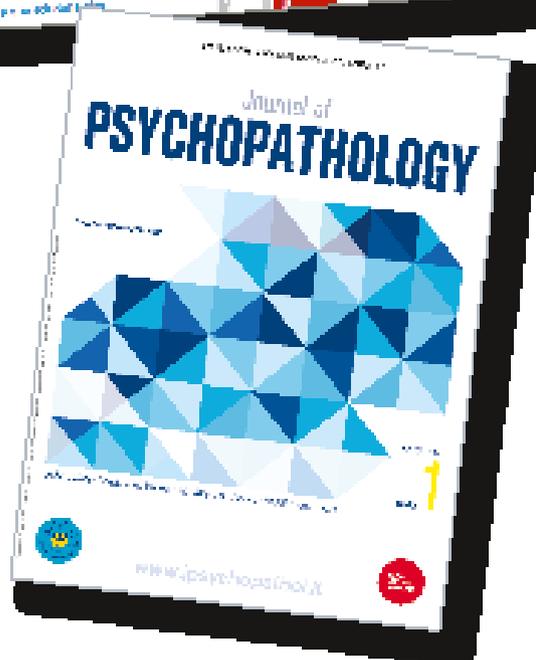
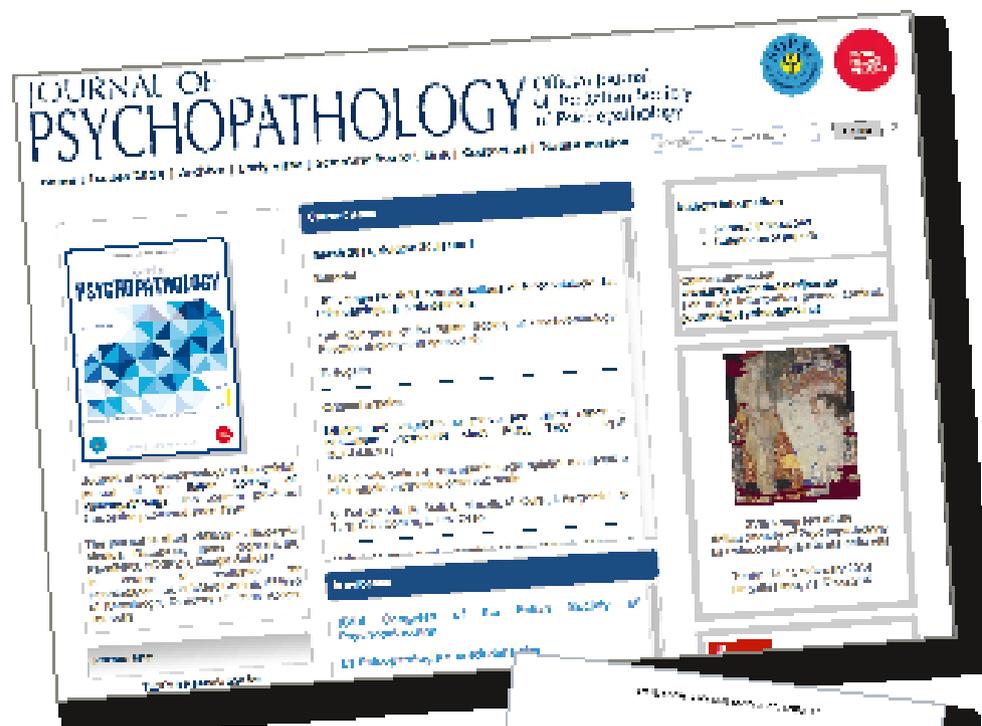
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